Progressive Thinning of Regional Macular Thickness After Epiretinal Membrane Surgery

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PURPOSE. To determine the long-term changes in the regional macular thickness after idiopathic epiretinal membrane (ERM) excision and to determine whether there were correlations between the pre- and postoperative central macular thickness and the best-corrected visual acuity (BCVA).

METHODS. This was a prospective, interventionai case series study of 53 eyes of 53 patients that underwent ERM removal with internal limiting membrane (ILM) peeling. Examinations were performed before, 1, 2, 3, 6, 9, 12, 24, 36, 48, and 60 months after the surgery. The average macular thicknesses in nine sectors outlined by the Early Treatment Diabetic Retinopathy Study were measured by spectral-domain optical coherence tomography. The final macular thicknesses of nine sectors of the 35 patients were compared with that of the normal fellow eyes.

RESULTS. All patients were followed for 36 months, and 21 patients were followed for 48 months. The thicknesses of all sectors progressively decreased for 48 months. The macula at 48 months was thinner than at 36 months (P < 0.0001–0.037) in all sectors. The final central and nasal sectors were significantly thicker than that of the fellow eyes. The final inner and outer temporal sectors were significantly thinner compared with the fellow eyes. There was no significant difference in the other sectors. The pre- and postoperative central macular thickness was significantly correlated with the postoperative BCVA at each examination.

CONCLUSIONS. A progressive thinning of the macula occurs with regional differences for at least 48 months. The temporal sector becomes thinner than the normal thickness.

Keywords: epiretinal membrane, internal limiting membrane, retinal thickness, spectral-domain optical coherence tomography

Excision of an idiopathic epiretinal membrane (ERM) with internal limiting membrane (ILM) peeling leads to a reduction in the thickness of the macular area and an improvement in vision.1–10 This decrease in the thickness has been documented by optical coherence tomography (OCT) as a recovery of retinal thickening.11–28 Earlier studies20,21 showed that this decrease continued for 24 months; however, it was not determined whether the decrease will continue for longer times.

Peeling the ILM is commonly done during ERM excision, and it can lead to a complete removal and reduction of recurrences of an ERM. However, ILM peeling has been associated with some complications, and whether ILM peeling should be performed is still controversial.24

The internal limiting membrane is the basement membrane of the Müller cells, and Müller cells play important roles in the physiology and function of the retina. Peeling the ILM has been demonstrated histologically and electroretinographically to damage Müller cells.29–32 Optical coherence tomography has shown that vitrectomy with ILM peeling leads to changes in the morphology and thickness of the macular area.33–38 We recently reported that there was a progressive decrease in the macular thickness for at least 2 years after successful macular hole surgery with ILM peeling.39 Some of the outer sectors became thinner than the baseline thickness, indicating that ILM peeling caused degenerative thinning of the retina. Thus, retinal changes associated with ERM surgery with ILM peeling may also continue for a long time, and may differ for the different sectors. In addition, it is not known whether the central macular thickness (CMT) and postoperative visual acuity continues to be correlated during a long-term follow-up.

Thus, the purpose of this study was to determine the long-term changes in the thicknesses of the different macular sectors after ERM surgery with ILM peeling. The thicknesses were determined by spectral-domain OCT for at least 36 months after the surgery. In addition, we determined whether there were significant correlations between the central macular thickness and the best-corrected visual acuity (BCVA) at the different postoperative times during the 36-month follow-up.

METHODS

This was a prospective study. We studied 59 eyes of 59 consecutive patients who underwent ERM surgery at the Shinjo Ganka Institute, Miyazaki, Japan, and the Nishigaki Ganka, Nagoya, Japan, between June 2008 and June 2010. The inclusion criteria were: (1) the presence of an idiopathic ERM; (2) successful surgery after 25-gauge transconjunctival three port pars plana vitrectomy with ILM peeling; and (3) returned for all scheduled examinations after the surgery. Eyes
were excluded if they had pseudomacular hole, myopia greater than 6 diopters, a history of ocular surgeries, and poor OCT images (signal strength < 7). Eyes were also excluded if they required a reoperation to treat postoperative complications, such as a retinal detachment. In addition, eyes were excluded if the patient had any ocular or systemic disorder that could affect the retinal thickness (e.g., glaucoma, optic nerve diseases, age-related macular degeneration, and diabetes mellitus).

