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Does Internal limiting membrane peeling size matter ?

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Abstract

Purpose: A variety of retinal topographical changes occur after internal limiting membrane (ILM) peeling for macular holes including a movement of the fovea towards the optic nerve. *This study was carried out to assess the effect of the extent of ILM peeled area on these changes and postoperative visual acuity.*

Methods: Prospective single centre study of a consecutive series of patients undergoing macular hole surgery. Pre and postoperative optical coherence tomography images were used to assess a variety of measures of retinal morphology. Transmission electron microscopy of the peeled ILM was used to assess residual retinal and vitreous side debris. The area of the ILM peeled was calculated from intraoperative images.

Results : 56 eyes of 56 patients were included. The mean area of ILM peeled was 9.5 mm^2 (2.4 - 28.3 mm^2). The mean disc to fovea distance (DFD) preoperatively was 3703 microns with a mean reduction of 52 microns postoperatively representing a change of -1.29 % with a wide range of -7.04% to +1.36%. Using step wise linear regression ILM peel area was significantly associated with change in DFD ($p<0.001$), extent of a dissociated optic nerve fibre layer appearance ($p<0.001$) as well as postoperative visual acuity ($p=0.025$). Nasotemporal retinal thickness asymmetry was associated with the minimum linear diameter ($p<0.001$).

Conclusion: ILM peel area has a significant effect on changes in retinal topography and postoperative visual acuity separate from macular hole size. Further study is needed to assess the effect of ILM peel size on visual function and to guide clinical practice.

Introduction

Peeling of the internal limiting membrane (ILM) has been proven to improve the closure rate of macular holes when combined with vitrectomy and gas tamponade.[1] There is no consensus regarding the extent of the area of ILM that should optimally be peeled, and peel radii of 0.5 to 3 disc diameters have been described.[2] A variety of retinal changes after ILM peeling occur, including a movement of the fovea towards the optic nerve head which has been associated with thickening of the nasal retina and a thinning of the temporal retina.[3,4] The retinal movement is centripetal but with greater movement in the horizontal meridian than vertical, and greater movement of the temporal retina towards the disc than nasal.[4,5] The observed retinal displacement has been related to the extent of postoperative metamorphopsia and also the appearance post-operatively of a dissociated optic nerve fibre layer (DONFL).[5,6] The factors that control the extent of these changes are incompletely understood. The extent of the retinal movement has been correlated with the size of the macular hole.[4] We have also recently related the extent of DONFL to the extent of Muller cell fragments on the retinal side of the ILM.[7] We postulated that the size of the ILM peel area could also have an effect on these changes and other postoperative outcomes and explored this possibility further in a consecutive cohort of patients undergoing surgery.

Method

Consecutive patients undergoing surgery by one surgeon for idiopathic macular holes were included in the study. The study followed the tenets of the Declaration of Helsinki, with approval from the local institutional review board. Informed consent was obtained from the subjects after explanation of the nature of the study. Patients with traumatic macular holes, an axial length of greater than 26 millimetres, previous retinal surgery, second eyes, less than 3 months follow up, inadequate imaging or those in whom the hole failed to close were excluded. Holes were considered closed, indicating anatomical success, if there was complete circumferential hole rim reattachment without a full thickness foveal neurosensory retinal defect demonstrated on OCT. All patients underwent trans-conjunctival 25 or 27gauge vitrectomy using wide field non-contact viewing with combined phacoemulsification and intraocular lens implantation if phakic. Brilliant Blue G [ILM Blue, Dorc international, The Netherlands] was used to stain the ILM and peeled using a pinch technique and 25g end gripping forceps (Grieshaber revolution DSP ILM forceps, Alcon Grieshaber AG, Schaffhausen, Switzerland). A peel radius of approximately 0.5 - 1.5 disc diameters was aimed for. The peeled ILM was removed from the eye and placed in glutaraldehyde for analysis by transmission electron microscopy

Either 25 % SF6 or 20% C2F6 gas was used as a tamponade and the patients instructed to position face down for 3 days. All surgeries were recorded via a beam splitter from the microscope (OPMI Lumera T, Carl Zeiss Meditec AG, Jena, Germany) and a digital recorder (Medlife Mind Stream, Carl Zeiss Meditec AG, Jena, Germany). At the end of each peeling procedure care was taken to obtain a well centred clear sequence of the peeled area. Patients were reviewed at 4 months post operatively. Preoperative and postoperative BCVA at 3 months was measured using a standard Snellen acuity chart and converted to logarithm of the minimum angle of resolution (logMAR) scores for the purposes of statistical analysis.

