Comparison of Individual Retinal Layer Thicknesses after Epiretinal Membrane Surgery with or without Internal Limiting Membrane Peeling

Chul Hee Lee, Min Woo Lee, Eun Young Choi, Suk Ho Byeon, Sung Soo Kim, Hyoung Jun Koh, Sung Chul Lee, and Min Kim

1Department of Ophthalmology, Institute of Vision Research, Gangnam Severance Hospital, Yonsei University College of Medicine, Seoul, Republic of Korea
2Department of Ophthalmology, Institute of Vision Research, Severance Hospital, Yonsei University College of Medicine, Seoul, Republic of Korea

Correspondence should be addressed to Min Kim; minkim76@gmail.com

Received 3 March 2018; Revised 19 July 2018; Accepted 9 August 2018; Published 21 October 2018

Academic Editor: Glenn Yiu

Copyright ©2018 Chul Hee Lee et al. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Purpose. To compare changes in the retinal layer thickness and visual outcomes in patients undergoing epiretinal membrane (ERM) surgery with or without internal limiting membrane (ILM) peeling. Methods. Seventy-six eyes of 76 patients who underwent ERM surgery from January 2013 to March 2015 at the Department of Ophthalmology, Yonsei University College of Medicine, Seoul, South Korea, were analyzed. While ERM removal with ILM peeling was performed in ILM peeling (P) group (n = 39), ILM peeling was not performed in non-ILM peeling (NP) group (n = 37). Retinal layer segmentation was performed using optical coherence tomography images. Individual retinal layer thicknesses before and at 6 months after ERM surgery were compared. Postoperative best-corrected visual acuity (BCVA) was also compared. Results. In the P group, the thicknesses of retinal nerve fiber layer (RNFL), ganglion cell layer (GCL), and inner plexiform layer (IPL) were significantly reduced. In the NP group, significant decreases in the RNFL, GCL, IPL, inner nuclear layer, and outer plexiform layer were observed. The P group manifested a greater mean postoperative GCL (35.56 ± 1.53 µm vs 29.86 ± 2.16 µm; p = 0.033) and less loss of GCL (−10.26 ± 1.91 µm vs −19.86 ± 2.74 µm; p = 0.004) compared to the NP group. No statistically significant differences were observed when comparing the changes in BCVA. Conclusions. This study demonstrates that ILM peeling for ERM surgery may result in better preservation of GCL compared to no ILM peeling.

1. Introduction

The epiretinal membrane (ERM) is an avascular proliferative fibrous tissue composed of extracellular matrix and a polymorphous population of cells, which develops between the vitreous and the internal limiting membrane (ILM). Tangential tractional force on the retina asserted by an ERM leads to distortion of normal retinal structure and layers, causing symptoms such as impairment of central vision, metamorphopsia, macropsia, and monocular diplopia [1, 2]. For many years, the treatment of choice for symptomatic ERMs had been pars plana vitrectomy (PPV) with membranectomy [3]. As ILM peeling has greatly improved the anatomical success rate of macular hole surgery in randomized controlled trials [4, 5], ILM removal has been favored in the treatment of ERM. Although previous studies have described some advantages of ILM peeling for ERM surgery [6, 7], there is still debate over the visual outcomes, safety, and indications for ILM peeling in patients with ERM.

The advantages of ILM removal during ERM surgery include better anatomical outcomes, lower recurrence rates, and better final visual acuity [6–9]. ILM is a transparent structure that defines the boundary between the retina and the vitreous body. It serves as the footplate of Müller cells, astrocytes, and fibroblasts, permitting adhesion and gliosis...
2 Journal of Ophthalmology

