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Optic Nerve Head Development in Healthy Infants and Children Using Handheld Spectral-Domain Optical Coherence Tomography

Aarti Patel, BSc, MBChB,[1] Ravi Purohit, MSc, BMedSci,[1] Helena Lee, PhD, FRCOphth,[2] Viral Sheth, BMedSci,[1] Gail Maconachie, BMedSci, PhD,[1] Eleni Papageorgiou, MSc, PhD,[3] Rebecca J. McLean, MSc, PhD,[1] Irene Gottlob, MD, FRCOphth,[1] Frank A. Proudlock, MSc, PhD[1]

Purpose: To determine feasibility of optic nerve head (ONH) imaging and to characterize ONH development in full-term infants without sedation using handheld spectral-domain optical coherence tomography (SD OCT).

Design: Prospective cross-sectional study.

Participants: Three hundred fifty-two children aged between 1 day and 13 years.

Methods: All participants were imaged using handheld SD OCT without sedation during a single scan session. The percentage of successful scans was calculated. Interexaminer reproducibility and differences between right and left eyes were assessed using intraclass correlation coefficients (ICCs). Images were analyzed using ImageJ software. The developmental trajectories over time for ONH parameters were calculated using fractional polynomial modelling.

Main Outcome Measures: Disc and cup diameter (expressed as distance in micrometers and visual angle in degrees), cup depth, Bruch's membrane opening–minimum rim width (BMO-MRW), retinal thickness, and retinal nerve fiber layer (RNFL; 1700 μm and 6° from the disc center).

Results: On average, 70% of participants were imaged successfully. Interexaminer reliability was excellent (ICC, >0.89) for diametric and retinal thickness parameters. Right and left eyes were similar for diametric measurements (ICC, >0.79), but more variable for nasal BMO-MRW, RNFL, and retinal thickness. The mean disc and cup diameter increase by 30% and 40%, respectively, between birth and 13 years of age when expressed as a distance measure, but remained constant (at 5°–5.5° and 2°, respectively) when expressed as a visual angle with reference to the eye nodal point. The peripapillary temporal RNFL demonstrated a marked initial decrease of nearly 35% between birth and approximately 18 months of age. This was followed by a slow increase up to 12 years of age when measured at 1700 μm from the disc center, although there was little change when measured at 6° from the disc center.

Conclusions: We demonstrated feasibility of handheld SD OCT imaging of the ONH in full-term infants and children without anaesthesia or sedation. This is the first in vivo handheld SD OCT study to describe the development of ONH parameters during the critical early years of visual maturation. Our results provide a normative database for use in routine practice and further studies of ONH pathologic features. *Ophthalmology 2016;123:2147-2157 © 2016 by the American Academy of Ophthalmology. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/).*

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The appearance of the optic nerve head (ONH) can indicate both ocular and central nervous tissue pathologic features. Although the ONH retains some plasticity during the early years of life, damage to the ONH can result from conditions such as pediatric glaucoma, one of the leading causes of childhood blindness worldwide.[1,2] Other conditions, including central nervous system tumors, craniofacial syndromes, neuropathies, and congenital anomalies, also can involve the visual pathway including the optic nerve and can affect vision.[3–5]

Clinical evaluation of the ONH is a combination of functional assessment (for example, visual field and color vision testing) and anatomic assessment (for example, direct visualization and imaging). In young children, many of these tests are not possible because of limited cooperation, communication, and fixation. Routine examination of the ONH often is restricted to funduscopy, providing a quick, noninvasive subjective assessment of ONH appearance. Until recently, fundus photography was the only method for quantifying the ONH of children objectively.

Optical coherence tomography (OCT), first described in 1991, has revolutionized imaging and the subsequent clinical management of many ocular conditions in adults.[6] Current OCT machines with a theoretical axial resolution of a few micrometers can take a so-called optical biopsy

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of retinal structures within seconds in vivo and without direct ocular contact.

Optical coherence tomography studies of older children who are able to position at a head chin rest and maintain fixation have provided important information about ONH parameters in childhood. For example, the average retinal nerve fiber layer (RNFL) thickness measured with spectral-domain (SD) OCT in children between 5 and 18 years of age has been reported to be 102 to 113 μm, with only a small degree of change over this period.[7–11] Critically, these studies miss the early years, during which time cadaveric and histologic studies suggest that most maturation takes place.[12,13]

The recent advent of handheld ultra–high-resolution SD OCT has the potential to improve our understanding of ocular development and pediatric ophthalmic care, just as table-mounted OCT has accomplished for adult patients. Avery et al[14] demonstrated excellent intravisit and intervisit reliability of optic nerve RNFL analysis for 59 children younger than 13 years imaged with handheld SD OCT. All participants were sedated during imaging and had a diagnosis of optic nerve glioma, neurofibromatosis type 1, or both. Studies of premature infants and full-term neonates imaged with handheld SD OCT without sedation have reported increased cup diameter associated with prematurity and thinning of the RNFL at increased arc distance from disc center, consolidating earlier studies using fundus photography.[15,16]

