Retinal Imaging in Infants

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Abstract

Digital retinal imaging is at the core of a revolution that is continually improving the screening, diagnosis, documentation, monitoring, and treatment of infant retinal diseases. Historically, imaging the retina of infants had been limited and difficult to obtain. Recent advances in photographic instrumentation have significantly improved the ability to obtain high-quality multimodal images of the infant retina. These include color fundus photography with different camera angles, ultrasonography, fundus fluorescein angiography, optical coherence tomography, and optical coherence tomography angiography. We provide a summary of the current literature on retinal imaging in infants and highlight areas where further research is required.

Key words
color fundus photography (CFP); fundus fluorescein angiography (FFA); optical coherence tomography (OCT); optical coherence tomography angiography (OCT-A); narrow-field; wide-field; wide-angle; ultra-widefield; retinal imaging; retinal imaging in infants
1. Introduction

The chief limitation of imaging the retina of infants has been the lack of equipment designed to allow quick and easy image acquisition, particularly in unanesthetized, preverbal, and uncooperative patients. Over the past two decades, multiple advancements in technology have produced imaging modalities and techniques that allow the acquisition of retinal images in infants, opening up new areas of clinical research and information in our understanding of the anatomy, as well as in evaluating pathology in these eyes. We provide a summary of the literature on retinal imaging in infants and highlight areas where further research is required.

2. Definition of infant

The American Academy of Pediatrics define an infant as a live born child younger than 365 days of age.

3. Methods of retinal imaging in infants

3.1 Ultrasonography

3.1.1 B-scan ultrasonography

Ultrasound is a high-frequency sound wave using frequencies outside the normal hearing range of humans (20 Hz to 20 kHz). Higher sound frequencies have less tissue penetration, but higher tissue resolution. Contact ophthalmic ultrasonography typically uses a 10 MHz handheld transducer probe. A 20 MHz probe can be used but its field of view is insufficient to evaluate the entire globe. The ultrasound probe used contains quartz or ceramic crystals that vibrate when stimulated by an electric current, generating a sound wave of constant amplitude and frequency. This is known as the piezoelectric effect. When the vibration stops, the quartz crystal is used as a detector. Reflected sound waves (echoes) cause the crystals to vibrate, which in turn produces an electric current. These are analyzed and processed into a visual display by the ultrasound machine. Echoes are produced at the junction of ocular tissues with different acoustic impedances. The greater the difference in
density between the two ocular tissues, the stronger the echo. Weaker echoes are produced when imaging deeper ocular structures. Increasing the gain of the amplifier can correct the decrease in signal strength with time of flight. There are two ways of displaying ultrasonography: A and B scans. Display of the echo from a longitudinal sound wave along a single line of sight is called an amplitude scan (A-scan). A summation of multiple A-scans produces a two-dimensional image known as a brightness scan (B-scan). B-scan ultrasonography is performed with the infant in a supine position. A coupling agent is applied to the tip of the transducer probe, which is then placed on the infant’s closed eyelids.

3.1.2. Prenatal ultrasonography

Ultrasonographic imaging of the prenatal eye to detect congenital ocular abnormalities can be performed at 18 to 20 weeks of gestational age. Typically, a 3-5 MHz curvilinear probe is used to obtain detailed anatomic features of the fetal eye. An alternative 1-5 MHz convex probe or 5-10 MHz transvaginal probe can be used if the higher frequency curvilinear probe has not obtained adequate sonographic images.

3.2. Color fundus photography

For infant retinal diseases, color fundus photography (CFP) is a valuable tool for disease evaluation, documentation, treatment monitoring, parental education and for medicolegal purposes. Traditional color fundus cameras have limited use in infants since their stationary table-top designs restrict their use to cooperative patients who can maintain an upright seated position during image acquisition. Technological advances and refinements to existing imaging techniques have allowed for easier image acquisition in infants. Various narrow-field (standard field), wide-field, and ultra-widefield retinal imaging devices are available to ophthalmologists for obtaining color fundus images in infants (Table 1). The term wide-field describes devices that capture, in a single fundus image, all 4 quadrants of the retina posterior to and including the vortex vein ampulla. The term ultra-widefield describes devices that capture in a single fundus image all 4 quadrants of the retina anterior to the vortex vein ampulla.
3.2.1. Historical imaging devices

3.2.1.1. Zeiss fundus camera

The first narrow-angle color fundus image of the infant retina was obtained by Bulpitt and coworkers in 1969 using a vertically mounted Zeiss fundus camera (Carl Zeiss, Inc., Thornwood, NY). One assistant stabilized the infant’s head with the eyelids held open, while another was responsible for photography. Gentle rotation of an infant's head enabled different angles of the retina to be captured.

3.2.1.2. NIDEK digital fundus camera

The NIDEK NM200D® (Nidek, Gamagori, Japan) is a hand-held, non-contact, narrow-angle digital imaging system. It is capable of capturing up to 30° of the retina in a single fundus image using a charge coupled device camera. Skalet and coworkers utilized the device in 2008 for examining telemedicine retinopathy of prematurity (ROP) diagnosis in a developing country because of its affordability, portability, and ease of use.

3.2.2. Current imaging devices

3.2.2.1. Pictor

Pictor® (Volk Optical Inc, Mentor, OH) is a hand-held, non-contact and narrow-field digital fundus camera approved by the Food and Drug Administration (FDA) for capturing digital images of the fundus and surrounding area. Prakalapakorn et al were able to capture images of sufficient quality with this device on a sample of prematurely born infants, showing promise for its use as a ROP screening tool. This device is light weight, portable, and can capture CFP that include up to 45° of the retinal field.

3.2.2.2. Video indirect ophthalmoscopy

Binocular indirect ophthalmoscopy with or without scleral depression is the gold-standard method for examining the infant retina. Shanmugam and coworkers described a technique in 2011 of using a standard hand-held digital video camera with an attached torch light, to capture retinal images and videos, during indirect ophthalmoscopy in anesthetized infants. A digital video camera is held up to the examiner’s eye with one hand, while a condensing lens is held in front of the infant eye with the other hand of the examiner. The handheld video camera controls are manipulated to capture dynamic or still images of the
infant retina. Scleral depression is not possible with this technique given both hands are employed. More recently, color fundus images of the infant retina have been obtained with the Vantage Plus® LED digital binocular indirect ophthalmoscope system (Keeler Instruments Inc, Broomall, PA). This device consists of an indirect ophthalmoscope with an integrated camera that captures video or still images of the retina (Fig. 1A). The retinal field of view is similar to that of standard indirect ophthalmoscopy.

