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# Impact of Cataract Surgery on Low Luminance Visual Acuity Deficit Measurements

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***Purpose:*** The impact of cataract surgery on low luminance visual acuity deficit (LLVAD) measurements was investigated by measuring the LLVAD before and after cataract surgery.

***Design:*** Prospective, longitudinal study.

***Participants:*** Patients undergoing cataract surgery.

***Methods:*** Photopic luminance (PL)−best-corrected visual acuity (BCVA) and low luminance (LL)−BCVA were obtained using the ETDRS chart. Low luminance visual acuity deficit scores were calculated by subtracting the LL-BCVA letter score from the PL-BCVA letter score. To demonstrate the reproducibility of these visual acuity measurements, we used data from drusen-only eyes previously published in the Complement Inhibition with Eculizumab for the Treatment of Nonexudative Age-Related Macular Degeneration (COMPLETE) study. The PL-BCVA, LL-BCVA, and LLVAD measurements obtained at an interval of 3 months in this cohort were used for comparison. In the current study, the impact of cataract surgery on LLVAD measurements was analyzed by comparing the PL-BCVA, LL-BCVA, and LLVAD measurements before and after cataract surgery.

***Main Outcome Measures:*** The reproducibility of the visual acuity measurements and the changes in LLVAD measurement after cataract surgery.

***Results:*** In the COMPLETE study, no clinically significant differences were found in the PL-BCVA, LL-BCVA, or LLVAD measurements between baseline and the 3-month follow-up visits with a change of −1.1 letters, −1.3 letters, and 0.1 letters, respectively ($P = 0.02$, $P = 0.11$, and $P = 0.88$, respectively). In the current study, significant increases were found in the PL-BCVA and LL-BCVA measurements, with a change of 7.3 letters and 10.2 letters after cataract surgery ($P < 0.001$ for both), and a statistically significant decrease in LLVAD measurements was found, with a change of −3.0 letters after cataract surgery ($P = 0.002$).

***Conclusions:*** Because of the variable effect of cataracts on LL-BCVA measurements and the significant change in LLVAD measurements after cataract surgery, investigators should be aware that cataract surgery during a trial will have an unpredictable impact on LLVAD measurements, and pseudophakic and phakic patients should be analyzed separately. *Ophthalmology Science 2022;2:100170 © 2022 Published by Elsevier Inc. on behalf of the American Academy of Ophthalmology. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).*

Low luminance visual acuity deficit (LLVAD) measurements were carried out first by Sunness et al[1] in a natural history study that prospectively followed up eyes with geographic atrophy (GA) secondary to age-related macular degeneration (AMD). In these eyes with GA, a high correlation was found between the LLVAD measurements obtained at baseline and, after 2 years, the loss of photopic luminance (PL)−best-corrected visual acuity (BCVA), also known as normal luminance BCVA or standard BCVA.[2] Yehoshua et al[3] subsequently showed that the LLVAD measurements obtained at baseline correlated with the growth rate of GA after 6 and 12 months without impacting PL-BCVA. Moreover, this association was the strongest in eyes with noncentral GA with a PL-BCVA of 60 letter or better, which is equivalent to a Snellen BCVA of 20/60 or better. Because a reliable LLVAD measurement requires a foveal cone function,[1,4–8] an explanation of how a decreased foveal LLVAD measurement predicts the growth of GA away from the foveal center remains unexplained. However, this correlation between baseline LLVAD measurements and the growth of GA in AMD has been confirmed in several subsequent clinical trials.[9–14]

Low luminance visual acuity deficit testing is obtained first by using the standard ETDRS chart under PL to obtain a PL-BCVA score, followed by low luminance (LL)−BCVA testing, which is performed by placing a 2.0-log unit neutral density filter in front of the eye.[1] This filter lowers the ambient luminance by 100-fold, and this visual acuity examination under LL is performed immediately after



https://doi.org/10.1016/j.xops.2022.100170
ISSN 2666-9145/22

placing the neutral density filter in front of the eye without allowing any time for dark adaptation, to be consistent with tests that measure cone function.[1,4–8] The LLVAD measurement is calculated by subtracting the LL-BCVA score from the PL-BCVA score.

