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Factors Associated with Development of Dissociated Optic Nerve Fiber Layer (DONFL) Appearance in the PIONEER Intraoperative OCT Study

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Abstract

Purpose—To assess the relationship of dissociated optic nerve fiber layer (DONFL) and intraoperative membrane peeling dynamics as visualized with intraoperative OCT, and to evaluate the functional implications of DONFL.

Methods—This was a post-hoc analysis of eyes undergoing membrane peeling for vitreomacular interface disorders in the prospective PIONEER intraoperative OCT study. Retinal layer measurements in pre-incision and post-peel intraoperative OCT images were obtained. The primary outcome was development of DONFL appearance on SD-OCT at 6 months follow-up. Secondary outcomes included correlation of DONFL with surgical technique, surgical indication, intraoperative OCT findings, retinal sensitivity.

Results—Ninety-five eyes were included. The prevalence of DONFL at 6 months was 36%. Increased inner retinal layer thickness on intraoperative OCT immediately following membrane peeling was associated with development of DONFL ($p < 0.01$). Macular hole (MH) repair was significantly associated with DONFL appearance. Peel technique (forceps vs. diamond-dusted membrane scraper) was not associated with DONFL. There was no difference in retinal sensitivity or visual acuity between eyes with or without DONFL.

Conclusions—Acute post-peel increase in inner retinal thickness and MH repair were associated with development of DONFL appearance. However, it is unclear whether the surgical indication (e.g., MH) or the surgical manipulations performed (e.g., ILM peeling) is the major factor that has an impact on DONFL appearance. Overall, these findings suggest that one mechanism in the development of DONFL appearance may be intraoperative trauma to the inner retina, potentially during internal limiting membrane peeling (e.g., MH repair).

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Keywords

Dissociated Optic Nerve Fiber Layer Appearance; DONFL; Microperimetry; OCT; Optical Coherence Tomography

Introduction

Pars plana vitrectomy (PPV) and membrane peeling are frequently performed for the management of many vitreomacular interface (VMI) disorders, such as macular hole (MH), epiretinal membrane (ERM), and vitreomacular traction (VMT)¹⁻⁵. While internal limiting membrane (ILM) peeling has been shown to decrease epiretinal membrane recurrence and enhance macular hole closure rates, it is also known to cause mechanical trauma to the inner retina, and the long-term consequences of ILM and/or membrane peeling remain unknown^{6, 7}. In 2001, Tadayoni et al reported that following ILM peeling, an unusual “moth-eaten” appearance of the retina was noted, characterized by dark arcuate striae along the course of the optic nerve fibers⁸. This finding was named “dissociated optic nerve fiber layer (DONFL) appearance” and appeared 1-3 months after surgery in 42-62% of eyes that underwent ILM peeling. A subsequent investigation using spectral-domain OCT showed that the striae were caused by small dimples in the regions of the retina where the ILM had been removed⁷. In addition, while DONFL appearance does not seem to cause alterations in overall visual acuity, several studies have suggested that it may be associated with retinal sensitivity loss and paracentral scotoma^{9, 10}.

There is not a current consensus about the pathophysiology of DONFL appearance. Many mechanisms have been proposed, including Müller cell damage due to direct contact with surgical instruments, deep inner retinal layer damage, damage due to visualization dye, or thinning of the temporal retina due to traction^{4, 7, 8, 11}. All of these mechanisms are related to direct trauma or sequelae of trauma during surgical repair. Intraoperative OCT provides a unique opportunity to visualize the underlying alterations to the retinal tissue and the potential implications for DONFL.¹² Intraoperative OCT provides a high-resolution, cross-sectional view of the eye, allowing the capture of images showing the microstructure of each layer of the retina both before and immediately after membrane peeling procedures^{12, 13}.

In this study, we use intraoperative OCT data to investigate the association between several intraoperative retinal alterations and the development of DONFL appearance. In addition, this report examines the impact of surgical technique and underlying preoperative diagnosis on DONFL appearance development, as well as the association of DONFL appearance with retinal function.

