Reading Speed as an Objective Measure of Improvement Following Vitrectomy for Symptomatic Vitreous Opacities

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Reading speed as a reliable outcome measure to assess visual improvement following vitrectomy for symptomatic vitreous opacities in patients with clear lenses

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Declaration of Conflicting Interests

The authors declare no potential conflicts of interest with respect to the research, authorship or publication of this article. In addition, Dr. Calabrese reports receiving royalties for sales of the MNREAD iPad app through a licensing agreement between the University of Minnesota and

Precision Vision outside of the present work. Dr. Ryan reports royalties for patents related to vitrectomy surgery from Alcon Surgical.

Abstract

Background and Objective: There is currently no objective measure of the visual deficits experienced by patients with symptomatic vitreous opacities (SVO) that would also correlate with the functional improvement they report following vitrectomy. This study aims to determine whether reading speed can be used as a reliable outcome measure to assess objectively the impact of both SVO and vitrectomy on patients' visual performance.

Study Design/Materials and Methods: 20 adult patients seeking surgery for SVO were included. Measures of visual function were obtained before and after vitrectomy using the ETDRS acuity chart, the NEI-VFQ and the MNREAD.

Results: In patients with non-opacified lenses (N=10), maximum reading speed increased significantly from 138 to 159 words per minute after complete removal of SVO by vitrectomy (95%CI = [14, 29], $p < 0.001$).

Conclusion: Reading speed is impaired with SVO, and improves following vitrectomy in phakic and pseudophakic eyes with clear lenses. Reading speed is a valid objective measure to assess the positive effect of vitrectomy for SVO on near-distance daily life activities.

Keywords

Vitrectomy, symptomatic vitreous opacities, lens opacity, reading speed, daily-life function, functional improvement, objective measurement

Background and Objective

Patients with symptomatic vitreous opacities (SVO) experience visual impairment from multiple dense particles floating in the vitreous gel, which often cast a mobile dark shadow on the retina. However, standard objective measures of visual function, such as Snellen visual acuity, remain often excellent in the presence of SVO[1,2]. Nonetheless, patients with SVO report significant visual improvement after their removal by vitrectomy[3,4]. For instance, previous studies have shown post-operative improvement in subjective visual quality of life[5,6]. These results were obtained with the National Eye Institute Visual Function Questionnaire (NEI-VFQ), which assesses the level of difficulty experienced by individuals with chronic eye diseases during daily-living activities, such as driving or reading[7].

To complement such subjective evaluations, there is a need for establishing a quantifiable measure to assess objectively (1) the impairment in visual function caused by SVO and (2) the improvement in visual function following vitrectomy[3]. First, such a clinical measure would help detect patients with functional impairment from vitreous floaters. Second, it would bring valuable insight to help resolve the existing controversy over vitrectomy's clinical relevance. So far, intraocular straylight[8] and contrast sensitivity[6] have been proposed as independent objective measures of visual perception with symptomatic floaters. Despite their impact on vision-related quality of life, these measures do not evaluate daily life function directly.

A frequent complaint from patients with prominent opacities is interference with ease of reading. Even if unilateral, these patients often complain of interference with binocular visual function[9,10].

Patients usually report moderate or extreme difficulty in reading small print[5]. In the low-vision literature reading speed is already considered a strong objective predictor of visual ability and vision-related quality of life for patients with ocular disorders, such as macular degeneration[11,12,13,14]. Here we conducted a prospective study to test whether reading performance can also be used as reliable outcome measure to investigate the impact of SVO and therapeutic vitrectomy on patients' visual performance.

Our main objective was to investigate whether reading performance, evaluated with the standardized MNREAD test, could provide an objective measure of functional improvement in patients with SVO treated with pars plana vitrectomy. To this aim, we compared pre and post-operative measures of (1) vision-related quality of life (subjectively obtained with the NEI VFQ) and (2) reading performance (objectively obtained with the MNREAD test). Given that reading performance is rapidly degraded with reduced contrast from cloudy ocular media[15], these comparisons were performed while controlling for patients' lens status (clear vs. mildly opacified). Additionally, we investigated whether a potential improvement in these subjective and objective measures following vitrectomy would be correlated with pre-operative opacity severity.

Patients/Materials and Methods

Patients

Patients over 21 years old were included in the present work if they (1) elected to undergo vitrectomy, (2) presented symptoms consistent with examination findings of dense opacities for at least 6 months, (3) had visual acuity of 20/80 (0.6 logMAR) or better in both eyes before surgery and (4) did not experience a significant drop in acuity in the non-operated eye between the pre- and post-surgery measurements. Phakic and pseudophakic patients were included, as well as patients with or without a vitreous detachment. History of scleral buckle for retinal detachment (RD) was acceptable if the macula was not involved. If an epiretinal membrane was noted on OCT but not clinically visible or deemed significant, patients were included in the study. Patients were excluded if they had history of cognitive impairment, macula-off RD, severe glaucoma, macular degeneration, diabetic macular edema, or other confounding ocular disorders. A total of 20 patients were recruited, tested and treated at two different sites: 11 at a private retina practice in Minnesota and 9 at an academic retina practice in California. Figure 1 illustrates the protocol sequence. Institutional Review Board (IRB)/Ethics Committee approval was obtained and written informed consent was obtained before the study from each patient according to IRB guidelines. The study also complied with tenets of the Declaration of Helsinki and HIPAA.

