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Postoperative Photoreceptor Integrity Following Pneumatic Retinopexy vs Pars Plana Vitrectomy for Retinal Detachment Repair

A Post Hoc Optical Coherence Tomography Analysis From the Pneumatic Retinopexy Versus Vitrectomy for the Management of Primary Rhegmatogenous Retinal Detachment Outcomes Randomized Trial

Rajeev H. Muni, MD; Tina Felfeli, MD; Srinivas R. Sadda, MD; Verena R. Juncal, MD; Carolina L. M. Francisconi, MD; Muneeswar Gupta Nittala, OD, PhM; Sophiana Lindenberg, BS; Frederic Gunnemann, MD; Alan R. Berger, MD; David T. Wong, MD; Filiberto Altomare, MD; Louis R. Giavedoni, MD; Radha P. Kohly, PhD; Peter J. Kertes, MD; David Sarraf, MD; Roxane J. Hillier, MBChB

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IMPORTANCE Pneumatic retinopexy (PnR) is associated with superior visual acuity and reduced vertical metamorphopsia compared with pars plana vitrectomy (PPV) for primary rhegmatogenous retinal detachment (RRD). It is important to determine postoperative photoreceptor integrity with both surgical techniques.

OBJECTIVE To compare photoreceptor integrity on spectral domain-optical coherence tomography (SD-OCT) between PnR and PPV at 12 months postoperatively.

DESIGN, SETTING, AND PARTICIPANTS Post hoc analysis of the Pneumatic Retinopexy Versus Vitrectomy for the Management of Primary Rhegmatogenous Retinal Detachment Outcomes Randomized Trial (PIVOT) conducted between August 2012 and May 2017 at St Michael's Hospital, Toronto, Ontario, Canada. Primary RRDs with specific criteria were included. Data were analyzed between April and August 2020.

INTERVENTION Randomization to PnR vs PPV stratified by macular status.

MAIN OUTCOMES AND MEASURES Difference in proportion of patients with discontinuity of the ellipsoid zone (EZ) and external limiting membrane (ELM) between groups assessed independently by 2 masked graders at an external masked image reading center.

RESULTS A total of 150 participants completed the 12-month follow-up visit. A total of 145 patients (72 PPV and 73 PnR) had gradable spectral-domain optical coherence tomography at 12 months. Analysis of the central 3-mm (foveal) scans found that 24% (n = 17 of 72) vs 7% (n = 5 of 73) displayed EZ discontinuity (difference, 17%; odds ratio [OR], 4.204; 95% CI, 1.458-12.116; *P* = .005) and 20% (n = 14 of 71) vs 6% (n = 4 of 73) displayed ELM discontinuity (difference, 14%; OR, 4.237; 95% CI, 1.321-13.587; *P* = .01) in the PPV and PnR groups, respectively. Analysis of the 6-mm (foveal and nonfoveal) scans revealed that EZ and ELM discontinuity was greater in the PPV vs PnR groups (EZ, 32% [n = 23 of 72] vs 11% [n = 8 of 73]; difference, 21%; OR, 3.814; 95% CI, 1.573-9.249; *P* = .002; ELM, 32% [n = 23 of 71] vs 18% [n = 13 of 73]; difference, 14%; OR, 2.211; 95% CI, 1.015-4.819; *P* = .04).

CONCLUSIONS AND RELEVANCE Discontinuity of the EZ and ELM was more common at 12 months postoperatively following PPV vs PnR for RRD repair. The findings of this post hoc analysis suggest that less discontinuity of the EZ and ELM may provide an anatomic basis for the previously reported superior functional outcomes with PnR, although the analysis does not prove a cause-and-effect relationship.

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Author Affiliations: Author affiliations are listed at the end of this article.

Corresponding Authors: Rajeev H. Muni, MD, Department of Ophthalmology, St Michael's Hospital, Unity Health Toronto, 30 Bond St, 8th Floor, Donnelly Wing, Toronto, ON M5B 1W8, Canada (rajeev.muni@gmail.com); Roxane J. Hillier, MBChB, Newcastle Eye Centre, Royal Victoria Infirmary, Queen Victoria Road, Newcastle upon Tyne NE1 4LP, England (roxanehillier@gmail.com).

Rhegmatogenous retinal detachment (RRD) repair has been central to vitreoretinal surgical practice since the early 1900s, when Ohm injected air into the vitreous cavity.[1] The first randomized trial to compare surgical interventions for RRD was carried out by Tornambe et al in 1989.[2,3] The Pneumatic Retinopexy Trial demonstrated superior visual acuity (VA) with pneumatic retinopexy (PnR) compared with scleral buckle for patients meeting trial criteria.