Although the LLVAD measurements have been shown to be correlated statistically with GA growth and to be helpful in predicting future disease progression in eyes with GA secondary to AMD, the Pearson correlation coefficients tend to be in the moderate range, between 0.2 and 0.4.[3] We hypothesized that one of the reasons for the moderate correlations between LLVAD and GA growth rates could be the variable effect of cataracts on LLVAD measurements because cataracts would be expected to decrease both PL-BCVA and LL-BCVA measurements, but these decreases resulting from the cataracts may not be correlated. Because LLVAD measurements are calculated as the difference between the PL-BCVA and LL-BCVA scores and cataracts may have a variable effect on each of these scores, the LLVAD obtained from pseudophakic eyes may be a more reliable measurement and a more robust predictor of future disease progression. As a result, investigators may need to analyze phakic and pseudophakic eyes separately. Furthermore, if the presence of cataract influences the LLVAD measurements, then this issue is of importance not only for baseline LLVAD measurements but also when tracking LLVAD measurements during a study because intervening cataract surgeries may influence the LLVAD measurements unpredictably. To date, we are unaware of any studies that investigated the influence of cataracts on the LLVAD measurements.[3,15]

To test the impact of cataract surgery on the LLVAD measurements, we designed a prospective study entitled the Comparison of Low-Luminance Visual Acuity Testing before and after Cataract Surgery (COMPARE) Study. However, before we could explore the impact of cataract surgery, we needed to show that our visual acuity measurements were reproducible over a 3-month period that would approximate the testing interval before and after cataract surgery. To test the reproducibility of LLVAD measurements in the absence of cataract surgery, we report herein on the reproducibility of LLVAD measurements from the previously published study entitled the Complement Inhibition with Eculizumab for the Treatment of Non-exudative Macular Degeneration (COMPLETE) Study. In the COMPLETE Study, which investigated eculizumab in patients with AMD with either drusen-only eyes or eyes with GA, the LLVAD measurements were obtained at 3-month intervals using the same ETDRS visual acuity measurement protocols as used in the current COMPARE Study.

## Methods

The COMPARE and COMPLETE Studies were approved by the institutional review board of the University of Miami Miller School of Medicine. Informed consent was obtained from all participants. Both studies were performed in accordance with the tenets of the Declaration of Helsinki and complied with the Health Insurance Portability and Accountability Act of 1996.

The COMPLETE Study (ClinicalTrials.gov identifier: NCT00935883) was designed to evaluate the safety and efficacy of systemic eculizumab for treatment of patients with dry AMD, including eyes with only drusen[15] and eyes with GA.[3] However, to allow for a fair comparison of the participants in the COMPLETE and the COMPARE Studies, we used only the drusen-only eyes from the COMPLETE Study for the reproducibility analysis. Patients with at least 1 druse having a diameter of 250 μm or more observed on fundus microscopy or color fundus photography and a total drusen volume 0.03 $mm^3$ or more as obtained by spectral-domain OCT within a 3-mm circle centered on the fovea were included. The visual acuity examinations and different fundus imaging methods, including autofluorescence, fluorescein angiographic imaging, and spectral-domain OCT, were performed at baseline and at 3 months, 6 months, and 12 months of follow-up. In the present study, we analyzed visual acuity measured only at baseline and the month 3 visit to test the reproducibility of visual acuity measurements, and none of these eyes underwent cataract surgery between the baseline and month 3 follow-up visits. The visual acuity examinations included both PL-BCVA and LL-BCVA measurements. The PL-BCVA was obtained using an ETDRS chart at 4 m under standard luminance, and the LL-BCVA was obtained by inserting a 2.0-log unit neutral density filter in front of the lenses in the trial frame for the eye being examined. This neutral density filter decreased the ambient luminance by 100-fold (Wratten filter; Kodak). Before performing the LL-BCVA measurement, we first performed standard BCVA measurement for both eyes, using chart 1 for the right eye and then chart 2 for the left eye. Then, we tested LL-BCVA for both eyes, using chart 1 for the right eye and then chart 2 for the left eye. The LL-BCVA testing is a mesopic measurement that does not require dark adaptation. Standard back illuminated ETDRS charts were used in our study, and the room was illuminated such that not more than 15-footcandles of light were measured at the center of the chart (with the illuminator cabinet switched off). The surface luminance level at the center of the ETDRS chart with the room lights off was 160 $cd/m^2$. The LLVAD then was calculated by subtracting the LL-BCVA ETDRS letter score from the PL-BCVA ETDRS letter score as described previously.[1,3,15]

