Double Peeling During Vitrectomy for Macular Pucker

The Charles L. Schepens Lecture

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Epiretinal membranes are commonly encountered in retinal practice, and they result in decreased vision. The present work addresses whether peeling of the internal limiting membrane is necessary during vitrectomy for macular pucker. We performed a retrospective analysis to investigate the effects of "single peeling," in which only the epiretinal membrane was peeled, and "double peeling," in which the internal limiting membrane was also stained and peeled. Although significantly more patients in the single-peeling group had an epiretinal membrane remaining in the central fovea postoperatively, visual acuity was not found to differ between the 2 groups in the short term. Patients who had an epiretinal membrane for more than 18 months had significantly worse visual acuity outcomes. Unexpectedly, there was a greater proportional decrease in central macular thickness in the single-peeling group than in the double peeling group, a finding that deserves further study.

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I would like to thank the American Academy of Ophthalmology, the Retina Research Foundation, and particularly Dr Alice McPherson for the special privilege of giving this lecture honoring Dr Charles L. Schepens (**Figure 1**). I was very fortunate to have been a resident at the Massachusetts Eye and Ear Infirmary in Boston when he was active, and during that time, his extraordinary charisma and leadership definitely inspired me to pursue a career in retinal surgery.

People who worked with Dr Schepens often say that he was the most amazing person that they ever knew—a man totally dedicated to his work. In addition to being a gifted physician and surgeon, he had many other talents. He was a scientist, innovator, teacher, administrator, and entrepreneur.

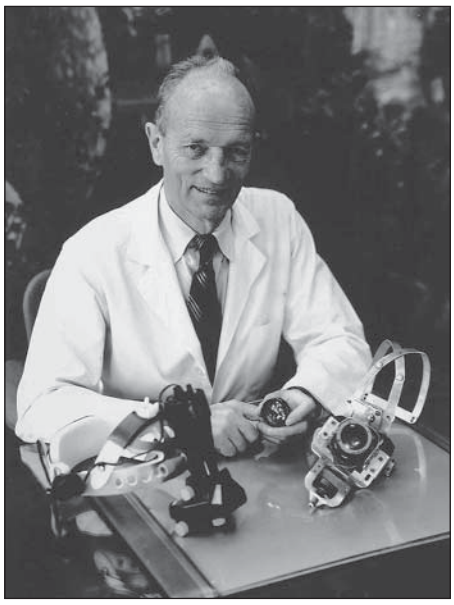

Figure 1. Charles L. Schepens, MD.

His contributions—the invention of the indirect ophthalmoscope, seminal observations about the peripheral retina, and work on the evolution of surgical techniques, materials, and instrumentation—laid the basic foundation for the modern treatment of retinal detachment. In addi-

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tion, he founded the Retina Society and the Schepens Eye Research Institute, a huge enterprise that supports more than 200 scientists working in vision science.

Dr Schepens was a master teacher and mentor; one who motivated his students to perform at their best—and many of them did. He trained more than 500 research fellows and more than 400 clinical fellows from around the world. I would like to share some comments from two of my contemporaries who were fellows with Dr Schepens:

> Despite the brilliant contributions that he made throughout his life, you had the feeling that he was always trying to learn something new. He never dismissed any suggestion that you may have had, and always responded as to whether your thoughts would work.
> Francis Cangemi, MD, 2011.

> The large retinal drawing was the cornerstone of his diagnostic workup. . . . After the fellow had examined both eyes of the patient and recorded his findings with a large drawing, Dr Schepens would take a look. The highest accolade he could accord was "I agree." If he agreed with your drawing, he would place his initials—a tiny "CS" in the corner of it. Our hearts sank if he picked up an entirely new piece of paper, and began sketching from scratch. He never said "Your drawing is terrible, inadequate, or hopelessly wrong." Instead he would diplomatically observe "I see it this way."
> James A. Valone, MD, 2011.

Dr Schepens believed that a careful, detailed study of the retina, vitreous, and eye should always be performed before surgery to learn as much as possible and plan the surgical approach properly. This was an important lesson that he passed on to his students; however, it seems to be a lesson that is not usually practiced in contemporary eye care.

