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Comparison of Parafoveal Retinal Thickness in Eyes with Idiopathic Macular Hole to that with Rhegmatogenous Retinal Detachment after Vitrectomy

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Abstract

Background: The foveal contour is asymmetrical in the horizontal optical coherence tomographic (OCT) images in idiopathic macula holes (IMHs) successfully closed by pars plana vitrectomy (PPV). The purpose of this study was to compare the parafoveal retinal contour after PPV followed by gas tamponade for IMHs to that after vitrectomy for rhegmatogenous retinal detachment (RRD).

Design: Retrospective study.

Participants: Eleven eyes of 11 IMH patients and 10 eyes of 10 RRD patients who underwent PPV.

Methods: The internal limiting membrane (ILM) was stained with indocyanine green and peeled in the IMH group but not in the RRD group. The postoperative retinal thickness was measured by spectral-domain OCT.

Main outcome measures: The parafoveal thicknesses of the operated eyes were compared to the corresponding areas of the fellow un-operated eyes.

Results: In the IMH group, the average postoperative thickness of the temporal sector was 312.6 μm and that of the corresponding area of the fellow eyes was 330.2 μm (P <0.05). Similarly, the thickness of the nasal sector was 362.6 μm and that of the fellow eyes was 345.8 μm (P<0.05). These differences were not observed in the RRD group. Additional measurements showed that the inner retinal layer was thinner in the temporal retina and the outer retinal layer was thicker in the nasal retina in the IMH group.

Conclusions: The postoperative asymmetrical foveal contour was observed in only the IMH group. We suggest that these alterations were caused by procedures, such as ILM peeling, rather than the gas tamponade.

Keywords: Idiopathic macular hole; Retinal thickness; Rhegmatogenous retinal detachment; Spectral-domain optical coherence tomography; Vitrectomy

Introduction

Kelly and Wendel reported that idiopathic macular holes (IMHs) can be closed by pars plana vitrectomy (PPV) with fluid-gas exchange [1,2]. Later studies showed that the anatomical closure rates after the initial PPV ranged from 45% to 73% [1-4]. The surgical technique for closing an IMH has been significantly modified, e.g., removal of the internal limiting membrane (ILM), which has increased the anatomic success rates and improved the functional results [5-9]. However, the parafoveal temporal retina was found to be thinner than the nasal parafoveal area in the spectral domain (SD)-optical coherence tomographic (OCT) images even in successfully closed IMHs [10,11]. The cause of this anatomical asymmetry has not been determined.

We measured the retinal thickness before and after vitrectomy in eyes with an IMH by SD-OCT and found that the parafoveal nasal retina was significantly thicker and the parafoveal temporal retina was significantly thinner than the corresponding areas of the fellow eyes [12]. However, we did not determine whether this asymmetry in retinal thickness was specific to IMH or was different for other retinal diseases that undergo PPV followed by gas tamponade. In addition, this asymmetry was not observed in 3 cases that did not have ILM removed. In addition to ILM peeling, there are several surgical differences between IMH and RRD. We could exclude the effect of gas tamponade, when this asymmetry is IMH specific.

Thus, the purpose of this study was to compare the parafoveal retinal thicknesses after PPV for IMHs and for macula-on rhegmatogenous retinal detachment (RRD).

Patients and Methods

We studied the medical records of 11 eyes of 11 Japanese patients with a full-thickness IMH (4 men, 7 women) and 10 eyes of 10 patients (7 men and 3 women) with a macula-on RRD that were treated at the Shinshu University Hospital and Matsumoto Dental University Hospital between 2004 and 2009. They were followed at the Matsumoto Dental University Hospital postoperatively. Eight of 11 eyes with IHM were same eyes studied in our former report. [12] Patients with other ocular diseases such as glaucoma, diabetic retinopathy, uveitis and pathological myopia were excluded.

All of the procedures adhered to the tenets of the Declaration of Helsinki. This study was approved by the Institutional Review Board

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and Ethics Committee of Matsumoto Dental University, and a written informed consent for the examination and surgery was obtained from all of the patients.

The vitreoretinal surgery was performed with standard 20-gauge (20-G) or 23-G instruments and was performed by a single surgeon (KO). Phacoemulsification and placement of a posterior chamber intraocular lens was done in 19 of the 21 eyes (phakia in a 50-year-old patient with IMH patient and pseudophakia in a RRD patient). After core vitrectomy, a posterior vitreous detachment (PVD) was created by suction with the vitrectomy cutter after a triamcinolone acetonide injection (Kenakolt-A; Bristol Pharmaceuticals KK, Tokyo, Japan) as required [13].