Although data from the COMPLETE Study were used to document the reproducibility of visual acuity measurements over 3 months, the effect of cataract surgery on BCVA and LLVAD measurements was investigated in the COMPARE Study. The COMPARE Study enrolled patients with phakic lenses who were scheduled to undergo cataract surgery. These patients were examined before and after cataract surgery. Exclusion criteria included confounding ocular conditions such as an axial length of 23 mm or less or of 26 mm or more, glaucoma, and any evidence of macular atrophy or a hypertransmission defect with a greatest linear dimension of 250 mm or more within a 1-mm circle centered on the fovea, as determined using swept-source OCT angiography imaging as described previously.[16–19] To investigate the effect of cataract surgery on the LLVAD measurement, we measured the BCVA and LLVAD outcomes before and after cataract surgery.

Because the same VA examination protocol was performed in both the COMPLETE and COMPARE Studies, the reproducibility of PL-BCVA, LL-BCVA, and LLVAD measurements at baseline and 3 months in the COMPLETE Study was used as evidence that these measurements should be reproducible before and after cataract surgery in the COMPARE Study. Changes in the BCVA measurements before and after cataract surgery in eyes with different underlying pathologic features also were assessed. In

addition, the correlation between the changes in BCVA examinations and different types of intraocular lenses was analyzed.

Generalized estimating equation (GEE) models with exchangeable correlation structure were used to account for the inclusion of 2 eyes of some participants when assessing change in PL-BCVA, LL-BCVA, and LLVAD over time or before and after cataract surgery. Bland−Altman plots were used to assess reproducibility and potential bias in BCVA measurements between baseline and the 3-month follow-up visits. Histograms were used to summarize the differences in BCVA and LLVAD examinations before and after cataract surgery. Statistical analysis was performed using the IBM Statistical Package for the Social Sciences software, version 24 (IBM Corporation), with a $P$ value of $< 0.05$ considered to be statistically significant.

## Results

A total of 37 eyes with drusen from 26 patients in the COMPLETE Study were included in the current analysis. The average age of the participants was 71 years, and 14 participants (54%) were women. The PL-BCVA, LL-BCVA, and LLVAD measurements from baseline and the month 3 follow-up visits are shown in Table 1. The mean differences in PL-BCVA, LL-BCVA, and LLVAD between the baseline and month 3 follow-up visits were −1.1 letters, −1.3 letters, and 0.1 letters, respectively. Although a statistically significant difference was found in PL-BCVA over 3 months ($P = 0.02$, GEE), this difference of only 1 letter was not considered clinically significant (Fig 1). Moreover, no statistically or clinically significant differences were found in the LL-BCVA and LLVAD measurements over this interval of 3 months ($P = 0.11$ and $P = 0.88$, respectively, GEE), including both phakic and pseudophakic eyes (Fig 1). Bland−Altman plots demonstrated good agreements in PL-BCVA, LL-BCVA, and LLVAD measurements between baseline and the 3-month follow-up visits, with no obvious bias related to PL-BCVA (Fig 2). This analysis of the COMPLETE data demonstrated that PL-BCVA, LL-BCVA, and LLVAD measurements are reproducible and do not change significantly over a 3-month period.

Table 1. Visual Acuity Measurements at Baseline and Month 3 in the Complement Inhibition with Eculizumab for the Treatment of Nonexudative Macular Degeneration Study

| | Baseline | 3-Month Follow-up | Differences (Baseline vs. 3 Months) | P Value |
|---|---|---|---|---|
| PL-BCVA | | | | |
| Mean (SD) | 81.5 (5.7) | 82.6 (6.1) | −1.1 (2.9) | 0.02 |
| Minimum −maximum | 69−90 | 69−94 | −7 to 4 | |
| LL-BCVA | | | | |
| Mean (SD) | 65.3 (9.7) | 66.5 (10.3) | −1.3 (4.7) | 0.11 |
| Minimum −maximum | 37−84 | 43−83 | −11 to 8 | |
| LLVAD | | | | |
| Mean (SD) | 16.2 (5.8) | 16.1 (6.1) | 0.1 (5.3) | 0.88 |
| Minimum −maximum | 4−36 | 5−28 | −9 to 13 | |

BCVA = best-corrected visual acuity; LL = low luminance; LLVAD = low luminance visual acuity deficit; PL = photopic luminance; SD = standard deviation.
All the visual acuity measurements are ETDRS letter scores.