3.2.2.3. Smartphones
Smartphone-based fundus photography provides a cost-effective and widely available method of capturing narrow-field color fundus images in infants. Modern smartphone cameras have an optical system and a co-axial inbuilt light source that can be used to capture retinal images. The simplest method of smartphone-based color photography involves coupling a condensing lens to a smartphone camera functioning as an indirect ophthalmoscope. With the infant in a supine position, a condensing lens is held in front of the eye with one hand, and with the other hand, the smartphones continuous flash is used to both illuminate the retina and capture snapshots from a video of the fundus. In contrast other smartphone devices use the principle of direct ophthalmoscopy. This includes the D-Eye® (D-Eye, Truckee, CA) portable optical device (Fig. 1B), the RetinaScope® (Fig. 1C) optical device and the panoptic ophthalmoscope (Fig. 1D) with the iExaminer® adapter (iExaminer, Welch Allyn, Skaneateles, Falls, NY) that connects to a smartphone to capture images of the infant retina.

3.2.2.4. 3nethra Neo (Neo)
The 3nethra Neo® (Forus Health, Bangalore, India), developed by Forus Health in 2012, is a portable, hand-held, wide-field digital imaging system. It is a low-cost infant retinal device that has been primarily used in developing countries for photographic documentation of the posterior segment during ROP screening. The device captures up to 120° of the retina in a single fundus image using a light-emitting diode (LED) illumination system. When using the 3nethra Neo, a lightweight hand-piece is applied directly onto the cornea of the infant’s eye using a coupling agent. Vinekar and coworkers found no systemic or ocular adverse events with this imaging technique in premature infants.
3.2.2.5. Panocam
The Panocam® (Visunex Medical Systems, Inc., Fremont, CA, USA) is a contact lens-based, wide-field digital imaging system approved by the FDA for capturing color fundus images in newborn infants. The device is wireless and uses LED lighting to capture a 130° field of view of the retina in a single image. Pertinent features of the Panocam include its portability, excellent resolution, and wide-angle camera system. In 2016, Wood et al performed a literature review that included a description of the Panocam and its application for ROP screening in premature infants. There is no clinical data available from research studies or clinical trials for this imaging device in infants.

3.2.2.6. RetCam
The RetCam® (Clarity Medical Systems, Inc., Pleasanton, CA), developed by Bert Massie in 1997, is a contact-lens based wide-field digital imaging system that uses fiberoptic illumination to capture up to 130° of the infant retina in a single fundus image (Fig. 1E). It is the most established and widely used imaging device for obtaining images in infants. It is portable with a hand-held probe (Fig. 1F) allowing the device to be used in the operating room, office or inpatient settings. Optimal images are obtained with wide dilation of the pupil and minimal media opacity. Imaging through media opacities is possible, but may produce suboptimal retinal images in infants owing to the inability of the image capturing unit to illuminate the interior of the globe and scattering of light from irregular surfaces.

3.2.2.7. Phoenix ICON
The Phoenix ICON® (Phoenix Technology Group, Pleasanton, CA) is a portable, cart-based pediatric contact wide-field imaging system that utilizes a LED light source to capture up to 100° of the retina in a single fundus image. The Phoenix ICON is similar to the RetCam imaging device, but provides better image resolution in pigmented fundi.

3.2.2.8. Optos
Optos® (Optos, Dunfermline, Scotland) is a non-contact, non-invasive, ultra-widefield digital imaging system utilizing confocal scanning laser ophthalmoscopy (cSLO) to obtain high-resolution retinal images. cSLO is an imaging technique whereby a near-infrared diode laser beam rapidly scans across the fundus in a raster pattern to illuminate point-by-point...
elements of the retina. After passing through a confocal pinhole, the intensity of the reflected light at each point is detected by a photomultiplier, and a two-dimensional digitized image is generated. To minimize scatter, chromatic aberration and improve image contrast, the confocal pinhole ensures that only light reflected from each retinal spot is recorded. Using a large ellipsoid mirror, the Optos imaging system is capable of capturing up to 200° of the retina in a single fundus image (Fig. 1G). Patel and coworkers described a technique in 2013 that allowed non-anesthetized infants to be imaged, whilst being held horizontally up to the Optos imaging system in an office setting (Fig. 1H). The Optos system captures optimum images with wide dilation of the pupil, although it is still possible to obtain high-quality images through small pupils, with or without placement of an eyelid speculum. There have been no reports of adverse ocular or systemic effects in premature and term infants with this imaging technique; however, the Optos device is not commonly used in infants, and there are no studies evaluating the safety and practicalities of using this device on infants attached to different forms of ventilatory support.

3.3. Fluorescein angiography

Fundus fluorescein angiography (FFA) allows the study of the circulation of the infant retina in normal and diseased states. Fluorescein is stimulated by blue light at a wavelength of 465-490 nm and emits a green-yellow light at a wavelength of 520-530 nm. To obtain a fluorescein angiogram, white light from a digital imaging system is passed through a blue filter, and blue light enters the eye. The blue light excites the unbound fluorescein molecules within the blood vessels or unbound molecules that have leaked out of the blood vessels. The blue light then causes those structures in the eye containing fluorescein to emit a green-yellow light. The blue reflected light and the green-yellow fluorescent light exit the eye and are directed back towards the digital imaging system. A green-yellow filter allows the green-yellow light through but blocks out the reflected blue light.

Traditionally, FFA has been difficult to perform on infants. Recent advances in photographic instrumentation have made it possible to obtain high-quality fluorescein angiograms in infants. Typically, images are taken after intravenous administration of fluorescein sodium 10% at a dose of 0.1ml/kg body weight, followed by an isotonic saline flush.
Alternatively, images can be taken at 15 minutes after oral administration of fluorescein sodium 2% (25mg/kg body weight). Studies have reported fluorescein angiography to be safe in infants with no systemic adverse effects.

3.3.1. Historical imaging devices
3.3.1.1. Zeiss fundus camera
FFA was first utilized on infants with retrolental fibroplasia in the 1960s by Flynn and colleagues using a vertically mounted Zeiss fundus camera (Carl Zeiss, Inc., Thornwood, NY) equipped with spectrotec fluorescein filters. At that time, FFA was reserved for studying infants with “peculiar or puzzling fundus pictures”. In 1982, Shields and associates used the same vertically mounted Zeiss fundus camera to perform FFA on anesthetized infants with retinoblastoma.

3.3.2. Current imaging devices
3.3.2.1. RetCam
In 2006, Ng and coworkers first demonstrated the feasibility of imaging the peripheral retinal vasculature in infants using the FFA RetCam digital imaging system. A total of 51 intravenous fluorescein angiography sessions were performed on 23 infants. No adverse events were observed by the authors.

3.3.2.2. Phoenix ICON
The Phoenix ICON imaging system offers fluorescein angiography capabilities; however, there have been no reports in the literature evaluating its use in the infant population.

