

Presence of Foveal Bulge in Optical Coherence Tomographic Images in Eyes With Macular Edema Associated With Branch Retinal Vein Occlusion

TAIJI HASEGAWA, TETSUO UEDA, MASAHIRO OKAMOTO, AND NAHOKO OGATA

- **PURPOSE:** To determine whether a significant correlation exists between the presence of a bulge in the photoreceptor inner segment/outer segment (IS/OS) line and the best-corrected visual acuity (BCVA) in eyes with resolved macular edema associated with branch retinal vein occlusion (BRVO).
- **DESIGN:** Retrospective, observational case series.
- **METHODS:** We retrospectively reviewed the medical records of patients who had a complete resolution of macular edema and had an intact IS/OS line in the central fovea in the spectral-domain optical coherence tomographic (SDOCT) images. Thirty-one eyes with macular edema associated with BRVO (BRVO group) and 31 unaffected fellow eyes (control group) of 31 patients were evaluated. In normal eyes, the intact IS/OS line determined by SDOCT has a bulge at the central fovea, called the foveal bulge. The eyes in the BRVO group were classified by the presence or absence of foveal bulge, and the characteristics of the 2 groups were compared.
- **RESULTS:** A foveal bulge was present in 7 of 31 eyes in the BRVO group. The incidence of a foveal bulge was significantly lower in the BRVO group (22.6%) than in the control group (100%; $P < .0001$). All 7 eyes with foveal bulge had a decimal BCVA of ≥ 1.0 at the final visit. The incidence of a foveal bulge was significantly higher in eyes with BCVA of ≥ 1.0 (77.8%) than in the eyes with BCVA of < 1.0 (0%; $P < .0001$).
- **CONCLUSIONS:** The foveal bulge is a good marker of the functional properties of the fovea in eyes with resolved macular edema associated with BRVO. (Am J Ophthalmol 2014;157:390–396. © 2014 by Elsevier Inc. All rights reserved.)

MACULAR EDEMA IS A MAJOR COMPLICATION associated with branch retinal vein occlusion (BRVO). The macular edema occasionally resolves spontaneously,¹ but it can also remain for a long period and lead to a decrease in visual acuity.^{2,3} Thus,

various treatments have been used to try to reduce macular edema, such as grid laser photocoagulation,^{4,5} pars plana vitrectomy combined with internal limiting membrane peeling,⁶ intravitreal injections of triamcinolone acetate,^{7,8} and intravitreal injections of bevacizumab⁹ or ranibizumab.¹⁰ After resolution of the macular edema, the visual acuity of most of the eyes recovers to a relatively good level. However some patients have poor visual acuity in spite of a complete resolution of the macular edema.

The reason for this lack of complete recovery was partially answered by the results of recent studies using spectral-domain optical coherence tomography (SDOCT). The SDOCT images showed that the photoreceptor inner and outer segment (IS/OS) line was disrupted at the central fovea in the eyes of patients who had poor visual acuity despite complete resolution of the macular edema.¹¹ It has also been shown that the integrity of the IS/OS line was significantly and positively correlated with visual acuity in eyes with resolved macular edema associated with BRVO. However, we have examined patients who had only limited visual improvement, although their eyes had an intact IS/OS line at the central fovea after resolution of the macular edema. We were not able to determine why the visual acuity did not completely recover in these eyes.

Careful examination of the SDOCT images of normal eyes shows that the IS/OS line has a bulge at the central fovea, named a foveal bulge. Recent OCT studies have shown that the presence or absence of a foveal bulge at the central fovea was significantly correlated with visual acuity in eyes with albinism,^{12,13} occult macular dystrophy,¹⁴ and amblyopia.¹⁵ However, as best we know, no study has reported on the presence or absence of a foveal bulge in eyes with BRVO.

Thus, the purpose of this study was to determine whether the foveal bulge was significantly correlated with visual acuity after resolution of the macular edema associated with BRVO. In addition, we studied the macular status at the initial visit and assessed the factors related to visual acuity after resolution of the macular edema.

PATIENTS AND METHODS

- **PROCEDURES AND PATIENTS:** The procedures used in this study conformed to the tenets of the Declaration of

Accepted for publication Oct 16, 2013.

From the Department of Ophthalmology, Nara Medical University, Nara, Japan.

Inquiries to Taiji Hasegawa, Department of Ophthalmology, Nara Medical University, 840 Shijo-cho, Kashihara, Nara 634-8522, Japan; e-mail: taijiha@naramed-u.ac.jp

Helsinki. Treatment of an intravitreal injection of bevacizumab was approved by the Institutional Review Board for Nara Medical University. An informed consent was obtained from all of the patients after an explanation of the procedures to be used and possible complications.