During the IMH surgery, the ILM was stained in all of the eyes with approximately 0.5 mL of 0.25% indocyanine green (ICG) injected intravitreally for 1 min then washed out. The ILM was grasped at the temporal raphe and peeled over 1 to 3 disc diameters around the MH. The ILM was not removed in eyes with a macula-on RRD. During the fluid-air exchange, the air pressure was set at 35 mmHg, and the air-gas exchange was performed with 20% sulfur hexafluoride (SF_6) in eyes with an IMH and 20% or 25 % SF_6 in eyes with a RRD. The patients were instructed to remain in a face-down position for at least 7 days.

Thus, the major difference in the surgical procedures between the IMH and RRD patients was the ILM peeling in the IMH eyes and lack of peeling in the RRD eyes.

The postoperative retinal thickness was measured with a Spectralis HRA-OCT (Heidelberg Engineering GmbH, Heidelberg, Germany) at least 4 months after the PPV at the Matsumoto Dental University Hospital (Table 1). The macular thickness and volume were obtained with the volume scan mode of the instrument. The retinal thickness was determined from a 30×20 degree raster consisting of 25 line scans, and the distance between the lines was 240 μm. At each retinal position, twelve B-scans were averaged with the automatic real time mode program to reduce the speckle noise. The mean retinal thickness and volume maps were determined for nine sectors in three concentric circles of diameters 1, 3, and 6 mm [14]. The inner and outer rings were divided into four quadrants. With the retinal thickness map analysis protocol of the Spectralis (ver. 4c software), the full retinal thicknesses of the fovea (within a circle of 1 mm diameter), of the parafovea (within annulus diameters of 1 and 3 mm), and of the perifovea (within annulus diameters of 3 and 6 mm) were automatically measured [15]. We did not analyze the data for the perifoveal thicknesses because they were not collected in all cases.

To investigate the morphology of the macular area in more detail [16], we measured the thickness of each retinal layer by moving the cursor lines manually. For this, single horizontal and vertical images were enlarged on a monitor screen, and the inner retinal layer was measured as the distance between the vitreoretinal surface to the outer border of the inner plexiform layer (IPL). In the same way, the outer retinal layer thickness was determined by measuring the distance between the outer border of the IPL to the inner/outer segment (IS/OS) junction. In addition, the inner retinal layer was divided into the retinal nerve fiber layer (RNFL) and sum of the ganglion cell layer (GCL) and the IPL.

Data were analyzed using SPSS for Windows (version 11.0J, SPSS, Chicago, IL). The Bonferroni correction was used to adjust the statistical significance of differences for continuous data between each group, viz., operated eyes vs. fellow eyes in the IMH group, operated eyes vs. fellow eyes in the RRD group, and operated eyes of the IMH vs. RD group. A difference was considered to be statistically significant when the P was <0.05.

Results

The clinical characteristic of all of the eyes are summarized in (Table 1). All patients had a successful closure of the IMH and a re-attachment of the retina in the RRD group after the first operation. The mean age and the mean interval between the examination and the time of surgery did not differ significantly in both groups (Table 1). In the 11 eyes with an IMH, there were two eyes at stage 2 and 9 eyes at stage 3. The difference in the mean refractive errors between the two groups was significant (-0.82 D vs -3.98 D). A PVD was observed preoperatively in all RRD but not in the IMH patients.

The mean central foveal and parafoveal thicknesses of eyes with an IMH and those with a RRD are shown Table 2 for each sector. In the RRD group, 3 of the 10 fellow eyes were excluded because 2 had undergone vitrectomy for a RRD and one for an epiretinal membrane (ERM). The central foveal thickness was 301.6 μm in eyes with an IMH which was significantly thicker than that in the fellow eyes at 253.4 μm (P <0.001).

The thickness of the nasal sector in the parafoveal region was 362.6 μm in eyes with an IMH which was significantly thicker than that in the fellow eyes at 345.8 μm (P = 0.024). On the other hand, the temporal parafoveal sector was significantly thinner at 312.6 μm in the IMH group than in the fellow eyes at 330.2 μm (P = 0.006). The central foveal and parafoveal sectors in the RRD group were thicker than that of the fellow eyes. However, the differences were not significant.

