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Computer-assisted quantification of pre-plus and plus disease in images obtained using Pictor versus video indirect ophthalmoscopy: a pilot study

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Abstract

Subjectivity in the diagnosis of plus disease in retinopathy of prematurity has prompted the creation of computer programs to objectively measure vascular characteristics. ROPTool is a semiautomated computer program that analyzes retinal vascular dilation and tortuosity. To explore its ability to trace images taken with a FDA-approved, portable, handheld noncontact digital fundus camera (Pictor), we compared ROPTool analysis of Pictor still images acquired by nonophthalmologists to video indirect ophthalmoscopy (VIO) still images acquired by ophthalmologists. ROPTool could trace more Pictor versus VIO images. In addition, receiver operating characteristic curves showed that accuracy for diagnosing pre-plus or plus disease was higher using Pictor versus VIO images.

Retinopathy of prematurity (ROP) is a major cause of preventable childhood blindness, and plus disease is usually present in eyes requiring treatment. Disagreement between expert ROP-trained ophthalmologists in identifying plus disease demands more objective measures.¹ ROPTool (v2.1.8, FocusROP, Trumbauersville, PA) can analyze images obtained by RetCam (Clarity Medical Systems Inc, Pleasanton, CA),² video indirect ophthalmoscopy (VIO),³ and Pictor (Volk Optical Inc, Mentor, OH).⁴ In one study, ROPTool could not analyze 29% of VIO images due to inadequate image quality.³ It is unknown whether ROPTool can trace more images acquired by Pictor versus VIO. The present study compares ROPTool's ability to trace retinal vessels and its accuracy of diagnosing pre-plus and plus disease in Pictor versus VIO images and assesses ROPTool's ability to trace Pictor images obtained by nonophthalmologists as they acquired more imaging experience.

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Drs. Freedman and Wallace have developed the technology (ROPTool) that is being used in the study. ROPTool has been purchased by FocusROP, and the developers and Duke University may benefit financially from sales of FocusROP.

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Methods

This retrospective study was approved by the Duke Health System Institutional Review Board and conformed to the requirements of the US Health Insurance Portability and Accountability Act of 1996. We used images previously acquired as part of a study evaluating the feasibility of using Pictor as an ROP screening tool. On the same day infants were screened for ROP by one of two ROP-trained ophthalmologists (DKW, SFF), one of two nonophthalmologists imaged their retinas using Pictor. During routine ROP screening, we record videos using a VIO system (Keeler Ophthalmic Instruments, Broomall, PA).

We included infants who had both VIO and Pictor images acquired on the same day. For each infant, we selected one examination date based on the date with the most severe posterior pole disease (plus disease > pre-plus > normal), determined by clinical examination and closest to postmenstrual age of 36 weeks. This enhanced sample included a higher number with pre-plus and plus disease. Within those dates, we chose one Pictor and one VIO still image per infant with the optic disk most centered and blood vessels most in focus. One eye was included per infant. We excluded images acquired after ROP treatment, lacking a view of the optic disk, or with <4 visible quadrants (defined as having 1 vessel visible for 1 optic disk diameter length). Part one of the study assessed ROPtool's ability to trace and accurately analyze VIO versus Pictor images. Part two (change in traceability of Pictor images as imagers gained imaging experience) analyzed ROPtool's ability to trace images acquired during the first-versus second-half of each imager's imaging period.

We uploaded VIO and Pictor images into ROPtool and, when possible, traced 2 major vessels in each quadrant. Each image was assessed for traceability, defined as having 1 vessel in all 4 quadrants traceable by ROPtool for a distance of 1 optic disk diameter length. For each image, even those deemed untraceable, ROPtool analyzed three indices: tortuosity index (TI),² the second-most tortuous quadrant's tortuosity (T2max), and tortuosity-weighted-plus (TWP, a measurement combining vessel dilation and tortuosity and giving dilation more weight as tortuosity increases).⁵ Because the diagnosis of plus disease requires at least 2 quadrants exhibit sufficient dilation and tortuosity, we considered the second-most tortuous quadrant when determining whether an eye had plus disease. Using the clinical examination diagnoses of plus and pre-plus disease as the reference standards, we generated receiver operating characteristic (ROC) curves for these indices.

Results

Twenty-three infants examined from May 2013 to May 2015 met inclusion criteria (Table 1). Overall, traceability was higher for Pictor compared to VIO images (21/23 [95% CI, 73%–98%] vs 13/23 [95% CI, 37%–74%], resp., $P=0.02$; Figure 1). Change in traceability for Pictor images acquired during the imagers' early versus later imaging was minimal (8/9 [95% CI, 56%–98%] to 5/5 [95% CI, 57%–100%] and 4/4 [95% CI, 51%–100%] to 6/7 [95% CI, 49%–97%], resp., for imagers 1 and 2).

