

# Peripapillary Retinal and Choroidal Perfusion in Nonarteritic Ischemic Optic Neuropathy Using Optical Coherence Tomography Angiography

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## ABSTRACT

**Significance:** Nonarteritic ischemic optic neuropathy (NAION) has been linked with vascular insufficiency, although the pathophysiology remains elusive. Optical coherence tomography angiography (OCTA) is a promising technology that noninvasively evaluates optic disc perfusion and that may help to characterize peripapillary vascular changes in NAION.

**Purpose:** This study aimed to evaluate peripapillary vascularity in NAION eyes and to compare it with fellow unaffected eyes and healthy control eyes using OCTA.

**Methods:** In this cross-sectional study, OCTA of the optic nerve head was obtained in 10 nonacute unilateral NAION and 12 healthy age-matched controls using ZEISS Angioplex. Quantitative analysis of peripapillary retinal and choroidal vascularity of NAION eyes was done using the instrument's inbuilt algorithm and ImageJ software and compared with fellow and control eyes.

**Results:** Mean total peripapillary superficial retinal vessel and perfusion density as calculated by the instrument was significantly reduced in NAION eyes compared with fellow eyes ( $13.93 \pm 4.27$  mm/0.36  $\pm$  0.07 for NAION eyes

17.7± 1.26 mm/0.43 ± 0.08 for fellow eyes; P = .01/P = .05). Using the ImageJ software technique, the mean superficial retinal perfusion was found to be significantly reduced in NAION eyes (0.17 ± 0.07) compared with fellow eyes (0.25 ± 0.06; P < .01) and control eyes (0.25 ± 0.04; P < .01). At the level of choriocapillaris, it was not significantly affected in NAION eyes (0.37 ± 0.13) versus fellow (0.34 ± 0.14; P = .1) and control eyes (0.31 ± 0.34; P = .83). Analysis with the two techniques yielded differing results: the ImageJ analysis technique found a 32% reduction in superficial retinal perfusion in NAION eyes, whereas the instrument's inbuilt algorithm found a 16% reduction compared with fellow and control eyes (P ≤.01).

**Conclusions:** Peripapillary vascularity can be estimated both at the retinal and choroidal levels using ImageJ software to analyze OCTA images. Retinal peripapillary vascularity is compromised in NAION eyes, but vascularity is not significantly affected at the choroidal level.

# Vortex Vein Anastomosis at the Watershed in Pachychoroid Spectrum Diseases

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## ABSTRACT

### **Purpose:**

To evaluate the vascular changes in vortex veins at the posterior pole in pachychoroid spectrum diseases, including central serous chorioretinopathy (CSC), pachychoroid neovascularopathy without polypoidal lesions (PNV), and pachychoroid neovascularopathy with polypoidal lesions (polypoidal choroidal vasculopathy [PCV]).

**Design:** Retrospective case-control study.

**Participants:** Ninety-two eyes of 89 patients with CSC, 61 eyes of 59 patients with PNV, 63 eyes of 61 patients with PCV, and 25 healthy control eyes of 25 age- and gender-matched participants for each pachychoroid spectrum disease.

**Methods:** Clinical records of patients with pachychoroid spectrum diseases and healthy controls were reviewed. Multimodal images of each group were analyzed. Swept-source OCT was performed to obtain B-mode and en face images in patients with pachychoroid spectrum diseases and healthy controls. All patients underwent fluorescein angiography, indocyanine green angiography, and OCT.

**Main outcome measures:** Vortex vein anastomosis at the watershed, determined using en face OCT, and central choroidal thickness (CCT), measured using B-mode OCT, were examined in patients and healthy controls. Patient ages also were taken into consideration.

**Results:** Patients with CSC were the youngest, followed by patients with PNV, and then those with PCV ( $P < 0.01$ , CSC vs. PNV and PNV vs. PCV), whereas CSC eyes showed the highest CCT values, followed by the PNV and then the PCV eyes ( $P < 0.01$ , CSC vs. PNV;  $P < 0.05$ , PNV vs. PCV). Central choroidal thickness was significantly greater in pachychoroid spectrum diseases than in healthy controls. No significant CCT differences were found among healthy controls. Anastomosis between superior and inferior vortex veins was observed in more than 90% of eyes with pachychoroid spectrum diseases, making this finding significantly more frequent than in healthy controls ( $P < 0.01$ , each pachychoroid spectrum disease vs. control). Polypoidal choroidal vasculopathy showed a significantly higher rate of anastomosis than CSC ( $P < 0.05$ ).