Methods

Subjects

This study examined patients in the Prospective Assessment of Intraoperative and Perioperative OCT for Ophthalmic Surgery (PIONEER) study who underwent pars plana vitrectomy (PPV) with membrane-peeling procedure for VMI disorders including MH, and ERM. The PIONEER study is a single-site multi-surgeon investigational device study

approved by the Cleveland Clinic Institutional Review Board¹⁴. The study adhered to the tenets of the Declaration of Helsinki, and written informed consent was obtained from all enrolled patients. Patients were recruited from the pool of all adult patients seen at the Cole Eye Institute. As described previously, the PIONEER study utilized a standard imaging protocol to obtain intraoperative OCT images using a microscope-mounted intraoperative OCT system¹⁴. The inclusion criteria for eyes included in this post-hoc analysis were: underwent PPV with membrane-peeling procedure for MH or ERM, intraoperative OCT was obtained, intraoperative OCT was of sufficient quality for quantitative assessment, and follow-up SD-OCT was obtained between 3-12 months post-operatively. Exclusion criteria included eyes with poor-quality intraoperative OCT, poor-quality follow-up SD-OCT (defined as signal strength less than 7/10), or evidence of other significant macular pathology on OCT (*e.g.*, diabetic macular edema, age-related macular degeneration). Additional IRB approval was obtained to contact subjects who met all inclusion and exclusion criteria to return voluntarily for functional assessment with microperimetry and follow-up SD-OCT.

Surgical Procedure

Patients underwent standard three-port PPV (either 23- or 25-gauge) by one of four vitreoretinal surgeons. The surgeons used their preferred choice of two techniques for membrane peeling: initiation of the peel with the Diamond-Dusted Membrane Scraper (DDMS [Synergetics, Inc., Fort Collins, CO]) and completion of the peel with vitreoretinal forceps, or initiation and completion of the peel with vitreoretinal forceps alone (*e.g.* “pinch-and-peel”). Indocyanine green (ICG) was used for membrane visualization in all cases. ILM peeling was completed in all cases of MH and was performed at surgeon discretion for ERM peeling.

Intraoperative OCT and SD-OCT Systems

Intraoperative images were obtained with the microscope-mounted Bioptigen Envisu intraoperative OCT system (Bioptigen, Research Triangle Park, NC, USA), as previously described.^{14, 15} The PIONEER study intraoperative imaging protocol directed surgeons to perform intraoperative OCT scanning during key surgical milestones (*e.g.* pre and post membrane-peeling), as determined by the operating surgeon. Per protocol, the following scans were obtained: 10 mm × 10 mm cubic volume scans (at 0 and 90 degrees), 10 mm × 5 mm volume scans, and 10 mm radial volume scans.

Post-operative follow-up OCT images were obtained using the Cirrus 3D-OCT 1000 (Carl Zeiss Meditec, Dublin, CA, USA) using the macular cube 512 × 128 scan and HD five-line raster (both horizontal and vertical) patterns. Follow-up OCT images were selected at the closest visit to 6-months post-operatively, with a range of 3-12 months.

OCT Image Analysis

Intraoperative OCT image raw data were exported into proprietary OCT analysis software, which was used to obtain quantitative measurements of pre- and post-peel scans. Manual microarchitectural measurements were obtained as previously described¹². Retinal thickness measurements were taken at 1.2 mm nasal, temporal, superior, and inferior to the fovea. The

zones measured were as follows: inner retinal thickness (i.e., nerve fiber layer), middle retinal thickness (ganglion cell layer, inner plexiform layer, outer plexiform layer), and outer retinal thickness (i.e., outer nuclear layer, EZ, RPE). The mean retinal thickness was calculated from these 4 measurements before and after membrane peeling.

