Widefield Imaging in Pediatric Retinal Disease

Widefield imaging can detect peripheral pathology not typically seen with standard imaging, often before patients are symptomatic.

BY ANTONIO CAPONE JR, MD; ANKOOR SHAH, MD; ASHKAN ABBEY, MD; KIMBERLY DRENSER, MD, PHD; AND MICHAEL TRESE, MD

Digital imaging is at the at the core of a revolution that is improving the evaluation and management of retinal vascular pathologies. Ultrahigh-resolution optical coherence tomography (OCT), enhanced-depth OCT, dual-wavelength autofluorescence, retinal oximetry, retro-mode imaging, time-based autofluorescence, and multispectral imaging are a few of the cutting-edge imaging technologies likely to have an impact on patient care in the short- to intermediate-term future.

CURRENT TECHNOLOGY

Traditional photographic images of the fundus were limited to a 30° field of view. The notion of imaging beyond the 30° field was popularized by the ETDRS method of overlapping seven standard stereoscopic fields, which in aggregate provided a 75° field view of the fundus.[1] Up to 200° of the fundus is now imaged routinely with currently available retinal imaging technology (Figure 1).[2]

Over the past 10 years, we have increasingly integrated widefield imaging into the routine care of pediatric patients at our practice. Our workhorse widefield tools are the RetCam (Clarity Medical Systems) for infants and small children in the neonatal intensive care unit (Figure 2) and the OR; and the Optos (Optos plc) for children and adults in the office (Figure 3). The RetCam uses a contact camera handpiece and a fiberoptic light source, with digital image capture displayed on a computer monitor. Imaging in older children and adults is precluded by the limits on fundus illumination related to aging changes in the crystalline lens. The Optos uses confocal scanning laser ophthalmoscopy (SLO) and an elliptical mirror construct, and it requires neither contact with the ocular surface nor mydriasis.

The biggest impact of widefield imaging has been in the surveillance of retinopathy of prematurity (ROP). We demonstrated the utility of this approach in a clinical trial in 2001[3]; others have since replicated this work[4-7]; and the approach was further validated by the recent eROP study.[8] Our surveillance paradigm consists of weekly digital fundus imaging by a nurse practitioner, followed

Widefield Fundus Imaging

• ETDRS 7-standard fields – 35-mm stereoscopic color 30° fundus photographs	75°
• RetCam 120 with 13° lens	130°
• Heidelberg noncontact UWF module	130°
• Heidelberg Spectralis and HRA2 platform – Ocular Staurenghi 230 SLO contact lens	150°
• Optos 200Tx imaging system	200°

Figure 1. Widefield fundus imaging options with corresponding approximate field of view.

Figure 2. We routinely use the RetCam for imaging infants and small children in the neonatal intensive care unit.

Figure 3. The Optos 200Tx is a useful piece of equipment. In our office, we use it frequently in the office to image both children and adults.

by remote interpretation by a physician. The physician employs a smart software platform with montage capability that facilitates zone 1 determination (Figure 4) and quantification of the vascular changes typical of plus disease (Figure 5). This paradigm is consistent with the recently published Joint Technical Report: Telemedicine for Evaluation of Retinopathy of Prematurity.[9]

Advantages of a telemedicine approach include the potential to integrate the procedure into contemporary electronic health record (EHR) initiatives, to objectively assess the quality of evaluations, to increase the number of infants evaluated, to fortify the "ROP safety net" construct of disease surveillance, to improve parent and staff education about ROP, and to make more widely available the experience of ROP experts.[9]

UNIVERSAL SCREENING

We are also strong proponents of universal fundus imaging of neonates. Most recently, at the 2014 American Academy of Ophthalmology Annual Meeting, Moshfeghi and colleagues reported on a study of universal screening of all infants within 72 hours of birth to identify any eye disease as part of the GUEST (Global Universal Eye Screen Testing) program at Stanford University. GUEST was initiated in part as a result of a clinical study including more than 3500 newborns born in the Kunming Maternal and Child Healthcare Hospital, China, by Lihong Li, MD, and colleagues,[10] wherein a significant number of healthy newborns were found to have ocular diseases requiring

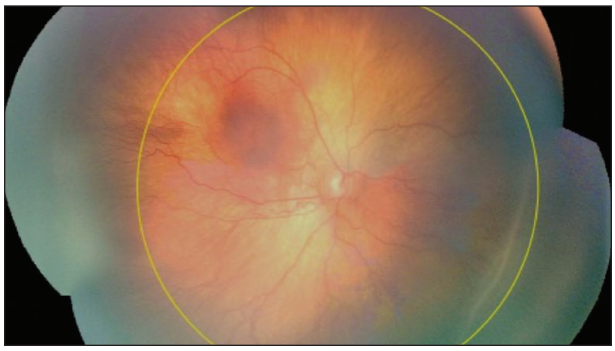

Figure 4. Depiction of zone 1 disease on the RetCam.

