Published in final edited form as:

Retina. 2018 August ; 38(8): 1588–1594. doi:10.1097/IAE.0000000000001735.

Handheld spectral domain optical coherence tomography imaging through the undilated pupil in infants born preterm or with hypoxic injury or hydrocephalus

Du Tran-Viet, BS¹, Brittany M. Wong¹, Shwetha Mangalesh, MBBS¹, Ramiro Maldonado, MD¹, C. Michael Cotten, MD,MHS², and Cynthia A. Toth, MD^{1,3}

¹Department of Ophthalmology, Duke University School of Medicine, Erwin Road, Durham 27710 NC

²Department of Neonatology, Duke University School of Medicine, Erwin Road 27710 NC

³Department of Biomedical Engineering, Pratt School of Engineering, Duke University, Durham 27708 NC

Abstract

Purpose—We investigated feasibility of undilated handheld spectral-domain optical coherence tomography (SDOCT) retinal imaging in preterm infants and children with neurological abnormalities.

Methods—Under an IRB approved protocol, we attempted handheld SDOCT imaging of the retina, choroid, and optic nerve in infants and young children without pupil dilation. Scans were analyzed for quality and successful capture of foveal, optic nerve, and retinal structural parameters and abnormalities.

Results—We obtained images through an undilated pupil in 11 infants/children over 28 eye imaging sessions, 27 at the bedside without sedation and one under anesthesia. Infants had: retinopathy of prematurity (n=8), hypoxic ischemic encephalopathy (n=2), or obstructive hydrocephalus (n=1 child). Pupil sizes ranged from 1.0 to 3.5 mm. We captured fovea and optic nerve scans in 25/28 eye imaging sessions, with scans of adequate quality to discern pre-specified foveal and optic nerve morphology and out of the 25 sessions, the choroidal-scleral junction was visible in all but 6 sessions.

Conclusion—Undilated, handheld SDOCT imaging is a potential alternative method to evaluate retina and optic nerve in patients with relative contraindication to pharmacological pupil dilation. This approach will enable the study of the eye-brain connection and ocular manifestations of neurologic diseases.

Corresponding Author: Cynthia Ann Toth, Department of Ophthalmology, Duke University Eye Center, 2351 Erwin Road, Durham 27710 NC, Phone: 919-684-5741, cynthia.toth@duke.edu.

Conflict of Interest: Dr. Toth receives royalties through her university from Alcon. She also has unlicensed patents pending in OCT imaging and analysis. No other authors have financial disclosures. No authors have a proprietary interest in the current study.

Meeting Presentation: This study was presented in part at Association for Research in Vision and Ophthalmology, Seattle, Washington, United States, May 6, 2013.

Keywords

brain injury; hie; hypoxic injury; hypoxic ischemic encephalopathy; imaging; infants; OCT; optical coherence tomography; preterm infants; pupil; retina; retinopathy of prematurity; sdoct; undilated

Introduction

While table-top optical coherence tomography (OCT) has become a common diagnostic tool for adult eye examinations, pediatric imaging poses unique obstacles including patient cooperation and pre-verbalism. As a solution for these difficulties, handheld spectral domain (SD) OCT has been optimized in recent years for bedside, non-sedated, non-contact imaging in infants and for imaging of young children during supine examination under anesthesia.^{12, 3} Handheld SDOCT imaging has proved to be a valuable adjunct to standard indirect ophthalmoscopy in preterm infants; the method has shed light on macular findings such as cystoid macular edema,^{4, 5} delayed photoreceptor development at the fovea,⁶ and inner retinal immaturity⁷ not visible in conventional ophthalmic examinations.

SDOCT findings have reminded us that the retina, known to be an extension of the diencephalon, is central nervous system (CNS) tissue.^{6, 8} In adults, abnormal retinal findings on OCT have been associated with multiple sclerosis, Parkinson's disease, and Alzheimer's disease.^{9–11} The status of these neurodegenerative conditions appears to correlate with optic nerve axonal and neuronal damage manifested in retinal nerve fiber layer (RNFL) thinning, quantified by OCT.^{8–11} Recent handheld SDOCT studies in preterm infants have shown a correlation between thinner RNFL and increased brain injury visible on magnetic resonance imaging and between optic nerve cupping and CNS abnormalities.^{12–14} Cystoid macular edema in preterm infants has been associated with poorer language and motor neurodevelopmental outcomes at age 2 years.¹⁵ These point to the potential for SDOCT to revolutionize the diagnosis and monitoring of retinal, optic nerve, and neurological diseases in both adults and infants.