This lecture addresses the question of whether peeling of the internal limiting membrane (ILM) is necessary during vitrectomy for macular pucker or epiretinal membranes (ERMs). The first series of patients undergoing vitrectomy for macular pucker was reported in 1978.[1] In this report,[1] 5 of 6 eyes had improvement in visual acuity postoperatively. For the next 20 or more years after that report,[1] there was little change in the surgical technique. Forceps were developed to replace the membrane pick, and small-gauge surgery with transconjunctival entry was introduced. During most of this time, most surgeons only removed the ERM without specifically addressing the ILM. Yet outcomes were favorable, with visual acuity improving in 65% to 90% of patients. A recurrence rate of 1% to 5% was reported.[2-4]

In recent years, there has been an unexplained trend to specifically stain and peel the ILM after peeling the ERM for macular pucker. Those surgeons who do not peel the ILM argue that visual outcomes are good and that peeling the ILM can sometimes be harmful.[5] Internal limiting membrane fragments are visible in 76% of surgically removed membranes.[6] Furthermore, there is a low recurrence rate that requires reoperation in only a few cases.[2] Those surgeons who peel the ILM routinely argue that retinal striae are more likely to disappear after removal of the ILM and that there is a lower rate of reproliferation postoperatively.[7] The development of methods to highlight or stain the ERM and the ILM, using triamcinolone, indocyanine green, trypan blue, or brilliant blue G (BBG), has made the visualization easier and more selective.[8-12] Triamcinolone creates a "dusting" effect when the particles lodge in the spaces between fibers in the cortical vitreous or ERM, but it does not stain the ILM.[12] Indocyanine green and trypan blue stain both the ERM and the ILM, whereas BBG only stains the ILM.[11]

In recent surveys, retinal surgeons were asked how often they peeled the ILM in a routine vitrectomy for ERMs, and it was found that the numbers of surgeon who did had increased. The number of surgeons reporting that they routinely peeled the ILM increased from 25% in 2008 to 44% in 2010. Conversely, the number of surgeons who have never peeled the ILM during vitrectomy decreased from 24.7% in 2008 to 10.9% in 2011 (American Society of Retinal Specialists, Preferences and Trends Survey [http://www.asrs.org]).

In recent years, the incorporation of spectral-domain optical coherence tomography (OCT) has made it possible to image the layers of the retina with greater precision.[13] This has allowed the surgeon to study the anatomic sequelae of membrane peeling after macular surgery in greater detail.

We studied the effect of "double peeling" during vitrectomy for macular pucker on the completeness of membrane removal and noted whether any potentially harmful effects occurred in the retina over the short term after ILM peeling. Visual outcomes were also assessed. Specifically, we performed a retrospective analysis to investigate the effects of "single peeling," in which only the ERM was peeled, and "double peeling," in which the ILM was also stained and peeled, on visual acuity.

METHODS

A retrospective study was performed of consecutive patients who underwent vitrectomy and membrane peeling for treatment of idiopathic macular pucker by one of the authors (S.C.) during the period from May 2009 to May 2011. Investigational review board approval was obtained at the Columbia University Medical Center in New York, New York, for conducting a retrospective chart review. In May 2010, the surgeon changed from the practice of single peeling, in which triamcinolone was used to highlight the ERM, to double peeling, in which triamcinolone was used to highlight the ERM and then BBG was subsequently used to stain and remove the ILM. Patients were excluded if they had a comorbid ophthalmic pathology that was likely to affect visual acuity (eg, proliferative diabetic retinopathy, diabetic macular edema, advanced glaucoma, or high myopia with foveoschisis), if they had a history of recurrent macular pucker, or if they did not undergo a preoperative OCT scan or a postoperative OCT scan within 1 year of surgery.

