# Internal limiting membrane peeling during idiopathic epiretinal membrane removal: a systematic review

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## ABSTRACT

Idiopathic epiretinal membrane (ERM) is characterised by the growth of fibrocellular tissue on the internal limiting membrane (ILM). The ERM could range from a subtle cellophane-like film not causing any visual disturbance to significant contractile membranes with folds in the underlying and adjacent retina causing metamorphopsia and a decline in visual acuity. Vitrectomy with ERM removal is beneficial in improving visual acuity and foveal contour and is well accepted as the treatment for symptomatic macular pucker. However there is still debate whether the concurrent removal of the ILM peeling affords any additional benefit. Overall a review of the literature suggests that there is no difference in final visual acuity between ILM peeling vs non-ILM peeling. When comparing ERM recurrence ILM peeling may offer some benefit although many recurrences are not visually significant. While ILM peeling could ensure complete removal of the cortical vitreous and ERM, the use of ICG dye could have a deterious effect. Therefore it still remains unclear whether removing the ILM during ERM surgery affords any additional benefit.

*Keywords:* macular pucker, epiretinal membrane, internal limiting membrane, pars plana vitrectomy.

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## Introduction

Idiopathic epiretinal membrane (ERM) is characterised by the growth of fibrocellular tissue on the internal limiting membrane (ILM). The ERM could range from a subtle cellophane-like film not causing any visual disturbance to significant contractile membranes with folds in the underlying and adjacent retina causing metamorphopsia and a decline in visual acuity. Although the exact pathogenesis of ERM formation is unclear it is known to be associated with posterior vitreous detachment[1] leading to hypertrophy of glial (Müller) cell processes and the accumulation of extracellular matrix components on the ILM (the ILM is the basement

membrane of the Müller cells.[2,3]

## Epiretinal membrane surgery

### *Pars plana vitrectomy*

While there are rare cases where an ERM spontaneously separates from the retina and induces regression of the macular distortion[4,5] in almost all cases it remains stable or slowly progresses. Progression of an ERM often results in underlying retinal changes with thickening and/or folds which could lead to a decline in visual acuity. Standard pars plana vitrectomy to remove the vitreous gel and the ERM has been the standard of therapy for visually significant ERM resulting in significant regression of the retinal thickening and/or folds. However reports show that the recurrence rate of ERM after surgery varies from 10% to 21% possibly due to remnants of cortical vitreous or incomplete removal of ERM.[6-9]

### *Internal limiting membrane peeling*

As the ERM is adherent to the ILM varying degrees of ILM fragments were identified on histopathology after removal of ERM. In some cases there was a positive correlation between the amount of ILM removal and the visual prognosis.[10-13] This started the debate whether the additional removal of ILM may be beneficial during ERM removal with the presumption that the removal of ILM ensures complete removal of cortical vitreous and epiretinal membrane from the macular surface and may also aid in the regression of the retina folds.[14]

To aid in visualisation and removal of the thin ILM various dyes have been used including indocyanine green (ICG) Trypan Blue (TB) and Brilliant Blue G (BBG). With or without the use of dyes to stain the ILM various instruments such as a pick bent micro vitreoretinal (MVR) blade or vitreoretinal forcep are used to remove the thin membrane. Some surgeons create a flap of ILM which is then grasped with forceps while others pinch a small portion of ILM and then peel a larger area using only forceps.

