

## BRIEF REPORTS

## Semiautomated Analysis of Retinal Vessel Diameter in Retinopathy of Prematurity Patients With and Without Plus Disease

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**PURPOSE:** To determine the feasibility of using semiautomated analysis of digital fundus images to quantify the differences in retinal vascular diameter between retinopathy of prematurity (ROP) patients with and without plus disease.

**DESIGN:** Case-control study.

**METHODS:** Thirty eyes of 15 patients with ROP were included in this study. Fourteen eyes of seven patients had plus disease and 16 eyes of eight patients had no evidence of plus disease. Digital fundus images were captured using an NM200D (Nidek, Inc, Aichi, Japan) camera. Vessel diameters were determined using VesselMap software (Imedos, Jena, Germany). The student *t* test analysis was used to compare diameters of vessels with and without plus disease.

**RESULTS:** We found that the average venous diameter is significantly larger by 15% in the group with plus disease.

**CONCLUSIONS:** VesselMap analysis of digital images is feasible. This method is able to distinguish between veins with and without plus disease, and may be useful in telemedicine screening strategies. (Am J Ophthalmol 2006;xx:xxx. © 2006 by Elsevier Inc. All rights reserved.)

**T**IMELY RECOGNITION OF POSTERIOR RETINAL VASCULAR changes (plus disease) is critical to optimize clinical outcome in retinopathy of prematurity (ROP). Plus disease is diagnosed clinically by subjective comparison of vascular dilation and tortuosity to a standard photograph used in the Cryotherapy for Retinopathy of Prematurity Study.<sup>1</sup> The need for a quantitative means to diagnose plus disease

has been recognized.<sup>2,3</sup> Various image analysis techniques have been investigated toward this goal.<sup>2-5</sup> We measured vessel diameter using VesselMap (Imedos, Jena, Germany) semiautomated analysis of digital fundus images from infants with ROP, with and without plus disease. Our aim was to assess mean vessel diameters in eyes with plus and no plus disease.

Thirty eyes of 15 patients were included in this study. These patients were selected from a larger study involving digital imaging of 54 infants at risk for developing ROP who had birth weights less than 1250 grams and gestational ages younger than 32 weeks. Parents of all infants signed an institutional review board–approved consent form after they were informed of the purpose and protocol of the study. This study complied with all Health Insurance Portability and Accountability Act (HIPAA) regulations. Fourteen eyes were clinically diagnosed with plus disease; 16 control eyes were matched for birth weight and gestational age. Digital fundus images of the disk and posterior pole were captured during routine ROP exams in awake infants using the NM200D fundus camera (Nidek, Inc, Aichi, Japan). Images were taken by both ophthalmologists and nonophthalmologists. Using VesselMap semiautomated software, retinal vascular diameters were measured from the digital images in a masked fashion. Four temporal vessels (two veins, two arteries) were measured from each eye. For each subject, the average diameters of four veins and four arteries (two vessels measured in each eye) were calculated. Measurement sites approximately 600 arbitrary units in length were chosen on straight portions of the vessels away from branching points. All measurements were performed within two disk diameters from the optic nerve (Figure 1). Veins and arteries were analyzed separately. Vessels with plus disease were compared with those without plus disease using the Student *t* test. A post hoc screening paradigm was applied to assess sensitivity and specificity for detecting plus disease. All results are shown in arbitrary units.

High-quality images were obtained from all 30 eyes. A total of 99 images were analyzed (average, 3.5 photographs per eye). Figure 2 summarizes the diameter measurements of the average retinal veins and arteries in each subject. Four veins and arteries were averaged for each data point. The mean venous diameter was significantly larger in the plus group by the Student *t* test analysis ( $P = .039$ ) (Table). Although the mean arterial diameter was larger in the plus group, the difference did not reach statistical

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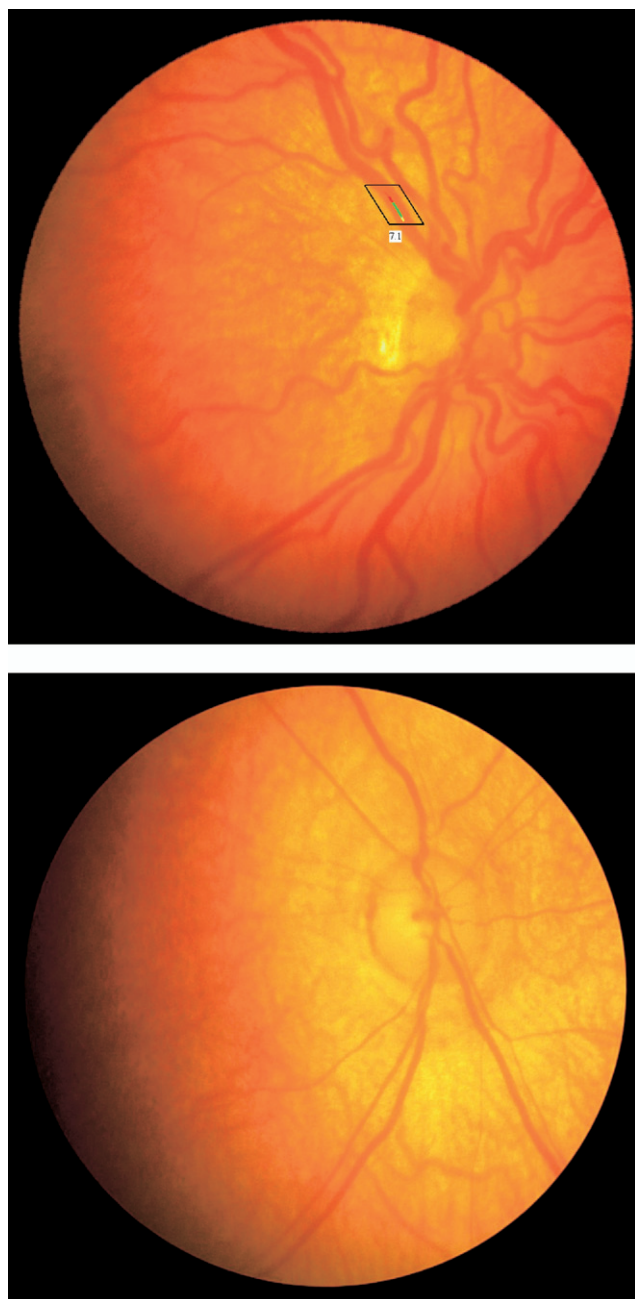