We studied the medical records of patients with a resolved macular edema associated with BRVO and with an intact IS/OS line at the central fovea in the SDOCT images. All of the patients were examined at the Nara Medical University Hospital from June 1, 2011 to April 30, 2013. Eyes with coexisting ocular diseases (eg, epiretinal membrane, glaucoma, diabetic retinopathy, vitreous hemorrhage, vitreous opacity, and senile cataract) were excluded. In the end, 31 eyes of 31 patients with macular edema associated with BRVO (BRVO group) were studied. We also studied the 31 unaffected fellow eyes as controls (control group). Twenty-seven of the 31 affected eyes received an intravitreal injection of bevacizumab and a posterior sub-Tenon injection of triamcinolone acetonide to treat the macular edema. The macular edema resolved spontaneously in the other 4 eyes. All of the patients underwent a complete ophthalmic examination including the measurement of the best-corrected visual acuity (BCVA), slit-lamp biomicroscopy, fundus examination including slit-lamp biomicroscopy with a noncontact fundus lens, fundus photography, and SDOCT.

• **EVALUATION OF OPTICAL COHERENCE TOMOGRAPHIC IMAGES:** The Spectralis SDOCT (Heidelberg Engineering, Heidelberg, Germany) was used to obtain the SDOCT images. We evaluated the horizontal cross-sectional images that were recorded at the initial and final visit after resolution of the macular edema. The central foveal thickness (CFT) was measured as the distance between the internal limiting membrane (ILM) and the outer border of the retinal pigment epithelium (RPE) at the central fovea. The CFT was measured automatically with the caliper measurement tool embedded in the SDOCT system (Figure 1). We also measured the outer nuclear layer (ONL) thickness as the distance between the outer border of the ILM and the external limiting membrane (ELM), and the photoreceptor inner segment (IS) length as the distance between the ELM and the inner border of the highly reflective line representing the IS/OS line at the central fovea. The photoreceptor outer segment (OS) length was measured as the distance between the IS/OS line and the inner border of the RPE at the center of the fovea (Figure 1). The ONL thickness and the photoreceptor IS and OS lengths were measured manually by 2 of the authors (T.H. and M.O.), who were masked to the visual acuity and other information of the eyes. The values obtained by the 2 authors were averaged for the statistical analyses. The intraclass correlation coefficient (ICC) was calculated as an interobserver reproducibility measure.

We focused on the foveal bulge as seen in normal eyes (Figure 1) in the 31 BRVO eyes of 31 patients. The eyes

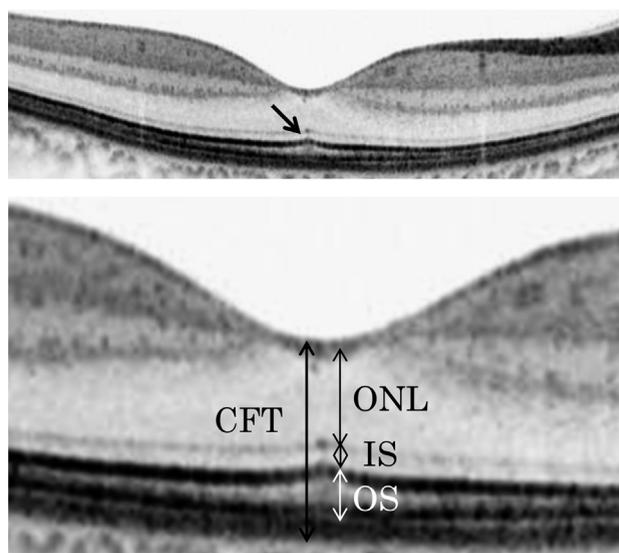


FIGURE 1. Spectral-domain optical coherence tomography (SDOCT) image of a normal eye of a 53-year-old woman whose decimal best-corrected visual acuity was 1.2. (Top) Horizontal scan across the central fovea that was obtained at a 30-degree angle. SDOCT image shows that the photoreceptor inner segment/outer segment (IS/OS) line has a bulge at the central fovea, named a foveal bulge (arrow). (Bottom) Magnified view. The central foveal thickness (CFT) is the distance between the surface of the internal limiting membrane (ILM) and the outer border of the retinal pigment epithelium (RPE) at the central fovea. The thickness of the outer nuclear layer (ONL) is the distance between the outer border of the ILM and the external limiting membrane (ELM). The length of the photoreceptor inner segment (IS) is the distance between the ELM and the inner border of the IS/OS line. The length of the photoreceptor outer segment (OS) is the distance between the inner border of the IS/OS and the inner border of the RPE.

were classified into those with a foveal bulge and those without a foveal bulge. The same retinal specialists (T.H. and M.O.) evaluated the foveal shape in the OCT images and were masked to the clinical characteristics of the eyes, and a third reviewer (T.U.), who was also masked to the patients' data, made the final decision regarding the presence or absence of a foveal bulge in cases of disagreement.

• **STATISTICAL ANALYSES:** Statistical analyses were performed using StatView software (version 5.0; SAS Institute, Cary, North Carolina, USA). The BCVA was measured with a Landolt chart, and the decimal acuities were converted to the logarithm of the minimal angle of resolution (logMAR) for the statistical analyses. All values are presented as the means \pm standard deviations. The Mann-Whitney *U* test was used to determine the significance of differences in the patient characteristics and the retinal thicknesses. The significance of the differences in the incidence of an intact the ELM, presence of serous

retinal detachment (SRD), and foveal bulge was analyzed with the Fisher exact probability test. A *P* value <.05 was considered statistically significant.

