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From Peel to Plug: Sealing The Gap With Surgical Innovations For Macular Hole Repair

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Historical Context and Evolution

The surgical management of macular holes (MH) has evolved significantly over the past few decades. In 1991, Kelly and Wendel revolutionized MH repair by introducing pars plana vitrectomy combined with air fluid exchange.[1] Eckardt et al. in 1997 further advanced and improved the success of macular hole closure by introducing internal limiting membrane (ILM) peeling, establishing the gold standard for idiopathic MH treatment.[2] The subsequent development of micro-incision vitrectomy systems, particularly 25- and 27-gauge instrumentation, has resulted in better wound sealing, reduced postoperative inflammation, and faster visual recovery.[3] These technological advancements laid the foundation for more complex surgical approaches, especially in complex cases such as large, recurrent, persistent, traumatic or myopic MHs. Contemporary techniques now include a variety of ILM flap methods (e.g., inverted, temporal, single-layer, and multilayered/petal flaps), autologous ILM transplantation (AILMT), human amniotic membrane (hAM) grafts, and autologous retinal transplantation (ART).[4]

Modern Techniques For Routine and Challenging Cases

Before the advent of ILM flap techniques, the standard surgical approach for MH repair involved peeling the ILM surrounding the hole. Surgeons differed in their technique preference, with some advocating for a limited ILM peel centred around the MH, while others favoured a more extensive arcade-to-arcade peel. This conventional ILM peeling approach remains the standard of care for small idiopathic MHs measuring less than 400 μm in diameter.

In recent years, a range of advanced surgical techniques have been developed to address large (>400 μm), recurrent, or otherwise complex MHs. These innovations aim to improve anatomical closure rates and enhance visual recovery, particularly in cases with poor prognostic indicators. Among these, ILM flap techniques—such as inverted, temporal, single-layer, and multilayered flaps—have become critical tools for managing challenging MHs.

Inverted ILM Flap Technique

The inverted ILM flap technique, introduced by Michalewska et al. in 2010, involves preserving a portion of the ILM attached to the edges of the MH during the peeling process, rather than removing it entirely.[5] This remaining ILM is then flipped over to cover the MH. Next, an air–fluid exchange is carried out, and patients are instructed to maintain a face-down position for 3 to 4 days.[5] The rationale behind this technique is that the ILM flap contains Müller cell fragments that promote gliosis and serve as a biological scaffold, encouraging retinal tissue to bridge the defect. Compared to conventional ILM peeling, the inverted flap technique has demonstrated higher anatomical closure rates, particularly in large MHs. In their original randomized controlled trial, Michalewska et al. reported a 98% closure rate with the inverted flap technique, compared to 88% with traditional peeling. Subsequent meta-analyses have confirmed that the inverted ILM flap technique results in superior anatomical outcomes and, in many cases, improved visual acuity for large MHs.[6,7] However, some studies have noted that visual acuity improvements may converge with standard techniques after 6 months.[8] Further multicenter randomized trials are warranted to definitively determine the functional advantages of the inverted flap in the long term.