A total of 80 patients were identified, 40 of whom underwent single peeling and 40 of whom underwent double peeling. All patients underwent 23-gauge vitrectomy with membrane peeling followed by injection of air and face-down positioning (1-2 days), and for some patients, this procedure was combined with phacoemulsification with intraocular lens insertion. Air tamponade was used to seal the sclerotomy incisions internally and decrease the likelihood of postoperative hypotony and endophthalmitis. A chart re-

view identified the preoperative best-corrected visual acuity (BCVA) and postoperative BCVA (closest to 3 months after surgery) converted from Snellen to logMAR units, the number of months between the date of surgery and the date of diagnosis and symptom onset, the staining used intraoperatively, and lens status. Spectral-domain OCT scans (Cirrus; Carl Zeiss Meditec, Inc) were reviewed for the preoperative and postoperative (closest to 1 month after surgery, between 3 and 5 weeks) central macular thickness calculated by OCT software. The OCT macular cube scans at 1 month after surgery (or closest date to this) and the most recent OCT scan were reviewed, with every slice of the 6 × 6-mm cube viewed and rated for the presence or absence of an ERM in the central fovea (within a 3 × 3-mm square centered on the fovea) and in the peripheral fovea (within a 6 × 6-mm square centered on the fovea but outside the 3 × 3-mm square centered on the fovea).

Two investigators (E.M.G.R. and Q.V.H.) independently rated all OCT scans for the presence or absence of ERMs in these 2 areas, and when their ratings were not in concordance, a third investigator (S.P.) rated the scan to determine the majority outcome. In comparing the OCT scans for the single-peeling and double-peeling groups, the main outcome measure was the presence or absence of ERM tissue on OCT imaging 1 month after surgery. Other outcome measures were BCVA 3 months after surgery, central macular thickness on OCT imaging 1 month after surgery, and the change in these variables before and after surgery. We also compared the results of the eyes of patients who had macular pucker symptoms for more than 18 months or whose condition was diagnosed more than 18 months ago with a group of patients with a history of macular pucker for 18 months or less. Furthermore, we examined the overall rate of ERM recurrence on OCT imaging at the most recent follow-up time point. Data were analyzed using the Stata 8.0 statistical package (StataCorp). For continuous variables, an independent 2-tailed *t* test was performed, and for binary variables, the Fisher exact test was performed. Statistical significance was defined as $P \leq .05$.

RESULTS

There were no statistically significant differences between the single-peeling and double-peeling groups with respect to age, sex, preoperative BCVA, and other potential confounding factors such as preoperative central macular thickness, lens status, measures of macular pucker chronicity, or length of time between surgery and outcome measurements (**Table**). Intraoperatively, triamcinolone (10 mg/mL) was used to highlight the ERM in all cases. In the single-peeling group, if any ILM was visible (usually seen as a thin, elevated residual membrane), it was also removed without staining. In the double-peeling group, BBG was used to stain the ILM, which became more visible (**Figure 2**A). In some cases, the ILM was removed when the ERM was peeled (Figure 2B), but staining helped to identify any edges of ILM and sometimes was helpful in differentiating the ERM from the ILM because of irregular, patchy staining (Figure 2C). Generally, the double-peeling group had more extensive removal of ILM around the macula because it was more visible after staining.

Table. Comparison of Baseline Characteristics and Potentially Confounding Variables Between Single-Peeling and Double-Peeling Groups

Variable	Mean Value: Double-Peeling Group	Mean Value: Single-Peeling Group	*P* Value[a]
Age, y	70.1	70.5	.89
Interval from surgery to 3-mo BCVA, d	78.6	71.0	.36
% of patients			
Who underwent vitrectomy in combination with CE/IOL	40	47.5	.65
With phakic interocular lens after surgery	25	30	.80
Preoperative BCVA			
logMAR units	0.52	0.44	.15
Snellen equivalent	20/66	20/55	
Preoperative central macular thickness, µm	456	473	.39
Interval			
From surgery to 1-mo OCT, d	29.9	33.0	.40
From symptom onset to surgery, mo	22.2	32.3	.22
From macular pucker diagnosis to surgery, mo	40.9	43.9	.82

Abbreviations: BCVA, best-corrected visual acuity; CE/IOL, cataract extraction by phacoemulsification with intraocular lens implantation; OCT, optical coherence tomography.
[a] Significance was defined as $P < .05$. Note that none of the *P* values were statistically significant.

