

Advances in retinopathy of prematurity imaging

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Abstract:

Retinopathy of prematurity (ROP) remains the leading cause of childhood blindness worldwide. Recent advances in ROP imaging have significantly improved our understanding of the pathogenesis and pathophysiological course of ROP including the acute phase, regression, reactivation, and late complications, known as adult ROP. Recent progress includes various contact and noncontact wide-field imaging devices for fundus imaging, smartphone-based fundus photography, wide-field fluorescein angiography, handheld optical coherence tomography (OCT) devices for wide-field en face OCT images, and OCT angiography. Images taken by those devices were incorporated in the recently updated guidelines of ROP, the International Classification of Retinopathy of Prematurity, Third Edition (ICROP3). ROP imaging has also allowed the real-world adoption of telemedicine- and artificial intelligence (AI)-based screening. Recent study demonstrated proof of concept that AI has a high diagnostic performance for the detection of ROP in a real-world screening. Here, we summarize the recent advances in ROP imaging and their application for screening, diagnosis, and management of ROP.

Keywords:

Angiography, imaging, retinopathy of prematurity

INTRODUCTION

Retinopathy of prematurity (ROP) continues to be a leading cause of blindness in preterm children worldwide.^[1] Timely screening examinations are essential in optimizing outcomes.^[2] Binocular indirect ophthalmoscopy has long been the gold standard for evaluating ROP.^[3] However, advances in various imaging techniques, such as fundus imaging, wide-field fluorescein angiography (FA), optical coherence tomography (OCT), and OCT angiography (OCTA), have provided additional insights into the pathogenesis, disease progression, and response to treatment in patients with ROP. Advances in retinal imaging have also facilitated the emergence of telemedicine- and artificial intelligence (AI)-based evaluations for ROP.^[4] In this review, we summarize the recent advances in ROP imaging with a focus on findings that may be difficult to otherwise identify on conventional ophthalmoscopic examinations.

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FUNDUS IMAGING

Binocular indirect ophthalmoscopy, performed by an experienced ophthalmologist, remains the gold standard for ROP screening.^[3] However, fundus imaging/photography is useful in capturing and recording the fundus findings, including zone (anteroposterior location), extent, and severity (stage and plus disease) [Figure 1a and b]. Abnormal retinal findings are used to classify ROP stage according to the guidelines described by the International Classification of Retinopathy of Prematurity, Third Edition (ICROP3), and these include demarcation line (Stage 1), ridge (Stage 2), extraretinal neovascular proliferation (Stage 3), partial retinal detachment that spares (Stage 4A) or involves (Stage 4B) the fovea, total retinal detachment (Stage 5), and the dilation and tortuosity of retinal vessels (plus disease).^[5]

The digital imaging systems for fundus imaging include contact and noncontact cameras. Examples of contact cameras include the RetCam[®] (Natus Medical Systems, Inc., Pleasanton, CA, USA), RetCam Shuttle[®] (Natus Medical Systems, Pleasanton, CA, USA),

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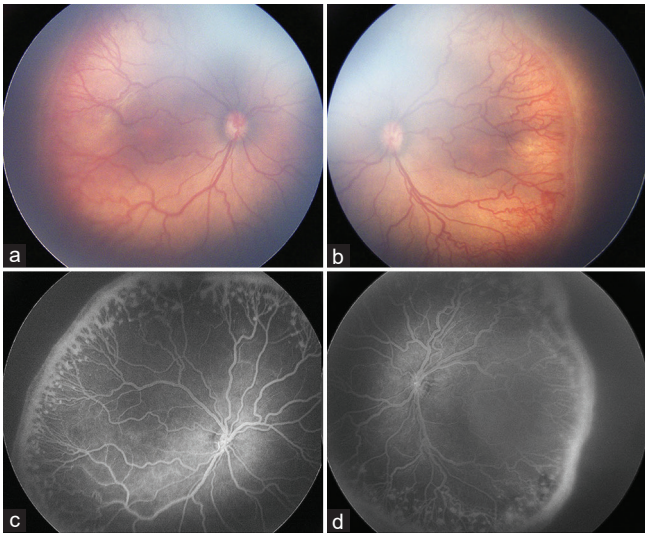