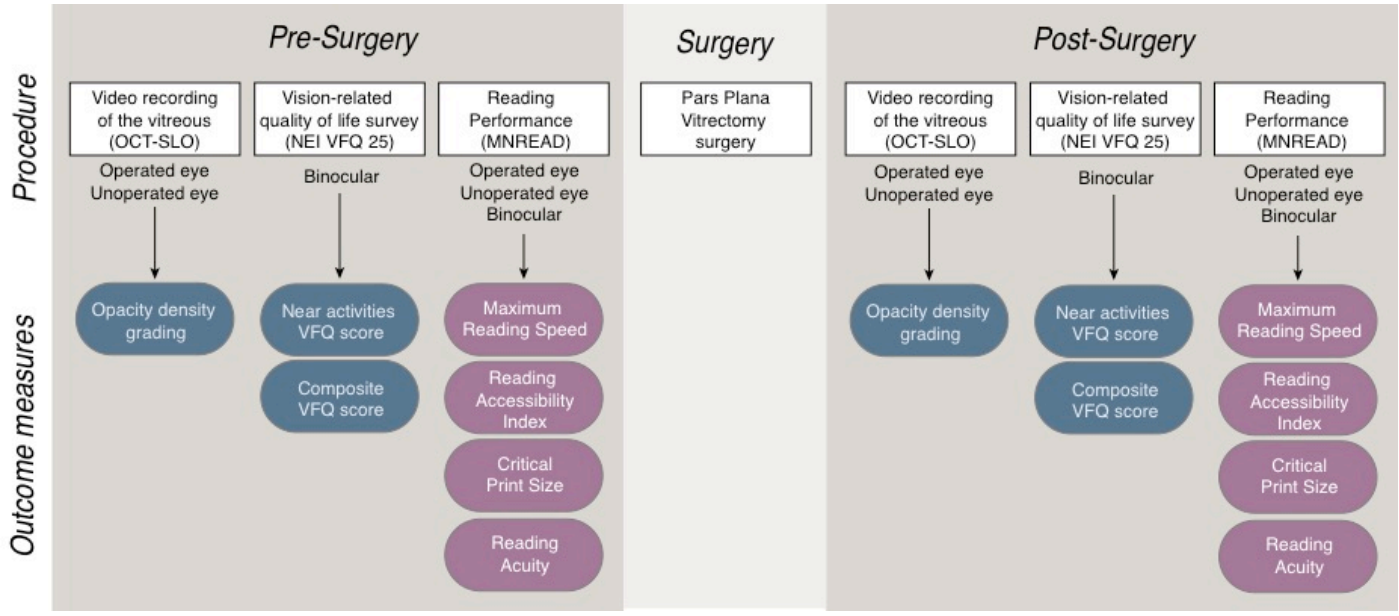

Figure 1: Protocol schematic showing the different test procedures along with the resulting outcome measures. Subjective measures are represented in blue; objective measures are represented in pink.

Surgery

20 eyes of 20 patients underwent outpatient three-port 25-gauge pars plana vitrectomy using the Alcon Constellation system. Inspection of the peripheral retina with indirect ophthalmoscopy and scleral depression was performed at surgery conclusion. Leaking sclerotomies were sutured. Postoperative examinations were at 1 day, 1-2 weeks, and 4-6 weeks. Presence or absence of a posterior vitreous detachment (PVD) was confirmed intraoperatively. Visual acuity, intraocular pressure, dilated funduscopic exam and any postoperative complications including high or low intraocular pressure, retinal tear or detachment, and/or endophthalmitis were recorded. For each patient, the non-operated eye served as control.

144 ***Subjective grading of opacity density***

145 Before and after surgery, patients went through video recording of the vitreous using the infrared
146 confocal scanning laser ophthalmoscope (SLO) combined with optical coherence tomography
147 (OCT)[16,17]. The movie created with this technique reveals motion of the shadows projected by
148 the opacities onto the retinal surface, enabling a subjective grading of the opacity density.
149 Recording was performed in each eye. Patients were instructed to look to one side and then re-
150 fixate, which set the vitreous opacities in motion. This step was repeated to each side several
151 times. The pre and post-surgery videos were assessed by two experienced, masked surgeons and
152 given a score of 0-3, with 0 corresponding to no floaters and 3 corresponding to very dense
153 floaters (see supplementary material for a pre-op movie graded as 2 and a post-op movie graded
154 as 0).

155

156 ***Subjective measure of vision-related quality-of-life***

157 Before and after surgery, patients were interviewed with the NEI-VFQ-25, the 25-item version of
158 the VFQ test[7]. Data were scored using the standard method to calculate: 1-the near activities
159 VFQ score (involving reading) and 2- the composite VFQ score (encompassing many vision-
160 related functions). Scores ranged from 0 to 100, with higher scores representing better function.

161

162 ***Objective measure of reading speed***

163 Before and after surgery, patients' reading performance was measured with the MNREAD acuity
164 chart, a standardized test designed to measure binocular and monocular reading performance[18].

Test measures were obtained with the MNREAD app running on an iPad[19]. Viewing distance was 60 cm and screen luminance was set to 200cd/m2. Patients went through six iterations of the test (operated eye, non-operated eye and binocular, each condition being repeated twice), all in black print on white background. MNREAD testing was performed pre-operatively and again 4-8 weeks after surgery. For each test performed, the four MNREAD measures were estimated internally by the app[18]: (1) Maximum Reading Speed (MRS), (2) Critical Print Size (CPS), (3) Reading Acuity (RA) and (4) reading ACCessibility index (ACC - a single-valued measure that represents one's visual access to commonly encountered printed material, ranging from 0 (i.e. no access to print) to 1 (i.e. average normal access) or above)[20].

Statistical analysis

Pre and post-operative scores of NEI-VFQ were compared with a Wilcoxon signed-rank test. For each of the four MNREAD parameters, a different linear mixed-effects model including data from all 20 patients was designed to compare values before and after vitrectomy for the operated eye, the non-operated eye and the binocular condition[21,22]. To control for covariate factors, the following variables were also included in the models: binocular lens opacity ('clear' vs. 'mild opacity'), presence of epiretinal membrane (ERM) in the operated eye ('yes' vs. 'no'), presence of SVO in the non-operated eye ('yes' vs. 'no'), presence of posterior vitreous detachment (PVD) in the non-operated eye ('yes' vs. 'no') and testing location ('Minnesota' vs. 'California'). The same random structure was chosen for all four models and included a random intercept for "eyes nested within patients", assuming a different baseline performance level for each patient and each eye. Post-hoc pairwise comparisons were performed using Tukey's

correction. In the Results section, mean values estimated by the models and post-hoc pairwise comparisons are reported with their 95% confidence intervals (95%CI) and p-values.

Results

Patients

Preoperative clinical examination revealed the presence of SVO and clinical evidence of PVD in all patients. Thirteen patients had bilateral but asymmetric opacities noted on clinical examination, and were asymptomatic in the fellow eye. Six patients had concurrent minimally significant epiretinal membrane. One patient had a history of scleral buckling for a macula-sparing retinal detachment. Vitreous opacities symptoms had been present for 6 to 24 months. Table 1 presents the patients' preoperative individuals characteristics.