The Pneumatic Retinopexy Versus Vitrectomy for the Management of Primary Rhegmatogenous Retinal Detachment Outcomes Randomized Trial (PIVOT) was a randomized clinical trial that compared PnR with PPV for primary RRD.[4] The primary outcome was Early Treatment Diabetic Retinopathy Study (ETDRS) VA at 1 year. The ETDRS letter score was superior in PnR vs PPV at every point including the 1-year end point. Of note, long-acting gas tamponade (perfluoropropane) was used in a proportion of patients (38%) in the PPV arm only. This difference could have influenced the anatomic success in favor of the PPV group with enhanced cataract formation in the PPV arm, which in turn could have influenced the VA outcomes favoring the PnR group. Most patients with phakic lenses who underwent PPV developed a cataract judged clinically relevant; these patients underwent phacoemulsification and intraocular lens implantation before the 1-year end point. However, the effect of these changes and interventions could have introduced bias to one of the groups. Nevertheless, PIVOT demonstrated that vertical metamorphopsia was significantly more prevalent and severe following PPV vs PnR. Unlike VA, objectively measured metamorphopsia is unlikely to be affected by refraction or lens opacity and is largely dependent on the integrity of the retina after reattachment.

The PIVOT trial also investigated additional functional outcomes beyond VA. Subjective visual function among unmasked participants was assessed using the 25-Item National Eye Institute Visual Function Questionnaire and demonstrated that patients undergoing PnR reported superior vision-related function during the first 6 months postoperatively compared with PPV.[5]

The pathophysiology of reduced VA and metamorphopsia after RRD repair is likely multifactorial and associated with abnormal physiology and/or structure of the photoreceptors. Hypoxic and structural injury owing to loss of contact between the neurosensory retina and the RPE may result in long-term compromise of retinal physiology. Structural abnormalities may include misalignment or poor orientation of the photoreceptors with the RPE.[6] The retinal tissue undergoes stress during (1) the process of detachment, (2) the period of detachment, and (3) the process of reattachment. Because the duration of macular detachment was similar between both surgical groups in PIVOT, the data are well positioned to establish which of these 2 different methods of achieving retinal reattachment are associated with better postoperative photoreceptor recovery. The purpose of this study was to compare the microstructural integrity of the outer retina using spectral-domain optical coherence tomography (SD-OCT) following PPV vs PnR for RRD.

Key Points

Question Does postoperative photoreceptor integrity vary with surgical technique used to repair primary rhegmatogenous retinal detachment?

Findings In this post hoc analysis of a randomized clinical trial, patients undergoing pneumatic retinopexy had less discontinuity of the ellipsoid zone and external limiting membrane on optical coherence tomography compared to pars plana vitrectomy at 12 months postoperatively. Ellipsoid zone and external limiting membrane discontinuity were associated with worse Early Treatment Diabetic Retinopathy Study visual acuity at 12 months postoperatively.

Meaning Postoperative photoreceptor integrity can vary with surgical technique, and pneumatic retinopexy is associated with superior photoreceptor integrity at 12 months postoperatively compared with pars plana vitrectomy.

Methods

Detailed PIVOT methods were published previously.[4] This randomized clinical trial of patients with primary RRD included eyes with a single retinal break or group of breaks within 1 clock hour in detached retina, above the 8-o'clock and 4-o'clock meridians, and associated with any number, location, and size of breaks or lattice degeneration in the attached retina. Stratified randomization by macular status was performed. A detailed description of the PPV and PnR techniques has been previously published.[4] The primary outcome was VA (ETDRS letter score) at 12 months following intervention. Standardized ETDRS testing was performed at 4 m and if less than 20 letters were read, then testing at 1 m was performed. The trial was approved by the research ethics board at St. Michael's Hospital, Toronto, Ontario, Canada, and patients were recruited from August 2012 to May 2016, with 1-year follow-up of the last patient completed in May 2017. Written consent was obtained from all patients who were enrolled in the study, and patients did not receive a stipend for their participation. The OCT image analysis at the Doheny Image Reading Center (DIRC) was initiated in April 2020 and completed in July 2020, with statistical analyses completed in August 2020. The described research adhered to the tenets of the Declaration of Helsinki and was registered at ClinicalTrials.gov.

Image Analysis

Retinal images were obtained with SD-OCT (Cirrus high-definition OCT; Carl Zeiss). Horizontal 5-line raster scans were performed for each eye using Cirrus HD-OCT analysis software, version 11.5.1.47041 (2019). Images were graded for quality and signal strength and rated on a scale of 1 to 10. Images with signal strength less than 5 were excluded from analysis.

