

Postoperative changes in the retinal thickness and volume after vitrectomy for epiretinal membrane and internal limiting membrane peeling

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Abstract

The aim of the study was to investigate the thickness and volume profiles of each retinal layer in postoperative patients with epiretinal membranes.

Twenty-four patients who underwent pars plana vitrectomy with internal limiting membrane (ILM) peeling for epiretinal membrane were included. The best corrected visual acuity, thickness, and volume were recorded from the medical records through a retrospective review. Spectral domain optical coherence tomography was used to measure the average thickness and volume of each retinal layer before surgery and 6 months postoperatively.

All 24 patients were monitored for 60 months after surgery. In all Early Treatment Diabetic Retinopathy Study (ETDRS) subfields, the thickness and volume of the retinal nerve fiber layer and the inner retinal layer decreased significantly. In contrast, the thickness and volume of the ganglion cell layer, inner nuclear layer, inner plexiform layer, and outer plexiform layer only decreased in some ETDRS subfields. Finally, there was no significant change in the thickness or volume of the outer nuclear layer (ONL), retinal pigment epithelium (RPE), and photoreceptor layers in all ETDRS subfields.

The thickness and volume of the inner retina layer decreased significantly after pars plana vitrectomy using ILM peeling. However, there was no significant change in the thickness and volume of the outer retinal layers (ONL, RPE, and photoreceptor) after surgery.

Abbreviations: BCVA = best corrected visual acuity, ETDRS = Early Treatment Diabetic Retinopathy Study, GCL = ganglion cell layer, ICG = indocyanine green, INL = inner nuclear layer, IPL = inner plexiform layer, IR = inner retina, ONL = outer nuclear layer, OPL = outer plexiform layer, PC = photoreceptor, RNFL = retinal nerve fiber layer, RPE = retinal pigment epithelium, SD-OCT = spectral domain optical coherence tomography.

Keywords: epiretinal membrane, inner retinal layer, optical coherence tomography, outer retinal layer, vitrectomy

1. Introduction

Epiretinal membranes (ERM) are semitransparent membranes between the internal limiting membrane (ILM) and the vitreous that occur in approximately 7% of individuals over 49 years old. The prevalence increases significantly with age, and approaches 15.1% in individuals 70 to 79 years old.^[1] An ERM occurs on the retinal surface, affecting both the inner and outer retina and may lead to macular constriction and thickening.^[2,3] As the membrane contracts, it decreases and distorts vision. Surgical treatment is required for ERM. The standard treatment involves pars plana vitrectomy with ERM removal, with or without ILM removal.^[4] However, there is controversy regarding the necessity of ILM peeling.^[5] Many vitreoretinal surgeons favor ILM peeling

during ERM surgery because it facilitates retinal striae resolution and reduces the recurrence rate of EMR.^[6] However, the visual outcomes without ILM peeling are generally favorable.^[7] In addition, ILM peeling using indocyanine green (ICG) staining can damage the retina and affects the final best corrected visual acuity (BCVA). Müller cells have been identified in up to 63.4% of ILM specimens after ERM with ILM peeling.^[8] Therefore, ILM peeling during ELM removal is currently debated. Many studies using spectral domain optical coherence tomography (SD-OCT) have reported that the postoperative integrity of the photoreceptor (PC) inner/outer segment (IS/OS) junction is an important factor that predicts visual outcomes after ERM surgery.^[9–11] Since ERMs occur on the surface of the retina, the inner retina (IR) should theoretically be impaired more than is the outer retina. Despite the importance of the IR with regard to the visual outcome, there are few studies that have evaluated it because of technical difficulty.

With the recent availability of SD-OCT, quantitative maps of the retina can be generated with high spatial resolution. This technology can also measure the thickness and volume of all retinal layers. The purpose of this study was to investigate the thickness and volume changes of all 10 retinal layers after pars plana vitrectomy, ERM removal, and ILM peeling using SD-OCT.

2. Methods

2.1. Subjects

The medical charts of 24 patients who underwent PPV with ILM peeling for unilateral, idiopathic ERM at Seoul St. Mary's

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Hospital between January 2008 and October 2013 were reviewed. This study was conducted according to the guidelines of the Association for Research in Vision and Ophthalmology. It adheres to the tenets of the Declaration of Helsinki and all protocols were approved by the Institutional Review Board of the Catholic University of Korea.