3.3.2.3. Optos
Patel and coworkers first reported oral ultra-widefield FFA in a 3-month-old infant using the Optos digital imaging system in 2013. Infant formula milk mixed with fluorescein sodium 2% was given 30 minutes prior to imaging. Following pupillary dilation and placement of a lid speculum, FFA was performed with the infant held up to the device. Fung et al have since performed oral ultra-widefield FFA using the Optos digital imaging system in premature infants with stage 3 ROP. Fung and coworkers described a method in 2014 for ultrawidefield intravenous FFA in infants, using the Optos digital imaging system. A total of
12 infants with a variety of proliferative retinopathies were imaged, with a mean age of 3.4 months. To obtain high-resolution images, a team-based approach was used, with one assistant holding the infant horizontally up to the Optos imaging device, whilst other team members performed the photography and intravenous fluorescein injection.\textsuperscript{94}

3.3.2.4. Heidelberg Spectralis
The Heidelberg Spectralis\textsuperscript{®} (Heidelberg Engineering, Heidelberg, Germany) is a table-top, multi-modal, non-contact digital imaging system that utilizes cSLO to obtain high-resolution retinal images. It is capable of imaging up to 102° of the retina in a single fundus image. In 2014, Fung and colleagues demonstrated ultrawidefield intravenous FFA on anesthetized infants in the operating room using a prototype arm-mounted Heidelberg Spectralis (Fig. 2).\textsuperscript{44}

3.4. Optical coherence tomography
Optical coherence tomography (OCT), developed by Huang and associates in 1991, is a non-invasive, non-contact imaging modality that produces micron-scale resolution cross-sectional retinal images.\textsuperscript{57} Most commercially available OCT imaging systems are vertically orientated which preclude the imaging of supine infants. Recent advances in photographic instrumentation have made it possible to obtain high-quality OCT images in infants with a variety of retinal disorders.

Time-domain OCT (TD-OCT) imaging devices rely on low coherence interferometry, in which the signal carrying light returning from the retina is allowed to interfere with light that has traveled a known path length.\textsuperscript{57} This is achieved with a Michelson interferometer that splits low coherence light emitted from a source that is split into a reference arm and a sample arm. Light from the reference arm interferes with light from the sample arm, and an interference signal is generated when the path lengths from both arms are the same or nearly the same. The interference signal is processed to form cross-sectional images of the retina.
Spectral-domain OCT (SD-OCT) imaging devices use a low coherence light source and measures the interference spectrum using a high-speed line charge-coupled device (CCD) and spectrometer. The spectrometer analyzes the spectrum of reflected light on the retina, transforming it into information on the depth of the structures, using the Fourier principle. The main advantage of SD-OCT over TD-OCT is that the former provides better resolution and faster acquisition speeds. This diminishes motion artifact and makes it more efficient for imaging the infant eye, where accurate scans must be obtained in the shortest period of time.

3.4.1. Zeiss fundus camera

Patel and coworkers first presented the feasibility of TD-OCT imaging in 2006 on an infant using a Zeiss Stratus OCT 3000 (Carl-Zeiss, Jena, Germany) imaging device. Under general anesthesia, the infant was placed in a prone and reverse Trendelenburg position in front of the OCT device.

3.4.2. Envisu

Envisu® (Leica Microsystems, Wetzlar, Germany) is a non-contact, hand-held SD-OCT imaging system that uses a superluminescent diode light source to produce in-vivo high-resolution images of the retina. A hand-held imaging probe is connected via a 1.3m fiberoptic cable to a portable cart holding the SD-OCT technology. Scott et al demonstrated in 2009 that retinal images could be obtained using this device on sedated or anesthetized full-term infants with shaken baby syndrome (SBS). Chavala and coworkers used the same system to image sedated or non-sedated premature infants with ROP. The system provides the maximum area of SD-OCT imaging within zone I and can capture images in posterior zone II if the handheld probe is tilted. In 2013, Lee and coworkers extended the application of this imaging system to infants with nystagmus. To optimize hand-held SD-OCT imaging in infants, Maldonado and coworkers created an age-dependent model to estimate the axial length of the infant eye in order to extrapolate lateral measurements.

3.4.3. Heidelberg Spectralis

Vinekar and coworkers described in 2010 a technique for converting the table-top chin-rest Heidelberg Spectralis SD-OCT system into a hand-held device for imaging supine non-
The Spectralis SLO camera head is disassembled from its mount by removing the screw that secures it at the bottom of the arc guide. Standing at the head end of the infant, the technician positions the freed camera head downwards in close alignment with the infant’s eye. Captured OCT images are laterally inverted since the infant’s eye is close to the camera head and the technician stands at the cranial end of the infant.

3.5. Optical coherence tomography angiography

OCT angiography (OCT-A) is a functional extension of OCT that provides information on the microvasculature of the retina without the need for intravascular dyes. It uses laser light reflectance from the surface of moving erythrocytes to identify blood vessels in different segments of the retina. In 2016 Vinekar and coworkers obtained OCT-A images in a non-anesthetized infant using the table-top Avanti RTVue XR® imaging device (Optovue Inc, Fremont, CA). Image acquisition was performed with the infant swaddled and held upright on the chin-rest of the device. In 2017 Chen and coworkers used a microscope-integrated scanning device to obtain OCT-A images in anesthetized infants in the operating room. The OCT-A scanner, containing a 100-kHz swept-source laser with a center wavelength of 1050 nm, was capable of capturing a 30° field of view of the retina. Campbell and coworkers have since developed a prototype hand-held non-contact OCT-A system to image non-anesthetized supine infants. This system utilizes a 100-kHz laser with a lateral resolution of 17 μm and an axial resolution of 5 μm to capture up to 40° of the infant retina in a single OCT-A image. More recently, Kothari et al demonstrated the feasibility of using a non-contact, arm-mounted SD-OCT with integrated OCT-A software (Spectralis HRA+OCT with Flex module, Heidelberg Engineering, Heidelberg, Germany) to image supine infants in the neonatal unit or operating room with or without sedation. En face OCT-A images of the superficial and deep parafoveal retinal microvasculature can be generated using the automated segmentation of retinal layers by the Spectralis software after imaging.