### *Controversies regarding ILM peeling*

ILM peeling was initially performed during macular hole surgery to aid in complete removal of cortical vitreous and epiretinal membrane possibly leading to higher anatomical and functional success rates compared to results without ILM peeling.[15,16] However the methods used in removing the ILM have raised some questions about possible mechanical and functional damage to the underlying retina. First the mechanical peeling of the ILM may lead to anatomic changes such as focal retinal haemorrhages[17] swelling of the arcuate nerve fiber layer[18] and dissociated optic nerve fiber layer or inner retina dimpling[19]. In addition long term follow-up after ILM peeling demonstrates a progressive reduction in macular volume.[20,21] These changes have been shown to be positively correlated with the shortening of the papillofoveal distance leading to foveal migration. Secondly there are concerns regarding the possible toxicity of various staining modalities used to visualise the ILM.[20] Although the mechanism is unclear why ICG could be toxic it is postulated that the ICG could migrate to the sub retinal space causing damage to the retina and RPE[21-24] visual defects[25-27] and optic atrophy.[28,29] Moreover a meta-analysis of ICG-assisted ILM peeling in macular hole surgery showed no differences in the closure rate a worse VA and an increased risk of RPE changes. An additional meta-analysis[30,31] has also shown that there is no evidence of clinical superiority in outcomes for ICG-assisted ILM peeling in macular hole surgery compared to ILM peeling without the use of ICG.

### *Surgical outcome comparing PPV with ILM peeling vs without ILM peeling*

In theory ILM peeling for ERM would enable a more complete removal of the epiretinal membrane and might also inhibit reproliferation of the ERM.[15] However to date there is no evidence from randomised trials showing that peeling of the ILM leads to a better anatomic and functional result or reduces the rate of ERM recurrence. Even with the lack of evidence peeling both ERM and ILM during ERM surgery is becoming more popular among surgeons. There are several histologic reports demonstrating remnants of ILM found in specimens with intended ERM removal alone.[11-13] Interestingly a recent study showed that although portions of ILM could be identified within the ERM specimens in 5 out of 17 cases (29%) a whole layer of ILM was present and able to be peeled during a second surgery in these 5 cases. In the remaining cases isolated cells or small cellular foci were found on the ILM in six specimens and portions of ERM were found in conjunction with ILM in over a third of specimens. These findings support the notion that removal of ILM in ERM surgery leads to a more complete removal of epiretinal elements.

### *Literature review for surgical management of ERM*

Table 1. Change in visual acuity before and after vitrectomy for epiretinal membrane without internal limiting membrane peeling

| First author | Year | # of eyes | Mean age (yrs) | Mean follow-up period (months) | Mean preop logMAR VA (mean+/-SD) | Mean postop logMAR VA (mean+/-SD) | Stable or improved VA (%) | VA improved >/ =2 lines (%) | Recurrent ERM (%) | Complications (%) |
|---|---|---|---|---|---|---|---|---|---|---|
| Park et al.[9] | 2003 | 24 | NA | 13 | NA | NA | 100 | 50 | 21 | none |
| Kwok et al.[3] | 2005 | 15 | 68.0 | 50.2 | 0.9+/-0.29 | 0.67+/-0.3 | 93.3 | 80 | 20 | 1RD |
| Lee et al.[33] | 2010 | 19 | 65.5 | 18.3 | 0.67+/-0.34 | 0.32+/-0.23 | NA | NA | 0 | none |
| Pournaras et al.[36] | 2011 | 15 | 41.9 | 77.1 | 0.48+/-0.22 | 0.37+/-0.42 | 73 | NA | NA | none |
| Chang et al.[34] | 2013 | 40 | 70.5 | 3 | 0.44 | 0.24 | NA | NA | 52.5 | NA |

### *with and without ILM peeling*

A PubMed search was undertaken using the following keywords: macular pucker, epiretinal membrane, internal limiting membrane and pars plana vitrectomy. Only articles describing primary research from peer-reviewed journals in English were collected. Only studies regarding vitrectomy for idiopathic ERM which provided initial and final visual acuity and/or categorised eyes with visual acuity that was the same better or worse using standard methods of reporting such as logarithm of minimal angle of resolution (logMAR) or Snellen acuity were included in the analysis. Studies with secondary ERM from uveitis, prior retinal detachment, vascular occlusion, diabetic retinopathy, trauma or vitreomacular traction were excluded as were those that included air gas or oil tamponade. The review identified 12 articles of sufficient quality to undergo review.