Follow-up Cirrus SD-OCT images were visualized using *en face* assessment for analysis of DONFL appearance using the Advanced Visualization feature of the Cirrus software (Figure 1), in a similar manner to the one described by Alkabes et. al.¹⁶ The default settings were changed to select a “Slab” with a thickness of 100 microns¹⁷, with the top of the slab fit to the top of the “ILM” (as determined by the Cirrus software). The resulting *en face* images were then converted to grayscale and de-identified. Two independent raters examined each image and determined whether DONFL appearance was present or absent (Figure 2). Cohen’s kappa coefficient for inter-rater reliability was 0.89. For final analysis, presence or absence of DONFL appearance was determined by rater consensus.

Functional Assessment with MP-1 Microperimetry

Each patient in this sub-analysis was contacted by telephone about follow-up imaging, and 42 patients consented to microperimetry testing. Retinal sensitivity was measured using the Microperimeter-1 (NIDEK, Vigonza, Italy) in both the study and control eye. The MP-1 protocol used a 4-2 threshold strategy with a Goldman III stimulus (200 ms) to test 33 locations in the central 20°, with a white background and a maximal stimulus of 20 dB. Images were analyzed by measuring mean sensitivity of the study and fellow eyes. In addition, each scan was manually reviewed for focal reductions in sensitivity particularly in the area of DONFL.

Statistical Analysis

All statistical analysis was performed using JMP Pro 12.1.0 Software (SAS Institute, Cary, NC, USA). Fisher’s exact test was performed to determine the association between categorical factors (*e.g.*, choice of surgical instrument) and development of DONFL appearance. The two-tailed t-test was used to determine the association between microarchitectural measurements and development of DONFL appearance, as well as to determine the association between DONFL appearance and mean sensitivity on microperimetry analysis. A P value of <0.01 was considered statistically significant for microarchitectural measurements, and a P value of <0.05 was considered statistically significant for all other tests.

Results

Demographics and Clinical Characteristics

Ninety-five eyes from ninety-six patients were included in the study (Table 1). Preoperative diagnosis included epiretinal membrane (ERM) in 54 eyes (57%), macular hole (MH) in 41 eyes (43%).

Perioperative Factor Analysis

The OCT-defined prevalence of DONFL at 6 months was 36% (Table 2). DONFL appearance occurred in 13.0% of eyes with ERM and 65.9% of eyes with MH ($p = 0.003$). In the MH group, forceps-only peeling was performed in 37% (15/41) of cases, compared to 63% (26/41) of cases with combined diamond-dusted membrane scraper and forceps peeling. In the ERM group, forceps-only peeling was performed in 52% (28/54) of cases, and combined peeling was performed in 48% (26/54) of cases. DONFL appearance was identified in 32.6% of eyes with forceps-only peeling and in 38.5% of eyes with combined diamond-dusted membrane scraper and forceps peeling ($p = 0.67$).

Microarchitectural Analysis

The intraoperative percentage change in mean inner retinal (i.e., nerve fiber layer) thickness from pre-peel to post-peel was found to be +10.8% in eyes that developed DONFL appearance at follow-up, and -10.7% in eyes that did not develop DONFL appearance (Table 2). Alterations in middle retinal (i.e., ganglion cell layer, inner plexiform layer, outer plexiform layer), outer retinal (i.e., outer nuclear layer, EZ, RPE), and ellipsoid zone-retinal pigment epithelium thickness were not found to be significantly associated with the development of DONFL appearance.

Functional and Microperimetry Outcome Analysis

Thirty nine eyes (41%) were evaluated using MP-1 microperimetry. Five subjects were excluded from analysis due to other coexisting ocular pathology (e.g. glaucoma). Of the thirty-four remaining eyes, fifteen had ERM as the initial surgical indication, and nineteen had MH as the initial surgical indication. The mean retinal sensitivity of the study eye was 17.7 ± 1.7 dB in eyes with DONFL appearance and 16.7 ± 2.7 dB in eyes that did not develop DONFL appearance ($p=0.22$). In fellow eyes, mean sensitivity was 17.5 ± 2.3 dB in patients whose study eye developed DONFL appearance, and 17.0 ± 1.9 dB in those who did not ($p=0.56$). In eyes with DONFL appearance, there was found to be no difference in mean nasal and temporal sensitivity, with mean sensitivities of 17.7 ± 1.9 dB and 18.0 ± 1.7 dB, respectively. Additionally, there was no significant difference in visual acuity between the two groups. The mean final visual acuity in eyes with DONFL appearance was 20/34 (logMAR: 0.24 ± 0.14) and the mean final visual acuity in eyes without DONFL appearance was 20/33 (logMAR: 0.22 ± 0.25).