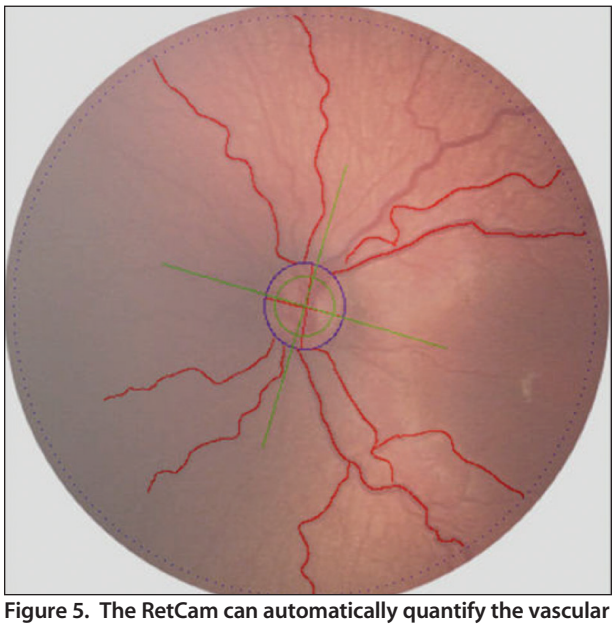

Figure 5. The RetCam can automatically quantify the vascular changes seen in typical plus disease.

medical intervention. Based on these results, Stanford University initiated its own program to determine whether early intervention can prevent vision loss by early identification and treatment of visually significant ocular disease.[11]

OFFICE MANAGEMENT OF PEDIATRIC RETINAL VASCULAR DISEASE

Widefield imaging is particularly useful for the identification of clinically inapparent pathology in pediatric retinal vascular pathologies such as familial exudative vitreoretinopathy,[12] Coats disease, Norrie disease, and persistent fetal vasculature syndrome (PFVS). Figure 6A depicts the normal appearing companion left eye in an infant with advanced PFVS in the right eye. Digital angiography reveals an irregular foveal structure (Figure 6B), and widefield images demonstrate a quietly avascular periphery (Figure 6C).

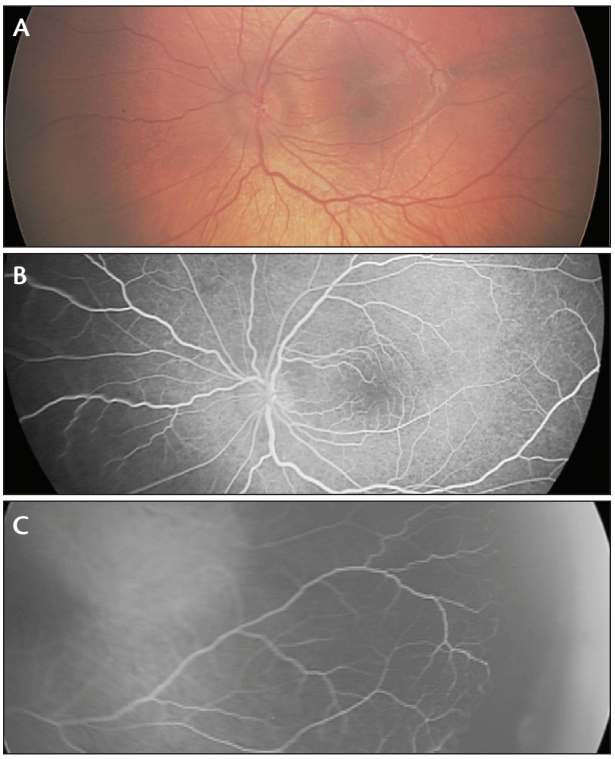

Figure 6. The left eye of a patient with diagnosed PFVS in the right eye (A). Digital angiography reveals foveal changes (B), and widefield imaging reveal an avascular periphery (C).