In this post hoc analysis of PIVOT, microstructural changes of the outer retina were assessed by 2 masked graders at the DIRC, with any disagreements adjudicated by a third senior masked grader at DIRC. No individual at DIRC was aware of treatment assignment. Spectral-domain OCT images at the 12-month end point were assessed for continuity vs discontinuity of the outer retinal layers, specifically the external limiting membrane (ELM) and the ellipsoid zone (EZ). The interdigitation zone (IZ) was also assessed, despite concerns regarding the ability to consistently identify and assess this layer relating to potential artifactitious alterations in reflectivity attributable to the directionality or tilt of the OCT B-scan. Macrostructural changes that could potentially influence functional outcomes and indirectly affect the continuity of the outer retinal layers were also assessed. Images were graded using the central 3 mm of the foveal B-scan of the 5-line raster scans as well as an additional analysis of all scans (foveal and nonfoveal) over the entire 6 mm.

Statistical Analysis

Tests of association were performed using the χ^2 test and *t* tests for categorical and continuous data, respectively, when the data were normally distributed. The Mann-Whitney *U* test was used for continuous data that was not normally distributed. For categorical analyses, the Fisher exact test was used in place of the χ^2 test when cell counts were less than 5. In this image investigation, the primary outcome measure was the difference in proportion of patients with discontinuity of the EZ and ELM between the PPV and PnR groups for the central 3-mm foveal B-scan of the 5-line raster scan. An additional post hoc analysis specified in section 2.6 of the PIVOT Final Statistical Analysis Plan that included the entire 6-mm 5-line raster scan (foveal and nonfoveal B-scans) was also carried out. All inferential statistical analyses were conducted using 2-sided *P* values. *P* values were not adjusted for multiple analyses. Interobserver agreement was assessed using Cohen κ. All analysis was performed using IBM SPSS, version 26 (IBM Corp).

Results

A total of 176 patients were randomized to PPV vs PnR. A total of 150 participants completed the 12-month follow-up visit (**Figure 1**). A detailed description of participants who did not attend the 12-month visit was previously published.[4] Most of these participants did not follow up because of travel distance and were reached by telephone to confirm that they did not have any additional complications or re-detachments. A total of 96.6% of patients (n = 145 of 150; 72 PPV and 73 PnR) had gradable SD-OCT at 12 months. Baseline characteristics were similar between groups (**Table 1**).

Participants with poor-quality scans (signal strength <5) were not assessed at baseline by the masked graders. There were no differences identified in the mean (SD) SD-OCT quality (signal strength) between the PPV (7.44 [1.58]) and PnR (7.81 [1.51]) groups for the entire 6-mm 5-line raster (mean difference, −0.47; 95% CI, −0.01 to 0.94; *P* = .15). Interobserver agreement (κ) for the central 3-mm foveal scan ELM discontinuity was 0.91 (95% CI, 0.79-0.98), with 1.2% disagreement and for EZ discontinuity was 0.81 (95% CI, 0.62-0.99), with 4.9% disagreement.