When the mean retinal thickness was compared between the IMH and RRD groups, the parafoveal temporal sector was significantly thinner in the IMH group (P <0.001). The parafoveal thicknesses in the other sectors did not differ significantly between the two groups.

Characteristic	Idiopathic Macular Hole	Rhegmatogenous Retinal Detachment
Eyes/patients (n/n)	11/11	10/10
Male/female (n/n)	4/7	7/3
Age (years), mean (SD) (range)	64.3 (8.0) (50 to 79)	57.9 (7.0) (48 to 70)
Examination (months) from surgery	12.6 (12.9) (6 to 48)	19.6 (20.4) (4 to 70)
Macular hole stage (n)		
2	2	-
3	9	-
Preoperative macula status (n)		
on	-	10
Preoperative PVD	0/11	10/11
Refractive error (Dioptor), mean (SD)	-0.82 (1.17) (0 to -3.0)	-3.98 (2.65) (0 to -8.75) *
Preoperative mean VA, logMAR units	0.48	N/A (some data missing)
Postoperative mean VA, logMAR units	0.00064	-0.11
ILM peeling with ICG staining (n)	11	0

ICG, indocyanine green; ILM, internal limiting membrane; PVD, posterior vitreous detachment
*P value is 0.0002 by unpaired t-test between two groups
There are not significant differences in age and visual acuities between both groups

Table 1: Descriptive data of eyes undergoing pars plana vitrectomy.

To investigate the contribution of the inner and outer retinal layer to the overall postoperative thickness, we measured the retinal thickness of inner layer and outer layer at 1,000 μm from the fovea on the horizontal and vertical images because the thickness of each retinal layer could not be obtained using the version of the Spectralis-OCT we used. We selected this point because this is the center of the parafoveal region measured automatically. The total retinal thickness was expressed as the sum of the inner layer and outer layer thicknesses (Table 3). Each value was smaller than those in (Table 2) because the thicknesses were measured from the vitreoretinal interface to the IS/OS junction in this manual analysis, and not to the choroid as in the automatic analysis [17].

The mean temporal thickness of the inner layer was 74.5 μm which was 23.4 μm thinner than that of the fellow eyes at 97.9 μm. On the other hand, the thickness of the outer layer was 161.8 which was significantly thinner than that of the fellow eyes at 170.8 μm. In contrast, the outer layer was significantly thicker in the nasal sector (194.8 μm vs. 177.2 μm). However, the inner layer in the nasal sector was not significantly thicker (117.4 μm vs. 109.5 μm). The differences in the mean thickness between the postoperative eyes and fellow eyes were not significant (Table 3). The mean thickness of the inner layer in all regions was thicker in the RRD group than that in the fellow eyes although the differences were not significant. However, the mean thickness of inner layer in IMH group was thinner than that in the RRD group except in the nasal region.

We also measured the thicknesses of the RNFL and GCL/IPL (Table 4). The RNFL was thinner than that of the fellow eyes in all 4 regions in the IMH group, although the differences were not significant. In contrast, there was a significant decrease of GCL/IPL in the temporal region in the IMH group than that of the fellow eyes. The differences in the GCL/IPL in the other sectors were not significant in the fellow eyes or in the eyes with a RRD.

Discussion

Our results showed that the nasal retina was significantly thicker than that of the fellow eyes postoperatively in eyes who are IMHs were successfully closed by PPV. In addition, the temporal retina was significantly thinner than the corresponding sector of the fellow eyes in the IMH group. These results confirmed our earlier results [12]. Our results also showed that the thinning of the temporal parafoveal retina was due to a thinning of the inner layer of the retina. Such a thinning was not observed in postoperative RRD eyes. Thus, the postoperative asymmetry appeared to be IMH-specific.

	Idiopathic Macula Hole (IMH)			**Rhegmatogenous Retinal Detachment (RRD)**			**IMH vs RRD**
	Operated eyes	Fellow eyes	p Value*	Operated eyes	Fellow eyes (n=7)	p Value†	p Value‡
Central Fovea	301.6 (21.7)	253.4 (20.6)	<0.001	290.7 (24.8)	274.9 (16.5)	0.862	1.000
Parafovea							
Nasal	362.6 (13.4)	345.8 (12.4)	0.024	357.1 (15.1)	346.7 (7.3)	0.644	1.000
Superior	343.6 (13.4)	342.3 (12.7)	1.000	353.3 (13.5)	341.3 (10.2)	0.382	0.529
Inferior	342.7 (10.5)	340.6 (10.2)	1.000	349.5 (13.4)	338.6 (10.8)	0.343	1.000
Temporal	312.6 (12.0)	330.2 (12.2)	0.006	341.5 (11.4)	331.3 (9.5)	0.486	<0.001