Widefield imaging is useful for screening asymptomatic family members of patients with familial exudative vitreoretinopathy (FEVR).[13] Figure 7A shows the right eye of an affected child, and Figure 7B depicts the silently affected asymptomatic mother. Interestingly, the father did not show findings typical of FEVR but had relatively minor peripheral vascular abnormalities, as shown in Figure 7C.

This last case underscores the challenge in trying to distinguish eyes with minimally abnormal variants of normal from those with disease but with subtle phenotypic expression. Any critical discussion of pathologic widefield imaging retinal vascular findings must include a comparison to patients who have "normal" retinal peripheries as a reference standard. To the best of our knowledge, published data on widefield imaging fundus angiography findings in "normal" patients (ie, patients lacking any identifiable retinal pathology) are lacking.

To better understand "normal" peripheral retinal changes, we evaluated peripheral vascular anatomy and the prevalence of peripheral fundus findings in patients with epiretinal membrane (ERM) and choroidal nevi using Optos. We also evaluated peripheral fundus features and angiographically apparent retinal vascular findings in a cohort of patients without known underlying conditions

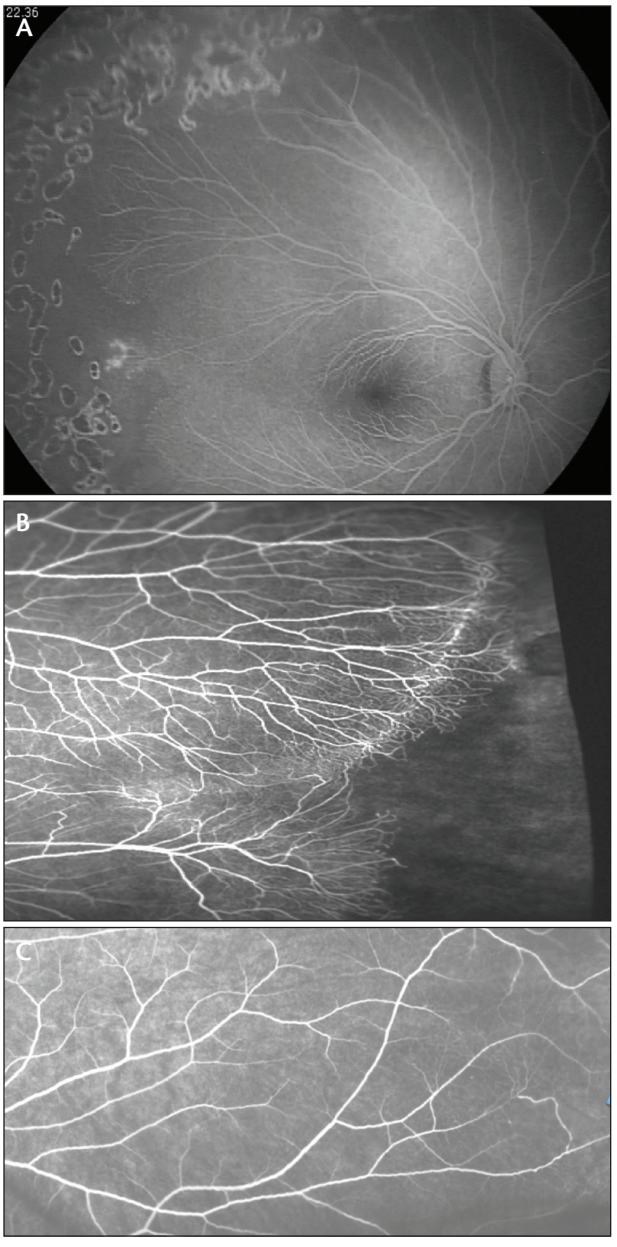

Figure 7. Right eye of a patient with FEVR on widefield imaging (A). The child's mother was asymptomatic (B) but examination of the father showed peripheral vascular abnormalities (C).

that are known to predispose to peripheral retinal vascular pathology. Our review of widefield imaging findings revealed a high prevalence of peripheral vascular anatomic variations in eyes expected to have "normal" peripheral retinal vasculature.[14] These findings provide a reference base for future studies addressing putative pathologic peripheral retinal angiographic findings.