After confirming the overall reproducibility of the VA measurements from the COMPLETE Study, we compared the PL-BCVA, LL-BCVA, and LLVAD measurements before and after cataract surgery in the COMPARE Study. A total of 25 eyes from 20 participants were included in this group from January 2018 to August 2020. The average age of these participants was 71 years, and 12 participants (60%) were women. The average follow-up time was 2.4 months (range, 1.4−7.1 months). Of these 25 eyes, 9 eyes were considered normal without any history of ocular disease, 14 eyes had a diagnosis of intermediate AMD, 1 patient had a history of Plaquenil use for 15 years without retinopathy, and 1 patient had a diagnosis of diabetes mellitus without any retinopathy. Of these 25 eyes, 22 eyes were implanted with monofocal intraocular lenses and 3 eyes were implanted with a monofocal toric intraocular lens during cataract surgery. No complications occurred in any of the patients at the time of cataract surgery.

The PL-BCVA, LL-BCVA, and LLVAD measurements in eyes from the COMPARE Study before and after cataract surgery are shown in Table 2. The differences in PL-BCVA, LL-BCVA, and LLVAD before and after cataract surgery were 7.3 letters, 10.2 letters, and 3.0 letters, respectively. Of note, although PL-BCVA and LL-BCVA measurements were increased significantly after cataract surgery (both $P < 0.001$, GEE), which was as expected, the LLVAD measurements were decreased significantly after cataract surgery ($P = 0.002$, GEE; Fig 3), which suggested that, on average, cataract removal surgery improved LL-BCVA more than it improved PL-BCVA. In Figure 3, this trend toward greater improvement in LL-BCVA than PL-BCVA can be appreciated by comparing the plots in Figure 3A, B. The overall decrease in LLVAD after cataract surgery was not correlated with different eye pathologic features such as intermediate AMD ($P = 0.93$, GEE) or with different types of intraocular lenses ($P = 0.30$, GEE). Histogram plots demonstrated the trends of PL-BCVA, LL-BCVA, and LLVAD measurement changes after cataract surgery (Fig 4).

## Discussion

In this study, we first controlled for the reproducibility of PL-BCVA, LL-BCVA, and LLVAD measurements by showing no clinically significant changes in these measurements over an interval of 3 months by using the data from the COMPLETE Study. With the reproducibility of the LLVAD measurement confirmed, we then investigated the changes of LLVAD measurements after cataract surgery. Our results showed that the LLVAD obtained from phakic eyes is different from the LLVAD obtained in the same eyes after cataract surgery and intraocular lens implantation.