Patient ID	Location	Gender	Age	Lens opacity in both eyes	Operated eye				Non-operated eye		
					Pathology	SVO	Acuity	OCT-SLO Opacity grading	Pathology	SVO	Acuity
P1	Minnesota	M	58	Clear	PVD	Yes	20/25	2	ERM	No	20/25
P2	Minnesota	M	59	Clear	PVD	Yes	20/20	1.5	--	Yes	20/25
P3	California	M	61	Clear	PVD	Yes	20/20	3	ERM	No	20/40
P4	Minnesota	M	62	Clear	PVD+ ERM	Yes	20/20	1.5	Scleral buckling + ERM	No	20/20
P5	Minnesota	M	64	Clear	PVD+ ERM	Yes	20/15	2	PVD	Yes	20/25
P6	Minnesota	F	64	Clear	PVD	Yes	20/25	2.5	--	Yes	20/20
P7	Minnesota	F	64	Clear	PVD	Yes	20/20	2.5	PVD	Yes	20/25
P8	Minnesota	F	68	Clear	PVD	Yes	20/30	1	PVD	Yes	20/15
P9	California	M	69	Clear	PVD	Yes	20/20	2.5	PVD	Yes	20/20
P10	Minnesota	F	72	Clear	PVD	Yes	20/25	2	PVD	Yes	20/25
P11	California	F	32	Mild opacity	PVD	Yes	20/25	1	PVD	Yes	20/80

P12	California	M	52	Mild opacity	PVD+ ERM	Yes	20/25	2.5	Vitreous Syneresis	No	20/20
P13	California	M	54	Mild opacity	PVD+ ERM	Yes	20/40	3	NPDR	No	20/20
P14	California	F	54	Mild opacity	PVD	Yes	20/25	2.5	PVD	Yes	20/80
P15	Minnesota	M	63	Mild opacity	PVD+ ERM	Yes	20/40	2.5	ERM	Yes	20/25
P16	California	M	63	Mild opacity	PVD+ ERM	Yes	20/80	2	ERM	No	20/25
P17	Minnesota	M	64	Mild opacity	PVD	Yes	20/20	2.5	Vitreous Syneresis	Yes	20/20
P18	California	F	65	Mild opacity	PVD	Yes	20/30	2.5	PVD	Yes	20/25
P19	California	F	67	Mild opacity	PVD	Yes	20/30	2.5	ERM	No	20/25
P20	Minnesota	M	68	Mild opacity	PVD	Yes	20/20	1.5	PVD	Yes	20/25

Table 1: Patients' individual characteristics prior to surgery. SVO stands for symptomatic vitreous opacities; ERM stands for epiretinal membrane. PVD stands for posterior vitreous detachment; NPDR stands for non-proliferative diabetic retinopathy; Visual acuity is given in Snellen notation.

Surgery

No complications were seen. No cataract progression was observed in phakic patients during the short period of follow-up (6 weeks). Complete removal of the central vitreous opacities was documented by examination and video SLO in all 20 cases. Prior to surgery, OCT-SLO grading of opacity was on average 2.2, ranging from 0 to 3 (Table 1). After vitrectomy, opacity grading score was 0 for all 20 patients.

Visual function

In the operated eye, mean visual acuity was 0.11±0.16 logMAR before surgery and 0.09±0.16 logMAR after surgery. The difference between pre- and post-op visual acuity was not significant ($p = 0.36$). Both NEI-VFQ scores improved significantly after vitrectomy, but this improvement was dependent on the lens opacity (Figure 2). Among patients with clear lenses (N=10), the

average near activities sub-score went from 47.5 to 74.2. This significant increase of 26.7 points (95%CI = [16.2, 37.1], $p < 0.001$) corresponds to an overall 56.2% improvement (Figure 2A-left). For patients with opacified lenses however (N=10), vitrectomy did not improve the near activities sub-score. For patients with clear lenses, the average pre-op composite score was 64.6 and increased by 19.8 points (95%CI = [13.9, 25.7], $p < 0.001$) after vitrectomy, representing a 30.6% improvement (Figure 2B-left). The improvement was somewhat smaller for patients with opacified lenses, whose score went from 71.4 to 85.8, representing a significant gain of 20.2% (14.4 points, 95%CI = [-6.3, 23.4], $p = 0.003$). The overall improvement for both subgroups on the composite score was 26.3%. There was no correlation between the opacity grading score prior surgery and the amount of NEI-VFQ score improvement following surgery (Pearson's correlation coefficients was -0.36 and -0.39 for the near activities sub-score and the composite score respectively).

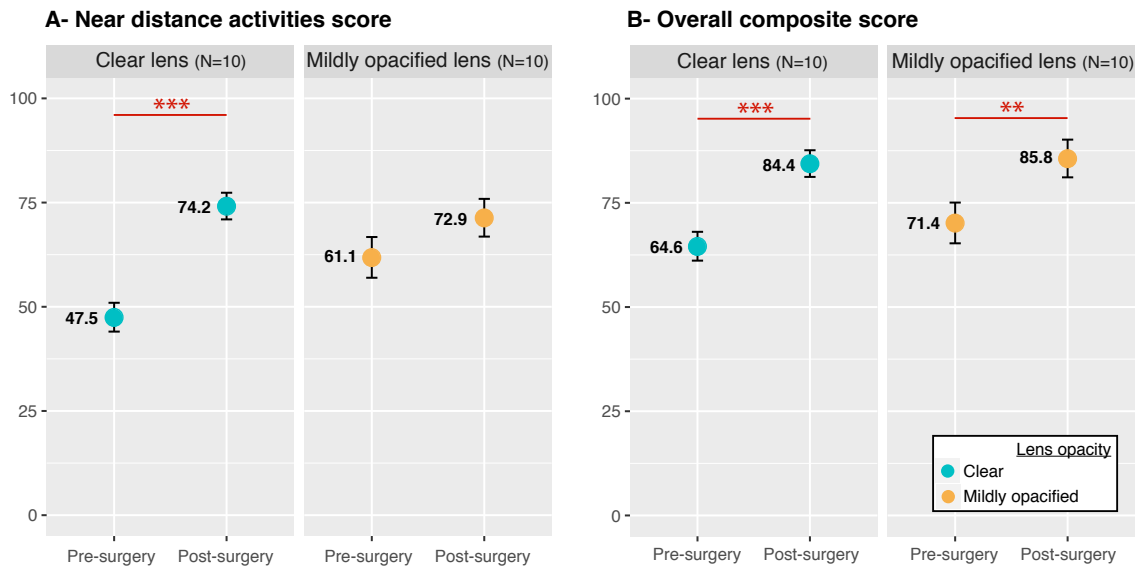

Figure 2: Pre and post-operative NEI-VFQ scores grouped by lens opacity status. Points show the mean estimates for the near activity sub-score (A) and the overall composite score (B), both before and after surgery, as estimated by the mixed effects models, for patients with clear lenses in blue

(N=10) and patients with mildly opacified lenses in orange (N=10). Error bars represent the 95% confidence intervals.

