

ILM: To Peel or Not to Peel

I was first introduced to Internal Limiting Membrane (ILM) peeling in 1996 by Prof. Eckardt on his visit to Moorfields Eye Hospital. His elegant videos of ILM peeling were carried out *without* the help of any dye and were inspiring. Prof Eckardt subsequently published his work in 1997¹. Morris et al had performed ILM peeling in 1990 for Haemorrhagic retinal cysts and published their 7 year followup in 1997². This report also demonstrated the long term safety of ILM peeling.

ILM is only 6 micron thick and is the structural boundary between the retina and the vitreous. It is adherent to the collagenous cortex of the vitreous on its one side, and to the Muller (glial) cell end feet on the Retinal side³.

ILM peeling is now an established procedure in Vitreo Retinal Surgery mainly for the following indications:

1. Macular Hole Surgery.
2. Diabetic Macular Oedema.
3. Vitreo Macular Traction.
4. Epiretinal Membrane peel.
5. Vitrectomy for Retinal Detachment.

However the literature on ultrastructural effects of ILM peeling on "human retina" are scant. of particular importance is the effect on Muller Cells and its end feet. Wolf et al⁴ carried out ILM peel with ICG on post mortem eyes (within 60 minutes of death) and subjected it to Electron Microscopy. They made the following observation:

"In the peeled area proper, many end-feet remained apparently intact may be because the human Muller cell endfoot membranes are not tightly fixed at the basal lamina (e.g., by hemidesmosomes); thus, some end-feet may be dissociated from the basal lamina without forces strong enough to disrupt the cells."

"Although direct evidence cannot be obtained from enucleated eyes, these observations suggest that only the endfeet and adjacent parts of some of the Muller cells were destroyed, whereas their somata and some cell processes could have survived by sealing the disrupted cell membranes."

There were suggestions that the effects could have resulted from the use of ICG during surgery which was refuted by the authors of the study. On the other hand this type of cellular injury in vivo stimulates regenerative mechanisms in the Muller cells that then may contribute to the closure of the macular hole⁵.

The effects of ILM peel on Muller Cells in Porcine eyes has been adequately studied. There was excellent growth in culture⁶ of Muller cells following ILM peel in porcine eyes. In addition the long term functional status of ILM peeled retina in human retina was also established by carrying out multifocal ERG after 1 year of ILM peel⁷.

The role of ILM peeling during Vitrectomy for various indications can be established by carrying out meta analysis of Randomised Control trials and the results in the literature are reproduced below.

1. Macular Hole: The role of ILM peeling in Macular Hole surgery is now well established. A Meta analysis of *Randomised Control Trials* comparing ILM peel versus Non ILM peel in Vitrectomy in Stage 2, 3 and 4 holes was carried out by Cornish et al⁸. It was observed:
 - There was NO evidence of difference in Visual Acuity at 6 months between the peel and non peel group.
 - ILM peel group had statistically superior closure of Macular Hole. This was present both for primary and final closure.
 - ILM peeling was found to be cost effective with no difference in the complications between the two groups and ILM peeling in macular holesurgery and is recommended as the treatment of choice.
2. Diabetic macular oedema: The ILM of patients with diabetes has a higher expression of collagen, fibronectin, and laminin,^{9,10} is thicker than that of non diabetic eyes¹¹. It would make sense to remove ILM in all cases of Diabetic macular oedema however the superiority of ILM peeling versus non peeling combined with patients with Diabetic macular oedema *cannot be statistically proven*.

In a review of 644 reports on the role of vitrectomy in DMO only 5 studies directly compared ILM peeling with non peeling in vitrectomy for DMO (4 of them were not RCTs). Nakajima¹² et al carried out meta analysis of these studies and concluded that:

The mean postoperative BCVA improved in patients who underwent vitrectomy regardless of ILM peeling in four of five studies.