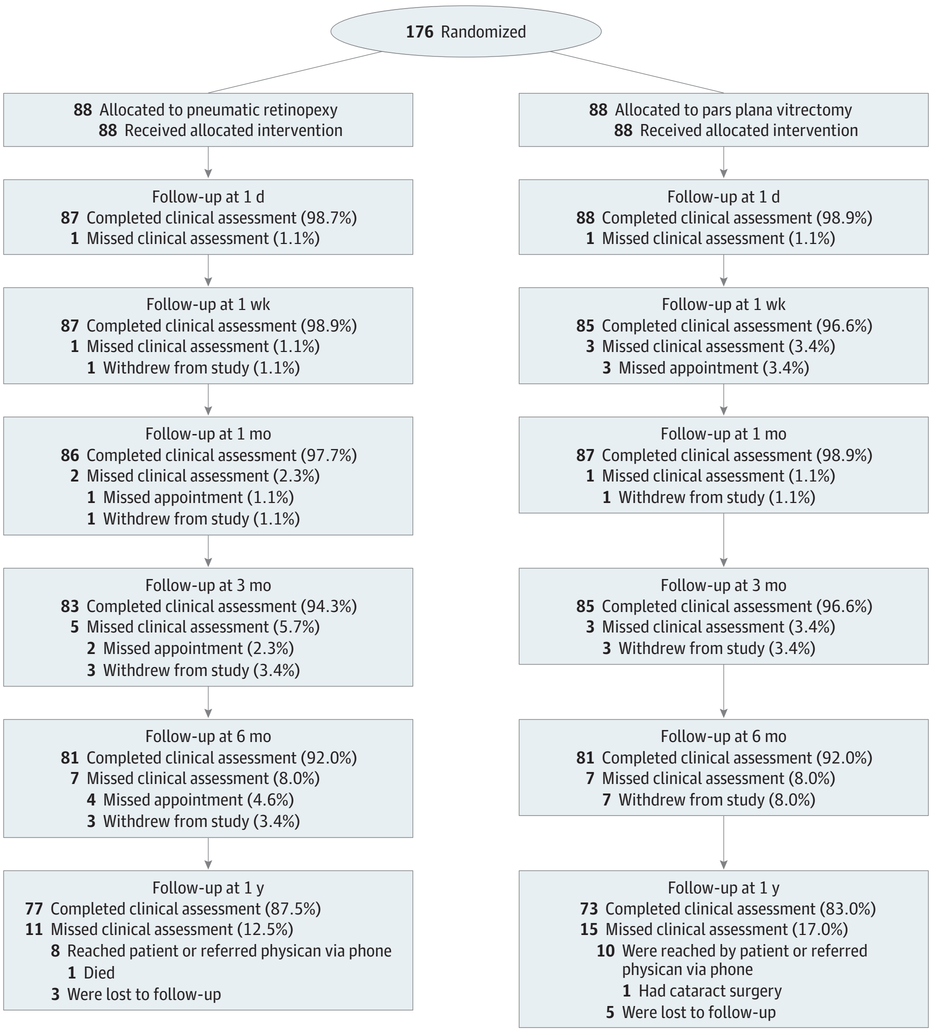
Spectral-domain OCT analysis of the central 3-mm (foveal) scans showed that 24% of patients (n = 17 of 72) in the PPV group vs 7% (n = 5 of 73) in the PnR group displayed EZ discontinuity (OR, 4.204; 95% CI, 1.458-12.116; *P* = .005), and 20% of patients (n = 14 of 71) in the PPV group vs 6% (n = 4 of 73) in the PnR group demonstrated ELM discontinuity (OR, 4.237; 95% CI, 1.321-13.587; *P* = .01) at 12 months (**Table 2**). Among patients in the PnR group with EZ and ELM discontinuity, 3 of 5 and 2 of 4 cases, respectively, had undergone PPV after failed PnR. Analysis of all the foveal and nonfoveal 6-mm scans showed that the proportion of patients with EZ and ELM discontinuity was greater for PPV vs PnR (EZ, 32% [n = 23 of 72] vs 11% [n = 8 of 73]; OR, 3.814; 95% CI, 1.573-9.249; *P* = .002 and ELM, 32% [n = 23 of 71] vs 18% [n = 13 of 73]; OR, 2.211;95% CI, 1.015-4.819; *P* = .04) respectively. **Figure 2** and **Figure 3** demonstrate typical discontinuity of the ELM and EZ that were seen more often following PPV vs PnR. There was no difference in the proportion of patients with epiretinal membrane, cystoid macular edema or residual subretinal fluid (SRF) in either the 3-mm or 6-mm scans between PPV and PnR (eTable in the Supplement).

Additional exploratory analysis was performed to determine the association of ETDRS letter score with continuous vs discontinuous EZ and ELM at 12 months. Mean ETDRS letter score was 79.5 (approximate Snellen equivalent 20/25; SD, 11) for patients with continuous ELM vs 69 (20/40; SD, 11.7) for patients with discontinuous ELM (difference, 9.3; 95% CI, 3.06-15.612; *P* = .004). Mean ETDRS letter score was 79.1 (20/25; SD, 11.2) for patients with continuous EZ vs 69.7 (20/40; SD, 19.8) for patients with discontinuous EZ (difference, 10.8; 95% CI, 5.1-16.4; *P* < .001).

Discussion

This study showed a difference in the proportion of patients with discontinuity of the EZ and ELM in study participants undergoing PPV vs PnR in the context of a randomized clinical trial. While these findings are post hoc in nature and should be used for hypothesis building rather than presumed to represent cause and effect, these findings suggest that patients undergoing PPV may be more likely to have discontinuity of the outer retinal layers compared with patients undergoing PnR at 12 months post RRD repair. The outer retina on SD-OCT demonstrates hyperreflective lines that correspond to the ELM (a row of tight junctions between the muller cells and photoreceptor layers, thought to play a key role in photoreceptor alignment and maintenance) and the EZ (considered to represent the mitochondria-rich ellipsoid portion of photoreceptor inner segments).[7] In this study, we found that the foveal EZ and ELM were discontinuous in 24% and 20% of eyes that had undergone PPV, vs 7% and 6% in eyes that had undergone PnR, respectively. Among the few cases of PnR with EZ or ELM discontinuity, about half had undergone secondary PPV after failed PnR, further supporting the notion that PPV may increase the risk of outer retinal discontinuity compared with successful PnR.