Patients underwent Spectral domain optical coherence tomography (SD OCT) on the Heidelberg Spectralis immediately preoperatively and at 3 months post-operatively. A high density central horizontal scanning protocol with 30 micron line spacing was used in the central 15 degrees as well as a broader 20 by 30 degree horizontal line scan pattern with a line spacing of 240 microns. All scans used a 25 automatic real time (ART) setting enabling multisampling and noise reduction over 25 images and were matched to a corresponding high-quality 768 by 768 pixel 30 degree infrared image. The follow up images were registered to the baseline image using the Spectralis AutoRescan function.

Image measurements

On the preoperative OCT the position of the centre of the hole was marked and the minimum linear diameter and base diameter of the hole measured. An identifiable landmark on the temporal disc margin where it was crossed by a vessel was chosen and the distance from the foveal centre to this point measured using the Spectralis measuring tools (Disc fovea distance (DFD)). Three vessel bifurcations were then chosen approximately 1.5 disc diameters superior, inferior and temporal to the fovea. The distance between the inferior and superior points ('vertical gap' (VG)) and between the temporal bifurcation and the optic disc landmark ('horizontal gap' (HG)) were then measured. The mean of the VG and HG was then used to calculate the area of this virtual circular which we termed the 'Macula area' (MA). These measurements were then repeated using the same landmarks on the post-operative OCT. In this case the foveal centre was taken as the point of minimal retinal thickness and sometimes also accompanied by a small outer retinal defect.

The difference between the pre and post-operative MA was calculated and expressed as a percentage change compared to baseline. The same calculation was performed for DFD change. (Figure 1)

The thickness of the retina was measured from the inner retinal surface to the RPE at points 1.5mm nasal and 1.5mm temporal to the fovea using the Spectralis measuring tools pre and postoperatively. A value which we called the nasal temporal difference (NTD) was calculated as the change in nasal retinal thickness minus the change in temporal retinal thickness. (Figure 1)

The fellow eye of 10 randomly selected patients in the study without macular pathology and with less than 1 dioptre of anisometropia were used as controls for the retinal measurement technique and any variability with repeat scanning.

The recording of the intraoperative video was imported into a video editing program, a snapshot image of a well centred post peel view saved and this then imported into the image viewing software GIMP (www.gimp.org). The ILM peeled area was calculated using the actual vertical disc diameter taken from the OCT to calibrate the measurements. ('ILM Peel area': ILM PA)

Quantifying DONFL

The number of focal depressions characteristic of DONFL in the retinal surface were counted in each slice of the 3 month post-operative 20 by 30 degree OCT and summed to produce a total DONFL score as previously described.[8] The technique is shown in figure 2 and the relationship between red free and en face images shown for illustrative purposes. We also calculated the number of dimples per mm^2 using the peeled area in each case.

One observer, masked to their previous count, counted the depressions on two occasions. There was high concordance between the two counts with a correlation coefficient of 0.92. The measurements showed no systematic relationship with the extent of DONFL and the repeatability coefficient was 2.2 which we considered clinically acceptable.

Transmission electron microscopy

ILM samples were fixed in 2% glutaraldehyde in 0.1M sodium cacodylate buffer. The ILM was enrobed in low-melting point agarose [4%] to form a small block to make the ILM easier to handle. After secondary fixation in 2% osmium tetroxide, the samples were dehydrated in graded acetone, embedded in epoxy resin and polymerised at 60^{o}C. Ultrathin sections of 70nm were taken at 2 levels through the block, stained with uranyl acetate and lead citrate and viewed on a Philips CM100 TEM (Philips/FEI Corp., Eindhoven, Holland). Detailed examination of the tissue was then performed to determine the occurrence of any cellular debris on the retinal and vitreous sides of the ILM. For estimation of the amount of cellular debris, images were taken at x7900 from 14 randomly sampled areas of the ILM. An unbiased method was used to quantify the amount of debris on the retinal side of the ILM as previously described.[9] The same technique was used for estimation of the extent of vitreous side material present on the ILM.

