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Imaging Infant Retinal Vasculature with OCT Angiography

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To date, visualization of the healthy infant perifoveal microvasculature has been limited mostly to histopathologic studies.¹ The advent of optical coherence tomography angiography (OCT-A) has enabled in vivo depth-resolved imaging of the retinal microvasculature and provided significant insights into the pathogenesis of many retinal vascular diseases.^{2,3} OCT-A brought into the operating room further allows for imaging of infants and young children in a supine position.^{4,5} However, prior studies have not distinguished the superficial and deep vascular complex in healthy, full-term infants. We report the depth-resolved visualization of retinal microvasculature in full-term infants 47 to 56 weeks postmenstrual age (PMA) using a portable OCT-A system while supine during examination under anesthesia. We show the images of the superficial and deep parafoveal retinal microvasculature in healthy full-term infants (PubMed search on March 11, 2018, terms “infant” AND “OCT angiography”), which are comparable to those in children aged 4 to 5 years.

The study was approved by the Duke University Health System institutional review board and adhered to the Health Insurance Portability and Accountability Act and all tenets of the Declaration of Helsinki. Parents or legal guardians gave written informed consent for the infants and children to participate in the research study. We imaged the macula of 3 full-term infants (47, 50, and 56 weeks PMA; 1 white male, 1 white female, 1 black female) and 3 children born full term (4, 4, and 5 years old; 1 white male, 1 biracial female, 1 white female) using a noncontact confocal scanning laser ophthalmoscope and spectral domain OCT camera head mounted on a portable arm integrated with OCT-A software (Spectralis

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HUMAN SUBJECTS: Human subjects were included in this study. The human ethics committees at the Duke University approved the study. All research adhered to the tenets of the Declaration of Helsinki. All participants provided informed consent.

No animal subjects were used in this study.

HRA+OCT with Flex module, Heidelberg Engineering, Heidelberg, Germany). All infants and children were imaged in the operating room while supine with both eyes dilated for clinically indicated examinations under anesthesia. For each patient, imaging was performed in 1 unaffected eye without retinal pathology (in the fellow affected eye: 2 infants had persistent fetal vasculature, 1 infant had a combined hamartoma of retina and retinal pigment epithelium, 2 children underwent strabismus surgery, and 1 child underwent surgery for traumatic cataract). An eyelid speculum was used, and frequent artificial tears were applied to maintain cornea clarity. We aligned the camera head without contacting the patient (Fig 1A) to capture OCT-A images of the macula. Images were acquired at 512 A-scans/B-scan and 512 B-scans/volume with scan sizes of $10^{\circ} \times 10^{\circ}$ and approximately 6 μm resolution.

En face OCT-A images of the superficial vascular complex (SVC) and deep vascular complex (DVC) were generated using the automatic segmentation of retinal layers by the Spectralis software after imaging (Fig 1B–G). A grader (STH) reviewed the automated segmentation for manual correction as necessary. The upper and lower segmented boundaries of the SVC were the internal limiting membrane and 17 μm above the bottom border of the internal plexiform layer, respectively. The DVC boundaries were from 17 μm above the bottom border of the inner plexiform layer to the bottom of the outer plexiform layer (Supplemental Fig S1, available at www.aaojournal.org). Projection artifact removal was applied to the en face OCT-A image of the DVC within the Spectralis software. To measure the size of the foveal avascular zone (FAZ) on OCT-A, a masked grader (HTN) used ImageJ (National Institutes of Health, Bethesda, MD) to manually trace and measure the FAZ for each eye. A custom MATLAB program (MathWorks, Natick, MA) and ImageJ were used to process the images and calculate the parafoveal vessel area density and vessel length density.

We successfully captured the retinal microvasculature of the superficial and deep vascular complexes in all 3 infants at 47 to 56 weeks PMA using the Spectralis with Flex module. The automatic segmentation of the retinal layers using the Spectralis software was accurate in segmenting B-scan images from infants and children. Manual correction was not needed, because the developed retinal layers in the infants facilitated the automated segmentation of the retina.

Comparison of the retinal vasculature in infants and young children showed both qualitative and quantitative similarity. The SVC and DVCOCT-A images of these full-term infants (Fig 1B–D) showed similar vascular patterns to those seen in young children 4 to 5 years of age (Fig 1E–G) and adults with healthy retinas.² The SVC and DVC of each eye appeared as distinct, organized meshwork with a circular vascular ring demarcating the boundary of the FAZ. Quantitative analysis of FAZ areas and vessel densities in the infant eyes were comparable to those of young children (Supplemental Table S1, available at www.aaojournal.org). Thus, similar to previous histologic reports,¹ our data suggest that the parafoveal microvasculature in both the SVC and DVC are formed by 47 weeks PMA (Fig 1B).

The feasibility of OCT-A imaging of supine infants with retinal pathologies has been demonstrated in research systems (handheld contact or microscope-mounted systems).^{4,5}

Our study adds to the armamentarium of neonatal retinal vascular imaging by depth-resolved visualization and quantification of the parafoveal vasculature, which demonstrated formation of the FAZ, SVC, and DVC in healthy term infants compared with young children. Limitations of this study include the small sample size that disallows for further statistical analysis and being able to image infants only under anesthesia. The next steps include imaging a wider range of ages in pediatric patients, establishment of normative measures of FAZ and parafoveal vessel length density in infants and children, and study of pathologic changes in infants with retinal vascular diseases.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations and Acronyms

DVC	deep vascular complex
FAZ	foveal avascular zone
OCT-A	OCT angiography
PMA	postmenstrual age
SVC	superficial vascular complex

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Figure 1.

Noncontact optical coherence tomography angiography (OCT-A) imaging was performed in supine pediatric patients during examination under anesthesia using the Spectralis (Heidelberg Engineering, Heidelberg, Germany) with Flex module (A). The microvascular pattern in the superficial and deep vascular complexes (SVC and DVC, respectively) of full-term infants (B, 47 weeks PMA male; C, 50 weeks PMA female; D, 56 weeks PMA female) were comparable to those of young children (E, 4-year-old male; F, 4-year-old female; G, 5-year-old female). DVC = deep vascular complex; PMA = post-menstrual age; SVC = superficial vascular complex.