Figure 1: Wide-field fundus imaging and fluorescein angiography in retinopathy of prematurity (a and b) Wide-field fundus imaging showing posterior Zone II, Stage 3 retinopathy of prematurity with plus disease. (c and d) Wide-field fluorescein angiography shows leakage of the neovascular ridge with anterior avascular retina

ICON® (Phoenix Technology group, Pleasanton, CA, USA), Panocam® (Visunex Medical Systems, Inc., Fremont, CA, USA), and 3nethra neo® (Forus Health, Bangalore, India). The RetCam® is a mydriatic, handheld wide-field imaging device with the ability to image 130° of the fundus and FA using various lenses (30°, 80°, 120°, 130°, and portrait which is for external images). The RetCam Shuttle® is a more portable, laptop version of the RetCam. The ICON® camera is also a mydriatic, handheld imaging device that can capture 100° of high-resolution color fundus photographic and FA images. The Panocam is a wireless, nonmydriatic handheld camera that can image 130° of the fundus. The 3nethra neo® is a mydriatic, compact, handheld wide-field imaging modality that offers a field of fundus view of 120°.

Noncontact cameras include various Optos (Optos, Dumferline, MA, USA) cameras, and other wide-field imaging devices commonly used in outpatient settings. Large-scale studies have not been performed on such devices, as they are not portable and less amenable to inpatient neonatal intensive care unit (NICU) use. Feasibility has been shown for infants who can be imaged as outpatients, but care should be used when positioning the infants.^[6,7] Further studies would be required to assess their safety and efficacy. Another emerging fundus imaging technique is via smartphone-based fundus photography.^[8-10] Images can be obtained in a low-cost manner, but image quality is often limited, and peripheral views are challenging to obtain. Similar to other conventional noncontact cameras, there are limited data regarding its diagnostic reliabilities. Further studies are indeed required before widespread adoption, as accuracy is essential in ROP screening.

On the other hand, advances in contact-based fundus imaging and favorable data from numerous validation studies have

allowed the real-world adoption of telemedicine-based ROP screening.^[11] For example, the Stanford University Network for Diagnosis of Retinopathy of Prematurity (SUNDROP) is a telemedicine initiative to screen for ROP that warrants treatment.^[12] In one SUNDROP study, 608 preterm infants who met ROP screening criteria were evaluated via remote fundus imaging taken with the RetCam® II/III over a 6-year period. The results showed that sensitivity was 100% and specificity was 99.8% for the detection of ROP that warranted treatment when compared with binocular indirect ophthalmoscopy. Elsewhere, the e-ROP study, a multicenter clinical trial, evaluated the validity of a telemedicine system that used fundus imaging for ROP screening.^[4] The fundus photographs were obtained with the RetCam Shuttle® by nonphysicians and interpreted remotely by nonphysicians. Of the 1257 infants screened, 19.4% had the characteristics of ROP that warranted referral, and the remote grading of images had a sensitivity of 81.9% and specificity of 90.1%. These studies indicate the usefulness of fundus imaging in telemedicine-based screening for ROP. Some limitations of fundus imaging with contact cameras include the need for experienced photographers and the high initial cost of the cameras.