Data collection included 1) study design and study period; 2) visual acuity before and after surgery or % of eyes with visual acuity that was the same better or worse after surgery;

Table 2. Change in visual acuity before and after vitrectomy for epiretinal membrane with internal limiting membrane peeling

| First author | Year | # of eyes | Mean age (yrs) | Dye use | Mean follow-up period (months) | Mean preop logMAR VA (mean+/-SD) | Mean postop logMAR VA (mean+/-SD) | Stable or improved VA (%) | VA improved >/ =2 lines (%) | Recurrent ERM (%) | Complications |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Park et al.[9] | 2003 | 24 | NA | none | 13 | NA | NA | 79 | 50 | 0 | none |
| Kawk et al.[53] | 2003 | 11 | 63.4 | ICG | 9.6 | 0.51+/-0.35 | 0.38+/-0.32 | 81.8 | 45.5 | 0 | none |
| Haritoglou et al.[42] | 2003 | 48 | 68.4 | ICG/none | | 0.65+/-0.3 | 0.34+/-0.21 | 100 | 75 | NA | 2RD, 7 VF defect |
| Haritoglou et al.[44] | 2004 | 43 | 69.4 | TB | 5.5 | 0.5 | 0.3 | NA | 72.7 | 4.5 | 1RD, 3 ME |
| Kwok et al.[32] | 2005 | 20 | 64.0 | ICG | 23.6 | 0.65+/-0.42 | 0.41+/-0.37 | 100 | 52.3 | 10 | none |
| Tari et al.[51] | 2007 | 10 | 63.9 | none | 3 | 0.4+/-0.11 | 0.19+/-0.13 | 100 | 70 | NA | NA |
| Von Jagow et al.[43] | 2009 | 6 | 75.7 | ICG | 87.6 | 0.68+/-0.29 | 0.43+/-0.41 | 83 | 50 | NA | 2 optic atrophy |
| Lee et al.[33] | 2010 | 21 | 63.4 | ICG | 18.1 | 0.68+/-0.21 | 0.2+/-0.17 | NA | NA | 0 | none |
| Pournaras et al.[36] | 2011 | 24 | 73.3 | BBG | 24 | 0.58+/-0.4 | 0.32+/-0.39 | 83 | NA | NA | none |
| Chang et al.[34] | 2013 | 40 | 70.1 | BBG | 3 | 0.52 | 0.31 | NA | NA | 2.5 | NA |
| Panos et al.[54] | 2013 | 30 | 72 | ICG | 12 | 0.41+/-0.12 | 0.26+/-0.2 | 86.7 | 40 | 0 | 1RD |
| Ripandelli et al.[52] (ETDRS) | 2014 | 30 | 72.3 | BBG | 12 | 0.9 | 0.65 | NA | NA | NA | none |

3) whether or not the eyes underwent peeling of the ILM at the time of surgery and whether or not dye was used for visualization of ILM; 4) recurrence of ERM and postoperative complications such as visual filed defect optic atrophy and retinal detachment.

To analyse the visual outcome across studies individual and mean visual acuity data were converted into logMAR units. Among the 12 studies that were identified 3 studies were prospective and 9 were retrospective cases series.[9,32-43] Six were comparative studies between ILM peeling vs no ILM peeling for idiopathic ERM. A total of 411 eyes with idiopathic ERM were included from the 12 studies in which visual acuity was reported before and after the surgery (Table 1 and 2).

### *Change in visual acuity after ILM peeling vs no ILM peeling*

Among the 6 studies[9,34-38] showing results after vitrectomy without ILM peeling for ERM the mean age ranged from 41.9 to 75.7 years. In all the studies without ILM peeling the mean logMAR visual acuity showed improvement after surgery. Mean logMAR visual acuity before surgery in the non-ILM peel group ranged from 0.44 to 0.9, with improved postoperative visual acuity which ranged from 0.24 to 0.67. In three of the studies[9,37,38] visual acuity changes were categorised into stable worse or improved after surgery. It was noted that 73.3-100% of the eyes without ILM peeling showed either stable or improved visual acuity at follow-up with 50-80% gaining lines or more.