Data are mean micrometer (standard deviation).
*Statistically significant difference between operated eyes and fellow eyes of patients with IMH after Bonferroni post hoc test
†Statistically significant difference between operated eyes and fellow eyes of patients with RRD after Bonferroni post hoc test
‡Statistically significant difference between operated eyes of patients with IMH and those with RRD after Bonferroni post hoc test
There are not significant differences between fellow eyes of patients with IMH and those with RRD after Bonferroni post hoc test (data not shown)

Table 2: Comparison of mean macular thickness (μm) by volume scan analysis between idiopathic macula hole and rhegmatogenous retinal detachment .

	Idiopathic Macula Hole (IMH)			**Rhegmatogenous Retinal Detachment (RRD)**			**IMH vs RRD**
	Operated eyes	Fellow eyes	p Value*	Operated eyes	Fellow eyes (n=7)	p Value†	p Value‡
Total retina							
Nasal	312.2 (20.4)	286.6 (14.0)	0.003	301.4 (14.1)	291.7 (8.6)	1.000	0.717
Superior	287.2 (20.0)	288.7 (10.0)	1.000	302.1 (14.8)	292.3 (9.1)	1.000	0.153
Inferior	287.9 (16.8)	292.1 (9.8)	1.000	299.6 (13.3)	291.9 (11.7)	1.000	0.314
Temporal	234.3 (20.3)	268.7 (10.4)	<0.001	281.0 (15.1)	271.6 (7.6)	1.000	<0.001
Inner retina							
Nasal	117.4 (12.7)	109.5 (14.6)	0.920	122.6 (12.6)	120.0 (9.1)	1.000	1.000
Superior	113.4 (11.5)	122.1 (11.1)	0.579	137.0 (14.9)	129.4 (8.8)	1.000	<0.001
Inferior	118.6 (10.7)	127.8 (13.2)	0.443	141.8 (13.1)	140.9 (8.5)	1.000	<0.001
Temporal	72.5 (16.8)	97.9 (9.1)	0.001	113.3 (18.6)	103.3 (7.3)	0.973	<0.001
Outer retina							
Nasal	194.8 (22.3)	177.2 (9.3)	0.035	178.8 (6.8)	171.7 (10.7)	1.000	0.081
Superior	173.8 (14.0)	166.6 (12.3)	1.000	165.1 (8.8)	162.9 (13.2)	1.000	0.665
Inferior	169.4 (14.1)	164.3 (11.6)	1.000	157.8 (7.2)	151.0 (17.7)	1.000	0.271
Temporal	161.8 (14.1)	170.8 (8.7)	0.562	167.7 (13.9)	168.3 (12.0)	1.000	1.000

Data are mean micrometer (standard deviation)
*Statistically significant difference between operated eyes and fellow eyes of patients with IMH after Bonferroni post hoc test
†Statistically significant difference between operated eyes and fellow eyes of patients with RRD after Bonferroni post hoc test
‡Statistically significant difference between operated eyes of patients with IMH and those with RRD after Bonferroni post hoc test
There are not significant differences between fellow eyes of patients with IMH and those with RRD after Bonferroni post hoc test (data not shown)

Table 3: Comparison of mean macular thickness (μm) at 1 mm form the center between idiopathic macula hole and rhegmatogenous retinal detachment.

		Idiopathic Macula Hole (IMH)			Rhegmatogenous Retinal Detachment (RRD)		IMH vs. RRD	
		Operated eyes	Fellow eyes	p Value*	Operated eyes	Fellow eyes (n=7)	p Value†	p Value‡
RNFL								
	Nasal	19.5 (3.9)	19.4 (2.9)	1.000	24.8 (2.9)	23.7 (4.1)	1.000	0.007
	Superior	25.6 (4.1)	26.8 (3.2)	1.000	33.5 (8.1)	27.0 (9.0)	0.244	0.038
	Inferior	27.9 (5.0)	29.8 (5.0)	1.000	37.6 (5.5)	38.0 (7.7)	1.000	0.002
	Temporal	11.1 (1.3)	14.6 (2.4)	0.475	14.3 (2.1)	18.9 (9.9)	0.279	0.661
GCL+IPL								
	Nasal	97.9(10.8)	90.1(13.3)	0.718	97.8 (12.4)	96.3 (7.1)	1.000	1.000
	Superior	87.7 (10.1)	95.3 (8.8)	0.640	103.5 (10.5)	102.4 (14.1)	1.000	0.011
	Inferior	90.6 (8.8)	98.0 (11.9)	0.618	104.2 (11.5)	102.9 (7.6)	1.000	0.029
	Temporal	61.4 (16.3)	83.4 (8.3)	0.003	99.0 (17.2)	84.4 (9.1)	0.220	<0.001