This was a single-center prospective study. We analyzed patient records, operative reports, and operation videos of 103 patients (103 eyes) who underwent ERM surgery by two surgeons (MK and SSK) at the Department of Ophthalmology, Yonsei University College of Medicine, Seoul, South Korea, between January 2013 and March 2015. The patients were classified into two groups depending on whether they underwent ILM peeling: ILM peeling (P) group with PPV plus epiretinal membrane peeling and non-ILM peeling (NP) group with PPV plus epiretinal membrane peeling. Only patients diagnosed with idiopathic ERM were included. Patients with other combined forms of maculopathy, such as macular hole, lamellar macular hole, diabetic macular edema, or retinal vein occlusion were excluded. Patients were also excluded from the analysis if they required reoperation or intravitreal injections within the 1-year follow-up period to treat postoperative complications such as retinal detachment, dislocation of intraocular lens, pseudophakic cystoid macular edema, and choroidal neovascularization. Only those patients who did not show significant posterior capsular opacity after the ERM surgery were included in the study. This study was approved by the institutional review board of Yonsei University College of Medicine (IRB approval number: 3-2016-0278) and was conducted in accordance with the tenets of the Declaration of Helsinki.

2.2 Preoperative Examination and Automated Segmentation. All past medical history and preoperative ophthalmologic data for each patient were reviewed. Results of the following preoperative evaluations were recorded: BCVA obtained by the Snellen visual acuity chart, which was converted to a logarithm of the minimum angle of resolution (logMAR) value for statistical analysis; slit-lamp biomicroscopy; intraocular pressure, as determined using a noncontact tonometer; color fundus photography; biometry measurements, obtained by the ZEISS IOLMaster® 500 (Carl Zeiss AG; Heidenheim, Germany); and OCT images, taken by the spectral domain OCT (SD-OCT; Spectralis®; Heidelberg Engineering, Heidelberg, Germany).

Automated segmentation of retinal layers was performed by the built-in software, which automatically calculated the average retinal thickness in each of the individual retinal layers: retinal nerve fiber layer (RNFL), GCL, inner plexiform layer (IPL), inner nuclear layer (INL), outer plexiform layer (OPL), outer nuclear layer (ONL), photoreceptor layer (PRL), and retinal pigment epithelium (RPE). The segmentation analysis was performed by two independent observers (CHL and EYC). Analysis was performed within a 6-mm diameter circle centered on the fovea, as defined in the Early Treatment of Diabetic Retinopathy Study (ETDRS) [19]. The diameters of the central circle, inner ring, and outer ring were 1 mm, 3 mm, and 6 mm, respectively (Figure 1).

2.3 Surgical Technique. For all patients, a 25-gauge PPV was performed (CONSTELLATION® Vision System, Alcon, Fort Worth, TX, USA). After performing core vitrectomy, triamcinolone was injected intravitreally to better visualize the vitreous gel and ERM. After removing the detached vitreous gel and the posterior hyaloid membrane, removal of the ERM was performed using intracocular forceps.

In the P group, the ILM was stained with 0.2mL of 1 mg/mL indocyanine green (ICG) solution (DID-Indocyanine Green inj, Dongindang Pharmaceutical, Siheung, Republic of Korea). Both surgeons used the same concentration of ICG dye. After injecting the 1 mg/mL ICG solution at the macula area, the infusion was turned on immediately followed by aspiration of ICG dye with the vitrectomy cutter for minimal ICG dye circulation within the vitreous cavity. The ILM was peeled of an area of approximately 2 to 3 disc diameters centered on the macula using a 25-gauge ILM forceps. After the initial ILM peeling, ICG dye solution was reinfused to visualize residual ILM. Residual ILM was peeled until there was no ILM visible by ICG dye staining within 2 to 3 disc diameters of the macular center (Figure 2(a)).

In the NP group, ICG dye solution was injected over the macula region after epiretinal membrane peeling to ensure that ILM remained intact. Patients with ILM unstained after simple membrane peeling were excluded from the NP group (Figure 2(b)).
2.4. Postoperative Examination. To determine the effects of ILM peeling on BCVA and anatomical structure of the retinal layers, the BCVA and automated segmentation analysis of SD-OCT at 6 months after the operation were analyzed. The change in retinal layer thickness was determined by subtracting the preoperative retinal layer thickness from the postoperative retinal layer thickness at the 1 mm central circle. The change in BCVA was calculated by subtracting the preoperative BCVA from the postoperative BCVA at 6 months follow-up.