Grading the presence or absence of ERMs on OCT scans was subjective. There was agreement between the 2 graders in 75% of ratings for the 1-month postoperative OCT scans and in 79% of ratings for the latest OCT scans. Overall, there was agreement in 77% of ratings. The OCT imaging results indicated that, compared with the single-peeling procedure, the double-peeling procedure more effectively removed the ERM from the central foveal area (defined as a 3 × 3-mm square centered on the fovea) but not the peripheral macular area (defined as the area bounded by a 6 × 6-mm square but outside the 3 × 3-mm square centered on the fovea) (**Figure 3**). At the 1-month postoperative time point, the prevalence of ERMs on OCT scans in the central fovea was 52.5% in the single-peeling group, which was significantly greater than the 2.5% prevalence in the double-peeling group ($P < .001$). In the peripheral macular area, the prevalence of ERMs on OCT scans was 77.5% in the single-peeling group, which was not significantly different from the 70% prevalence in the double-peeling group ($P = .61$).

After surgery, an ERM was commonly present on the most recent follow-up OCT scan. With regard to the central fovea, 39% of patients had an ERM present on their latest follow-up OCT scan. With regard to the peripheral macular area, 74% of patients had an ERM present on their latest follow-up OCT scan. The mean follow-up from surgery to latest OCT scan was 224 days (range, 15-696 days). In comparison, 1 month after surgery, only 28% of patients had an ERM present in the central fovea, and 73% had an ERM present in the peripheral fovea. The presence or absence of an ERM at latest follow-up was not compared between the single- and double-peeling groups because the mean follow-up period between

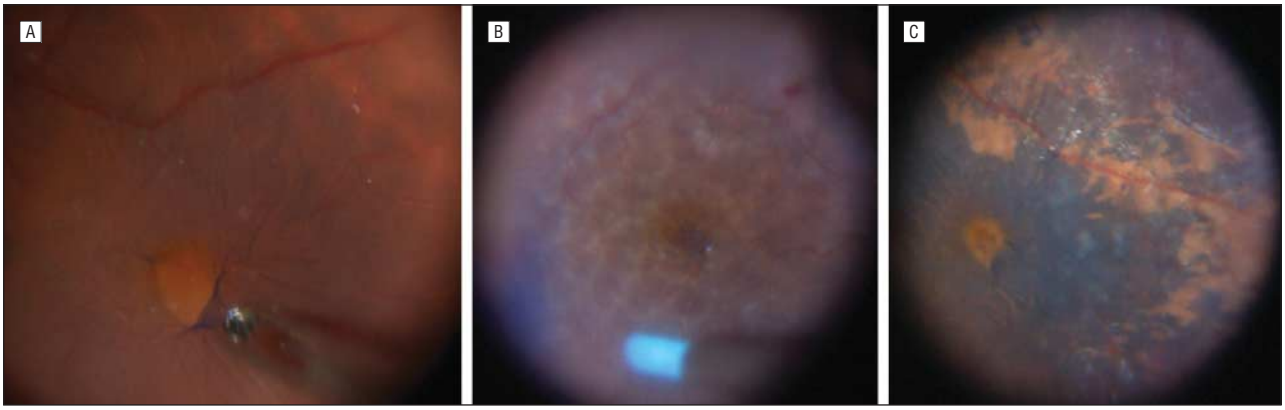

Figure 2. Intraoperative images after the removal of the epiretinal membrane (ERM) and the staining of the internal limiting membrane (ILM) with brilliant blue G dye showing the range of staining patterns, including an almost completely intact ILM (A), a minimal residual amount of the ILM (B), and irregular, patchy staining of the ILM likely representing a residual amount of the overlying ERM (C).