Monitoring pupil size and response has been an important component of neurological evaluation in both adult and pediatric populations.^{16, 17} Increased intracranial pressure and edema from brain injury can cause damage to the nerve fibers and bulb, leading to pupillary reflex abnormality; therefore the light-reflex test is a useful assessment of neurological status. The afferent pupillary light reflex arc begins at the retina and the ganglion cell fibers travel through the optic tract to the Edinger-Westphal nucleus.¹⁸ In the efferent pathway, fibers in the oculomotor nerve transmit signals from the midbrain through the superior orbital fissure to the ciliary sphincter. This pathway can be affected by pressure,¹⁷ cranial herniation,¹⁹ ischemia,²⁰ and optic pathway tumors, making a reflex test an essential tool.²¹ Therefore, it is critical in some neurological conditions to evaluate the brain without pharmacologically altering the pupil. In several of these conditions, pupillary size and reflex is conventionally used to track change and progression of disease and thus pharmacologic pupil dilation in an ocular exam would be avoided.^{16, 17, 22, 23}

In neurological assessment of infants, a non-invasive, non-contact modality to image retina and optic nerve without pupil dilation may prove effective in monitoring disease progression, assessing the extent of disease and treatment response. In this pilot study, our goal was to investigate the feasibility of handheld OCT imaging of the optic nerve and retina without pupil dilation in infants, for potential future use in those who cannot be dilated.

Methods

This observational study was conducted as a subset of a larger prospective study approved by the Duke University Institutional Review Board and conducted in accordance with the Health Insurance Portability and Accountability Act and tenets of the Declaration of Helsinki.

Stable preterm infants and children eligible for SDOCT imaging were enrolled from February 2010 through October 2015 with informed consent of a parent or legal guardian. The participants were imaged either in the Duke Intensive Care Nursery (ICN) outside of normal clinical eye examination or in the surgical suite under anesthesia.

Demographic information, including gestational age, birth weight, sex, race, disease status, were noted at the initial imaging session. Participants under this study were imaged without the use of topical dilation drops. Imaging was thus performed outside of normal clinical eye examination either at a single or multiple sessions. Pupil size was recorded for all imaging sessions and participants with pupils larger than 3.5 mm were not included in the study. All imaging followed the age-specific pediatric protocol laid out by Maldonado et al. for a portable, handheld, non-contact SDOCT system (Envisu C2200 and C2300 Bioptigen, Inc, Research Triangle Park, NC).¹ Volumetric rectangular scans of the macula and optic nerve were attempted for one or both eyes at each imaging session.

Image Analysis

Two trained graders (BMW, DT) reviewed the retinal SDOCT volumes in the InVivoVue Clinic software (Bioptigen, Research Triangle Park, NC) and assessed for both feasibility and image quality while masked to the other grader's findings. In this study, image acquisition was performed by a team including one of the graders. To avoid bias, all patient identifiers were removed and replaced by a study ID before graders analyzed scans. The scans were analyzed using the raw image files and were not post-processed to enhance the image quality.

Feasibility was determined by the successful capture of the fovea and optic nerve. Image quality of the fovea was based on ability to distinguish inner retinal layers, outer retinal layers, ability to visualize the choroidal-scleral junction (CSJ), and ability to distinguish retinal morphology such as cystoid macular edema (CME) or subretinal fluid (SRF). Image quality of the optic nerve was based on visibility of the optic nerve cup and of the lateral retinal pigment epithelium (RPE) boundaries. Further morphology analysis was performed by expert reviewers (DT, SM, CAT).