All of the patients had a comprehensive ophthalmological examination including; measurements of the refractive error, measurements of the BCVA with a Landolt chart (Richmond Products, Albuquerque, NM, USA) at 5 m, slit-lamp examinations, measurements of the intraocular pressure with a Goldmann applanation tonometer (Haag-Streit AG, Koeniz, Switzerland), dilated slit-lamp biomicroscopy with and without a contact lens, fundus photography, and Cirrus high definition optical coherence tomographic (HD-OCT; Carl Zeiss Meditec, Dublin, CA, USA) examinations.

This study adhered to the tenets of the Declaration of Helsinki. Approval for the data collection and analyses was obtained from the Institutional Review Board of the Shinjo Ganka Institute and Nishigaki Ganka Hospital. A written informed consent was obtained from all of the patients for the surgery.

Patients were examined preoperatively, and after 1 day, 1 and 2 weeks, and 1, 2, 3, 6, 9, and 12 months postoperatively. Therefore, the examinations were performed every 3 to 6 months.

All surgeries were performed by one surgeon (NO). All of the phakic patients underwent pars plana vitrectomy with phacoemulsification and placement of a posterior chamber intraocular lens to avoid a decrease in the postoperative BCVA because of nuclear cataract progression. After core vitrectomy, a posterior vitreous detachment was created by aspiration with a backflush needle in eyes that did not have a posterior vitreous detachment. After the removal of the detached vitreous gel and the posterior hyaloid membrane, the ERM was peeled from the entire macular surface using end-gripping forceps. Triamcinolone-assisted ILM peeling was subsequently performed. The area of ERM or ILM peeling was 6 mm in diameter which is equivalent to the entire Early Treatment Diabetic Retinopathy Study area sector.

We used the retinal thickness map analysis protocol of the HD-OCT system. A macular cube scan of 200 × 200 pixels and the five-line raster scan were performed at every visit by experienced OCT examiners. The examiners discarded poor quality images with signal strength less than 7 and any scans with visible eye movements or blink artifacts (discontinuous jumps), poor centration, or incorrect segmentation.

The built-in software automatically calculated the average retinal thickness in each of the nine macular sectors in a 6-mm diameter circle centered on the fovea as defined in the ETDRS. The standard retinal sectors were the central, and the superior, temporal, inferior, and nasal quadrants of the inner and outer rings. The diameter of the central circle was 1 mm, that of the inner ring was 3 mm, and that of the outer ring was 6 mm. A reduction in the macular thickness was determined by subtracting the postoperative thickness from the preoperative thickness at each time.

The preoperative baseline macular thickness differed in all sectors. Therefore, it was important to compare the relative reduction as the average postoperative regional thicknesses relative to the baseline thickness. The percentage reduction was determined by dividing the difference between the preoperative thickness and postoperative thickness by the preoperative thickness.

The decimal BCVAs were converted to their logMAR values for all statistical analyses. The significance of differences between paired samples was determined by t tests. The thicknesses of the central circle, the four sectors in the inner ring and in the outer ring were compared by analysis of variance with post hoc comparisons by the Scheffe procedure. Correlations between the BCVA and CMT were determined by the Pearson correlation tests. Multiple regression analyses were performed to determine the factors significantly correlated with the postoperative BCVA at 12 months. A value of \( P < 0.05 \) was accepted as statistically significant. The statistical analyses of the data were carried out with statistical software (StatView 5.0; SAS Institute Inc., Cary, NC, USA).

**RESULTS**

**Subjects**

We studied 59 eyes of 59 patients but 6 eyes of 6 patients were excluded because the scheduled return visits were not met. In the end, 53 eyes of 53 patients were analyzed with a mean follow-up of 42.1 ± 8.4 months and a range of 36 to 60 months. Twenty-one patients were followed for 48 months after surgery. The patients included 39 women (73.6%) and 14 men (26.4%), and their average age was 66.2 ± 7.5 years with a range from 49 to 81 years. The preoperative decimal BCVA ranged from 0.15 to 1.5 (median, 0.7), and it ranged from 0.3 to 1.5 (median, 1.2) at 24 months after the surgery.