In the ILM peeling group[9,34-43] baseline mean logMAR visual acuity ranged from 0.4 to 0.9 which improved to a range of 0.19 to 0.65. In all the studies with ILM peeling the mean logMAR visual acuity improved after surgery. In nine of the studies[9,37-43] visual acuity changes were categorised into stable worse or improved after surgery. Stable or improved visual acuity in eyes with ILM peeling was noted in 79-100% with 40-75% gaining 2 or more lines. These studies suggest that improvement of visual acuity is achieved after vitrectomy for ERM regardless of ILM peeling may not add any visual acuity benefit.

### *Recurrence of ERM and foveal contour after ILM peeling vs no ILM peeling*

In the non-ILM peeling group 4 studies reported postoperative ERM recurrence (Table 1).[9,34,36,37] The follow-up period ranged from 3 to 77 months and ERM recurrence was 0-52.5%. In the ILM peeling group 8 studies[9,34,36,37,40,42,43] reported postoperative ERM recurrence. Follow-up ranging from 3 to 88 months and ERM recurrence was 0-10%.

Park et al.[9] reported that none of their eyes undergoing ILM peeling had recurrent ERM. In contrast 21% of eyes that did not undergo ILM peeling showed recurrence or persistant contraction of the ILM and distortion of macular retinal vessels. However many of these recurrent ERMs were not visually significant and the final visual acuity results were similar between the two groups. In addition Kwok et al.[32] showed that there was biomicroscopic evidence of recurrence in 3 out of 15 eyes (20%) after ERM surgery without ILM peeling while 2 out of 20 eyes (10%) showed recurrence after ILM peeling. All of the recurrent membranes occurred within 12 months in the non-ILM peel group. In the ILM peel group asymptomatic and faint ERM was noted at the edge of the peeled ILM. Lee et al.[33] reported that none of the eyes showed recurrent ERM in both groups. In this study 16 eyes (84.2%) in the ERM peeling alone group had a normal foveal contour on postoperative OCT while nine eyes (42.9%) in the ERM with ILM peeling group had a normal foveal depression (p=0.01) suggesting that macular thickening with loss of the normal foveal contour was more common in the ERM with ILM peeling group. However regardless of the appearance of the fovea on OCT the visual outcome did not differ. Chang et al.[34] reported that there was a greater decrease in the central macular thickness in the non-ILM peel group compared to the ILM peel group. The cause of this is unknown but it is possible that removing the ILM could result in Muller cell trauma.[18,35] Regardless of OCT findings functional results remain unchanged by ILM peeling with no influence on postoperative visual acuity.[36] The development of spectral domain OCT may further clarify these findings.[37]

### *Possible dye-associated retinal toxicity*

A possible cause for the anatomic results after ILM peeling is ICG toxicity. It is well known that ICG dye has a photosensitising effect on the retina and may induce photo toxicity.[38,39] Experimental animal studies show that there are ICG-induced dose-dependent morphologic and functional changes in the retina and retinal pigment epithelium.[40,41] In a clinical study Haritoglou et al.[42] reported that eyes with ILM peeling without ICG experienced a significant improvement in visual acuity from 20/63 to 20/40; however there was no improvement in visual acuity in those with ICG- assisted peeling (p=0.013). Moreover in the group with ICG staining 7 out of 20 eyes showed large visual field defects. In follow-up study by the same group there was no significant change in the visual field defect after 7 years; however col-

our vision changes and optic atrophy were additional findings suggestive of long-term inner retinal damage caused by ICG-assisted ILM peeling.[43] Histologic assessment showed that epiretinal cells lost their cellular integrity after ICG-assisted vitrectomy. Because of the potential adverse effects of ICG various dyes including trepan blue (TB) and brilliant blue G (BBG) were introduced. Although clinical studies[44,45] have shown that TB has no toxic effect on the human retina experimental reports are controversial.[46,47] Moreover TB does not stain ILM as selectively as ICG. On the other hand BBG stains for ILM selectively with no known adverse effects at present.[48-50]