2.5. Statistical Analyses. For all segmentation data, only the retinal layer thicknesses in the central circle at 1 mm were compared. The mean age and preoperative BCVA, biometry data, and segmentation data of the two groups (P group and NP group) were compared using independent Student’s t-tests. The mean postoperative BCVA and segmentation data of the two groups were also compared using independent Student’s t-tests. Within each group, the significance of the change in thickness of each retinal layer from before surgery to 6 months after surgery was determined by paired sample t-tests. The correlation between the thickness of each layer and postoperative BCVA was calculated by Pearson’s correlation coefficient. A value of $p < 0.05$ was accepted as statistically significant.

Inter-rater agreement between the two observers was analyzed for all segmentation data by calculating intraclass correlation coefficients (ICCs). All statistical analyses of the data were performed using IBM SPSS 23.0 software for
3. Results

3.1. Baseline Characteristics. Out of the 103 patients who underwent ERM surgery, 76 patients (76 eyes) with clinically confirmed idiopathic ERM satisfied the inclusion criteria and were included in the final analysis (P group \( n = 39 \), NP group \( n = 37 \)). Sample size calculation was done by using the modified Cochran’s formula. By using this formula, the sample size of 76 eyes met 95% confidence level with 6% margin of error about the population of 103 cases that underwent ERM surgery by two surgeons (MK and SSK) at the Department of Ophthalmology, Yonsei University College of Medicine between January 2013 and March 2015. There were no significant differences in patient age, BCVA, axial length, and spherical equivalent diopter between the two groups (Table 1). In addition, the mean preoperative segmented retinal layer thicknesses at each macular sector did not exhibit any significant differences (Table 1). Simultaneous cataract surgery was performed for all phakic eyes (P group: 61.5%; NP group: 62.2%; independent Student’s \( t \)-tests, \( p = 0.999 \), and posterior capsular opacities were removed in all pseudophakic patients (P group: 38.5%; NP group: 37.8%; \( p = 0.999 \)). In the P group, the average ILM removal time was 2.4 ± 0.5 minutes for surgeon 1 (MK) and 2.3 ± 0.7 for surgeon 2 (SSK) (\( p = 0.999 \)). In the NP group, the average ERM removal time was 2.2 ± 0.2 minutes for surgeon 1 (MK) and 2.2 ± 0.4 minutes for surgeon 2 (SSK) (\( p = 0.999 \)).

3.2. Individual Retinal Layer Segmentation and BCVA at 6 Months Postoperatively. At 6 months postoperatively, the mean GCL thickness was significantly higher in the P group than in the NP group (P group: 35.56 ± 1.53 \( \mu \)m; NP group: 29.86 ± 2.16 \( \mu \)m; \( p = 0.033 \); Table 2). There was no significant difference in BCVA between the two groups (P group: 29.86 ± 2.16 \( \mu \)m; \( p = 0.033 \); Table 2). There was no significant correlation between postoperative GCL and postoperative BCVA was observed in both groups (P group: Pearson \( r = 0.218, p = 0.182 \); NP group: Pearson \( r = 0.049, p = 0.775 \)).

In the analysis of mean differences in retinal layer thickness before and after 6 months operation, the P group exhibited less loss of GCL thickness when compared to the NP group (P group: \( -10.26 \pm 1.91 \mu m \); NP group: \( -19.86 \pm 2.74 \mu m \); \( p = 0.004 \); Table 3). The mean change in thickness in all other segmented layers showed no significant differences (Table 3).

In paired \( t \)-test analysis, the P group showed significant reduction in the RNFL, GCL, and IPL thicknesses at 6 months after surgery. On the other hand, significant decreases in thickness that extended into the deeper layers, including the RNFL, GCL, IPL, INL, and OPL, were observed in the NP group (Table 3). The BCVA of both groups improved significantly after surgery (P group: \( p < 0.0001 \); NP group: \( p = 0.006 \); paired \( t \)-tests).
The ICCs for the preoperative and postoperative segmentation data indicated excellent interrater agreement in all layers.

4. Discussion

ILM peeling for ERM surgery resulted in less loss of GCL thickness compared to no ILM peeling.

A novel finding of this study is that the P group exhibited significantly lower reduction of GCL thickness compared to the NP group. This contradicts many previous concerns regarding iatrogenic trauma and retinal toxicity produced by ICG dye guided ILM peeling.

