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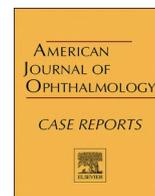
### Publication Date

2025-06-01

### DOI

10.1016/j.ajoc.2025.102294

Peer reviewed



## Outer retinal reflectivity and visual function loss after anatomically successful macula-off rhegmatogenous retinal detachment repair

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### ARTICLE INFO

#### Keywords:

Retinal detachment  
Adaptive optics  
Optical coherence tomography

### ABSTRACT

**Purpose:** Rhegmatogenous retinal detachment (RRD) can cause permanent photoreceptor damage with subsequent vision loss, even after prompt repair. Here we compared photoreceptor structure in retinal areas with varying levels of residual visual function loss following anatomically successful macula-off RRD repair.

**Observations:** Five eyes of four individuals (2 male, 2 female; ages 18–77 years) with successful macula-off RRD repair were included. Two were repaired via scleral buckle, one via vitrectomy, and two with both. Postoperative visual acuity measured 4–11 months after surgical repair ranged from 20/20 to 20/100. In each eye, areas of previously detached macula exhibited reduced or variable cone reflectivity on adaptive optics scanning light ophthalmoscopy (AOSLO) images. This was typically associated with reduced or variable inner segment/outer segment junction (IS/OS) band reflectivity on optical coherence tomography (OCT) images. Areas of the macula with reduced photoreceptor reflectivity also showed lower sensitivity on microperimetric testing.

**Conclusions:** Despite anatomically successful repair, RRD results in photoreceptor changes, including reduced reflectivity of cone profiles and the IS/OS band that were associated with reduced macular sensitivity. As ophthalmologic imaging progresses towards higher resolution modalities, AOSLO may be useful in monitoring outcomes after RRD repair. Low cone reflectivity, cataract, high axial length, and poor visual fixation may be barriers to quantification of cone structure in this patient population.

### 1. Introduction

Rhegmatogenous retinal detachment (RRD), a vision-threatening condition in which the neurosensory retina is separated from the underlying retinal pigment epithelium, is the most common indication for vitreoretinal surgery.<sup>1</sup> Even after prompt surgical repair (e.g. via pars plana vitrectomy [PPV] or scleral buckle), macula-off RRDs (in which subretinal fluid detaches the macular retina) cause a variable extent and severity of visual deficits.<sup>2</sup> Pre-operative clinical factors that have been associated with postoperative visual outcomes include the duration of macular detachment, extent of detachment, and pre-operative visual acuity (VA).<sup>3–5</sup> Several studies have sought to elucidate retinal structural factors contributing to variable postoperative visual outcomes after RRD.<sup>3–10</sup> Using high resolution retinal imaging, such as optical coherence tomography (OCT), researchers have also identified post-operative factors associated with visual outcomes after RRD. In particular,

disrupted integrity of the inner segment/outer segment junction (IS/OS) or ellipsoid zone (EZ) band, residual foveal detachment, and persistent subretinal fluid have been associated with worse VA after successful RRD repair.<sup>3,6–10</sup>

Given the observed association of IS/OS band integrity with post-operative visual outcomes, there has been interest in characterizing photoreceptor structure with high resolution after RRD. Some researchers have utilized adaptive optics scanning light ophthalmoscopy (AOSLO), a noninvasive technique that compensates for higher order ocular aberrations to image light waveguided by photoreceptors and produce images with single cell resolution.<sup>11–13</sup> Using AOSLO, Saleh et al. reported a nearly 30 % lower cone density in eyes after macula-off RRD repair compared to the fellow eye.<sup>11</sup> Additionally, lower cone density was associated with worse VA in that study.<sup>11</sup>

Existing studies characterizing OCT and AOSLO predictors of post-operative RRD outcomes have mainly used VA to describe visual

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<https://doi.org/10.1016/j.ajoc.2025.102294>

Received 8 December 2024; Received in revised form 30 January 2025; Accepted 21 February 2025

Available online 24 February 2025

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outcome. In contrast, Reumueller et al. assessed retinal morphology using adaptive optics OCT and retinal function with fundus-guided microperimetry in five patients after RRD repair,<sup>12</sup> which allowed for localized assessment of macular structure and function in regions beyond the fovea. They demonstrated an association between photoreceptor density and macular sensitivity one year postoperatively.<sup>12</sup>