- Postoperative BCVA itself the superiority in BCVA by additional ILM peeling was equivalent to 2 ETDRS letters and not statistically significant.
- Change in BCVA before and after surgery by additional ILM peeling was equivalent to 2 ETDRS letter) and not statistically significant.

The Results of Internal Limiting Membrane peeling on central macular thickness:

- When evaluated by the change in CMT before and after surgery the further decrease in CMT by additional ILM peeling was not statistically significant.

Since 4 of these studies were not RCTs hence the bias/influence of PVD, PDR, previous laser therapy and HbA1c cannot be eliminated hence the need for a large RCT!

Kumagai Kazuyuki¹³ et al had reduced the bias of Diabetic control (HbA1c) and duration of Diabetes by carrying out Vitrectomy in *each eye of the same patient* with one eye having ILM peel and the fellow eye no peel. However their results were not different from those in the previous meta-analysis. They concluded that the differences in the best-corrected visual acuity between the two groups were not significant at any time point.

3. Vitreomacular traction: Once again the role of ILM peeling is not entirely clear with lack of statistically significant data (lack of Randomised Clinical Trial). A meta analysis¹⁴ of the available data fails to establish any benefit of Vitrectomy with ILM peel over the non-peel group. However the results of ILM peel in myopic traction maculopathy are encouraging with improved BCVA in cases with foveal detachment and macular retinoschisis but not in the Macular Hole associated with High Myopia¹⁵.
4. Epiretinal membrane: the role of ILM peeling in Epiretinal Membrane is well established by the excellent histological study carried out by Gandorfer et al¹⁶. In 2 of 3 patients with idiopathic ERM, the vitreous cortex splits when the ERM is

removed leaving cells on the ILM. As these cells are capable of proliferation and causing ERM recurrence, staining of the ILM with subsequent removal seems beneficial in macular pucker surgery.

This is further corroborated by a large but retrospective study of 440 patients¹⁷. It was found out that ILM peeling was the only factor preventing ERM recurrence.

5. Retinal detachment: Apart from anatomical success the occurrence of macular pucker can affect visual acuity after repair of retinal detachment. The epiretinal membrane in retinal detachment differs from those idiopathic cases and stains for myofibroblasts and retinal pigment epithelial cells with a propensity to contract. In a retrospective study¹⁸ comparing PPV with No ILM peel and ILM peel the following observations were made:

- Post-operative macular pucker: 34.4% of eyes in Non-peel vs. 3.3% in ILM peel group.
- Re operation for macular pucker: 9.4% in Non ILM group (almost 1 in 10 patients require re operation!!) and NONE in ILM peel group.
- Post-operative VA: No difference between the 2 groups but only 1 in 4 patients were Macula on before surgery.

In a larger retrospective study it was observed¹⁹:

- No ERM occurred in the ILM peeling group, whereas ERM occurred 21.5% of non-peeling group. This difference was significant ($P < 0.001$).
- In the macula on group, the overall mean best-corrected visual acuity was better in the ILM peeling group and was significantly higher 12 months postoperatively ($P = 0.03$).

ILM peeling in cases of retinal detachment prevents macular pucker formation. However there is no statistical difference in vision when ILM peel group is compared to non-peel group in macula off retinal detachments.

Safety of ILM peeling: ILM peeling can be associated with some side effects.

The Dyes used in ILM peeling especially ICG can cause retinal dysfunction at least temporarily and it is recommended to use a lower concentration of ICG²⁰. A reduction of GCIPL layer thickness was also observed when ILM peeling was combined with ICG staining²¹.

The development of para central retinal Holes is well documented²² and reported regularly.

In conclusion ILM peeling is now an established and safe procedure procedure in vitreo retinal surgery. The indications for ILM peeling are gradually expanding however concrete and statistically proven efficacy of ILM peeling is lacking and requires large multicentrerandomised control Trials. The surgeon should aware of the available data on the subject and evidence based treatment should be carried out.

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