Published in final edited form as:

Retina. 2011 September ; 31(8): 1470–1482. doi:10.1097/IAE.0b013e31821dfa6d.

Macular Features From Spectral Domain Optical Coherence Tomography as an Adjunct to Indirect Ophthalmoscopy in Retinopathy of Prematurity

Annie C. Lee, MD¹, Ramiro S. Maldonado, MD¹, Neeru Sarin, MBBS¹, Rachelle V. O'Connell, BS¹, David K. Wallace, MD, MPH^{1,2}, Sharon F. Freedman, MD^{1,2}, Michael Cotten, MD², and Cynthia A. Toth, MD^{1,3}

¹ Department of Ophthalmology, Duke University Medical Center, Duke University, Durham, North Carolina

² Department of Pediatrics, Duke University Medical Center, Duke University, Durham, North Carolina

³ Department of Biomedical Engineering, Pratt School of Engineering, Duke University, Durham, North Carolina¹

Abstract

Purpose—To compare vitreoretinal pathology imaged with portable handheld spectral domain optical coherence tomography (SDOCT) to conventional indirect ophthalmoscopic (IO) examination in neonates undergoing screening for retinopathy of prematurity (ROP).

Methods—SDOCT images were collected from 76 eyes of 38 neonates during 118 routine ROP examinations. Imaging sessions in the neonatal intensive care unit were performed immediately after the subjects underwent a standard ophthalmic examination with IO by a pediatric ophthalmologist. Masked certified SDOCT graders evaluated scans for preretinal and retinal findings including material in the vitreous, epiretinal membrane, intraretinal cystoid structures and deposits, optic nerve and vascular features, as well as severity and location of ROP. The frequency of detection of these features by clinical examination and evaluation of SDOCT images was compared to determine potential clinical advantages for each modality.

Results—Portable SDOCT imaging characterized macular features of retinal cystoid structures in 39% of exams and epiretinal membrane in 32% of exams. Neither feature was visualized by indirect ophthalmoscopy in any cases. The clinician using indirect ophthalmoscopy detected stage of ROP and the presence or absence of plus or pre-plus disease. These were not visualized with SDOCT.

Conclusions—SDOCT provides new information about the premature infant retina that is of unknown importance relative to visual development and acuity. As used in this study, SDOCT does not replace indirect ophthalmoscopy for evaluation of ROP.

Correspondence and requests for reprints should be addressed to: Cynthia A. Toth, MD, Duke Eye Center, DUMC Box 3802, Durham, North Carolina 27710, cynthia.toth@duke.edu, Phone: 919-684-5631, Fax: 919-681-6474.

Meeting Presentation: The American Academy of Ophthalmology Annual Meeting, Chicago, IL, October 2010

Disclosures: The following authors have the ensuing financial disclosures:

Dr. Sharon F. Freedman:

Pfizer: Consulting

Dr. Cynthia A. Toth:

Alcon: Consulting, Research Support and Royalties; Biopogen: Research Support and Royalties; Genentech: Consulting and Research Support

Keywords

Macular edema; Premature neonates; ROP; SDOCT; Visual development

Retinopathy of prematurity (ROP) remains a major cause of vision loss in neonates despite advances in treatment [1, 2]. Examination of the retina with indirect ophthalmoscopy has been the gold standard for the evaluation of neonates at risk for ROP [3]. However, imaging technology has progressed to allow detection of pathologic findings not evident on conventional clinical examination [4]. The ability to identify clinical features that herald fibrovascular proliferation and subsequent risk for subsequent retinal detachment may lead to earlier intervention and improved visual outcomes.

Optical coherence tomography (OCT) has become a standard diagnostic imaging tool in the management of macular disease in adults [5]. Applications of OCT to the pediatric population have been limited by patient motion and positioning. Modifications to this modality have led to the development of a portable hand-held SDOCT unit (Biotigen, Inc., Research Triangle Park, North Carolina) that has been optimized for use in neonates, infants and children [6]. This system has been used to successfully image infants with shaken baby syndrome and children with albinism [7, 8]. More recently, imaging of three ROP infants with this device revealed posterior retinal pathologic findings such as preretinal structures, retinoschisis and retinal detachment that were not observed clinically [4]. These preretinal structures may represent posterior neovascularization such as with aggressive posterior retinopathy of prematurity or incomplete regression of the hyaloid [9].

SDOCT is a rapid and well-tolerated modality that offers the advantages of quantitative, reproducible, and 3-dimensional cross-sectional assessment of retinal pathology. While indirect ophthalmoscopy or color fundus imaging will likely remain advantageous in many aspects, we hypothesize that SDOCT imaging may be more sensitive than standard indirect ophthalmoscopy in detecting critical early vitreoretinal abnormalities in the developing eye. This additional information may optimize timing of treatment and visual outcomes, and augment current practices of ROP evaluation.