We hypothesize that after RRD repair, localized differences in cone photoreceptor reflectivity may explain differences in retinal sensitivity. To test this hypothesis, we used AOSLO, spectral domain OCT (Heidelberg Spectralis, Heidelberg Engineering Inc., Franklin, MA), and mesopic fundus-guided microperimetry testing using a Humphrey 10-2 grid and a Goldmann III spot (MAIA, iCare, San Jose, CA) to subjectively assess structural and functional changes after surgical repair of macula-off RRD (Table 1). The extent of retinal detachment in each case is shown in Supplement 1. The methods used to obtain AOSLO images have been previously described in detail.<sup>14-17</sup> AOSLO imaging of normal retinas demonstrates a confluent mosaic of hyperreflective dots representing normal cone profiles.<sup>18-20</sup> The current study assessed cone reflectance profiles, which represent light waveguided from cones with intact and organized inner and outer segments,<sup>18,19</sup> and highlighted challenges in using high resolution retinal imaging, in individuals with anatomically successful RRD repair. This information will contribute to improved understanding of the etiology of postoperative visual deficits in RRD patients.

**2. Findings**

**2.1. Case 1 (UCSF AOSLO #40220)**

An 18-year-old male with high myopia (-9.00 + 0.25 × 060 in the right eye, -7.00 + 0.75 × 030 in the left eye) presented 5 days after losing central vision with RRD involving the entire macula in the right eye (Supplement 1a). Initial repair was achieved via scleral buckle, external drainage, and cryotherapy 11 days after losing central vision. The patient developed recurrent macula-off RRD 1 week after the initial surgical repair, and the second retinal detachment was repaired with PPV, endolaser, and perfluoropropane gas bubble. Although postoperative vision was 20/25 11 months after surgical repair, microperimetry testing revealed decreased sensitivity in the central inferonasal macula (Fig. 1a, middle). AOSLO imaging revealed lower cone reflectivity in areas with lower microperimetry sensitivity (Fig. 1a, top).

This individual subsequently developed a RRD in the left eye involving nearly the entire macula (Supplement 1b) 2 weeks after laser retinopexy treatment of peripheral lattice degeneration. Anatomically successful repair was achieved 4 days after being diagnosed with macula-off RRD via PPV, endolaser, perfluoropropane gas bubble, and scleral buckle. Postoperative visual acuity was 20/40-1 8 months after repair. Microperimetry testing, AOSLO, and OCT imaging demonstrated a similar pattern in which areas with lower macular sensitivity also had lower cone reflectivity and greater disruption of the IS/OS junction

band, along with inner retinal cysts nasal to the fovea (Fig. 1b).

At some locations in each eye, AOSLO image resolution did not permit reliable quantification of cone density, partially attributable to high myopia (axial length 27.7 mm in the right eye; 26.5 mm in the left eye) and inability to maintain the fovea stably on the fixation target. Repeat AOSLO imaging was attempted at 4 visits over an 11-month period without significant improvement in image quality.

**2.2. Case 2 (UCSF AOSLO #40219)**

A 47-year-old female developed RRD involving the inferotemporal half of the left macula (Supplement 1c), which was repaired 3 months after developing peripheral visual field loss and 7 days after being diagnosed with macula-off RRD using scleral buckle with external drainage. Postoperative VA was 20/25 4 months after surgical repair. Macular sensitivity and AOSLO cone reflectivity were reduced in the temporal macula (Fig. 2). There was decreased IS/OS junction band reflectivity immediately nasal to the fovea in a region with variable cone reflectivity (Fig. 2, top) where sensitivity was preserved, and slightly higher than in the temporal macula where cone reflectivity in AOSLO images was reduced (Fig. 2, blue inset). AOSLO, OCT, and microperimetry images of the fellow eye (the unaffected right eye) are provided in Supplement 2a, which demonstrates less heterogeneity in cone reflectivity.