4. Foveal development in infants

SD-OCT has provided insight into the development of the different layers of the normal and diseased infant fovea. Maldonado and coworkers reported on their SD-OCT investigation of
foveal development from 31 weeks postpartum age up to adulthood, describing, with segmentation and 3D mapping techniques, the dual processes of centripetal displacement of the outer retinal structures toward the fovea and a centrifugal displacement of the inner retinal layers away from the fovea.\(^5\) Hendrickson and coworkers confirmed these developmental patterns with histological studies on human foveal development, which showed progressive thickening of the foveal outer nuclear layer after birth as cone packing and elongation occurred.\(^6\) In 2012, Vajzovic and coworkers directly correlated SD-OCT images with histological specimens of the prenatal and postnatal human fovea.\(^{130}\) They demonstrated a progressive increase in neurosensory retinal thickness from 30 weeks postmenstrual age to 16 years of age and maturation of photoreceptors over several years after birth. Vajzovic and coworkers later compared photoreceptor development from SD-OCT imaging in very preterm infants, born at less than 32 weeks gestational age, with those of term infants.\(^{129}\) They found that the ellipsoid zone (EZ) developed in the foveal center in only 14% of very preterm infants, compared to 47% of term infants. For those infants without an EZ at the fovea, there was a greater mean distance of the visible EZ to the foveal center in very preterm infants versus term infants. The study concluded that very preterm infants have delayed photoreceptor inner and outer segment development when compared to term infants, which could contribute to poor visual acuity in children with a history of prematurity. In a cross-sectional quantitative comparative study of 43 children, aged 6-8 years and born prematurely without retinopathy treatment (20 full-term controls), SD-OCT and OCT-A imaging of the fovea and parafovea showed a significantly higher central foveal thickness, inner retinal thickness, outer retinal thickness, parafoveal nasal retinal thickness, superficial and deep capillary plexus vessel densities compared with full-term controls.\(^{32}\) The clinical significance of these structural and vascular characteristics in the fovea and parafovea of untreated prematurely-born children is yet to be determined. In 2015, Lee and coworkers demonstrated the developmental time course and trajectories for each retinal layer at the fovea in full term infants using SD-OCT.\(^{74}\) The reported features pertinent to foveal development are as follows: there is a logarithmic increase in central foveal thickness from birth until 48.6 months postmenstrual age; regression of inner retinal layers from the fovea is complete by 17.5 months postmenstrual age; the outer retinal layers at the fovea reach maturity by 75 months postmenstrual age. In a cohort of ten infants and young children with genetically confirmed achromatopsia, Lee and coworkers used hand-held SD-
OCT to show that all retinal layers at the fovea develop at a reduced rate and magnitude in comparison with controls. Lee and coworkers later demonstrated with the same method that inner retinal layer migration from the fovea is delayed and arrested prematurely in infants and young children with a diagnosis of albinism.

5. Retinal imaging in retinal vascular diseases

5.1. Retinopathy of prematurity

ROP is a vascular disease of the premature retina that results in abnormal blood vessel formation at the boundary of the vascularized and avascular peripheral retina. It is classified based on the zone or location, stage or severity (Fig. 3 and Fig. 4), extent of disease described by clock hour(s), and vascular abnormalities in the posterior pole (plus disease, pre-plus disease, aggressive posterior ROP). Multimodal retinal imaging is useful for the evaluation and management of ROP.

5.1.1. Ultrasonography

5.1.1.1. B-scan ultrasonography

De Juan and coworkers reviewed the ultrasonographic appearance of 54 eyes with advanced ROP in 1988. They demonstrated the value of ultrasonography in evaluating the configuration of retinal detachments and detecting subretinal and choroidal hemorrhage in eyes with advanced ROP. In eyes with stage 5 ROP, Jabbour and coworkers found preoperative ultrasonographic findings correlated well with surgical findings. In 2004, Jokl and colleagues reported on the use of 10-MHz B-scan ultrasonography for the detection of ROP stages in 34 eyes of 18 infants. Findings on ultrasonography were in agreement with those on clinical ophthalmoscopy in 24 eyes. In one eye that was underdiagnosed, a stage 4a ROP was misclassified as stage 2 ROP. The same authors have since compared 20-MHz B-scan ultrasonography with clinical ophthalmoscopy in the staging of ROP. They found that 20-MHz B-scan ultrasonography was able to offer a sensitivity of 72% and a specificity of 95% for the detection of all stages of ROP.

5.1.1.2. Ultrasound biomicroscopy
In 2001, Brent and coworkers imaged two infants with ROP using ultrasound biomicroscopy (UBM). In one infant with stage II ROP, UBM demonstrated the stage II ridge on the retina posterior to the ora serrata. In another infant with stage III ROP, UBM showed a neovascular frond in the retina, present nasally in zone II. The authors concluded that UBM may be useful for screening ROP when the posterior segment is difficult to visualize with other optical methods. UBM is not used for standard ROP screening.

5.1.2. Color fundus photography
5.1.2.1. Telemedicine
Indirect ophthalmoscopy, with scleral depression as required, is the gold standard method for the detection of ROP. Screening for ROP by this technique is difficult, as it requires an experienced ophthalmologist, and adequate ophthalmic expertise is often limited to larger academic centers worldwide. In addition, there are a limited number of ophthalmologists trained and willing to provide screening for infants at risk of developing ROP because of concerns regarding medicolegal liability, poor reimbursement, lack of cover for physicians' time and expertise, compensation for time away from the office, and the requirement of constantly being available for diagnosis and treatment. One strategy for improving the accessibility and delivery of ROP care is ‘store and forward’ telemedicine, which is a technology where medical data and images are captured and transmitted to a storage system for subsequent retrieval and interpretation by a remote expert. A number of studies have evaluated the detection of moderate and severe ROP using wide-angle digital photography. In 2003, Ells and colleagues showed that remote interpretation of wide-angle digital color fundus photographs by a single masked reader had a sensitivity of 100% and a specificity of 96% in detecting referral-warranted ROP. In 2006 Chiang et al examined the accuracy and reliability of telemedical ROP diagnosis by three image readers based on wide-angle images captured by an experienced ophthalmic photographer. They showed that masked interpretation of wide-angle images by multiple image readers resulted in a sensitivity of 85% or greater, and a specificity of 96% or greater for detecting ROP requiring treatment. For detection of type 2 prethreshold ROP, the image readers had a sensitivity greater than 72% and specificity greater than 90%. Wu et al found that wide-field digital photography had a sensitivity of 100% and a specificity of 97% for the detection of prethreshold and threshold ROP compared with ophthalmoscopic diagnosis. In 2007
Chiang and coworkers examined the accuracy and reliability of telemedical ROP diagnosis by multiple image readers, based on wide-angle images captured by a trained neonatal nurse. For images taken from infants at 31 to 33 weeks postmenstrual age, the specificity for the diagnosis of mild or worse ROP was 91% and sensitivity was 100%. For images obtained from infants at 35 to 37 weeks postmenstrual age, the specificity for the diagnosis of type 2 prethreshold or worse ROP was 91% and the sensitivity was 100%. The specificity for the diagnosis of treatment requiring ROP was 89% and the sensitivity was 100%. The subsequent photographic screening for ROP study evaluated the utility of remote wide-field images as compared to dilated ophthalmoscopy to screen for ROP. Wide-field digital photography had a sensitivity of 92% and a specificity of 37% for the detection of clinically significant ROP, compared with ophthalmoscopic diagnosis. In 2014, Quinn and coworkers evaluated the validity of remote wide-field retinal image grading, by trained nonphysician imagers and readers, to detect referral-warranted ROP. When remote grading of images of one eye at a single session was compared with ophthalmoscopic findings, the specificity for the detection of referral-warranted ROP was 90.1% and the sensitivity was 81.9%. When both eyes were considered, the specificity was 87%, and the sensitivity was 90%.