**Changes of Regional Macular Thickness**

The changes in the thicknesses of the central and inner four sectors with time are shown in Figure 1A and those of the outer four sectors in Figure 1B. Statistical comparisons of average regional macular thickness between each time points are shown in Table 1. The postoperative time when the average macular thickness became significantly smaller than that of preoperative time differed among the sectors. In the central and inner four sectors, a significant reduction in retinal thicknesses was found in the inner superior, inner temporal, and inner inferior sectors as early as 1 month (all, \( P < 0.0001 \)), and in the central and inner nasal sector at 2 months (\( P = 0.0011, 0.012 \), respectively). In the four outer sectors, a significant reduction in the retinal thickness was found in the temporal sector at 1 month (\( P = 0.0005 \)), in the inferior and nasal sectors at 2 months (\( P = 0.020 \) and 0.027, respectively), and in the superior sector at 6 months (\( P = 0.0007 \)).

The postoperative macular thickness at 24 months was significantly thinner than that at 12 months for all of the sectors (\( P < 0.0001–0.0074 \)). The postoperative macular thickness at 36 months was significantly thinner than that at 24 months for all of the sectors (\( P < 0.0001–0.0045 \)). For the 21 eyes with a 48-month follow-up period, the macular thickness at 48 months was significantly thinner than at 36 months for all of the sectors (\( P < 0.0001–0.037 \)).

**Comparisons of Macular Thickness Changes of Different Sectors**

The reduction of the macular thickness in the central, the four inner sectors, and the four outer sectors are shown in Figures 2A and 2B, respectively. The reductions in the macular thickness were significantly different for the central and the four inner sectors at all times after the surgery (\( P < 0.0001–0.0004 \)). The inner temporal sector had a significantly greater reduction in thickness than the inner nasal sector at all times after the surgery (\( P < 0.0001–0.004 \)). The reductions in the
macular thickness were not significantly different for the four outer sectors at all times after the surgery ($P = 0.057–0.75$).

The percentage reductions in the central and inner four sectors and in the outer four sectors are shown in Figures 3A and 3B, respectively. The percentage reduction was significantly different for the central and four inner sectors at all times after surgery (all, $P < 0.0001$) in the order of temporal $>$ superior $>$ inferior $>$ central $>$ nasal sectors. The inner temporal sector had a significantly greater reduction than the inner nasal sector at all times (all, $P < 0.0001$). The inner temporal sector had a significantly greater reduction than the central sector at 1, 2, 3, 6, 9, 12, and 24 months postoperatively ($P < 0.0001–0.023$).

The percent reduction was significantly different for the outer four sectors only at 1 month after surgery ($P = 0.015$). The outer temporal sector had a significantly greater reduction than the outer superior sector ($P = 0.045$).

**Interocular Differences in Regional Macular Thickness**

Comparisons of the regional macular thickness at the final visit with that of the normal fellow eyes in 35 patients are shown in Table 2. Final measurements were performed with a mean

<table>
<thead>
<tr>
<th>Sectors</th>
<th>Preop vs. 1 mo</th>
<th>Preop vs. 2 mo</th>
<th>Preop vs. 3 mo</th>
<th>Preop vs. 6 mo</th>
<th>6 vs. 12 mo</th>
<th>12 vs. 24 mo</th>
<th>24 vs. 36 mo</th>
<th>36 vs. 48 mo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Central</td>
<td>0.29</td>
<td>0.0011</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
<td>0.0002</td>
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<tr>
<td>Inner superior</td>
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<td>$&lt;0.0001$</td>
<td>$&lt;0.0001$</td>
<td>$&lt;0.0001$</td>
<td>$&lt;0.0001$</td>
<td>$&lt;0.0001$</td>
<td>$&lt;0.0001$</td>
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<tr>
<td>Inner nasal</td>
<td>0.20</td>
<td>0.012</td>
<td>0.0067</td>
<td>0.0002</td>
<td>0.0001</td>
<td>0.0001</td>
<td>0.0001</td>
<td>0.0005</td>
</tr>
<tr>
<td>Outer superior</td>
<td>0.89</td>
<td>0.27</td>
<td>0.065</td>
<td>0.0007</td>
<td>0.0007</td>
<td>0.0029</td>
<td>0.0009</td>
<td>0.0075</td>
</tr>
<tr>
<td>Outer nasal</td>
<td>0.0003</td>
<td>0.0007</td>
<td>0.0002</td>
<td>$&lt;0.0001$</td>
<td>$&lt;0.0001$</td>
<td>0.0006</td>
<td>0.0007</td>
<td>0.0003</td>
</tr>
<tr>
<td>Outer inferior</td>
<td>0.12</td>
<td>0.020</td>
<td>0.0033</td>
<td>$&lt;0.0001$</td>
<td>$&lt;0.0001$</td>
<td>0.0063</td>
<td>$&lt;0.0001$</td>
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</table>

$P$ values are shown. Paired t-test was used.