Methods

Patient Selection

Eligible subjects included all infants in the Neonatal Intensive Care Unit (NICU) undergoing routine ROP screening by Duke pediatric ophthalmologists (SFF and DKW) between January 20, 2009 and January 12, 2010, using standard screening criteria. Medical clearance to participate in this study was first obtained from the neonatologist, and consent for the study was obtained from parents or legal guardians in accordance with the Duke University Medical Center Institutional Review Board. The study conformed to the tenets of the Declaration of Helsinki. Data Collection

Imaging was performed in study subjects following clinical examination by pediatric ophthalmologists as part of the standard of care for ROP screenings. Both pupils had been dilated with cyclomydril (cyclopentolate 0.2% and phenylephrine 1.0%). In most cases during imaging, the eyelids were held open by the examiner using two fingers, although a lid speculum was used when needed. Artificial tears (Systane, Alcon Inc., Fort Worth, TX) were applied topically to improve the corneal surface and enhance imaging. Oral sucrose 24% 0.5 mL with pacifier was used to decreased infant stress as reported in previous studies [10, 11]. Image acquisition time was limited to 15 minutes with monitoring of vital signs every minute. If monitoring indicated a change in health status, defined as a deviation of

heart rate, respiratory rate, or oxygen saturation of greater than 20% from baseline, study imaging was stopped until these stabilized. If a second change in health status occurred, the study imaging session was stopped. The nurse was queried one to two hours following imaging for adverse events such as apnea, bradycardia, desaturation and feeding problems that may have been related to the imaging session.

All subjects were imaged in a supine position using a non-contact portable handheld SDOCT system (Bioptigen Inc., Research Triangle Park, North Carolina) optimized for pediatric use [6] (Figure 1). Capture and analysis of SDOCT images were performed in a manner similar to a protocol described previously using volumetric and lateral-repeated scanning techniques [7].

Up to nine total SDOCT scans were collected for each eye. During the preceding indirect ophthalmoscopic examination, the clinician (SF or DW) completed a clinical case report form for each eye, documenting the presence or absence of the same vitreoretinal features as were graded on later SDOCT review. Each feature was recorded as present, absent or indeterminate, and further characterization of pathology type or extent was documented where applicable. The features included: vitreous material shadowing (and location), preretinal tissue (and location), vitreoretinal attachment (and whether deforming retina), epiretinal membrane (and whether deforming foveal), optic nerve abnormality (elevation, large cup, pallor, hyaloidal remnants), retinal cystoid structures or splitting (and whether single, foveal location), intraretinal deposits (lipid, blood, other), subretinal fluid (and whether foveal), subretinal lesions (CNV, blood, pigment, etc), retinal pigment epithelial (RPE) atrophy, stage and zone of ROP, and plus disease.

In a later review, certified OCT readers masked to the clinical findings selected three representative SDOCT scan sets per eye with the goal of choosing optimal images that captured the region of interest, either fovea or optic nerve, and captured an adequate field of scan and allowed differentiation of retinal layers and foveal contour. The graders evaluated each of the three SDOCT scans for characteristics of the same vitreoretinal features as on the clinical examination grading form. Each feature was recorded as present, absent or indeterminate, and further characterization of pathology type or extent was documented where applicable. A subset of ten scans was reevaluated by an independent grader to confirm intergrader agreement, and intergrader agreement was seen in all in the subset of cases. Detection frequencies of pathologic features found on SDOCT and clinical examination were compared.

Results

Patient Enrollment and Demographics

Table 1 provides the baseline characteristics for enrolled subjects. Thirty-eight subjects were included in the study. Of the 168 premature infants undergoing ROP screening, 42 patients were not medically cleared by the neonatologist, 77 patients had legal guardians that were not approached due to availability, 9 declined consent, 1 patient was discharged prior to imaging, and 1 patient's legal guardian withdrew prior to imaging. Images were obtained in parallel with clinical examinations scheduled as part of standard of care. Subjects were imaged over multiple visits, for a total of 118 visits (228 individual eye sessions). All but 3 imaging sessions were performed in the NICU. Of those, two were obtained during clinic examination following discharge from the NICU, and one was obtained during examination under anesthesia. Imaging was not attempted if dense vitreous hemorrhage was present, as occurred in 1 session for 1 infant.

Image Acquisition and Safety

Of 118 imaging visits, imaging was paused in 3 (2%), once due to a respiratory rate fluctuation, twice because of heart rate fluctuation and none due to drop in oxygen saturation. Two of the three sessions were resumed with permission from the nurse. Although the nurse gave permission to resume in the third case, the imager decided not to resume the imaging due to persisting elevated heart rate that was, however, still within acceptable parameter by protocol. No adverse events related to the study activity were reported.

Modality Agreement and Ability to Grade Vitreoretinal Features

Comparison of agreement between SDOCT and clinical examination for the detection of vitreoretinal features showed that the two modalities had a high rate of agreement for many categories (Table 2) with the highest agreement in subretinal fluid, subretinal lesion and RPE atrophy categories. Whereas SDOCT graders used all three scoring options including the designations present, absent, and “unable to determine”, the clinical examiners almost never scored the latter designation and instead scored all features as present or absent.

Comparison of Features of the Vitreous and Vitreoretinal Interface

Both SDOCT and clinical examination were able to detect cases of vitreous material shadowing, preretinal tissue and vitreoretinal attachment that were not graded as present by the other modality (Table 2). The vitreous material reported on clinical examination, but not noted as shadowing on SDOCT, was blood in all cases and was within zone I in 2 of the 8 sessions. Nineteen of 23 (83%) cases of preretinal tissue found clinically and not seen on SDOCT were at the anterior border of Zone I or in Zone II. The typical appearance of preretinal tissue as graded on SDOCT was a discrete hyperreflective laterally elongated structure often with shadowing (Figure 2). In the 29 sessions where preretinal tissue was seen on SDOCT (presumably within zone I) the ROP was staged as 3 or greater in 11 sessions (38%).

