Internal Limiting Membrane: Making the Decision to Peel

The decision should be based on the patient's disease condition.

BY CHI-CHUN LAI, MD

The internal limiting membrane (ILM) is a very thin and transparent acellular membrane on the surface of the retina. It plays an important role in the early stages of retinal development; however, its function in adults is not yet understood.[1] The ILM might participate in the pathogenesis of vitreoretinal interface diseases, such as macular hole (MH), macular pucker (MP), and macular traction maculopathy in highly myopic eyes, as well as other maculopathies.[2-4] It has been well accepted that ILM peeling can improve the hole closure rate and postoperative BCVA after MH surgery, and these ideas might also be true for other traction maculopathies requiring vitrectomy.[4-6]

Because the ILM is a barely visible membrane, identification of the ILM is a challenging step in surgery, and removal is difficult even for experienced retina surgeons. Therefore, staining the ILM with vital dyes is essential for increased visibility of the ILM, and staining might decrease surgical trauma to the retina during ILM removal.

Available staining materials can be classified as staining dyes or coating materials. Most of the staining dyes are chemicals, including indocyanine green (ICG), which was the first dye to be used in macular surgery, trypan blue (TB), and brilliant blue G (BBG).[4,7] Coating materials that have been used clinically include triamcinolone acetonide (TA) and blood.[8-10]

Staining dyes can selectively stain and penetrate the ILM, resulting in a well-visualized margin during the peeling process. However, studies have shown toxicity to the retinal pigment epithelium (RPE) and neurosensory retina, as well as cases of optic nerve atrophy, after the use of ICG.[11] Alternative dyes have emerged for staining the ILM with less toxicity, such as TB and BBG. TB demonstrated lower toxicity to retinal tissue and an excellent affinity for staining the epiretinal membrane (ERM) but not for the ILM. BBG provides good staining capability for the ILM and was not toxic in experimental studies or case series in humans, and it was recently made available in the European market.[7,12] Long-term retention of chemical dye after application could raise safety and toxicity concerns, but these have not been seen with TB or BBG.[13]

Coating materials only coat the membrane surface and do not actually stain the ILM. They are easier to remove and result in less retention after surgery; their dispersion during application is the main concern. The perfect dye has not yet been found.

ILM peeling continues to incur potential risks and costs. Therefore, several questions must be answered for this procedure: Should we peel the ILM completely or partly or not peel the ILM for every case of traction maculopathy? Which dye should we use when we need to preserve the stained ILM? This article explores these issues as they apply in several disease states.

MACULAR HOLE

Combined vitrectomy, ILM peeling, and gas tamponade are the standard treatment for the repair of MH. ILM peeling has become even more popular since the introduction of vital dyes because staining makes the procedure easier and safer. Many retina surgeons enjoy peeling procedures and will try to peel ILM if they can.

Historically, ILM has been viewed as an entity which should be removed as completely as possible.[5] ILM peeling was considered a necessary and harmless step; however, ILM peeling can cause morphologic changes to the macula, such as a dissociated optic nerve fiber (DONF) layer. Nevertheless, no functional consequences have been attributed to this anatomic change.[14] Some studies showed that electrophysiologic changes occurred after

ILM peeling in MH cases. The clinical impact of these abnormalities remains to be elucidated.[15]

Regardless of the above issues, ILM peeling does require more surgical time and greater expense (for dyes and forceps), and it incurs the potential risk of iatrogenic trauma. Whether ILM peeling is needed at all stages of MH remains an open question, and debate may persist into the future.

Recent evidence has shown that ILM peeling might not be necessary for all types of MH. Ocriplasmin (Jetrea, Thrombogenics), a protease with proteolytic activity against fibronectin and laminin that induces vitreous liquefaction and posterior vitreous detachment, has demonstrated a nearly 40% MH closure rate with a single injection.[16] Not all patients require ILM peeling, even without gas tamponade and prone positioning.

These data indicate that, for some selected MH patients, it is not necessary to peel the ILM for MH closure. Studies have also shown better success rates in cases with smaller holes with vitreous traction. Therefore, a more conservative approach may be not to peel the ILM for such cases in the future. Ideal candidates would include patients with symptomatic vitreomacular traction and those with MH sizes smaller than 250 µm with vitreous traction, if ocriplasmin is not available or not effective.

By contrast, to improve the closure rate of large MHs of sizes larger than 400 µm, the inverted ILM flap technique was introduced to improve MH closure rate and postoperative BCVA in idiopathic chronic MH.[17] In this procedure, the ILM is not removed completely from the retina but is left attached to the edge of the MH. Then the ILM is gently inverted and is used to cover the MH from all sides (Figure 1). The inverted ILM flap has also been applied to close holes in small case series of MHs in highly myopic eyes with or without retinal detachment.[18] In these cases, the ILM can facilitate hole closure.

These newly emerging concepts indicate that complete ILM peeling may not be necessary for all cases of MH.