* 48 months ($n = 21$)
follow-up of 41.9 ± 8.4 months with a range of 36 to 60 months.

The central and nasal sectors were significantly thicker than that of the normal fellow eyes (all, \( P < 0.0001 \)). The final thicknesses of the inner and outer temporal sectors were significantly thinner than that of the normal fellow eyes (\( P = 0.043, 0.052 \), respectively). There was no significant difference in the other sectors.

**Temporal Changes of BCVA After Surgery**

The temporal changes of the BCVA in logMAR units are shown in Figure 4. The average BCVA improved over the 12-month follow-up period. The postoperative BCVA was significantly better at 1 month than before surgery (\( P < 0.0001 \)), also at 3, 6, and 12 months than 1 month after surgery (all, \( P < 0.0001 \)), at 6, 12, and 24 months than at 3 months (\( P = 0.16, 0.0087 \), and \( P = 0.0006 \), respectively) and at 24 months than at 12 months (\( P = 0.059 \) after the surgery. None of the eyes had a decrease in the BCVA by more than 2 lines during the follow-up period.

**Correlation Between BCVA and CMT**

The coefficients of correlation between the BCVA and central macular thickness at each follow-up period are showed in Table 3. The pre- and postoperative central macular thicknesses were significantly correlated with the postoperative BCVA at each of the follow-up times. Multiple regression analysis showed that the central macular thickness at 1 month was significantly correlated with the BCVA at 12 months (CMT at 1 month, \( r = 0.27 \), \( P = 0.014 \); age, \( r = 0.019 \), \( P = 0.85 \); sex, \( r = 0.097 \), \( P = 0.53 \); BCVA at baseline, \( r = 0.57 \), \( P < 0.0001 \)) and at 24 months (CMT at 1 month, \( r = 0.24 \), \( P = 0.028 \); age, \( r = 0.001 \), \( P = 0.99 \); sex, \( r = 0.049 \), \( P = 0.62 \); BCVA at baseline, \( r = 0.60 \), \( P < 0.0001 \)).

**Temporal Changes of Macular Surface Maps of Representative Cases With and Without ILM Peeling**

The retinal surface maps reconstructed from the 3-dimensional cube scans showing the differences in the macular appearance with (Fig. 5A) and without (Fig. 5B) ILM peeling are shown in Figure 5. In eyes with ILM peeling, the thicker macula areas became thinner with increasing postoperative time for 24 months, and the depression in the temporal region became deeper with time for 24 months. This depression was seen only in eyes with ILM peeling, and never seen in eyes without ILM peeling. We previously used the temporal to nasal ratio (T/N ratio) to compare the temporal-nasal differences in eyes with and without ILM peeling. \(^{23} \) In the current study, the T/N ratio after surgery ranged from 0.78 to 0.84 in the ILM peeled eyes and from 0.89 to 0.93 in the ILM preserved eyes.

**DISCUSSION**

The results of this study showed the temporal changes in the regional macular thicknesses after ERM surgery. A decrease in the macular thickness continued for at least 48 months after
the surgery with some regional variations. The average postoperative macular thicknesses returned to normal by 36 months except in the central, inner nasal, and inner temporal sectors. The inner temporal sector in the operated eyes became thinner than that in the normal fellow eyes at final visit (36–60 months), whereas the central and inner nasal sectors remained thicker. The pre- and postoperative central macular thicknesses were negatively correlated with the postoperative BCVA at each follow-up time.