Discussion

Since it was first described in 2001 by Tadayoni et.al., many different imaging methods have been used to investigate DONFL appearance, including blue-filter fundus photography, cross-sectional SD-OCT, and *en face* SD-OCT^{8, 10, 16, 18–21}. Most theories for DONFL etiology are related to intraoperative trauma that occurs during surgical manipulation. The visualization of these retinal alterations in the retinal microenvironment have been previously described with intraoperative OCT, but have not been previously assessed for their implications in DONFL development. To our knowledge, this study is the first to use intraoperative OCT to investigate the development of DONFL appearance.

We also found a significant association between increase in intraoperative inner retinal thickness and development of DONFL appearance post-operatively. There are several possible explanations for this. It may represent an acute reaction to direct surgical trauma on the inner retina during membrane peeling. Previous intraoperative OCT studies have identified broad changes likely-related to tractional forces from membrane peeling as well as focal changes due to direct instrument-tissue instrument interaction (e.g., engaging the membrane with forceps).^{12, 14} Given the findings in this study, the retinal alterations appear to be more consistent to broad-based peeling tractional forces rather than direct tissue-instrument interaction. One recent study by Pan et al²² described how intraoperative trauma to the retinal nerve fiber layer led to postoperative central scotoma and reduced visual acuity in several patients who underwent membrane peeling for macular hole. Another possible explanation is that membrane peeling may induce damage to the Müller cell footplates which are attached to the ILM. Swelling of the inner retina one day post-operatively after membrane peeling procedures has been previously described by Clark et al, who named the finding swelling of the arcuate retinal nerve fiber layer (SANFL)²³. Additionally, there have been multiple reports that have demonstrated sub-ILM debris following membrane peeling that may be linked to DONFL development.^{24, 25} The association of debris on the sub-ILM surface following peeling with DONFL is consistent with a trauma-related etiology related to the broad tractional forces of ILM peeling rather than direct instrument-tissue interaction trauma.^{12, 24, 25} Individual tissue characteristics related to ILM adherence may be a key factor in the tractional forces applied during membrane peeling. Our study builds on this prior research, and demonstrates that inner retinal swelling may be appreciated directly post-peel. In addition, our study is the first to report that this inner retinal thickness increase is associated with development of DONFL appearance at 3-12 months follow-up.

One potential concern in this study is that by sampling at different final time points, the OCTs in those eyes that had an endpoint at 3 months may have underestimated DONFL incidence. However, the mean follow-up OCT time was 5.9 months and was not significantly different between ERM and MH groups. Previous studies on DONFL appearance have demonstrated that DONFL appearance develops between 1-3 months, and then stabilizes.^{19,20} In these previous studies DONFL appearance was evaluated at 1, 3, and 12 months, and there were no new cases of DONFL appearance at 12 months that had not already been observed at 3 months. Therefore, it is unlikely that any significant underestimate bias would have occurred in this study.

There was also a strong correlation between surgical indication and development of DONFL appearance, with eyes undergoing internal limiting membrane peeling for MH having the highest prevalence of DONFL appearance at 6-month follow-up. This is consistent with prior reports that describe a strong association between ILM peeling and development of DONFL appearance²⁶. While ILM peeling was performed in all eyes in our study that underwent membrane peeling for MH, ILM peeling was not mandated in eyes with ERM. For ERM cases, ERM peeling was initiated with elevating an edge of ILM in all cases, but not all cases utilized restraining for confirmation of ILM peeling. Intraoperative OCT was utilized to confirm complete ERM removal. It is unclear whether the underlying surgical indication is an independent risk factor, particularly given the high frequency of ILM peeling in the MH group and unknown frequency of ILM peeling in the ERM group. One possibility

is that eyes with MH have different tissue adherence characteristics. The applied trauma during membrane peeling could potentially be different between the two pathologies. Further research is needed to evaluate this question in more detail.