### *Conclusions*

Vitrectomy with ERM removal is beneficial in improving visual acuity and foveal contour and is well accepted as the treatment for symptomatic macular pucker. However there is still debate whether the concurrent removal of the ILM peeling affords any additional benefit. A recent American Society of Retina Specialists survey shows that 72-91% of retina surgeons routinely peel the ILM while performing macular hole surgery. While ICG is the most commonly used dye for ILM peel in the United States BB is most commonly used in other parts of the world. To date there are only two prospective comparative studies[44,51] addressing the functional and structural outcomes for ERM removal with and without ILM peeling. Overall a review of the literature suggests that there is no difference in final visual acuity between ILM peeling vs non-ILM peeling. Regardless of ILM peeling at least 70% of eyes included in these studies showed stable or improved visual acuity after surgery with 40-50% improving more than 2 lines in both groups. When comparing ERM recurrence ILM peeling may offer some benefit although many recurrences are not visually significant.

While ILM peeling could ensure complete removal of the cortical vitreous and ERM there is some suggestion that ILM peeling and the use of ICG dye could have a deterious effect. These effects are most likely detectable by visual field testing and/or microperimetry retinal sensitivity analysis. Therefore it still remains unclear whether removing the ILM during ERM surgery affords any additional benefit.[51-53]

## REFERENCES

1. Appiah AP, Hirose T, Kado M. A review of 324 cases of idiopathic premacular gliosis. Am J Ophthalmol 1988; 106(5):533-535.

2. Hiscott P, Sheridan C, Magee RM, Grierson I. Matrix and the retinal pigment epithelium in proliferative retinal disease. Prog Retin Eye Res 1999; 18(2):167-190.

3. Wollensak G, Spoerl E, Grosse G, Wirbelauer C. Biomechanical significance of the human internal limiting lamina. Retina 2006; 26(8):965-968.

4. Messner KH. Spontaneous separation of preretinal macular fibrosis. Am J Ophthalmol 1977; 83(1):9-11.

5. Sumers KD, Jampol LM, Goldberg MF, Huamonte FU. Spontaneous separation of epiretinal membranes. Arch Ophthalmol 1980; 98(2):318-320.

6. Grewing R, Mester U. Results of surgery for epiretinal membranes and their recurrences. Br J Ophthalmol 1996; 80(4):323-326.

7. Pesin SR, Olk RJ, Grand MG, Boniuk I, Arribas NP, Thomas MA, Williams DF, Burgess D. Vitrectomy for premacular fibroplasia. Prognostic factors, long-term follow-up, and time course of visual improvement. Ophthalmology 1991; 98(7):1109-1114.

8. Donati G, Kapetanios AD, Pournaras CJ. Complications of surgery for epiretinal membranes. Graefes Arch Clin Exp Ophthalmol 1998; 236(10):739-746.

9. Park DW, Dugel PU, Garda J, Sipperley JO, Thach A, Sneed SR, Blaisdell J. Macular pucker removal with and without internal limiting membrane peeling: pilot study. Ophthalmology 2003; 110(1):62-64.

10. Kuhn F. Point: to peel or not to peel, that is the question. Ophthalmology 2002; 109(1):9-11.

11. Mittleman D, Green WR, Michels RG, de la Cruz Z. Clinicopathologic correlation of an eye after surgical removal of an epiretinal membrane. Retina 1989; 9(2):143-147.