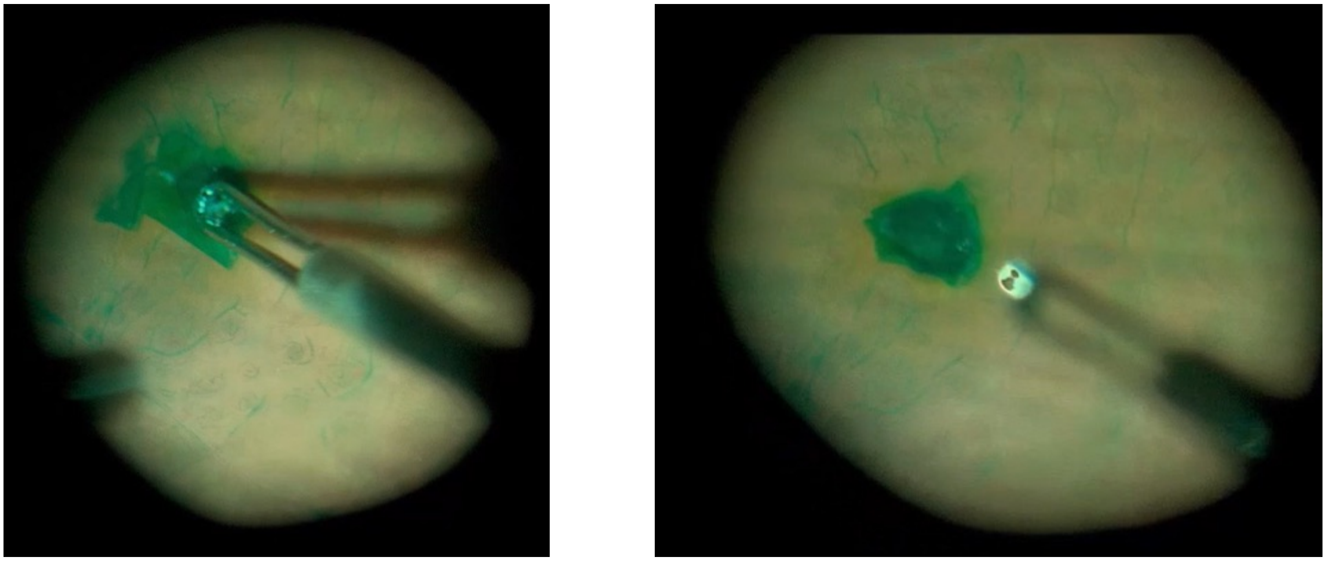


Figure 1. Intraoperative view of the multilayered or petal internal limiting membrane (ILM) flap technique, visualized with indocyanine green (ICG) staining; *courtesy of Peng Yan, MD, FRCSC*

Temporal Inverted ILM Flap

To further minimize surgical trauma, Michalewska et al. later introduced the temporal inverted ILM flap technique, a modification designed to reduce the extent of ILM peeling and better preserve the retinal nerve fiber layer.[9] In this approach, the peel begins on the temporal side of the MH and spans an area approximately equivalent to two optic disk diameters, leaving the nasal side of the fovea attached. This modified method has demonstrated comparable MH closure rates and improvements in visual acuity to those achieved with the original inverted ILM flap technique.[9] Notably, a randomized controlled trial published in 2023 reported a lower incidence of dissociated optic nerve fiber layer (DONFL) appearance postoperatively associated with the temporal technique. DONFL is seen as numerous arcuate retinal striae running along the optic nerve fibers in the macular area and has been considered to be related to ILM removal. However, functional outcomes such as best-corrected visual acuity and retinal sensitivity were comparable to those achieved with standard ILM peeling in holes larger than 250 μm.[10] This technique may be especially useful in eyes where minimizing trauma to the inner retina is a priority, such as in younger patients, those with thinner retinas, or those with concerns involving the preexisting nerve fiber layer.

Single-layer ILM Flap

The single-layer ILM flap technique, introduced by Shin et al., represents a refinement aimed at reducing excessive tissue layering while maintaining anatomical efficacy. This technique involves positioning a thin, single-layer ILM flap over the MH, assisted by perfluoro-n-octane (PFO) to stabilize the flap during surgery.[11] Unlike the original inverted flap technique, which creates a multilayered fold, this method avoids excessive tissue buildup and ensures a more physiological scaffold over the fovea. In initial studies, it achieved favourable results, with anatomical closure in 10 out of 12 eyes and significant improvement in visual acuity over 6 months, suggesting it is a simpler yet effective alternative. Further studies have confirmed the technique's effectiveness for large MH,[12] and found that the single-layered inverted ILM flap was better than ILM peeling for the closure of large MHs.[13]

Multilayered/petal Flaps

The multilayered or petal ILM flap technique **(Figure 1)** is another innovative variation designed to enhance scaffold stability over large MHs. Often referred to as the "flower-petal" technique, it involves creating multiple ILM segments that are inverted and layered sequentially over the hole to form a thickened, multilayered construct.[14,15] This approach provides a robust platform for glial proliferation and tissue remodelling, especially in cases where hole size, chronicity, or high myopia reduce the likelihood of spontaneous closure. In