We found that there was no association between choice of surgical instrument (forceps alone or combined DDMS and forceps) for membrane peeling and postoperative development of DONFL appearance. This is consistent with an earlier report by our group, which showed no association between choice of surgical instrument and intraoperative macroarchitectural changes.¹² One previous study by Steel et. al. compared DDMS and forceps for ILM peeling, and reported the DDMS group showed a significant increase in both the prevalence and severity of DONFL appearance.²⁷ These results may differ from ours because in our study, surgeons using the DDMS used it solely for membrane peel initiation, and completed the peel with forceps, while surgeons in the previous study used the DDMS for the entire peel. As Steel hypothesized, the use of the DDMS for the entire peel may influence development of DONFL appearance by either changing the plane of cleavage from the retina or by increasing the pressure applied to the retina throughout the peel; by only examining the DDMS for peel-initiation, these mechanisms were not present in our study.

In terms of retinal sensitivity, this study did not identify a significant association between DONFL appearance and either visual acuity or mean retinal sensitivity as measured by microperimetry. There are several potential explanations for this finding. First, there is no current consensus whether DONFL appearance affects retinal sensitivity. While several studies have described the lack of association between DONFL and mean retinal sensitivity, other studies have reported findings including decreased retinal sensitivity and paracentral scotoma after ILM peeling.^{22, 28} A second possible explanation is that microperimetry alone is not sufficient to fully evaluate retinal sensitivity after membrane peeling. A recent study by Nguyen et al²⁹ evaluated visual function after macular pucker surgery using Freiburg acuity contrast testing, and found that while gross visual acuity was not affected, contrast sensitivity was altered.

There are several limitations to this report that should be acknowledged. First, although the PIONEER study was a prospective study, this is a post-hoc analysis of the PIONEER data. Additionally, the variability in surgical techniques and challenges around identifying the surgeons' definitive approach to ILM peeling during ERM surgery complicates the overall specific impact of ILM peeling in ERM repair. Due to lack of definitive information on ILM peeling during ERM removal, additional analysis of ILM removal in relation to DONFL development is precluded in this dataset. It is not clear whether the underlying diagnosis of MH is a risk factor for DONFL, or if instead the ILM was peeled at a much higher rate in that group, resulting in a significant difference in the development of DONFL. Additionally, ICG was used in all cases. Given the theoretical concerns around potential ICG toxicity, there is some possibility that ICG could have influenced DONFL appearance. Finally, microperimetry testing was all conducted post-operatively; ideally patients in future studies would receive microperimetry testing both pre- and post-operatively.

In conclusion, this study presents unique data on the long-term impact of membrane peeling procedures. In our study, the development of DONFL appearance was associated with

surgical indication (*i.e.* MH), but not associated with choice of surgical instrument (forceps-alone or combined DDMS and forceps). However, it is unclear whether the surgical indication (e.g., MH) or the surgical manipulations performed (e.g., ILM peeling) is the major factor that has an impact on DONFL appearance. Interestingly, an intraoperative increase in inner retinal thickness was also shown to be associated with the development of DONFL appearance, suggesting that intraoperative trauma or traction to the inner retina may be a mechanism leading to development of DONFL appearance. As intraoperative OCT technology advances, there may be a role for intraoperative OCT in the development of minimally traumatic membrane peeling techniques. In addition, more research is needed in evaluating the role of ILM peeling in DONFL development in the context of the underlying surgical indication.

