Recovery of photoreceptor inner and outer segment layer thickness after reattachment of rhegmatogenous retinal detachment

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ABSTRACT

Aims To evaluate the recovery of retinal function and the thicknesses of the photoreceptor inner (IS) and outer segment (OS) layers after a reattachment of a rhegmatogenous retinal detachment (RRD).

Methods 49 eyes of 49 patients (mean age, 57.4 ±10.3 years) with successfully reattached RRD were retrospectively studied. Spectral-domain optical coherence tomography was used to obtain images of the foveal area, and the thicknesses of the IS and OS were measured before and 1, 3, 6 and 12 months after surgery. The thicknesses of the corresponding structures of the healthy fellow eye served as control.

Results The thickness of the IS layer was 20.4±5.0 μm and that of the OS layer was 34.4±9.7 at 1 month after surgery, which was significantly thinner than the IS (28.9±2.9) and OS (55.4±5.2) layers of the fellow eyes. The thicknesses gradually increased and were not significantly different from that in the fellow eye at 12 months (IS, 28.4±4.4 μm and OS, 50.7±6.6 μm). The IS and OS thicknesses at 1 month after surgery in eyes that had a decimal visual acuity of 1.0 at 6 months were significantly thicker than those in eyes that had a visual acuity of <1.0.

Conclusions The increase in the thicknesses of the IS and OS layers of the photoreceptors during the recovery phase of eyes with RRD indicates that the recovery process was slow and gradual. Quantitative analysis of the IS and OS thicknesses may be useful to follow the disease process.

INTRODUCTION

A rhegmatogenous retinal detachment (RRD) causes anatomical degeneration of the photoreceptor outer segments (OSs), resulting in a decrease in the visual acuity (VA). Reattachment of the retina leads to a recovery of the OSs and vision. However, the degree of visual recovery differs among patients despite successful reattachment in all.[1] It has been reported that the degree of recovery is related to the preoperative VA and the presence of a foveal detachment.[2] The limited visual recovery after successful retinal reattachment may be due to macular abnormalities such as the presence of an epiretinal membrane, cystoid macular oedema,[1] retinal folds[3] and a persistent foveal detachment.[4 5]

Spectral-domain optical coherence tomography (SD-OCT) has been used to evaluate the microstructures of the photoreceptors. A significant association was found between the final VA and the integrity of the microstructures of the photoreceptors[6] in several types of retinal diseases.[5 7 8] In addition, recent improvements in the resolution of OCT instruments have made it possible to obtain more precise evaluations of the retinal microstructures, that is, not only the integrity of each structure[5 7 8] but also a quantitative analysis on the degree of integrity.[9–15]

The purpose of this study was to determine the thicknesses of the inner segment (IS) and OS layers of the photoreceptors (IS thickness and OS thickness) in the SD-OCT images before and after a reattachment of an RRD. We also followed the recovery of the best-corrected visual acuity (BCVA) during the recovery process.

PATIENTS AND METHODS

The inclusion criterion was the patient who underwent pars plana vitrectomy (PPV) for unilateral RRD, the eye for which OCT image at 1, 3, 6 or 12 months' postoperative periods was available. The eyes that required second surgery, the eyes with persisted foveal detachment at any of the 1, 3, 6 or 12 months' postoperative periods, the eyes that developed epiretinal membrane after surgery and the eyes with accompanying eye disease that may affect each of the retinal layer thickness such as retinitis pigmentosa and retinal vein occlusion were excluded from the study.

In total, 49 eyes of 49 patients that had a successful reattachment of a unilateral RRD with macular involvement were evaluated. There were 39 men and 10 women, and their mean age was 57.4 ±10.3 years (±SD). The surgery consisted of PPV in 32 eyes, and combined PPV and encircling scleral buckling in 17 eyes. Combined cataract surgery was done in 31 eyes. The tamponade was air in 38 eyes, sulfur hexafluoride in 6 eyes and silicone oil in 5 eyes.