The purpose of the current study was to create a clinically useful pathway for using the handheld SD OCT to assess ONH morphologic features of children in vivo. To achieve this, our aims were (1) to test the feasibility of handheld SD OCT for imaging the ONH in full-term children without sedation, (2) to estimate interexaminer reliability and intereye similarity of ONH measures in children, (3) to describe ONH development between birth and 13 years of age, and (4) to provide normative estimates with 95% confidence intervals for 13 age bands between birth and 13 years of age for ONH parameters that can be measured in a clinical setting for future studies of ocular development in children.

Methods

Participants

Three hundred fifty-two children up to 13 years of age born after 37 weeks' gestation and without prior neurologic or ophthalmic diagnoses were recruited to the study. Potential participants were all identified from the Leicestershire region within the National Health Service representing a varied socioeconomic background. All participants underwent ophthalmic examination including fundus examination and orthoptic assessment on the same day. Retinoscopy was performed after dilation with cyclopentolate 0.5% eye drops for younger participants. For older children who did not prefer to undergo dilation, uncycloplegic refraction was performed. Neonatal infants were examined in the delivery suite between 1 and 7 days after birth. Older babies and children were assessed during routine pediatric outpatient clinic appointments.

Participants were excluded if initial assessment revealed an ophthalmic abnormality or a spherical equivalent refractive error of more than ±3 diopters (D). Age-appropriate visual acuity assessments, including Keeler Acuity Cards (Windsor, Berkshire, UK) for preverbal children, Crowded LogMAR Kay Picture Tests (Tring, Hertfordshire, UK) for toddlers, and Snellen letters for older children, were performed before dilation. Participants unable to perform visual acuity assessment at recruitment were invited for repeat testing at a later date. Ten participants were excluded if initial or follow-up assessment demonstrated a visual acuity recording of less than the 99% confidence level for age.[17,18] Fifteen further participants did not return for repeat assessment and also were excluded. Five participants were excluded because of high refractive error, and 1 participant was excluded after review of medical notes found that the gestational age at birth was 36 weeks. Interexaminer reproducibility and intereye similarity were assessed for 30 participants in different age groups.

The study adhered to the tenets of the Declaration of Helsinki, and ethics committee approval was granted. Informed consent was obtained from all parents or guardians of participants, and older children also gave their assent to the study.

Handheld Spectral-Domain Optical Coherence Tomography Image Acquisition

A noncontact handheld SD OCT device (ENVISU C class 2300; Bioptigen, Inc., Research Triangle Park, NC; axial resolution, 3.3 μm; scan depth, 3.4 mm; 32 000 A-scans per second) was used to image the ONH of all participants without sedation. Pacifiers and visual fixation devices, including cartoons played on screens, toys, and books, were used to minimize movement of the child during imaging. The acquisition protocol used a 10×5-mm scanning window. If the ONH was not imaged successfully, a larger 10×10-mm scanning window was used. The 3-dimensional raster scan program for both scan sequences consisted of 100 B-scans and 500 A-scans per B-scan line. The short acquisition time (2.9 seconds) enabled operators to obtain images of the ONH with minimal disruption of image quality.

Image Analysis

Analysis was based primarily on a single B-scan through the deepest part of the optic cup to derive normative estimates for parameters that can be measured mainly in a clinical setting without the need for custom software (i.e., can be measured mainly using calipers). The B-scan image was randomized before analysis and was analyzed by 1 of 2 assessors (A.P. and R.P.) masked to the age of the participant to minimize bias. B-scan images were assessed and analyzed (Fig 1) using ImageJ software version 1.48 (available at: http://imagej.nih.gov/ij/ and provided in the public domain by the National Institutes of Health, Bethesda, MD).

The edges of the Bruch's membrane were identified manually by the examiner and were used to define the optic disc diameter. A semiautomated ImageJ software program flattened the image and identified the contour of the inner limiting membrane (ILM) using the ABSnake plugin, which was corrected manually where necessary. The neuroretinal rim was measured using Bruch's membrane opening–minimum rim width (BMO-MRW), defined as the shortest distance between the disc edge (termination of Bruch's membrane) and the ILM. The optic cup diameter was calculated at half-cup depth from the axial distance between the height of the nasal and temporal neuroretinal rims to the optic cup base (Fig 1A). Comparison measurements for optic cup diameter were obtained at a plane 200 μm anterior to the disc. The cup-to-disc ratio calculated using OCT defined measurements has been termed C/DOCT to distinguish from that derived from fundoscopy in previous studies (C/DFUND). The total retina and RNFL thicknesses were calculated at 1.7 mm distance laterally after adjusting for axial length, which was estimated from the age