Reading performance

Maximum Reading Speed (MRS)

First, we included data from all 20 patients in the mixed-effects model without any distinction on their lens opacity status. MRS before surgery was on average 137 words/minute (wpm) for the operated eye (95%CI = [125, 149]). It was significantly higher by 13 wpm in the non-operated eye (95%CI = [5, 22], p = 0.003) and by 15 wpm in the binocular condition (95%CI = [7, 24], p < 0.001). After surgery, MRS in the operated eye increased significantly to 146 wpm (i.e. a 9 wpm increase; 95%CI = [3, 15], p = 0.007). Post-operatively, MRS did not change significantly in the non-operated eye (1 wpm increase; 95%CI = [-12, 14]; p = 0.8) or in the binocular condition (3 wpm increase; 95%CI = [-9, 17]; p = 0.23).

Second, we included an interaction between the "surgery" and "lens opacity" factors in the model. For patients with clear lenses only (N=10), MRS prior surgery was on average 138 words/minute (wpm) for the operated eye (95%CI = [120, 156]; Figure 3-left panel). It was significantly higher by 13 wpm in the non-operated eye (95%CI = [6, 20], p < 0.001) and by 14 wpm in the binocular condition (95%CI = [7, 22], p < 0.001). After surgery, MRS in the operated eye increased significantly to 159 wpm (i.e. a 21 wpm increase; 95%CI = [14, 29], p < 0.001). In the non-operated eye, MRS did not change post-operatively, with a non-significant increase of 3 wpm (95%CI = [-7, 39], p = 0.43). In the binocular condition, the limited increase of 8 wpm following vitrectomy barely reached significance (95%CI = [-0.38, 45], p = 0.04).

For patients with mildly opacified lenses (N=10), there was no significant difference in MRS before and after surgery in any of the three conditions tested (operated eye, un-operated eye and binocular; Figure 3-right panel).

For all 20 patients there was no correlation between the opacity grading score in the operated eye prior surgery and the amount of MRS improvement following surgery (Pearson's correlation coefficients was -0.13).

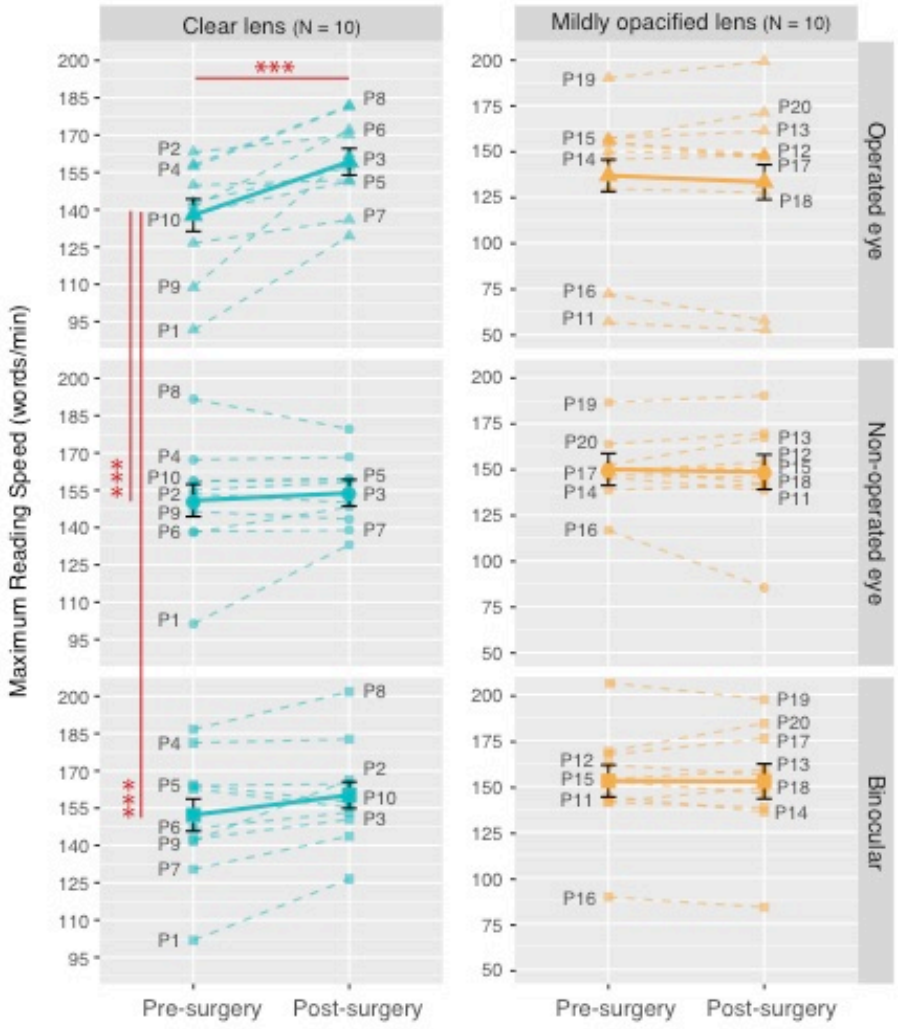

Figure 3: **Effect of pre/post-surgery condition on MRS for the operated eye (top – triangles), the non-operated eye (center - circles) and the binocular condition (bottom – squares) grouped by lens opacity: clear (left – blue) vs. mildly opacified (right - orange). Solid lines connect the estimates for**

each sub-group as given by the mixed-effects model. Errors bars (black) represent their standard errors. Dashed lines connect the MRS values for each patient, numbered from P1 to P20.