The entire macular area was scanned with an SD-OCT instrument (Cirrus OCT; Carl Zeiss Meditec) with scan lengths of 9 mm for horizontal scans and 6 mm for vertical scans. High-quality images were obtained by using the five-line raster mode. The distance between the internal limiting membrane (ILM) and the external limiting membrane (ELM) was taken to be the ILM-ELM thickness, the distance between the inner border of the ELM and the ellipsoid zone (EZ),[16] which had previously been called as the photoreceptor IS and OS junction line, was taken to be the IS thickness, and the distance between the EZ and the inner border of the retinal pigment epithelium (RPE) was taken to be the OS thickness. The measurements were made on the OCT images passing through the

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fovea and were made with the software of the system (figure 1). Each thickness was calculated by averaging the values of the vertical and horizontal images. An experienced investigator (GT) who was masked to the patients' information including the time after surgery and the BCVA made the measurements. Scans with a signal strength of >7/10 were considered appropriate, and a representative image was selected for the measurements.

The mean thicknesses of the ILM-ELM, IS and OS of the diseased eyes in the SD-OCT images were determined before the surgery (baseline) and at 1, 3, 6 and 12 months after the surgery. The thicknesses of the corresponding layers in the healthy fellow eye served as control.

The BCVA was measured with a Landolt chart, and the decimal values were converted to the logarithm of the minimum angle of resolution (logMAR) units. Mann–Whitney U tests were used to assess the significance of the changes from the baseline for the BCVA and changes in the thickness of each segment of the photoreceptor. For comparisons between the two groups, the eyes were divided into two groups according to the BCVA at 6 months after surgery; Group G consisted of eyes whose BCVA was 1.0 (Snellen 20/20), and group P consisted of eyes whose BCVA was <1.0. Mann–Whitney U tests were used to determine whether the differences were significant. Pearson's correlation coefficient was used to determine the correlation between the BCVA at 6 month and thickness of each retinal layer. p Values <0.05 were taken to be statistically significant.

RESULTS

The mean±SD of the BCVA of the eyes with RRD before surgery was 1.09±0.65 logMAR units. A significant improvement was observed at 1, 3, 6 and 12 months compared with the baseline BCVA after surgery (figure 2). The mean interval between the diagnosis and surgery was 11.2±15.9 days.

The changes in the mean thicknesses of the ILM-ELM, IS and OS are shown in figure 3. The IS and OS thicknesses were not measurable preoperatively in most of the diseased eyes because the EZ was not clear in the detached retina. At 1 month after surgery, each layer was thinner than the corresponding layer of the healthy fellow eye, and the IS and OS thicknesses gradually became thicker with time. The IS thickness was still significantly thinner at 3 and 6 months than the corresponding layer in the fellow eye, and the IS thickness was not significantly different from that of the fellow eye at 12 months after surgery. The OS thickness was significantly thinner than the corresponding layer in the fellow eye throughout the study period. The thickness of the retina between the ILM-ELM was significantly thinner than that in the fellow eye at 1 month after surgery and became not significantly different to that in the healthy fellow eye at 3 months and thereafter.

No significant correlation of the ILM-ELM, IS or OS layer thicknesses with the interval until surgery for each period after surgery was found except the OS thickness at 6 months after surgery. At this time, there was a significant correlation with the interval until surgery (r=−0.49, p=0.004, figure 4).

The number of eyes in group G was 24 and in group P was 25. The thickness of each retinal layer at each time after surgery is shown in table 1. No significant differences were observed in

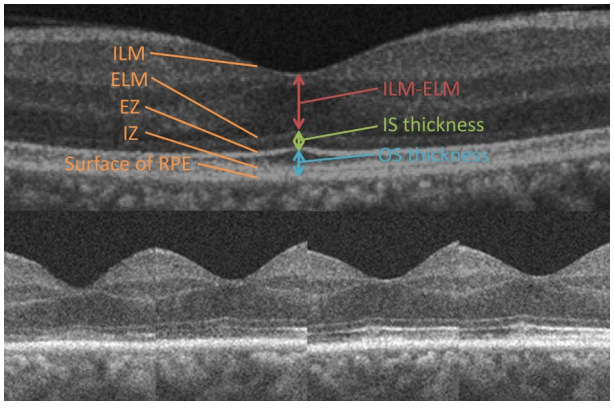

Figure 1 Analysis of the retinal layer thickness at the fovea. Measurements were made in the optical coherence tomographic (OCT) image crossing the fovea. (Upper) Each layer is indicated. The internal limiting membrane–external limiting membrane (ILM-ELM) thickness is the distance between the surface of the ILM to the surface of the ELM. The photoreceptor inner segment (IS) thickness is the distance between the ELM to the ellipsoid zone (EZ). The photoreceptor outer segment (OS) thickness is the distance between the EZ to the border of the retinal pigment epithelium (RPE). (Lower) Representative pictures of the foveal OCT images. The first column shows the foveal OCT image in the healthy fellow eye, and the second to fourth columns show the foveal OCT images at different postoperative periods. Second column=1 month after surgery; third column=3 months after surgery; and fourth column=6 months after surgery. IZ, interdigitation zone.