In previous studies using electron microscopy, findings indicated possible Müller cell damage caused by the ILM peeling procedure [20, 21]. However, these peeled ILM samples only contained Müller cells and myofibroblasts and were void of ganglion cells, photoreceptors, or RPE cells [20]. Another recent study showed that specimens acquired from ILM abrasion using a tano diamond-dusted membrane scraper did not contain RNFL or neuronal cells that lay beneath the ILM [22]. In accordance with our results, these scraper did not contain RNFL or neuronal cells that lay from ILM abrasion using a tano diamond-dusted membrane [20]. Another recent study showed that specimens acquired including the RPE layer. In agreement with our results, Kwok et al. have demonstrated that there was no clinically significant ICG toxicity after ILM peelingangiographically [23]. There have been some case reports of poor visual outcomes due to ICG dye toxicity after successful macular surgery.

### Table 1: Baseline characteristics and preoperative automated retinal layer segmentation.

|                      | P group (ILM peeling) | NP group (non-ILM peeling) | p value |
|----------------------|-----------------------|-----------------------------|---------|
| **Age (years)**      | Mean ± SD             | Mean ± SD                   |         |
| Preoperative BCVA (logMAR) | 66.59 ± 1.41         | 68.73 ± 1.14                | 0.245   |
| Spherical equivalent (D) | 0.23 ± 0.03           | 0.27 ± 0.03                 | 0.255   |
| Axial length (mm)    | 23.72 ± 0.20          | 23.31 ± 0.18                | 0.135   |
| Total retinal thickness (µm) | 466.4 ± 11.31       | 458.7 ± 10.25               | 0.616   |
| RNFL thickness (µm)  | 84.46 ± 11.79         | 70.78 ± 9.81                | 0.378   |
| GCL thickness (µm)   | 45.82 ± 1.39          | 49.73 ± 1.97                | 0.106   |
| IPL thickness (µm)   | 45.97 ± 1.76          | 46.43 ± 1.86                | 0.858   |
| INL thickness (µm)   | 50.49 ± 1.70          | 52.38 ± 1.71                | 0.435   |
| OPL thickness (µm)   | 37.82 ± 1.32          | 40.46 ± 1.68                | 0.217   |
| ONL thickness (µm)   | 114.2 ± 4.60          | 111.4 ± 4.35                | 0.660   |
| PRL thickness (µm)   | 71.56 ± 0.09          | 70.84 ± 0.64                | 0.444   |
| RPE thickness (µm)   | 16.21 ± 0.47          | 16.84 ± 0.52                | 0.369   |

**BCVA** = best-corrected visual acuity; **SD** = standard deviation; **ILM** = internal limiting membrane; **RNFL** = retinal nerve fiber layer; **GCL** = ganglion cell layer; **IPL** = inner plexiform layer; **INL** = inner nuclear layer; **OPL** = outer plexiform layer; **ONL** = outer nuclear layer; **PRL** = photoreceptor layer; **RPE** = retinal pigment epithelium. Independent Student’s t-test for statistical analysis between Group 1 and Group 2 for retinal layers, BCVA, age, spherical equivalent, and axial length.

### Table 2: Automated retinal layer segmentation and best-corrected visual acuity at 6 months after epiretinal membrane surgery.

|                      | P group (ILM peeling) | NP group (non-ILM peeling) | p value |
|----------------------|-----------------------|-----------------------------|---------|
| **Total retinal thickness (µm)** | 378.9 ± 5.89         | 360.8 ± 8.94                | 0.091   |
| RNFL thickness (µm)  | 21.67 ± 1.47          | 23.95 ± 1.80                | 0.327   |
| GCL thickness (µm)   | 35.56 ± 1.53          | 29.86 ± 2.16                | 0.033   |
| IPL thickness (µm)   | 34.05 ± 1.17          | 31.41 ± 1.81                | 0.219   |
| INL thickness (µm)   | 45.46 ± 1.55          | 44.49 ± 2.45                | 0.735   |
| OPL thickness (µm)   | 35.05 ± 1.16          | 33.30 ± 1.49                | 0.353   |
| ONL thickness (µm)   | 117.5 ± 3.90          | 109.5 ± 2.98                | 0.112   |
| PRL thickness (µm)   | 72.77 ± 0.72          | 72.05 ± 0.67                | 0.470   |
| RPE thickness (µm)   | 17.13 ± 0.93          | 17.24 ± 0.80                | 0.926   |
| BCVA (logMAR)        | 0.11 ± 0.02           | 0.16 ± 0.02                 | 0.099   |