RESULTS

THE INTEROBSERVER ICC FOR THE MEASUREMENT OF THE ONL thickness was 0.957, for the photoreceptor IS length was 0.871, and for the photoreceptor OS length was 0.970. These findings suggest that the measurement of each retinal layer had good reproducibility.

The average age of the 31 patients (15 men and 16 women) was 67.3 ± 8.6 years, with a range of 49-81 years. At the initial visit, all 31 affected eyes had macular edema associated with BRVO, and the macular edema had resolved completely and an intact IS/OS line was observed at the central fovea in the SDOCT images in all of the cases.

• COMPARISONS BETWEEN CONTROL GROUP AND BRANCH RETINAL VEIN OCCLUSION GROUP: The clinical characteristics of the eyes in the BRVO group and control fellow eyes at the final visit are summarized in Table 1. In the BRVO group, the mean BCVA was 0.18 ± 0.22 logMAR units with a range of -0.08 to 0.52 logMAR units, the mean CFT was 221.8 ± 20.5 μm, and the mean photoreceptor OS length at the central fovea was 47.3 ± 9.4 μm. For the eyes in the control group, the mean BCVA was -0.03 ± 0.05 logMAR units, the mean CFT was 221.2 ± 15.9 μm, and the mean photoreceptor OS length was 58.5 ± 4.2 μm. The BCVA in eyes of the control group was significantly better than that in eyes of the BRVO group (*P* < .0001). The photoreceptor OS length in eyes of the BRVO group was significantly shorter than that in eyes of the control group (*P* < .0001), but the CFT, ONL thickness, and photoreceptor IS length were not significantly different between the eyes of the 2 groups.

In the control group, a foveal bulge was present in all 31 eyes (100%) at the final visit, but a foveal bulge was present in 7 eyes (22.6%) and absent in 24 (77.4%) in the BRVO group at the final visit. This difference in the incidence of a foveal bulge at the final visit was significant (*P* < .0001).

• COMPARISONS OF EYES WITH OR WITHOUT FOVEAL BULGE IN BRANCH RETINAL VEIN OCCLUSION GROUP: At the final visit, a foveal bulge was present in 7 and not present in 24 eyes of the BRVO group. The clinical characteristics of the eyes in the foveal bulge (+) group (n = 7) and foveal bulge (-) group (n = 24) are presented in Table 2. At the final visit in the foveal bulge (+) group, the mean BCVA was -0.06 ± 0.04 logMAR units, the mean CFT was 237.0 ± 17.7 μm, and the mean photoreceptor OS length at the central fovea was 58.6 ± 3.8 μm. In the foveal bulge (-) group, the mean BCVA

TABLE 1. Patient Characteristics and Optical Coherence Tomographic Findings at the Final Visit After Resolution of Macular Edema Associated With Branch Retinal Vein Occlusion

| | BRVO Group (n = 31) | Control Group (n = 31) | <i>P</i> Value |
|---------------------------------|------------------------|---------------------------|-------------------|
| Age (y) | 67.3 ± 8.6 | | |
| Follow-up period (mo) | 7.5 ± 4.3 | | |
| LogMAR | 0.18 ± 0.22 | -0.03 ± 0.05 | <.0001 |
| CFT (μm) | 221.8 ± 20.5 | 221.2 ± 15.9 | .8880 |
| ONL thickness (μm) | 106.3 ± 11.8 | 101.6 ± 15.5 | .1314 |
| Photoreceptor IS length (μm) | 28.1 ± 1.6 | 28.0 ± 2.8 | .5375 |
| Photoreceptor OS length (μm) | 47.3 ± 9.4 | 58.5 ± 4.2 | <.0001 |
| Detection of foveal bulge n (%) | 7 (22.6%) | 31 (100%) | <.0001 |

BRVO = branch retinal vein occlusion; CFT = central foveal thickness; IS = inner segment; logMAR = logarithm of minimal angle of resolution; ONL = outer nuclear layer; OS = outer segment.

was 0.24 ± 0.21 logMAR units, the mean CFT was 217.3 ± 19.3 μm, and the mean photoreceptor OS length was 44.0 ± 7.8 μm at the final visit. At the final visit, the BCVA was significantly better in the foveal bulge (+) group than in the foveal bulge (-) group (*P* < .0001). The CFT was significantly thicker and the photoreceptor OS length was significantly longer in the foveal bulge (+) group than in the foveal bulge (-) group (*P* = .0248, *P* = .0001, respectively). On the other hand, the ONL thickness and photoreceptor IS length were not significantly different in the 2 groups.