**Conclusions:** Anastomosis between superior and inferior vortex veins was found to be a common feature in pachychoroid spectrum diseases. Longstanding vortex vein congestion may lead to the development of pachychoroid spectrum diseases. Choroidal congestion may be compensated for by new drainage routes formed via vortex vein anastomosis.

# Inverted Internal Limiting Membrane Flap versus Internal Limiting Membrane Peeling for Macular Hole Retinal Detachment in High Myopia

Matsumae H, Morizane Y, Yamane S, Yanagisawa S, Sakurai T, Kobori A et al.

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## ABSTRACT

**Purpose:** To compare surgical outcomes between the inverted internal limiting membrane (ILM) flap technique and ILM peeling for macular hole retinal detachment (MHRD) in eyes with high myopia.

**Design:** Multicenter cohort study.

**Participants:** We retrospectively reviewed medical records of consecutive patients treated between June 2008 and September 2018 at 7 hospitals and included 100 eyes with MHRD associated with high myopia in our study. All eyes underwent vitrectomy with the inverted ILM flap technique (57 eyes) or ILM peeling (43 eyes) and were followed up for more than 6 months.

**Methods:** We estimated odds ratios and their 95% confidence intervals (CIs) for macular hole (MH) closure using multivariate logistic regression analysis. We also examined factors associated with the postoperative best-corrected visual acuity (BCVA) at the final visit using multiple linear regression analysis.

**Main outcome measures:** Macular hole closure and postoperative BCVA at the final visit.

**Results:** The MH closure rate was significantly higher in the inverted ILM flap group (80.7%) than in the ILM peeling group (37.2%;  $P < 0.001$ ). Moreover, postoperative BCVA at the final visit was significantly better in the former group ( $0.88 \pm 0.48$  vs.  $0.99 \pm 0.48$ ;  $P = 0.03$ ). The retinal attachment rate (ILM flap, 91.2%; ILM peeling, 79.5%;  $P = 0.229$ ) and recovery rates for the external

limiting membrane and ellipsoid zone line (ILM flap, 10.9%; ILM peeling, 0%;  $P = 0.12$ ) showed no significant intergroup differences. After adjustment for age, axis, tamponade substance, and dye for ILM staining, the inverted ILM flap technique was associated strongly and positively with MH closure (odds ratio, 7.14; 95% CI, 2.72-18.7;  $P = 0.001$ ). Moreover, the inverted ILM flap technique and preoperative BCVA were associated significantly and positively with the postoperative BCVA at the final visit.

**Conclusions:** Our findings suggest that the MH closure rate and postoperative visual outcome for eyes with high myopia-associated MHRD are better with the inverted ILM flap technique than with ILM peeling. Thus, vitrectomy with the inverted ILM flap technique should be considered as the initial surgery for MHRD associated with high myopia.

# Orbital Magnetic Resonance Imaging Demonstrates Better Contact between the Gas and Anterior Inferior Retina in Side versus Face-Down Position

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## ABSTRACT

**Purpose:** To demonstrate the relationship between an intraocular gas bubble, the retina, and the residual intraocular fluid in different head positions using orbital magnetic resonance imaging (MRI) in 3 patients who underwent pars plana vitrectomy (PPV) with gas tamponade.

**Design:** Novel study.

**Participants:** Patients undergoing PPV with gas-fluid exchange (sulfurhexafluoride [SF<sub>6</sub>] or perfluoropropane [C<sub>3</sub>F<sub>8</sub>]).

**Methods:** Magnetic resonance imaging scans were obtained in 3 patients undergoing PPV with gas-fluid exchange (SF<sub>6</sub> or C<sub>3</sub>F<sub>8</sub>). All surgeries were performed by a single surgeon (E.D.M.). On the first postoperative day, the volume of intraocular gas fill was estimated separately by 2 surgeons (A.H. and E.D.M.). Four orbital MRI scans were obtained from different head positions, including face up (supine), face down (prone on a massage pillow), flat on the right side, and flat on the left side.

**Main outcome measure:** Relationship between the gas bubble and residual vitreous fluid.

**Results:** The MRI images demonstrated, with excellent contrast, the gas and fluid locations in the vitreous cavity in all scans. The relationship between the gas bubble and residual vitreous fluid showed a rapid shift when the patient's head position changed. The MRI images demonstrated that with both 70% gas

fill and 95% gas fill, lying on the side can give better support to the inferior retina than face-down positioning. The images demonstrated the importance of accurate head positioning, because a slight change in head position resulted in inadequate contact between the anterior inferior retina and the gas bubble.

