ILM peeling a vital intervention for many vitreoretinal disorders

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The internal limiting membrane (ILM) is the structural interface between the vitreous and retina. As the basement membrane of retinal Müller cells, it serves as a protective barrier and provides biomechanical strength for the central retina.\textsuperscript{1-3} It also acts as a scaffold for cellular proliferation for myofibroblasts, fibrocytes, and retinal pigmented epithelial cells. ILM removal ensures separation of the posterior hyaloid from the macular surface, which can relieve macular traction\textsuperscript{4,5} and prevent postoperative epiretinal membrane formation.\textsuperscript{6,7} Thus, vitrectomy with ILM peeling has become an increasingly utilized and vital component in surgical intervention for various vitreoretinal disorders.

Indications

Macular hole repair

Since Kelly and Wendel’s initial report of macular hole repair surgery, success rates for hole closure have improved, in large part due to ILM peeling.\textsuperscript{8,9} Cellular proliferation on the ILM can induce tangential traction.\textsuperscript{10} ILM removal relieves the tractional component and has been shown to achieve anatomic success in macular hole closure.\textsuperscript{9} Data from retrospective studies, prospective trials, and meta-analyses indicate that vitrectomy with ILM peeling results in higher closure rates and greater visual acuity improvement than does vitrectomy without ILM peeling.\textsuperscript{4,11-13} Given the lower reoperation rate, ILM peeling is a cost-effective maneuver in initial macular hole surgery.\textsuperscript{14} ILM peeling is particularly important when other variables limit closure rates, such as in holes that are large, chronic, or traumatic.
Most vitreoretinal surgeons agree that ILM peeling is an essential maneuver in macular hole repair.

**Epiretinal membrane removal**

Removal of epiretinal membranes (ERM) may be complicated by recurrence. Histologic examination of recurrent ERM revealed that the ILM was the source of recurrent cellular proliferation. Further, histolopathologic examination of unremoved ILM after ERM removal has detected residual ERM cells on the surface of the ILM. ERM recurrence rates have been shown to range from 7.5% to 56% after 2 years. When compared with single intravitreal removal of ERM and a reduced recurrence rate.

**Diabetic macular edema**

Vitrectomy for diabetic macular edema improves oxygenation to the retina and removes growth factors promoting vascular permeability. ILM removal provides the additional benefit of removing tractional forces, which conceptually assists in reducing macular edema. A review of studies in which diabetic macular edema was treated with vitrectomy and ILM peeling showed that the majority of studies showed significant reduction of foveal thickness. A retrospective review found that the decrease in foveal thickness was sustained for over 2 years. When compared with single intravitreal triamcinolone injection, vitrectomy with ILM peeling provided better sustained efficacy. However, visual improvement after vitrectomy with ILM peeling remains equivocal, possibly resulting from the inherent case selection of eyes with refractory diabetic macular edema, lipid deposition, and suboptimal macular perfusion.

**Retinal vein occlusion**

Mandelcorn postulated that a macular decompression achieved from ILM peeling may reduce elevated intraretinal tissue pressure and facilitate egress of hemorrhage and extracellular fluid from inner retinal layers to a vitrectomized cavity, subsequently reducing macular edema. In a series of 14 patients with vein occlusion–related macular edema not eligible for laser photocoagulation who underwent vitrectomy with ILM peeling, all cases resulted in reduced retinal thickening. Other studies also indicate a significant reduction in retinal thickness after ILM peeling. Visual improvements remain equivocal, again possibly due to factors of chronicity of macular edema and macular ischemia. With advances in pharmacotherapy for retinal vein occlusion–related macular edema, vitrectomy with ILM peeling is a viable but less frequently utilized therapeutic adjuvant.

**Retinal detachment**

Macular hole following retinal detachment has been reported, and epiretinal membrane formation after primary vitrectomy has been reported at a rate as high as one-third of cases, often requiring additional surgery. A retrospective review by Rao et al showed that 34.4% of eyes undergoing primary vitrectomy without ILM peeling developed postoperative ERM, compared to only 3.3% of eyes with ILM peeling. In the group without ILM peeling, 9.4% underwent subsequent vitrectomy for ERM removal, whereas no patients who underwent ILM peeling underwent subsequent vitrectomy for ERM removal. The number needed to treat to prevent postoperative ERM was four, and the number needed to treat to prevent subsequent ERM removal was 11. It is important to note that ERM following retinal detachment is a limited form of proliferative vitreoretinopathy and carries different implications for surgical repair and prognosis. Vitrectomy with ILM peeling has also been shown to prevent postoperative ERM formation in complicated retinal detachments undergoing vitrectomy with retinectomy and silicone oil tamponade.

**Other indications**

ILM peeling has also been reported to be effective in surgery for vitreomacular traction, optic pit maculopathy, and Terson’s syndrome.