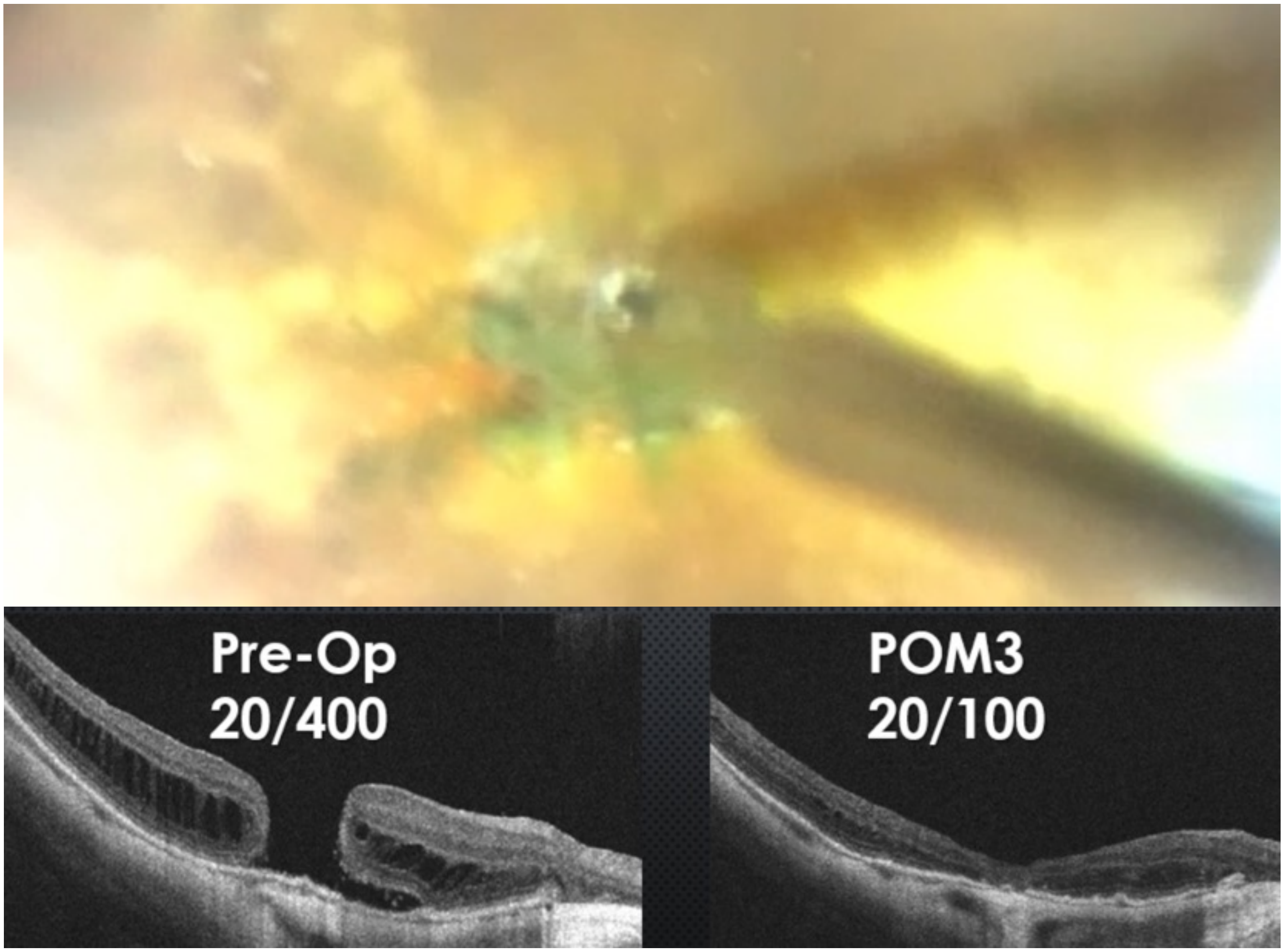


Figure 2. In myopic macular hole (MH) repair, an autologous internal limiting membrane (ILM) graft is harvested from a separate retinal area and transplanted into the MH. Postoperative outcomes show successful MH closure and improved visual acuity; *courtesy of Peng Yan, MD, FRCSC*

a study of 103 eyes with large full-thickness MHs (average minimum linear diameter of 712 µm), Joshi et al. performed this method under PFO and achieved an anatomic closure rate of 92.2%.[16] This approach may be especially beneficial for highly myopic eyes with posterior staphyloma, where the ILM is often fragmented or discontinuous.[16] While PFO is frequently used to stabilize the multilayered flaps during surgery, surgeons can use alternative anchoring methods, such as autologous blood or platelet plugs to anchor the flaps in place, which offers an alternative strategy when PFO use is not feasible or desired. This technique may be best suited for very large, chronic, or myopic holes where standard inverted or single-layer flaps are insufficient to promote closure.

Despite the high anatomical success rates associated with primary MH surgery, persistent, recurrent, or refractory MHs remain a significant challenge for vitreoretinal surgeons. These cases are often characterized by larger hole diameters, higher degrees of myopia, increased chronicity, and minimal residual ILM, all of which negatively impact the likelihood of successful closure. In response, a variety of advanced surgical techniques and supportive agents have been developed to improve outcomes in these difficult scenarios.