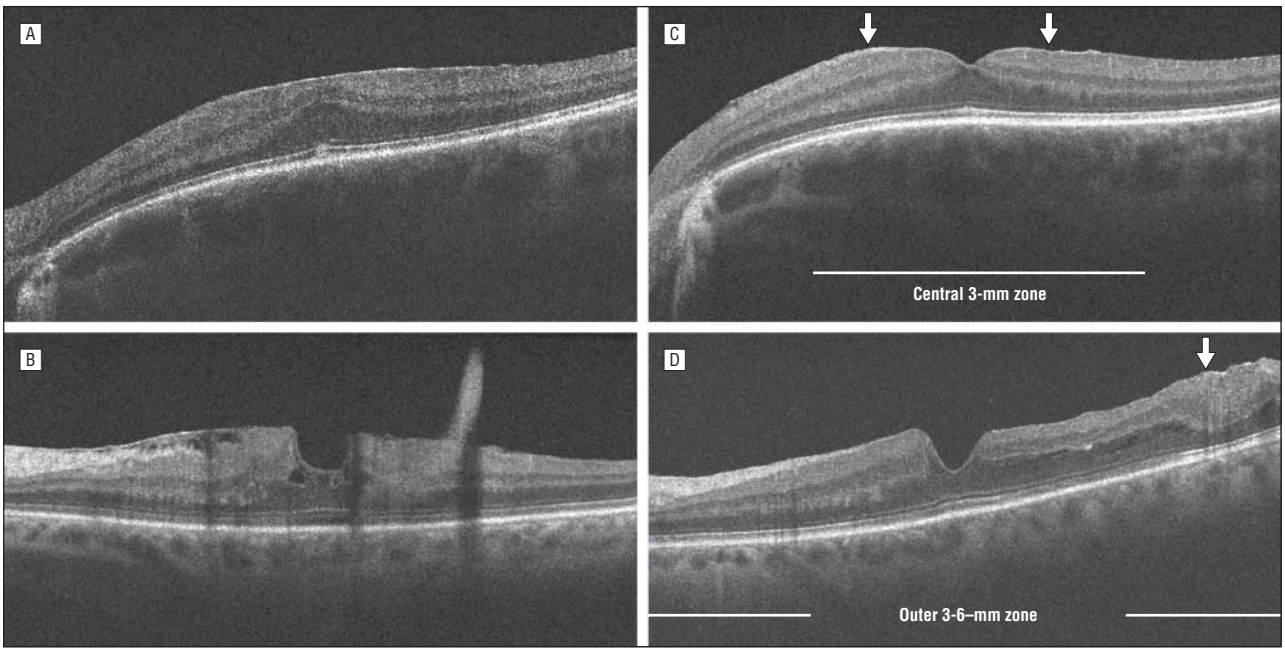

Figure 3. Optical coherence tomographic scans before (A and B) and after (C and D) pars plana vitrectomy and membranectomy with double peeling depicting the eye of a patient with residual tissue at the vitreoretinal interface in the central 3-mm zone (C) and the peripheral macula (outer 3-6–mm zone [D]).

surgery and the latest OCT scan was much longer for the single-peeling group than for the double-peeling group (mean follow-up period, 319 days for the single-peeling group vs 129 days for the double-peeling group; $P < .001$).

There was no significant difference in measures of postoperative BCVA between the single-peeling group and the double-peeling group. The mean BCVA at the 3-month postoperative time point was 0.24 logMAR units (Snellen equivalent of 20/35) in the single-peeling group and 0.31 logMAR units (Snellen equivalent of 20/41) in the double-peeling group, which was not a statistically significant difference ($P = .13$). The percentage of patients with a postoperative BCVA of 20/40 or better was 77.5% in the single-peeling group and 62.5% in the double-peeling group, which was not statistically significantly different between the 2 groups ($P = .22$). Because the preoperative BCVA was better in the single-peeling group (0.44 logMAR units [Snellen equivalent of 20/55]) than in the double-peeling group (0.52 logMAR units [Snellen equivalent of 20/66]), we examined the change in BCVA before and after surgery in the 2 groups. The mean improvement in BCVA was 0.20 logMAR units in the single-peeling group and 0.21 logMAR units in the double-peeling group, which was not a statistically significant difference ($P = .88$).