Results

Eleven infants and young children between the ages of 35 weeks post menstrual age (PMA) and 2 years were imaged under the research protocol without dilation and were included in this study (Figure 1). This included 8 infants with retinopathy of prematurity (ROP), 2 with hypoxic ischemic encephalopathy (HIE), and one child aged 2 years undergoing ventriculoperitoneal (VP) shunt surgery for obstructive hydrocephalus. The median pupil size was 2.5 mm, with range of 1.0 to 3.5 mm. Out of 28 possible eye imaging sessions, 2 eyes were not imaged due to health care team request, one with ROP and one with obstructive hydrocephalus. In 25 of the 26 (96%) attempted eye imaging sessions, at least one successful scan was obtained of the optic nerve in each eye. One ROP infant was restless, making the optic nerve imaging session difficult. In all 25 optic nerve imaging sessions, the location and quality of the scans were sufficient to view the optic nerve cup and the lateral RPE boundaries. In 25 of 26 (96%) eye imaging sessions, at least one successful scan was obtained of the fovea in each eye. We were unable to capture the fovea of one ROP infant due to early termination of the imaging as advised by the infant's nurse, who expressed concern that the infant was not sufficiently stable for imaging. While the choroidal-scleral junction was visible in 19 (76%) of 25 foveal imaging sessions, in all 25 foveal imaging sessions (100%), the location and quality of the scans were sufficient to view the foveal center, distinguish retinal layers and determine presence or absence of macular edema and subretinal fluid.

In the ROP subgroup, eight preterm infants in the ICN underwent ROP exams and were imaged without sedation between the ages of 35 weeks to 42 weeks PMA. At the time of imaging, 7 infants had pupil size from 2.0 to 3.0 mm and one infant had 3.5 mm. Of the 15 eyes imaged, fovea was captured successfully in 14/15 (93%) eyes. Foveal scan was not obtained in one eye due to health care team intervention. Optic nerve was captured in 14/15 (93%) eyes. In one eye, we were unable to capture optic nerve due to infant movement and restlessness, resulting in a difficult imaging session.

There was 100% agreement between the masked graders in the qualitative grading of the fovea and optic nerve scans obtained, and the image quality was good enough to visualize inner and outer retinal layers and to assess for presence or absence of CME in all foveal scans (Table 1). CME (Figure 2C) was present in 4/14 (29%) scans. CSJ (Figure 2) was visible on 11/14 (79%) scans. In all 14 eyes (100%) with an optic nerve scan (Figure 3), the image quality was good enough to visualize the optic nerve cup and the lateral RPE boundaries (Table 1).

In the HIE subgroup two infants were imaged at bedside in the ICN (born at 34 and 40 weeks GA and imaged at ages 35 and 41 weeks PMA respectively, after initiation of therapeutic hypothermia). One infant had one imaging session in both eyes and the other infant had four imaging sessions in both eyes. Pupil sizes ranged from 2.5 to 3.5 mm. Imaging was feasible in all 10 eye imaging sessions, with fovea and optic nerve captured in all 10 imaging sessions. In all 10 imaging sessions with a foveal scan, the image quality was good enough to visualize inner and outer retinal layers and to assess for presence or absence of CME. There was no CME observed in any of these scans. CSJ was visible on 7/10 (70%)

scans. In all 10 eye imaging sessions with an optic nerve scan, the image quality was good enough to visualize the optic nerve cup and the lateral RPE boundaries (Table 1). Quality was also sufficient to visualize retinal morphology. One infant with moderate HIE had severe retinal abnormalities which included thinning of all retinal layers, an immature photoreceptor layer, and a thin choroid. The other infant with severe HIE demonstrated the presence of sub-retinal fluid with an otherwise normal appearing retina (Figure 2B). The second HIE infant was imaged on four separate imaging sessions with comparable image quality at each visit.

In our final group, a 2-year-old child with obstructive hydrocephalus and a history of preterm birth was imaged in one eye (pupil size 1.0 mm) in the operating room following a craniotomy, cyst fenestration and external ventricular drain placement. Both the fovea and optic nerve of the eye were captured during this imaging session. In the foveal scan, the inner and outer retinal layers as well as the CSJ were visible. In the optic nerve scan, the optic nerve cup and the lateral RPE boundaries were visible (Table 1). In the fovea, CME caused bulging of the foveal contour, while the optic nerve head was elevated (Figure 3C) but appeared less elevated than it was in the dilated imaging session during an ophthalmic examination one week prior.