Patients were included if they were >18 years old and required elective PPV to treat idiopathic ERM with a postoperative evaluation of >12 months. Exclusion criteria included secondary ERM arising from uveitis, previous retinal detachment surgery or laser treatment, venous occlusion, glaucoma, anisometropia (>2 diopters), high myopia (spherical equivalent of >-6.0 diopters or axial length >26 mm), intraocular pressure (IOP) >21 mm Hg after surgery, and any other ocular condition that could affect the postoperative results.

Ocular examinations were performed preoperatively and 6 months postoperatively. The BCVA was measured using log MAR. The IOP was measured with Goldmann tonometry. Slit lamp biomicroscopy was used to examine the anterior segment and fundus. SD-OCT with HEYEX 6.0C software was used to measure the retinal thickness and volume preoperatively and 6 months postoperatively (Heidelberg Engineering, Heidelberg, Germany). And additional manual segmentation of retina was used to measure the retinal thickness and volume in some patients.

A single, experienced vitreo-retinal surgeon performed all the procedures at Seoul St. Mary's Hospital using standardized surgical procedures. The procedure involved 3-port vitrectomy with the Constellation system (Alcon Surgical, Ft. Worth, TX) using 23-gauge, valved trocars and a widefield viewing system (MiniQuad XL VIT contact lens; Volk, Mentor, OH). If a clinically significant cataract was identified, phacoemulsification and intraocular lens implantation were conducted simultaneously. After removal of the vitreous gel and posterior hyaloid, ERM peeling was performed using 25-gauge forceps. The ILM was stained with 0.25% ICG solution through the posterior pole. After staining, the ILM was peeled from an area within 2 to 3 disc diameters from the fovea using 25-gauge forceps. In order to minimize damage of the papillomacular

bundle, the ERM and ILM peeling was initiated at the temporal region around the fovea. If needed, intraocular endolaser photocoagulation and fluid-air exchange or intravitreal gas injection were performed.

2.2. SD-OCT measurements

OCT images underwent automated segmentation of individual retinal layers: retinal nerve fiber layer (RNFL), ganglion cell layer (GCL), inner plexiform layer (IPL), inner nuclear layer (INL), outer plexiform layer (OPL), outer nuclear layer (ONL), IR from ILM to external limiting membrane, PC layer, and retinal pigment epithelium (RPE) (Fig. 1). Three retinal areas were demonstrated in each layer according to the Early Treatment Diabetic Retinopathy Study (ETDRS) grid: the fovea (or central circle with a diameter of 1mm); the pericentral ring (1-3mm from the center of the fovea); and the peripheral ring (3-6mm from the center of the fovea) (Fig. 2). Automated and manual measurements of their mean macular thickness and volume were done in 9 separate areas based on ETDRS sectors. The mean macular thickness and volume of each retinal layer was measured at the fovea and 4 sectors (superior, inferior, nasal, and temporal) of the pericentral and peripheral rings.

2.3. Statistical analysis

All statistical analyses were performed using SPSS version 22.0 software (SPSS Inc., Chicago, IL). A paired *T*-test was used to compare the baseline and postoperative data at each layer and sector. *P*-values <.05 were considered statistically significant.

3. Results

A total of 24 eyes from 24 patients (16 women and 8 men) with idiopathic ERM were included. The mean patient age was 64.3 years (range: 54-79 years). Six patients underwent concomitant cataract surgery. Eighteen patients were found to