The mean central macular thickness at the 1-month postoperative time point was 400 μm in the double-peeling group and 389 μm in the single-peeling group. This difference was not statistically significant ($P = .43$). However, the mean preoperative central macular thickness was thicker in the single-peeling group (473 μm) than in the double-peeling group (456 μm), although not statistically significant ($P = .39$). We also calculated the reduction in central macular thickness, before and after surgery, as a percentage of the preoperative central macular thickness. The postoperative proportional decrease in central macular thickness was greater in the single-peeling group than in the double-peeling

group. The reduction in macular thickness was 16.8% for the single-peeling group and 10.3% (95% CI, 0.5%-12.3%) for the double-peeling group, and this difference was statistically significant ($P = .03$).

Analysis indicated that measures of postoperative BCVA at 3 months did not differ overall between those with an ERM postoperatively and those without an ERM postoperatively. There were 58 patients without an ERM and 22 patients with an ERM within the central fovea at the 1-month postoperative time point. The mean postoperative BCVA was 0.27 logMAR units (Snellen equivalent of 20/38) in the group without ERMs and 0.27 logMAR units (Snellen equivalent of 20/37) in the group with ERMs ($P = .98$). However, results indicated that BCVA was affected by the presence or absence of an ERM in the single-peeling group. For the single-peeling group, those with an ERM had a mean BCVA at 3 months of 0.29 logMAR units (Snellen equivalent of 20/39), which is significantly worse than the mean BCVA of 0.18 logMAR units (Snellen equivalent of 20/30) for those without an ERM ($P = .03$). Because only 1 patient in the double-peeling group had a persistent ERM in the central fovea postoperatively, a statistical comparison of postoperative visual acuity with patients having a persistent ERM in the single-peeling group was not meaningful. However, for patients in the double-peeling group without an ERM in the central fovea postoperatively, the mean logMAR visual acuity was 0.32 (Snellen equivalent of 20/42), which was significantly worse than that for patients in the single-peeling group without an ERM ($P = .04$). These results indicate that, although complete removal of a central foveal ERM was more common when double peeling was performed than when single peeling was performed, the successful removal of a central foveal ERM with single peeling resulted in superior visual acuity than did the successful removal with double peeling.

There were 35 patients with macular pucker who had symptoms for 18 months or less and whose condition was diagnosed 18 months ago or less, and there were 37 patients with macular pucker who had symptoms for more than 18 months or whose condition was diagnosed more than 18 months ago. Eight patients had no definite record of their duration of symptoms or diagnosis. The mean improvement in BCVA for those with a duration of symptoms or diagnosis of 18 months or less was 0.27 logMAR units, whereas the mean improvement in BCVA for those with a duration of symptoms or diagnosis of more than 18 months was 0.15 logMAR units. This was a statistically significant difference ($P = .005$; 95% CI, 0.040-0.216 logMAR units). Postoperative BCVA was 20/40 or better in 83% of patients with a duration of symptoms or diagnosis of 18 months or less compared with 59% in those with duration of symptoms or diagnosis of more than 18 months ($P = .04$). The mean reduction in central macular thickness in those with a duration of symptoms or diagnosis of 18 months or less was 15.1%, whereas the mean reduction in central macular thickness in those with a duration of symptoms or diagnosis of more than 18 months was 13.0%. This was not statistically significant ($P = .47$).

COMMENT

These results indicate that, based on OCT analysis, the double-peeling procedure for idiopathic macular pucker, using triamcinolone to remove the ERM and BBG to remove the ILM, results in a much more effective removal of the ERM within a 3×3-mm square centered on the fovea compared with the single-peeling procedure with triamcinolone. We believe that performing OCT 1 month after surgery is the correct time point at which to determine the amount of residual tissue left after membrane peeling and before any significant remodeling at the vitreoretinal interface has occurred. Although OCT evidence of a residual ERM remained in the central foveal area in 52.5% of single-peeling patients, this tissue was present in only 2.5% of double-peeling patients. To our knowledge, the outcomes of ERM-peeling surgery as gauged by OCT have not previously been reported. However, the 3-month visual acuity outcomes did not differ between the 2 groups. This is consistent with previous data using indocyanine green staining of the ILM, which has shown that peeling both the ERM and the ILM may not result in better postoperative visual acuity compared with peeling only the ERM.[14] An alternative explanation for our finding may be that visual acuity had not yet stabilized postoperatively at the 3-month time point we examined and that longer-term follow-up of visual acuity may have revealed a significant difference. We examined 3-month postoperative visual acuity to limit confounding effects of postvitrectomy nuclear sclerosis and cataract on visual acuity. In other studies, a longer follow-up did not appear to change the finding that there was a difference in BCVA after ILM peeling.[15] However, it has been shown that, following ERM removal, the macular thickness is significantly reduced 3 months after surgery, yet, in some patients, recovery of visual acuity takes at least 9 months.[16] Effective ERM removal in the peripheral macula (within a 6×6-mm square centered on the fovea but outside a 3×3-mm square centered on the fovea) would not be expected to affect visual acuity significantly, and we found no difference between the 2 treatment groups with regard to the presence of a postoperative ERM in this area (ie, 70% of patients in the double-peeling group and 77.5% of patients in the single-peeling group).