Subretinal Balanced Salt Solution (BSS) Injection

The technique of creating subretinal fluid to shift the released retina towards the center of refractory macular hole has been described in literature.[17] The mechanism involved in this technique includes: the release of centripetal force by ILM removal, followed by the release of RPE-photoreceptor adherence to mobilize retina

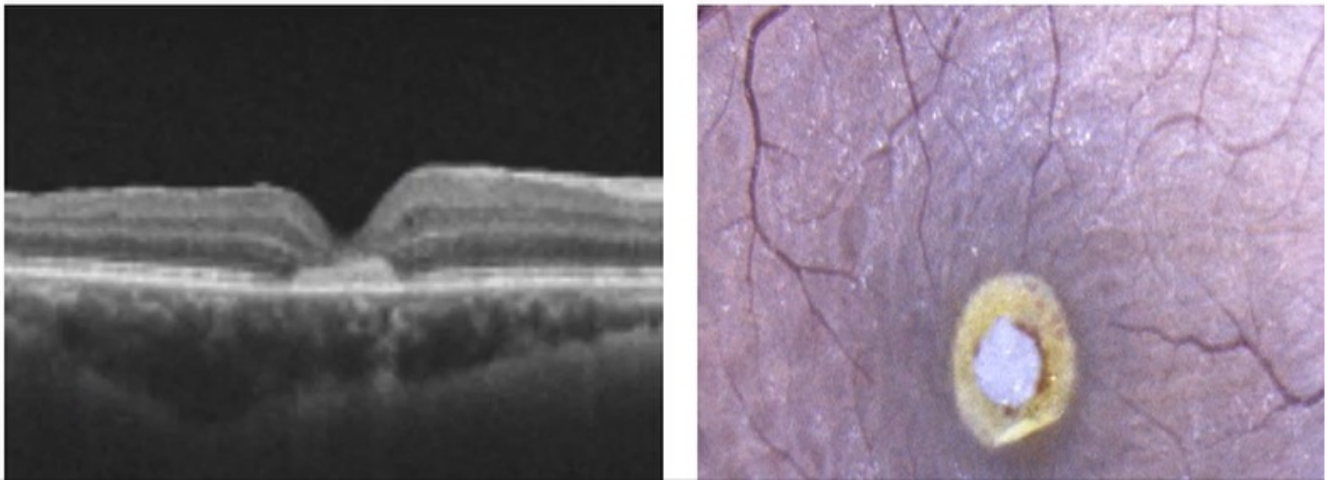


Figure 3. A human amniotic membrane graft is inserted into subretinal space as a plug over the macular hole (MH). Optical coherence tomography illustrates the role of the amniotic membrane in assisting with MH closure; *courtesy of Peng Yan, MD, FRCSC*

from epiretinal and subretinal adhesions, then stretching the retina with subretinal fluid and tactile massage to enlarge retinal surface covering large macular holes. Small studies have reported success of 78% of closure of refractory macular hole using subretinal BSS injection with objective visual improvement with no complications.[18]