5.1.2.2. Quantitative image analysis for ‘plus disease’

‘Plus disease’, characterized by retinal dilation and tortuosity, is the primary criterion for laser treatment in ROP. The minimum level of vascular abnormality required for plus disease was defined using a standard photograph, which was selected by expert consensus. The presence of plus disease is typically determined by an examiner during indirect ophthalmoscopy, but this assessment is highly subjective. Chiang and coworkers evaluated agreement among ROP experts for plus disease diagnosis in 2007, and showed that 23 ROP experts disagreed about the presence of plus disease for 27 of 34 wide-angle images (79%). To overcome the subjectivity of plus disease diagnosis, many studies have explored the use of automated techniques. Gelman and coworkers evaluated a semiautomated image analysis program called Retinal Image multiscale Analysis (RISA), which calculates quantitative values for diameter, integrated curvature, and tortuosity index for arteries and veins from wide-angle photos. Eyes with plus disease had vessels with significantly higher diameter, integrated curvature, and tortuosity index than those without plus disease. Rabinowitz and coworkers evaluated a semiautomated program called...
VesselMap© that measures diameters of arteries and veins on wide-angle images by creating brightness indexes perpendicular to vessel lengths. Average retinal vessel diameter measurements were shown to be significantly larger in infants who developed severe ROP requiring treatment, than in infants who developed no or less severe ROP. Johnson et al also used VesselMap to analyze images captured with the NIDEK NM200D device. A significant increase in retinal vein diameter with plus disease was observed compared to that without plus disease. Wallace et al developed a semiautomated image analysis software called ROPtool, which traces retinal blood vessels and measures their dilation and tortuosity. They reported a 78% specificity and 95% sensitivity for diagnosing tortuosity sufficient for plus disease compared with two expert readers. Wilson and coworkers developed a semiautomated program called Computer-Aided Image Analysis of the Retina (CAIAR), which measures vessel dilation and tortuosity based on model-fitting in a scale space framework. Compared to expert grading, CAIAR correlated moderately with tortuosity grades but less well with width grades. More recently, Brown and coworkers showed that a fully automated system using a deep convolutional neural network achieved a sensitivity of 93% and a specificity of 94% for the diagnosis of plus disease from retinal color fundus photographs.

5.1.3. Fluorescein angiography

In 1971 Cantolino and coworkers presented the feasibility of fluorescein angiographic imaging of the peripheral vasculature in nine infants with acute retrolental fibroplasia. The authors noted the presence of changes seen on FFA that were not visible with indirect ophthalmoscopy. Images were obtained using a Zeiss fundus camera, but due to limitations in obtaining angiograms in infants with this device, only a few good examples of FFA of ROP were reported for many subsequent years. Recent refinements in photographic instrumentation have made it possible to obtain high quality FFA in infants with ROP (Fig. 5). Ng and coworkers demonstrated in 2006 that clear wide-angle angiograms can be obtained as part of ROP screening using the fluorescein angiographic RetCam digital system. In 2011 Lepore and coworkers provided a FFA atlas of the vascular abnormalities associated with severe ROP. The major fluorescein angiographic findings reported with the RetCam imaging device were: (1) leakage from neovascular tissue at the vascular-avascular junction, (2) arteriovenous shunting at the vascular-avascular junction, (3) capillary tuft formations...
just beyond the vascular-avascular junction, (4) focal dilatation of capillaries, (5) rosary-bead-like hyperfluorescent lesions inside retinal vessels, (6) hyperfluorescent “popcorn-like” lesions with well-defined contours posterior to the ridge, (7) absence of a foveal avascular zone and (8) periarteriolar loss of capillary bed at the vascularized retina and posterior pole. Yokoi and coworkers demonstrated with wide-angle fluorescein angiography the presence of a continuous demarcation line, composed of circumferential vessels and shunts at the vascular-avascular junction, and extensive capillary bed loss throughout the vascularized posterior retina in infants with aggressive posterior ROP.  

The role of FFA in the diagnosis and management of ROP remains unclear. Klufas and coworkers reported a significant increase in sensitivity for the diagnosis of stage 3 ROP or worse disease when wide-field FFA was used in addition to CFP. Studies have utilized wide-field FFA to evaluate retinal vascular morphologic features in eyes receiving intravitreal bevacizumab (Avastin®, Genentech, San Francisco, CA) for zone I and posterior zone II ROP. Fung and coworkers demonstrated the usefulness of ultrawidefield FFA for guiding laser treatment to areas of peripheral avascular retina in infants with stage 3 ROP.  

5.1.4. Indocyanine green angiography  
In 2017, Patel and coworkers presented the feasibility of ultra-widefield indocyanine green (ICG) angiographic imaging of the peripheral vasculature in five infants with active type I ROP. Peripheral attenuation of the choroidal circulation corresponded to regions of avascularity seen on clinical examination and FFA.  

5.1.5. Optical coherence tomography  
Chavala and coworkers evaluated the SD-OCT findings in five eyes of three severely premature infants with advanced ROP. Posterior retinal pathologic findings such as preretinal structures, retinoschisis and macular retinal detachment (RD) were revealed with SD-OCT that were not detected clinically. The nature of the preretinal structures was not elucidated, but the authors postulated they may represent abnormal vasculogenesis or incomplete regression of the hyaloid. In a study of 228 SD-OCT imaging sessions from 38 infants undergoing ROP screening, Lee and coworkers found the presence of an epiretinal membrane (ERM) in 32%, and macular cystoid structures or schisis in 39% of imaging
sessions. Neither of these findings were clinically evident in any of the infants during indirect ophthalmoscopy. Clinical features regarding the zone and stage of ROP, and the presence of pre-plus or plus disease were not detected in infants during SD-OCT imaging. Chen and coworkers have since visualized retinal neurovascular microstructures at the vascular-avascular junction during different stages of ROP. A prominent inner retinal ridge was evident with SD-OCT for stage 2 ROP. In stage 3 ROP there was significant inner retinal thickening and preretinal neovascular tissue was present at the vascular-avascular junction (Fig. 6).

In 2012, Maldonado and coworkers utilized SD-OCT to detect subclinical cystoid macular edema (CME) in 50% of premature infants. They reported that, while there was no correlation of CME with stage of ROP, markers of CME severity such as central foveal thickness, the foveal-to-parafoveal thickness ratio, and the thickness of the inner retinal layers were greater in eyes that required laser treatment or that developed plus disease or ROP stage 3. In 2015, Rothman and coworkers evaluated the association of CME and neurodevelopmental outcomes in very preterm infants at 18 to 24 months corrected age. SD-OCT imaging was performed during routine ROP examinations and Bayley Scales were performed at 18 to 24 months corrected age to assess neurodevelopment. The results showed that infants with CME had poorer language and motor skills as well as lower cognitive scores at 18 to 24 months corrected age. Vinekar and coworkers reported reduced visual acuity as early as three months corrected age in infants with CME.