Discussion

In this pilot study, we demonstrate the feasibility and potential utility of handheld undilated imaging in preterm infants and in infants with CNS instability in order to visualize foveal contours and distinguishing retinal characteristics. Macular scans captured through the undilated pupil were of sufficient quality to visualize inner and outer retinal layers, reveal presence or absence of macular edema, and visualize the CSJ (Table 1 and Figure 2). We also discovered subfoveal fluid in an infant with severe HIE in the third day of life (Figure 2B), noting however, that subfoveal fluid has previously been found in 14% of healthy term-born infants on OCT examination within 48 hours after birth.^{24, 25}

Optic nerve scans were of sufficient quality to visualize optic nerve cup and the lateral RPE boundaries, allowing for three-dimensional visualization and revealing retinal nerve fiber layer thickness, vessel abnormalities and optic nerve head elevation (Table 1 and Figure 3).

In this small series, imaging was performed through multiple volumes obtained at the same session per infant. While images could vary in quality, from our assessment, we could find no difference in the appearance of macular or optic nerve scans between those volumes.

Advances in pediatric handheld SDOCT imaging have not only enabled bedside OCT imaging in the ICN, but also added to our knowledge base of retinal findings not previously described in infants.^{4–6} In the current study, we were able to capture both the fovea and optic nerve scans successfully, through pupil size 1.0 to 3.5 mm which revealed a difference in the presence of microstructural changes between two infants and reflected severity of MRI findings. We have not tried to image infants with pupil size less than 1 mm. It is important to recognize that systemic medications may affect pupil size; for example, one child had received morphine prior to imaging, which likely contributed to the 1 mm pupil. Also, while

ambient lighting has no impact on OCT image quality, it will affect pupil size. Thus we reported pupil size for each eye imaged in this study. Because it is easier to direct the OCT imaging through a larger pupil, we would recommend avoiding bright ambient lighting while imaging an undilated patient.

A current goal in neonatal care is to provide a healthy neurodevelopmental trajectory for preterm infants with attention to limiting invasive procedures among other factors.²⁶ In infants with HIE, long term neurological and visual outcomes have an impact on quality of life, and limit the ability to achieve full potential for healthy productive life. In addition to the current gold standard treatment, hypothermia, newer therapies are being evaluated.^{27, 28} Evaluating retinal and optic nerve injury at the micron-scale, which likely reflects injury and response to injury in the CNS, could be extremely useful as shown in this study. The methodology would offer a valuable for, first, determination of the acute neuronal cellular tissue damage and, second, repeated assessments to monitor changes in response to treatment. For example, RNFL thinning has been found to be associated with hydrocephalus in preterm infants,¹² and it may be useful to monitor for optic nerve head swelling or thinning in these infants in a prospective study of intervention timing and prognosis. We have demonstrated in the current study feasibility of capturing OCT scans in the operating room, through a pin-point pupil, in a child with obstructive hydrocephalus. The ability to visualize CNS tissue real-time in the operating room can provide relevant information in the future regarding the acute status of the optic nerve tissue in response to surgical intervention.

There are multiple techniques we use to help us efficiently obtain high quality images at the bedside. We have an additional person operate the computer software, while the imager holds the handheld probe and obtains the scans. It is important that the viewing screen is positioned where it is readily visible to the imager without twisting away from the infant. The additional person can provide support in comforting the infant by swaddling beforehand and by resting his/her hands around the head or body to hold and soothe the infant. Pacifiers and sucrose are often useful to calm a restless infant. Aligning the imager so that the top of the infant's head is towards the imager's chest, simplifies positioning the handheld probe over the head and not the entire body. Lateral alignment is critical when pupils are small, since any small movement not centered at the point of interest will cause the scan quality to diminish. Artificial tears (single use, preservative free packets) may be useful to help lubricate the cornea and obtain sharper images. We have commented on some of these techniques in Maldonado et al.¹