Reading Accessibility Index (ACC)

As for MRS, we first included data from all 20 patients in the mixed-effects model, without any distinction on their lens opacity status. Before surgery, ACC was on average 0.61 for the operated eye (95%CI = [0.55, 0.68]). It was significantly higher by 0.09 wpm in the non-operated eye (95%CI = [0.04, 0.15], p = 0.002) and by 0.11 in the binocular condition (95%CI = [0.05, 0.17], p < 0.001). After surgery, ACC in the operated eye increased significantly to 0.67 (i.e. a 0.06 increase; 95%CI = [0.01, 0.10], p = 0.01). Post-operatively, ACC did not change significantly in the non-operated eye (0.002 increase; 95%CI = [-0.09, 0.09]; p = 0.95) or in the binocular condition (0.03 increase; 95%CI = [-0.06, 0.12]; p = 0.22).

Second, we included an interaction between the "surgery" and "lens opacity" factors in the model. For patients with clear lenses only (N=10), ACC was 0.65 in the operated eye before surgery (95%CI = [0.56, 0.74], p < 0.001; Figure 4 - left). It was marginally but significantly better for the non-operated eye, with a value of 0.72 (0.07 difference; 95%CI = [0.01, 0.14], p = 0.02) and significantly better in the binocular condition, with a value of 0.75 (0.1 difference; 95%CI = [0.04, 0.17], p = 0.002). Following surgery, ACC was significantly increased by 0.1 in the operated eye (95%CI = [0.05, 0.16], p < 0.001), reaching a value of 0.75. In the non-operated eye, ACC remained unchanged after surgery (0.01 difference; 95%CI = [-0.09, 0.28], p = 0.5). In the binocular condition, ACC increased by 0.05 after vitrectomy but this change did not reach significance (95%CI = [-0.03, 0.34], p = 0.06).

For patients with mildly opacified lenses (N=10), there was no significant difference in ACC before and after surgery in any of the three conditions tested (operated eye, un-operated eye and binocular; Figure 4 – right panel).

For all 20 patients, there was no correlation between the opacity grading score prior surgery in the operated eye and the ACC increase following surgery (Pearson's correlation coefficient was -0.41).

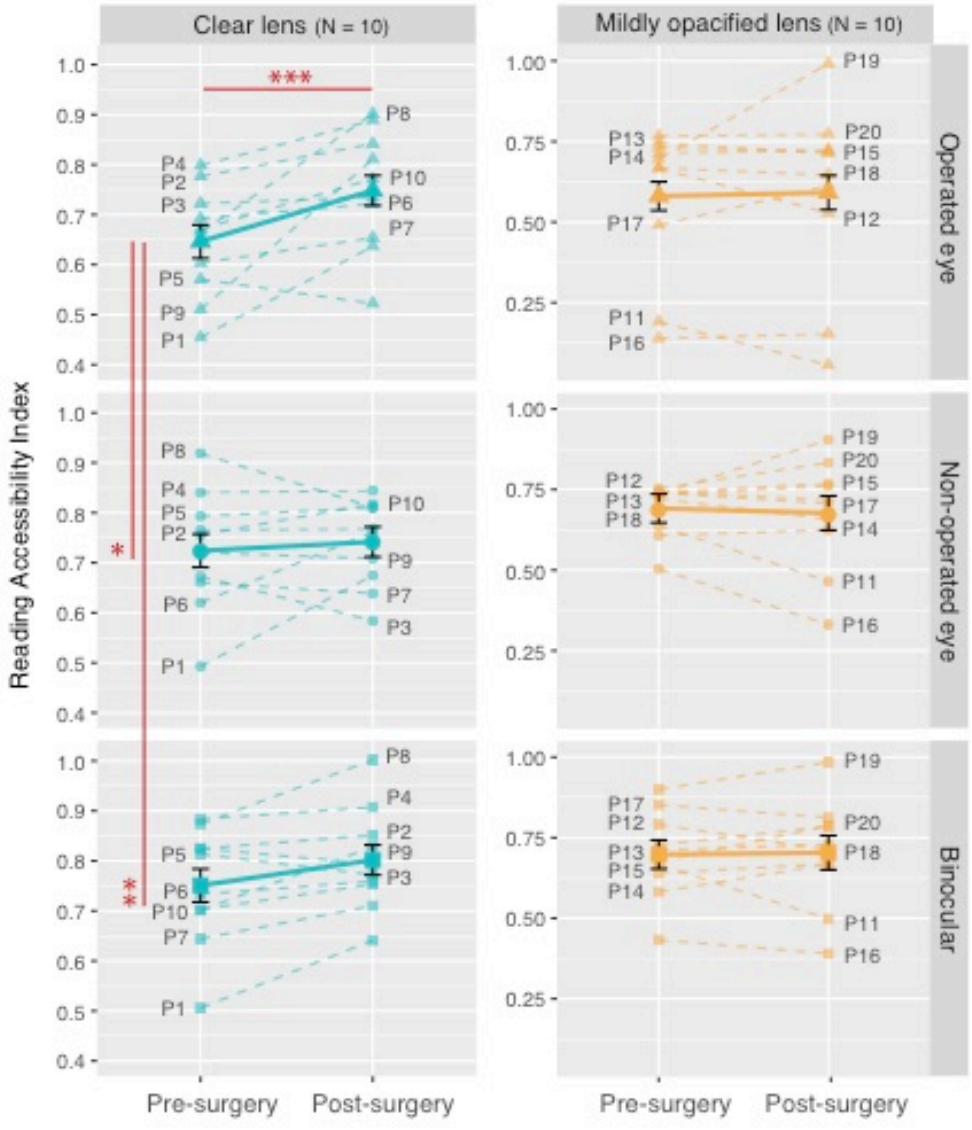

Figure 4: Effect of pre/post-surgery condition on ACC for the operated eye (top – triangles), the non-operated eye (center - circles) and the binocular condition (bottom – squares) grouped by lens opacity: clear (left – blue) vs. mildly opacified (right - orange). Solid lines connect the estimates for each sub-group as given by the mixed effects model. Errors bars (black) represent their standard errors. Dashed lines connect the MRS values for each patient, numbered from P1 to P20.