Statistical analysis

Descriptive and statistical analysis was performed using Minitab 16 statistical package (Minitab Ltd, Coventry, UK). Pre, intra and post-operative variables are presented in terms of mean, standard deviation and range when normally distributed, and median, interquartile range and range when not normally distributed, and percentage as appropriate.

Paired t-tests and Chi squared tests were used to compare the continuous and categorical variables respectively between the pre and post-operative measurements. Statistical significance was considered with a p-value of 0.05 or less.

Association between continuous data were assessed using correlations and between categorical data using two sample t-tests or analysis of variance. Stepwise linear modelling was then used on the % change in DFD, % change in macular area, NTD, postoperative visual acuity, postoperative minimal foveal thickness and the extent of DONFL represented by the total DONFL score, to pick out the most important pre and intraoperative variables.

Results

During the study period 69 patients (72 eyes) underwent surgery. Sixteen were excluded for incomplete follow up (2), inadequate imaging (10), non-closure (1) and second eye status (3) leaving 56 eyes for analysis.41 of these eyes had the ILM examined by TEM. The baseline features are show in table 1.

There was a significant correlation between BD and MLD ($R=0.76$, $p<0.001$), and between both variables and preoperative visual acuity ($R=0.45$ and 0.53, $p<0.001$ both). No other preoperative variables were significantly associated with each other and specifically the size of the ILM peel area was not correlated with the size of the macular hole.

The mean area of ILM peeled was ~10mm^2 equating to a peel radius of 1.8 mm i.e. approximately 1 disc diameters. There was however a wide range of ILM peel areas ranging from ~2.4 mm^2 (~1/2 disc diameter peel radius) to ~28 mm^2 (~2 disc diameters in radius).

The visual acuity improved from a mean of 0.93 logMAR preoperatively to 0.36 postoperatively. (Table2)

The mean nasal retinal thickness increased by 16 microns and the mean temporal thickness reduced by 21 microns resulting in a mean NTD of +37 microns, but with a wide range of -13 microns (representing a thinning of the nasal retina and thickening of the temporal retina) to +96 microns.

The mean DFD preoperatively was 3703 microns with a mean reduction of 52 microns postoperatively representing a change of -1.29 % with a wide range of -7.04% to +1.36%.

The MA similarly reduced by a mean of 0.38% with a range of -5.14% to +2.8%.

The fellow eyes used as controls showed a low level of variability pre and postoperatively representing a high level of test-retest reliability. (Table 3)

Using step wise linear regression the association between the preoperative and intraoperative variables and the postoperative outcomes was analysed.

For percentage change in DFD, the only significant variable associated was peel area ($p<0.001$), R^2 =25.8%. (Figure 3) The greater the peel area, the greater the reduction in DFD observed.

For percentage change in MA, peel area was strongly associated ($p<0.001$) as well as age ($p=0.019$) and the amount of vitreous side debris on the ILM ($p=0.045$). R^2 =46.7%. The greater the peel area, age and the greater the vitreous side debris, then the greater the reduction in macular area. (Figure 4)

For NTD, MLD ($p<0.001$) and male sex ($p=0.001$) were associated , R^2 =47.1%.

The extent of DONFL was associated with peel area ($p<0.001$), BD ($p=0.014$) and retinal debris ($p=0.012$), R^2 =67.2%. (Figure 5) Peel area was not significant when the same analysis was performed for DONFL per mm^2.

For postoperative visual acuity the significantly associated variables were the duration of the hole ($p=0.002$), BD ($p=0.038$) and peel area ($p=0.025$), R^2 =46.7%.

Discussion

The extent of the area of ILM removed was strongly associated with a number of postoperative changes including a shortening of the fovea to disc distance, a reduction in the virtual measure of 'Macular area', the extent of DONFL observed and importantly the postoperative visual acuity.