Data are mean micrometer (standard deviation)
RNFL, retinal nerve fiber layer; GCL, ganglion cell layer; IPL, inner plexiform layer
*Statistically significant difference between operated eyes and fellow eyes of patients with IMH after Bonferroni post hoc test
†Statistically significant difference between operated eyes and fellow eyes of patients with RRD after Bonferroni post hoc test
‡Statistically significant difference between operated eyes of patients with IMH and those with RRD after Bonferroni post hoc test
There are not significant differences between fellow eyes of patients with IMH and those with RRD after Bonferroni post hoc test (data not shown)

Table 4: Comparison of mean inner macular thickness (μm) at 1 mm form the center between idiopathic macula hole and rhegmatogenous retinal detachment.

PPV with SF_6 gas tamponade was used on both types of eyes although the percentage of SF_6 was slightly higher (25 vs 20%) in some of the RRD eyes. The main difference in the surgical procedures was the removal of the ILM with ICG in the eyes with an IMH and non-removal in the eyes with a RRD. In addition, PVD was created by suction with the vitrectomy cutter for only the IMH group, because a PVD was already present in all of the eyes with a RRD. However, the creation of a PVD probably did not contribute to our findings because this asymmetry was not observed in 3 IMH cases where the ILM was not removed. But it must be remembered that the number of these cases is small, and the statistical reliability may be low.

ILM removal has also been reported to change the appearance of the retina by Tadayoni et al. They reported the development of a dissociated nerve fiber layer (DONFL) appearance after ILM peeling [18]. Mitamura et al. also observed the DONFL appearance after ILM peeling and reported that the depth of the DONFL was about 28.6 μm. [19] However, the DONFL was observed in superior or inferior sectors rather than the temporal sector [19]. In addition, the thickness of RNFL in temporal retina was thinner in the horizontal images. Thus, we suggest that the thinning of inner layer in the temporal region was not due to the same mechanism that causes the DONFL.

Nerve fiber layer defects were reported in the SD-OCT images after ILM peeling for an IMH in another study [10]. In our study, the ILM peeling was done by grasping the ILM at the temporal raphe to avoid damaging the RNFL or the retinal vessels. Thus, small defects or cleavages of not only the RNFL but also the GCL/IPL in this area cannot be excluded as contributing to the thinning of the temporal parafoveal retina.

On the other hand, the nasal parafoveal thickening in the IMH group could not be due to the same mechanism, although the retina was not significantly thicker than the preoperative thickness [12]. The reason for this was not determined. However, we suggest several possible mechanisms. First, the differences in the RNFL thickness around the fovea may be because the RNFs pass to the optic disc in this sector. Thus, the removal of the ILM may induce a mild shrinkage of the RNFL or resistance to recovery from a thickened retina.

The RNFL was thinner than that of the fellow eyes in the IMH group, but in contrast to our previous report [12], the difference was not significant due to the small number of eyes studied by ANOVA.

Because the ILM is made up of the footplates of the Müller cells, the ILM contributes to the normal foveal depression, and damage of the Müller footplates may be related to this shrinkage or resistance. Because Müller cells support the retina longitudinally, this support is lost after removal of the ILM. Similar damage of the Müller cells has been suggested to account for the DONFL appearance [18]. However, we cannot explain whether the loss of the longitudinal support results in the thickening of outer layer rather than the inner one (Table 3).

Another explanation for the asymmetrical parafoveal thicknesses is the change of the foveal contour after PPV in the IMH eyes. Imai et al reported that the foveal contour in the time-domain OCT images was different after successful closure of an IMH [20]. Even in closed IMHs after a single PPV in our study, the bottom of the IMH was shallower and more V-shaped. In contrast, the contour of the macula in normal eyes and eyes with a RRD appeared wider. So we might have measured the change in the shape of the outer retina. This may partially contribute to the increase of outer retinal thickness in only the nasal sector (Table 3).