Critical Print size (CPS) and Reading Acuity (RA)

For both CPS and RA, we found no significant difference between the operated eye and the non-operated eye or the binocular condition before surgery. None of these measures changed significantly after surgery in the tested eyes.

Correlation between reading performance change and daily life visual function improvement

Lastly, we inspected the correlation between the improvement in reading performance and the improvement in NEI-VFQ near activities sub-score in the operated eye of all 20 patients. We found no correlation between the percentage of improvement in MRS and the increase in NEI-VFQ near activities sub-score ($r = 0.4$, 95%CI $= [-0.12, 0.75]$, $p = 0.12$). On the other hand, the improvement in ACC was significantly correlated with the near activities sub-score ($r = 0.74$, 95%CI $= [0.39, 0.90]$, $p = 0.001$; Figure 5).

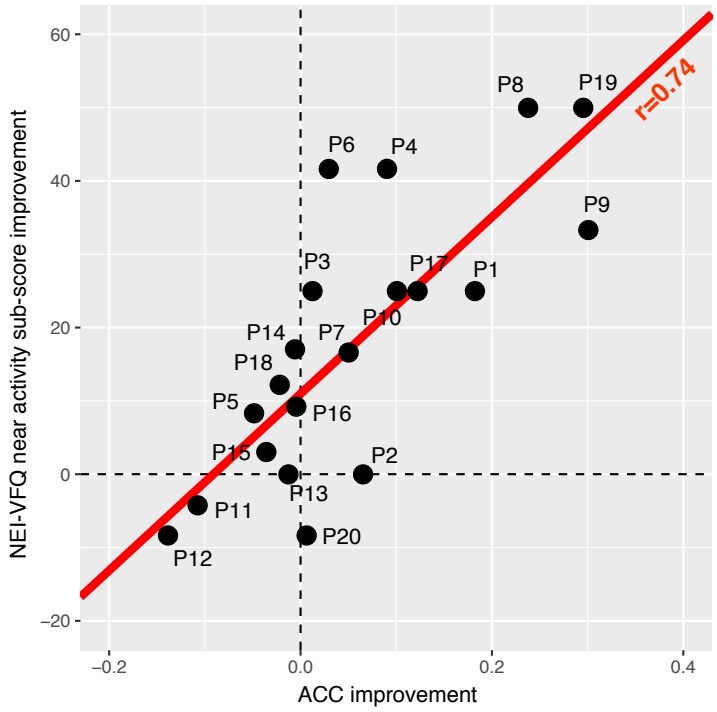

Figure 5: Post-operative NEI-VFQ near activity sub-score improvement as a function of post-operative reading accessibility index improvement for all 20 patients.

Discussion

The symptomatic relief experienced by patients following vitrectomy has been demonstrated before by the use of the NEI-VFQ subjective test[5,6]. Our study confirmed the literature results, with a significant overall improvement of 26% on the test composite score. This value is in line with previously reported improvement results, ranging from 19% to 29%, in patients treated for symptomatic floaters[6,23]. The present analysis also revealed a significant interaction between the impact of surgery on the VFQ scores and the opacity status of the patient's lenses. For near distance activities, vitrectomy only improved patients' score if their lenses were clear, whereas the overall composite score (which includes both near- and far-distance activities) improved even

if the lenses were mildly opacified. To our knowledge, this result was never reported before and suggests that the removal of SVO may have a significant impact on near-distance daily life activities, but only in the absence of cataract or lens opacification. Because near distance activities rely on fine central vision, for which performance is rapidly degraded past a critical contrast threshold[24], SVO removal may not be sufficient to help improve performance if contrast sensitivity is still reduced from lens opacification.

Our second result is the poor MRS achieved in all 10 patients with SVO and clear lenses (138 wpm on average in the operated eye prior surgery) compared to normal values. According to Calabrèse et al., 2016, normal readers between 58 to 68 years old should reach a MRS comprised between 183.2 and 189.2 wpm when reading with one or both eyes[25,26]. This 35% decrease suggests that reading speed may be considered as an objective measure of functional impairment in the presence of SVO. However, this finding should be interpreted with caution, given that other confounding clinical factors (e.g. cognitive or visual) may have also contributed to reducing reading speed.

Our third outcome is the significant change in MRS, measured after vitrectomy in patients with clear lenses, with a 15% improvement in the operated eye. For these patients, the non-operated eye served as control and showed no improvement post-surgery, confirming that the improvement measured in the fellow eye was not due to a practice effect. More importantly, this improvement did not occur in eyes with mildly opacified lenses, either from cataract (phakic eyes) or posterior capsule opacification (pseudophakic eyes). Taken all together, these results suggest that reading speed may be a valid objective measure to quantify the positive impact of

vitrectomy on visual function, but only if contrast sensitivity is not still altered by lens opacification. There is evidence that a main effect of vitrectomy is to restore normal contrast sensitivity function for individuals with clear lenses[6,27]. We hypothesize that for patients with mildly opacified lenses, who experienced no post-surgery improvement in MRS, reduced contrast sensitivity from cloudy ocular media created a bottleneck for any potential increase in reading speed. We noted that binocular MRS was not improved post-surgery. Since, our population was not restricted to patients with non-pathological fellow eyes, we did not expect to see monocular vitrectomy having a significant impact on binocular performance.

ACC showed the same pattern as MRS, suggesting that this measure, which is potentially quicker to obtain (in terms of testing and calculation time), could be a good alternative in clinical settings where time is often limited. More interestingly, the improvement in ACC induced by vitrectomy was significantly correlated with the improvement in near distance activities score measured with the NEI-VFQ. This result alone suggests that improved reading performance following vitrectomy will also have a positive impact on the overall patients' quality of life. The simple objective assessment of ACC post-operatively may therefore provide some insight to the patient and his/her care team about his/her overall quality of life improvement.

Surprisingly, neither CPS nor RA were sensitive to the presence of dense floaters. Even more, we found no effect of vitrectomy on any of these measures. In their study of 110 treated eyes, Nie et al., 2013 reported that 71% of their patients had difficulty in reading small print, which markedly improved after surgery[5]. Based on their results, we had hypothesized that RA (i.e. the smallest print one can read) would improve following vitrectomy. However, our results do not

support this hypothesis and suggest that these reading measures may not be valid to quantify the impact of floaters on daily visual function.