The results of two previous studies indicated that the central macular thickness continued to decrease for 2 years after ERM surgery. 20,21 However, it was not stated whether there was a significant difference between the thickness at 12 months and 24 months. Our results showed that the

<p>| Table 3. Correlations Between BCVA and CMT at Each Follow-Up Period |
|-------------------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|------------- |</p>
<table>
<thead>
<tr>
<th></th>
<th>BCVA Preop</th>
<th>BCVA, 1 mo</th>
<th>BCVA, 2 mo</th>
<th>BCVA, 3 mo</th>
<th>BCVA, 6 mo</th>
<th>BCVA, 9 mo</th>
<th>BCVA, 12 mo</th>
<th>BCVA, 24 mo</th>
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<tr>
<td>CMT, preop</td>
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<td>$r = 0.35$</td>
<td>$r = 0.39$</td>
<td>$r = 0.42$</td>
<td>$r = 0.43$</td>
<td>$r = 0.37$</td>
<td>$r = 0.36$</td>
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<tr>
<td>$P = 0.012$</td>
<td>$P = 0.0095$</td>
<td>$P = 0.0037$</td>
<td>$P = 0.0017$</td>
<td>$P = 0.0015$</td>
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<tr>
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<td>$r = 0.52$</td>
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<td>$r = 0.48$</td>
<td>$r = 0.47$</td>
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<tr>
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<td>$r = 0.38$</td>
<td>$r = 0.43$</td>
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The T/N ratio is defined as the inner temporal/inner nasal thickness.

Figure 5. Temporal changes of macular appearance on retinal surface map of representative cases with and without ILM peeling. (A) A 60-year-old man underwent ERM surgery with ILM peeling in his left eye. (B) A 65-year-old woman underwent ERM surgery without ILM peeling in her left eye. The T/N ratio is defined as the inner temporal/inner nasal thickness.
postoperative macula was significantly thinner at 24 months than 12 months, and even at 36 months than at 24 months for all ETDRS sectors. As best we know, our study is the first to show a significant progressive decrease in the macular thickness for at least 36 months after ERM surgery.

The time course of the changes in macular thickness of the nine sectors after ERM surgery has not been reported. The present results showed a progressive macular thinning with regional differences, such as a higher percentage reduction in the inner temporal sector, and lower percentage reductions in the central and inner nasal sectors. These regional differences are consistent with the results we reported after macular hole surgery with ILM peeling.59

In 2001, Massin et al.13 reported that the macular profile rarely returned to normal at 3 months after surgery. Subsequently, several authors reported that the central macular area was thicker in the operated eyes than in the normal eyes 9 to 46 months after ERM surgery with ILM peeling.17,20,22 Treumer et al.22 reported that the central and nasal sectors remained thickened, whereas the temporal sector returned to normal thickness. Our results generally agree with the results of these previous studies, and also showed that the macular thickness in the inner and outer temporal sectors became thinner than that in the normal fellow eyes after a long follow-up period.

The retina in the outer temporal sector became significantly thinner than the preoperative baseline thickness at 24 months after macular hole surgery.59 Thus, it is likely that the progressive thinning of the temporal sectors to less than the preoperative or normal levels is a common change after vitrectomy with ILM peeling. Macular surface maps indicated that the depression in the temporal macular sectors after ERM surgery and also after macular hole surgery59 with ILM peeling. It has been reported that ILM peeling caused inner retinal defects deeper than the ganglion cell layer. Several alterations to the inner retina may be involved in the marked thinning of the temporal macula after vitrectomy with ILM peeling.

Several studies have reported that the central macular thickness was not significantly correlated with the postoperative visual acuity.1,15,19,20,22 In contrast, Kim et al.21 reported that there was a significant correlation between the early postoperative central macular thickness and the final BCVA. In our study, the pre- and postoperative central macular thickness was significantly correlated with the postoperative BCVA at each follow-up examination. We confirmed that the central macular thickness 1 month after surgery was a significant factor for BCVA at 12 and 24 months using multiple regression analyses.

The exact reason for the contradictory findings has not been determined.

In conclusion, successful epiretinal membrane surgery with ILM peeling led to progressive changes in the retinal thickness in all sectors of the macular area for at least 48 months. The preoperative retinal thickening in all sectors except in the central and inner nasal sectors returned to near the normal level by 24 to 48 months after surgery. However, it did not appear to return to normal thickness in the central and nasal sectors. On the other hand, the temporal sectors became thinner than the normal thickness at 36 months. Further studies are needed to determine the effect of the progressive retinal thinning on retinal physiology and associated with adverse effects on extrafoveal retinal function.

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References