The presence of foveal detachment in ROP, which can be detected using SD-OCT, is important in decision-making and for predicting visual outcomes. In 2006 Patel and coworkers described the use of OCT in an infant with active progressive stage 4a ROP despite laser photocoagulation. They demonstrated how OCT changed the staging of ROP from 4a to 4b, and suggested that OCT could help guide optimal timing of lens-sparing vitrectomy when there is evidence of progression despite full laser photocoagulation. Similarly, Chavala and coworkers described an infant who appeared to have stage 4a ROP on indirect ophthalmoscopy but was found to have stage 4b ROP on SD-OCT imaging. Muni and colleagues described a case series of three infants with progression of their ROP despite laser photocoagulation. In one case, presumed retinoschisis was noted in the region just
posterior to the temporal ridge on SD-OCT, which was not visible on clinical examination. This OCT finding helped guide the investigator’s decision to proceed with lens-sparing vitrectomy.  

In 2014, Maldonado and coworkers analyzed vascular and perivascular abnormalities on SD-OCT in eyes with ROP, and proposed a Vascular Abnormality Score by OCT (VASO) to quantify abnormalities graded on SD-OCT such as hyporeflective vessels, vessel elevation, perivascular spaces, and scalloping of retinal layers. The authors found a significantly higher VASO score in infants with plus disease.

5.1.6. Optical coherence tomography angiography
Experience with OCT-A in ROP is limited. In one case report, OCT-A was used to detect and monitor regression of a neovascular complex in an infant with aggressive posterior ROP. Campbell et al obtained OCT-A in four infants with various stages of ROP. In one infant with type I ROP requiring surgery for a retinal detachment (RD), OCT-A demonstrated attenuated retinal flow in regions of previous laser treatment, absence of flow in the preretinal membranes and loss of the choriocapillaris with sparing of the larger choroidal vessels. Recently, Kothari and coworkers reported on the effectiveness of OCT-A for studying the foveal avascular zone area in seven infants with treated ROP.

5.2. Coats disease

Coats disease is an idiopathic condition characterized by vascular telangiectasia, aneurysmal retinal vessels, and capillary microaneurysms with subretinal and intraretinal exudation and fluid. Ancillary imaging can be useful when the diagnosis of Coats disease is suspected.

5.2.1. Ultrasonography
B-scan ultrasonography can be used in infants to differentiate between Coats disease and other clinical entities, most notably retinoblastoma. In the early stages of Coats disease, ultrasonographic findings are non-specific, showing areas of RD with or without subretinal opacities. In advanced stages, the most common abnormal ultrasonographic findings are a
closed funnel RD with looping of the peripheral retina, poor retinal mobility, and low to medium reflective subretinal opacities.²

5.2.2. Fluorescein angiography

FFA is useful for documenting the findings in Coats disease. Blair and coworkers reported the FFA findings in the fellow eye of 17 patients with unilateral Coats disease.⁷ In one infant, subtle telangiectatic vessels and microaneurysms, not detected clinically, were identified with wide-field FFA in the fellow eye. In a study by Jung et al, wide-angle FFA of the fellow eye of a 1-year-old boy with unilateral Coats disease demonstrated far peripheral avascularity and adjacent telangiectatic vasculature, that was not visible with indirect ophthalmoscopy.⁶⁴

5.3. Familial exudative vitreoretinopathy

Familial exudative vitreoretinopathy (FEVR) is a rare heritable disorder of retinal vascular development often associated with subretinal exudation, macular and vascular dragging, and tractional RD (Fig. 7).²⁸

5.3.1. Fluorescein angiography

Kashani and coworkers described the angiographic findings of FEVR in infants and young children using the wide-field RetCam digital imaging system.⁶⁵ The major findings described with the wide-field RetCam digital imaging system were: (1) arterial tortuosity adjacent to the optic disc and in the peripheral retina, (2) bulbous vascular endings or telangiectasias in the macular or peripheral retina, (3) supernumerary vascular branching at the vascular-avascular junction, (4) diffuse or segmental delayed or absent choroidal perfusion, (5) venous-venous shunting in the far peripheral retina, and (6) aberrant circumferential vessels in the far peripheral retina that travels parallel to the ora serrata.⁶⁵ Fung and coworkers utilized ultrawidefield FFA to demonstrate peripheral capillary non-perfusion and subclinical neovascularization in a 3-month-old infant with FEVR.⁴⁴

5.3.2. Optical coherence tomography
Day and coworkers demonstrated the presence of preretinal and intraretinal exudates in a 6-month-old infant with FEVR using a hand-held SD-OCT device. Lee and coworkers evaluated SD-OCT images of 26 eyes from 16 infants and young children with FEVR. They identified a broad spectrum of features: vitreopapillary traction, vitreomacular traction, prepapillary membrane, premacular or preretinal exudates, neurosensory retinal displacement, retinal elevation along the vasculature, focal vitreous condensation, and membrane-like posterior hyaloid thickening.

5.4. Incontinentia pigmenti

Incontinentia pigmenti (IP) is a rare X-linked dominant disease with ocular, neurological, dermatologic, and dental abnormalities. Ancillary imaging can help identify the area and extent of retinal ischemia with or without neovascularization (Fig. 8).

5.4.1. Fluorescein angiography

Goldberg reported on the presence of an irregularly enlarged or distorted foveal avascular zone in nine eyes of nine infants with IP on FFA. Shaikh and coworkers evaluated the peripheral retinal vasculature in a 5-month-old infant with IP. Using widefield FFA, they showed areas of retinal neovascularization with late leakage posterior to an area of avascular peripheral retina that was not visible with dilated ophthalmoscopy. DeVetten and coworkers also demonstrated the ability of wide-angle FFA to detect fronds of neovascularization at the vascular-avascular junction in a 4-month-old infant with IP that was not visible on indirect ophthalmoscopy or wide-angle CFP. Patel et al reported the use of ultrawidefield oral FFA in a 3-month-old infant with IP in the office setting. High-resolution late phase images provided accurate identification of retinal neovascularization and avascular retinal zones that enabled targeted laser treatment.

5.4.2. Optical coherence tomography

Two studies have examined the SD-OCT findings of infants with IP. In the first study, Basilius and coworkers reported on the finding of inner retinal disorganization and thinning of the nasal fovea on SD-OCT in a 3-month-old infant with IP. Although the exact pathophysiology of inner retinal thinning in IP remains unknown, the authors postulated...
that the neural tissue changes in the retina are secondary to vascular events. The second study evaluated one eye of an infant with IP. They found inner and outer retinal thinning temporally in the parafoveal region, without RPE abnormalities or increased OCT signal into the choroid. They hypothesized that outer retinal thinning may result from defective development of deeper vessels during retinal vascularization.

5.5. Persistent Hyperplastic Primary Vitreous

Persistent hyperplastic primary vitreous (PHPV) is caused by failure of the primary vitreous to regress, leaving a stalk of fibrovascular tissue extending from the posterior lens capture to the optic nerve. Ancillary imaging is useful for differentiating PHPV from other entities, most notably retinoblastoma.