Epiretinal membrane was found in 74 (32%) SDOCT imaging sessions and was never identified on clinical examination (Figure 3). In almost one third of these cases (22 imaging sessions), the epiretinal membrane was graded as deforming the fovea with loss of the foveal depression. Unlike the adult eye, neonatal ERMs appeared more adherent across the retinal surface without retinal folds. In some cases of subtle ERMs, in secondary review we debated whether these could be prominent internal limiting membranes.

Comparison of Optic Nerve Features

Optic nerve characteristics could be analyzed by SDOCT by review of cross-sectional images as well as by evaluation of the sum voxel projection (SVP), a 2-dimensional image analogous to a fundus image created by the axial projection of 3-dimensional volumetric scans. The optic nerve was incompletely or poorly imaged in 65 sessions (28%) on SDOCT, particularly early in the series. The 124 (54%) sessions with SDOCT optic nerve findings not detected by clinical examination included hyaloid artery remnants (Figure 4) and large optic cup (Figure 5), but no case of elevated optic nerve head. Clinical examination identified large optic cup at 14 (6%) sessions, and SDOCT also detected large cup at 4 of these sessions. Clinical examination identified optic nerve pallor at 4 (2%) sessions. SDOCT did not identify optic nerve pallor.

Comparison of Intraretinal Features

On SDOCT we characterized 88 (39%) imaging sessions with retinal cystoid structures or schisis (Figure 6) not identified on clinical examination. Thirty-nine eyes of 23 patients

(61% of all subjects) showed retinal cystoid structures or schisis during the study. In secondary analysis of our SDOCT category “retinal cystoid structures or schisis”, no cases of retinal schisis inner to the inner nuclear layer were found, unlike the finding of schisis adjacent to traction RD reported in other studies [4]. Thus all eyes demonstrated “cystoid structures”, which ranged from milder rounded hyporeflective sites often without complete loss of foveal depression (Figure 7) to severe vertically elongated hyporeflective structures with thin strands of hyperreflectivity between them and grossly elevating the central fovea (Figure 8). Rarely was there a single cystoid structure (five sessions, all in different neonates). The macular cystoid structures were always present in the inner nuclear layer with infrequent associated thickening and deformation of (and rarely a cystoid structure within) the photoreceptor layer elevating the outer plexiform layer (Figure 6). One third of the sessions with macular cystoid structures had concurrent macular epiretinal membrane (29 sessions). Hyperreflective intraretinal deposits were also present in 13 of 88 (15%) sessions with cystoid structures and occurred in 0 of 126 sessions without cystoid structures. Macular cystoid structures were observed in all stages of ROP and in the presence or absence of plus disease (Table 3). Because neonates were first available for imaging at different ages and because imaging was not at standard intervals, the time of onset and exact duration of cystoid structures could not be compared across subjects. Cystoid structures were visible as early as 32.7 weeks PMA and as late as 50 weeks PMA. In the majority of cases the edema was bilateral and persisted on repeat examinations, when these occurred. The longest duration of cystoid structures present on interval examinations was 6 weeks.

Comparison of Subretinal Features

At six sessions, clinical examination identified retinal detachment not graded on SDOCT. All were cases of Stage 4A, or more peripheral detachments not involving the macula. In one case, we found subretinal fluid tracking into the fovea on SDOCT, signaling a more advanced retinal detachment than the 4A RD described on clinical examination (Table 2).

Comparison of Vascular Features

Retinal vascular abnormalities such as tortuosity and dragging was assessed on all clinical sessions but could not be assessed by evaluation of the cross-sections of SDOCT images. The retinal summed images from the SDOCT sessions were of inadequate quality to evaluate vessels in many sessions and the time to sum and extract images was prohibitive.

ROP Disease and Severity

The clinician was able to determine stage and zone of ROP after indirect ophthalmoscopy in all except for 4 sessions in which vitreous hemorrhage was present. The stage and zone of ROP could not be determined from any of the SDOCT images with the exception of the single session in which SDOCT graded subretinal fluid tracking under fovea. Twenty-one eyes in 12 subjects reached ROP stage 3 or greater and, of these, 3 eyes progressed to retinal detachment.

Discussion

Using SDOCT imaging, we identified many retinal features in premature infants that were not detected on clinical examination by experienced pediatric ophthalmologists. Macular features identified on SDOCT images and not seen by clinical examination included macular cystoid structures (39% of all sessions), epiretinal membranes (32% of all sessions), intraretinal deposits and subclinical macular detachment. Clinical features of zone and stage of ROP were not detected by portable handheld SDOCT imaging of the awake infant in the NICU. This is in large part due to the smaller field of view with SDOCT imaging which restricted assessment of the peripheral retina (Figure 9).

In a previous study, Muni et al. used a handheld SDOCT to image progressive posterior tractional retinoschisis in laser-treated ROP both during examination under anesthesia and in the NICU [12]. They documented SDOCT imaging of a stage 3 elevated neovascular complex in zone 1 in an infant eye in the NICU. With the current system and our technique, we could not readily view the anterior border of zone I ROP, which is quite restricted, compared to a wide-field fundus camera (e.g. RetCAM, Clarity Medical Systems, Pleasanton, CA). Because of this limitation, SDOCT in this study was most useful for visualizing macular pathology, and not a useful tool for routine imaging of the border between vascular and avascular retina.

The presence of plus disease also could not be assessed by SDOCT. Although retinal vascular features may be evaluated by SDOCT using the retinal summed image, these were of limited quality in many infants and showed motion artifact. As our imaging techniques and protocol have improved, so have the retinal summed images, perhaps allowing evaluation of these features in the future (Figure 10).