Lighter, more compact and higher speed handheld OCT technology would address the major limitation to this study. Although images were of a quality comparable to those captured with pupil dilation, a highly skilled imager was required to align the handheld imaging system and capture the key structural retinal features through very small pupils with the current Bioptigen handpiece of moderate weight and size. Because of the limitations of the rate of SDOCT capture with the current commercial system, infant eye movement made alignment more challenging. We recently initiated use of an investigational ultracompact system with high-speed swept source OCT imaging. Use of these novel systems with higher capture speed and the addition of pupil alignment, are likely to improve the utility of this infant imaging.²⁹

This is a preliminary study towards our long-term goal to advance methods and tools for visual and neurodevelopmental outcomes of a vulnerable infant population. Bringing portable OCT imaging to the neonatal realm has been developed over the last decade. From literature published so far, we believe it is highly likely that ongoing brain injury in infants with neurological diseases will be reflected in the eye throughout the stages of injury and sequelae. Our pilot study, although with limited sample size, has provided an auxiliary method to monitor ophthalmic and neurologic microstructural abnormalities in infants with pharmacologically undilated pupils.

Acknowledgments

The authors would like to thank Vincent Tai, MS (Duke University Eye Center) and Christian Viehland, BS (Duke Biomedical Engineering) for assistance with image processing.

Financial Support: The Hartwell Foundation; The Andrew Family Charitable Foundation; Research to Prevent Blindness; Retina Research Foundation; NIH Grants: 1UL1RR024128, NIH Roadmap for Medical Research, 1UL1TR001117, National Center for Advancing Translational Sciences, R01 EY025009, Center Core Grant for Vision Research, P30 EY005722.

References

- 1Maldonado RS, Izatt JA, Sarin N, et al. Optimizing hand-held spectral domain optical coherence tomography imaging for neonates, infants, and children. *Invest Ophthalmol Vis Sci*. 2010; 51(5): 2678–2685. [PubMed: 20071674]
- 2Chavala SH, Farsiu S, Maldonado R, Wallace DK, Freedman SF, Toth CA. Insights into advanced retinopathy of prematurity using handheld spectral domain optical coherence tomography imaging. *Ophthalmology*. 2009; 116(12):2448–2456. [PubMed: 19766317]
- 3Scott AW, Farsiu S, Enyedi LB, Wallace DK, Toth CA. Imaging the infant retina with a hand-held spectral-domain optical coherence tomography device. *Am J Ophthalmol*. 2009; 147(2):364–373.e362. [PubMed: 18848317]
- 4Maldonado RS, O’Connell R, Ascher SB, et al. Spectral-domain optical coherence tomographic assessment of severity of cystoid macular edema in retinopathy of prematurity. *Arch Ophthalmol*. 2012; 130(5):569–578. [PubMed: 22232366]
- 5Vinekar A, Avadhani K, Sivakumar M, et al. Macular edema in premature infants. *Ophthalmology*. 2012; 119(6):1288–1289.e1281. author reply 1289–1290.e1281. [PubMed: 22656902]
- 6Vajzovic L, Rothman AL, Tran-Viet D, Cabrera MT, Freedman SF, Toth CA. Delay in retinal photoreceptor development in very preterm compared to term infants. *Invest Ophthalmol Vis Sci*. 2015; 56(2):908–913. [PubMed: 25587063]
- 7Maldonado RS, O’Connell RV, Sarin N, et al. Dynamics of human foveal development after premature birth. *Ophthalmology*. 2011; 118(12):2315–2325. [PubMed: 21940051]
- 8Simao LM. The contribution of optical coherence tomography in neurodegenerative diseases. *Curr Opin Ophthalmol*. 2013; 24(6):521–527. [PubMed: 24100368]
- 9Gordon-Lipkin E, Chodkowski B, Reich DS, et al. Retinal nerve fiber layer is associated with brain atrophy in multiple sclerosis. *Neurology*. 2007; 69(16):1603–1609. [PubMed: 17938370]
- 10Garcia-Martin E, Satue M, Fuertes I, et al. Ability and reproducibility of Fourier-domain optical coherence tomography to detect retinal nerve fiber layer atrophy in Parkinson’s disease. *Ophthalmology*. 2012; 119(10):2161–2167. [PubMed: 22749083]
- 11Paquet C, Boissonnot M, Roger F, Dighiero P, Gil R, Hugon J. Abnormal retinal thickness in patients with mild cognitive impairment and Alzheimer’s disease. *Neurosci Lett*. 2007; 420(2):97–99. [PubMed: 17543991]
- 12Rothman AL, Sevilla MB, Mangalesh S, et al. Thinner Retinal Nerve Fiber Layer in Very Preterm Versus Term Infants and Relationship to Brain Anatomy and Neurodevelopment. *Am J Ophthalmol*. 2015; 160(6):1296–1308.e1292. [PubMed: 26386157]