5.5.1. Ultrasonography
5.5.1.1. Prenatal ultrasonography
Esmer and coworkers reported on the prenatal findings in two fetuses with PHPV. In both fetuses, sonography revealed hyperechoic lenses and a thick hyperechoic band between the lenses and posterior walls of the eyes, representing cataracts and hyaloid artery persistence respectively. In one fetus, a conical structure, with the base at the lens and the apex towards the retina, was present suggesting the presence of a retinal non-attachment.

5.5.1.2. B-scan ultrasonography
B-scan ultrasonography can be used to narrow the differential when an infant has a lens opacity that precludes ophthalmoscopic examination of the posterior segment. The commonest abnormal ultrasonographic findings in PHPV are RD, microphthalmia, and vitreous membranes with a stalk going from the membrane to the optic nerve head.

6. Retinal imaging in Shaken Baby Syndrome (SBS)

SBS is a form of child abuse associated with significant mortality and morbidity in infants. Retinal imaging is important for evaluating and documenting the ocular sequelae of SBS.
6.1. Ultrasonography
The role of ophthalmic ultrasonography in SBS is limited. Riggs and coworkers have demonstrated in a series of 11 infants with SBS that emergency practitioner-performed ocular point-of-care ultrasonography can be used to diagnose traumatic retinoschisis.\textsuperscript{109}

6.2. Color fundus photography
The presence of retinal hemorrhages in the context of intracranial injuries in infants is highly predictive of SBS.\textsuperscript{140} Given the medicolegal implications of making a diagnosis of SBS, accurate documentation of retinal hemorrhages is imperative. Conventionally, retinal hemorrhages are documented by freehand drawings. However, such drawings may not accurately reflect the severity and detail of pathological retinal features. Contact wide and non-contact ultra-wide field digital imaging provides high-quality CFP which can objectively document the number and severity of retinal hemorrhages (Fig. 9).\textsuperscript{89,142} CFPs also enable the sequelae of SBS, such as perimacular retinal folds and traumatic macular retinoschisis, to be documented to determine the timing and necessity of any intervention.

6.3. Fluorescein angiography
Caputo and coworkers reported on the complication of retinal neovascularization with tractional RD in two 4-month-old infants with a history of SBS.\textsuperscript{16} FFA was not used to document or observe areas of retinal ischemia in this study. The authors postulated that retinal ischemia plays a role in the pathogenesis of these lesions and hypothesized that vigorous shaking induces direct vitreous shearing of the capillary network, with subsequent retinal ischemia and late neovascularization.\textsuperscript{16} Goldenberg and coworkers evaluated the retinal vasculature of seven eyes of five full term infants with SBS using FFA.\textsuperscript{52} They showed that all eyes had marked areas of peripheral capillary non-perfusion and two eyes exhibited vascular shunting. None of the eyes developed neovascularization or a RD. The authors concluded that close observation of eyes with retinal ischemia for the development of neovascularization is warranted.\textsuperscript{52}

6.4. Optical coherence tomography
Sturm and coworkers evaluated morphological retinal changes in three infants with SBS using SD-OCT.\textsuperscript{127} The OCT images revealed extensive vitreoretinal traction, perimacular folds, and macular retinoschisis, which was not seen by indirect ophthalmoscopy. Scott and coworkers have demonstrated a double layer of ERM, with distortion of the underlying foveal architecture, in a 6-month-old infant with SBS using a hand-held SD-OCT device.\textsuperscript{117} Seider and coworkers detected a macular pseudohole with SD-OCT in a 4-month-old girl with SBS.\textsuperscript{118}

7. Retinal imaging in nystagmus

Lee and coworkers demonstrated that foveal morphology can be reliably assessed in infants and young children with infantile nystagmus using a hand-held SD-OCT device.\textsuperscript{76,77} They suggested that identification of foveal abnormalities such as typical and atypical foveal hypoplasia on SD-OCT can prioritize further investigations, facilitating a more timely and cost-effective diagnosis in infants and young children with infantile nystagmus.\textsuperscript{76} Rufai and coworkers, in a longitudinal study, demonstrated that structural grading of foveal hypoplasia in infants and young children with infantile nystagmus could predict future visual acuity.\textsuperscript{113}

8. Retinal imaging in retinoblastoma

Retinoblastoma is the most common intraocular malignancy in the pediatric population.\textsuperscript{67} Ancillary imaging is helpful for the evaluation and management of infants with this condition.\textsuperscript{15,53,66,111,115,121,126}

8.1. Ultrasonography

B-scan ultrasonography is used in infants with retinoblastoma to demonstrate the size and presence of a hyperechoic calcified intraocular mass with or without a secondary retinal detachment.\textsuperscript{126}

8.2. Fluorescein angiography
In 1982, Shields and coworkers evaluated the retinovascular findings on FFA in 31 children with retinoblastoma. The authors reported that FFA was valuable in visualizing the following: (1) confinement of a small tumor to the sensory retina, (2) presence of vitreous seeding, (3) residual viable retinoblastomas in a previously treated lesion or scar, and (4) very early retinoblastomas that are not well appreciated with ophthalmoscopy alone. Later Kim et al described the FFA findings of group D and E retinoblastomas in a retrospective review of 100 eyes of 87 infants and young children. Pertinent findings included: (1) identification of subclinical iris neovascularization, (2) large retinal vessel dilatation and tortuosity, (3) small retinal vessel abnormalities such as telangiectasia, arteriovenous shunts, microaneurysms, and intraretinal microvascular abnormalities (4) retinal or tumor non-perfusion, and (5) retinal venous leakage in eyes with subretinal fluid.

8.3. Optical coherence tomography

Rootman and coworkers evaluated the utility of hand-held SD-OCT in detecting very small tumors, monitoring treatment response, and identifying edge recurrence in anesthetized infants with retinoblastoma. Cao and coworkers utilized the same device to determine foveal morphology before and after therapy in infants and young children with macular retinoblastoma, providing an estimation of visual potential. Saktanasate and coworkers reported on the ability of SD-OCT to detect a tiny regressed retinoblastoma which was not visible in CFP or FFA in a 2-month-old infant. Gonzalez-Montpetit and coworkers further demonstrated subclinical recurrence within a previous regression scar with SD-OCT in a 2-month-old infant with retinoblastoma.