We had expected patients with the eyes having the most prominent vitreous opacities to exhibit the greatest improvement in both NEI-VFQ scores and reading performance. This was not the case. In clinical practice, patients with a wide range of vitreous debris are seen, and often individuals with very substantial opacities can be essentially asymptomatic (as in asteroid hyalosis)[28]. Our result, as well as the wide variability in dysfunction among patients with similar vitreous opacities, suggests that the location and motion characteristics of the opacities may be more significant drivers than the level of opacity itself in the decision to seek symptomatic relief with surgery. However, the ability to show the degree of vitreous opacification using the video SLO was found to be helpful for educational purposes, both pre- and post-operatively. First, to show family members dynamically what the patients were seeing. Second, to help persuading patients with significant complaints but mild opacities on SLO testing that surgery would not be prudent. Finally, to document the absence of the opacities post-surgery.

Our work presents some limitations. The main one is the restricted number of patients. In the future, our results should be replicated with larger sets of patients to confirm our findings. Another limitation is that, given the nature of the MNREAD, the current study only measured fluent reading for short sentences. Therefore, it remains to be determined whether speed is also improved (and to what extent) for spot reading (i.e. for isolated words, such as tag labels) and sustained reading (i.e. for long texts).

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Ethical Approval

This study was conducted in accordance with the Declaration of Helsinki. Ethical approval for this study was obtained from the Institutional Review Board (IRB) at the University of South Carolina. The collection and evaluation of all protected patient health information was performed in a Health Insurance Portability and Accountability Act (HIPAA)-compliant manner.

Statement of Informed Consent

Written informed consent was obtained before the study from each patient according to IRB guidelines, including permission for publication of all videos included herein.

References

1. Schulz-Key S, Carlsson J, Crafoord S (2011) Longterm follow-up of pars plana vitrectomy for vitreous floaters: complications, outcomes and patient satisfaction. Acta Ophthalmol 89: 159-65.

2. Tan HS, Mura M, Lesnik Oberstein SY, Bijl HM (2011) Safety of vitrectomy for floaters. Am

J Ophthalmol 151: 995-8.

3. Ivanova T, Jalil A, Antoniou Y, et al. (2016) Vitrectomy for primary symptomatic vitreous opacities: an evidence-based review. Eye (Lond) 30: 645-55.

4. Schiff WM, Chang S, Mandava N, Barile GR (2000) Pars plana vitrectomy for persistent, visually significant vitreous opacities. Retina 20: 591-6.

5. de Nie KF, Crama N, Tilanus MAD, Klevering BJ, Boon CJF (2013) Pars plana vitrectomy for disturbing primary vitreous floaters: clinical outcome and patient satisfaction. Graefes Arch Clin Exp Ophthalmol 251: 1373-82.

6. Sebag J, Yee KMP, Nguyen JH, Nguyen-Cuu J (2018) Long-Term Safety and Efficacy of Limited Vitrectomy for Vision Degrading Vitreopathy Resulting from Vitreous Floaters. Ophthalmology Retina 2: 881--887.

7. Mangione CM, Lee PP, Gutierrez PR, Spritzer K, Berry S, Hays R (2001) Development of the 25-list-item national eye institute visual function questionnaire. Archives of Ophthalmology 119: 1050-1058.

8. Castilla-Marti M, van den Berg TJTP, de Smet MD (2015) Effect of vitreous opacities on straylight measurements. Retina 35: 1240-6.

9. Delaney YM, Oyinloye A, Benjamin L (2002) Nd:YAG vitreolysis and pars plana vitrectomy: surgical treatment for vitreous floaters. Eye (Lond) 16: 21-6.

10. Mason JO 3rd, Neimkin MG, Mason JO 4th, et al. (2014) Safety, efficacy, and quality of life following sutureless vitrectomy for symptomatic vitreous floaters. Retina 34: 1055-61.

11. Hazel CA, Petre KL, Armstrong RA, Benson MT, Frost NA (2000) Visual function and subjective quality of life compared in subjects with acquired macular disease. Invest Ophthalmol Vis Sci 41: 1309-15.

12. McClure ME, Hart PM, Jackson AJ, Stevenson MR, Chakravarthy U (2000) Macular degeneration: do conventional measurements of impaired visual function equate with visual disability?. Br J Ophthalmol 84: 244-50.

13. Murro V, Sodi A, Giacomelli G, et al. (2017) Reading Ability and Quality of Life in Stargardt Disease. Eur J Ophthalmol 27: 740-745.

14. Rubin GS (2013) Measuring reading performance. Vision Res 90: 43-51.

15. Rubin GS, Legge GE (1989) Psychophysics of reading VI - The role of contrast in low vision. Vision Res 29: 79-91.

16. Kakehashi A, Ishiko S, Konno S, Akiba J, Kado M, Yoshida A (1995) Vitreous videography using the scanning laser ophthalmoscope. Jpn J Ophthalmol 39: 377-83.

17. Mojana F, Kozak I, Oster SF, et al. (2010) Observations by spectral-domain optical coherence tomography combined with simultaneous scanning laser ophthalmoscopy: imaging of the vitreous. Am J Ophthalmol 149: 641-50.

18. Mansfield JS, Ahn SJ, Legge GE, Luebker A (1993) A new reading-acuity chart for normal and low vision. Ophthalmic and Visual Optics/Noninvasive Assessment of the Visual System Technical Digest, (Optical Society of America, Washington, DC., 1993.) 3: 232--235.

19. Calabrèse A, To L, He Y, Berkholtz E, Rafian P, Legge GE (2018a) Comparing performance on the MNREAD iPad application with the MNREAD acuity chart. J Vis 18: 8.

20. Calabrèse A, Owsley C, McGwin G, Legge GE (2016a) Development of a Reading Accessibility Index Using the MNREAD Acuity Chart. JAMA Ophthalmol 134: 398-405.

21. R Core Team (2018) R: A Language and Environment for Statistical Computing. Vienna, Austria: R Foundation for Statistical Computing. , https://www.R-project.org/.

