Published in final edited form as:

J AAPOS. 2012 October ; 16(5): 411–412. doi:10.1016/j.jaapos.2012.08.001.

Image analysis for retinopathy of prematurity: Where are we headed?

Michael F. Chiang, MD

Departments of Ophthalmology & Medical Informatics and Clinical Epidemiology, Casey Eye Institute, Oregon Health & Science University, Portland, Oregon

Within several decades, remarkable progress has occurred in retinopathy of prematurity (ROP) management. One reason for improved clinical outcomes is that clear criteria for identifying disease that requires treatment have been established through the Cryotherapy for ROP (CRYO-ROP) and Early Treatment for ROP (ETROP) trials.^{1,2} These studies have shown that the most critical feature that determines whether to treat is the presence of plus disease, which is defined as arterial tortuosity and venous dilation in the posterior pole greater than or equal to that of a standard published photograph.^{1,3}

What are the challenges with clinical ROP diagnosis? Retinal vascular features such as tortuosity and dilation would appear to be subjective and qualitative, and significant variability in plus disease diagnosis among experts has been demonstrated in several studies.^{4–7} From this perspective, it is challenging that rigorous ROP research studies have found that the most important clinical findings may produce the most disagreement among clinicians. Computer-based image analysis has potential to address these limitations by providing objective and quantitative measures of retinal vessels.^{8–9} The most recent issues of the *Journal of AAPOS* include three papers examining the role of digital image analysis for ROP care^{10–12} that extend our understanding of these methods and their applications.

What is currently known in this area? Algorithms have been created for identification (“segmentation”) of retinal vessels, but they generally require manual correction by experts because of difficulty in distinguishing retinal versus choroidal vessels, difficulty distinguishing branching versus intersecting vessels, and other obstacles. Using these segmentation methods, several semiautomated, computer-based image analysis systems have been developed for ROP: Retinal Image multiScale Analysis (RISA), ROPtool, Computer-Aided Image Analysis of the Retina (CAIAR), and VesselMap.⁹ These systems have been used to quantify retinal vascular parameters such as arterial tortuosity and venous dilation, and pilot studies have demonstrated that they have the potential to identify plus disease with comparable or better accuracy than experts.^{8–9}

How do these three new studies contribute to existing knowledge? Kwon and colleagues¹⁰ applied the CAIAR system to narrow-angle images taken using a non-contact fundus camera (NM200D; Nidek, Aichi, Japan) to demonstrate that retinal vascular width and tortuosity decreased in eyes with type 1 ROP after laser photocoagulation. That is certainly not

© 2012 American Association for Pediatric Ophthalmology and Strabismus. Published by Mosby, Inc. All rights reserved.

Correspondence: Michael F. Chiang, MD, Casey Eye Institute, Oregon Health & Science University, 3375 SW Terwillger Boulevard, Portland, OR 97239 (chiangm@ohsu.edu).

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

surprising, and it is consistent with what is seen clinically. However, their finding that vascular width decreased before regression of tortuosity is interesting. This raises questions about the pathophysiology of vascular abnormality in plus disease and about future strategies utilizing quantitative analysis to monitor disease regression after laser treatment.

Ghadasra and colleagues¹¹ applied the CAIAR system to narrow-angle Nidek NM200D images and wide-angle images (RetCam; Clarity Medical Systems, Pleasanton, CA) to quantify changes in vascular parameters in eyes at risk for ROP. They demonstrated that the rate of change in arterial tortuosity and venous width was higher in eyes that developed type 1 ROP than in eyes that did not, consistent with previous findings.^{13–15} An interesting implication is that current ROP classification is based on findings from discrete retinal examinations, without regard to disease tempo.³ Yet experienced clinicians will often informally note the significance of changes in retinal vascular appearance between serial examinations. These studies show that such changes can be quantified and suggest possible strategies for ROP diagnosis and prognosis that incorporate the rate of disease progression.

Finally, Wilson and colleagues¹² applied CAIAR to narrow-angle images cropped from RetCam images, with the goal of gaining insight about which specific retinal vessels should be analyzed. They found that quantitative arterial tortuosity and venous tortuosity increased with worsening clinical stage of ROP and that this finding was consistent regardless of whether 4 vessels or 8 vessels were analyzed per image. On the other hand, quantitative vascular width did not differ significantly based on clinical disease stage. These results are noteworthy because distinguishing between retinal arteries and veins in infants with ROP is challenging for computer systems, and even for experienced clinicians. If it can definitively be shown that quantitative identification of clinically significant ROP can be performed without the need to manually select specific vessels for analysis, then adoption of these methods will become far more practical.