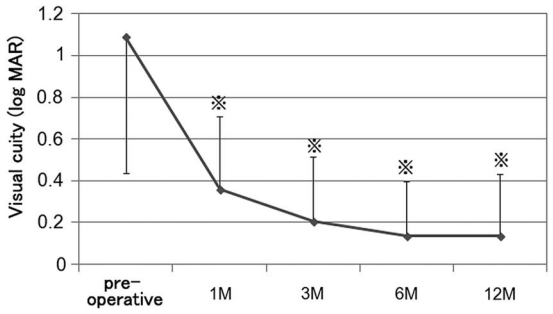

Figure 2 Changes of the mean best-corrected visual acuity (BCVA) before and after vitreous surgery for rhegmatogeneous retinal detachment. The BCVA improved significantly at each time after surgery. Bar represents SD. *p<0.05. logMAR, logarithm of the minimum angle of resolution.

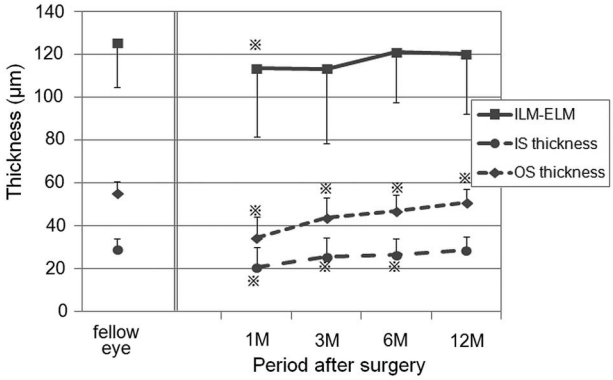

Figure 3 Change in the mean retinal layer thickness at the fovea after surgery. At 1 month after surgery, each layer was thinner than the healthy fellow eye. With increasing postoperative times, the thickness gradually increased. The thickness of internal limiting membrane–external limiting membrane (ILM-ELM) was comparable to that of the healthy fellow eye at 3 months and thereafter. The photoreceptor inner segment (IS) layer thickness was comparable to that of the fellow eyes at 12 months after surgery. The photoreceptor outer segment (OS) layer thickness was significantly thinner than the corresponding layer in the fellow eye throughout the study period. . Bar represents SD. *p<0.05.

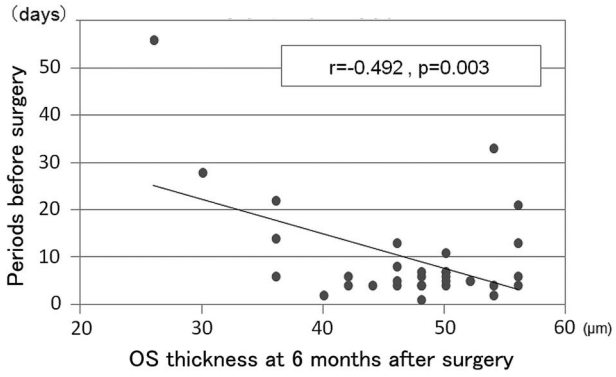

Figure 4 Relationship between the period until surgery and photoreceptor outer segment (OS) thickness at 6 months after surgery. There was significant correlation between the period until surgery and OS thickness at 6 months after surgery (Pearson's rank correlation coefficient). The OS layer was thinner in eyes with longer period until surgery.

the thickness of the ILM-ELM between the two groups at any time after surgery. On the other hand, a significant difference was observed in the IS thickness between the two groups at 1, 3 and 12 months after surgery. A significant difference was observed in the OS thickness between the two groups at 1, 3 and 6 months after surgery. Although the difference in some comparisons did not reach significance, the thickness of each segment in group G eyes was thicker than that in group P at all times after surgery.

