Relationship between preoperative foveal microstructure and visual acuity in macula-off rhegmatogenous retinal detachment : imaging analysis by swept source optical coherence tomography

Abbreviated title:

SS-OCT in retinal detachment

Authors:

Hiroshi Noda*, MD, Shuhei Kimura*, MD, PhD, Yuki Morizane, MD, PhD, Shinji Toshima, MD, Mio Morizane Hosokawa, MD, Yusuke Shiode, MD, PhD, Shinichiro Doi, MD, Kosuke Takahashi, MD, Mika Hosogi, MD, Atsushi Fujiwara, CO, PhD, Fumio Shiraga, MD, PhD

* Hiroshi Noda and Shuhei Kimura contributed equally to this work.

Institutional Affiliation:

Department of Ophthalmology, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, 2-5-1 Shikata-cho Kita-ku, Okayama City, Okayama 700-8558, Japan

Corresponding author:

Yuki Morizane, MD, PhD

Department of Ophthalmology, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, 2-5-1 Shikata-cho Kita-ku, Okayama City, Okayama 700-8558, Japan

E-mail: moriza-y@okayama-u.ac.jp

Competing interests

Conflicts of Interest:

There are no conflicting or proprietary interests to declare for any of the authors.

Financial disclosure:

None of the authors received funding for this work from any external organization.

Keywords

ellipsoid zone, external limiting membrane, foveal microstructure, rhegmatogenous retinal detachment, swept source optical coherence tomography

Brief summary statement

We visualized preoperative foveal microstructures of patients with macula-off rhegmatogenous retinal detachment using swept source optical coherence tomography and found that continuity of the external limiting membrane and the ellipsoid zone is a novel prognostic factor for postoperative visual acuity.

Abstract

Purpose: To visualize the foveal microstructures of macula-off rhegmatogenous retinal detachment (RRD) using swept source optical coherence tomography (SS-OCT) before and after surgery and to investigate the relationship between foveal microstructures and postoperative visual acuity.

Methods: We retrospectively analyzed 42 eyes of 42 consecutive patients diagnosed as macula-off RRD who underwent anatomically successful repair surgery and were followed up for 6 months. We used SS-OCT to investigate the relationship between pre- and postoperative continuity of both the external limiting membrane (ELM) and the ellipsoid zone (Ez) and pre- and postoperative best-corrected visual acuity (BCVA).

Result: Both preoperative ELM and Ez were continuous in 9 eyes (21%; ELM+/Ez+ eyes), only the ELM was continuous in 25 eyes (60%; ELM+/Ez- eyes), and neither were continuous in 8 eyes (19%; ELM-/Ez- eyes). The postoperative BCVA in ELM+/Ez+ eyes (-0.05±0.04 in logarithm of the minimum angle of resolution units, Snellen equivalent 20/18) was significantly better than that in both ELM+/Ez- eyes (0.16±0.16, 20/29; P=0.03) and ELM-/Ez- eyes

(0.86±0.37, 20/145; P<0.001). The postoperative BCVA was significantly better in ELM+/Ez- eyes than ELM-/Ez- eyes (P<0.001).

Conclusion: In eyes with macula-off RRD, preoperative continuity of the ELM and the Ez may be a predictor of postoperative BCVA.

Introduction

Patients with macula-off rhegmatogenous retinal detachment (RRD) can have poor visual recovery, specific color vision defects, and metamorphopsia even after successful retinal reattachment.[1-3] Several factors have been reported as predictors of postoperative best-corrected visual acuity (BCVA) in eyes with macula-off RRDs that undergo retinal reattachment, including preoperative BCVA,[4,5] duration of retinal detachment,[6,7] foveal detachment height,[5,8-11] the distance from the central fovea to the nearest undetached retinal point, [5] patient age,[12] postoperative onset of epiretinal membrane,[13,14] and foveal microstructure.[15-18] Results from studies using time domain optical coherence tomography (TD-OCT) and spectral domain OCT (SD-OCT) have reported that postoperative continuity of the external limiting membrane (ELM) and ellipsoid zone (Ez),[1,16,18-22] preoperative outer retinal corrugation (ORC),[17,21,23,24] pre- and postoperative macular edema (ME),[23,25,26] postoperative retinal thickness,[15,27-31] and postoperative foveal bulge[32] are significant predictors of postoperative BCVA. Among these, postoperative continuity of the ELM/Ez, which is representative of photoreceptor integrity, has been reported to be strongly correlated with postoperative BCVA. However, because it is difficult to obtain high-resolution images of the ELM/Ez in detached retinas using TD-OCT and/or SD-OCT,[23,25,26] the relationship between preoperative continuity of the ELM/Ez and postoperative BCVA remains unknown.