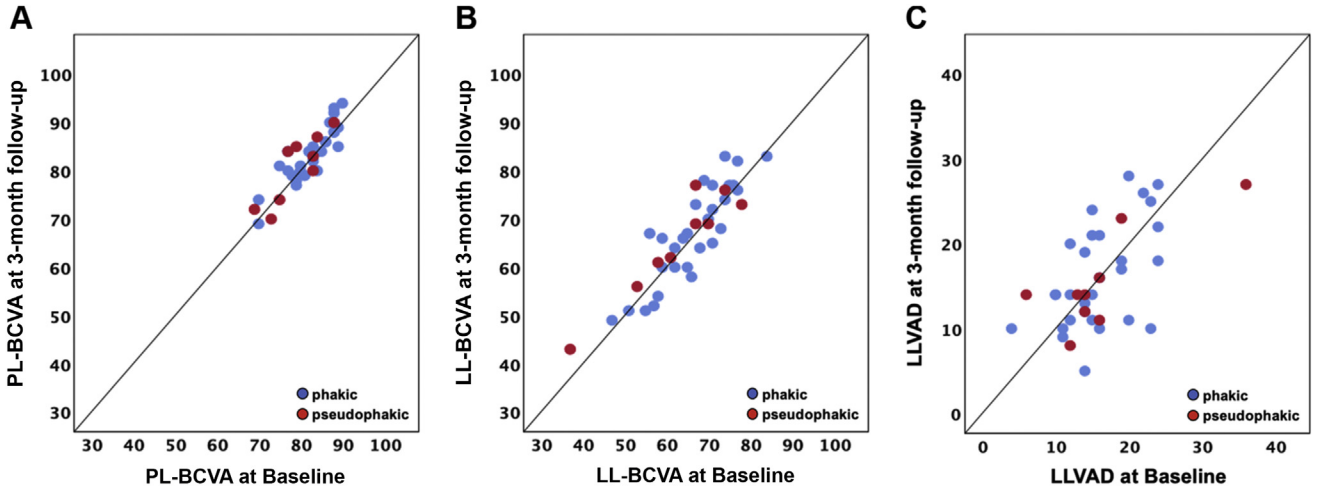


**Figure 1.** Scatterplots showing visual acuity letter score measurements at baseline and the month 3 follow-up visit in the Complement Inhibition with Eculizumab for the Treatment of Non-Exudative Macular Degeneration Study. **A**, Photopic luminance (PL)—best-corrected visual acuity (BCVA) measurements obtained at baseline and the month 3 follow-up visit. Although a statistically significant difference was detected ($P = 0.02$), this change was not considered clinically significant because of the small standard deviation in the variability of these visual acuity measurements. **B**, Low luminance (LL)—BCVA obtained at baseline and the month 3 follow-up visit. No statistically significant difference between the baseline and 3-month follow-up visits was detected ($P = 0.11$). **C**, Low luminance visual acuity deficit (LLVAD) measurements obtained at baseline and the month 3 follow-up visit. No statistically significant difference between baseline and the month 3 follow-up visits was detected ($P = 0.88$). All the visual acuity measurements are ETDRS letter scores.

Therefore, the LLVAD measurements from eyes with cataracts may not be equivalent to the LLVAD measurements obtained from pseudophakic eyes, which has direct implications for the use of LLVAD when monitoring disease progression in AMD. If the cataract itself has a variable impact on the LLVAD measurements, it would affect the design and analysis of clinical trials attempting to use baseline LLVAD measurements to predict future disease progression. This implies that it may not be possible to combine both patients with phakia and patients with pseudophakia in the same analysis or, at least, that caution should be exercised if doing so. Moreover, investigators should be aware that the LLVAD measurements may change unpredictably when cataract surgery is performed during a study.

The impact of cataract surgery on LLVAD measurements resulted from the greater improvement in LL-BCVA than in PL-BCVA after cataract surgery. This finding confirms that LL-BCVA is a more sensitive measurement and can be an independent indicator of foveal function, as reported previously.[1,5–7,20–22] Puell et al[5] found that the impairment of LL-BCVA presented earlier than PL-BCVA in early-stage AMD. Chandramohan et al[6] also found that LL-BCVA was decreased significantly in patients with intermediate