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References

1. Williams GA. Retina. United States: 2006. Macular holes: the latest in current management; S9–12.
2. Kumagai K, et al. Retina. United States: 2004. Vitreous surgery with and without internal limiting membrane peeling for macular hole repair; 721–727.
3. Almony A, et al. Techniques, rationale, and outcomes of internal limiting membrane peeling. Retina. 2012; 32:877–891. [PubMed: 22105502]
4. Pichi F, et al. Early and late inner retinal changes after inner limiting membrane peeling. Int Ophthalmol. 2014; 34:437–446. [PubMed: 23864285]
5. Walia HS, Shah GK, Hariprasad SM. ILM peeling a vital intervention for many vitreoretinal disorders. Ophthalmic Surg Lasers Imaging Retina. 2014; 45:92–96. [PubMed: 24635150]
6. Spiteri Cornish K, et al. Vitrectomy with internal limiting membrane (ILM) peeling versus vitrectomy with no peeling for idiopathic full-thickness macular hole (FTMH). Cochrane Database Syst Rev. 2013; (6):CD009306. [PubMed: 23740611]
7. Spaide RF. Retina. United States: 2012. “Dissociated optic nerve fiber layer appearance” after internal limiting membrane removal is inner retinal dimpling; 1719–1726.
8. Tadayoni R, et al. Dissociated optic nerve fiber layer appearance of the fundus after idiopathic epiretinal membrane removal. Ophthalmology. 2001; 108:2279–2283. [PubMed: 11733271]
9. Tadayoni R, et al. Decreased retinal sensitivity after internal limiting membrane peeling for macular hole surgery. Br J Ophthalmol. 2012; 96:1513–1516. [PubMed: 23077227]
10. Nukada K, et al. Invest Ophthalmol Vis Sci. United States: 2013. Tomographic features of macula after successful macular hole surgery; 2417–2428.
11. Azad S, Takkar B. Invest Ophthalmol Vis Sci. United States: 2016. Comments on Progressive Thinning of Regional Macular Thickness After Epiretinal Membrane Surgery; 1235
12. Ehlers JP, et al. Membrane Peeling-Induced Retinal Alterations on Intraoperative OCT in Vitreomacular Interface Disorders From the PIONEER Study. Invest Ophthalmol Vis Sci. 2015; 56:7324–7330. [PubMed: 26559478]