The clinical significance of the large number of subclinical macular cystoid structures and schisis is not yet known. Cystoid structures were observed in eyes with or without stage 3 ROP and in the presence or absence of plus disease. They were documented from 33 to 50 weeks PMA and often persisted through several interval examinations (Table 3). The cystoid changes always involved the inner nuclear layer and were rarely seen in the photoreceptor or other layers except in the most deformed foveas. Because vascular endothelial growth factor (VEGF) has been demonstrated to increase vascular permeability leading to macular edema [13, 14] and is known to be present in the eyes of infants with ROP [15], we believe these cystoid structures may be a VEGF-related process. The presence of cystoid structures might serve as a marker for VEGF levels in these infants although it could also reflect a stage of *ex utero* development in these very young eyes. As the infants in this study were imaged at different gestational ages, it was not possible to correlate patient age with onset of cystoid changes. A more in-depth study is in progress to correlate macular findings including macular thickness with the complex systemic findings and with severity of ROP.

We do not know whether macular cystoid changes early in retinal development play any role in ultimate visual outcome. Final visual acuity results from the Early Treatment of Retinopathy of Prematurity Study showed that although visual acuity is improved with early treatment, 65.4% of eyes receiving early treatment developed visual acuity worse than 20/40 [16]. However, in another study, very low birth weight infants without advanced ROP and without serious neurologic sequelae of premature birth showed no difference from term infants on three measures of visual function [17]. Anatomic macular abnormalities detected by SDOCT may also partially explain the poor visual outcomes after surgical intervention in advanced cases of ROP [18]. Although we had few retinal detachments in this series, precise macular assessment in eyes with retinal detachment may influence timing of future intervention and improve visual outcomes.

This study must be viewed in light of several limitations. The comparison of modalities in this study is descriptive and not statistical. Also, the sample presented in this study may not be representative since enrollment in the study was limited to neonates that had been medically cleared to participate and who had parents available for, and willing to provide consent. In addition, some infants were examined for more sessions than others, weighing results toward those with more sessions. Differing interpretations of grading form elements may also have contributed to scoring differences between clinical examiners and SDOCT graders. Unlike the SDOCT graders, the clinical examiners almost never used the “unable to determine” category. In a large number of sessions, optic nerve findings noted on SDOCT were not recorded on clinical examination, although the scoring forms for both had the same

options to record large cup, hyaloidal remnants, optic nerve pallor and optic nerve elevation. The clinician may not have been as attentive to the optic nerve section of the grade form as to the ROP-pertinent sections. For the optic nerve, we lacked an objectively defined threshold for abnormalities to assure similar attention to structures such as small hyaloidal remnants that would be recorded as present on SDOCT grading but may not have been considered notable for clinical scoring. In addition, the clinician scored findings based upon a brief indirect ophthalmoscopic examination in a moving infant, while the SDOCT graders made their interpretations based upon evaluation of digital images displayed on a computer screen, which could be replayed as needed for evaluation of graded features. Color fundus photography would provide a similar reader experience reviewing images as one is moving through a grade form. In future study, it would be interesting to identify how characteristics identified on SDOCT relate to a corresponding fundus photograph.

In conclusion, SDOCT images may provide subclinical information on early critical vitreoretinal changes and enhance standard clinical examination in the management of ROP. As used in this study, SDOCT does not replace standard clinical examination of ROP, but may serve as a useful adjunct. Further study is needed to evaluate the clinical significance and predictive value of novel SDOCT findings in premature infants.

References

1. Tasman W. Multicenter trial of cryotherapy for retinopathy of prematurity. *Arch Ophthalmol.* 1988; 106(4):463–4. [PubMed: 3281639]
2. Early Treatment For Retinopathy Of Prematurity Cooperative, G. Revised indications for the treatment of retinopathy of prematurity: results of the early treatment for retinopathy of prematurity randomized trial. *Arch Ophthalmol.* 2003; 121(12):1684–94. [PubMed: 14662586]
3. Screening examination of premature infants for retinopathy of prematurity. *Pediatrics.* 2001; 108(3): 809–11. [PubMed: 11533356]
4. Chavala SH, et al. Insights into Advanced Retinopathy of Prematurity Using Handheld Spectral Domain Optical Coherence Tomography Imaging. *Ophthalmology.* 2009
5. Mirza RG, Johnson MW, Jampol LM. Optical coherence tomography use in evaluation of the vitreoretinal interface: a review. *Surv Ophthalmol.* 2007; 52(4):397–421. [PubMed: 17574065]
6. Maldonado RS, et al. Optimizing Hand-Held Spectral Domain Optical Coherence Tomography Imaging for Neonates, Infants and Children. *Invest Ophthalmol Vis Sci.*
7. Scott AW, et al. Imaging the infant retina with a hand-held spectral-domain optical coherence tomography device. *Am J Ophthalmol.* 2009; 147(2):364–373. e2. [PubMed: 18848317]
8. Chong GT, et al. Abnormal foveal morphology in ocular albinism imaged with spectral-domain optical coherence tomography. *Arch Ophthalmol.* 2009; 127(1):37–44. [PubMed: 19139336]
9. Flynn JT, Chan-Ling T. Retinopathy of prematurity: two distinct mechanisms that underlie zone 1 and zone 2 disease. *Am J Ophthalmol.* 2006; 142(1):46–59. [PubMed: 16815250]
10. Stevens B, Yamada J, Ohlsson A. Sucrose for analgesia in newborn infants undergoing painful procedures. *Cochrane Database Syst Rev.* 2004;CD001069. [PubMed: 15266438]
11. Elserafy FA, et al. Oral sucrose and a pacifier for pain relief during simple procedures in preterm infants: a randomized controlled trial. *Ann Saudi Med.* 2009; 29(3):184–8. [PubMed: 19448377]
12. Muni RH, et al. Retinoschisis detected with handheld spectral-domain optical coherence tomography in neonates with advanced retinopathy of prematurity. *Arch Ophthalmol.* 128(1):57–62. [PubMed: 20065217]
13. Funatsu H, et al. Vitreous levels of vascular endothelial growth factor and intercellular adhesion molecule 1 are related to diabetic macular edema. *Ophthalmology.* 2005; 112(5):806–16. [PubMed: 15878060]
14. Micieli JA, Surkont M, Smith AF. A systematic analysis of the off-label use of bevacizumab for severe retinopathy of prematurity. *Am J Ophthalmol.* 2009; 148(4):536–543. e2. [PubMed: 19660736]