Fundus imaging has also been central in developing AI-assisted ROP screening.^[13] In the past few years, deep-learning (DL) algorithms using convolutional neural networks have shown great promise in automated diagnosis of ROP from fundus imaging. For example, Wang *et al.* reported that the algorithm DeepROP achieved a sensitivity of 97% and a specificity of 99% for distinguishing ROP cases from normal cases based on fundus photographs obtained with the RetCam®.^[14] Brown and colleagues from the Imaging and Informatics in Retinopathy of Prematurity group, a multicenter ROP imaging consortium, developed an algorithm to automatically distinguish the presence of plus disease on fundus images obtained with the RetCam®.^[15] This system achieved high sensitivity (93%) and specificity (94%) for the diagnosis of plus disease. A recent study further showed that the ROP DL system, originally developed for a North American population of premature infants, had high diagnostic accuracy in a real-world ROP screening in India using fundus photographs obtained with the Retcam Shuttle®.^[16] Another study also demonstrated proof of concept that AI can have high diagnostic performance for detection of Type 2 or worse ROP in real-world ROP screening with the RetCam®.^[17] AI using fundus images may benefit ROP management by improving the efficiency, accuracy, and objectivity of ROP diagnosis, and to widen the reach of ROP screening worldwide. The performance of AI algorithms for analyzing fundus images from different cameras and populations with variable image quality should be investigated in further studies.

WIDE-FIELD FLUORESCIN ANGIOGRAPHY

FA has been used for more than 50 years in ROP, since Flynn *et al.* introduced it as a method to study retrolental fibroplasia in the late 1960s.^[18] FA has been shown to be safe in children

with minimal adverse effects.^[19] Portable wide-angle cameras have increased its utility in pediatric retinal diseases. It is particularly useful for atypical cases.

The role of wide-field fluorescein angiography in retinopathy of prematurity diagnosis

Several studies have suggested that wide-field FA (WFA) improves the diagnosis of zones in ROP owing to the high-contrast images of the peripheral retina [Figure 1c and d]. WFA is a useful adjunct for visualizing the borders of avascular zones in the peripheral retina. In 2006, Ng *et al.* described a case series of 23 patients who underwent WFA and found that clear angiograms could be obtained during ROP screening.^[20] Lepore *et al.* reported an atlas of WFA findings in eyes undergoing laser treatment for ROP and showed that WFA was useful for clearly distinguishing the deceptively featureless Zone I junction between vascularized and nonvascularized retina.^[21]

Further studies have established that the combination of FA and color fundus photography improved the accuracy of the classification of ROP stages. Klufas *et al.* demonstrated that, compared with color fundus imaging alone, the addition of WFA resulted in a significant increase in the sensitivity of the diagnosis of Stage 3 or worse disease, type 2 or worse disease, and preplus or plus disease.^[22] The addition of WFA to color fundus photography also led to a significant improvement in intergrader agreement for a diagnosis of ROP that requires treatment.

WFA also has the potential to assist with the diagnosis of aggressive ROP (A-ROP) early on in the course of the disease. Aggressive ROP, a severe, rapidly progressive form of ROP, was added to the ICROP in 2005 as aggressive posterior ROP (AP-ROP).^[23] In ICROP3 (the third edition and the most recent update), the term “A-ROP” replaced “AP-ROP.”^[5] Eyes with A-ROP often demonstrate so-called flat neovascularization, which can be difficult to visualize using a 28-D lens and ophthalmoscopy; however, the use of FA may allow early diagnosis. Yokoi *et al.* described the characteristic FA features in A-ROP as capillary nonperfusion throughout the vascularized retina, shunting in the vascularized retina, a circumferential demarcation line, and limited vessel development, which were difficult to identify using ophthalmoscopy.^[24]

The role of wide-field fluorescein angiography in monitoring treatment response

WFA may also facilitate monitoring the effects of ROP treatment. Kusaka *et al.* reported a reduction in neovascular activity on FA in 14 (93%) of 15 eyes after intravitreal bevacizumab for Stage 3–4B ROP.^[25] Yokoi *et al.* evaluated the efficacy of scleral buckling for active neovascularization in eyes with Stage 4A ROP.^[26] They reported a decrease in fluorescein leakage from the fibrovascular tissue in all eyes, which indicated the efficacy of scleral buckling in reducing both tractional forces and neovascular activity. Nishina *et al.* assessed the effect of early vitrectomy on A-ROP using FA as well.^[27] More recently, Harper *et al.*^[28] found that ranibizumab was effective in the initial cessation of Type 1 ROP, but

vascularization to Zone III was only achieved in 50% of eyes; most eyes had evidence of vascular anomalies, such as blunting, dilatation, and/or capillary dropout on FA.^[28]