Autologous ILM Transplantation

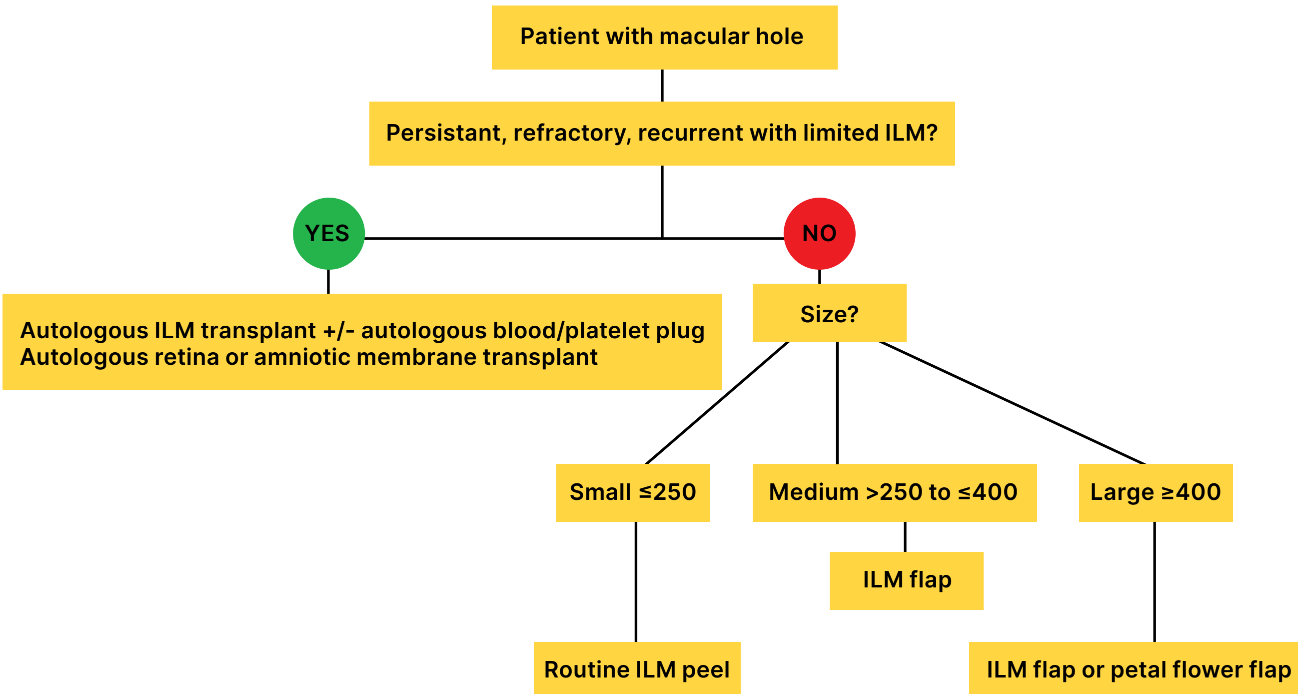
In patients who lack sufficient ILM around the MH for secondary surgery, Morizane et al. introduced autologous ILM transplantation **(Figure 2)**. This method involves harvesting a small ILM flap from a different retinal area and placing into the MH, using viscoelastic to anchor it, followed by gas tamponade.[19] This method achieved a 90% closure rate and visual improvement in 80% of eyes. Studies have demonstrated that AILMT can achieve high closure rates and is associated with minimal complications.[20–22] A limitation of this technique is that the free ILM flaps are prone to displacement and are positioned in the MH in a non-physiological orientation, which might limit their ability to promote glial cell growth. One way to help minimize this effect is to use autologous blood or platelet plugs to prevent displacement of the ILM. Additionally, this approach may not restore the neurosensory retina across the hole.

Autologous Retinal Transplantation

First described by Grewal and Mahmoud in 2016, the ART technique involves transplanting a segment of the patient's own retina to cover the MH.[23] This technique involves harvesting a free flap of autologous neurosensory retina and positioning it over the refractory MH, where it serves as both a mechanical plug and a biological scaffold to promote glial proliferation and tissue integration.[23] ART is particularly useful in cases with no residual ILM, chronic holes exceeding 750 µm, or in eyes associated with high myopia and retinal atrophy. A multicenter international study reported an 87.8% anatomical closure rate and a mean visual acuity improvement of 0.08 logarithm of the Minimum Angle of Resolution (logMAR) in eyes with full-thickness MH refractory to prior vitrectomy with ILM peel and tamponade.[24] A meta-analysis published in 2024 involving 322 cases demonstrated a 94% overall closure rate and significant improvement in postoperative visual acuity across all subgroups of large MHs, including refractory MH, high myopia associated with MH, primary MH, and MH with retinal detachment.[25] While ART has demonstrated excellent anatomical success, visual outcomes can be variable due to potential disorganization of the outer retina and disruption of photoreceptor alignment. Nevertheless, ART remains a powerful salvage technique for cases where traditional or ILM-based strategies are not feasible.

Human Amniotic Membrane Grafts

The hAM is the innermost layer of fetal membranes. It possesses anti-inflammatory, anti-fibrotic, and pro-regenerative properties. In this technique **(Figure 3)**, hAM is inserted as a plug into the epiretinal or subretinal space over the MH, where it acts as a biological scaffold to support



Flow diagram of the surgical decision-making algorithm for macular hole management; *courtesy of Peng Yan, MD, FRCSC*

Abbreviations: ILM: internal limiting membrane

tissue repair and cell proliferation, helping to achieve hole closure.[26]

