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

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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. 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. 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). Several studies have sought to elucidate retinal structural factors contributing to variable postoperative visual outcomes after RRD. 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. $^{3,6-10}$

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. ^{11–13} Using AOSLO, Saleh et al. reported a nearly 30 % lower cone density in eyes after macula-off RRD repair compared to the fellow eye. ¹¹ Additionally, lower cone density was associated with worse VA in that study. ¹¹

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

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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, ¹² 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. ¹²

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 maculaoff 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. 14-17 AOSLO imaging of normal retinas demonstrates a confluent mosaic of hyperreflective dots representing normal cone profiles. 18-20 The current study assessed cone reflectance profiles, which represent light waveguided from cones with intact and organized inner and outer segments, 18,19 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 $(-9.00+0.25\times060)$ in the right eye, $-7.00+0.75\times030$ 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 post-operative 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 ₃ F ₈ gas bubble	11 days	11 months	20/200	20/25
1 (40220)	18	Left	PPV, endolaser, C ₃ F ₈ 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 ₃ F ₈ gas bubble	About 2 weeks	6 months	Counting Fingers	20/25 + 2
4 ^a (TC_12383)	71	Left	PPV, endolaser, and C3F8 gas bubble.	1.5 months	5 Months	20/100	20/20

PPV: Pars-Plana Vitrectomy; SB: Scleral Buckle; C₃F₈: perfluoropropane.

^a Surgery was done at an outside center.

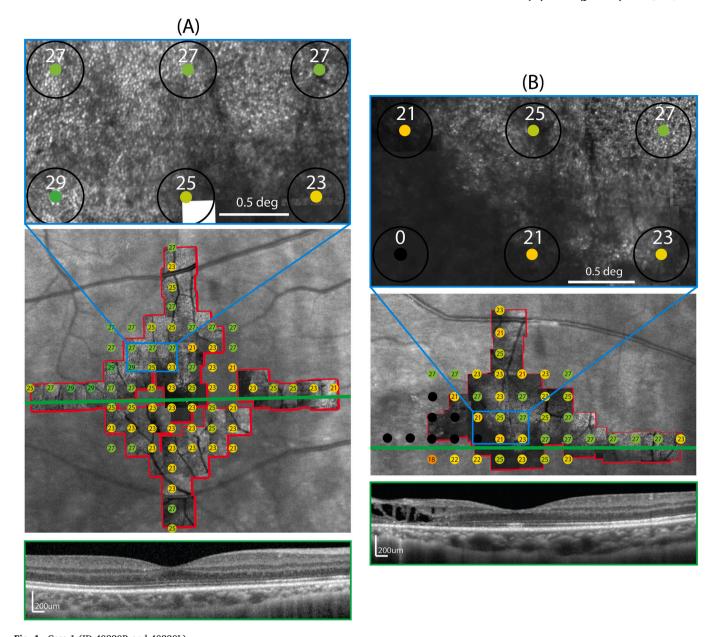


Fig. 1. Case 1 (ID 40220R and 40220L)
Image overlay of adaptive optics scanning light ophthalmoscopy, optical coherence tomography, and microperimetry data of an 18-year-old male with rhegmatogenous retinal detachment in the right (1a) and left (1b) eyes. Lower microperimetry sensitivity was detected 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.

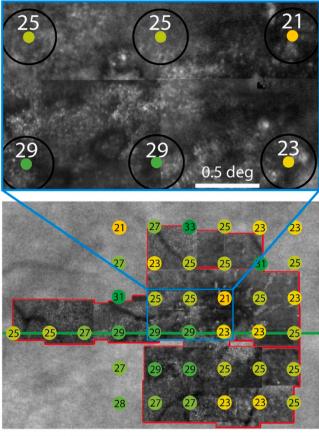
3. Discussion

Several studies have reported high variability in VA outcomes after RRD repair. ^{2–5} In turn, there has been interest in using high resolution retinal imaging to detect structural changes that may account for differences in VA. ^{3,6–11,21} 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. ²² 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



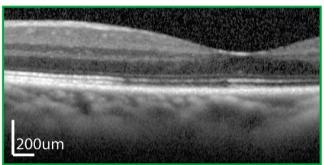


Fig. 2. Case 2 (ID 40219L)

Image overlay of adaptive optics scanning light ophthalmoscopy, optical coherence tomography, and microperimetry data of a 47-year-old female with rhegmatogenous retinal detachment in the left eye. Nasal to the fovea, there is an area with preserved microperimetry sensitivity despite decreased IS/OS band reflectivity and variable cone profile reflectivity.