Figure 1. Randomization and Follow-up of the Intention-to-Treat Population for the Pneumatic Retinopexy vs Vitrectomy for the Management of Primary Rhegmatogenous Retinal Detachment Outcomes Randomized Trial



This randomized data set that included masked external grading by a retinal image reading center provides, for the first time to our knowledge, evidence to suggest that the type of RRD surgery undertaken is associated with the postoperative integrity of anatomic reattachment, as visualized in the outer retinal layers on SD-OCT.

Given the intimate association of these structures with other photoreceptor components and their supporting cells, the preservation of outer retinal microstructural anatomy on SD-OCT, in particular the EZ and ELM, has consistently been found to be associated with VA across a range of retinal diseases.[8-10] Specifically, abnormalities of the EZ and ELM have been associated with metamorphopsia and reduced VA following successful RRD repair.[11-14] Furthermore, recovery of VA after retinal reattachment has been shown to be associated with restoration of the outer retinal integrity.[11,15-17] The precise cellular mechanisms governing functional improvement following RRD repair are incompletely understood, but it has been suggested that ELM disruption likely signifies absence or

Table 1. Patient and Study Eye Characteristics

Variable	No. (%) Pneumatic retinopexy (n = 73)	No. (%) Pars plana vitrectomy (n = 72)
Age, mean (SD), y	60.6 (9.3)	60.5 (7.9)
Male	51 (70)	43 (60)
Macular status		
Macula retinal detachment		
On	38 (52)	35 (49)
Off	35 (48)	37 (51)
No. of quadrants of retinal detachment, mean (SD)	1.85 (0.84)	1.64 (0.68)
Preoperative lens status		
Pseudophakic	24 (33)	19 (26)
Phakic	49 (67)	53 (74)
Baseline ETDRS visual acuity, mean (SD)	46 (36)	44 (37)

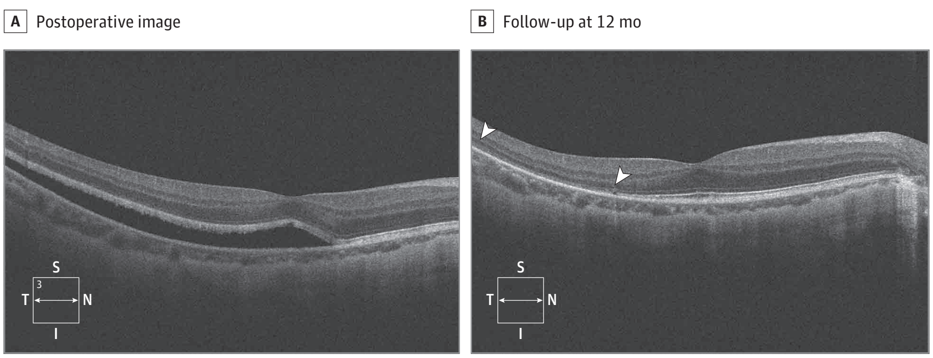
Abbreviation: ETDRS, Early Treatment Diabetic Retinopathy Study.

Table 2. Outer Retinal Integrity in Pneumatic Retinopexy vs Pars Plana Vitrectomy

Variable	No. (%) Pneumatic retinopexy (n = 73)	No. (%) Pars plana vitrectomy (n = 72)	Odds ratio, pars plana vitrectomy vs pneumatic retinopexy (95% CI)	*P* value
ELM discontinuity				
3-mm Foveal scans	4 (5.5)	14 (19.7)	4.237 (1.321-13.587)	.01
6-mm Foveal and nonfoveal scans	13 (17.8)	23 (32.4)	2.211 (1.015-4.819)	.04
EZ discontinuity				
3-mm Foveal scans	5 (6.8)	17 (23.6)	4.204 (1.458-12.116)	.005
6-mm Foveal and nonfoveal scans	8 (11.0)	23 (31.9)	3.814 (1.573-9.249)	.002
IDZ discontinuity				
3-mm Foveal scans	41 (56.2)	44 (61.1)	0.699 (0.421-1.581)	.54
6-mm Foveal and nonfoveal scans	45 (61.6)	48 (66.7)	0.804 (0.407-1.586)	.53
RPE discontinuity				
3-mm Foveal scans	0	1 (1.4)	0.036 (0.002-0.618)	.50
6-mm Foveal and nonfoveal scans	0	3 (4.2)	0.135 (0.007-2.663)	.12

Abbreviations: ELM, external limiting membrane band; EZ, ellipsoid zone; IDZ, interdigitation zone; RPE, retinal pigment epithelium.