**BCVA** = best-corrected visual acuity; **SD** = standard deviation; **ILM** = internal limiting membrane; **RNFL** = retinal nerve fiber layer; **GCL** = ganglion cell layer; **IPL** = inner plexiform layer; **INL** = inner nuclear layer; **OPL** = outer plexiform layer; **ONL** = outer nuclear layer; **PRL** = photoreceptor layer; **RPE** = retinal pigment epithelium. Independent Student’s t-test for statistical analysis between Group 1 and Group 2 for retinal layers and BCVA.
Table 3: Difference in segmented retinal layer thicknesses and best-corrected visual acuity before and at 6 months after epiretinal membrane surgery.

| Difference                                      | P group (ILM peeling) | $p$ value (preop vs POD 6 month) | NP group (non-ILM peeling) | $p$ value (preop vs POD 6 month) | $p$ value (P group vs NP group) |
|------------------------------------------------|-----------------------|---------------------------------|-----------------------------|---------------------------------|---------------------------------|
| Total retinal thickness ($\mu m$)               | $-87.51 \pm 9.87$    | $<0.0001^\dagger$               | $-97.95 \pm 8.35$          | $<0.0001^\dagger$               | 0.425                           |
| RNFL thickness ($\mu m$)                        | $-62.79 \pm 11.43$   | $<0.0001^\dagger$               | $-46.84 \pm 9.21$          | $<0.0001^\dagger$               | 0.283                           |
| GCL thickness ($\mu m$)                         | $-10.26 \pm 1.91$    | $<0.0001^\dagger$               | $-19.86 \pm 2.74$          | $<0.0001^\dagger$               | 0.004$^\ast$                     |
| IPL thickness ($\mu m$)                         | $-11.92 \pm 1.89$    | $<0.0001^\dagger$               | $-15.03 \pm 2.37$          | $<0.0001^\dagger$               | 0.306                           |
| INL thickness ($\mu m$)                         | $-5.03 \pm 2.49$     | 0.050                           | $-7.89 \pm 3.29$           | 0.022$^\ast$                     | 0.486                           |
| OPL thickness ($\mu m$)                         | $-2.77 \pm 1.71$     | 0.114                           | $-7.16 \pm 1.58$           | 0.002$^\ast$                     | 0.064                           |
| ONL thickness ($\mu m$)                         | $3.26 \pm 5.29$      | 0.542                           | $-1.89 \pm 4.88$           | 0.721                           | 0.478                           |
| PRL thickness ($\mu m$)                         | $1.21 \pm 0.77$      | 0.126                           | $1.22 \pm 0.82$            | 0.194                           | 0.992                           |
| RPE thickness ($\mu m$)                         | $0.92 \pm 0.93$      | 0.326                           | $0.41 \pm 0.78$            | 0.672                           | 0.672                           |
| BCVA (logMAR)                                   | $-0.11 \pm 0.02$    | $<0.0001^\dagger$               | $-0.11 \pm 0.03$          | 0.006$^\ast$                     | 0.950                           |

BCVA = best-corrected visual acuity; POD = postoperative day; SD = standard deviation; ILM = internal limiting membrane; RNFL = retinal nerve fiber layer; GCL = ganglion cell layer; IPL = inner plexiform layer; INL = inner nuclear layer; OPL = outer plexiform layer; ONL = outer nuclear layer; PRL = photoreceptor layer; RPE = retinal pigment epithelium. Independent Student’s $t$-test for statistical analysis between Group 1 and Group 2 for difference of retinal layers and BCVA: $^* p < 0.05$, $^\ast p < 0.01$, $^\dagger p < 0.001$. Paired sample $t$-test within Group 1 and Group 2 for statistical analysis: $^\ast p < 0.05$, $^\ast\ast p < 0.01$, $^\dagger\dagger p < 0.001$. hole closure [24]. However, with a macular hole, the RPE and other retinal layers at the fovea are directly exposed to the vitreous cavity, whereas in the presence of an ERM, these layers are enclosed by the fibrotic membrane and ILM. We speculate that the risk of foveal exposure to ICG dye would be lower in patients with an ERM.