22. Zuur AF, Ieno EN, Elphick CS (2010) A protocol for data exploration to avoid common

460 statistical problems. Methods in Ecology and Evolution 1: 3-14.
461 23. Sebag J, Yee KMP, Wa CA, Huang LC, Sadun AA. Vitrectomy For Floaters: Prospective
462 Efficacy Analyses And Retrospective Safety Profile. Retina 2014;34:1062-8.
463 24. Owsley C (2003) Contrast sensitivity. Ophthalmol Clin North Am 16: 171-7.
464 25. Calabrèse A, Cheong AMY, Cheung S, et al. (2016c) Baseline MNREAD Measures for
465 Normally Sighted Subjects From Childhood to Old Age. Invest Ophthalmol Vis Sci 57: 3836-43.
466 26. Johansson J, Pansell T, Ygge J, Seimyr GÖ (2014) Monocular and binocular reading
467 performance in subjects with normal binocular vision. Clin Exp Optom 97: 341-8.
468 27. Garcia GA, Khoshnevis M, Yee KMP, Nguyen-Cuu J, Nguyen JH, Sebag J (2016)
469 Degradation of Contrast Sensitivity Function Following Posterior Vitreous Detachment. Am J
470 Ophthalmol 172: 7-12.
471 28. Khoshnevis M, Rosen S, Sebag J (2019) Asteroid Hyalosis - A comprehensive review. Surv
472 Ophthalmol.

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475 Figure legends

476 Figure 1: Protocol schematic showing the different test procedures along with the resulting
477 outcome measures. Subjective measures are represented in blue; objective measures are
478 represented in pink.

479

Figure 2: Pre and post-operative NEI-VFQ scores grouped by lens opacity status. Points show the mean estimates for the near activity sub-score (A) and the overall composite score (B), both before and after surgery, as estimated by the mixed effects models, for patients with clear lenses in blue (N=10) and patients with mildly opacified lenses in orange (N=10). Error bars represent the 95% confidence intervals.

Figure 3: Effect of pre/post-surgery condition on MRS for the operated eye (top – triangles), the non-operated eye (center - circles) and the binocular condition (bottom – squares) grouped by lens opacity: clear (left – blue) vs. mildly opacified (right - orange). Solid lines connect the estimates for each sub-group as given by the mixed-effects model. Errors bars (black) represent their standard errors. Dashed lines connect the MRS values for each patient, numbered from P1 to P20.

Figure 4: Effect of pre/post-surgery condition on ACC for the operated eye (top – triangles), the non-operated eye (center - circles) and the binocular condition (bottom – squares) grouped by lens opacity: clear (left – blue) vs. mildly opacified (right - orange). Solid lines connect the estimates for each sub-group as given by the mixed effects model. Errors bars (black) represent their standard errors. Dashed lines connect the MRS values for each patient, numbered from P1 to P20.

Figure 5: Post-operative NEI-VFQ near activity sub-score improvement as a function of post-operative reading accessibility index improvement for all 20 patients.

Tables

Patient ID	Location	Gender	Age	Lens opacity in both eyes	Operated eye				Non-operated eye		
					Pathology	SVO	Acuity	OCT-SLO Opacity grading	Pathology	SVO	Acuity
P1	Minnesota	M	58	Clear	PVD	Yes	20/25	2	ERM	No	20/25
P2	Minnesota	M	59	Clear	PVD	Yes	20/20	1.5	--	Yes	20/25
P3	California	M	61	Clear	PVD	Yes	20/20	3	ERM	No	20/40
P4	Minnesota	M	62	Clear	PVD+ ERM	Yes	20/20	1.5	Scleral buckling + ERM	No	20/20
P5	Minnesota	M	64	Clear	PVD+ ERM	Yes	20/15	2	PVD	Yes	20/25
P6	Minnesota	F	64	Clear	PVD	Yes	20/25	2.5	--	Yes	20/20
P7	Minnesota	F	64	Clear	PVD	Yes	20/20	2.5	PVD	Yes	20/25
P8	Minnesota	F	68	Clear	PVD	Yes	20/30	1	PVD	Yes	20/15
P9	California	M	69	Clear	PVD	Yes	20/20	2.5	PVD	Yes	20/20
P10	Minnesota	F	72	Clear	PVD	Yes	20/25	2	PVD	Yes	20/25
P11	California	F	32	Mild opacity	PVD	Yes	20/25	1	PVD	Yes	20/80
P12	California	M	52	Mild opacity	PVD+ ERM	Yes	20/25	2.5	Vitreous Syneresis	No	20/20
P13	California	M	54	Mild opacity	PVD+ ERM	Yes	20/40	3	NPDR	No	20/20
P14	California	F	54	Mild opacity	PVD	Yes	20/25	2.5	PVD	Yes	20/80
P15	Minnesota	M	63	Mild opacity	PVD+ ERM	Yes	20/40	2.5	ERM	Yes	20/25
P16	California	M	63	Mild opacity	PVD+ ERM	Yes	20/80	2	ERM	No	20/25
P17	Minnesota	M	64	Mild opacity	PVD	Yes	20/20	2.5	Vitreous Syneresis	Yes	20/20
P18	California	F	65	Mild opacity	PVD	Yes	20/30	2.5	PVD	Yes	20/25
P19	California	F	67	Mild opacity	PVD	Yes	20/30	2.5	ERM	No	20/25
P20	Minnesota	M	68	Mild opacity	PVD	Yes	20/20	1.5	PVD	Yes	20/25

Table 1: Patients' individual characteristics prior to surgery. SVO stands for symptomatic vitreous opacities; ERM stands for epiretinal membrane. PVD stands for posterior vitreous detachment; NPDR stands for non-proliferative diabetic retinopathy; Visual acuity is given in Snellen notation.

Supplementary material

Movie 1. Video 1, preoperative video SLO. The video is live streaming of scanning laser ophthalmoscopic images from the Heidelberg OCT machine. This is recorded in "Movie Max" mode, (in avi) then converted to .mov. A patient with prominent vitreous opacities months post scleral buckling was instructed to look left and re-fixate, then look right and re-fixate. Shadows from mobile vitreous opacities were projected on the stabilized retinal surface and thus imaged with the infrared camera.

Movie 2. Video 2, postoperative video SLO. The video is recorded in the same manner (with saccades) as Video 1, and of the same eye one week post vitrectomy. Absence of shadowing from vitreous opacities is noted.