Figure 2. Spectral-Domain Optical Coherence Tomography (SD-OCT) for Macula-On Detachment Randomized to Pars Plana Vitrectomy (PPV)

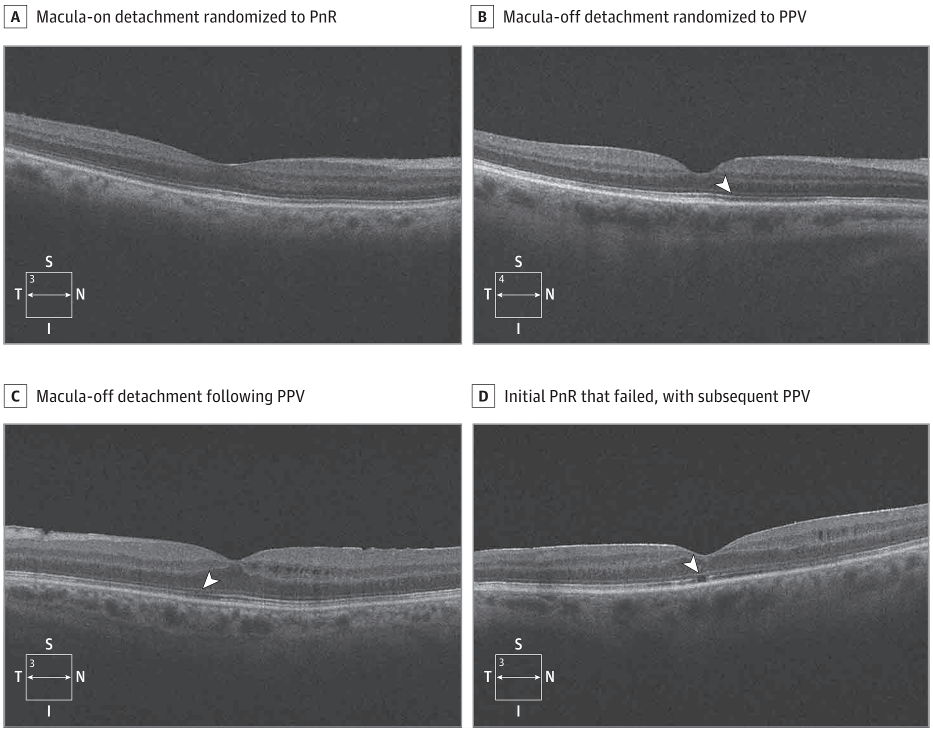


Representative SD-OCT 5-line raster images for macula-on detachment randomized to PPV, which became macula off postoperatively (A) and underwent repeated PPV. Secondary reattachment achieved with ellipsoid zone and interdigitation zone discontinuity (arrowheads) at the 12-month follow-up (B).

regression of the Muller cells and irreversible photoreceptor cell death.[8,18] Regarding the EZ, changes in mitochondrial morphology have been proposed to modify light scattering and thereby alter the appearance of the corresponding OCT line.[19,20] Given that mitochondrial function is central to cellular function, EZ continuity may be indicative of photoreceptor health.[20] A proposed theory for the observed disruption in the outer retinal integrity with RRD is apoptotic photoreceptor cell death, as shown in animal and human studies.[21,22] Furthermore, adaptive optics imaging has enabled the detection of reduced cone density and abnormal cone mosaic patterns following PPV for macula-off RRD, and associated these changes with postoperative VA.[23] The PIVOT trial demonstrated superior VA, reduced vertical metamorphopsia, and better self-reported visual function after PnR compared with PPV. Analysis of SD-OCT data from this clinical trial has found a significant corresponding disparity in the postoperative integrity of key outer retinal layers, thereby providing a compelling rationale for the difference in functional outcomes between the 2 surgical techniques. Together, these anatomic and functional findings attest to the fact that retinal reattachment taking place following PPV vs PnR occurs as a result of 2 very different surgical processes.