The reason for the relative preservation of postoperative GCL in the P group is unclear. However, we hypothesize that induction of Müller cell injury during ILM peeling may have triggered reactive gliosis, resulting in subsequent thickening of GCL compared to the NP group. On the retinal side of the ILM obtained after ERM surgery, electron micrographs revealed segments of Müller cell footplates in ILM specimens, which shows that ILM peeling generates Müller cell injury [21]. In addition, injured Müller cells have a role in retinal neural regeneration and repair as described in previous studies performed on rodent and human retinal tissues [25–28]. Hypothetically, ILM peeling, having induced Müller cell injury, may have activated reactive gliosis at the GCL level with the RNFL serving as Müller cell footplate.

However, it is unclear whether greater GCL thickness as shown by our study necessarily means a recovery of healthy neuronal cells. Previous studies have shown decreased retinal function on multifocal electroretinogram and visual field sensitivity after ILM peeling [21, 29]. Our study showed that there was no correlation between postoperative GCL thickness and postoperative BCVA in the P group (Pearson $r = 0.218$, $p = 0.182$). The relative preservation of GCL after ILM peeling may be a result of a reactive gliosis after initial injury on Müller cells, rather than a healthy regeneration of ganglion cells. Further study about the changes that occur at cellular level after ILM peeling is required to clarify these results.

There is no significant difference in postoperative BCVA between ILM peeling and no ILM peeling for ERM surgery.

Both groups exhibited significant improvements in BCVA after ERM surgery. However, ILM peeling did not result in superior visual outcomes regarding central visual acuity. Our results agree with a recent randomized controlled study that compared the BCVA of ILM peeling and no ILM peeling [30]. In other studies, some have reported superior outcomes in ILM peeling group, while some have reported opposing results [6, 7, 31]. However, the advantage of our study over these previous studies is that the proportion of eyes with and without ILM peeling was similar (P group: 51.3% versus NP group: 48.7%), which adds representativeness and objectivity to our data.

Our study has a few limitations. First, although the surgical protocols in the two groups were identical except for ILM peeling, two surgeons performed operations. However, there was no significant difference between the two surgeons in operation time, ERM removal time, or ILM removal time. Also, since there were a sufficient and approximately equal number of each surgeon’s patients in both groups, the surgeon factors may have been minimized. Second, epiretinal membranes without ILM peeling does not necessarily result in complete preservation of the ILM, as ILM could be removed along with the ERM during the membrane removal procedure. Unfortunately, we could not perform a histological study proving that the ILM was completely preserved after ERM removal in the NP Group. As an alternative to a histological study, we have done the best we could clinically by thoroughly reviewing our surgical videos to include only those eyes that showed complete peeling of ILM in the P group and cases with ILM as completely preserved as possible in the NP Group grossly (Figure 2). Third, there are insufficient data about the changes that occur at cellular levels after surgical manipulation of the ILM, a key finding to explain our data.

In conclusion, this study demonstrates a novel finding that ILM peeling during ERM surgery may result in better preservation of GCL compared to ERM surgery without ILM peeling. We cautiously speculate that the removal of ILM and subsequent Müller cell injury may have induced reactive...
gliosis. Future studies regarding the changes inflicted on Müller cells after ILM removal in the human retina are required to support our results and confirm our findings.

Data Availability

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request. All data generated or analyzed during this study are included in this article.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Acknowledgments

This study was supported by a faculty research grant of Yonsei University College of Medicine, 2017-32-0037.

References

[1] H. Liu, S. Zuo, C. Ding, X. Dai, and X. Zhu, “Comparison of the effectiveness of pars plana vitrectomy with and without internal limiting membrane peeling for idiopathic retinal membrane removal: a meta-analysis,” *Journal of Ophthalmology*, vol. 2015, Article ID 974568, 10 pages, 2015.