15. Chen J, Smith LE. Retinopathy of prematurity. *Angiogenesis*. 2007; 10(2):133–40. [PubMed: 17332988]
16. Good WV, et al. Final visual acuity results in the early treatment for retinopathy of prematurity study. *Arch Ophthalmol*. 128(6):663–71. [PubMed: 20385926]
17. Mirabella G, et al. Visual development in very low birth weight infants. *Pediatr Res*. 2006; 60(4): 435–9. [PubMed: 16940247]
18. Joshi MM, Trese MT, Capone A Jr. Optical coherence tomography findings in stage 4A retinopathy of prematurity: a theory for visual variability. *Ophthalmology*. 2006; 113(4):657–60. [PubMed: 16581425]

Figure 1. Color photograph showing a portable spectral domain optical coherence tomography (SD OCT) workstation connected to a handheld probe for imaging of infants in the neonatal intensive care unit.

Figure 2.

Cross-sectional SD OCT image shows a laterally elongated preretinal structure with shadowing. As these preretinal structures were sometimes found adjacent to blood vessels, we hypothesize that they may represent early proliferative changes. In the sessions where preretinal tissue was seen on SDOCT (presumably within zone I) the ROP was staged as 3 or greater in 38% of sessions.

Figure 3.

The cross-sectional SD OCT image on the left demonstrates a prominent epiretinal membrane deforming fovea. The cross-sectional SD OCT image on the right shows an epiretinal membrane adjacent to blood vessel. Neither case of epiretinal membrane was noted on clinical examination.

Figure 4.
Cross-sectional SD OCT image shows hyaloidal remnant.

Figure 5. Cross-sectional SD OCT image on left with corresponding en-face retinal summed image on right.

Figure 6.

Cross-sectional SD OCT image showing retinal cystoid structures or schisis present in the inner nuclear layer with associated thickening and deformation of the photoreceptor layer elevating the outer plexiform layer. This session had been graded by the clinical examiner as stage II ROP disease in zone 2, no cystoid structures.

Figure 7. Cross-sectional SD OCT image demonstrating single intraretinal cystic structure without complete loss of foveal depression. The optic nerve is visible to the right.

Figure 8. Cross-sectional SD OCT image showing a severe case of macular edema with gross elevation of the central fovea and vertically elongated hyporefective structures alternating with thin strands of hyperreflectivity. This eye reached stage 2 disease in zone III and did not receive laser treatment.

Figure 9. Schematic diagram showing range of retinal imaging with the portable handheld SD OCT unit. This system provides high magnification imaging within zone I and can only infrequently capture images at the anterior border of zone I.

Figure 10.

Early retinal summed image on left showing motion artifact and incomplete view of optic nerve and vascular arcades. Example of a later retinal summed image on the right demonstrating improved image of optic nerve and vascular arcades.

Table 1

Baseline Characteristics of Enrolled Subjects (n= 38)

Mean birth weight (g, SD)	810 ($\pm$ 245)
Mean gestational age (wk, SD)	26.3 ($\pm$ 2.5)
Mean postmenstrual age at time of imaging (wk, SD)	37.5 ($\pm$ 4.8)
Gender (n, % male)	17 (45%)
Race or Ethnicity (n, %)	
Asian	0
Black/African American	21 (55%)
Hispanic	1 (3%)
White	16 (42%)

Table 2
Comparison of SD OCT and Clinical Examination for the Detection of Vitreoretinal Features