**2.3. Case 3 (UCSF AOSLO #40216)**

A 77-year-old male presented with a RRD involving the entire macula in the right eye (Supplement 1d), which was repaired 6 days after losing central vision via PPV, internal drainage, endolaser, and perfluoropropane gas bubble. Postoperative visual acuity was 20/25 + 2 at 6 months. In the inferotemporal macula, there was reduced sensitivity on microperimetry in regions with reduced reflectivity of the IS/OS junction band (Fig. 3). Postoperatively, he developed a nuclear sclerotic and posterior subcapsular cataract, which precluded acquisition of unambiguous AOSLO images of photoreceptor structure. AOSLO, OCT, and microperimetry images of the fellow eye (with nuclear sclerotic cataract but without posterior subcapsular cataract) are provided in Supplement 2b for reference.

**2.4. Case 4 (MCW #TC\_12383)**

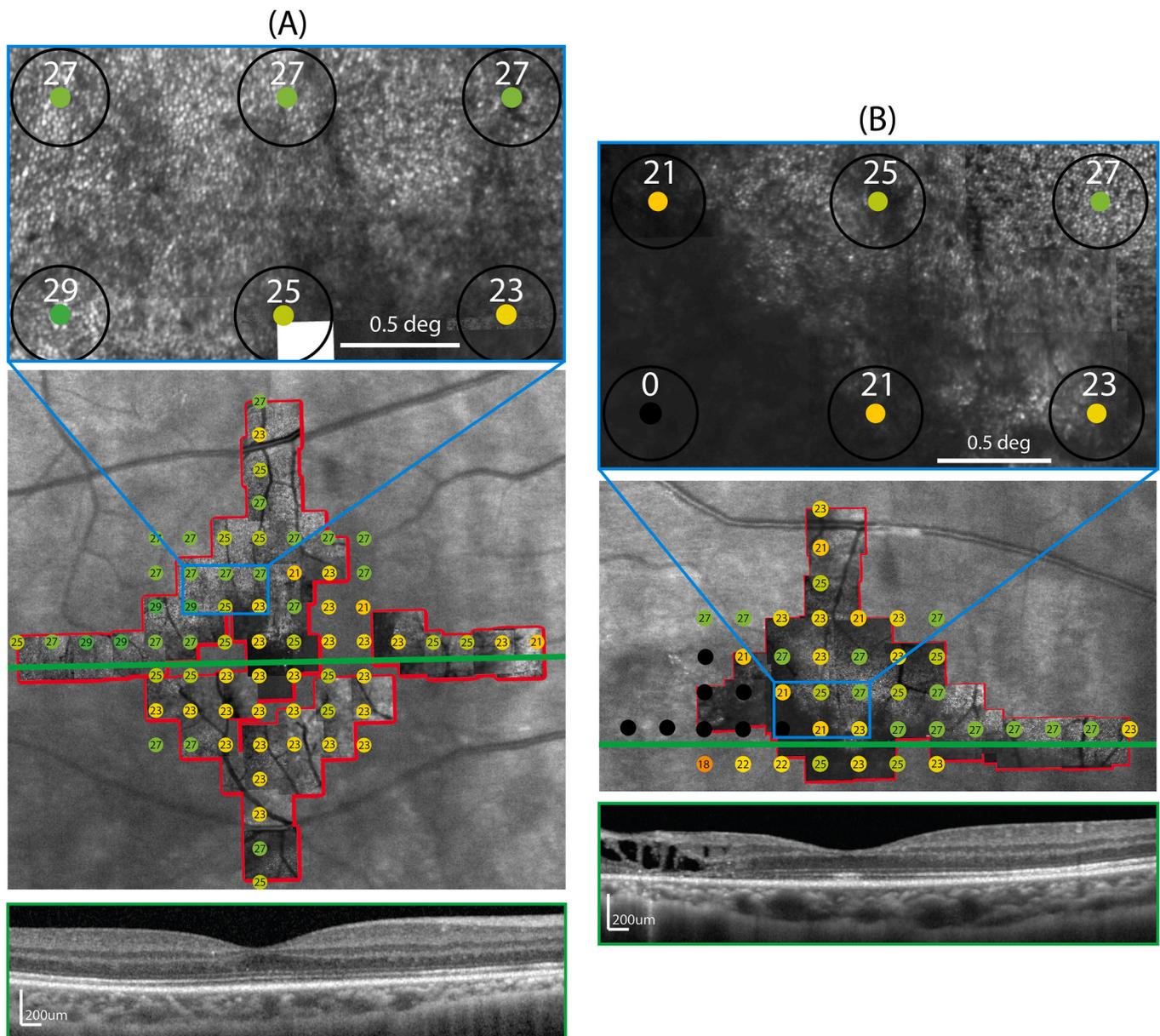
A 71-year-old female presented with an RRD involving the entire macula in the left eye, which was repaired via PPV, perfluorocarbon liquid, endolaser, and perfluoropropane gas bubble. Postoperative visual acuity was 20/20 at 5 months. Imaging demonstrated mild variability in AOSLO cone profile reflectivity and mild IS/OS junction band disruption throughout the horizontal foveal OCT scan (Fig. 4). Microperimetry was not assessed in this case.