[2] F. S. Ting and A. K. Kwok, “Treatment of epiretinal membrane: an update,” *Hong Kong Medical Journal*, vol. 11, no. 6, pp. 496–502, 2005.

[3] H. Shimada, H. Nakashizuka, T. Hattori, R. Mori, Y. Mizutani, and M. Yuzawa, “Double staining with brilliant blue G and double peeling for epiretinal membranes,” *Ophthalmology*, vol. 116, no. 7, pp. 1370–1376, 2009.

[4] N. Lois, J. Burr, J. Norrie et al., “Full-thickness Macular H et al: internal limiting membrane peeling versus no peeling for idiopathic full-thickness macular hole: a pragmatic randomized controlled trial,” *Investigative Ophthalmology & Visual Science*, vol. 52, no. 3, pp. 1586–1592, 2011.

[5] L. Ternent, L. Vale, C. Boachie, J. M. Burr, and N. Lois, “Full-Thickness Macular H, Internal Limiting Membrane Peeling Study G: cost-effectiveness of internal limiting membrane peeling versus no peeling for patients with an idiopathic full-thickness macular hole: results from a randomised controlled trial,” *British Journal of Ophthalmology*, vol. 96, no. 3, pp. 438–443, 2012.

[6] D. W. Park, P. U. Dugel, J. Garda et al., “Macular pucker removal with and without internal limiting membrane peeling: pilot study,” *Ophthalmology*, vol. 110, no. 1, pp. 62–64, 2003.

[7] E. H. Bovey, S. Uffer, and F. Achache, “Surgery for epimacular membrane: impact of retinal internal limiting membrane removal on functional outcome,” *Retina*, vol. 24, no. 5, pp. 728–735, 2004.

[8] S. R. Tari, O. Vidne-Hay, C. Greenstein, G. R. Barile, D. C. Hood, and S. Chang, “Functional and structural measurements for the assessment of internal limiting membrane peeling in idiopathic macular pucker,” *Retina*, vol. 27, no. 5, pp. 567–572, 2007.

[9] R. Sorcinelli, “Surgical management of epiretinal membrane with indocyanine-green-assisted peeling,” *Ophthalmologica*, vol. 217, no. 2, pp. 107–110, 2003.

[10] A. M. Maguire, W. E. Smiddy, S. K. Nanda, R. G. Michels, Z. de la Cruz, and W. R. Green, “Clinicopathologic correlation of recurrent epiretinal membranes after previous surgical removal,” *Retina*, vol. 10, no. 3, pp. 213–222, 1990.

[11] I. Iandiev, O. Uckermann, T. Pannicke et al., “Glial cell reactivity in a porcine model of retinal detachment,” *Investigative Ophthalmology & Visual Science*, vol. 47, no. 5, pp. 2161–2171, 2006.

[12] K. Kumagai, M. Hangai, and N. Ogino, “Progressive thinning of regional macular thickness after epiretinal membrane surgery,” *Investigative Ophthalmology & Visual Science*, vol. 56, no. 12, pp. 7236–7242, 2015.

[13] H. N. Oh, J. E. Lee, H. W. Kim, and I. H. Yun, “Clinical outcomes of double staining and additional ILM peeling during ERM surgery,” *Korean Journal of Ophthalmology*, vol. 27, no. 4, pp. 256–260, 2013.

[14] J. Tian, B. Varga, G. M. Somfai, W. H. Lee, W. E. Smiddy, and D. C. DeBuc, “Real-time automatic segmentation of optical coherence tomography volume data of the macular region,” *PLoS One*, vol. 10, no. 8, Article ID e0133980, 2015.

[15] D. Y. Kim, H. S. Yang, Y. J. Kook, and J. Y. Lee, “Association between microperimetric parameters and optical coherent tomographic findings in various macular diseases,” *Korean Journal of Ophthalmology*, vol. 29, no. 2, pp. 92–101, 2015.

[16] C. I. Falkner-Radler, C. Glittenberg, S. Hagen, T. Benesch, and S. Binder, “Spectral-domain optical coherence tomography for monitoring epiretinal membrane surgery,” *Ophthalmology*, vol. 117, no. 4, pp. 798–805, 2010.