FEATURE	AGREEMENT			DISAGREEMENT				
	Present (%)	Absent (%)	Total (%)	Present on Clinical		Present on OCT		Absent on OCT
				Absent on OCT (%)	Indeterminate on OCT (%)	Absent on Clinical (%)	Indeterminate on Clinical (%)	
Vitreous Material*	7 (3)	200 (88)	207 (91)	8 (4)	0	4 (2)	0	9 (4)
Over Fovea	0	213 (93)	213 (93)	5 (2)	0	0	0	10 (4)
Preretinal Tissue (not ERM)	15 (7)	155 (68)	170 (75)	23 (10)	0	29 (13)	0	6 (3)
Vitreoretinal Attachment	2 (1)	197 (86)	199 (87)	10 (4)	1 (<1)	9 (4)	0	9 (4)
Deforming Retina	1 (<1)	204 (89)	205 (90)	3 (1)	0	8 (4)	0	12 (5)
Epiretinal Membrane	0	144 (63)	144 (63)	0	0	74 (32)	0	10 (4)
Deforming Fovea	0	190 (83)	190 (83)	0	0	22 (10)	0	16 (7)
Optic Nerve Abnormality	13 (6)	26 (11)	39 (17)	0	5 (2)	124 (54)	0	60 (26)
Retinal Cystoid Structures	0	126 (55)	126 (55)	0	0	88 (39)	0	14 (6)
Single	0	208 (91)	208 (91)	0	0	5 (2)	0	15 (7)
Foveal	0	147 (64)	147 (64)	0	0	64 (28)	0	17 (7)
Intraretinal Deposits	0	200 (88)	200 (88)	5 (2)	0	12 (5)	1 (<1)	10 (4)
Subretinal Fluid**	2 (1)	219 (96)	221 (97)	6 (3)	0	0	0	1 (<1)
Foveal	0	218 (96)	218 (96)	0	0	1 (<1)	0	9 (4)
Other Subretinal Lesion	0	214 (94)	214 (94)	5 (2)	0	0	0	9 (4)
RPE Atrophy/Absence	0	213 (93)	213 (93)	1 (<1)	0	5 (2)	0	9 (4)
Foveal	0	218 (96)	218 (96)	0	0	1 (<1)	0	9 (4)

* Graded on SD OCT as Vitreous Shadowing

† Graded on SD OCT and clinical examination as either Subretinal Fluid or Retinal Detachment

Table 3

Summary of Indirect Ophthalmoscopy and OCT Findings

Subject	Imaging Session	Birth wt (g)	G.A at birth (wks)	PMA at imaging (wks)	Indirect Ophthalmoscopy Findings OD	OCT Findings OD	Indirect Ophthalmoscopy Findings OS	OCT Findings OS
1	1	880	28	33.3	ZII S0; stalk at optic disc		ZII S0	HR
1	2	880	28	41.4	ZIII S2	HR	ZIII S2	HR
2	1	660	24	37.7	ZI S4A; VH; fibrous stalk, ridge NV; VRA; SRF; SR exudate	ERM; CME; IR deposits	ZI S4B; VRA; dragged vessels; SRF; SR exudate; RPE atrophy	ERM; CME; IR deposits
2	2	660	24	38.1	ZI S3; VH; VRA	ERM; HR; CME	ZI S4A; VRA; SRF; SR exudate	PR tissue; ERM; CME; IR deposits; SRF
2	3	660	24	38.7	ZI S4A; PRH; dragged vessels; IR lipid; SRF	vitreous shadowing; HR; CME	VH	ERM
2	4	660	24	38.7	ZII; VH; PRH; VRA	CME	VH	
2	5	660	24	40.7	ZII regressing; VH		VH	
2	6	660	24	43.0	ZII regressing; VH	vitreous shadowing; HR	ZII regressing	PR tissue; CME; IR deposits; RPE atrophy
3	1	560	23	41.9	ZII regressing; LC	HR; CME; IR deposits	ZII regressing; VRA; LC	PR tissue; ERM; HR; CME
3	2	560	23	43.0	ZII S1	HR; CME; IR deposits	ZII S1; fibrous PR material	CME
4	1	542	25	50.7	ZI S3; VRA; NV PR material; LC; vascular abnormality	PR tissue; VRA; ERM; HR; CME; IR deposits	ZI S3; NV PR material; LC	ERM; CME
4	2	542	25	53.7	ZI regressing; LC	PR tissue; VRA; ERM; HR	ZI regressing; fibrous PR material; LC	vitreous shadowing; PR tissue; VRA; HR; LC
4	3	542	25	56.7	ZI regressing; LC; vascular abnormality	PR tissue; VRA; HR	ZI regressing; VRA; NV PR material; LC; vascular abnormality	PR tissue
5	1	860	26	40.0	ZII S3; NV PR material; pre-Plus	CME	ZII S3; NV PR material	
6	1	690	26	31.9	ZII S2		ZII S2	ERM; HR; LC
6	2	690	26	33.9	ZII S2		ZII S2	LC
6	3	690	26	35.9	ZII S3; pre-Plus	HR; LC	ZII S3; pre-Plus	
6	4	690	26	36.9	ZII S3; pre-Plus		ZII S3; pre-Plus	LC
7	1	610	25	31.4	ZI S0		ZI S0	