ROC curves for diagnosing plus and "pre-plus or plus" disease using TI, T2max, and TWP showed that diagnostic accuracy, measured using areas under curves, was greater for Pictor

versus VIO images but was statistically significantly different only for pre-plus or plus (Figure 2).

Discussion

ROPtool could trace more retinal images acquired by Pictor versus VIO and was more accurate in diagnosing pre-plus or plus disease when analyzing Pictor versus VIO images. Nonophthalmologists could obtain images traceable by ROPtool early in their experience using Pictor and did not require extensive imaging experience.

In one study, 98% of RetCam images could be analyzed by ROPtool.⁶ Contrarily, 2 vessels in each of 4 quadrants could be traced in only 24% of VIO still images.⁷ In this study, ROPtool could trace more Pictor than VIO images.

While Pictor and RetCam images are both highly traceable by ROPtool, Pictor offers advantages over RetCam. Pictor is less expensive, smaller, and more portable (weight < 500 g). Also, compression artifact during RetCam imaging can decrease retinal vascular diameter, which can mask the presence of plus disease and lead to false negative results.⁸ As a noncontact camera, Pictor exerts no corneal pressure, does not require topical anesthesia, and minimizes infection risk. While RetCam offer a wider field of view versus Pictor (120°–130° vs 45°, resp.), Pictor images have sufficient quality and field of view for accurate grading of pre-plus and plus disease.⁹

ROPtool can accurately detect plus disease using images obtained by different imaging devices. In one study using RetCam images, ROPtool's accuracy was similar and sensitivity compared favorably to those of experts.¹⁰ In another, ROPtool achieved high sensitivity and specificity when analyzing *high-quality* VIO images.⁷ In the present study, ROPtool more accurately analyzed Pictor compared to VIO images when diagnosing pre-plus *or* plus disease.

As imagers gained experience imaging premature infants with Pictor, we did not observe a significant change in ROPtool's ability to trace images, suggesting that nonophthalmologist imagers can quickly become proficient at acquiring high-quality images with Pictor for ROP screening.

This study had several limitations. Because images were not collected for computer-assisted analysis, imagers did not prioritize centering the optic disk. We had a small sample size and only two Pictor imagers. Quality of image acquisition for both imaging modalities is user dependent. The investigator who traced images could not be masked to the image type being analyzed. Also, because ROPtool is semiautomated, it required user input to identify the vessels. Finally, the results of this study may not be generalizable to other vessel analysis programs (eg, CAIAR, RISA, and VesselMap). Nevertheless, the combination of Pictor imaging and ROPtool analysis offers promise for ROP screening.

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FIG 1. ROPtool tracing of retinal images from an infant with a normal posterior pole: Best video indirect ophthalmoscopy (VIO) still image (A), Pictor still image (B), and ROPtool tracings of the VIO still image (C) and Pictor still image (D). ROPtool was able to trace more vessels in the Pictor image compared to the VIO image.

FIG 2.

Receiver operating characteristic curves for diagnosing either “pre-plus or plus disease” or plus disease using three indices calculated by ROPtool: tortuosity index (A,D), tortuosity-weighted-plus (B,E), and second-most tortuous quadrant (C,F). Area under the curve is presented in parentheses for each type of imaging technique (ie, Pictor and video indirect ophthalmoscopy [VIO]).

Table 1

Characteristics of infants imaged using the Pictor camera by imager 1 and imager 2

	Infants imaged by imager 1 (n = 14)		Infants imaged by imager 2 (n = 11)		Overall
	First half of his imaging period	Second half of his imaging period	First half of his imaging period	Second half of his imaging period	
Clinical trait, mean $\pm$ SD					
GA, weeks	25.9 $\pm$ 2.1	25.0 $\pm$ 0.7	24.5 $\pm$ 1.0	25.7 $\pm$ 2.0	25.5 $\pm$ 1.8 ^a
Birth weight, g	782 $\pm$ 338	778 $\pm$ 109	740 $\pm$ 82	876 $\pm$ 170	805 $\pm$ 234 ^a
PMA at time of imaging, weeks	35.0 $\pm$ 1.0	35.4 $\pm$ 0.9	37.6 $\pm$ 2.7	35.3 $\pm$ 2.4	35.6 $\pm$ 1.9
Retinal images, no.					
No pre-plus or plus disease ^b	6	2	3	5	16
Pre-plus ^b	1	3	0	1	5
Plus disease ^b	2	0	1	1	4

GA, gestational age; PMA, postmenstrual age; SD, standard deviation.

^aTwo infants were imaged by both imagers. Each infant was only counted once in these calculations.

^bDiagnosis based on clinical examination using indirect ophthalmoscopy and a 28 D lens.