**Conclusions:** To our knowledge, this is the first time that the relationship between an intraocular gas bubble and contact with the retina has been evaluated in different head positions in vivo using MRI imaging. The MRI images demonstrated that side positioning gives better contact between the gas bubble and the inferior and anterior retina than prone positioning even when the gas fill is only 70% of the vitreous cavity.



# **Detrimental Effect of Delayed Re-treatment of Active Disease on Outcomes in Neovascular Age-Related Macular Degeneration: The RAMPS Study**

Chong Teo KY, Saxena N, Gan A, Wong TY, Gillies MC, Chakravarthy U et al.

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## **ABSTRACT**

**Purpose:** To assess the impact of delaying anti-vascular endothelial growth factor (VEGF) treatment of active disease at any point during a patient's treatment journey on clinical outcomes in a real-world cohort of patients with neovascular age-related macular degeneration (nAMD).

**Design:** Longitudinal cohort study.

**Participants:** Consecutive treatment-naive nAMD eyes commencing anti-VEGF monotherapy (bevacizumab, ranibizumab, or aflibercept) from January 2014 from a tertiary eye center in Singapore.

**Methods:** We conducted a real-world study using registry data comparing delayed re-treatment (defined as not receiving treatment at 2 or more monitoring visits when disease was graded as active) versus timely re-treatment (defined as receiving treatment when disease was active).

**Main outcome measures:** The primary outcome was the change in visual acuity (VA) in the timely and delayed re-treatment groups at 12 months.

**Results:** Data from 286 eyes were included and categorized into the timely (188 [66%]) or the delayed (98 ([34%]) group. The mean numbers of anti-VEGF injections over 12 months were similar: 5.6 (standard deviation [SD], 2.9) versus 4.9 (SD, 3.2;  $P = 0.11$ ) for the timely and delayed groups, respectively. Timely treated patients showed larger gains in VA (6.4 letters [SD, 8.1 letters] vs. 1.2 letters [SD, 5.3 letters;  $P = 0.04$ ), a higher proportion with VA of 6/12 or

better (30% vs. 8%;  $P = 0.01$ ), and greater reduction in OCT-measured central subfield thickness ( $135 \mu\text{m}$  [SD,  $154 \mu\text{m}$ ] vs.  $87.8 \mu\text{m}$  [SD,  $129 \mu\text{m}$ ];  $P = 0.04$ ) at 12 months. A longer delay between detection of active disease and re-treatment was associated with poorer vision outcomes (0.02-letter decrease/day;  $P = 0.03$ ;  $R^2 = 0.29$ ).

**Conclusions:** Although it has been established that adequate numbers of injections are required for favorable outcomes, timely re-treatment of active disease also is important. This should be emphasized to patients to ensure optimal outcomes in real-world clinical settings.

# RATES AND RISK FACTORS FOR RECURRENCE OF RETINOPATHY OF PREMATUREITY AFTER LASER OR INTRAVITREAL ANTI-VASCULAR ENDOTHELIAL GROWTH FACTOR MONOTHERAPY

Ling KP, Liao PJ, Wang NK, Chao AN, Chen KJ, Chen TL et al.

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## ABSTRACT

**Purpose:** To determine the rates and risk factors of recurrent retinopathy of prematurity (ROP) treated by laser photocoagulation, intravitreal bevacizumab (IVB) monotherapy, or intravitreal ranibizumab (IVR) monotherapy.

**Methods:** In this retrospective cohort study, consecutive infants with Type 1 ROP who received laser, IVB, or IVR treatments were followed for at least 75 weeks of postmenstrual age. Data analysis was performed between March 2010 and February 2017 in Chang Gung Memorial Hospital, Linkou, Taiwan.