Subject	Imaging Session	Birth wt (g)	GA at birth (wks)	PMA at imaging (wks)	Indirect Ophthalmoscopy Findings OD	OCT Findings OD	Indirect Ophthalmoscopy Findings OS	OCT Findings OS
7	2	610	25	32.4	ZII S1		ZII S1	
7	3	610	25	33.4	ZII S2	HR	ZII S2	
7	4	610	25	34.4	ZII S2	ERM	ZII S2	
7	5	610	25	35.4	ZII S2		ZII S2	HR
8	1	770	26	34.3	ZI S0; pre-Plus	ERM; HR	ZI S0; pre-Plus	ERM; HR
8	2	770	26	35.3	ZI S0; pre-Plus	PR tissue; ERM; HR	ZI S0; pre-Plus	
8	3	770	26	36.3	ZI S0; Plus	PR tissue; ERM; HR; CME	ZI S0; Plus	PR tissue; ERM
8	4	770	26	37.3	ZII S0; Plus	PR tissue; ERM; HR	ZII S0; Plus	PR tissue; ERM; HR
8	6	770	26	39.6	ZII S0; pre-Plus	PR tissue; ERM; CME	ZII S0; pre-Plus	PR tissue; ERM; HR
8	7	770	26	45.3	ZI S0; PRH	PR tissue; ERM; CME	ZI S0	ERM; HR; CME
9	1	1010	27	33.4	ZI S0	ERM; HR; LC	ZI S0	LC
9	2	1010	27	37.4	ZII S2	CME	ZII S2	
10	1	1050	30	34.0	ZII S0	ERM	ZII S0	ERM; HR
11	1	860	26.4	33.7	ZII S1	HR; LC	ZII S0	HR; LC
11	2	860	26.4	36.0	ZII S1		ZII S1	ERM; HR; LC
12	1	520	28	41.4	ZII S1; LC		ZII S1; LC	
12	2	520	28	42.3	ZII S2; LC	ERM; LC; CME	ZII S2; LC	ERM; LC
12	3	520	28	44.3	ZII S2; NV PR material; LC; pre-Plus; IRH	ERM	ZII S2; NV PR material; LC; vascular abnormality; IRH	ERM; LC
13	2	478	23	33.0	ZI S1	PR tissue; ERM; HR; LC	ZI S1	
13	3	478	23	35.0	ZI/II S3; NV PR material; Plus	PR tissue; ERM; HR	ZI/II S3; NV PR material; pre-Plus	PR tissue; ERM; HR
13	4	478	23	36.0	ZI/II S3; PRH; VRA; pre-Plus	vitreous shadowing; PR tissue; ERM; HR	ZI/II S3; PRH; VRA; pre-Plus	HR
13	5	478	23	37.0	ZII S2; VH; PRH; pre-Plus	ERM; HR	ZII S2; PRH; pre-Plus	vitreous shadowing; PR tissue; VRA; ERM; HR; CME
13	6	478	23	38.0	ZII S2; PRH; pre-Plus	PR tissue; VRA; ERM; HR	ZII S3; PRH; pre-Plus	PR tissue; HR
13	7	478	23	39.0	ZII S0; PRH	vitreous shadowing; ERM; HR; CME	ZII S0; PRH	vitreous shadowing; ERM; HR; CME;

Subject	Imaging Session	Birth wt (g)	GA at birth (wks)	PMA at imaging (wks)	Indirect Ophthalmoscopy Findings OD	OCT Findings OD	Indirect Ophthalmoscopy Findings OS	OCT Findings OS
14	1	790	25.7	31.4	ZII S1	LC	ZII S1	LC
15	1	1060	28	32.4	ZI/II S0	LC	ZI/II S0	LC
16	1	550	23.2	31.3	ZI/II S0; optic nerve pallor		ZI/II S0; optic nerve pallor	
16	2	550	23.2	34.3	ZI S2; pre-Plus	PR tissue; ERM; CME	ZI S2; pre-Plus	PR tissue; ERM; CME
16	3	550	23.2	35.3	ZI S2; NV PR material; Plus	CME	ZI S3; NV PR material; Plus	ERM; CME; IR deposits
16	4	550	23.2	36.3	ZI S0; Plus	ERM	ZI S0; Plus	PR tissue
16	5	550	23.2	49.0	ZII S0; optic nerve pallor	PR tissue; ERM; CME; IR deposits; RPE atrophy	ZII S0; optic nerve pallor	HR
17	1	640	24.1	31.1	ZI S0		ZI S0	ERM; LC
17	2	640	24.1	32.1	ZI/II S2		ZI/II S2	
17	3	640	24.1	33.1	ZII S0		ZII S0	
18	1	850	25	32.7	ZII S1	HR; CME	ZII S1	HR
19	1	1060	28	32.7	ZII S0		ZII S0	HR
20	1	720	28	32.7	ZII S0	HR	ZII S0	ERM; HR
21	2	1160	28	40.1	ZII S2	HR; CME; IR deposits	ZII S2	ERM; CME
22	1	1580	29	35.1	ZIII S0		ZIII S0	HR
23	1	660	24.4	38.0	ZII S2	HR	ZII S2	HR
24	1	650	27	34.0	ZII S1	HR	ZII S1	
24	2	650	27	35.0	ZII S1	CME	ZII S1	HR; CME
25	1	930	27	32.0	ZII S0	LC; CME	ZII S0	
26	1	495	24	40.0	ZII S4A; fibrous PR material; VRA; SRF	HR	ZII S3	PR tissue; HR; CME
26	2	495	24	41.0	ZII S4A; fibrous PR material; VRA; SRF	PR tissue; HR	ZII S3	
26	3	495	24	42.0	ZII S4A; fibrous PR material; VRA; SRF	vitreous shadowing; PR tissue; VRA; SRF; RPE atrophy	ZII S3	PR tissue; VRA
26	4	495	24	43.0	ZII S4A; fibrous PR material; VRA; SRF	vitreous shadowing; PR tissue; HR; RPE atrophy	ZII S3	vitreous shadowing; HR
26	5	495	24	45.0	ZII S3; fibrous PR material	PR tissue	ZII S3	PR tissue; HR