Swept source OCT (SS-OCT) is a third generation OCT technique that was developed after TD-OCT and SD-OCT.[33-35] By using a wavelength-tunable laser and a balanced photo detector, SS-OCT achieves deeper penetration and a faster acquisition time. These advantages of SS-OCT overcome the difficulties of TD-OCT and SD-OCT and allow visualization of foveal microstructures in the detached retina. However, to our knowledge, no reports have used SS-OCT to analyze preoperative foveal microstructures in eyes with macula-off RRD.

In this study, we used SS-OCT to visualize foveal microstructures in detached retinas and investigated the relationships between pre- and postoperative foveal microstructures and postoperative BCVA.

Patients and Methods

Study design and patients

We retrospectively reviewed 116 consecutive eyes of 113 patients with RRD who underwent surgical treatment. All patients were treated at Okayama

University Hospital between January and December in 2016. This study was approved by the Institutional Review Board of the Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, and all procedures were in accordance with the tenets of the Declaration of Helsinki. Each patient was informed of risks and benefits of the surgery and provided written, informed consent. Patients were excluded if they showed signs of other ocular diseases, such as vitreous hemorrhage, macular hole, epiretinal membrane, age-related macular degeneration, retinal vein occlusion, or proliferative vitreoretinopathy..

Ophthalmic examinations

All patients underwent comprehensive ophthalmologic examinations before and 6 months after surgery. These examinations included measurement of BCVA with refraction using the 5-m Landolt C acuity chart and indirect and contact lens slit-lamp biomicroscopy. All eyes were examined by SS-OCT using a commercially available instrument (DRIOCT-1 Atlantis, TOPCON Corporation, Tokyo, Japan) before and 6 months after surgery. We used horizontal and vertical OCT images that included the fovea, and we termed ”macula-off retinal detachment” as any retinal detachment detect in macular area including the fovea in both vertical and horizontal OCT images. The foveal detachment height was measured between the inner border of the retinal pigment epithelium and the outer border of the backreflection.[21] We also assessed the presence of preoperative ORC and ME.[23] Analyses of OCT images were performed by three retinal specialists (H.N., S.K., and S.T.).

Main outcome measures

The main outcome measures were the correlations between preoperative foveal microstructures (ELM, Ez), foveal detachment height, ORC, ME, and pre- and postoperative BCVA in patients with macula-off RRD.

Surgical procedure

Based on the direction of the patient’s physician, each patient underwent either pars plana vitrectomy (PPV) or scleral buckling (SB). When PPV was performed, patients underwent 25-gauge transconjunctival, sutureless, microincision vitrectomy using the Constellation Vision System (Alcon Laboratories, Inc., Fort Worth, TX, USA). We released the vitreous traction around the retinal breaks and drained the subretinal fluid from the intentional retinal hole. Then, we performed a total gas-fluid exchange using a 20% SF_6 gas tamponade and endo-laser photocoagulation to create chorioretinal adhesions. We also performed cataract surgery in elderly patients (i.e., patients over 50 year old). When SB was performed, chorioretinal adhesions were created with cryopexy around the retinal breaks. A silicone explant was used to support the peripheral retinal breaks. External drainage of subretinal fluid was performed when necessary.

Statistical analysis

BCVAs were recorded as decimal values and converted to the logarithm of the minimum angle of resolution (logMAR) for statistical analysis. All visual acuity results are presented as logMAR units with Snellen equivalents in parentheses. All statistical analyses were performed using SPSS ver. 22.0 (IBM, Armonk, NY, USA). To evaluate surgical outcomes, pre- and postoperative BCVA values were compared using a one-way ANOVA with a Bonferroni correction, and categorical data were analyzed using Fisher's exact test. Comparisons of preoperative and postoperative BCVA values were performed using Pearson's correlation analysis. The correlations between foveal detachment height and pre- and postoperative BCVAs were performed using Spearman's correlation analysis. P values less than 0.05 were considered significant. Data are presented as mean ± SD.

Results

Of the 113 eyes of 116 patients with RRD who underwent surgical treatment at our institution, 42 eyes showed preoperative foveal detachment and retinal microstructures that were evaluable with SS-OCT. Among the 42 eyes, 31 eyes underwent PPV and 11 eyes underwent SB. Among the 31 eyes that underwent PPV, 13 eyes were preoperatively pseudophakic and 18 eyes were preoperatively phakic. All phakic eyes underwent PPV, phacoemulsification and aspiration, and intraocular lens implantation simultaneously.