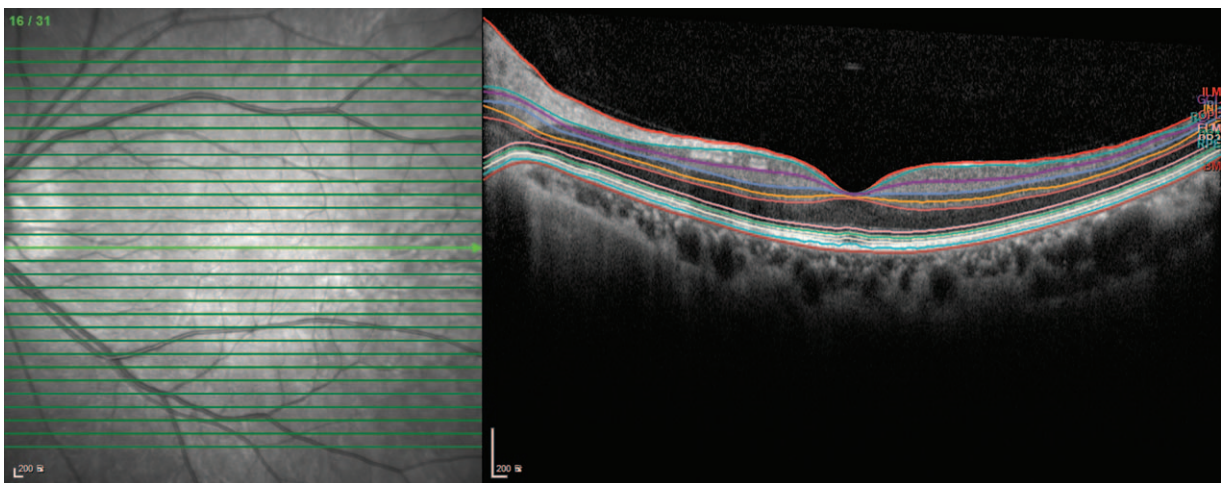


Figure 1. Normal retinal segmentation in SD-OCT. Nine retinal layers were identified by automatic segmentation: retinal nerve fiber layer (layer 1), ganglion cell layer (layer 2), inner plexiform layer (layer 3), inner nuclear layer (layer 4), outer plexiform layer (layer 5), outer nuclear layer (layer 6), inner retina layer (from internal limiting membrane to external limiting membrane) (layer 7), photoreceptor layer (layer 8), and retinal pigment epithelium (layer 9). SD-OCT = spectral domain optical coherence tomography.

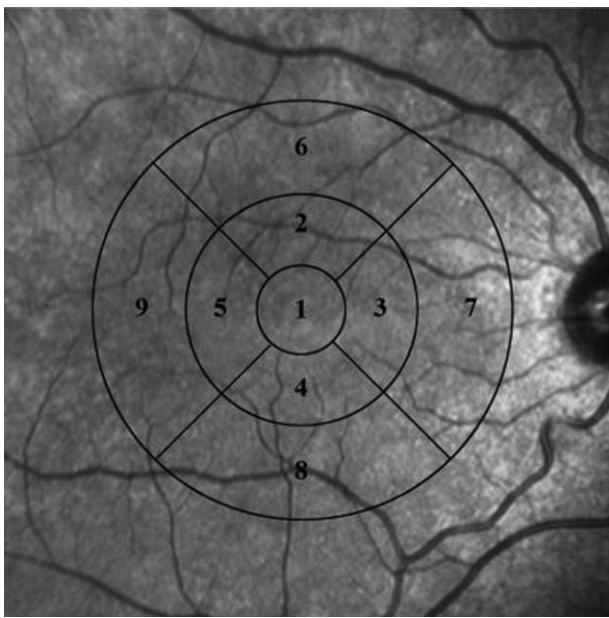


Figure 2. The 9 ETDRS regions in OCT. Fovea (region 1 of the 9 ETDRS regions); the pericentral ring (ETDRS regions 2–5); and the peripheral ring (ETDRS regions 6–9). ETDRS = Early Treatment Diabetic Retinopathy Study, OCT = optical coherence tomography.

have pseudophakia at the time of diagnosis. The mean visual acuity (log MAR) at baseline was 0.52. All patients underwent ILM peeling using ICG dye. Because 20 patients had some lesion-like lattice or suspicious retinal hole, 20 patients got the intraocular endolaser at peripheral retina. Fluid–air exchange was performed in 7 patients, and intravitreal gas injection (e.g., C3F8 or SF6 gas) was performed in 14 patients (Table 1). No intraocular or postoperative complications, such as retinal

Table 1
Baseline patient characteristics (n=24).

Characteristic	Number
Gender	
Male	16
Female	8
Age, years	
Range	54–79
Mean (SD)	64.3 (6.8)
Lens status	
Phakia	6
Pseudophakia	18
BCVA (log MAR)	
Range	0.3–1.0
Mean (SD)	0.52 (0.22)
Cataract operation	6
Internal limiting membrane peeling	
No peeling	0
With ICG	24
Without	0
ICG	
Intraocular endolaser	20
Fluid–air exchange	7
Intravitreal gas injection	14

BCVA=Best corrected visual acuity, ICG=indocyanine green, SD = standard deviation.

