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# Visual Acuity Is Correlated with the Area of the Foveal Avascular Zone in Diabetic Retinopathy and Retinal Vein Occlusion

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***Purpose:*** To determine if the area of the foveal avascular zone (FAZ) is correlated with visual acuity (VA) in diabetic retinopathy (DR) and retinal vein occlusion (RVO).

***Design:*** Cross-sectional study.

***Participants:*** Ninety-five eyes of 66 subjects with DR (65 eyes), branch retinal vein occlusion (19 eyes), and central retinal vein occlusion (11 eyes).

***Methods:*** Structural optical coherence tomography (OCT; Spectralis, Heidelberg Engineering) and OCT angiography (OCTA; Avanti, Optovue RTVue XR) data from a single visit were analyzed. FAZ area, point thickness of central fovea, central 1-mm subfield thickness, the occurrence of intraretinal cysts, ellipsoid zone disruption, and disorganization of retinal inner layers (DRIL) length were measured. VA was also recorded. Correlations between FAZ area and VA were explored using regression models. Main outcome measure was VA.

***Results:*** Mean age was 62.9±13.2 years. There was no difference in demographic and OCT-derived anatomic measurements between branch retinal vein occlusion and central retinal vein occlusion groups (all $P \geq 0.058$); therefore, data from the 2 groups were pooled together to a single RVO group for further statistical comparisons. Univariate and multiple regression analysis showed that the area of the FAZ was significantly correlated with VA in DR and RVO (all $P \leq 0.003$). The relationship between FAZ area and VA varied with age ($P = 0.026$) such that for a constant FAZ area, an increase in patient age was associated with poorer vision (rise in logarithm of the minimum angle of resolution visual acuity). Disruption of the ellipsoid zone was significantly correlated with VA in univariate and multiple regression analysis (both $P < 0.001$). Occurrence of intraretinal cysts, DRIL length, and lens status were significantly correlated with VA in the univariate regression analysis ($P \leq 0.018$) but not the multiple regression analysis ($P \geq 0.210$). Remaining variables evaluated in this study were not predictive of VA (all $P \geq 0.225$).

***Conclusions:*** The area of the FAZ is significantly correlated with VA in DR and RVO and this relationship is modulated by patient age. Further study about FAZ area and VA correlations during the natural course of retinal vascular diseases and following treatment is warranted. *Ophthalmology 2016;■:1–17 © 2016 by the American Academy of Ophthalmology.*

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Diabetic retinopathy (DR) is the leading cause of vision loss in the working-age population in developed countries.[1] According to data from the National Eye Institute, there were approximately 7.7 million diagnosed cases of DR in the United States alone in 2010.[2] Retinal venous occlusion (RVO), due to central retinal vein occlusion (CRVO) or branch retinal vein occlusion (BRVO), is the second most common retinal vascular disorder leading to significant vision loss, with an estimated number of global cases in 2010 exceeding 16.4 million.[3] The prevalence of DR and RVO is projected to increase to pandemic portions over the next 30 years, as is the socioeconomic burden associated with these conditions.[4] Thus, there is an urgent need to improve our understanding of the pathophysiologic mechanisms and anatomic correlates for significant visual loss due to these disorders.

The foveal avascular zone (FAZ) is a specialized region of the human retina that approximates the region of highest cone photoreceptor density and oxygen consumption.[5,6] Histologic techniques[7–9] and a range of in vivo imaging modalities[10–19] have highlighted the variability in FAZ topology in normal human eyes. In healthy eyes, the size of



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the FAZ does not seem to influence visual function,[9,17,20] but the relationship between FAZ size and visual acuity (VA) in retinal vascular diseases remains a matter of conjecture. Much of our understanding concerning the relationship between FAZ topology and visual function has been attained from studies that utilized fluorescein angiography (FA) techniques to visualize the retinal circulation.[21,22] Although these studies significantly aided our understanding of the pathogenic mechanisms leading to vision loss in retinal vascular diseases, they seldom accounted for the influence of other anatomic changes, such as ellipsoid zone (EZ) disruption,[23] that may have also affected visual function.

Volumetric imaging using optical coherence tomography angiography (OCTA) permits rapid, noninvasive evaluation of the retinal circulation.[24–29] Recent work has shown that OCTA permits reproducible measurement of FAZ dimensions and provides quantitative vascular information comparable to histologic examination.[9,30] The technique of OCTA thus appears suited for delineating relationships between the morphometric properties of the FAZ and VA. In this report, a biomorphometric analysis incorporating OCTA and structural optical coherence tomography (OCT) data is used to determine the significant predictors of VA in DR and RVO. We show that FAZ area is an independent predictor of VA in DR and RVO. We also demonstrate that patient age modulates the relationship between FAZ area and VA in retinal vascular diseases. The results of this report, therefore, have important clinical applications.