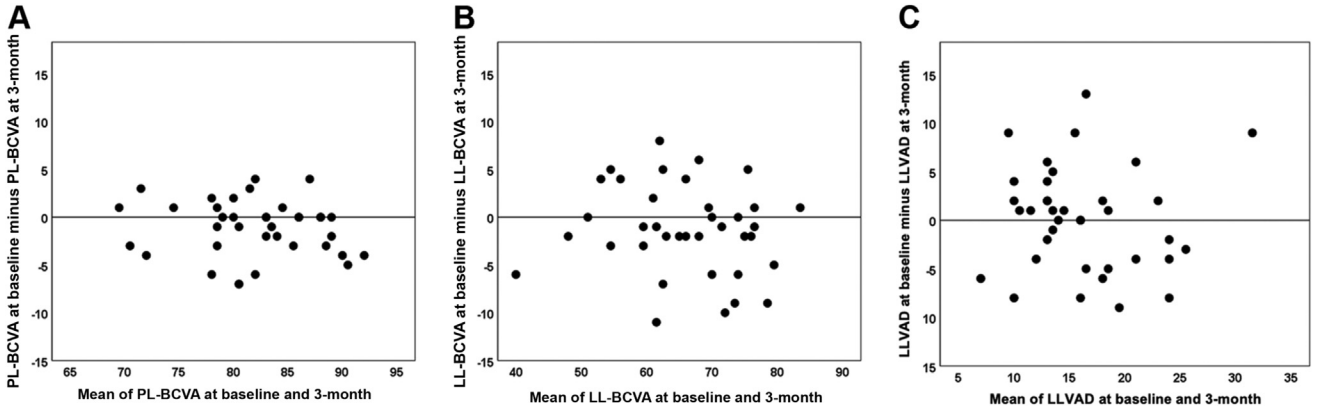


**Figure 2.** Bland-Altman plots showing the differences in (**A**) photopic luminance (PL)—best-corrected visual acuity (BCVA), (**B**) low luminance (LL)—BCVA, and (**C**) low luminance visual acuity deficit (LLVAD) at baseline and the month 3 follow-up visits. The Bland—Altman plots demonstrate agreement in BCVA measurements between baseline and month-3 follow-up in the Complement Inhibition with Eculizumab for the Treatment of Nonexudative Macular Degeneration Study. **A**, **B**, **C**, Good agreement among the PL-BCVA, LL-BCVA, and LLVAD measurements was found at baseline and the month 3 follow-up visit with no obvious bias. All the visual acuity measurements are ETDRS letter scores.

Table 2. Visual Acuity Measurements before and after Cataract Surgery in the Comparison of Low Luminance Visual Acuity Testing before and after Cataract Surgery and Its Association with Choriocapillaris Perfusion Study

| | Before Cataract Surgery | After Cataract Surgery | Differences (before vs. after Cataract Surgery) | *P* Value |
|---|---|---|---|---|
| PL-BCVA | | | | |
| Mean (SD) | 79.0 (6.8) | 86.3 (5.7) | 7.3 (6.3) | <0.001 |
| Minimum–maximum | 57–93 | 74–99 | −2 to 28 | |
| LL-BCVA | | | | |
| Mean (SD) | 63.4 (6.6) | 73.6 (7.8) | 10.2 (6.9) | <0.001 |
| Minimum–maximum | 51–82 | 57–86 | −2 to 20 | |
| LLVAD | | | | |
| Mean (SD) | 15.6 (4.2) | 12.7 (5.3) | −3.0 (5.3) | 0.002 |
| Minimum–maximum | 6–24 | 0–24 | −15 to 10 | |

BCVA = best-corrected visual acuity; LL = low luminance; LLVAD = low luminance visual acuity deficit; PL = photopic luminance; SD = standard deviation.
All the visual acuity measurements are ETDRS letter scores.

AMD compared with healthy control participants. Moreover, LL-BCVA and LLVAD may be a more sensitive measurement of the impact that cataract have on foveal function, so these measurements may be useful for cataract surgeons in assessing the severity of cataracts and how they impact patients' quality of life. One possible explanation for why cataracts affect the LL-BCVA more than the PL-BCVA is the increase in intraocular light scattering, which reduces the retinal image contrast and causes a more substantial decrease in LL vision than in PL vision.[23,24] However, more studies are needed to appreciate how LL-BCVA and LLVAD measurements may be used by cataract surgeons.

One of the limitations of our study is its small sample size (25 eyes). However, the statistical correlations were strong enough to show the impact of cataract surgery on the LLVAD measurements. Another limitation of our study is that we included eyes with ocular pathologic features and different types of intraocular lenses, although most of the eyes were implanted with monofocal intraocular lenses. However, the presence of different pathologic features and lenses showed no statistically significant effect on our finding that LLVAD measurements changed after cataract surgery.

In conclusion, we found that LLVAD measurements were decreased significantly after cataract surgery, and this was because of a greater increase in the LL-BCVA letter score measurements than in PL-BCVA letter scores after surgery. Because it seems that LL-BCVA measurement is a more sensitive visual function measurement than PL-BCVA measurement, the use of LL-BCVA and LLVAD measurements may be useful for monitoring patients with conditions that involve foveal visual function, such as AMD. However, if these measurements are to be used in AMD clinical trials