Table 2
Change in the retinal thickness (µm) of the macular sector in SD-OCT.

	Sector 1		Sector 2		Sector 3		Sector 4		Sector 5		Sector 6		Sector 7		Sector 8		Sector 9	
	Preop	Postop	Preop	Postop	Preop	Postop	Preop	Postop	Preop	Postop	Preop	Postop	Preop	Postop	Preop	Postop	Preop	Postop
RNFL	86±24	47±10	127±40	39±15	138±52	30±8	131±45	32±11	87±27	44±8	83±23	38±10	128±48	31±10	134±40	35±13	96±28	46±13
GCL	40±9	36±10	56±10	50±9	44±12	38±10	51±11	48±9	41±11	30±7	44±11	40±11	52±10	47±10	52±8	50±10	39±6	36±7
IPL	34±8	30±6	48±9	41±6	52±9	38±10	41±7	35±10	40±11	26±5	53±14	35±9	50±10	41±9	45±8	35±7	43±6	30±4
INL	45±11	40±10	52±10	52±12	692	57±11	54±11	53±9	43±8	37±10	45±9	44±12	53±13	51±10	56±11	52±10	375	44±8
OPL	32±8	28±4	40±8	36±6	131	39±10	40±7	38±9	32±5	28±3	32±5	30±4	41±8	35±4	41±7	37±6	35±7	30±3
ONL	78±25	72±11	83±29	81±18	689	108±33	80±37	77±20	68±25	60±14	72±26	70±11	90±39	89±18	86±46	86±19	68±7	66±12
RPE	14±3	13±1	14±2	15±2	263	18±9	14±3	14±2	14±1	13±1	16±5	14±2	15±2	14±2	18±10	16±5	401	14±2
PC	80±3	80±3	82±3	82±3	777	88±9	83±3	81±4	81±5	79±4	81±5	80±3	83±4	82±3	86±0	84±5	278	81±4
IR	318±76	253±42	407±91	298±53	447±99	289±35	402±96	227±30	306±86	257±47	317±65	296±42	414±103	308±43	415±84	252±37	316±74	283±33

* Significantly different, P < .05; paired T-test.

GCL = ganglion cell layer, INL = inner nuclear layer, IPL = inner plexiform layer, IR = inner retina, ONL = outer nuclear layer, OPL = outer plexiform layer, PC = photoreceptor, RNFL = retinal nerve fiber layer, RPE = retinal pigment epithelium