What follow-up studies are needed, and how might this eventually affect practice? Computer-based image analysis has potential to improve the accuracy and reproducibility of ROP diagnosis. This may eventually improve quality of care, facilitate education and workforce training, add value to telemedicine systems, and reduce medico-legal liability. Based on these three new studies and many previous ones, it is now well-established that quantitative analysis of retinal images can correlate with results from clinical ROP examinations. However, remaining gaps in knowledge must be addressed before these systems can be deployed for real-world use. The interesting study by Wilson and colleagues¹² should be replicated in larger data sets, using wider-field images to examine the diagnostic significance of vessels outside the posterior pole.¹⁶ The precise nature of vascular abnormality in plus disease requires additional research, so that key vessel features may be better understood and modeled using computer-based algorithms. Mathematical techniques for combining individual features values such as “tortuosity” and “dilation” into overall diagnoses may be needed. Improved retinal image segmentation methods are required to reduce dependence on manual editing by experts. Such efforts will rely on continued multidisciplinary collaborative efforts involving pediatric ophthalmologists, and these three papers are steps in the right direction.

Acknowledgments

Financial disclosure: MFC is an unpaid member of the Scientific Advisory Board for Clarity Medical Systems (Pleasanton, CA). MFC is supported by grant EY19474 from the National Institutes of Health (Bethesda, MD), and by unrestricted departmental funding from Research to Prevent Blindness (New York, NY).

References

1. Cryotherapy for Retinopathy of Prematurity Cooperative Group. Multicenter trial of cryotherapy for retinopathy of prematurity: Preliminary results. *Arch Ophthalmol.* 1988; 106:471–479. [PubMed: 2895630]
2. Early treatment for Retinopathy of Prematurity Cooperative Group. Revised indications for the treatment of retinopathy of prematurity: results of the Early Treatment for Retinopathy of Prematurity randomized trial. *Arch Ophthalmol.* 2003; 121:1684–1694. [PubMed: 14662586]
3. An International Committee for the Classification of Retinopathy of Prematurity. The international classification of retinopathy of prematurity revisited. *Arch Ophthalmol.* 2005; 123:991–999. [PubMed: 16009843]
4. Reynolds JD, Dobson V, Quinn GE, et al. Evidence-based screening criteria for retinopathy of prematurity: Natural history data from the CRYO-ROP and LIGHT-ROP studies. *Arch Ophthalmol.* 2002; 120:1470–1476. [PubMed: 12427059]
5. Chiang MF, Jiang L, Gelman R, Du YE, Flynn JT. Interexpert agreement of plus disease diagnosis in retinopathy of prematurity. *Arch Ophthalmol.* 2007; 125:875–880. [PubMed: 17620564]
6. Wallace DK, Quinn GE, Freedman SF, Chiang MF. Agreement among pediatric ophthalmologists in diagnosing plus and pre-plus disease in retinopathy of prematurity. *J AAPOS.* 2008; 12:352–356. [PubMed: 18329925]
7. Slidsborg C, Forman JL, Fielder AR, et al. Experts do not agree when to treat retinopathy of prematurity based on plus disease. *Br J Ophthalmol.* 2012; 96:549–553. [PubMed: 22174097]
8. Chiang MF, Gelman R, Martinez-Perez ME, et al. Image analysis for retinopathy of prematurity diagnosis. *J AAPOS.* 2009; 13:438–445. [PubMed: 19840720]
9. Wittenberg LA, Jonsson NJ, Paul Chan RV, Chiang MF. Computer-based image analysis for plus disease diagnosis in retinopathy of prematurity. *J Pediatr Ophthalmol Strabismus.* 2012; 49:11–19. [PubMed: 21366159]
10. Kwon JY, Ghodasra DH, Karp KA, et al. Retinal vessel changes after laser treatment for retinopathy of prematurity. *J AAPOS.* 2012; 16:350–353. [PubMed: 22824490]
11. Ghodasra DH, Thuangtong A, Karp KA, et al. The rate of change in retinal vessel width and tortuosity in eyes at risk for retinopathy of prematurity. *J AAPOS.* In press.
12. Wilson CM, Wong K, Ng J, Cocker KD, Ells AL, Fielder AR. Digital image analysis in retinopathy of prematurity: a comparison of vessel selection methods. *J AAPOS.* 2012; 16:223–228. [PubMed: 22681937]
13. Grunwald L, Mills MD, Johnson KS, et al. The rate of retinal vessel dilation in severe retinopathy of prematurity requiring treatment. *Am J Ophthalmol.* 2009; 147:1086–1091. [PubMed: 19286152]
14. Wallace DK, Freedman SF, Zhao Z. Evolution of plus disease in retinopathy of prematurity – Quantification by ROPTool. *Trans Am Ophthalmol Soc.* 2009; 107:45–52.
15. Thyparampil PJ, Park Y, Martinez-Perez ME, et al. Plus disease in retinopathy of prematurity: quantitative analysis of vascular change. *Am J Ophthalmol.* 2010; 150:468–475. e2. [PubMed: 20643397]
16. Rao R, Jonsson NJ, Ventura CVOC, Lindquist M, Casper DS, Chiang MF. Plus disease in retinopathy of prematurity: Diagnostic impact of field of view. *Retina.* 2012; 32:1148–1155. [PubMed: 22466473]