FA has also been used to evaluate the differences in peripheral findings after differing treatments. Several studies have shown more peripheral vascular abnormalities in anti-vascular endothelial growth factor (anti-VEGF)-treated eyes compared to laser-treated eyes. Lepore *et al.* compared FA findings 9 months and 4 years after either intravitreal bevacizumab or laser treatment.^[29] The majority of eyes that received bevacizumab compared to only a few laser-treated eyes had abnormalities, including leakage, tangles, shunts, and decreased foveal avascular zone (FAZ). The impact of these various peripheral findings on long-term anatomical and visual outcomes should be evaluated in future studies.

FA is also effective in highlighting the reactivation of ROP after anti-VEGF treatment [Figure 2].^[30] Reactivation is associated with the reappearance of neovascularization or worsening fibrovascular proliferation after a period of regression. The reappearance of neovascularization is subtle, but it can be detected clearly on FA.

OPTICAL COHERENCE TOMOGRAPHY

OCT is widely used to diagnose and monitor vitreoretinal diseases in adult patients. Its use in ROP patients has been

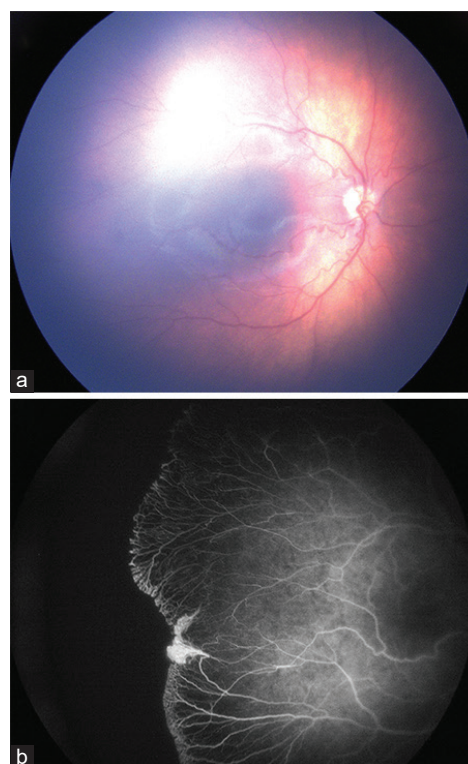


Figure 2: Wide-field fluorescein angiography showing reactivation. (a) Fundus imaging of a child at 65 weeks postmenstrual age who had a history of anti-vascular endothelial growth factor treatment for Type 1 retinopathy of prematurity. (b) Wide-field fluorescein angiography shows the reappearance of neovascularization

relatively limited due to several challenges, including the difficulty in positioning NICU patients, poor fixation, small eyes, various refractive errors, and other logistical and medical limitations. However, many of these difficulties have been minimized with the development of handheld OCT devices that enable OCT images to be taken during the bedside examinations or under anesthesia. A recent study indicated that the OCT imaging of ROP was less stressful for infants than binocular indirect ophthalmoscopy examinations by trained ophthalmologists.^[31] Handheld spectral-domain OCT (SD-OCT) has allowed the detection of subclinical findings (i.e., vitreous opacities,^[32] vitreous bands,^[33] preretinal neovascularization, epiretinal membrane, macular edema, photoreceptor immaturity, retinoschisis, retinal detachment, and choroidal thinning) that may not be obvious using conventional indirect binocular ophthalmoscopy. Some of these findings are potentially associated with ROP severity and may have prognostic value.