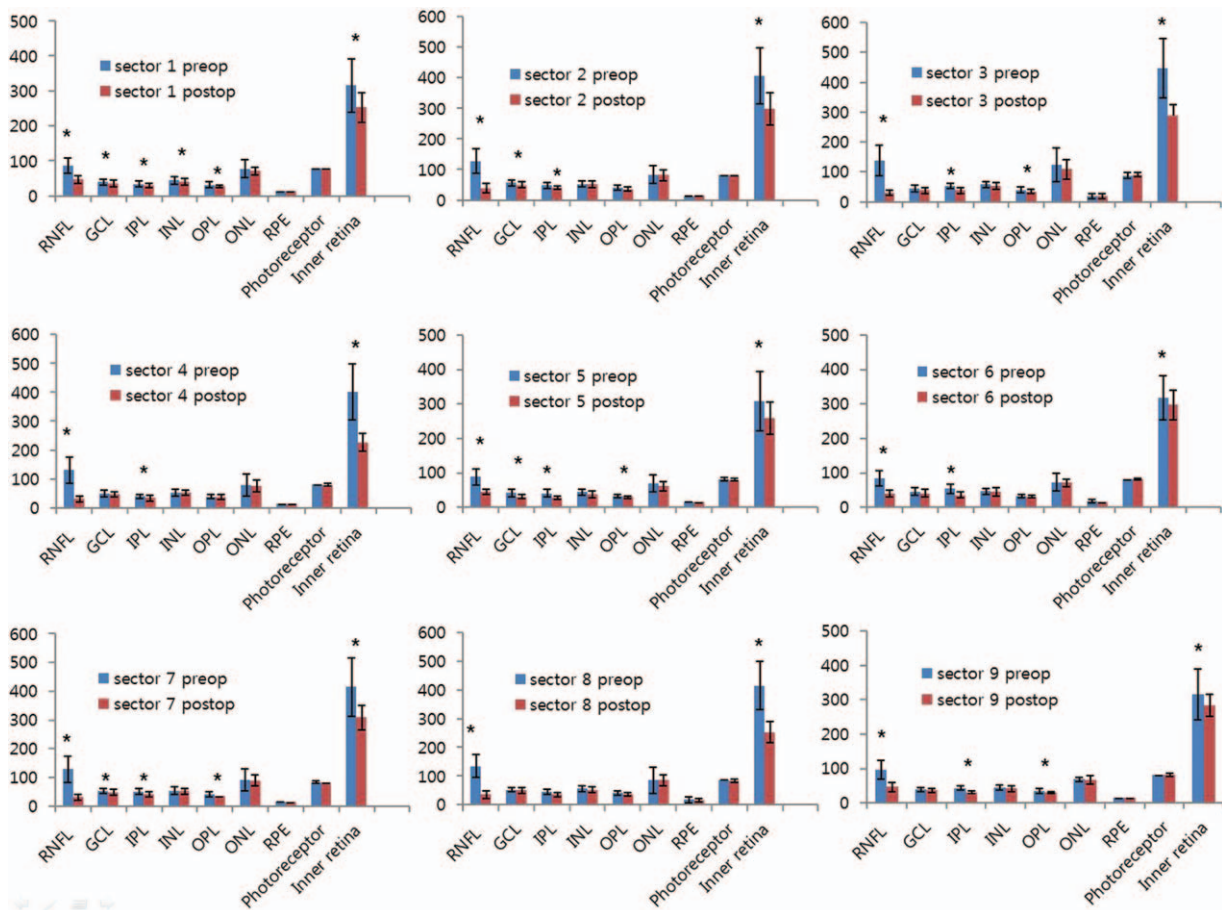


Figure 3. Change in the retinal thickness (μm) of the macular sector in SD-OCT. GCL = ganglion cell layer, INL = inner nuclear layer, IPL = inner plexiform layer, IR = inner retina, ONL = outer nuclear layer, OPL = outer plexiform layer, PC = photoreceptor, RNFL = retinal nerve fiber layer, RPE = retinal pigment epithelium, SD-OCT = spectral domain optical coherence tomography.

detachment, vitreous hemorrhage, or persistently elevated IOP, were observed.

Table 2 and Fig. 3 show the retinal thickness profile before and after surgery. In all ETDRS subfields, the thickness of the RNFL and IR layer thickness significantly decreased postoperatively. The GCL thickness significantly decreased in sectors 1, 2, 5, and 7 after surgery. The IPL thickness significantly decreased in all ETDRS subfields except sector 8. In contrast, the INL thickness significantly decreased only in sector 1 postoperatively. The OPL thickness significantly decreased in sectors 1, 3, 5, 7, and 9. There were no significant retinal thickness changes (in any of the ETDRS subfields) in the ONL, RPE, and PC layers.

Table 3 and Fig. 4 display the retinal volume profile before and after surgery. In all ETDRS subfields, the volume of the RNFL and IR layer decreased significantly after surgery. The GCL volume significantly decreased in sectors 1, 2, and 5 postoperatively. The IPL volume significantly decreased in all ETDRS subfields except sectors 4, 7, and 8 after surgery. The INL volume significantly decreased in sectors 1 and 5. The OPL volume significantly decreased in sectors 1, 5, and 9. There were no significant retinal thickness changes in any of the ETDRS subfields in the ONL, RPE, and PC layers.

In general, the thickness and volume of the RNFL and IR layer significantly decreased in all ETDRS subfields postoperatively. The thickness and volume of the GCL, INL, IPL, and OPL decreased in some subfields. There was no significant retinal thickness or volume change of the ONL, RPE, or PC layers in any of the ETDRS subfields (Fig. 5).

4. Discussion

ERM formation results from the fibrocellular proliferation over the ILM. Fibrocellular growth in the ERM induces a tangential tractional force on the retina, which causes it to wrinkle and distort. Ultimately, this results in decreased visual acuity and metamorphopsia.^[12]

Since the 1970s, pars plana vitrectomy has been used as a standard treatment for ERM removal. Recently, ILM peeling has been combined with ERM surgery to reduce recurrence.^[13] However, ILM peeling can be technically difficult because it is a transparent tissue. Therefore, staining materials were introduced to facilitate visualization and surgical removal of the ILM. Many surgeons have used the ICG dye for ILM peeling during retinal surgery. ICG is the most widely used ophthalmic dye. However, trypan blue or brilliant blue G can also be used to facilitate ILM

Table 3
Change in the retinal volume (μL) of the macular sector in SD-OCT.