[17] A. Shiono, J. Kogo, G. Klose et al., “Photoreceptor outer segment length: a prognostic factor for idiopathic epiretinal membrane surgery,” *Ophthalmology*, vol. 120, no. 4, pp. 788–794, 2013.

[18] S. W. Park, I. S. Byon, H. Y. Kim, J. E. Lee, and B. S. Oum, “Analysis of the ganglion cell layer and photoreceptor layer using optical coherence tomography after idiopathic epiretinal membrane surgery,” *Graefe's Archive for Clinical and Experimental Ophthalmology*, vol. 253, no. 2, pp. 207–214, 2015.

[19] Early Treatment Diabetic Retinopathy Study Research Group, “Early Treatment Diabetic Retinopathy Study design and baseline patient characteristics: ETDRS report number 7,” *Ophthalmology*, vol. 98, no. 5, pp. 741–756, 1991.

[20] R. G. Schumann, M. Remy, M. Grueterich, A. Gandorfer, and C. Haritoglou, “How it appears: electron microscopic evaluation during brilliant blue G assisted macular hole surgery,” *British Journal of Ophthalmology*, vol. 92, no. 3, pp. 330–331, 2008.

[21] S. R. Tari, O. Vidne-Hay, C. Greenstein, G. R. Barile, D. C. Hood, and S. Chang, “Functional and structural measurements for the assessment of internal limiting membrane peeling in idiopathic macular pucker,” *Retina*, vol. 27, no. 5, pp. 567–572, 2007.

[22] D. R. Almeida, E. K. Chin, R. M. Tarantola et al., “Effect of internal limiting membrane abrasion on retinal tissues in macular holes,” *Investigative Ophthalmology & Visual Science*, vol. 56, no. 5, pp. 2783–2789, 2015.

[23] A. K. Kwok, T. Y. Lai, D. T. Yew, and W. W. Li, “Internal limiting membrane staining with various concentrations of indocyanine green dye under air in macular surgeries,” *American Journal of Ophthalmology*, vol. 136, no. 2, pp. 223–230, 2003.

[24] D. Stanescu-Segall and T. L. Jackson, “Vital staining with indocyanine green: a review of the clinical and experimental studies relating to safety,” *Eye*, vol. 23, no. 3, pp. 504–518, 2009.
[25] A. V. Das, K. B. Mallya, X. Zhao et al., “Neural stem cell properties of Muller glia in the mammalian retina: regulation by Notch and Wnt signaling,” Developmental Biology, vol. 299, no. 1, pp. 283–302, 2006.

[26] J. M. Lawrence, S. Singhal, B. Bhatia et al., “MIO-M1 cells and similar muller glial cell lines derived from adult human retina exhibit neural stem cell characteristics,” Stem Cells, vol. 25, no. 8, pp. 2033–2043, 2007.

[27] S. Ooto, T. Akagi, R. Kageyama et al., “Potential for neural regeneration after neurotoxic injury in the adult mammalian retina,” Proceedings of the National Academy of Sciences, vol. 101, no. 37, pp. 13654–13659, 2004.

[28] J. Wan, H. Zheng, Z. L. Chen, H. L. Xiao, Z. J. Shen, and G. M. Zhou, “Preferential regeneration of photoreceptor from Muller glia after retinal degeneration in adult rat,” Vision Research, vol. 48, no. 2, pp. 223–234, 2008.

[29] J. W. Lim, J. H. Cho, and H. K. Kim, “Assessment of macular function by multifocal electroretinography following epiretinal membrane surgery with internal limiting membrane peeling,” Clinical Ophthalmology, vol. 4, pp. 689–694, 2010.

[30] P. Tranos, S. Koukoula, D. G. Charteris et al., “The role of internal limiting membrane peeling in epiretinal membrane surgery: a randomised controlled trial,” British Journal of Ophthalmology, vol. 101, no. 6, pp. 719–724, 2017.

[31] A. Sivalingam, R. C. Eagle Jr., J. S. Duker et al., “Visual prognosis correlated with the presence of internal-limiting membrane in histopathologic specimens obtained from epiretinal membrane surgery,” Ophthalmology, vol. 97, no. 11, pp. 1549–1552, 1990.