Optical coherence tomography cross-sectional images

Macular edema

Macular edema has been reported in approximately 50% of ROP cases (range, 38%–60%).^[34–37] The detailed etiology of the edema is unknown, but increased VEGF and mechanical traction have been proposed as causes. In a prospective case series, Dubis *et al.* reported that 54% (25/46) of patients had edema.^[34] It was found in every stage of ROP, including Stages 0, 1, 2, 3, and 4A; thus, they concluded that the disease stage was not associated with the finding. By contrast, Vinekar *et al.* reported that edema was not detected in Stage 1 ROP; however, it was observed in 29% (23/79 eyes) of patients with Stage 2 ROP.^[38] Macular edema peaked at 37 weeks postmenstrual age (PMA) and self-resolved without treatment by 52 weeks PMA or by the 3rd month. Maldonado *et al.* also sought to determine the association between edema severity in ROP and other systemic health conditions in neonates aged 31–36 weeks PMA.^[35] Macular edema was found in 50% (21/42) of the infants. The severity of edema, measured by retinal thickness or using the foveal/parafoveal thickness ratio, was shown to correlate with ROP stage, the presence of plus disease, and subsequent laser treatment, as well as systemic factors, including Apgar score, surgery for patent ductus arteriosus, and the presence of intraventricular hemorrhage.

In addition, Erol *et al.* reported that the prevalence of edema increased with an increase in ROP stage (i.e., 46%, 57%, and 88% in Stage 1, Stage 2, and Stage 3, respectively).^[36] Recently, Mangalesh *et al.*^[37] found that OCT identified macular edema in 60% of infants (50/85) at 36 ± 1 week PMA. Bilateral edema was identified in 82% of the infants (41/50), and severity was associated with higher ROP stages.^[37]

It is important to determine whether this edema of prematurity influences visual outcomes. Vinekar *et al.* reported that visual acuity was lower in infants with ROP with macular edema than in those without edema, or in infants without ROP.^[39] Rothman *et al.* also reported that eyes without edema had better

vision than those with edema.^[40] Taken together, the edema or prematurity seems to correlate with ROP severity and vision, but further studies are needed to confirm long-term outcomes.

Vascular abnormality score by optical coherence tomography

A vascular abnormality score, determined using OCT (i.e., VASO), was proposed by Maldonado *et al.* to identify vascular and perivascular abnormalities on SD-OCT images associated with plus disease.^[41] The score was based on the following features: retinal vessel elevation (1 point or 2 points if severe), scalloped retinal layers (1 point or 2 points if severe), hyporeflexive vessels (2 points), and retinal spaces (2 points). The VASO was higher in eyes with plus disease than in those without (4.1 vs. 1.4). Further studies are required to validate the findings, but this is an interesting and objective approach to assessing plus disease.

Retinoschisis and retinal detachment

In advanced ROP, both retinoschisis and retinal detachment have been described in the posterior pole by handheld OCT. Clinically, retinoschisis may sometimes be difficult to distinguish from retinal detachment on indirect ophthalmoscopy; however, OCT is effective in differentiating between these two pathologies. Chen *et al.* reported that all 12 infants diagnosed with Stage 4A ROP had retinoschisis of some degree on handheld OCT, and OCT imaging was effective in determining Stages 4A versus 4B, which is critical for visual prognosis.^[42] SD-OCT is also useful for monitoring reattachment of the posterior pole after surgery for Stage 4 and 5 ROP.

Photoreceptor immaturity

Compared with full-term infants, premature infants have shallower foveal depressions, attenuated external limiting membrane and photoreceptor ellipsoid zones (EZ), and thinner retinal layers, indicative of photoreceptor immaturity. Vajzovic *et al.* described the delay in the photoreceptor development of very preterm infants (<32 weeks gestational age), compared with term infants.^[43] EZ development was lower in very preterm infants (14%, 9/64 eyes) than in term infants (47%, 22/47 eyes) ($P < 0.001$). There was also a greater mean distance between the EZ and the foveal center in very preterm versus term infants, which further signified a delay in photoreceptor migration.