12. Sivalingam A, Eagle RC Jr, Duker JS, Brown GC, Benson WE, Annesley WH Jr, Federman J. Visual prognosis correlated with the presence of internal-limiting membrane in histopathologic specimens obtained from epiretinal membrane surgery. Ophthalmology 1990; 97(11):1549-1552.

13. Smiddy WE, Maguire AM, Green WR, Michels RG, de la Cruz Z, Enger C, Jaeger M, Rice TA. Idiopathic epiretinal membranes. Ultrastructural characteristics and clinicopathologic correlation. Ophthalmology 1989; 96(6):811-820; discussion 821.

14. Gaudric A, Fardeau C, Goberville M, Cohen D, Paques M, Mikol J. [Ablation of the internal limiting membrane, macular unfolding and visual outcome in surgery of idiopathic epimacular membranes]. J Fr Ophtalmol 1993; 16(11):571-576.

15. Kwok AK, Li WW, Pang CP, Lai TY, Yam GH, Chan

NR, Lam DS. Indocyanine green staining and removal of internal limiting membrane in macular hole surgery: histology and outcome. Am J Ophthalmol 2001;132(2):178-183.

16. Freeman WR, Azen SP, Kim JW, el-Haig W, Mishell DR 3rd, Bailey I. Vitrectomy for the treatment of full-thickness stage 3 or 4 macular holes. Results of a multicentered randomized clinical trial. The Vitrectomy for Treatment of Macular Hole Study Group. Arch Ophthalmol 1997; 115(1):11-21.

17. Oh HN, Lee JE, Kim HW, Yun IH. Clinical outcomes of double staining and additional ILM peeling during ERM surgery. Korean J Ophthalmol 2013; 27(4):256-260. doi: 10.3341/kjo.2013.27.4.256. Epub 2013 Jun 25.

18. Clark A, Balducci N, Pichi F, Veronese C. Swelling of the arcuate nerve fiber layer after internal limiting membrane peeling. Retina 2012; 32(8):1608-1613. doi: 10.1097/IAE.0b013e3182437e86.

19. Ito Y, Terasaki H, Takahashi A, Yamakoshi T. Dissociated optic nerve fiber layer appearance after internal limiting membrane peeling for idiopathic macular holes. Ophthalmology 2005; 112(8):1415-1420.

20. Rodrigues EB, Costa EF, Penha FM, Melo GB, Bottós J, Dib E, Furlani B, Lima VC, Maia M, Meyer CH, Höfling-Lima AL, Farah ME. The use of vital dyes in ocular surgery. Surv Ophthalmol 2009; 54(5):576-617. doi: 0.1016/j.survophthal.2009.04.011.

21. Arevalo JF, Garcia RA. Macular hole surgery complicated by accidental massive subretinal indocyanine green, and retinal tear. Graefes Arch Clin Exp Ophthalmol 2007; 245(5):751-753. Epub 2006 Oct 6.

22. Ejstrup R, la Cour M, Heegaard S, Kiilgaard JF. Toxicity profiles of subretinal indocyanine green, Brilliant Blue G, and triamcinolone acetonide: a comparative study. Graefes Arch Clin Exp Ophthalmol 2012; 250(5):669-677. doi: 10.1007/s00417-011-1886-3. Epub 2011 Dec 16.

23. Treumer F, Wacker N, Junge O, Hedderich J, Roider J, Hillenkamp J. Foveal structure and thickness of retinal layers long-term after surgical peeling of idiopathic epiretinal membrane. Invest Ophthalmol Vis Sci 2011; 52(2):744-750. doi: 10.1167/iovs.10-6310.

24. Kodjikian L, Richter T, Halberstadt M, Beby F, Flueckiger F, Boehnke M, Garweg JG. Toxic effects of indocyanine green, infracyanine green, and trypan blue on the human retinal pigmented epithelium. Graefes Arch Clin Exp Ophthalmol 2005; 243(9):917-925. Epub 2005 Apr 15.