A retrospective analysis of large MHs (>400 μm) or reoperations following unsuccessful ILM peeling, has shown a 100% closure rate with a single hAM intervention and no recurrences, along with a median of three lines of visual improvement.[26] A 2023 meta-analysis involving 103 eyes treated with hAM after failed vitrectomy and ILM peeling reported a 66% improvement in visual acuity and a 94% MH closure rate.[27] Cryopreserved hAM grafts have shown better outcomes than dehydrated grafts.[27]

Surgery Guided by Optical Coherence Tomography (OCT) Features

With an expanding array of surgical techniques available, selecting the optimal approach for MH repair increasingly relies on a detailed preoperative assessment, particularly using OCT. OCT offers high-resolution cross-sectional imaging that enables precise evaluation of MH characteristics—including size, shape, retinal thickness, and the presence of associated pathologies such as epiretinal membranes (ERMs). For small MHs measuring less than 400 μm, the standard ILM peel technique remains an effective technique of choice. However, for larger MHs, evidence suggests that the inverted ILM flap technique is likely to yield better anatomical outcomes.[6,7] In addition, a meta-analysis involving over 1,400 eyes showed that the inverted ILM flap technique results in significantly higher closure rates than ILM peeling alone. This advantage was consistent across various full-thickness MH sizes, including myopic eyes, and those complicated by retinal detachment.[28] A systematic review and meta-analysis reported that the inverted ILM flap technique provides superior anatomical closure and better short-term visual outcomes in large idiopathic MHs compared to traditional ILM peeling, ART, or ILM insertion.[29] While ART has been shown to be effective in treating refractory MHs, large hAM grafts, though associated with high closure rates, tend to result in less favourable visual acuity outcomes.[29] This meta-analysis recommends the inverted ILM flap technique as the preferred approach for large idiopathic MHs, while ART and hAM grafts are considered effective alternatives for refractory cases.[29] Thus, for large MH cases greater than 400 μm, the inverted ILM flap is the approach of choice provided sufficient ILM remains. In refractory MHs larger than 750 μm or in cases where the ILM is insufficient, ART or hAM grafts are the recommended approaches.

Additional OCT-derived features also guide surgical decision making:

- Chronicity: MHs persisting for more than 3–6 months often exhibit signs of retinal thinning, glial remodelling, and reduced tissue elasticity. In such cases, techniques such as inverted flaps, ILM free flaps, or ART are more suitable than standard ILM peeling.[30]
- ERM presence: ERMs exert tangential traction that can prevent hole closure. Their removal is essential, and in combined cases, more aggressive approaches such as inverted flaps or grafting should be considered to minimize recurrence.[31]
- Lamellar macular holes (LMH): Differentiating between tractional LMH (typically associated with highly reflective ERMs) and degenerative LMH (characterized by lamellar hole-associated epiretinal proliferation, or LHEP) is crucial. In degenerative LMH, traditional peeling can risk converting the defect into a full-thickness hole. Modified techniques, such as LHEP embedding combined with ILM flap inversion, have shown promise in reducing complications.[32]

Key strategies to minimize anatomical failure and optimize visual outcomes in MH surgery begin with a thorough preoperative assessment. OCT should be used to evaluate key features such as hole size, traction, ERM presence, and chronicity. Early surgical intervention is important, as shorter symptom duration is associated with higher closure rates and better visual recovery. Intraoperatively, careful use of vital dyes (indocyanine green [ICG], brilliant blue, or triamcinolone) and controlled endoillumination can help reduce retinal toxicity during ILM peeling. Surgical technique should be individualized—typically using the inverted ILM flap for large idiopathic holes, and ART or hAM grafts for refractory or recurrent cases. Postoperatively, the use of long-acting gas tamponades such as SF_6, combined with face-down positioning, can enhance closure. However, recent studies suggest that high closure rates can still be achieved without strict prone positioning when extensive ILM peeling is performed.[33]

Conclusion

MH surgery has evolved into a highly effective and nuanced discipline, driven by advances in imaging, instrumentation, and surgical techniques. Innovations such as the inverted ILM flap, ART, and hAM grafts have significantly improved outcomes, particularly in complex and refractory cases. Current evidence supports the inverted ILM flap as the preferred approach for large idiopathic holes, while ART and hAM grafts offer viable solutions when ILM is unavailable or if previous surgical attempts have failed.

Achieving successful outcomes in MH surgery now depend on individualized, OCT-guided surgical planning. Key factors such as hole size, chronicity, ILM availability, and associated pathologies must also be carefully evaluated. As both imaging and surgical technologies continue to advance, precision-based, tailored interventions are becoming the standard of care, offering patients the best possible anatomical and visual results in even the most challenging cases.

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