The correlations between the BCVA at 6 months after surgery and each retinal layer thickness are shown in table 2. There was a significant correlation between the BCVA and the OS thickness at 1, 3 and 6 months after surgery. Thus, eyes with a thicker OS thickness had a better BCVA. Also, ILM-ELM and IS thicknesses at 3 months after surgery were significantly and positively correlated with the BCVA.

DISCUSSION

Recent OCT studies have shown disruptions of the photoreceptor microstructures in several retinal diseases.[7–12 17] The studies showed that the presence of a continuous EZ was due to well-restored photoreceptor cells,[6] and the integrity of the ELM was correlated with the morphological changes in the photoreceptor cell bodies and Muller cells.[7 17] The interdigitation zone (IZ),[16] which had been called as the cone outer segment tips line, in normal eyes is visible because of the different thicknesses of the cone and rod OSs.[6]

Several investigators have examined the correlation between the integrity of the microstructures and the BCVA in eyes with a macular hole, occult macular dystrophy and the acute zonal occult outer retinopathy complex.[4 8 14 15 18 19] Recently, a significant correlation was found between foveal function, for example, the VA, and the quantitative parameters of the photoreceptor microstructures.[10 13 14] Thus, Itoh *et al*[10] made quantitative evaluations on the photoreceptors in the horizontal OCT images and reported that the mean total area and maximum lengths of the EZ defect at 12 months after macular hole surgery were significantly and negatively correlated with the postoperative BCVA. Although a decrease in the OS thickness in eyes with a retinal detachment has been reported,[9] only limited information is available on the changes of the OS thickness after the retina is reattached.[11 12] Our findings clearly showed that the IS and OS thicknesses increased in parallel with the improvement of the BCVA after successful retinal reattachment. The results showed that the IS and OS thickness were thin soon after the retina was reattached, and there was an increase in the thickness with increasing time. The thinner OS layer is caused by the absence of normal OS renewal caused by the separation of the OSs from the RPE.[20 21] This is supported by the studies on monkey retinas with experimental RDs.[20 21] The increase in the thickness in our results is also consistent with those experiment that reported that during the 7-day detachment period the majority of rod outer segments (ROS) and cone outer segments (COS) degenerated, but the ROS regained 72% of their normal thickness and COS regained approximately 48% by 30 days after reattachment.[20] After 150 days of reattachment, the mean OS thickness was not statistically different from that in the control areas.[20] In contrast, the OS thickness in the present study was still thinner than that of the healthy fellow eye at 12 months after surgery. This may be partly because the OS thickness in the present study mainly reflects COS, which was reported to have less recovery than ROS in an animal study.[20] Because the OS thickness may still become thicker, further longitudinal study is necessary to determine whether it finally recovers to the same level as the healthy fellow eye.

Our results showed that the IS thickness was significantly thinner in the early period after surgery. This is not consistent with a previous experimental RD study in rhesus monkey eyes, which reported that the IS thickness remained intact during the 7-day detachment period.[20] This may be due to the differences of several factors such as the analysis methods (histology and OCT), species (monkey and humans), subretinal fluid (balanced salt solution in the experiment and vitreous fluid in the patients), vitreous traction, tamponade agents used and duration of the RD. Recently, a change in the IS and OS thicknesses was found during the recovery phase of eyes with multiple

Table 1 Comparison of retinal layer thickness between two groups

	ILM-ELM			IS			OS		
	Group P	Group G	p Value	Group P	Group G	p Value	Group P	Group G	p Value
Fellow eye	122.6±19.39	128.1±22.35	>0.05	28.20±3.17	29.60±2.39	>0.05	54.00±4.90	56.85±5.18	>0.05
1 month	101.9±28.87	122.7±32.22	>0.05	17.73±5.06	22.53±3.94	***0.003***	28.93±10.22	38.63±6.87	***0.007***
3 months	98.27±38.42	126.5±26.00	>0.05	22.67±4.82	27.65±2.37	***0.001***	39.47±10.15	47.53±6.15	***0.025***
6 months	114.4±19.08	128.5±26.31	>0.05	25.33±3.82	27.73±2.25	>0.05	43.89±8.44	50.40±4.01	***0.016***
12 months	109.3±42.91	124.7±21.85	>0.05	23.33±5.03	30.57±1.51	***0.019***	44.83±7.75	53.14±4.60	>0.05

Data are shown as mean±SD (μm).
ELM, external limiting membrane; Group G, eyes with postoperative visual acuity at 6 months ≥1.0; Group P, eyes with postoperative visual acuity at 6 months <1.0; ILM, internal limiting membrane; IS, photoreceptor inner segment; OS, photoreceptor outer segment.
Significant values are shown in Bold/italics.