Subject	Imaging Session	Birth wt (g)	GA at birth (wks)	PMA at imaging (wks)	Indirect Ophthalmoscopy Findings OD	OCT Findings OD	Indirect Ophthalmoscopy Findings OS	OCT Findings OS
26	6	495	24	47.0	ZII S0	HR	ZII S0	HR
26	7	495	24	50.0	ZII S0	PR tissue	ZII S0	PR tissue; HR
27	1	630	27	31.0	ZI/II S0	ERM	ZI/II S0	ERM; HR; LC
27	2	630	27	32.0	ZI/II S0	ERM; HR	ZI/II S0	HR
27	3	630	27	33.0	ZII S0	PR tissue; ERM; HR	ZII S0	ERM; HR
27	4	630	27	34.0	ZII S0	ERM; HR; LC	ZII S0	ERM; HR
27	5	630	27	36.0	ZII S0	vitreous shadowing; ERM	ZII S0	HR
28	1	750	24	36.0	ZII S2; pre-Plus		ZII S2	
28	2	750	24	37.0	ZII S2; pre-Plus		ZII S2; pre-Plus	HR
28	3	750	24	38.0	ZII S2		ZII S2	
28	4	750	24	39.0	ZII S2; pre-Plus		ZII S2; pre-Plus	HR
28	5	750	24	40.0	ZII S2; pre-Plus	ERM; HR	ZII S2; pre-Plus	
28	6	750	24	41.0	ZII S2; pre-Plus	ERM	ZII S2; pre-Plus	HR
29	1	950	26	35.0	ZII S2	CME	ZII S2	CME
29	2	950	26	36.0	ZII S2	CME	ZII S2	HR; LC; CME
29	3	950	26	38.0	ZII S2	CME	ZII S2	LC; CME
30	1	1160	29	35.0	ZII S0		ZII S0	HR
30	2	1160	29	37.0	ZIII S0		ZIII S0	HR
31	1	1350	29	35.0	ZII S0	HR	ZII S0	HR
31	2	1350	29	37.0	ZIII S0	HR	ZIII S0	
32	1	870	25	33.0	ZII S2	HR; CME	ZII S2; pre-Plus	HR; CME
32	2	870	25	35.0	ZII S2	HR; CME	ZII S2; pre-Plus	CME
32	3	870	25	36.0	ZII S2	CME	ZII S2; pre-Plus	HR; CME
32	4	870	25	37.0	ZII S2	HR; CME	ZII S2; pre-Plus	HR; CME
32	5	870	25	38.0	ZII S2	ERM; HR; CME	ZII S3; pre-Plus	ERM; CME
32	6	870	25	39.0	ZII S2	ERM; HR; CME; IR deposits	ZII S2; pre-Plus	ERM; HR; CME; IR deposits
33	1	700	37	37.0	ZII S3; VH; pre-Plus	VRA	ZII S3; pre-Plus	HR; CME

Subject	Imaging Session	Birth wt (g)	GA at birth (wks)	PMA at imaging (wks)	Indirect Ophthalmoscopy Findings OD	OCT Findings OD	Indirect Ophthalmoscopy Findings OS	OCT Findings OS
33	2	700	37	38.0	ZII S3; VH; fibrous PR material	VRA; HR	ZII S3; fibrous PR material	PR tissue; VRA; ERM; HR; CME
33	3	700	37	39.0	ZII regressing; VH; fibrous PR material	ERM; CME	ZII regressing; fibrous PR material	CME
34	1	990	26	31.0	ZII S0	ERM; HR; LC	ZII S0	HR; LC
34	2	990	26	36.0	ZII S0	CME	ZII S0	HR; CME
35	1	800	25	33.0	ZII S1	HR; CME	ZII S1	ERM
35	2	800	25	34.0	ZII S3; Plus	ERM; HR	ZII S3; Plus	ERM; HR
35	3	800	25	35.0	ZII regressing; Plus	PR tissue; ERM; HR	ZII regressing; pre-Plus	ERM; HR
35	4	800	25	36.0	ZII S3; pre-Plus		ZII regressing; pre-Plus	HR
35	5	800	25	37.0	ZII S3	PR tissue; HR; CME	ZII regressing	CME
35	6	800	25	40.0	ZII regressed	HR; LC; CME	ZII regressed	CME
35	7	800	25	42.0	ZII regressed		ZII regressed	
36	1	680	25	33.0	ZII S0	HR; CME	ZII S0	HR
36	2	680	25	34.0	ZII S0		ZII S0	HR; CME
36	3	680	25	36.0	ZII S0	HR; CME	ZII S0	HR; CME
36	4	680	25	37.0	ZII S0	HR; CME	ZII S0	HR; CME
36	5	680	25	39.0	ZII S0	HR; CME	ZII S0	HR; CME
37	1	600	26	41.0	ZIII S3; IR deposit	HR; CME	ZIII S1	HR; CME
37	2	600	26	42.0	ZIII S2	PR tissue; HR; CME	ZIII S2	HR; CME
37	3	600	26	46.0	ZIII S3; IRH	CME	ZIII S0	HR; CME
38	1	700	25	34.0	ZI S2; pre-Plus		ZI S2; pre-Plus	
38	2	700	25	35.0	ZII S2; pre-Plus	HR; LC; CME	ZII S2; pre-Plus	CME
38	3	700	25	36.0	ZII S2; pre-Plus	CME	ZII S2; pre-Plus	CME
38	4	700	25	37.0	ZII S2	CME	ZII S2	HR; CME
38	5	700	25	42.0	ZIII S1	HR; CME	ZII S2	CME

CME=macular cystoid structures; ERM=epiretinal membrane; GA=gestational age; HR=hyaloidal remnants; IR=intraretinal; IRH=intraretinal hemorrhage; LC=large optic cup; NV=neovascular; PMA=postmenstrual age; PR=preretinal; PRH=preretinal hemorrhage; S=stage; SR=subretinal; SRF=subretinal fluid; VH=vitreous hemorrhage; VRA=vitreoretinal attachment; Z=zone