(Continued on page 60)

(Continued from page 44)

CONCLUSION

Widefield imaging is a powerful tool for the management of pediatric retinal disease. Digital fundus imaging with remote interpretation has great utility in ROP surveillance. Widefield imaging for universal screening remains underutilized, given that the incidence of detected visually significant disease is considerably higher than that for other commonly screened conditions, such as hearing loss. Asymptomatic family members of patients with FEVR are effectively screened with this technology as well, and it has evolved to become a standard component in the care of patients with conditions such as Coats disease, FEVR, and others.

Widefield imaging allows detection of peripheral pathology not typically seen with standard imaging, often before patients are symptomatic. Characterization of the range of "normal" peripheral vascular findings apparent on color and angiographic widefield images can provide a reference base for future studies addressing putative pathologic peripheral retinal findings. ■

Corresponding author Antonio Capone Jr MD, is a partner at Associated Retinal Consultants, Royal Oak, Michigan, and a professor at William Beaumont Hospital-Oakland University School of Medicine, Auburn Hills, Michigan. Dr. Capone may be reached at +1-248-288-2280; fax: +1-248-288-5644; or acaponejr@yahoo.com.

The authors are affiliated with Associated Retinal Consultants, PC, Royal Oak, Michigan. Drs. Capone, Drenser, and Trese are shareholders in FocusROP, LLC.

1. Early Treatment Diabetic Retinopathy Study Research Group. Fundus photographic risk factors for progression of diabetic retinopathy. ETDRS report number 12. *Ophthalmology*. 1991;98:823-33.
2. Silva PS, Cavallerano JD, Sun JK, Noble J, Aiello LM, Aiello LP. Nonmydriatic ultrawide field retinal imaging compared with dilated standard 7-field 35-mm photography and retinal specialist examination for evaluation of diabetic retinopathy. *Am J Ophthalmol*. 2012;154(3):549-559.e2.
3. Photographic Screening for Retinopathy of Prematurity (Photo-ROP) Cooperative Group. The photographic screening for retinopathy of prematurity study (photo-ROP). Primary outcomes. *Retina*. 2008;28(suppl 3):S47-S54.
4. Ells AL, Holmes JM, Astle WF, et al. Telemedicine approach to screening for severe retinopathy of prematurity: a pilot study. *Ophthalmology*. 2003;110(11):2113-2117.
5. Chiang MF, Keenan JD, Starren J, et al. Accuracy and reliability of remote retinopathy of prematurity diagnosis. *Arch Ophthalmol.* 2006;124(3):322-327.
6. Wu C, Petersen RA, VanderVeen DK. RetCam imaging for retinopathy of prematurity screening. *J AAPOS*. 2006;10(2):107-111.
7. Silva RA, Murakami Y, Jain A, Gandhi J, Lad EM, Moshfeghi DM. Stanford University Network for Diagnosis of Retinopathy of Prematurity (SUNDROP): 18-month experience with telemedicine screening. *Graefes Arch Clin Exp Ophthalmol*. 2009;247(1):129-136.
8. Quinn GE, Ying GS, Daniel E, et al; e-ROP Cooperative Group. Validity of a telemedicine system for the evaluation of acute-phase retinopathy of prematurity. *JAMA Ophthalmol*. 2014;132(10):1178-1184.
9. Fierson WM, Capone A Jr; American Academy of Pediatrics Section on Ophthalmology, American Academy of Ophthalmology, and American Association of Certified Orthoptists. Telemedicine for evaluation of retinopathy of prematurity. *Pediatrics*. 2015;135(1):e238-54. .
10. Li LH, Li N, Zhao JY, et al. Findings of perinatal ocular examination performed on 3573, healthy full-term newborns. *Br J Ophthalmol*. 2013;97(5):588-591.
11. Moshfeghi D. Ophthalmic trends in neonatal imaging: how retinopathy of prematurity screenings have exposed the need for universal neonatal ocular imaging. *Neonatology Today*. 2013;8(9):9-10.
12. Kashani AH, Brown KT, Chang E, et al. Diversity of retinal vascular anomalies in patients with familial exudative vitreoretinopathy. *Ophthalmology*. 2014;121(11):2220-2227.
13. Kashani AH, Learned D, Nudleman E, et al. High prevalence of peripheral retinal vascular anomalies in family members of patients with familial exudative vitreoretinopathy. *Ophthalmology*. 2014;121(1):262-268.
14. Shah AR, Abbey AM, Yonekawa Y, et al. Ultra-widefield angiography in patients without peripheral disease: a study of normal peripheral findings. Submitted for publication.