It has yet to be fully established what components of the PPV procedure predispose to the outer retinal alterations we describe. Generally, retinal reattachment during PPV occurs in a brisk and active manner, where SRF is forcibly evacuated from the subretinal space using an aspiration cannula, via a retinal break or retinotomy, with or without the aid of heavy liquid. Furthermore, there is significant fluid flow and turbulence in both the vitreous cavity and subretinal space. Most commonly, a near-complete air-fluid exchange is performed, and maximal fill of tamponade agent (gas or silicone oil) is sought. Conversely, retinal reattachment following PnR is largely passive. A small bubble of gas is injected into the vitreous cavity, and a steamroller maneuver is performed to express a portion of the SRF into the vitreous cavity with the remaining fluid gently reabsorbed by the action of the retinal pigment epithelial pump. We propose that this slower and more physiological retinal reapposition, with less intraocular turbulence, culminates in reduced stress on the photoreceptors and other retinal cells and improved alignment of the photoreceptors with

Figure 3. Spectral-Domain Optical Coherence Tomography (SD-OCT) for Macula-On Detachment Randomized to Pneumatic Retinopexy (PnR)



Representative SD-OCT 5-line raster images with no discontinuity of the outer retinal layers for macula-on detachment randomized to PnR (A). External limiting membrane, ellipsoid zone (EZ), and interdigitation zone (IZ) discontinuity (arrowhead) in foveal scan of macula-off detachment randomized to pars plana vitrectomy (PPV) (B). The EZ and IZ discontinuity (arrowhead) in foveal scans of macula-off detachment following PPV (C), as well as EZ and IZ discontinuity (arrowhead) in macula-off detachment following initial PnR that failed and underwent subsequent PPV (D).

the retinal pigment epithelial villi, thereby facilitating superior functional outcomes (**Video 1** and **Video 2**).

A second possible mechanism that accounts for the difference in outer retinal microstructural integrity between PPV and PnR is postoperative retinal displacement. Quite unlike PPV, where the tamponade agent makes contact with a large area of the retina and applies a greater buoyant force to the retina and SRF (including the macular region), the gas bubble in PnR will subtend a smaller angle of contact with the retina, localized to the vicinity of the retinal break(s), and will apply a smaller buoyant force to the retina and SRF. Several groups, including ours, have hypothesized that inferior displacement of residual SRF occurring during (and immediately after) PPV, as a result of a larger gas tamponade, may result in inferior stretch and displacement of the retina, with resultant photoreceptor misalignment. Our group has demonstrated that inferior displacement of the retina is commonplace after PPV and gas tamponade, whereas it is encountered much less frequently when PnR is used.[24-27] Furthermore, this displacement has been associated with worse functional outcomes, including metamorphopsia. It is possible that the direction and severity of retinal stretch may influence the severity of objectively measured vertical and horizontal metamorphopsia.

It is important to recognize that the functional and anatomic outcomes from the PIVOT trial were in the context of a randomized clinical trial and the results may not be generalizable to every patient and every surgeon. However, the authors believe that there is sufficient evidence to suggest that PnR should be a part of the armamentarium of surgical techniques available to a vitreoretinal surgeon so they can appropriately manage patients on a case-by-case basis. Specifically, all vitreoretinal surgeons who do not have experience with PnR should seek some training and/or experience with the procedure and may consider it in patients who meet the inclusion/exclusion criteria of the PIVOT trial. In the PIVOT trial, the primary reattachment rate was 81% in the PnR group vs 93% in the PPV group, a difference of 12%. One very important consideration is that patients who have a failed pneumatic should have a timely rescue procedure. Keeping this in mind, it has been demonstrated that in the PIVOT trial and the Pneumatic Retinopexy Trial that a PnR failure did not jeopardize future anatomic and visual outcomes, such that failed PnR had similar outcomes to primary PPV or scleral buckle, respectively.

Strengths and Limitations

This study has several strengths. First, these data pertain to a randomized trial of 2 commonly performed treatments for RRD repair. Second, the SD-OCT images were graded by masked graders from a retinal reading center that was not affiliated with the study site, with excellent interobserver agreement. These methods eliminate some potential sources of bias. Third, our key findings are likely to be highly clinically relevant because integrity of these layers on SD-OCT has been firmly established by others as a biomarker for the restoration of normal outer retinal microstructural anatomy following RRD surgery and has consistently been associated with functional outcomes.

One limitation of this study, as mentioned previously, is the post hoc nature of the analysis. Another limitation relates to the 2 primary outcomes, namely EZ and ELM discontinuity on the foveal 5-line raster scan. We did not adjust for multiple comparisons in the analysis, and this should be considered.

Conclusions

This study demonstrates that PPV is associated with greater risk of discontinuity of the EZ and ELM compared with PnR following RRD surgery. The superior photoreceptor integrity achieved with PnR likely explains some of the functional advantages found in PIVOT. The findings of this study are of key importance to contemporary vitreoretinal surgeons and their patients, who seek more than gross anatomic retinal reattachment. It is important for vitreoretinal surgeons to take these results into consideration when choosing retinal detachment repair techniques that are most likely to give patients the best functional outcomes. The results of this study suggest that patients with retinal detachment meeting PIVOT trial criteria undergoing PnR achieve superior photoreceptor integrity at 12 months postoperatively compared with PPV. This study supports the hypothesis that postoperative photoreceptor integrity varies with surgical technique in retinal detachment repair.