We also studied the differences in the age, BCVA, and OCT findings at the initial examination between the foveal bulge (+) group and the foveal bulge (-) group. The patients in the foveal bulge (+) group were significantly younger than those in the foveal bulge (-) group (*P* = .044). The BCVA was significantly better and the CFT was significantly thinner in the foveal bulge (+) group than that in the foveal bulge (-) group (*P* = .0034, *P* = .0011, respectively). At the initial visit, a disrupted ELM was present in 1 of 7 eyes (14.3%) in the foveal bulge (+) group but was disrupted in 17 of 24 eyes (70.8%) in the foveal bulge (-) group. In addition, an SRD was detected beneath the fovea in only 1 of 7 eyes (14.3%) in the foveal bulge (+) group, but in 20 of 24 eyes (83.3%) in the foveal bulge (-) group. The incidence of a disrupted ELM in the foveal bulge (+) group was significantly lower than that in the foveal bulge (-) group (*P* = .0124), and the incidence of an SRD in the foveal bulge (+) group was also significantly lower than that in the foveal bulge (-) group (*P* = .0017). At the initial visit, the foveal bulge could be detected in 6 of 7 eyes (85.7%) in the foveal

TABLE 2. Comparison of Eyes With or Without Foveal Bulge After Resolution of Macular Edema Associated With Branch Retinal Vein Occlusion

| | Foveal Bulge (+) (n = 7) | Foveal Bulge (-) (n = 24) | P Value |
|---------------------------------|--------------------------|---------------------------|---------|
| Age (years) | 59.1 ± 12.1 | 69.7 ± 5.6 | .0440 |
| Follow-up period (months) | 8.4 ± 5.4 | 7.3 ± 4.0 | .7210 |
| Initial examination | | | |
| LogMAR | 0.14 ± 0.13 | 0.45 ± 0.27 | .0034 |
| CFT (μm) | 300.4 ± 76.3 | 560.1 ± 168.6 | .0011 |
| Disrupted ELM n (%) | 1 (14.3%) | 17 (70.8%) | .0124 |
| Detection of SRD n (%) | 1 (14.3%) | 20 (83.3%) | .0017 |
| Detection of foveal bulge n (%) | 6 (85.7%) | 1 (4.2%) | <.0001 |
| Final examination | | | |
| LogMAR | -0.06 ± 0.04 | 0.24 ± 0.21 | <.0001 |
| CFT (μm) | 237.0 ± 17.7 | 217.3 ± 19.3 | .0248 |
| ONL thickness (μm) | 110.5 ± 10.7 | 105.0 ± 12.1 | .3443 |
| Photoreceptor IS length (μm) | 28.8 ± 1.6 | 27.9 ± 1.6 | .2631 |
| Photoreceptor OS length (μm) | 58.6 ± 3.8 | 44.0 ± 7.8 | .0001 |

CFT = central foveal thickness; ELM = external limiting membrane; IS = inner segment; logMAR = logarithm of minimal angle of resolution; ONL = outer nuclear layer; OS = outer segment; SRD = serous retinal detachment.

bulge (+) group, but the foveal bulge could be detected in only 1 of the 24 eyes (4.2%) in the foveal bulge (-) group ($P < .0001$).

• **CORRELATIONS BETWEEN CLINICAL CHARACTERISTICS AND FINAL VISUAL ACUITY:** We classified 31 BRVO eyes into eyes with a decimal BCVA of ≥ 1.0 ($n = 9$) and eyes with a decimal BCVA of < 1.0 ($n = 22$; Table 3). Seven of 9 eyes (77.8%) with a decimal BCVA of ≥ 1.0 had a foveal bulge after resolution of the macular edema. In eyes with a decimal BCVA of < 1.0 , none had a foveal bulge. This difference in the number of eyes with a foveal bulge after resolution of the macular edema was significant ($P < .0001$). Furthermore, the initial clinical characteristics (eg, age, BCVA, CFT, integrity of the ELM, SRD, and foveal bulge) were significantly different in the eyes with a decimal BCVA of ≥ 1.0 and the eyes with BCVA of < 1.0 .

• **CASE REPORTS:** *Case 1 with foveal bulge.* A 53-year-old woman presented with macular edema associated with BRVO. Her decimal BCVA at the initial visit was 0.4,

TABLE 3. Comparison of Eyes With or Without Decimal Best-Corrected Visual Acuity of ≥ 1.0 After Resolution of Macular Edema Associated With Branch Retinal Vein Occlusion

| | Decimal BCVA of ≥ 1.0 (n = 9) | Decimal BCVA of < 1.0 (n = 22) | P Value |
|---------------------------------|------------------------------------|----------------------------------|---------|
| Age (y) | 59.8 ± 10.6 | 70.4 ± 5.2 | .0088 |
| Follow-up period (mo) | 7.9 ± 4.8 | 7.3 ± 4.1 | .8780 |
| Initial examination | | | |
| LogMAR | 0.14 ± 0.14 | 0.48 ± 0.27 | .0005 |
| CFT (μm) | 343.0 ± 167.8 | 566.3 ± 155.9 | .0017 |
| Disrupted ELM n (%) | 2 (22.2%) | 16 (72.7%) | .0166 |
| Detection of SRD n (%) | 2 (22.2%) | 19 (86.4%) | .0013 |
| Detection of foveal bulge n (%) | 6 (66.7%) | 1 (4.5%) | .0007 |
| Final examination | | | |
| LogMAR | -0.04 ± 0.04 | 0.27 ± 0.21 | <.0001 |
| CFT (μm) | 232.9 ± 18.0 | 217.2 ± 20.0 | .0476 |
| ONL thickness (μm) | 109.3 ± 9.6 | 105.1 ± 12.6 | .5136 |
| Photoreceptor IS length (μm) | 28.5 ± 1.5 | 28.0 ± 1.6 | .4558 |
| Photoreceptor OS length (μm) | 56.6 ± 6.1 | 43.5 ± 7.6 | .0002 |
| Detection of foveal bulge n (%) | 7 (77.8%) | 0 (0%) | <.0001 |