- 13Rothman AL, Mangalesh S, Chen X, Toth CA. Optical coherence tomography of the preterm eye: from retinopathy of prematurity to brain development. *Eye and Brain*. 2016; 8:123–133. [PubMed: 28539807]
- 14Tong AY, El-Dairi M, Maldonado RS, et al. Evaluation of optic nerve development in preterm and term infants using handheld spectral-domain optical coherence tomography. *Ophthalmology*. 2014; 121(9):1818–1826. [PubMed: 24811961]
- 15Rothman AL, Tran-Viet D, Gustafson KE, et al. Poorer neurodevelopmental outcomes associated with cystoid macular edema identified in preterm infants in the intensive care nursery. *Ophthalmology*. 2015; 122(3):610–619. [PubMed: 25439600]
- 16Takata T, Kamada M, Ikeda K, et al. Unilateral mydriatic tonic pupil as an early isolated symptom of neurosyphilis. *J Neurol Sci*. 2014; 344(1–2):219–220. [PubMed: 24958595]
- 17Chen JW, Vakil-Gilani K, Williamson KL, Cecil S. Infrared pupillometry, the Neurological Pupil index and unilateral pupillary dilation after traumatic brain injury: implications for treatment paradigms. *Springerplus*. 2014; 3:548. [PubMed: 25332854]
- 18Spector RH. The Pupils. In: Walker HK, Hall WD, , Hurst JW, editors *Clinical Methods: The History, Physical, and Laboratory Examinations* Boston: Butterworths; 1990
- 19Manley GT, Larson MD. Infrared pupillometry during uncal herniation. *J Neurosurg Anesthesiol*. 2002; 14(3):223–228. [PubMed: 12172296]
- 20Ritter AM, Muizelaar JP, Barnes T, et al. Brain stem blood flow, pupillary response, and outcome in patients with severe head injuries. *Neurosurgery*. 1999; 44(5):941–948. [PubMed: 10232526]
- 21Avery RA, Fisher MJ, Liu GT. Optic pathway gliomas. *J Neuroophthalmol*. 2011; 31(3):269–278. [PubMed: 21857190]
- 22Koehler PJ, Wijdicks EF. Fixed and dilated: the history of a classic pupil abnormality. *J Neurosurg*. 2015; 122(2):453–463. [PubMed: 25415062]
- 23Scinto LF, Daffner KR, Dressler D, et al. A potential noninvasive neurobiological test for Alzheimer's disease. *Science*. 1994; 266(5187):1051–1054. [PubMed: 7973660]
- 24Cabrera MT, Maldonado RS, Toth CA, et al. Subfoveal fluid in healthy full-term newborns observed by handheld spectral-domain optical coherence tomography. *Am J Ophthalmol*. 2012; 153(1):167–175.e163. [PubMed: 21925640]
- 25Cabrera MT, O'Connell RV, Toth CA, et al. Macular findings in healthy full-term Hispanic newborns observed by hand-held spectral-domain optical coherence tomography. *Ophthalmic Surg Lasers Imaging Retina*. 2013; 44(5):448–454. [PubMed: 23938334]
- 26Stoll BJ, Hansen NI, Bell EF, et al. Trends in Care Practices, Morbidity, and Mortality of Extremely Preterm Neonates, 1993–2012. *Jama*. 2015; 314(10):1039–1051. [PubMed: 26348753]
- 27Higgins RD, Raju T, Edwards AD, et al. Hypothermia and other treatment options for neonatal encephalopathy: an executive summary of the Eunice Kennedy Shriver NICHD workshop. *J Pediatr*. 2011; 159(5):851–858.e851. [PubMed: 21875719]
- 28Davidson JO, Wassink G, van den Heuvel LG, Bennet L, Gunn AJ. Therapeutic Hypothermia for Neonatal Hypoxic-Ischemic Encephalopathy - Where to from Here? *Front Neurol*. 2015; 6:198. [PubMed: 26441818]
- 29LaRocca F, Nankivil D, DuBose T, Toth CA, Farsiu S, Izatt JA. In vivo cellular-resolution retinal imaging in infants and children using an ultracompact handheld probe. *Nature Photonics*. 2016; 10:580–584. [PubMed: 29479373]