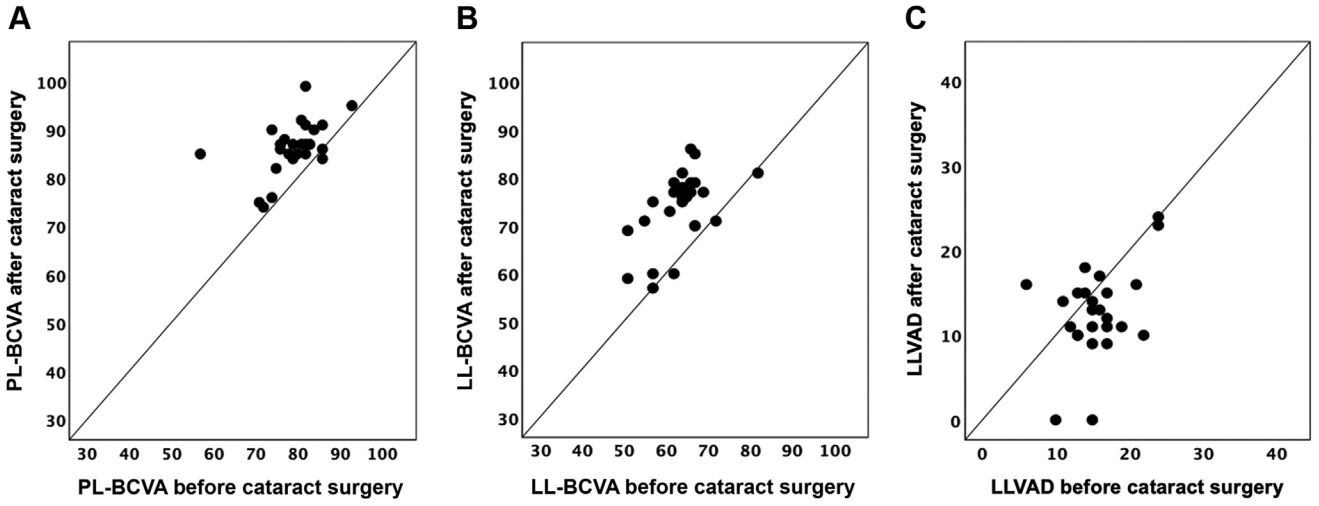


**Figure 3.** Scatterplots showing visual acuity measurements obtained before and after cataract surgery in the Comparison of Low Luminance Visual Acuity Testing before and after Cataract Surgery and Its Association with Choriocapillaris Perfusion Study. **A**, Photopic luminance (PL)–best-corrected visual acuity (BCVA) measurements increased significantly after cataract surgery ($P < 0.001$). **B**, Low luminance (LL)–BCVA measurements increased significantly after cataract surgery ($P < 0.001$). **C**, Statistically significant decrease in low luminance visual acuity deficit (LLVAD) after cataract surgery ($P = 0.002$). All the visual acuity measurements are ETDRS letter scores.