## Methods

This study followed the tenets of the Declaration of Helsinki and was approved by the Institutional Review Board at North Shore Long Island Jewish Health System. Data were stored and managed in compliance with guidelines from the Health Insurance Portability and Accountability Act.

### Subjects

Consecutive cases of DR, BRVO, and CRVO seen between August 2014 and October 2015 by 2 retina specialists (L.A.Y. and K.B.F.) at Vitreous Retina Macula Consultants of New York were enrolled in this study. Treatment-naïve and treated cases were included. The diagnosis of diabetes mellitus was based on the results of fasting blood samples and glycosylated hemoglobin (HbA1c). Only patients with clinical signs of diabetic retinopathy, according to the Early Treatment Diabetic Retinopathy Study (ETDRS) grading criteria,[31] were included in this study (Fig 1). Patients with diabetes mellitus without evidence of diabetic retinopathy (level 10 scale ETDRS criteria) were not included in this study. Central retinal vein occlusion was determined by the presence of retinal vein dilation, retinal edema, or scattered superficial or deep hemorrhages with or without the presence of optic disc edema/hyperemia (Fig 1). Branch retinal vein occlusion was determined by the presence of the same clinical features as CRVO, but confined to a focal region in the retina corresponding to a specific arteriovenous crossing (Fig 1). Long-standing vein occlusion was determined by the presence of occluded or sheathed retinal veins and/or vascular anastomoses. With the exception of 4 cases (1 case of BRVO and 3 cases of DR), the clinical evaluation of all subjects included imaging with FA (Optos 200Tx [Optos, Dunfermline, Scotland, United Kingdom], Topcon TRC 501x fundus camera [Topcon Imagenet, Tokyo, Japan], or Heidelberg Spectralis HRA+OCT [Heidelberg Engineering, Heidelberg, Germany]). Other inclusion criteria for this study included the following: (1) clear ocular media; (2) absence of significant refractive error; (3) absence of significant concurrent ocular diseases. Patients deemed to have unsatisfactory OCTA images such that FAZ area could not be reliably measured, as described below, were also excluded from this study. All subjects underwent slit-lamp biomicroscopy, dilated funduscopic examination, and measurement of pinhole VA on the day of OCTA imaging. Demographic and clinical information, including treatment history, lens status (phakic or pseudophakic), and duration of disease, was obtained from patient records.

### Optical Coherence Tomography–Derived Measurements of Foveal Anatomy

All patients were imaged with Spectralis spectral-domain OCT (SD OCT) (Heidelberg Engineering, Heidelberg, Germany) on the day of OCTA imaging. A raster scan protocol centered at the fovea (range, $20^\circ \times 25^\circ - 30^\circ \times 20^\circ$) was used. The following assessments of foveal structure were attained using the macular volume scan (Figs 2 and 3):

1. Point thickness of the central fovea (point foveal thickness, PFT): Determined using the B-scan image of the central fovea and defined as the distance between the retinal pigment epithelium and inner limiting membrane (ILM). Calipers provided by the OCT software were used to determine this measurement. Point thickness of the central fovea was measured by 2 independent examiners (M.I. and J.M.) and the average measurement was used for statistical analysis.
2. Occurrence of intraretinal cystoid changes: Categorically graded as being present or absent by 2 independent observers (M.I. and J.M.). Intraretinal cysts were identified using previously determined OCT criteria[32] and were defined as the occurrence of round or oval hyporeflective spaces arranged in linear aggregates at the level of the inner nuclear or outer nuclear/Henle fiber layers. When the evaluation was inconsistent between the 2 graders, a third masked reader (C.B.) made the final arbitration.
3. Integrity of the ellipsoid zone in the central fovea: The central 3 mm of the fovea, as circumscribed by the ETDRS grid, was evaluated. Disruption of the EZ was categorically graded as being present or absent by 2 independent observers (M.I. and J.M.). An absent grading was denoted if there was any disruption of the EZ on OCT. When the evaluation was inconsistent between the 2 graders, a third masked reader (C.B.) made the final arbitration.
4. Central 1-mm subfield thickness (CST): Recorded from the retinal thickness ETDRS grid generated by Spectralis software (Heidelberg Engineering, Heidelberg, Germany). The occurrence of diabetic macular edema, defined as a central foveal thickness of greater than 275 μm (ETDRS central subfield),[33] was also evaluated in the diabetic cohort.
5. Disorganization of the retinal inner layers (DRIL) length: Previously reported definitions of DRIL were used.[34,35] Disorganization of the retinal inner layers length was defined as the horizontal extent (in microns) for which any boundaries between the ganglion cell–inner plexiform layer complex, inner nuclear layer, and outer nuclear layer