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Author Affiliations: Department of Ophthalmology and Vision Sciences, University of Toronto, Toronto, Ontario, Canada (Muni, Felfeli, Juncal, Berger, Wong, Altomare, Giavedoni, Kohly, Kertes); Department of Ophthalmology, St Michael's Hospital, Unity Health Toronto, Toronto, Ontario, Canada (Muni, Juncal, Berger, Wong, Altomare, Giavedoni); Kensington Vision and Research Centre, University of Toronto, Toronto, Ontario, Canada (Muni, Kohly, Kertes); Keenan Research Centre for Biomedical Science/Li Ka Shing Knowledge Institute, Toronto, Ontario, Canada (Muni); Dalla Lana School of Public Health, University of Toronto, Toronto, Ontario, Canada (Felfeli); Doheny Image Reading Center, Doheny Eye Institute, Los Angeles, California (Sadda, Nittala, Lindenberg, Gunnemann); Department of Ophthalmology, David Geffen School of Medicine at University of California, Los Angeles (Sadda, Gunnemann, Sarraf); Department of Ophthalmology and Visual Sciences, Dalhousie University, Halifax, Nova Scotia, Canada (Francisconi); The John and Liz Tory Eye Centre, Sunnybrook Health Sciences Centre, Toronto, Ontario, Canada (Kohly, Kertes); Newcastle Eye Centre, Royal Victoria Infirmary, Newcastle upon Tyne, England (Hillier); Institute of Translational and Clinical Research, Newcastle University, Newcastle upon Tyne, England (Hillier).

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Concept and design: Muni, Felfeli, Francisconi, Wong, Kohly, Kertes, Hillier.
Acquisition, analysis, or interpretation of data: Muni, Felfeli, Sadda, Juncal, Francisconi, Nittala, Lindenberg, Gunnemann, Berger, Wong, Altomare, Giavedoni, Sarraf, Hillier.
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Invited Commentary

Understanding Visual Acuity Outcomes After Retinal Detachment Repair by Assessing Photoreceptor Integrity on Spectral-Domain Optical Coherence Tomography

Mårten E. Brelén, BMBCh, PhD; Carol Y. Cheung, PhD

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The annual incidence of rhegmatogenous retinal detachment is approximately 18 to 22 per 100 000 population[1,2] and reported techniques for reattaching the retina include pneumatic retinopexy (PnR), scleral buckle, and pars plana vitrectomy (PPV). Recently, it has become increasingly common to repair a retinal detachment using vitrectomy and gas, given the higher anatomical success rate of this procedure. However, the Pneumatic Retinopexy Versus Vitrectomy for the Management of Primary Rhegmatogenous Retinal Detachment Outcomes Randomized Trial (PIVOT) showed that even though the anatomical success of PnR is lower than that of PPV, visual acuity outcomes were better and rates of postoperative metamorphopsia were lower in patients treated with PnR.[3] It is important to note that long-acting gas tamponade (perfluoropropane) was used in 33 of 88 individuals (38%) in the PPV arm only. This difference could have influenced the anatomic success rates in favor of the PPV group with enhanced cataract formation in the PPV arm, which in turn could have influenced the visual acuity outcomes in favor of the PnR group. To understand further factors in the PnR arm that may have been associated with better functional outcomes, the study by Muni et al[4] investigated the microstructural integrity of the outer retina on optical coherence tomography (OCT) between PnR and PPV groups. The results show a better preservation of the ellipsoid zone and external limiting membrane in the PnR group vs the PPV group, which, although not proving a causal relationship, has some biologic rationale to account for better functional outcomes when performing a PnR. Of note, it would be interesting to have further explorations by Muni et al[4] to see if there were any confounding associations between use of perfluoropropane in the PPV group and worse microstructural integrity of the outer retina on OCT.

Having demonstrated this difference in functional outcomes between the 2 techniques, it is important to try to understand the mechanisms that may result in disruption and damage of the ellipsoid zone during a PPV. It might then be possible to modify existing techniques to obtain better functional outcomes during PPV if there is indeed a causal relationship and not just differences due to known or unknown confounding factors.

For example, Muni et al[4] suggest the difference between PnR and PPV could be attributed to the forceful evacuation of subretinal fluid during PPV when using heavy liquid compared with the more passive pumping of subretinal fluid by the retinal pigment epithelium following PnR, although this hypothesis may have been provided by the authors after they determined their results. Should we therefore leave some residual subretinal fluid at the end of PPV and allow the retina to reattach more passively, as occurs during PnR? Changes in