The mean pre- and postoperative BCVAs were 0.69 ± 0.51 (20/98) and 0.25 ± 0.37 (20/36), respectively. There was a significant positive correlation between preoperative and postoperative BCVA values ($y = 0.37x - 0.06$, r = 0.51, P < 0.01; see Figure, Supplemental Digital Content 1, which shows the correlation between preoperative and postoperative BCVA). Age was not significantly correlated with postoperative BCVA (P = 0.94). The mean postoperative BCVAs for patients who underwent PPV and explantation were 0.25 ± 0.32 (20/36) and 0.24 ± 0.50 (20/35), respectively (P = 0.98).

Classification of eyes based on preoperative foveal microstructure visualized with SS-OCT

We used SS-OCT to analyze preoperative foveal microstructure, and we classified eyes according to whether they showed continuity of the ELM and the Ez (Figure 1). Eyes were considered to be in group A if both the ELM and the Ez were continuous (ELM+/Ez+), group B if the ELM was continuous but the Ez was disrupted (ELM+/Ez-), and group C if both the ELM and the Ez were disrupted (ELM-/Ez-). None of the eyes showed a disrupted ELM and continuous Ez. There were no significant differences in age, gender, or surgical procedure among these 3 groups (Table 1).

Relationship between preoperative foveal microstructure and pre- and postoperative BCVA

The mean preoperative BCVA values of groups A, B, and C were 0.27 ± 0.43 (20/37), 0.65 ± 0.40 (20/89), and 1.29 ± 0.36 (20/390), respectively. The preoperative BCVA of group C was significantly worse than that of groups A and B ($P < 0.001$, $P < 0.01$, respectively; Figure 2). The difference between the preoperative BCVA of groups A and that of group B was not significant ($P = 0.06$). The postoperative BCVAs of group A, B, and C were -0.05 ± 0.04 (20/18), 0.16 ± 0.16 (20/29), and 0.86 ± 0.37 (20/145), respectively. The postoperative BCVA of group A was significantly better than that of groups B and C ($P = 0.03$, $P < 0.001$, respectively), and the postoperative BCVA of group B was significantly better than that of group C ($P < 0.001$). The mean postoperative BCVA was significantly improved compared to the preoperative BCVA in all groups (group A: $P = 0.04$, group B: $P < 0.001$, group C: $P = 0.03$).

Relationship between postoperative foveal microstructure and postoperative BCVA

We used SS-OCT to analyze postoperative foveal microstructure, and we classified the eyes according to whether they showed continuity of the ELM and the Ez. Similar to the preoperative groups, group A’ included eyes in which both the ELM and the Ez were continuous (ELM+/Ez+), group B' included eyes in which the ELM was continuous but the Ez was disrupted (ELM+/Ez-), and group C' included eyes in which both ELM and Ez were disrupted (ELM-/Ez-). As with the preoperative analysis, no eyes showed disrupted ELM and continuous Ez. The mean postoperative BCVAs of groups A', B', and C' were 0.06 ± 0.14 (20/23), 0.41 ± 0.28 (20/51), and 0.81 ± 0.43 (20/129), respectively (Figure 3A). The postoperative BCVA of group A' was significantly better than that of group B' and C' ($P < 0.01$, $P < 0.001$, respectively), and the postoperative BCVA of group B' was significantly better than that of group C' ($P < 0.01$).

Relationship between pre- and postoperative foveal microstructure

Figure 3B shows the postoperative foveal microstructure results for group of A, B, and C. In group A, all eyes showed postoperative continuity of both the ELM and the Ez. For group B, the Ez had recovered postoperatively 20 of 25 eyes (80%). In group C, all eyes showed postoperative discontinuity of the ELM and the Ez.