MACULAR PUCKER

Surgery for symptomatic MP or ERM, including vitrectomy and membrane peeling, has been a common vitreoretinal procedure for a long time. Without further ILM peeling, the rate of recurrence of ERM is approximately 5% to 10%. Of recurrent cases, approximately half required another operation after long-term follow-up.[19] To reduce recurrence, ILM peeling was introduced and has shown good results. In addition, most ERM recurrences that occurred in patients who had undergone ILM peeling were thin and asymptomatic. Removal of the ILM can limit the reproliferation of ERM in eyes undergoing MP surgery.[20,21]

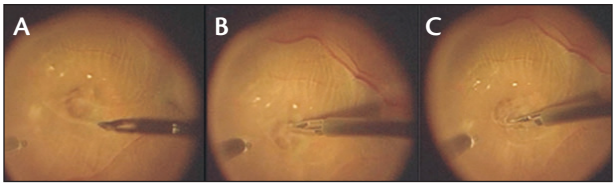

Figure 1. Inverted internal limiting membrane (ILM) flap for a large macular hole (MH). Part of the ILM was left attached to the edge of the MH (A). Then the ILM was gently inverted, covering the MH from all sides (B and C). Note that the ILM was not stained to prevent long-term retention of dye.

However, there has been debate about the necessity of ILM peeling for MP. Retinal surgeons who are opposed to ILM peeling are always concerned that its removal might be responsible for anatomic and functional damage to the retina. One study found that, when only the ERM is peeled without ILM peeling, approximately 50% of ERM tissues remain on the central fovea, while this tissue was present in only 2.5% of patients who also underwent ILM peeling.[20]

However, complete removal of the ILM assisted by dye has not shown any functional benefits in short-term follow-up. Rather, ILM peeling can increase central macular thickness, and it is possible that the additional trauma to the inner retina resulting from ILM peeling may cause more damage to the inner retinal layers postoperatively. One study found that, although no difference was seen in postoperative BCVA, recovery of mean retinal sensitivity occurred earlier and was better in the non-ILM–peeling group than in the ILM-peeling group.[21]

Although ILM peeling may prevent recurrence of MP, ERM does not recur often, and reoperation is performed only for symptomatic cases. Therefore, the notion of ILM peeling in ERM surgery may deserve reconsideration. ILM peeling should be considered only in selected cases in which ERM might recur, such as bilateral ERMs, secondary ERMs, and secondary surgery for recurrent ERMs. Additional ILM peeling might be necessary after complete ERM removal if the retina still has a severe wrinkle. Through more careful selection, the costs and benefits of ILM peeling can be better balanced in ERM surgery.

MYOPIC FOVEOSCHISIS AND RETINAL DETACHMENT DUE TO MH

Myopia is the most common eye disease, particularly in east Asia, and its prevalence is increasing around the world. Highly myopic eyes can be associated with tractional maculopathies, such as myopic foveoschisis (MF) and RD due to MH (MHRD), which can threaten the vision of patients.

When foveal detachment occurs in eyes with MF, surgery is necessary to prevent further deterioration. Vitrectomy and complete ILM peeling have been suggested to flatten

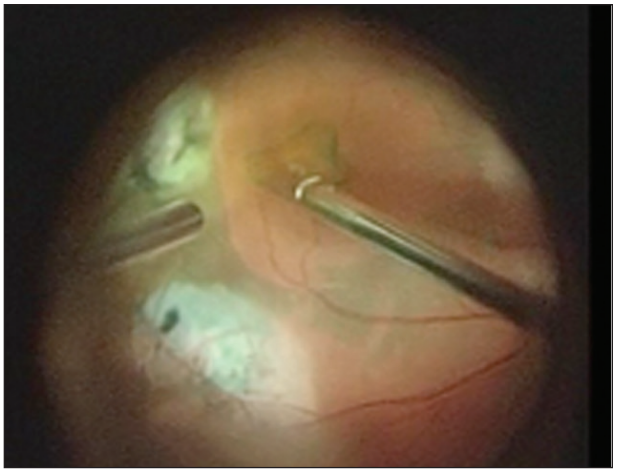

Figure 2. Fovea-sparing ILM peeling for myopic foveoschisis. A piece of ILM is preserved on the fovea to prevent postoperative MH. Note that the ILM was stained with indocyanine green dye, and the dye can remain within the ILM for a long duration.

the retina, but postoperative MH has been reported to occur in approximately 20% of cases.[6] ILM peeling removes the Müller cone cells, which form the base of the fovea and serve as a plug that binds the photoreceptor cells in the foveola and supports the foveola structurally. The stretched retina in a highly myopic eye can easily induce a MH without this structure. To prevent postoperative MH, fovea-sparing ILM peeling was introduced.[22,23] Studies have shown that this technique can prevent MH formation very effectively. A piece of ILM is preserved in the center of fovea to prevent damage to the Müller cone cells during surgery (Figure 2).

In the past, the ILM was peeled completely for MHRD, but the MH closure rate was less than 50% after surgery. Recently, the inverted ILM flap procedure has been applied not only for large and chronic MHs but also for MHRD.[17,18] This technique has reduced the occurrence of MH after MHRD surgery published in case series, but further studies are needed.

Overall, a trend toward ILM preservation is emerging in treatment of myopic tractional maculopathies.

CONCLUSION

Complete ILM peeling is no longer suitable for every type of macular surgery. The decision not to peel the ILM or to perform partial or complete peeling should be based on the surgical indication. Further, if the ILM must be partially preserved, the next question is whether staining material should be employed. Chemical dyes can remain on the fovea for a long time, and the safety of these dyes has not been clearly demonstrated. Next-generation staining materials may be required: for example, development of a dye without long-term toxicity, with excellent affinity for the ILM, and possibly even with neuroprotective qualities in these applications. It would be even better if such a dye could facilitate MH closure. ■

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