	Sector 1		Sector 2		Sector 3		Sector 4		Sector 5		Sector 6		Sector 7		Sector 8		Sector 9										
	Preop	Postop	Preop	Postop	Preop	Postop	Preop	Postop	Preop	Postop	Preop	Postop	Preop	Postop	Preop	Postop	Preop	Postop									
RNFL	0.46±0.12	0.25±0.05	.001*	0.20±0.06	0.09±0.02	.002*	0.11±0.04	0.02±0.01	.001*	0.21±0.07	0.02±0.01	.002*	0.46±0.14	0.23±0.04	.001*	0.44±0.12	0.29±0.06	.001*	0.20±0.07	0.05±0.01	.002*	0.21±0.07	0.05±0.02	.001*	0.51±0.15	0.25±0.07	.001*
GCL	0.21±0.05	0.19±0.05	.017	0.09±0.02	0.09±0.02	.039*	0.03±0.01	0.03±0.01	.316	0.08±0.02	0.08±0.01	.674	0.22±0.06	0.16±0.04	.005*	0.23±0.06	0.21±0.07	.203	0.08±0.02	0.07±0.02	.774	0.08±0.01	0.08±0.02	.475	0.21±0.03	0.19±0.04	.203
IPL	0.18±0.04	0.16±0.03	.032*	0.08±0.01	0.07±0.01	.032*	0.04±0.01	0.03±0.01	.030*	0.07±0.01	0.06±0.01	.721	0.19±0.05	0.14±0.03	.002*	0.22±0.06	0.18±0.05	.021*	0.08±0.02	0.07±0.01	.174	0.08±0.02	0.08±0.02	.066	0.19±0.04	0.16±0.02	.004*
INL	0.24±0.06	0.21±0.05	.044*	0.09±0.02	0.08±0.02	.135	0.05±0.01	0.04±0.01	.161	0.08±0.01	0.08±0.02	.948	0.23±0.04	0.20±0.05	.045*	0.24±0.05	0.23±0.06	.532	0.08±0.02	0.08±0.02	.734	0.09±0.02	0.08±0.02	.066	0.23±0.04	0.22±0.04	.322
OPL	0.17±0.04	0.15±0.02	.024	0.06±0.02	0.06±0.01	.530	0.03±0.01	0.03±0.01	.316	0.06±0.01	0.06±0.01	.817	0.17±0.03	0.15±0.02	.015	0.17±0.03	0.16±0.02	.052	0.06±0.01	0.06±0.01	.667	0.07±0.01	0.06±0.01	.204	0.19±0.03	0.16±0.02	.002
ONL	0.41±0.13	0.38±0.06	.820	0.19±0.05	0.13±0.03	.430	0.10±0.04	0.09±0.03	.187	0.13±0.06	0.12±0.03	.069	0.36±0.13	0.32±0.07	.112	0.39±0.14	0.37±0.06	.192	0.14±0.06	0.14±0.03	.359	0.14±0.07	0.14±0.03	.484	0.36±0.14	0.36±0.06	.543
RPE	0.07±0.02	0.07±0.01	.861	0.02±0.00	0.02±0.01	.317	0.01±0.01	0.01±0.01	.341	0.02±0.00	0.02±0.00	.705	0.08±0.02	0.07±0.01	.380	0.07±0.01	0.07±0.01	1.000	0.02±0.00	0.02±0.00	.257	0.03±0.01	0.02±0.01	.541	0.08±0.02	0.08±0.01	.739
PC	0.42±0.02	0.42±0.02	.754	0.13±0.01	0.13±0.01	.796	0.07±0.01	0.07±0.01	.408	0.43±0.03	0.42±0.02	.844	0.43±0.03	0.42±0.02	.655	0.49±0.01	0.49±0.02	.844	0.13±0.01	0.13±0.01	.248	0.13±0.01	0.14±0.02	.365	0.43±0.02	0.43±0.02	.525
IR	1.67±0.40	1.34±0.23	.001*	0.64±0.14	0.46±0.07	.002*	0.35±0.08	0.23±0.04	.001*	0.63±0.15	0.45±0.06	.001*	1.62±0.45	1.20±0.16	.002*	1.68±0.34	1.36±0.25	.001*	0.65±0.16	0.46±0.07	.001*	0.65±0.13	0.48±0.07	.001*	1.68±0.39	1.34±0.20	.001*

* Significantly different, P<.05; paired T-test.