BCVA = best-corrected visual acuity; CFT = central foveal thickness; ELM = external limiting membrane; IS = inner segment; logMAR = logarithm of minimal angle of resolution; ONL = outer nuclear layer; OS = outer segment; SRD = serous retinal detachment.

and the SDOCT image showed macular edema, which was located internal to the ELM line without contacting the line. A foveal bulge was present (Figure 2, Top). Seven months after the resolution of the macular edema, the OCT image showed a continuous IS/OS line at the central fovea and the presence of a foveal bulge (Figure 2, Bottom). Her BCVA improved to 1.2.

Case 2 without foveal bulge. A 71-year-old man presented with macular edema associated with BRVO. At the initial visit, his decimal BCVA was 0.3 and the SDOCT image showed significant macular edema with an SRD in contact with the ELM line. A foveal bulge could not be detected (Figure 3, Top left). Six months after the resolution of the macular edema, his BCVA improved to 0.7, and the OCT image showed an absence of a foveal bulge (Figure 3, Top right). However, the IS/OS line was continuous at the central fovea.

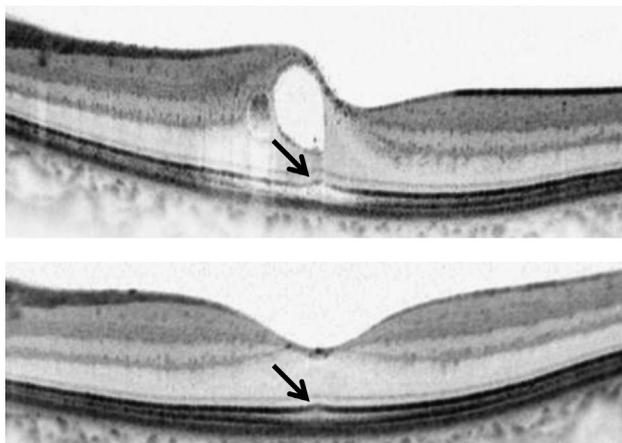


FIGURE 2. Spectral-domain optical coherence tomography (SDOCT) image of an eye with branch retinal vein occlusion in a 53-year-old woman. (Top) At the initial visit, the SDOCT image shows macular edema, which was located internal to the external limiting membrane line without contacting the line. A foveal bulge can be seen (arrow). The decimal best-corrected visual acuity (BCVA) was 0.4. (Bottom) Seven months after resolution of the macular edema, the SDOCT image shows the presence of a foveal bulge (arrow). The BCVA was 1.2.

Case 3 without foveal bulge. A 77-year-old man presented with macular edema associated with BRVO. At the initial visit, his decimal BCVA was 0.4, and the SDOCT image showed severe macular edema, which was located internal but not connected to the ELM line. A flat IS/OS line without a foveal bulge was present (Figure 3, Bottom left). Four months after the resolution of the macular edema, the BCVA was 0.5 and OCT image showed an absence of a foveal bulge (Figure 3, Bottom right).

DISCUSSION

OUR RESULTS SHOWED THAT THE FINAL DECIMAL BCVA varied from 0.3-1.2 after a resolution of the macular edema even with an intact IS/OS line at the central fovea. Thus, it appears that the presence of an intact IS/OS line at the central fovea may not be an indicator of good visual recovery.

Our study indicates that the presence of the foveal bulge in the SDOCT image is a good indicator of better BCVA after resolution of the macular edema associated with BRVO. Our results showed that the percentage of eyes with foveal bulge after resolution of the macular edema was only 22.6% in the BRVO group but was 100% in the control group. In the BRVO group, the BCVA was significantly better in the eyes with foveal bulge than in eyes without a foveal bulge, despite the fact that all eyes had a complete resolution of the macular edema and had an intact IS/OS line. All 7 eyes with a foveal bulge after resolution of the macular edema had a decimal BCVA of ≥ 1.0 .

In contrast, 22 of 24 eyes without foveal bulge after resolution of macular edema had a BCVA < 1.0 . Thus, we suggest that not only an intact IS/OS line but also a foveal bulge is important for a BCVA of ≥ 1.0 after resolution of the macular edema.