13. Ehlers JP, Tao YK, Srivastava SK. The value of intraoperative optical coherence tomography imaging in vitreoretinal surgery. *Current opinion in ophthalmology*. 2014; 25:221–227. [PubMed: 24614147]
14. Ehlers JP, et al. The Prospective Intraoperative and Perioperative Ophthalmic Imaging with Optical Coherence Tomography (PIONEER) Study: 2-year results. *American journal of ophthalmology*. 2014; 158:999–1007. [PubMed: 25077834]
15. Ehlers JP, et al. Integration of a spectral domain optical coherence tomography system into a surgical microscope for intraoperative imaging. *Invest Ophthalmol Vis Sci*. 2011; 52:3153–3159. [PubMed: 21282565]
16. Alkabes M, , et al. *Invest Ophthalmol Vis Sci*. United States: 2011. En face optical coherence tomography of inner retinal defects after internal limiting membrane peeling for idiopathic macular hole; 8349–8355.
17. Bendschneider D, et al. Retinal nerve fiber layer thickness in normals measured by spectral domain OCT. *J Glaucoma*. 2010; 19:475–482. [PubMed: 20051888]
18. Mitamura Y, , et al. *American journal of ophthalmology*. United States: 2004. Optical coherence tomographic findings of dissociated optic nerve fiber layer appearance; 1155–1156.
19. Ito Y, , et al. *Ophthalmology*. United States: 2005. Dissociated optic nerve fiber layer appearance after internal limiting membrane peeling for idiopathic macular holes; 1415–1420.
20. Kishimoto H, et al. Retinal surface imaging provided by Cirrus high-definition optical coherence tomography prominently visualizes a dissociated optic nerve fiber layer appearance after macular hole surgery. *Int Ophthalmol*. 2011; 31:385–392. [PubMed: 22057824]
21. Kusuha S, , et al. *Ophthalmologica*. Switzerland: 2014 S. Karger AG, Basel; 2014. Evaluating dissociated optic nerve fiber layer appearance using en face layer imaging produced by optical coherence tomography; 170–178.
22. Pan BX, , et al. *Invest Ophthalmol Vis Sci*. United States: 2014 The Association for Research in Vision and Ophthalmology, Inc.; 2014. Inner retinal optic neuropathy: vitreomacular surgery-associated disruption of the inner retina; 6756–6764.
23. Clark A, et al. Swelling of the arcuate nerve fiber layer after internal limiting membrane peeling. *Retina*. 2012; 32:1608–1613. [PubMed: 22495325]
24. Kenawy N, et al. Does the presence of an epiretinal membrane alter the cleavage plane during internal limiting membrane peeling? *Ophthalmology*. 2010; 117:320–323 e321. [PubMed: 20006906]
25. Steel DH, et al. The relationship between a dissociated optic nerve fibre layer appearance after macular hole surgery and Muller cell debris on peeled internal limiting membrane. *Acta Ophthalmol*. 2017; 95:153–157. [PubMed: 27572851]
26. Mitamura Y, Ohtsuka K. *Ophthalmology*. United States: 2005. Relationship of dissociated optic nerve fiber layer appearance to internal limiting membrane peeling; 1766–1770.
27. Steel DH, et al. ILM peeling technique influences the degree of a dissociated optic nerve fibre layer appearance after macular hole surgery. *Graefes Arch Clin Exp Ophthalmol*. 2015; 253:691–698. [PubMed: 25028313]
28. Tognetto D, et al. Macular edema and visual loss after macular pucker surgery with ICG-assisted internal limiting membrane peeling. *Eur J Ophthalmol*. 2005; 15:289–291. [PubMed: 15812777]
29. Nguyen JH, , et al. *Ophthalmology*. United States: 2016 American Academy of Ophthalmology Published by Elsevier Inc; 2016. Quantifying Visual Dysfunction and the Response to Surgery in Macular Pucker; 1500–1510.

Summary statement

This study uses intraoperative OCT images to investigate the relationship between intraoperative membrane dynamics and postoperative development of DONFL appearance. DONFL appearance was correlated with acute post-peel increase in inner retinal thickness and MH repair, and there was no correlation between choice of surgical technique and development of DONFL appearance.

Figure 1.

Generation of *en face* intraoperative SD-OCT image using Cirrus Advanced Visualization Software. (A) Final *en face* image overlaid on fundus photograph. (B) and (C) A “Slab” of 100 micron thickness is fit to the “ILM” layer as recognized by the Cirrus software. (D) The resulting grayscale *en face* SD-OCT. This example shows clear DONFL appearance.

Figure 2.
En face SD-OCT analysis. (A) DONFL present and (B) DONFL absent.

Table 1

Clinical and demographic data of patients undergoing membrane peeling procedures in the PIONEER study.

Gender	
Male	41 (43%)
Female	54 (57%)
Age (median)	67 (Range: 33-86)
Mean Preoperative Visual Acuity	20/88 (Range: 20/25-20/2000)
Lens status	
Phakic	71 (75%)
Pseudophakic	24 (25%)
Preoperative Diagnosis	
Epiretinal Membrane	54 (57%)
Macular Hole	41 (43%)

Table 2

Perioperative factor analysis of patients with and without development of DONFL appearance.

	DONFL Appearance	No DONFL Appearance	P-value
Preoperative Diagnosis			
Macular Hole (%)	65.9	34.1	p <0.001
Epiretinal Membrane (%)	13.0	87.0	
Membrane peeling technique			
Forceps-only technique	32.6	67.4	p = 0.67
DDMS/Forceps combined technique	38.5	61.5	
Inner Retinal Thickness (% change pre- to post-peel)	10.8	-10.7	p = 0.003