GCL = ganglion cell layer, INL = inner nuclear layer, IPL = inner nuclear layer, OPL = outer plexiform layer, ONL = outer nuclear layer, OPL = outer plexiform layer, PC = photoreceptor, RNFL = retinal nerve fiber layer, RPE = retinal pigment epithelium.

peeling. In our study, ILM peeling was performed in every patient. None of the patients experienced recurrent ERM. Regardless, ILM removal during ERM surgery still remains controversial.

Several previous studies with SD-OCT have suggested that the preoperative central retinal thickness, IS/OS status, cone outer segment tips, and PC outer segment length may be prognostic factors of visual acuity after ERM removal.^[14,15] Therefore, numerous studies have discussed the anatomical changes of the fovea and parafovea after ERM surgery. In 1 prior OCT study, the foveal thickness and macular volume decreased rapidly after ERM removal.^[16] However, no prior studies have addressed the thickness and volume changes of all of the retinal layers after ERM removal. In addition, previous studies have had limitations such as difficulty reproducing the measurements in each retinal layer (because of manual segmentation) and cross-sectional bias. This study is unique because we generally investigated the thickness and volume profiles of automatically segmented retinal layers (9 layers) and ETDRS subfields using HEYEX™ 6.0C software though manual segment of some IR layers (mostly RNFL layer) was used in some patients.

Several studies have reported structural changes in the RNFL after vitrectomy. Lee et al^[17] described a decrease RNFL thickness 12 months after vitrectomy in patients with ERM. In this study, we found that the thickness and volume of the RNFL decreased in all sectors. The recovery from RNFL swelling caused by traction forces of the ERM could induce the postoperative RNFL thinning. Several factors, such as increased intraoperative IOP, ICG toxicity, and mechanical damage induced by ILM peeling and fluid–air exchange, may explain why the RNFL thickness decreases after ERM removal.^[18] In our study, the fluid–air exchange was included in some patients and there was effect of this procedure on RNFL thickness change. Twenty patients got the intraocular endolaser at peripheral retina because of lattice or suspicious retinal hole. Endolaser could affect RNFL thickness. But in our study, the site of all lesions in 20 patients was more nearer to peripheral retina past equator area. Because the distance between lesion and ETDRS area was far, the endolaser wouldn't affect the RNFL thickness at ETDRS.^[19]

The GCL is the innermost and closest cell layer to the glial proliferation. Lee and Yu^[20] found that the GCL–IPL thickness decreased after vitrectomy with ILM peeling. In our study, we found that both the thickness and volume of the ganglion layers decreased in sectors 1, 2, and 5. Similarly, both the thickness and volume of the IPL decreased in all sectors except 4 and 8. These findings may have resulted from mechanical damage to the ganglion cell complex during ILM peeling or ICG cytotoxicity. Typically, the ERM of sectors 5 and 9 are first removed, and then the remaining sectors are removed clockwise. Therefore, we speculate that the thickness and volume of the GCL–IPL tended to decrease more in temporal and superior regions than in the nasal and inferior regions.

The IR thickness and volume decreased significantly after vitrectomy with ILM peeling. These findings are consistent with those of other reports. However, no significant changes were observed in the outer retina (ONL, RPE, and PC).

Our study has a few limitations. For example, the sample size (n=24) was small and the postoperative follow-up period was relatively short. Therefore, larger, longer studies (>1 year) are required to substantiate our findings.