**Table 1**  
Subject characteristics.

Subject (AOSLO ID)	Age	Eye	Surgical approach	Time from symptom onset to repair	Time from repair to study imaging	Preoperative Visual Acuity	Postoperative Visual Acuity
1 (40220)	18	Right	PPV, endolaser, and C <sub>3</sub> F <sub>8</sub> gas bubble	11 days	11 months	20/200	20/25
1 (40220)	18	Left	PPV, endolaser, C <sub>3</sub> F <sub>8</sub> gas bubble, and SB	5 days	8 months	20/200	20/40-1
2 (40219)	47	Left	SB and external drainage	3 months	4 months	20/400	20/25
3 (40216)	77	Right	PPV, internal drainage, endolaser, and C <sub>3</sub> F <sub>8</sub> gas bubble	About 2 weeks	6 months	Counting Fingers	20/25 + 2
4 <sup>a</sup> (TC_12383)	71	Left	PPV, endolaser, and C <sub>3</sub> F <sub>8</sub> gas bubble.	1.5 months	5 Months	20/100	20/20

PPV: Pars-Plana Vitrectomy; SB: Scleral Buckle; C<sub>3</sub>F<sub>8</sub>: perfluoropropane.

<sup>a</sup> Surgery was done at an outside center.



**Fig. 1.** Case 1 (ID 40220R and 40220L)

Image overlay of adaptive optics scanning light ophthalmoscopy, optical coherence tomography, and microperimetry data of an 18-year-old male with rhegmatogenous retinal detachment in the right (1a) and left (1b) eyes. Lower microperimetry sensitivity was detected in areas with lower cone reflectivity and inner segment/outer segment junction band reflectivity after retinal detachment repair, adjacent to regions with inner retinal cysts.