**Results:** A total of 176 infants (340 eyes) were included in this study. The mean follow-up was  $197.3 \pm 110$  weeks. All of the baseline demographic and ROP characteristics among the laser, IVB, and IVR groups were similar. The overall recurrence rate after treatment was 44 of 340 eyes (12.9%). The IVB group had a recurrence rate of 10.0%, followed by the laser group (18.0%) and the IVR group (20.8%); however, these rates were not significantly different ( $P = 0.0528$ ). Compared with the laser group, the IVB and IVR groups exhibited recurrence at later ages ( $43.4 \pm 3.5$  weeks for the IVB group,  $42.3 \pm 2.0$  weeks for the IVR group, and  $39.5 \pm 2.8$  weeks for the laser group;  $P = 0.0058$ ). The mean interval of recurrence from initial treatment in the laser group was  $3.6 \pm 1.4$  weeks compared with  $8.8 \pm 3.9$  weeks and  $8.3 \pm 1.6$  weeks in the IVB and IVR groups, respectively ( $P = 0.0001$ ). Overall, the independent risk factors of recurrence included an early postmenstrual age at initial treatment ( $P = 0.0160$ ), Zone I ( $P = 0.0007$ ), low Apgar score ( $P = 0.0297$ ), and multiple births

( $P = 0.0285$ ). There was no significant difference in progression to retinal detachment among the three groups (laser: 3/61, 4.9%; IVB: 2/231, 0.9%; and IVR: 1/48, 2.1%;  $P = 0.2701$ ).

**Conclusion:** Laser, IVR, and IVB are effective for Type 1 ROP. Retinopathy of prematurity recurrence requiring re-treatment was encountered as late as 50 weeks of postmenstrual age after IVB or IVR but earlier after laser. Longer follow-up for infants treated with anti-vascular endothelial growth factor is needed, especially in patients with significant risk factors such as an early postmenstrual age at initial treatment, Zone I ROP, low Apgar score, and multiple births.

# Longitudinal Panretinal Leakage and Ischemic Indices in Retinal Vascular Disease after Aflibercept Therapy: The PERMEATE Study

Figueiredo N, Srivastava SK, Singh RP, Babiuch A, Sharma S, Rachitskaya A et al

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## ABSTRACT

**Purpose:** To characterize the longitudinal panretinal retinal vascular dynamics in diabetic macular edema (DME) and retinal vein occlusion (RVO) over a 12-month period while being treated with intravitreal aflibercept injections (IAIs).

**Design:** Prospective open-label study (clinicaltrials.gov identifier, NCT02503540).

**Participants:** Thirty-one treatment-naive eyes with foveal-involving retinal edema secondary to DME and RVO.

**Methods:** Participants received 2 mg IAI every 4 weeks for the first 6 months, followed by 2 mg every 8 weeks. Ultra-widefield fluorescein angiography (UWFA; California Optos [Optos, Dunfermline, United Kingdom]) and spectral-domain OCT (Cirrus; Zeiss, Oberkochen, Germany) scans were obtained and analyzed using a novel quantitative assessment platform. Visual acuity, central subfield thickness, and adverse events also were collected.

**Main outcome measures:** The primary end point was the mean change in panretinal leakage index at month 12 from baseline as measured by UWFA.

**Results:** Mean age was 67.1 years. At month 12, visual acuity significantly improved by a mean of  $18.4 \pm 21.4$  letters ( $P < 0.0001$ ), and central subfield thickness also improved significantly, with a mean reduction of  $301.3 \pm 250.3$   $\mu\text{m}$  ( $P < 0.0001$ ). Mean panretinal leakage index improved significantly, decreasing from 3.4% at baseline to 0.5% at month 6 ( $P < 0.0001$ ) and 0.4% at

month 12 ( $P < 0.0001$ ). Panretinal ischemic index did not demonstrate any significant change but showed a nonsignificant increase from 5.5% at baseline to 6.1% at month 6 ( $P = 0.315$ ) and 8.7% at month 12 ( $P = 0.193$ ). Eyes with DME showed a decrease in leakage index from  $3.5 \pm 2.7\%$  at baseline to  $1.6 \pm 0.8\%$  at month 12 ( $P = 0.018$ ) and overall stability in ischemic index from  $5.0 \pm 4.1\%$  at baseline to  $4.7 \pm 3.5\%$  at month 12 ( $P = 0.689$ ). Participants with RVO showed a decrease in leakage index from  $3.3 \pm 1.1\%$  at baseline to  $0.02 \pm 0.03\%$  at 12 months ( $P < 0.0001$ ) and a nonsignificant increase in ischemic index from  $5.9 \pm 4.5\%$  at baseline to  $12.6 \pm 9.8\%$  at month 12 ( $P = 0.172$ ).

**Conclusions:** Intravitreal aflibercept injections resulted in a dramatic reduction in panretinal leakage index. Panretinal ischemic index did not improve and trended toward worsening.

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