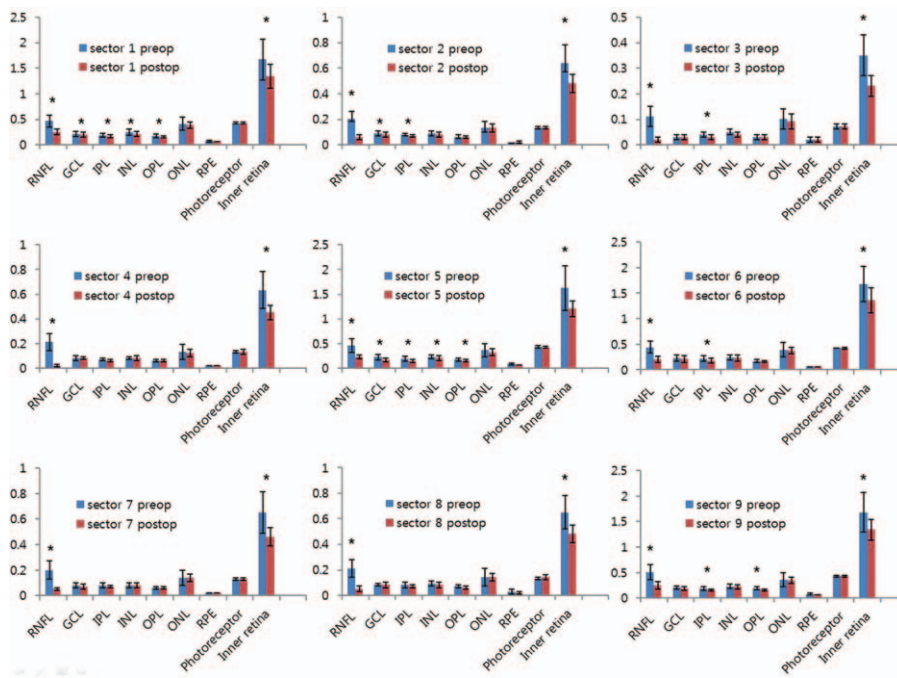


Figure 4. Change in the retinal volume (μL) of the macular sector in SD-OCT. GCL = ganglion cell layer, INL = inner nuclear layer, IPL = inner plexiform layer, IR = inner retina, ONL = outer nuclear layer, OPL = outer plexiform layer, PC = photoreceptor, RNFL = retinal nerve fiber layer, RPE = retinal pigment epithelium, SD-OCT = spectral domain optical coherence tomography. Paired *T*-test (*significantly different, $P < .05$).

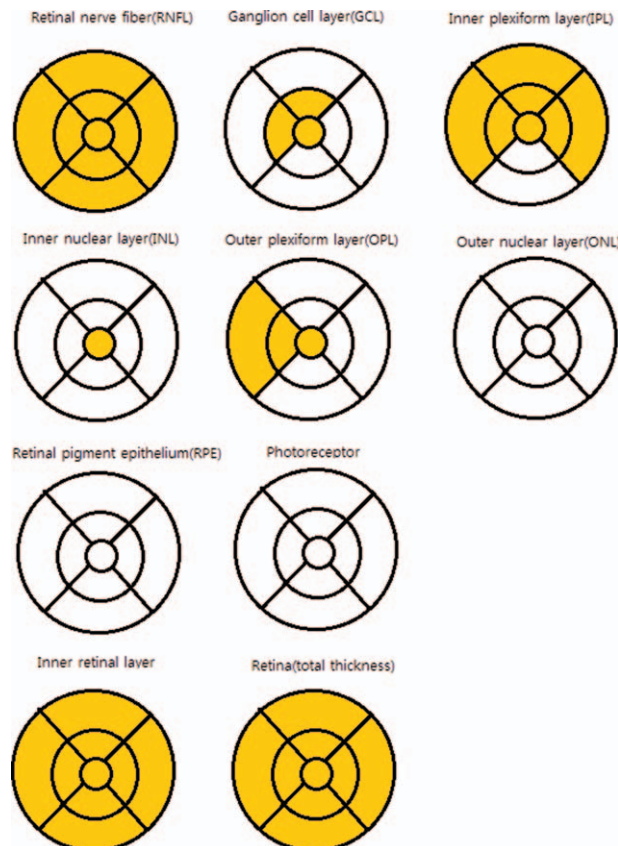


Figure 5. Postoperative retinal thickness and volume change analysis in ETDRS areas. Yellow areas indicate significant decreases in both the retinal thickness and volume. ETDRS = Early Treatment Diabetic Retinopathy Study.

5. Conclusions

The inner retina thickness and volume tend to decrease after pars plana vitrectomy using ILM peeling for removal of ERM. These postoperative decreases were associated with ILM and ERM removal. Further studies are needed to investigate the correlation between the retinal thickness and volume with visual acuity and metamorphopsia.

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