sensitivity after successful anatomic RRD repair. This relatively preserved macular function likely originates from the best-preserved cones exposed to the stimulus. It is possible that the variability in reflectivity represents disruption of the rod IS/OS junction and outer segment tips in a region with preserved cone outer segments; this would result in disruption of the IS/OS junction and OS/retinal pigmented epithelium bands on OCT given the greater number of rods than cones in the macula, but possibly may not alter cone profile reflectivity on AOSLO. This could explain the preserved macular sensitivity and AOSLO cone profile reflectivity in this area despite the OCT EZ reflectivity changes, which are of lower resolution than the en face AOSLO cone images. High-resolution retinal imaging may indicate subtle disruption or abnormality in cone structure that is not apparent from measurement of macular sensitivity after retinal detachment repair, which may contribute to patient experience of reduced visual function despite

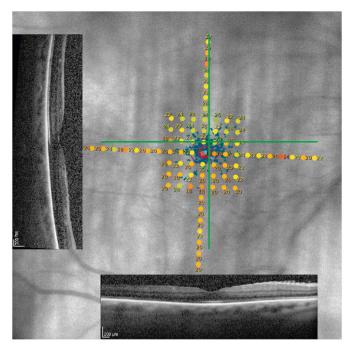


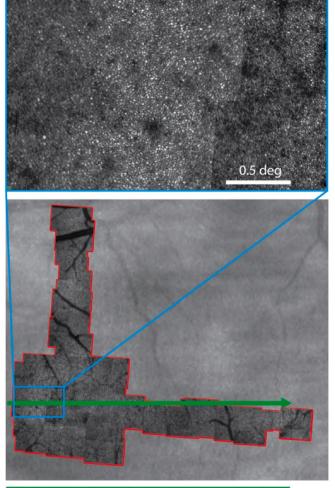
Fig. 3. Case 3 (ID 40216)

Image overlay of optical coherence tomography and microperimetry data of a 77-year-old male with rhegmatogenous retinal detachment in the right eye. In the inferotemporal macula, there was both reduced sensitivity on microperimetry and disruption of the IS/OS junction band.

recovery of visual acuity.

The resolution of AOSLO images in this study was limited by several factors. Myopia, high axial length, cataract, and poor fixation with excessive eye movement are all common in patients who have had RRD repair. AOSLO imaging in patients with any combination of these factors is challenging and image quality may be limited. In this case series, the image quality and variability of cone reflectivity in some images precluded the quantification of cone density (i.e. the number of reflective cone profiles per area of retina), which requires unambiguous identification of every cone in the mosaic for accurate measurement. Moreover, the decreased cone reflectivity after RRD repair may itself pose a barrier to cone quantification. If AOSLO were used to monitor cones in patients with RRD in the future, ophthalmologists may have to rely on qualitative interpretation of cone reflectivity since reduced reflectivity complicates quantification of cone spacing and density, similar to the current practice pattern for clinical use of OCT.^{8,23} Imaging with split detector AOSLO may reveal cone structure in the context of outer segment disruption, but the regions most affected in the current study were close to the foveal center, where resolution of AOSLO split detector images is limited. 18,24,25

A similar study was conducted by Reumueller et al. using adaptive optics OCT rather than AOSLO. ¹² That study similarly found irregularity of cone reflectivity patterns in eyes after retinal detachment repair compared to control fellow eyes. Images in that study demonstrated very limited visibility of cone structure in eyes with retinal detachment (Reumueller et al., Figs. 2–4)¹² in comparison to the AOSLO images shown in the present manuscript. Despite lower cone visibility, adaptive optics OCT provided 3-dimensional volume scans, allowing assessment of individual retinal layers over 1 year of follow up. Although the AOSLO image quality in our study was limited and reliable quantification of cone density over much of the affected area was not possible because not every cone in the mosaic was clearly visible, the resolution of AOSLO images was greater than the images shown using AO-OCT by Reumueller et al., permitting correlation with cross-sectional retinal images acquired using spectral domain OCT, and with measures of macular



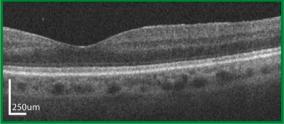


Fig. 4. Case 4 (ID TC_12383)
Adaptive optics scanning light of

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 2.12

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 12 and may reveal improvement in cone reflectivity after retinal detachment repair earlier 21 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. ²⁶ 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 week²¹ and can continue beyond one year after RRD repair. ¹² 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.²¹ 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.

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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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