Although we suggested that edema of the RNFL on the nasal side was the cause of the asymmetry earlier [12], we did not observe an increase of the RNFL in this study. Instead, a mild increase of the GCL/IPL and significantly larger increase of the outer retina contributed to the thickening of the nasal retina.

Our study has some limitations. The number of patients studied was low which may have affected the reliability of the statistical analyses. However, our measurements were most likely accurate based on the excellent reproducibility of the Spectralis OCT retinal thickness measurements [21]. In addition, the vitrectomy was done by single surgeon thus minimizing the effect of surgical procedures. Based on these points, we believe our findings are reliable.

Another limitation was the significant difference in the refractive error in the two groups with the refractive errors of the RRD group significantly more myopic. Because it is known that the refractive error, as well as age, gender and race, can affect the macular thickness, these factors must be matched in future studies [22-24]. However, there were no significant differences in the thicknesses of the corresponding retinal layers between fellow eyes of the two groups. The differences in the follow-up times between the two groups should also be considered. The follow-up of long-term changes of retinal thickness is an on-going study.

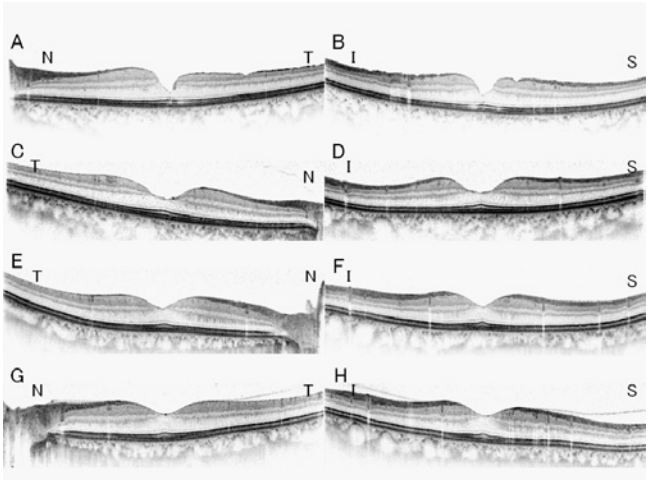

Figure 1: Postoperative Spectralis-OCT images of a 58-year-old Japanese woman with a stage 3 macular hole (A,B) and healthy fellow eye (C, D), and those of a 48-year-old Japanese man with macula-on rhegmatogenous retinal detachment (RRD; E, F) and healthy fellow eye (G, H).

A. Horizontal OCT image of a Japanese woman with a stage 3 macular hole showing a thinning of the temporal retina. Retinal ganglion cell layer (RGCL) and inner plexiform layer (IPL) are thinner which probably contributed to the thinness of the total retinal thickness in the temporal retina.

B. Vertical OCT image of the same woman showing symmetrical but steep foveal contour.

C. and D. In contrast, the foveal contour has a smooth concave shape in the fellow eyes.

E.- H. The postoperative OCT images in eyes with RRD and fellow eyes have normal foveal contours.

N, nasal; T, temporal; S, superior; I, inferior.

We cannot omit the possible effect of ICG for this asymmetric foveal contour. Although additional experiments on the effect of ICG are needed, we have stopped using ICG because of its possible toxicity [25].

The fact that we measured only one point of each retinal layer in the horizontal and vertical images as the representative value of thickness in each of the 4 sectors is also a limitation. Automated procedures programmed in other SD-OCT to measure the thickness of inner retina and outer retina may confirm our results.

Apart from the study design, we cannot explain this asymmetrical contour. We suggest that the asymmetrical contour resulted from anatomical changes rather than functional abnormalities. In support of this, we have not found any significant abnormalities in the postsurgical visual fields and electroretinograms in the cases where these tests were performed [12].

In conclusion, a thinning of the parafoveal temporal retina and thickening of nasal sector after PPV in patients with an IMH was confirmed. The surgical procedures were different, e.g., ILM peeling with or without ICG and creation of a PVD, between the IMH and RRD groups. These differences may have contributed to the asymmetrical contour in eyes with a closed MH. However, the gas-tamponade most likely was not the cause of the asymmetrical foveal contour.

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Ethics Approval

Ethics approval was provided by the Institutional Review Board of the Matsumoto Dental University, Shiojiri, Japan.

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