Ohta et al observed in 2010 that, after ILM peeling and macular hole closure, there was a change in the relative thicknesses of the parafoveal retina, with a thickening of the nasal retina and thinning of the temporal retina.[3] Subsequently others have reported a variety of changes including a reduction in fovea to disc distance and a centripetal movement of the parafoveal retina towards the disc and fovea. [4,10]

The ILM forms the inner boundary of the retina and is considered the basement membrane of the Muller cells, but is formed from proteins shed into the vitreous cavity during embryogenesis from the lens and ciliary body .[11] Its thickness varies across the fovea reaching a maximum at 1000 microns from the foveal centre of around 4 microns.[12] Although thin its mechanical strength is in the megapascal range similar to articular cartilage and about a 1000-fold stronger than cell layers, forming at least 50% of retinal rigidity.[13,14]

Its removal reduces retinal compliance and as Ishida et al showed, being anchored at the optic disc , after peeling there is a movement of the temporal retina towards the disc.[4]

Previous studies have found a large range of induced retinal movement. For example Nagakomi et al found a reduction in fovea to disc distance of -4.7% but with a range of -9.24% to +0.38%.[6] These studies did not however investigate the association between these induced changes and ILM peel area. Indeed it is perhaps intuitive that peeling ILM over a larger area will result in increased retinal movement and we found a mean reduction in DFD of -1.29% with a range of -7.04% to +1.36%, which was strongly associated with ILM peel area. Interestingly Nagakomi et al aimed for an ILM peel diameter of 3-4 disc diameters equating to a large peel area which would account for the difference in mean value.[6] The same discussion likely relates to MA. Rodrigues et al. found a reduction in macular area with a mean of -7.6% after macular hole surgery compared to our mean change of -0.38%.[5] Again differences in the size of ILM peel area may explain this but also differences in methodology for the measurement of 'MA'. Indeed the location of the points chosen for measuring the perimeter of the 'macular area' are likely to have an effect on changes in its area. Ishida et al. showed that the temporal retina undergoes greater movement postoperatively than the nasal retina.[4] Also points chosen within the ILM peel area may move differently to those chosen outside the perimeter of the peel, with residual peripheral ILM and any adherent vitreous, acting to 'pull' tissue towards it centrifugally, whilst tissue more centrally moves centripetally. Interestingly we found a weak association between the amount of vitreous debris on the peeled ILM and the change in MA which adds weight to this hypothesis.

We found that change in DFD and MA were related to each other and also to the extent of DONFL which in turn were all related to ILM peel area. Nakagomi et al related change in DFD to DONFL with a greater reduction in DFD being associated with a more frequent observation of DONFL and hypothesised that the appearance of DONFL was related to the retinal slippage occurring after surgery.[6] We found that a greater peel area was associated with a greater number of dimples on OCT characteristic of DONFL. However when the number of dimples per unit area of ILM peel area was analysed, the associations disappeared suggesting that the association is only related to the absolute number of dimples not their density. We have previously showed an association between the extent and size of retina side debris on the ILM and the extent of DONFL and we corroborated this finding in this study with retinal debris again being associated with the extent of DONFL.[7]

We didn't find a relationship between the change in retinal asymmetry which we quantified by NTD, and ILM peel area. We did find however that NTD postoperatively was associated with MLD and male sex. Ishida et al also found an association of retinal thickness asymmetry with macular hole size albeit basal diameter.[4] It is interesting that we didn't find an association between DFD and NTD and no association between DFD and macular hole size. Similarly neither Ishida et al nor Nakagomi et al found an association between the DFD and macular hole size and our findings suggest that macular hole size is more important in determining retinal thickness asymmetry ,whilst ILM peel area governs DFD and MA changes to a greater extent.[4,6] The association between NTD and male sex is also noteworthy. Population studies have shown that men have greater macular thickness and greater choroidal thickness than women in the central foveal areas with steeper foveal pits which may have aetiological significance for our findings.[15,16] Furthermore women have been previously shown to have larger holes on average than men which we also found; 343 microns in MLD for women versus 268 microns for men, p=0.03).[17]