Summary statement

We demonstrate the feasibility of imaging infants and young children with neurological abnormality using handheld SDOCT without dilation, by evaluating image quality and resolution of foveal and optic nerve characteristics. This approach will allow better understanding of the eye-brain connection and disease manifestation of brain injury in the retinal layers.

Figure 1.

Overview of study population and the ability to image fovea and optic nerve with handheld spectral domain optical coherence tomography imaging on undilated infants and children.

Figure 2.

Spectral domain optical coherence tomography (SDOCT) scans on undilated infants at the foveal center. **(A)** A 35-week postmenstrual age (PMA) infant with Retinopathy of Prematurity (ROP) imaged through a 2mm pupil showing normal foveal contour with persistent inner retinal layers. **(B)** A 41-week PMA infant diagnosed with severe hypoxic ischemic encephalopathy imaged through a 2.5mm pupil showing subretinal fluid at the fovea.^{24,25} **(C)** A 37 week PMA infant with ROP imaged through a 2.5mm pupil showing inner retinal thickening due to macular edema, with cystoid spaces in the inner nuclear layer.

In all three foveal images, the photoreceptor layer is immature (consistent with age) with absence of the ellipsoid zone at the foveal center in A and C (white arrows) and a short distance between the thin outer plexiform layer (black arrow) and the retinal pigment epithelium.⁶

Figure 3.

Spectral domain optical coherence tomography (SDOCT) three dimensional volumes including the optic nerve (left) from b-scans (right) on undilated infants at the optic nerve. (A) A 35-week postmenstrual age (PMA) infant with Retinopathy of Prematurity (ROP) imaged through a 2mm pupil. The fovea (black arrow) is distinct from optic nerve head (white arrow) and a hyaloidal vessel is extended from the optic nerve head. (B) A 35-week PMA infant diagnosed with hypoxic ischemic encephalopathy imaged through a 3.5mm pupil. The retinal vasculature was visible across the retinal surface (black arrows). (C) A 2-

year old child diagnosed with obstructive hydrocephalus imaged through a 1mm pupil revealed the elevated optic nerve head (white arrow). On the B scan, there is pronounced retinal thinning adjacent to the optic nerve and the choroid is thin.

Table 1

Ability to visualize retinal and choroidal features using optical coherence tomography without pupil dilation

Disease group (eye imaging sessions)	Foveal and choroidal development				Cystoid Macular Edema		Optic nerve	
	Inner retinal layers	Outer retinal layers	Choroidal-Scleral Junction		Present	Absent	Optic Nerve Cup	Lateral boundary at RPE
Retinopathy of Prematurity (n = 14)	14	14	11		4	10	14	14
Hypoxic Ischemic Encephalopathy (n = 10)	10 [*]	10 ^{**}	7		0	10	10	10
Obstructive hydrocephalus (n = 1)	1	1	1		1	0	1	1
All (n = 25)	25	25	19		5	20	25	25

* Severe thinning of inner and outer layers in two eyes for four visits;

** Subretinal fluid present in two eyes for one visit; RPE, retinal pigment epithelium