25. Kanda S, Uemura A, Yamashita T, Kita H, Yamakiri K, Sakamoto T. Visual field defects after intravitreous administration of indocyanine green in macular hole surgery. Arch Ophthalmol 2004; 122(10):1447-1451.

26. Tsuiki E, Fujikawa A, Miyamura N, Yamada K, Mishima K, Kitaoka T. Visual field defects after macular hole surgery with indocyanine green-assisted internal limiting membrane peeling. Am J Ophthalmol 2007; 143(4):704-705. Epub 2006 Dec 8.

27. Yonemura N, Hirata A, Hasumura T, Negi A. Fundus changes corresponding to visual field defects after vitrectomy for macular hole. Ophthalmology 2001; 108(9):1638-1643.

28. Rodrigues EB, Meyer CH, Farah ME, Kroll P. Intravitreal staining of the internal limiting membrane using indocyanine green in the treatment of macular holes. Ophthalmologica 2005; 219(5):251-262.

29. Rodrigues EB, Meyer CH, Kroll P. Chromovitrectomy: a new field in vitreoretinal surgery. Graefes Arch Clin Exp Ophthalmol 2005; 243(4):291-293. Epub 2004 Dec 10.

30. Wu Y, Zhu W, Xu D, Li YH, Ba J, Zhang XL, Wang F, Yu J. Indocyanine green-assisted internal limiting membrane peeling in macular hole surgery: a meta-analysis. PLoS One 2012; 7(11):e48405. doi: 10.1371/journal.pone.0048405. Epub 2012 Nov 7.

31. Gibran SK, Flemming B, Stappler T, Pearce I, Groenewald C, Heimann H, Hiscott P, Wong D. Peel and peel again. Br J Ophthalmol 2008; 92(3):373-377. Epub 2007 Nov 30.

32. Kwok AK, Lai TY, Yuen KS. Epiretinal membrane surgery with or without internal limiting membrane peeling. Clin Exp Ophthalmol 2005; 33(4):379-385.

33. Lee JW, Kim IT. Outcomes of idiopathic macular epiretinal membrane removal with and without internal limiting membrane peeling: a comparative study. Jpn J Ophthalmol 2010; 54(2):129-134. doi: 10.1007/s10384-009-0778-0. Epub 2010 Apr 18.

34. Chang S, Gregory-Roberts EM, Park S, Laud K, Smith SD, Hoang QV. Double peeling during vitrectomy for macular pucker: the Charles L. Schepens Lecture. JAMA Ophthalmol 2013; 131(4):525-530. doi: 10.1001/jamaophthalmol.2013.2176.

35. Smiddy WE, Feuer W, Cordahi G. Internal limiting membrane peeling in macular hole surgery. Ophthalmology 2001; 108(8):1471-1476; discussion 1477-8.

36. Pournaras CJ, Emarah A, Petropoulos IK. Idiopathic macular epiretinal membrane surgery and ILM peeling: anatomical and functional outcomes. Semin Ophthalmol 2011; 26(2):42-46. doi: 10.3109/08820538.2010.544237.

37. Falkner-Radler CI, Glittenberg C, Hagen S, Benesch T, Binder S. Spectral-domain optical coherence tomography for monitoring epiretinal membrane surgery. Ophthalmol 2010; 117(4):798-805. doi: 10.1016/j.ophtha.2009.08.034. Epub 2010 Jan 4.

38. Yam HF, Kwok AK, Chan KP, Lai TY, Chu KY, Lam DS, Pang CP. Effect of indocyanine green and illumination on gene expression in human retinal pigment epithelial cells. Invest Ophthalmol Vis Sci 2003; 44(1):370-377.

39. Kwok AK, Lai TY, Yeung CK, Yeung YS, Li WW,

Chiang SW. The effects of indocyanine green and endoillumination on rabbit retina: an electroretinographic and histological study. Br J Ophthalmol 2005; 89(7):897-900.