9. Imaging in retinal hamartomas

Chidambara and coworkers have described the angiographic and OCT findings of an infant with multiple retinal hamartomas. Dilated ophthalmoscopy revealed two retinal lesions in the right eye and one in the left eye. SD-OCT demonstrated that all retinal lesions involved the inner retinal layers and had a smooth fusiform appearance. Only one lesion was detected on FFA and it showed diffuse early hyperfluorescence with increasing intensity in the late phase.
10. Retinal imaging in X-linked retinoschisis

X-linked retinoschisis is a hereditary retinal degenerative disease caused by mutations in the RS1 gene at XP22.1.\textsuperscript{123} Ling and coworkers investigated the microanatomic retinal changes in infants and young children with juvenile X-linked retinoschisis using a hand-held SD-OCT device.\textsuperscript{80} A difference in the location of schisis between the foveal-parafoveal and the extrafoveal region was reported, in addition to ellipsoid zone disruption, vitreous traction, and RD in a number of eyes imaged.\textsuperscript{80}

11. Retinal imaging in congenital Zika syndrome

Congenital Zika syndrome (CZS) is a group of congenital malformations and disabilities associated with infection with the Zika virus.\textsuperscript{101} Freitas and coworkers reported in 2016 the ocular findings in 20 eyes of ten infants with CZS.\textsuperscript{34} The main ocular findings identified with indirect ophthalmoscopy and CFP, were focal pigment mottling and circumscribed areas of chorioretinal atrophy with or without the presence of a surrounding hyperpigmented halo. Ventura and coworkers have since evaluated the SD-OCT macular findings in nine eyes of eight infants with CZS\textsuperscript{131}, and reported that all eyes had discontinuation of the ellipsoid zone and hyperreflectivity underlying the atrophic retinal pigment epithelium. Less common findings were chorioretinal thinning and colobomatous-like excavation of the neuroretina, RPE, and choroid.\textsuperscript{131}

12. Conclusion

Technological advances and refined instrumentation have simplified retinal image acquisition in infants. The advent of wide-field and ultrawidefield digital imaging has been fundamental to the diagnosis, documentation, and management of a wide range of infant retinal diseases. The development of a hand-held SD-OCT imaging device for clinical use in the pediatric population has increased our understanding of normal anatomy, development, and pathologic events in infant retinal diseases. Future research will likely continue to modify newer imaging tools such as OCT-A for use in infants, and incorporate deep neural
networks into imaging devices or telemedicine systems to improve the automated detection of infant retinal diseases.

13. Method of literature search
The authors conducted a search of MEDLINE with PubMed. Several articles published prior to 1996 have been included to provide a historical overview, but the review is predominantly based on articles published in the past two decades. Search terms were: retinal imaging in infants, retinal imaging in pediatrics, optical coherence tomography in infants, optical coherence tomography in pediatrics, optical coherence tomography angiography in infants, optical coherence tomography angiography in pediatrics, widefield retinal imaging in infants, widefield retinal imaging in pediatrics, ultra-widefield retinal imaging in infants and ultra-widefield retinal imaging in pediatrics. The authors included original articles, review articles, and case reports that yielded new aspects of retinal imaging in infants with different imaging modalities. Translation of non-English literature was not performed for this review. Further articles were retrieved from the reference list of the articles found with the previously described method.

Disclosure
The authors have no other financial or personal relationships with other people or organizations that could potentially and inappropriately influence their work.

Conflict of Interest
All authors have no commercial or similar relationships to products or companies mentioned in or related to the subject matter of the article being submitted.

All authors declare that there are no conflicts of interest and no financial interests.
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anaesthetized infants: utility demonstrated in aggressive posterior retinopathy of prematurity. Eye (Lond) 2010; 24: 379-382


Figure 1. A: Color fundus photography, centered on the optic nerve, of the left eye of an infant, illustrating the field of view capable with video indirect ophthalmoscopy. B: Color fundus photography, centered on the optic nerve, of the right eye of an infant, illustrating the field of view capable with the D-Eye optical device. (Image courtesy of Giulio Galiano). C: The RetinoScope optical device. (Reprinted from Patel et al\textsuperscript{100} with permission of Yannis Paulus). D: Color fundus photography, centered on the optic nerve, of the right eye of an infant, illustrating the field of view capable with the panoptic ophthalmoscope with iExaminer adapter. (Reprinted from Day et al with permission of John Wiley and Sons – Books). E: Color fundus photography, centered on the optic nerve, of the left eye of an infant, illustrating the field of view capable with the RetCam widefield digital imaging system. F: RetCam widefield imaging of an infant demonstrating contact of the portable probe with the infant eye during imaging. (Image courtesy of Hoag Levins). G: Color fundus photography, centered on the optic nerve, of the right eye of an infant, illustrating the field of view capable with the Optos ultra-widefield digital imaging system. H: Optos ultra-widefield imaging of an infant held horizontally up to the imaging system (Reprinted from Patel et al\textsuperscript{87} with permission of Elsevier Ltd). I: Image demonstrating the use of an Optos machine between humidicribs in the neonatal intensive care unit.
Figure 2. Modified Heidelberg Spectralis imaging system designed to image infants in the operating room. (Reprinted from Fung et al.\textsuperscript{44} with permission of Elsevier Ltd.)
Figure 3. Ultra-widefield pseudocolor fundus photography of the different stages of ROP. (Reprinted from Fung et al\textsuperscript{47} with permission of the Infant journal)

Figure 4. Wide-field color fundus photography of the different stages of ROP. (Reprinted from Fung et al\textsuperscript{47} with permission of the Infant journal)
Figure 5. Ultra-widefield fluorescein angiogram of the right (A) and left (B) eye of an infant with stage 3 zone 2 retinopathy of prematurity after laser treatment. Leakage from neovascular tissue (black arrowhead) and areas of capillary non-perfusion (white arrow) at the vascular-avascular junction are demonstrated in both eyes. In the left eye, a skip area absent of laser treatment (white arrowhead) is demonstrated. (Reprinted from Fung et al\textsuperscript{44} with permission from Elsevier Ltd)
Figure 6. SD-OCT image of an infant with stage 3 retinopathy of prematurity reveals hyperreflective neovascular tufts extending from the inner retinal surface at the vascular-avascular junction.

Figure 7. Ultra-widefield pseudocolor fundus photography of the right eye of an infant with familial exudative vitreoretinopathy showing fibrovascular proliferation with subretinal exudates in the temporal periphery.
Figure 8. Ultra-widefield fluorescein angiography of the left eye of an infant with incontinentia pigmenti demonstrating an area of non-perfusion in the temporal periphery (white arrow). (Reprinted from Fung et al44 with permission from Elsevier Ltd)
Figure 9. Wide-field color fundus photography of the right eye of an infant with shaken baby syndrome shows multi-layered retinal hemorrhages in the posterior pole and peripheral retina.
Table 1 – Comparison of digital imaging systems available for infants

<table>
<thead>
<tr>
<th>Imaging system</th>
<th>Maximum field of view</th>
<th>Contact or non-contact</th>
<th>Imaging capabilities</th>
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<tr>
<td>NIDEK NM200D</td>
<td>30°</td>
<td>Non-contact</td>
<td>Color fundus</td>
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<tr>
<td>Pictor</td>
<td>45°</td>
<td>Non-contact</td>
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<td>Vantage Plus LED digital indirect ophthalmoscope</td>
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<td>Color fundus</td>
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