There are currently no prescribed parameters for the optimum extent of ILM to be peeled during surgery for macular holes. It has been observed that enlarging ILM peeled area can result in hole closure in failed cases undergoing revision surgery and some authors have argued for large ILM peels in all cases.[18] It is striking that the 7 holes in this series between 450 and 550 microns in MLD had ILM peel areas of 5-7mm^2 (i.e. less than 1dd in radius) and all closed. There have been two recent trials comparing different sizes of ILM peel radii. Modi et al carried out a prospective study of 50 patients undergoing surgery with ILM peel radii of 1 and 1.5 disc diameters.[19] They found no significant difference in hole closure rates but better visual results in the smaller peel radii group with less retinal nerve fibre layer thinning particularly temporally. Although we found that hole duration was the strongest association with postoperative visual acuity, we also found a significant association between peel area and visual acuity. Pilli et al found an association between inner retinal volume in the macular and postoperative visual outcome [20] and other authors have reported reduced retinal sensitivity in the peeled area and paracentral scotomata. [21,22] Conversely Bae et al. carried out a randomised controlled study of 65 eyes with ILM peeling radii of 0.75 and 1.5 disc diameters.[23] They found no difference in visual outcomes but did find a benefit of larger peels with regards to an improvement in metamorphopsia. Currently it is thus unclear as to the extent of ILM that should be optimally peeled during surgery for macular holes. We found a high rate of closure with widely differing peel areas but hypothetically there may be a minimum ILM peel area for a set size of macular hole to allow enough reduced retinal compliance to permit closure. This area may vary with hole chronicity and other factors.

Larger ILM peels would ensure that this threshold was passed but at the expense of greater inner retinal changes and potentially reduced visual function.

We acknowledge that this study has several weaknesses. It was a retrospective observational study and the size of the ILM peel was not predetermined. A peel radius of approximately 0.5 - 1.5 disc diameters was aimed for, but wide variability in peel radius was achieved based on the ease of peel, field of view and size of eye. The range of ILM peel areas we observed was therefore not evenly distributed across a range of sizes. We didn't quantify metamorphopsia in our cohort so are unable to comment on the effect of ILM peel area on relief of distortion. The strengths of the study include the fact that a single surgeon performed all the surgery with a single technique minimising confounding variables. Baseline scans were matched to postoperative scans allowing more accurate measurements. Histology was performed to assess the effect of ILM related variables on outcome. The fellow eyes used as controls showed a low level of variability pre and postoperatively verifying that the changes we observed were surgically induced.

In conclusion ILM peel area has a significant effect on retinal topography postoperatively. Further study is needed to assess the effect of these differences on visual function and to guide clinical practice as to an optimum ILM peel area for surgeons to aim for in any particular case.

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Disclosures

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References

1) Spiteri Cornish K, Lois N, Scott N, Burr J, Cook J, Boachie C et al. (2013) Vitrectomy with internal limiting membrane peeling versus vitrectomy with no peeling for idiopathic full-thickness macular hole. **Cochrane Database Syst Rev.** 6:CD009306.

2) Abdelkader E, Lois N. (2008) Internal limiting membrane peeling in vitreo-retinal surgery. **Surv Ophthalmol**. 53:368-96.

3) Ohta K, Sato A, Fukui E. (2010) Asymmetrical thickness of parafoveal retina around surgically closed macular hole. **Br J Ophthalmol.** 94:1545–1546.

4) Ishida M, Ichikawa Y, Higashida R, et al.(2014) Retinal displacement toward optic disc after internal limiting membrane peeling for idiopathic macular hole. **Am J Ophthalmol.** 157:971–977.

5) Rodrigues IA, Lee EJ, Williamson TH. (2016) MEASUREMENT OF RETINAL DISPLACEMENT AND METAMORPHOPSIA AFTER EPIRETINAL MEMBRANE OR MACULAR HOLE SURGERY. **Retina.** 36:695-702.

6) Nakagomi T, Goto T, Tateno Y, Oshiro T, Iijima H.(2013) Macular slippage after macular hole surgery with internal limiting membrane peeling. **Curr Eye Res.** 38:1255-60.

7) Steel DH, Dinah C, White K, Avery P. (2016) The relationship between a dissociated optic nerve fibre layer appearance after macular hole surgery and Muller cell debris on peeled ILM. **Acta Ophthalmol.** Aug 29. doi:10.1111/aos.13195. [Epub ahead of print]

8) Steel DH, Sandinha MT, White K. (2015) The Plane of Vitreoretinal Separation and Results of Vitrectomy Surgery in Patients Given Ocriplasmin for Idiopathic Macular Hole. **Invest Ophthalmol Vis Sci.** 56:4038-44.

9) Steel DH, Dinah C, Madi HA, White K, Rees J. (2014) The staining pattern of brilliant blue G during macular hole surgery: a clinicopathologic study. **Invest Ophthalmol Vis Sci.** 55:5924-31.