Maldonado and associates reported on the morphologic development of the human fovea from the SDOCT images.¹⁶ Accompanying the development of the fovea, the IS/OS line had a central bulge at the fovea. In an earlier histologic study on the development of the fovea, there was a centripetal migration of the cone photoreceptors toward the central fovea.^{17,18} The density of cone photoreceptors at the fovea increased from 11 200/mm² at a fetal age of 11 weeks to approximately 200 000/mm² in the adult eye.¹⁷ Then, the foveal cone OS underwent both a thinning in width and an increase in length. The foveal cone OS is approximately 1.2 μm wide and 3 μm long at birth and becomes 1.0 μm wide and 41-50 μm long in adults.¹⁷ The centripetal migration of the cone cells and the thinning of individual foveal cone OSs resulted in an increase in the foveal cone OS density.^{17,18} We suggest that not only the elongation of the foveal cone OS but also the foveal cone OS density are important components that contribute to construct the foveal bulge in normal eyes.

Histologic studies have shown that the severe macular edema can affect the photoreceptor layer in the fovea, which then results in photoreceptor dysfunction and photoreceptor cell loss.¹⁹ In our study, the CFT was significantly thinner and the photoreceptor OS length was also significantly shorter in the foveal bulge (-) group than in the foveal bulge (+) group. Thus, we suggest that the macular edema damages the foveal photoreceptors, which results in the absence of a foveal bulge. We examined only patients who had an intact IS/OS line at the central fovea after resolution of the macular edema associated with BRVO. Thus, patients with more severe macular edema were probably not included in our study, and this might explain our results that the ONL thickness did not significantly differ between the foveal bulge (+) group and the foveal bulge (-) group.

The initial clinical characteristics (eg, age, BCVA, CFT, integrity of the ELM, SRD, and foveal bulge beneath the fovea) were significantly correlated with the final BCVA. Several studies have shown that the baseline BCVA, age, and presence of an SRD are predictive factors for the final BCVA in eyes with macular edema associated with BRVO.²⁰⁻²² Yamaike and associates reported that an intact ELM line suggested an integrity of the photoreceptor layer.²³ The ELM functions as a barrier within the retina and consists of zonula adherens between the Müller cells and photoreceptor cells. Recently, Tsujikawa and associates reported that a breakdown of the barrier function of the ELM leads to a movement of intraretinal fluid into the subretinal space, resulting in an SRD.² Macular edema in contact with the ELM may lead to disruptions of the photoreceptor integrity (ie, the foveal bulge), which

