Identification of type 1 retinopathy of prematurity (ROP) relies heavily on the presence of characteristics of plus disease, especially tortuosity. However, a relatively infrequent subset of eyes with type 1 ROP, eyes with zone 1, stage 3 ROP without plus disease, is included in treatment indications. We examined if posterior pole vessel width is associated with type 1 ROP in a subset of eyes with zone 1, stage 3 ROP without plus disease and whether vessel width differentiates type 1 from non–type 1 ROP.

Treatment of eyes with type 1 ROP is based on results from the Early Treatment for Retinopathy of Prematurity (ETROP) Study. Type 1 ROP consists of the following: (1) any ROP in zone 1 with plus; (2) zone 1, stage 3 ROP without plus; and (3) zone 2, stage 2 or 3 ROP with plus disease. The ETROP Study investigators recommended treatment for eyes with type 1 ROP, which includes all eyes with plus disease (except for zone 2, stage 1) and eyes with zone 1, stage 3 ROP without plus disease. The presence of plus disease, a subjective clinical diagnosis made by comparison with standard reference photographs, is an essential component of 2 of the 3 categories of type 1 disease.

With the emphasis on eyes with plus disease as the current indication for ROP treatment, vascular changes in a subset of type 1 ROP—specifically those with zone 1, stage 3 ROP without plus disease—may be missed. We wanted to determine whether posterior pole vessel width using narrow-field images could identify eyes with zone 1, stage 3 ROP without plus disease and whether those changes differentiate type 1 from non–type 1 ROP.

Subjects and Methods
We conducted a retrospective case-control study. Institutional review board approval was obtained. ROP status was classified based on the diagnosis recorded by 3 pediatric ophthalmologists.

Table 1 displays mean vessel width increasing progressively among eyes without type 1 ROP, type 1 ROP without plus, and type 1 ROP with plus disease. A significant difference among the 3 groups was noted when venules alone (p = 0.01) and venules and arterioles (p = 0.02) were considered. Controls with type 1 and those without type 1 were significantly different for venules alone (p = 0.003) and both arterioles and venules (p = 0.003). When both groups of type 1 ROP eyes were compared, there were no significant differences for vessel width, with only a 2.7 μm difference in venule width between type 1 ROP...
eyes with and without plus disease. Although the mean values for vessel width suggest a difference between type 1 eyes without plus disease and controls without type 1 ROP (particularly for venules with a 17 μm difference), these results were not statistically significant ($p = 0.07$).

**Discussion**

Due to the restricted field of the fundus in narrow-field images, it is speculated that remote evaluation of its images may result in higher false-negative rates in detecting serious ROP, especially among zone 1 ROP without plus disease. The primary purpose of this study was to determine whether image analysis of eyes with type 1 ROP without plus disease could be distinguished from those eyes without type 1 ROP and, secondarily, from eyes with type 1 ROP with plus disease. We report that, based on a comparison of vessel width, the group of the ten eyes with type 1 ROP without plus disease can be distinguished from eyes without type 1 ROP. Given the marginal statistical significance after adjustment of multiple comparisons (adjusted $p = 0.07$) we acknowledge that this difference may be due to chance alone.

We found no statistically significant difference between mean vessel width of eyes with type 1 ROP without plus disease and eyes without type 1 ROP. However, we found that mean vessel width was greater for type 1 ROP without plus disease relative to eyes without type 1 ROP. Interestingly, when we compared our cases to eyes with type 1 ROP with plus disease, we found a very small difference in the mean vessel width between the 2 groups, which was not significant. Although vessel width abnormalities measured in type 1 ROP eyes without plus disease may not be sufficient to qualify on clinical examination as plus disease, they are sufficiently abnormal to be distinguished from eyes without type 1 using image analysis. Quantitative measurement of vessel changes associated with ROP may be more consistent and reliable than the clinical judgment required for the diagnosis of plus disease, a basically binary decision.7-9

There were several limitations to our study. Results from eye examinations were used as reference standards and, despite efforts to standardize clinical judgment of plus disease across examiners, inter-expert disagreement on diagnosis of plus disease is significant.7-9 Furthermore, ETROP recommendations do not suggest treatment of all eyes with plus disease, as in zone 2, stage 1 ROP and zone 3 ROP with plus disease.1,2

In conclusion, in our small sample, we found no significant differences on analysis of narrow-field digital images of eyes with type 1 ROP without plus disease from those without type 1 ROP, although a clear trend toward increased width of vessels was present in eyes with type 1 ROP without plus disease. Further study with a larger sample size of stage 3 zone 1 ROP without plus disease is necessary but can be difficult given its relatively low incidence.

**References**