Relationship between other OCT parameters and pre- and postoperative BCVA

To investigate the correlations between preoperative height of foveal detachment and pre and postoperative BCVA, we analyzed 40 eyes excluding 2 eyes, because the RPE lines were not detected in SS-OCT images. We observed negative correlations between preoperative foveal detachment height and pre- and postoperative BCVA ($y = 0.0006\,x + 0.36$, r = 0.62, $P < 0.001$; $y = 0.0001\,x + 0.15$, r = 0.45, $P < 0.01$, respectively; Figure 4A and B). The mean preoperative foveal detachment heights in groups A, B, and C were 108.9 ± 64.3, 652.7 ± 389.0, and 871.6 ± 725.9 µm, respectively (Figure 5). The preoperative foveal detachment height in group A was significantly lower than were the respective heights in groups B and C (both $P < 0.01$). We also analyzed the relationship between pre- and postoperative ORC and preoperative BCVA. There was no significant difference in mean preoperative BCVA between the 14 eyes with preoperative ORC and the 28 eyes without preoperative ORC (0.86 ± 0.48 (20/145) and 0.62 ± 0.54 (20/83), respectively; P = 0.17). Similarly, there was no significant difference in mean postoperative BCVA between the eyes with or without ORC (0.32 ± 0.28 (20/42), 0.21 ± 0.41 (20/32), respectively; P = 0.35). Finally, we also assessed the relationship between preoperative ME and both pre- and preoperative BCVA. We found no significant difference in mean preoperative BCVA between the 17 eyes with preoperative ME and the 25 eyes without preoperative ME (0.75 ± 0.44 (20/112), 0.60 ± 0.61 (20/80), respectively; P = 0.36). Similarly, there was no significant difference in mean postoperative BCVA between eyes with preoperative ME and those without preoperative ME (0.31 ± 0.46 (20/41), 0.21 ± 0.29 (20/32), respectively; P = 0.39). Figure 6 shows representative cases from groups A, B, and C.

Discussion

According to our PubMed search of the Medline database, this is the first report to use SS-OCT to investigate the relationship between preoperative foveal microstructure and postoperative BCVA after anatomically successful repair of macula-off RRD. Before the development of SS-OCT, it was difficult to observe details of foveal microstructure in macula-off RRD using first and second-generation OCT, which includes TD-OCT and SD-OCT.[23,25,26] There are two possible reasons for this. First, the OCT laser lights used in these technologies barely reach the retinal outer layer in macula-off RRD because the detached retina is tilted in a more parallel direction with respect to the OCT laser beam. Second, the captured image is often blurred because of the high mobility of the detached retina and because of poor fixation because of central visual loss. In this study, we used SS-OCT, which has deeper penetration and a faster acquisition time,[23,25,26] to analyze preoperative foveal microstructures (ELM/Ez continuity), and our results indicate that preoperative foveal microstructure can be a predictor of postoperative visual acuity. Cho et al.[23] reported that there was no significant relationship between preoperative foveal microstructures imaged with SD-OCT and postoperative BCVA. However, several possible reasons could explain the conflicting results between that study and the present study, including differences in OCT image resolution, sample size (12 eyes in Cho et al.'s study vs 42 eyes in our study), and follow-up period (1 month in Cho et al.'s study vs 6 months in our study).

In this study, eyes whose postoperative foveal microstructures were intact showed better postoperative BCVA values (Figure 3A). This result is similar to those of past studies using SD-OCT imaging.[1,16,18-22] For example, Wakabayashi et al.[16] analyzed postoperative foveal microstructures with SD-OCT and reported that postoperative continuity of the ELM was a predictor of subsequent restoration of the photoreceptor layer. Interestingly, as shown in Figure 3B, the present study found that 80% (20 of 25) of eyes that were preoperatively classified as ELM+/Ez- improved to ELM+/Ez+ postoperatively. In contrast, no eyes originally classified as ELM-/Ez- postoperatively improved to ELM+/Ez+. Because ELM comprises optical density due to the difference in reflection of the zonular adherens and other junctional complexes binding the Muller cells and photoreceptors, preoperative disruption of the ELM signifies absence or regression of the Muller cells and/or the photoreceptor cells. Muller cell degeneration eventually induces decline of photoreceptor viability, thus, preoperative disruption of the ELM maybe a sign of the irreversible photoreceptor cell death[16,29,36] to a greater degree than is disruption of the Ez.

Past reports on RRD eyes in humans[37] and animal models[38-43] indicate that the duration of RRD is one of the most important factors related to apoptotic photoreceptor cell death. Disturbance of nutritional supply from the choriocapillaris,[44] inflammation following microglia migration,[45,46] and translocation of apoptosis-inducing factor[38] to photoreceptor nuclei are the expected mechanisms behind this time dependence. Although we were unable to obtain accurate data on duration of RRD from patients in the current study, we did find a significantly negative correlation between preoperative foveal detachment height and postoperative BCVA, consistent with previously published results.[5,8-11] Because longer duration of RRD has been shown to increase subretinal fluid and foveal detachment height,[10] our results support the current body of evidence that duration of foveal detachment is positively correlated with photoreceptor cell apoptosis.