FIGURE 1. Fundus photograph of a typical patient with plus disease (Top) and without plus disease (Bottom). Measurement site on a main temporal vein is demonstrated as a black box (Top).

significance ( $P = .104$ ). Using a post hoc screening paradigm, our measurements yield sensitivity of 71% and specificity of 75% for predicting the presence of plus disease by vein diameter. Artery diameter had sensitivity of 86% and specificity of 100%.

These data demonstrate the feasibility of quantifying retinal vessel diameter using VesselMap analysis of digital images taken in awake infants with active ROP. Our results suggest that the mean venous diameter is signifi-

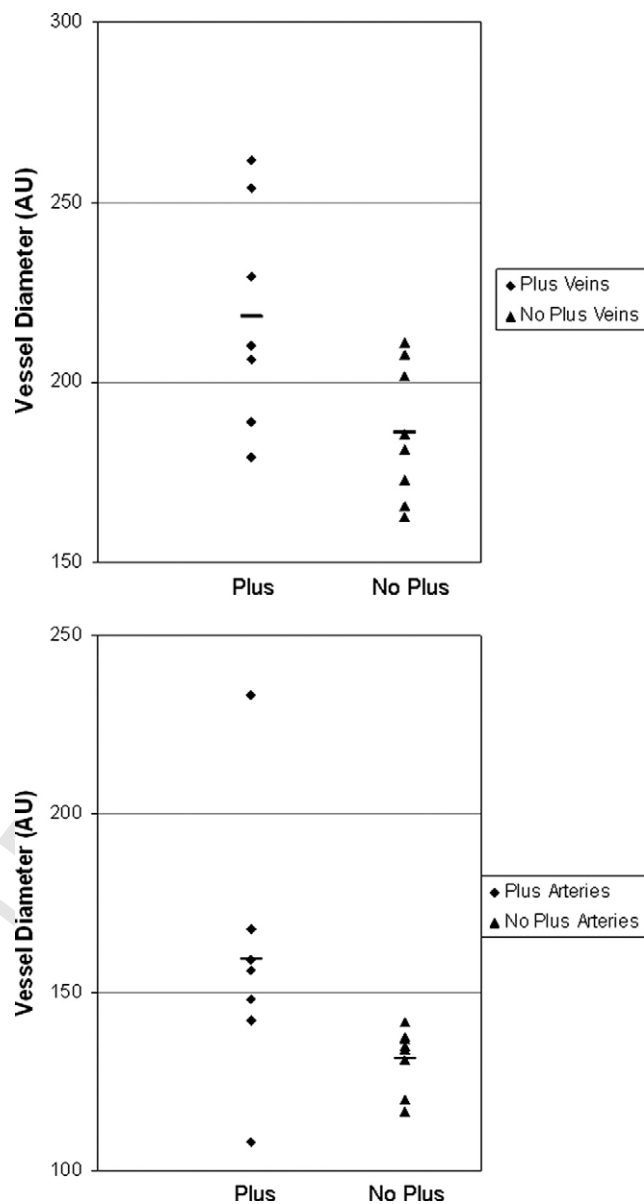


FIGURE 2. Scatterplot of average retinal vein (Top) and artery (Bottom) diameter in patients with plus disease (plus) and without plus disease (no plus). Each data point represents the average of four retinal vessels measured in each subject. The student  $t$  test,  $P = .039$  for veins and  $P = .104$  for arteries. The horizontal lines indicate the mean diameter for all subjects. Measurements are shown in arbitrary units (AU).

cantly larger in the plus group. Our post hoc screening paradigm yielded good sensitivity and specificity for detecting plus disease in the veins and arteries. Factors limiting a more accurate assessment of vessel diameters with our method include poor image quality and insufficient contrast because of red choroidal vasculature. Tortuosity, another important characteristic of plus disease, was not assessed in this study.

Screening for ROP remains a challenge because of the high volume of infants requiring examinations and the

**TABLE.** Analysis of Retinal Vessel Diameter in Retinopathy of Prematurity Patients With and Without Plus Disease

	Plus Disease Mean Diameter (SD)	No Plus Disease Mean Diameter (SD)	P value
Average vein	219 (31)	186 (19)	.039
Average artery	159 (38)	132 (9)	.104
SD = standard deviation.			

relatively few ophthalmologists with expertise, particularly in developing countries. Our images were captured by both nonophthalmologists and ophthalmologists. Other studies have shown that remote reading of digital images for ROP screening has promise.<sup>6,7</sup> Semiautomated analysis of digital images could allow objective diagnosis of plus disease remotely with a telemedicine strategy.

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