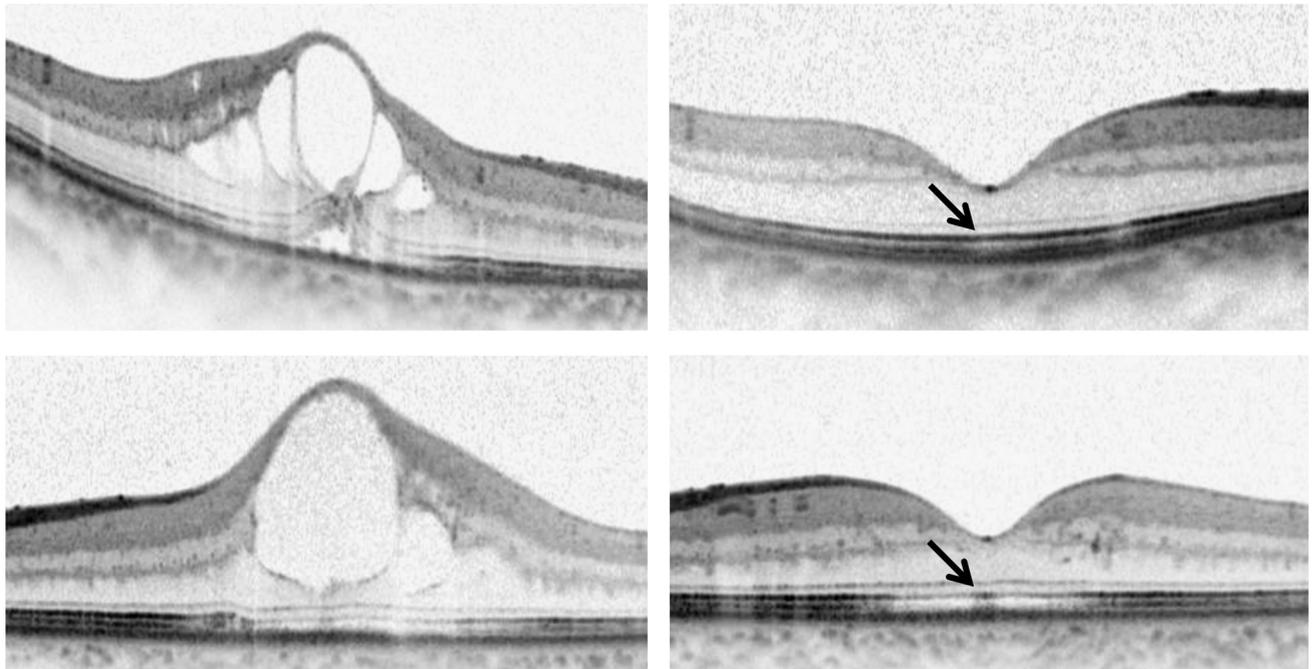


FIGURE 3. Spectral-domain optical coherence tomography (SDOCT) images of eyes with branch retinal vein occlusion. (Top left) SDOCT image from the eye of a 71-year-old man at the initial visit showed severe macular edema, which contacted the external limiting membrane (ELM) line. A disrupted ELM and a serous retinal detachment can also be seen. A foveal bulge cannot be seen. The decimal best-corrected visual acuity (BCVA) was 0.3. (Top right) Six months after resolution of the macular edema, the SDOCT image shows an absence of a foveal bulge (arrow), while the continuity of the photoreceptor inner segment/outer segment (IS/OS) line can be seen in the central fovea. The BCVA was 0.7. (Bottom left) SDOCT image from the eye of a 77-year-old man at the initial visit showed severe macular edema, which was located internal to the ELM line without contacting the line and a flat IS/OS line. The BCVA was 0.4. (Bottom right) Four months after resolution of the macular edema, the SDOCT image shows an absence of a foveal bulge (arrow). A continuity of the IS/OS line can be seen at the central fovea. The BCVA was 0.5.

can affect the BCVA. All 7 eyes with a foveal bulge at the initial visit also had an intact ELM. In these eyes, the macular edema was located internal to the ELM line and did not contact the ELM. Six of these 7 eyes with a foveal bulge at the initial visit had a foveal bulge and the BCVA was ≥ 1.0 after the resolution of the macular edema. We suggest that the presence of a foveal bulge in eyes with macular edema indicates that the photoreceptor integrity is preserved, which accounts for the better BCVA. It is noteworthy that 4 eyes with spontaneously resolved macular edema had an intact ELM and a foveal bulge at the initial visit. In addition, all 4 eyes had a decimal BCVA of ≥ 1.0 at the final visit. Thus, we suggest that eyes with an intact ELM and a foveal bulge be followed closely without any treatment, despite the presence of macular edema.

An association between the initial CFT and final BCVA is somewhat controversial. Ota and associates reported a significant correlation between the initial foveal thickness and final BCVA in BRVO patients with a persistent macular edema after the treatment.²⁴ However, other studies have reported no significant correlation between the baseline CFT and final BCVA.^{21,25} Tsujikawa and associates reported that the CFT of eyes with an SRD secondary to retinal vein occlusion was significantly thicker than that

of eyes without an SRD.² The thicker CFT, which represents the severity of macular edema, may lead to disruption of the ELM integrity. Thus, we suggest that a thicker CFT results in damage of the photoreceptors.

There are several limitations in this study. First, we studied only a small number of cases and the follow-up time was short. Although 6 of 7 eyes in the foveal bulge (+) group had a foveal bulge at the initial visit, the foveal bulge in another eye in the foveal bulge (+) group was detected 4 months after the resolution of the macular edema. It may be possible that the eyes in the foveal bulge (-) group will recover the foveal bulge with longer follow-up durations. Thus, additional studies with a larger number of patients and longer follow-up times are needed. Second, this study was a single-site retrospective analysis. Therefore, it may be necessary to confirm our findings at another medical center. Third, although all of the 31 unaffected fellow eyes in our patients with an age range of 49-81 years had a foveal bulge in this study, as best we know, no study has reported on an age-associated incidence of a foveal bulge. If the incidence of the foveal bulge varies with age, then that may have affected the findings. Thus, it is important to determine whether the foveal bulge varies with age.

In conclusion, determining the presence of a foveal bulge may be a useful parameter to determine the visual

properties of eyes with macular edema and eyes with resolved macular edema associated with BRVO.

ALL AUTHORS HAVE COMPLETED AND SUBMITTED THE ICMJE FORM FOR DISCLOSURE OF POTENTIAL CONFLICTS OF INTEREST and none were reported. The authors indicate no funding support. Contributions of authors: design of the study (T.H.); conduct of the study (T.H., N.O.); collection of the data (T.H., M.O.); management of the data (T.H., M.O.); analysis of the data (T.H., M.O., T.U.); interpretation of the data (T.H., M.O., T.U.); preparation of the manuscript (T.H.); review and approval of the manuscript (N.O.).