### 3. Discussion

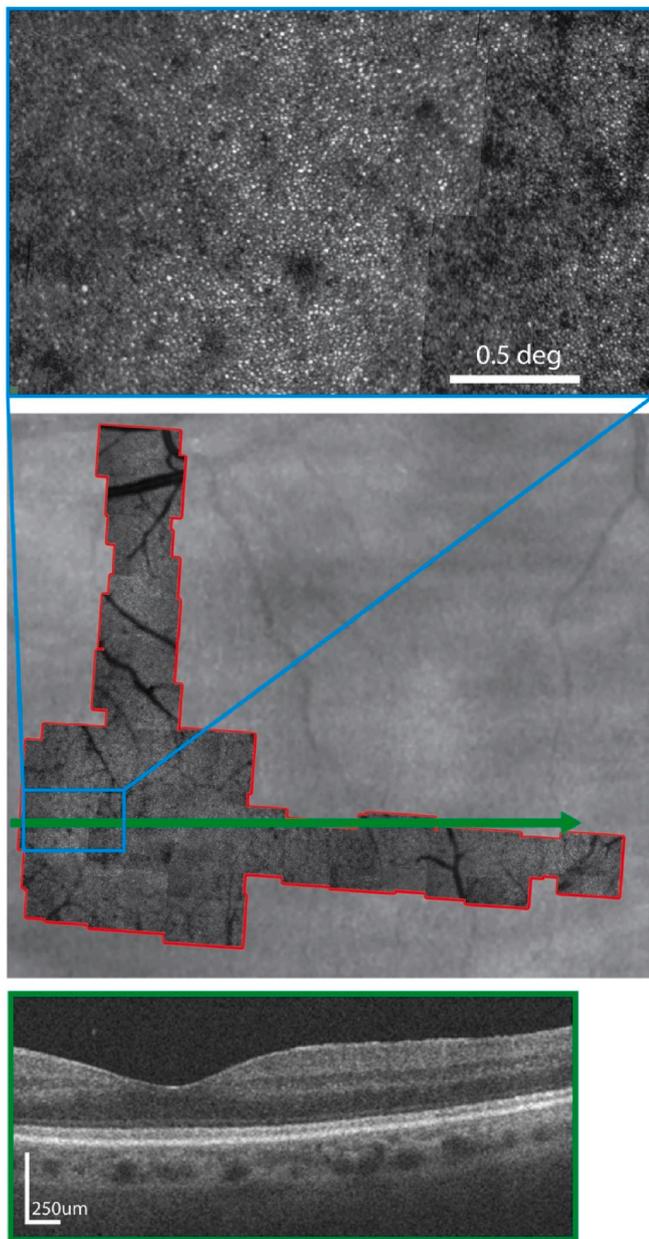
Several studies have reported high variability in VA outcomes after RRD repair.<sup>2-5</sup> In turn, there has been interest in using high resolution retinal imaging to detect structural changes that may account for differences in VA.<sup>3,6-11,21</sup> In this series of five cases of macula-off RRD in four individuals, there was significant variability in AOSLO cone reflectivity and OCT IS/OS junction band reflectivity after anatomically successful repair. In four cases, the variability in reflectivity was pronounced; on the other hand, there was very mild variability in reflectivity 5 months after repair in Case 4 despite detachment of the entire macula.

VA is only one component of visual function, and it does not capture all the impacts of RRD on vision. In fact, a study of 92 patients with RRD found that VA increased during the first postoperative year, but patient satisfaction with their vision did not.<sup>22</sup> Using microperimetry testing for

a more comprehensive assessment of visual function in the macula, the present study found reduced sensitivity in previously detached areas of the macula, even in the absence of persistent subretinal fluid, in most patients with excellent foveal VA.

Three eyes of two individuals were studied with both microperimetry and AOSLO. In each of these eyes, macular sensitivity was lower in areas with lower cone reflectivity. Four eyes of three individuals were assessed using both microperimetry and OCT. In three of these four eyes, disruption and reduced reflectivity of the IS/OS junction band corresponded with reduced macular sensitivity. However, in Case 2, macular sensitivity was preserved in a region of IS/OS junction band hyporeflectivity with significant accompanying disruption of the OS/retinal pigmented epithelium or interdigitation zone band (Fig. 2). The variability in outer retinal reflectivity observed with high-resolution retinal images, including AOSLO cone profiles and the IS/OS junction band, demonstrates retinal disruption even in regions with preserved retinal





**Fig. 4.** Case 4 (ID TC\_12383)

Adaptive optics scanning light ophthalmoscopy (AOSLO) and optical coherence tomography images from of a 71-year-old female with rhegmatogenous retinal detachment in the left eye. There was mild variability in the AOSLO cone profile and IS/OS junction band reflectivity.

function in cases 1 and 2.<sup>12</sup>

AOSLO and adaptive optics OCT are not widely used in the clinical setting due to factors such as cost, convenience, and availability. However, as these technologies continue to develop, it is possible that they may become useful tools for the prediction of visual functional outcomes after RRD. Compared to spectral domain OCT, AOSLO images provide greater resolution of cone structure; the additional resolution provided with AO may be more sensitive to detect changes in photoreceptor morphology<sup>12</sup> and may reveal improvement in cone reflectivity after retinal detachment repair earlier<sup>21</sup> in future studies of patients imaged longitudinally comparing AOSLO and standard measures.