Choroidal thinning

Recent studies have described choroidal thinning in ROP infants with lower gestational age and lower birth weight using handheld SD-OCT.^[37,44] In one study, subfoveal choroidal thickness in premature infants was seen to decrease in relation to ROP severity.^[44] Macular edema did not correlate with choroidal thickness in premature infants.

EN FACE OPTICAL COHERENCE TOMOGRAPHY IMAGING

With the advance of high-speed, high-density, volumetric scanning techniques, recently developed handheld OCT devices can provide wide-field *en face* OCT images of nearly

the entire retina [Figure 3].^[45] This technique will likely be able to offer objective diagnosis and quantification of zone, stage, and plus disease in ROP.

OPTICAL COHERENCE TOMOGRAPHY ANGIOGRAPHY

OCTA allows noninvasive visualization of retinal blood flow without the use of exogenous dyes. The recent development of prototype handheld OCTA by several groups revealed the potential of using OCTA to assess ROP. Campbell *et al.* first described a handheld OCTA system using a 100-kHz tunable laser to visualize retinal blood flow in ROP.^[46] Similarly, Viehland *et al.* visualized the vascular structure of a preretinal neovascular membrane using a handheld OCTA device with a 200 kHz swept-source probe,^[47] and Song *et al.* also reported on the use of an OCTA with a 200 kHz swept-source probe in infants.^[48]

However, these prototype handheld OCTA instruments did not have the wide-field imaging needed for the peripheral visualization required to identify most ROP pathologies.

Recent advances in laser light sources and high-performance computing systems have further improved the ability to capture a wide field of view. Ni *et al.* recently reported wide-field (55°) OCT/OCTA retinal imaging in infants with ROP using a 400-kHz handheld swept-source probe.^[49] They successfully

visualized the retinal vasculature and neovascularization in the peripheral retina via high-resolution *en face* OCT/OCTA images. High-speed, high-resolution, and wide-field handheld OCT/OCTA systems have potential as a screening tool in the future.

B-SCAN ULTRASONOGRAPHY IN TRACTION RETINAL DETACHMENT IN RETINOPATHY OF PREMATUREITY

B-scan ultrasonography is effective for diagnosis, preoperative evaluation, and surgical planning in cases of tractional retinal detachment in ROP. B-scans are particularly helpful in the setting of media opacity (i.e., corneal scars, poorly dilated pupils, cataracts, hyphema, and vitreous hemorrhage) in patients with Stage 5 ROP. In ICROP3, Stage 5 ROP was subclassified into Stage 5A, in which the optic disc is visible by ophthalmoscopy; Stage 5B, in which the optic disc is not visible because of retrolental fibrovascular tissue or closed-funnel detachment; and Stage 5C, in which Stage 5B is accompanied by anterior segment changes.^[5] In Stage 5B and C, the extent of detachment must be examined by B-scan ultrasonography.

Jabbour *et al.* described a series of 368 eyes of 184 patients with Stage 5 ROP. Of ultrasonography, indirect ophthalmoscopy, and biomicroscopy, ultrasonography was the most valuable tool for assessing the configuration of retinal detachment. Similarly, Muslubas *et al.* reported on a series of 300 eyes of 150 patients with Stage 5 ROP, and they determined that ultrasonography was effective in visualizing the following retinal detachment configurations: closed–closed (82%), open–closed (11%), open–open (6%), and closed–open (2%) retinal detachment configuration, as well as subretinal hemorrhage (26%), anterior loop traction (24%), retinal cyst (2%), and calcification (1%).^[50] Preoperative assessment of the retinal detachment configuration with B-scan ultrasonography is not only beneficial in surgical planning but also for predicting prognosis and therefore allows appropriate counseling for the family.