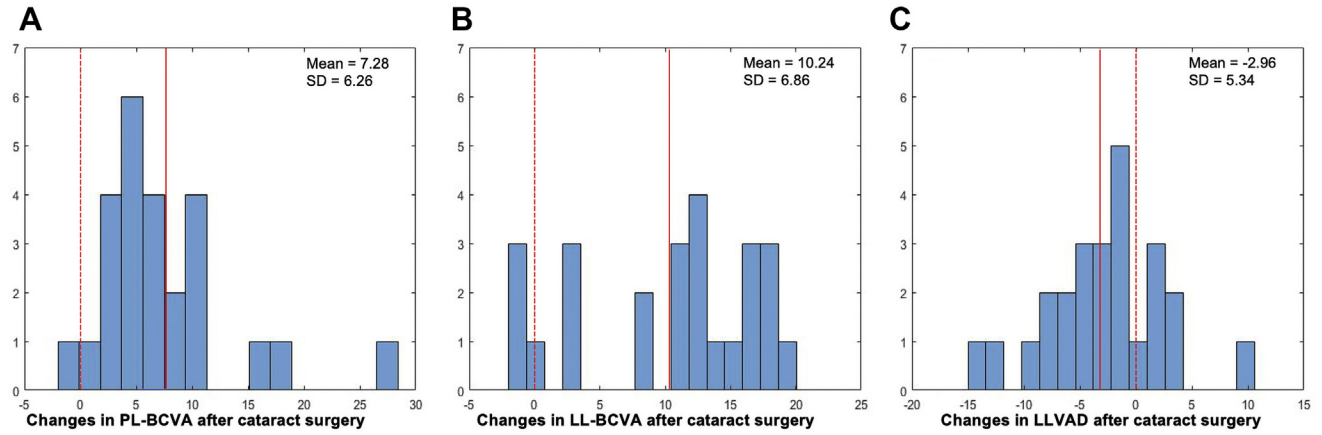


**Figure 4.** Histogram plots showing the changes in (**A**) photopic luminance (PL)—best-corrected visual acuity (BCVA), (**B**) low luminance (LL)—BCVA, and (**C**) low luminance visual acuity deficit (LLVAD) after cataract surgery. An increase in the PL-BCVA and LL-BCVA letter scores after cataract surgery (the solid line representing the mean value is larger than the dotted line at 0) can be appreciated in (**A**) and (**B**), whereas (**C**) shows a decrease in the LLVAD after cataract surgery (the solid line representing the mean value is smaller than the dotted line at 0). All the visual acuity measurements are ETDRS letter scores.

as reliable markers of foveal function and as a predictors of disease progression, then cataract surgery during the trial should be avoided, patients with phakia and pseudophakia should be stratified at baseline, and the protocol should prespecify that patients with pseudophakia and phakia should be analyzed separately.

## Footnotes and Disclosures

Originally received: February 5, 2022.
Final revision: April 24, 2022.
Accepted: May 12, 2022.
Available online: May 18, 2022. Manuscript no. XOPS-D-21-00232

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Disclosure(s):

All authors have completed and submitted the ICMJE disclosures form.

The author(s) have made the following disclosure(s):

J.F.R.: Consultant — Carl Zeiss Meditec

G.G.: Financial support and Patent — Carl Zeiss Meditec, Inc.

P.J.R.: Consultant — Apellis, Boehringer-Ingelheim, Carl Zeiss Meditec, Chengdu Kanghong Biotech, Ocunexus (InflammX) Therapeutics, Ocudyne, Regeneron Pharmaceuticals, Unity Biotechnology; Financial support — Gyroscope Therapeutics, Stealth BioTherapeutics, Carl Zeiss Meditec, Inc.; Equity owner — Apellis, Valitor, Verana Health, Ocudyne.

Supported by the National Eye Institute, National Institutes of Health, Bethesda, Maryland (grant no.: P30EY014801 to the Department of Ophthalmology, University of Miami Miller School of Medicine); the Salah Foundation; and Research to Prevent Blindness, Inc., New York, New York; The funding organizations had no role in the design or conduct of the present research.

HUMAN SUBJECTS: Human subjects were included in this study. The COMPARE and COMPLETE studies were approved by the institutional review board of the University of Miami Miller School of Medicine. Both studies were performed in accordance with the tenets of the Declaration of Helsinki and complied with the Health Insurance Portability and Accountability Act of 1996. Informed consent was obtained from all participants.

No animal subjects were included in this study.

Author Contributions:

Conception and design: Shen, Shi, Yoo, Rose, Habash, Amescua, Feuer, Gregori, Rosenfeld

Analysis and interpretation: Shen, Shi, Wang, Russell, Jiang, Laiginhas, Iyer, Trivizki, Thulliez, Yoo, Rose, Habash, Amescua, Feuer, Gregori, Rosenfeld

Data collection: Shen, Shi, Wang, Russell, Jiang, Laiginhas, Iyer, Trivizki, Thulliez, Yoo, Rose, Habash, Amescua, Feuer, Gregori, Rosenfeld

Obtained funding: N/A; Study was performed as part of the authors' regular employment duties. No additional funding was provided.

Overall responsibility: Shen, Shi, Wang, Russell, Jiang, Laiginhas, Iyer, Trivizki, Thulliez, Yoo, Rose, Habash, Amescua, Feuer, Gregori, Rosenfeld

Abbreviations and Acronyms:
**AMD** = age-related macular degeneration; **BCVA** = best-corrected visual acuity; **COMPARE** = Comparison of Low-Luminance Visual Acuity Testing before and after Cataract Surgery; **COMPLETE** = Complement Inhibition with Eculizumab for the Treatment of Nonexudative Age-Related Macular Degeneration; **GA** = geographic atrophy; **GEE** = generalized estimating equation; **LL** = low luminance; **LLVAD** = low luminance visual acuity deficit; **PL** = photopic luminance.

Keywords:
Cataract surgery, Low luminance visual acuity deficit.

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