Table 2 Correlation of each retinal layer thickness with the BCVA at 6 months after surgery

	ILM-ELM		IS		OS	
Postoperative period (months)	r	p Value	r	p Value	r	p Value
1	0.32	0.065	0.336	0.052	0.688	***<0.001***
3	0.4	***0.023***	0.468	***0.007***	0.544	***0.001***
6	0.268	0.132	0.311	0.078	0.675	***<0.001***

BCVA, best-corrected visual acuity; ELM, external limiting membrane; ILM, internal limiting membrane; IS, photoreceptor inner segment; OS, photoreceptor outer segment.
Significant values are shown in Bold/italics.

evanescent white dot syndrome.[14 15] Further studies are needed to clarify the changes in the IS thickness.

Whether the thinning of the IS and/or OS occurs in the detached retina, and if so when it occurs was not determined in our OCT study because the EZ was not clear in the detached retina.

The IS and OS thicknesses were significantly thicker in eyes with better BCVA than in eyes with worse BCVA at 1 month after surgery. Moreover, the BCVA at 6 months after surgery was significantly correlated with the OS thickness at 1 month after surgery. BCVA at 6 months after surgery was better in eyes with thicker OS at 1 month after surgery. These findings suggest that the IS and OS thicknesses at a relative early postoperative period may be a good indicator of the final BCVA. Significant positive correlations of the photoreceptor OS thickness and the BCVA in patients with diabetic macular oedema, epiretinal membrane and central serous chorioretinopathy have been reported.[11–13] Shin *et al*[12] measured the outer photoreceptor layer (PRL) thickness, which we called the OS thickness, in 10 eyes with macular involved RRD >6 months after a reattachment. They reported that the OS thickness was decreased compared with that of normal eyes. In addition, the mean OS thickness of the central subfield was significantly correlated with the postoperative BCVA. Kim *et al* reported[11] significant thinning of the outer nuclear layer and PRL in reattached retina 10.4±6.9 months after surgery, although the mean duration of RRD was <1 week. They did a cross-sectional study, and the measurement periods were not clear, whereas our study was a longitudinal study and we followed the course of recovery of the IS and OS thicknesses of the same eyes. Our findings on the foveal microstructure are in good agreement with those of earlier studies on other retinal diseases in terms of the pattern of changes and the recovery periods.

Our study has several limitations. The sample size was small, and the eyes had different baseline BCVAs, various durations of detachment and different surgical procedures. Therefore, definitive conclusions cannot be made about the influence of these clinical characteristics on the changes of the IS and OS thicknesses. Several investigators have reported on the postoperative changes in the foveal architecture after sclera buckling surgery and/or vitrectomy for RRD.[22–25] Because we did not include eyes that underwent sclera buckling, such comparison could not be made. However, our results suggest that the IS and OS thicknesses in eyes with a reattached RRD were significantly thinner immediately after surgery, and then gradually increased and became not significantly different from that of the normal fellow eyes at 12 months. In addition, our results showed that those thicknesses in the early period after surgery may be an indicator for the degree of recovery. If this can be shown in a larger number of eyes, then this can be a method to monitor the disease course non-invasively.

Contributors Conception and design of study: KS. Conduct of study: KS, CSM and GT. Collection of data: KS, CSM, and EW. Analysis and interpretation of data: KS and GT. Preparation of the manuscript: KS. Critical revision: KS. Data collection: KS, CSM and EW. Statistical expert: KS and GT. Obtain funding: KS. Literature search: KS. Administrative support: HM and AM. Review and approval of the manuscript: KS, CSM, EW, GT, HM and AM.

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Competing interests None.

Patient consent Obtained.

Ethics approval The procedures used conformed to the tenets of the Declaration of Helsinki. The study was a retrospective, consecutive, observational case series with approval of the Ethics Committee of the Teikyo University School of Medicine (study ID number: 12-053).

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