Ultrasonic color Doppler imaging has been utilized to investigate the association between flow velocity and ROP. Hartenstein *et al.* reported an increase in the central retinal artery and central retinal vein velocity in Stage 2 ROP, compared with those without ROP.^[51] Likewise, Silverman *et al.* recently reported that the use of plane-wave ultrasonic imaging, which provides improved spatial resolution, demonstrated that central retinal artery and central retinal vein velocities were higher in infants with ROP, compared to infants without ROP, and this correlated with ROP stage as well.^[52] Ultrasonic color Doppler imaging is not currently routinely used to screen for ROP, but such ancillary testing may potentially allow reduction of the frequency of dilated examinations in neonates with normal blood flow velocity, and, conversely, watching neonates with high blood flow velocity more closely. Another benefit of ultrasonography is that it is a nonmydriatic test that can be performed through closed lids.

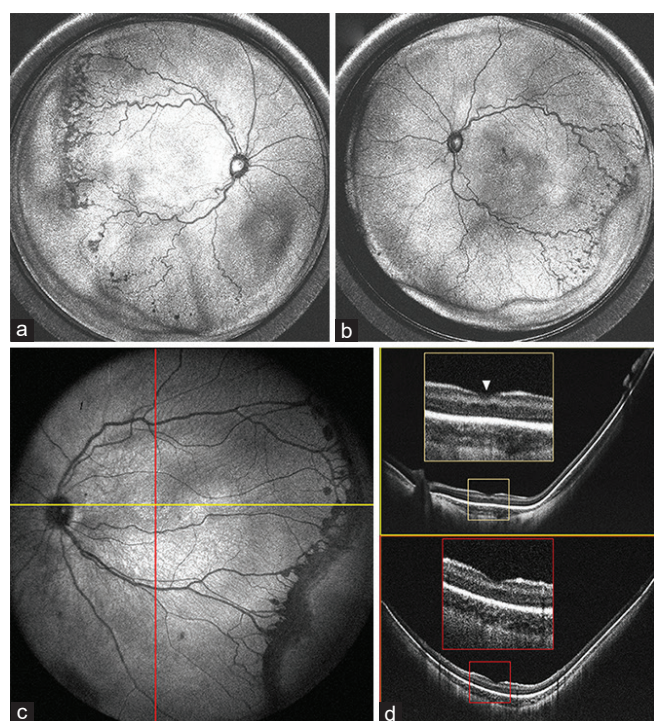


Figure 3: *En face* optical coherence tomography in retinopathy of prematurity. (a and b) Wide-field *en face* optical coherence tomography images in an infant with Stage 3 retinopathy of prematurity. Tortuous retinal vessels and the vascular-avascular border demarcated by the ridge are clearly observed. (c and d) Wide-field *en face* optical coherence tomography and corresponding cross-sectional images. The arrowhead indicates the persistent inner retinal layers at the fovea

MULTIMODAL IMAGING IN OLDER CHILDREN AND ADULTS WITH HISTORY OF RETINOPATHY OF PREMATURITY

In addition to being a neonatal disease, long-term effects of ROP extend into adulthood, making it a lifelong disease.^[53] Secondary ROP complications that may develop later in life include cataract, glaucoma, high myopia, corneal decompensation, persistent avascular retina (PAR), vitreous hemorrhage, retinal tears, and retinal detachment.^[30] Of these, increasing attention is being paid to the development of PAR. Imaging using wide-field fundus imaging and WFA is particularly useful in evaluating for PAR and associated complications. Optos FA can visualize areas of peripheral nonperfusion associated with PAR, as well as the location and extent of ridge and vascular abnormalities. In a recent multicenter study by Hamad *et al.*, ultra-WFA was shown to effectively identify subtle peripheral vascular abnormalities, including arteriovenous loops, microaneurysms, capillary avascularity, and neovascularization in adult patients with PAR and history of ROP.^[30] In their study, adult patients with PAR were reported to experience lattice degeneration (54%), retinal tears (31%), atrophic holes (35%), retinal detachment (39%), and tractional retinoschisis (12%). Atrophic holes and lattice-like changes were commonly found either along or just anterior to the vascular-avascular junction. Such findings are well-documented when a combination of optos fundus imaging and FA was used.