REFERENCES

1. Rogers SL, McIntosh RL, Lim L, et al. Natural history of branch retinal vein occlusion: an evidence-based systematic review. *Ophthalmology* 2010;117(6):1094–1101.
2. Tsujikawa A, Sakamoto A, Ota M, et al. Serous retinal detachment associated with retinal vein occlusion. *Am J Ophthalmol* 2010;149(2):291–301.
3. Spaide RF, Lee JK, Klancnik JK Jr, Gross NE. Optical coherence tomography of branch retinal vein occlusion. *Retina* 2003;23(3):343–347.
4. Esrick E, Subramanian ML, Heier JS, et al. Multiple laser treatments for macular edema attributable to branch retinal vein occlusion. *Am J Ophthalmol* 2005;139(4):653–657.
5. Arnarsson A, Stefánsson E. Laser treatment and the mechanism of edema reduction in branch retinal vein occlusion. *Invest Ophthalmol Vis Sci* 2000;41(3):877–879.
6. Mandelcorn MS, Nrusimhadevara RK. Internal limiting membrane peeling for decompression of macular edema in retinal vein occlusion: a report of 14 cases. *Retina* 2004;24(3):348–355.
7. Chen SD, Sundaram V, Lochhead J, Patel CK. Intravitreal triamcinolone for the treatment of ischemic macular edema associated with branch retinal vein occlusion. *Am J Ophthalmol* 2006;141(5):876–883.
8. Scott IU, Ip MS, VanVeldhuisen PC, et al. A randomized trial comparing the efficacy and safety of intravitreal triamcinolone with standard care to treat vision loss associated with macular edema secondary to branch retinal vein occlusion: the Standard Care vs Corticosteroid for Retinal Vein Occlusion (SCORE) study report 6. *Arch Ophthalmol* 2009;127(9):1115–1128.
9. Cekiç O, Chang S, Tseng JJ, et al. Intravitreal triamcinolone injection for treatment of macular edema secondary to branch retinal vein occlusion. *Retina* 2005;25(7):851–855.
10. Campochiaro PA, Heier JS, Feiner L, et al. Ranibizumab for macular edema following branch retinal vein occlusion: six-month primary end point results of a phase III study. *Ophthalmology* 2010;117(6):1102–1112.
11. Ota M, Tsujikawa A, Murakami T, et al. Association between integrity of foveal photoreceptor layer and visual acuity in branch retinal vein occlusion. *Br J Ophthalmol* 2007;91(12):1644–1649.
12. Thomas MG, Kumar A, Mohammad S, et al. Structural grading of foveal hypoplasia using spectral-domain optical coherence tomography a predictor of visual acuity? *Ophthalmology* 2011;118(8):1653–1660.
13. Mohammad S, Gottlob I, Kumar A, et al. The functional significance of foveal abnormalities in albinism measured using spectral-domain optical tomography. *Ophthalmology* 2011;118(8):1645–1652.
14. Scholl HP, Birch DG, Iwata T, Miller NR, Goldberg MF, Chen CJ. Characterizing the phenotype and genotype of a family with occult macular dystrophy. *Arch Ophthalmol* 2012;130(12):1554–1559.
15. Al-Haddad CE, El Mollayess GM, Mahfoud ZR, Jaafar DF, Bashshur ZF. Macular ultrastructural features in amblyopia using high-definition optical coherence tomography. *Br J Ophthalmol* 2013;97(3):318–322.
16. Maldonado RS, O'Connell RV, Sarin N, et al. Dynamics of human foveal development after premature birth. *Ophthalmology* 2011;118(12):2315–2325.
17. Yuodelis C, Hendrickson A. A qualitative and quantitative analysis of the human fovea during development. *Vision Res* 1986;26(6):847–855.
18. Hendrickson A, Possin D, Vajzovic L, Toth CA. Histologic development of the human fovea from midgestation to maturity. *Am J Ophthalmol* 2012;154(5):767–778.
19. Tso MO. Pathology of cystoid macular edema. *Ophthalmology* 1982;89(8):902–915.
20. Kondo M, Kondo N, Ito Y, et al. Intravitreal injection of bevacizumab for macular edema secondary to branch retinal vein occlusion: results after 12 months and multiple regression analysis. *Retina* 2009;29(9):1242–1248.
21. Kang HM, Chung EJ, Kim YM, Koh HJ. Spectral-domain optical coherence tomography (SD-OCT) patterns and response to intravitreal bevacizumab therapy in macular edema associated with branch retinal vein occlusion. *Graefes Arch Clin Exp Ophthalmol* 2013;251(2):501–508.
22. Ohashi H, Oh H, Nishiwaki H, Nonaka A, Takagi H. Delayed absorption of macular edema accompanying serous retinal detachment after grid laser treatment in patients with branch retinal vein occlusion. *Ophthalmology* 2004;111(11):2050–2056.
23. Yamaike N, Tsujikawa A, Ota M, et al. Three-dimensional imaging of cystoid macular edema in retinal vein occlusion. *Ophthalmology* 2008;115(2):355–362.
24. Ota M, Tsujikawa A, Murakami T, et al. Foveal photoreceptor layer in eyes with persistent cystoid macular edema associated with branch retinal vein occlusion. *Am J Ophthalmol* 2008;145(2):273–280.
25. Hoeh AE, Ruppenstein M, Ach T, Dithmar S. OCT patterns of macular edema and response to bevacizumab therapy in retinal vein occlusion. *Graefes Arch Clin Exp Ophthalmol* 2010;248(11):1567–1572.



Biosketch

Taiji Hasegawa, MD, graduated from the Fukushima Medical University School of Medicine, Fukushima, Japan in 2006. He is currently an Assistant Professor of the Department of Ophthalmology, Nara Medical University School of Medicine, Kashihara, Japan. He specializes in macular diseases.