Postoperative BCVA did not differ between those with an ERM and those without (when the single-peeling and double-peeling groups are combined), which suggests that complete ERM removal does not improve BCVA compared with incomplete ERM removal. This finding is consistent with the finding that there was no significant difference in postoperative BCVA between the single- and double-peeling groups, despite the higher rates of complete ERM removal in the double-peeling group. However, there was a significant improvement in BCVA within the single-peeling group when the ERM was absent in the central foveal area postoperatively compared with when the ERM was present. However, when the ERM was not present in the central foveal area postoperatively, the double-peeling group had a significantly lower proportional de-

crease in retina thickness and lower visual acuity than the single-peeling group. These findings suggest that complete ERM removal itself would improve visual acuity but that subsequent ILM peeling provides an additional insult to the retina that worsens visual acuity by the 3-month postoperative time point. It is not known whether a longer follow-up would have affected the final visual outcome in this double-peeling group, which would have had to be assessed after all of the eyes had become pseudophakic, to avoid the confounding effect of postvitrectomy cataract.

There was a greater proportional decrease in central macular thickness in the single-peeling group than in the double-peeling group. This finding was unexpected. One would have expected that the extra layer of ILM that was removed with double peeling (combined with the more effective ERM removal to decrease contraction forces that produce pucker) would have resulted in a greater decrease in thickness for the double-peeling group, yet the opposite occurred. The reason for this is unclear and not completely understood. It is possible that the additional trauma to the inner retina resulting from the double-peeling procedure may cause more disruption or swelling of the inner retinal layers postoperatively.[5,17]

Our results are consistent with previous studies of macular pucker showing that duration of symptoms correlates with postoperative visual acuity.[15] We found that patients with chronic macular pucker (with a duration of symptoms or diagnosis >18 months prior to surgery) had a worse visual outcome than patients whose puckers developed over a time period 18 months or less, although there was no difference in postoperative central macular thickness between the 2 groups. This is consistent with the theory that persistent neuronal stretching and disruption present over a long time period can result in permanent damage that impacts visual acuity and is not reversible when the stretching ceases as macular thickness decreases postoperatively.

Our study is limited by its retrospective nature, lack of randomization, and relatively small numbers of patients. However, a comparison of various potential confounders between the single-peeling group and the double-peeling group indicated no significant differences (Table). The rating of the presence or absence of an ERM was subjective, and we were not able to fully mask the graders to the treatment group because they were aware that the surgeon used a double-peeling procedure for recent cases. There was disagreement between graders in a small proportion of cases. However, any inaccurate classification of OCT scans would be expected to increase random variability and lead to reduced power of our study rather than to false-positive results. Given that we have a positive result for the primary outcome related to ERM removal, this is unlikely to be an issue.

The results of our study indicate that staining with BBG after removal of the ERM results in a more complete removal of the membrane. The effects on visual acuity and central macular thickness indicate that it may not offer other benefits over single peeling. However, the removal of the ILM should limit the reproliferation of ERMs in eyes undergoing macular pucker surgery and should reduce the recurrence rate. We plan to follow up with this group of patients to evaluate this possibility.

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Author Contributions: Dr Chang had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Conflict of Interest Disclosures: Dr Chang was a consultant for Alcon and for Alimera.

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