The results of this study should be interpreted in the context of its several limitations. First, this study subjectively compared results of different testing modalities within the same subject. The lateral

resolution of OCT and fundus-guided microperimetry are not commensurate with the lateral resolution of AOSLO images, which may limit the ability to precisely compare structure and function in different areas of the macula. Use of adaptive optics-guided microperimetry could yield more accurate comparisons, but challenges of unstable fixation and reduced cone reflectivity would complicate reliable measures of microperimetry with adaptive optics.<sup>26</sup> Second, this study included only five eyes, three of which underwent all three testing modalities. Third, due to the unexpected nature of RRD, pre-operative data was not available; for this reason, we compared areas that were not detached with areas that had been detached within the same eye. Fourth, image quality of some regions in the AOSLO images did not permit quantitative analysis of cone structure. Fifth, this study did not capture longitudinal changes in photoreceptor structure in all patients. Longitudinal imaging was not possible in several patients who developed cataract at later time points, including Case 3. Future longitudinal studies will be needed to assess changes in retinal structure and function, which may begin within one week<sup>21</sup> and can continue beyond one year after RRD repair.<sup>12</sup> Imaging in the early postoperative period was not done in these cases. AOSLO can be performed acutely after RRD in some cases repaired with pneumatic retinopexy after the gas has resorbed. One such case demonstrated return of cone profile reflectivity within the first week, followed by progressive increase in cone density.<sup>21</sup> The current study did not evaluate dynamic longitudinal changes in cone structure that occur after RRD repair, but demonstrated imaging challenges associated with high myopia and post-operative media imperfections that are common features after RRD repair.

#### 4. Conclusion

Despite prompt anatomically successful repair, RRD resulted in variable photoreceptor changes, including reduced reflectivity of the IS/OS junction band (on OCT) and cone profiles (on AOSLO). In most cases, low photoreceptor reflectivity was associated with reduced macular sensitivity. If these findings are corroborated in future research, AOSLO may be useful in monitoring structural outcomes or predicting visual function after RRD repair.

#### CRedit authorship contribution statement

**Ajay Kolli:** Writing – review & editing, Writing – original draft, Methodology, Formal analysis, Data curation. **Jessica Wong:** Writing – review & editing, Visualization, Methodology, Formal analysis, Data curation. **Stephanie Duret:** Writing – review & editing, Visualization, Methodology, Formal analysis, Data curation. **Jay M. Stewart:** Writing – review & editing, Data curation, Conceptualization. **Thomas B. Connor:** Writing – review & editing, Methodology, Investigation, Data curation. **Austin Roorda:** Writing – review & editing, Visualization, Project administration, Methodology, Formal analysis, Data curation, Conceptualization. **Joseph Carroll:** Writing – review & editing, Visualization, Project administration, Methodology, Formal analysis, Data curation, Conceptualization. **Jacque L. Duncan:** Writing – review & editing, Visualization, Supervision, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization.

#### Patient consent

Written consent to participate in the study and publish this data was obtained from each patient.

#### Disclosures

No author has any financial conflict of interest related to the work in this manuscript. The following authors have no financial disclosures: AK, JW, SD, TC, AR. JS has financial relationships with Zeiss, Merck,

Roche, Valitor, Long Bridge, and Twenty Twenty; unrelated to the topic of this work. JC has financial relationships with Translational Imaging Innovations and MeiraGTx, unrelated to the topic of this work. JLD has the following financial relationships: Acucela, AGTC, Allergan/Abbvie, Ascidian; Biogen/NightstaRx, ProQR, PYC Therapeutics, and Thea/SepulBio, all of which provide funding to UCSF for patients enrolled in clinical trials, and stock in RxSight (Spouse), which is unrelated to the current work.

### Authorship

All authors attest that they meet the current ICMJE criteria for Authorship.

### Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

### Grant Support:

Research reported in this publication was supported in part by the National Eye Institute of the National Institutes of Health under award numbers P30EY002162, R01EY023591, & U24EY029891. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health. Additional support from Foundation Fighting Blindness (FFB-BR-CL-0720-0784-MCW), Larry L. Hillblom Foundation Network Grant #2014-A-003-NET, and an unrestricted grant from Research to Prevent Blindness, New York, NY (JD). The funding sources did not have a role in the design, execution, or decision to publish this work.

### Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ajoc.2025.102294>.

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