40. Enaida H, Sakamoto T, Hisatomi T, Goto Y, Ishibashi T. Morphological and functional damage of the retina caused by intravitreous indocyanine green in rat eyes. Graefes Arch Clin Exp Ophthalmol 2002; 240(3):209-213. Epub 2002 Feb 15.

41. Sippy BD, Engelbrecht NE, Hubbard GB, et al. Indocyanine green effect on cultured human retinal pigment epithelial cells: implication for macular hole surgery. Am J Ophthalmol 2001; 132(3):433-435.

42. Haritoglou C, Gandorfer A, Gass CA, Schaumberger M, Ulbig MW, Kampik A. The effect of indocyanine-green on functional outcome of macular pucker surgery. Am J Ophthalmol 2003; 135(3):328-337.

43. von Jagow B, Höing A, Gandorfer A, Rudolph G, Kohnen T, Kampik A, Haritoglou C. Functional outcome of indocyanine green-assisted macular surgery: 7-year follow-up. Retina 2009; 29(9):1249-1256. doi: 10.1097/IAE.0b013e3181a91dd3.

44. Haritoglou C, Eibl K, Schaumberger M, Mueller AJ, Priglinger S, Alge C, Kampik A. Functional outcome after trypan blue-assisted vitrectomy for macular pucker: a prospective, randomized, comparative trial. Am J Ophthalmol 2004; 138(1):1-5.

45. Perrier M, Sébag M. Epiretinal membrane surgery assisted by trypan blue. Am J Ophthalmol 2003; 135(6):909-911.

46. Jin Y, Uchida S, Yanagi Y, Aihara M, Araie M. Neurotoxic effects of trypan blue on rat retinal ganglion cells. Exp Eye Res 2005; 81(4):395-400.

47. Narayanan R, Kenney MC, Kamjoo S, Trinh TH, Seigel GM, Resende GP, Kuppermann BD. Trypan blue: effect on retinal pigment epithelial and neurosensory retinal cells. Invest Ophthalmol Vis Sci 2005; 46(1):304-309.

48. Remy M, Thaler S, Schumann RG, May CA, Fiedorowicz M, Schuettauf F, Grüterich M, Priglinger SG, Nentwich MM, Kampik A, Haritoglou C. An in vivo evaluation of Brilliant Blue G in animals and humans. Br J Ophthalmol 2008; 92(8):1142-1147. doi: 10.1136/bjo.2008.138164.

49. Schumann RG, Remy M, Grueterich M, Gandorfer A, Haritoglou C. How it appears: electron microscopic evaluation of internal limiting membrane specimens obtained during brilliant blue G assisted macular hole surgery. Br J Ophthalmol 2008; 92(3):330-331. doi: 10.1136/bjo.2007.128421.

50. Kawahara S, Hata Y, Miura M, Kita T, Sengoku A, Nakao S, Mochizuki Y, Enaida H, Ueno A, Hafezi-Moghadam A, Ishibashi T. Intracellular events in retinal glial cells exposed to ICG and BBG. Invest Ophthalmol Vis Sci 2007; 48(10):4426-4432.

51. Tari SR, Vidne-Hay O, Greenstein VC, Barile GR, Hood DC, Chang S. Functional and structural measurements for the assessment of internal limiting membrane peeling in idiopathic macular pucker. Retina 2007; 27(5):567-572.

52. Ripandelli G, Scarinci F, Piaggi P, Guidi G, Pileri M, Cupo G, Sartini MS, Parisi V, Baldanzellu S, Giusti C, Nardi M, Stirpe M, Lazzeri S. Macular pucker: to peel or not to peel the internal limiting membrane? A microperimetric response. Retina 2015; 35(3):498-507. doi: 10.1097/IAE.0000000000000330.

53. Kwok AK, Lai TY, Yew DT, Li WW. Internal limiting membrane staining with various concentrations of indocyanine green dye under air in macular surgeries. Am J Ophthalmol 2003; 136(2):223-230.