This study has several important limitations. First, it was retrospective. Second, the retinal microstructures were subjectively evaluated and analyzed based on 2 foveal B-scans images. Therefore, it is possible that ORC was missed. Third, the number of cases was small, and the follow-up period was relatively short (6 months). Forth, the surgical procedure was not unified and we evaluated the data of the patients who underwent SB and PPV together. Although there was no significant difference in the frequency of surgical procedure among group A, B, and C (P = 0.29, Table 1), we consider it is necessary to investigate a larger number of the eyes with the same surgical procedure frequency in the future. Fifth, we did not account for cataract surgery potentially improving postoperative visual acuity. However, in this study, although the rate of the eyes that underwent PPV+PEA+IOL in group A (22%) was lower than those in group B and C (48%, 50%, respectively), postoperative BCVA in group A was better than those of group B and C. This fact increases the significance of our conclusion that preoperative continuities of the ELM and the Ez are important for better postoperative BCVA in eyes with macula-off RRD. Finally, we observed no correlations between postoperative BCVA and either ORC or ME despite the fact that these conditions have each been reported as predictors of postoperative BCVA.[17,21,23-26] Further studies with more cases and longer follow-up periods are thus needed.

In conclusion, our results suggest that preoperative continuity of the ELM and the Ez imaged by SS-OCT may be a predictor of postoperative BCVA in eyes with macula-off RRD.

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Figure legends

Figure 1

Classification of patients with macula-off rhegmatogenous retinal detachment based on preoperative foveal microstructures visualized with swept source optical coherence tomography.

ELM, external limiting membrane (arrow head); Ez, ellipsoid zone (arrow).

Figure 2

Relationship between preoperative foveal microstructures and pre- and postoperative BCVA

Error bars represent standard deviations. BCVA, best-corrected visual acuity. logMAR, logarithm of the minimum angle of resolution; ELM, external limiting membrane; Ez, ellipsoid zone, *$P < 0.05$; **$P < 0.01$.

Figure 3

A. Relationship between postoperative foveal microstructures and postoperative BCVA

B. Relationship between preoperative and postoperative foveal microstructures

Error bars represent standard deviations. BCVA, best-corrected visual acuity. logMAR, logarithm of the minimum angle of resolution. ELM, external limiting membrane; Ez, ellipsoid zone, *P < 0.01; **P < 0.001.

Figure 4

A. Correlation between preoperative foveal detachment height and preoperative BCVA

B. Correlation between preoperative foveal detachment height and postoperative BCVA

BCVA, best-corrected visual acuity; logMAR, logarithm of the minimum angle of resolution.

Figure 5

Relationship between preoperative foveal microstructure and foveal detachment height

ELM, external limiting membrane; Ez, Ellipsoid zone, n.s. not significant, *P < 0.01.

Figure 6

Three representative cases of macula-off rhegmatogenous retinal detachment with differing preoperative foveal microstructures.

A–C, preoperative color fundus photographs. D–F, preoperative swept source optical coherence tomography (SS-OCT) images. G–I, postoperative SS-OCT B-scan images. All of the SS-OCT images are vertical scan images and the left side of each image being superior, and the right side of each image being inferior.

All three cases had macula-off rhegmatogenous retinal detachment (A–F). Black arrowheads in A, B, and C represent the borders of retinal detachment.

Case 1 (A, D, and G): The patient is a 33-year-old male with intact external limiting membrane (ELM, white arrowheads in D) and intact ellipsoid zone (Ez, white arrows in D) in preoperative SS-OCT images. Preoperative best-corrected visual acuity (BCVA) was 20/20. The ELM and Ez were intact postoperatively, and postoperative BCVA was 20/17 (ELM, white arrowhead and Ez, white arrows in G).

Case 2 (B, E, and H): The patient is a 60-year-old female with intact ELM (white arrowheads in E) and disrupted Ez (white arrows in E) continuity in preoperative

SS-OCT images. Preoperative BCVA was 20/50. The postoperative ELM continuity remained intact (white arrowheads in H), and Ez continuity was restored (white arrows in H). Postoperative BCVA was improved to 20/33.

Case 3 (C, F, and I): The patient is a 21-year-old male with disrupted ELM (white arrowheads in F) and Ez (white arrow in F) continuity in preoperative SS-OCT images. Preoperative BCVA was 20/662. The postoperative ELM continuity was intact (white arrowheads in I), but Ez continuity remained disrupted (white arrows in I). Postoperative BCVA was 20/200.

Supplemental Digital Content 1.tiff

Correlation between preoperative and postoperative BCVA

BCVA, best-corrected visual acuity; logMAR, logarithm of the minimum angle of resolution.