In eyes with late reactivation or neovascular activity associated with PAR, laser treatment in areas affected by PAR can be considered. WFA is helpful in identifying residual vascular activity after such treatment. In eyes with rhegmatogenous retinal detachment, often from atrophic holes, scleral buckling-based surgery is recommended, and wide-field fundus imaging can be a useful tool [Figure 4].

Macular abnormality, such as a decrease in the size of the FAZ, is a common imaging finding in adults with ROP. Using FA, a smaller FAZ was first reported more than 20 years ago, but recent OCTA studies have quantitatively shown a significantly smaller FAZ in patients with a history of ROP compared to other individuals.^[54-58] Several studies have also demonstrated an association between a smaller FAZ and decreased visual acuity and lower gestational age and birth weight.^[59,60] The reason for a smaller FAZ is not fully understood, but an increase in the intraocular VEGF level during the FAZ formation period in ROP may contribute to excessive vasculature, leading to smaller FAZ. One study reported that laser-treated patients had significantly larger FAZs than patients with spontaneously regressed ROP.^[61] The impact of treatment (i.e. laser and anti-VEGF) on FAZ is not well elucidated, and further investigations using OCTA are warranted.

CONCLUSION

Recent advances in ROP imaging have improved our understanding of the pathogenesis and pathophysiological

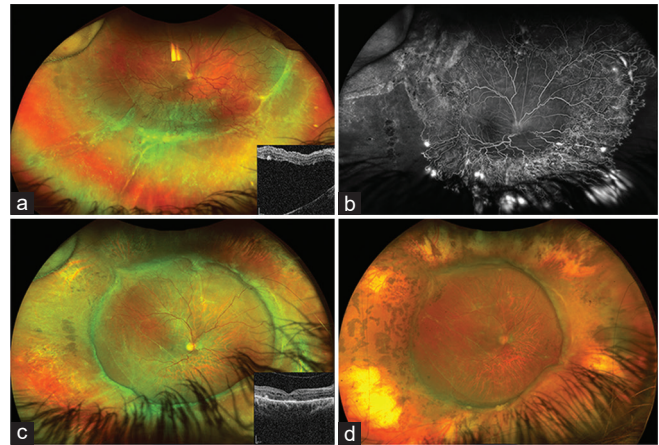


Figure 4: Adult retinopathy of prematurity with rhegmatogenous retinal detachment. (a) Preoperative ultra-wide-field fundus image showing a rhegmatogenous retinal detachment in a 15-year-old female from atrophic holes and contraction of the hyaloid adherent to the retinopathy of prematurity ridge. (b) Preoperative ultra-wide-field fluorescein angiography showing persistent avascular retina and leakage in the periphery. (c) Postoperative ultra-wide-field fundus image after successful scleral buckle. (d) After retinal reattachment, photocoagulation was performed in areas of persistent avascular retina

course of ROP including the acute phase, regression, and reactivation. Future imaging advances will hopefully further improve ROP care and treatment outcomes. The recently published ICROP3 indicated the areas that require additional research as follows: “methods for quantifying vascular changes, including the rate of disease progression; characterizing clinical findings using other imaging methods (e.g., FA, OCT); understanding long-term risks of PAR; and elucidating signs and timing of ROP reactivation.”^[5] Progress in these research areas will likely advance with further improvements in imaging technology, such as in the resolution (higher) and field (wider) of fundus imaging, FA, and OCT/OCTA, via the use of compact, handheld devices that are designed for pediatric eyes. ROP imaging in telemedicine-based screening with the potential for computer-based image analysis paradigms may also lead to improvements in diagnosis and management of ROP, and most importantly, to provide wider access to ROP care.

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Conflicts of interest

There are no conflicts of interest.

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