**Methods**

ILM peeling is generally performed after standard pars plana vitrectomy with removal of the posterior hyaloid. Removal of ILM is technically challenging due to the ILM’s transparency and thinness. Using an adjuvant dye to stain the ILM facilitates its removal. While various adjuvants exist, vitreoretinal surgeons most commonly utilize indocyanine green (ICG), trypan blue, brilliant blue, or triamcinolone acetonide to assist in removal.

**Adjuvant dyes**

ICG has long been used in choroidal angiography and more recently to facilitate ILM identification and peeling. There is no standard method for preparation of ICG; some surgeons dissolve the powder in D5W (5% dextrose in water) or sterile water before adding balanced salt solution. Likewise, there is no consensus regarding ideal concentration (ranging from 0.6 to 5 mg/mL), volume instilled (ranging from a few drops to 2 mL), or contact time required (ranging from a few seconds to 5 minutes). Viscoelastic material has been used as a
vehicle after dissolving it in water to limit the application area of the dye to the desired extent and to prevent access into the subretinal space. Concerns about possible toxic effects of the ICG on the retina exist. Engelbrecht et al reported RPE changes and ICG use, and theories regarding phototoxicity have subsequently been suggested as the mechanism for RPE damage. Visual field defects and reduction of retinal nerve fiber layer thickness after ICG use have also been reported. Some reports have also noted less visual acuity improvement associated with ICG use. Therefore, despite the improvement in visualization, some vitreoretinal surgeons prefer to limit or avoid ICG use. Trypan blue has been employed widely in anterior segment surgery and can also be an efficacious stain at a concentration of 0.06% for the posterior hyaloid, ERM, and ILM. No significant reports of toxicity have arisen, and trypan blue is advantageous in that it can be used in a fluid- or air-filled eye. However, the stain can be inconsistent, and its use has been associated with equivocal visual results.

Brilliant blue G was introduced in vitreoretinal surgery in 2006 at a concentration of 0.25 mg/mL that was instilled then immediately washed out. It was noted to selectively stain the ILM. While no animal studies have reported toxicity, further clinical and experimental studies are needed to fully evaluate its safety and efficacy in staining the ILM.

Intravitreal triamcinolone acetonide (TA) has frequently been used to visualize the posterior hyaloid and aid in ILM peeling. Within a minute of injection into the vitreous cavity, TA settles over the macula and any residual floating particles can be removed. The residual dusting of TA on the surface of the macula does not stain the ILM but rather highlights it and allows good visualization of the extent of ILM peel. Adverse effects of intravitreal TA injection are well known. Evaluations by Shah et al indicate that these complications have not been described following TA-assisted ILM peeling.

**Complications**

Minor complications including focal retinal hemorrhages and edema often resolve spontaneously. Direct mechanical trauma during the peeling can also cause nerve fiber layer damage, iatrogenic eccentric full-thickness retinal breaks, and full-thickness macular holes. Paracentral scotomas and visual field defects after ILM peeling have also been reported but not directly correlated to the removal of the ILM and could result from adjuvant stain or mechanical trauma.

It has been postulated that the removal of Müller cell basement membrane could cause glial apoptosis and retinal function. An investigation of focal macular electroretinogram changes after ILM removal showed that the a-wave amplitude increased 6 months after surgery but the b-wave amplitudes did not change significantly, suggesting an alteration in the physiology of the Müller cells located in the area where the ILM was removed. There was, however, no adverse effect on visual acuity. A study evaluating P1 amplitudes on multifocal electroretinogram testing showed that 18 eyes that underwent ILM peeling had decreased responses compared to preoperative values, but the difference was not statistically significant. This reduction was persistent for up to 1 year postoperatively but did not correlate to a decreased visual acuity; on the contrary, visual acuity had improved.

In 2001, Tadayoni et al reported changes in the inner retina after ERM removal. They described these as numerous arcuate striae in the posterior pole in the direction of the optic nerve visualized as dark striae on blue filter photographs and referred to the clinical scenario as dissociated optic nerve fiber layer (DONFL) appearance. They hypothesized that this was due to extensive peeling of the ILM but did not report any adverse functional effects on visual recovery. DONFL has been reported to occur early in the postoperative period, most commonly within the first 3 months. Studies have shown that the DONFL appearance is present on blue light photography in 54% to 62% of eyes undergoing ILM peeling and in no eyes without ILM peeling. Spaide later described DONFL appear-
ance inner retinal dimpling along the course of the nerve fiber layer occurring only after ILM peeling.\(^5^9\)

He suggested that the dimples result from trauma and the healing process constrained by the optic nerve fiber layer and not from a true defect or dissociation of optic nerve fibers. No reports have yet described DONFL with permanent adverse effects on visual function.\(^56,58,60\) No scotomas were found corresponding to DONFL, and when comparing the arcuate striae and surrounding normal retina, no difference in the microperimetry threshold value was found.\(^57,58\)

**Conclusion**

ILM peeling has been shown to improve anatomic and functional results in a variety of retinal diseases. Although technically challenging, ILM peeling is a commonly utilized, safe, effective component in vitreoretinal surgery. No permanent adverse effects on visual function corresponding to ILM removal have been reported.

**REFERENCES**


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