10) Itoh Y, Inoue M, Rii T, Ando Y, Hirakata A. (2014) Asymmetrical recovery of cone outer segment tips line and foveal displacement after successful macular hole surgery. **Invest Ophthalmol Vis Sci.** 55:3003-11

11) Halfter W, Dong S, Dong A, Eller AW, Nischt R. (2008) Origin and turnover of ECM proteins from the inner limiting membrane and vitreous body. **Eye (Lond).** 22:1207-13.

12) Henrich PB, Monnier CA, Halfter W, Haritoglou C, Strauss RW, Lim R et al.(2012) Nanoscale topographic and biomechanical studies of the human internal limiting membrane. **Invest Ophthalmol Vis Sci**. 53:2561-70.

13) Candiello J, Balasubramani M, Schreiber EM, Cole GJ, Mayer U, Halfter W et al.(2007) Biomechanical properties of native basement membranes. **FEBS J** 274: 2897–2908.

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

15) Patel PJ, Foster PJ, Grossi CM, Keane PA, Ko F, Lotery A et al; UK Biobank Eyes and Vision Consortium.(2016) Spectral-Domain Optical Coherence Tomography Imaging in 67 321 Adults: Associations with Macular Thickness in the UK Biobank Study. **Ophthalmology.** 123:829-40.

16) Zeng J, Liu R, Zhang XY, Li JQ, Chen X, Pan JY et al. (2012) [Relationship between gender and posterior pole choroidal thickness in normal eyes]. **Zhonghua Yan Ke Za Zhi.** 48:1093-6.

17) Kumagai K, Ogino N, Demizu S, Atsumi K, Kurihara H, Iwaki M et al. (2001)[Clinical features of idiopathic macular holes-differences between sexes and stages]. **Nippon Ganka Gakkai Zasshi.** 105:452-6.

18) Goker YS, Koc M, Yuksel K, Yazici AT, Demir A, Gunes H et al. (2016) Relationship between Peeled Internal Limiting Membrane Area and Anatomic Outcomes following

Macular Hole Surgery: A Quantitative Analysis. **J Ophthalmol.** 2016:5641273. doi: 10.1155/2016/5641273. Epub 2016 Jun 16.

19) Modi A, Giridhar A, Gopalakrishnan M. (2016) COMPARATIVE ANALYSIS OF OUTCOMES WITH VARIABLE DIAMETER INTERNAL LIMITING MEMBRANE PEELING IN SURGERY FOR IDIOPATHIC MACULAR HOLE REPAIR. **Retina.** Jul 14. [Epub ahead of print]

20) Pilli S, Zawadzki RJ, Werner JS, Park SS. (2012) Visual outcome correlates with inner macular volume in eyes with surgically closed macular hole. **Retina.** 32:2085–2095.

21) Ripandelli G, Scarinci F, Piaggi P, Guidi G, Pileri M, Cupo G et al.(2015) Macular pucker: to peel or not to peel the internal limiting membrane? A microperimetric response. **Retina.** 35:498-507.

22) Tadayoni R, Svorenova I, Erginay A, Gaudric A, Massin P.(2012) Decreased retinal sensitivity after internal limiting membrane peeling for macular hole surgery. **Br J Ophthalmol.** 96:1513-6.

23) Bae K, Kang SW, Kim JH, Kim SJ, Kim JM, Yoon JM.(2016) Extent of Internal Limiting Membrane Peeling and Its Impact on Macular Hole Surgery Outcomes: A Randomized Trial. **Am J Ophthalmol.** Jul 5. pii: S0002-9394(16)30315-4. doi: 10.1016/j.ajo.2016.06.041.

Legends

Figure 1: Top panel shows preoperative macular hole, and bottom panel postoperative appearance, with corresponding central slice of SDOCT showing measurements of retinal topography and thickness.

Figure 2: Red free (top left), en face OCT at the level of the ILM(bottom left), and two illustrative line scans of patient postoperatively (top right corresponding to black lines on red free and en face and bottom right corresponding to white line) . Edge of ILM peel area drawn on red free image as dotted black line.

Figure 3: Percentage change in disc foveal distance versus ILM peel area

Figure 4: Graph of percentage change in macular area versus ILM peel area

Figure 5: Graph of total DONFL score versus ILM peel area