Adaptive optics imaging, microperimetry and optoretinograhy following intravitreal injection of VP-001 in patients with *PRPF31*-associated retinitis pigmentosa

Jessica I. W. Morgan

Nivedhitha Govindasamy, Peiluo Xu, Yu You Jiang,
Raymond L. Warner, Thiran Jayasundera,
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SCHEIE EYE INSTITUTE
ESTABLISHED 1972
ESTABLISHED 1874
DEPARTMENT OF OPHTHALMOLOGY

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PYC Therapeutics

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Research to Prevent Blindness

Center for Advanced Retinal & Ocular Therapeutics
PennCAROT

The people who make it happen!

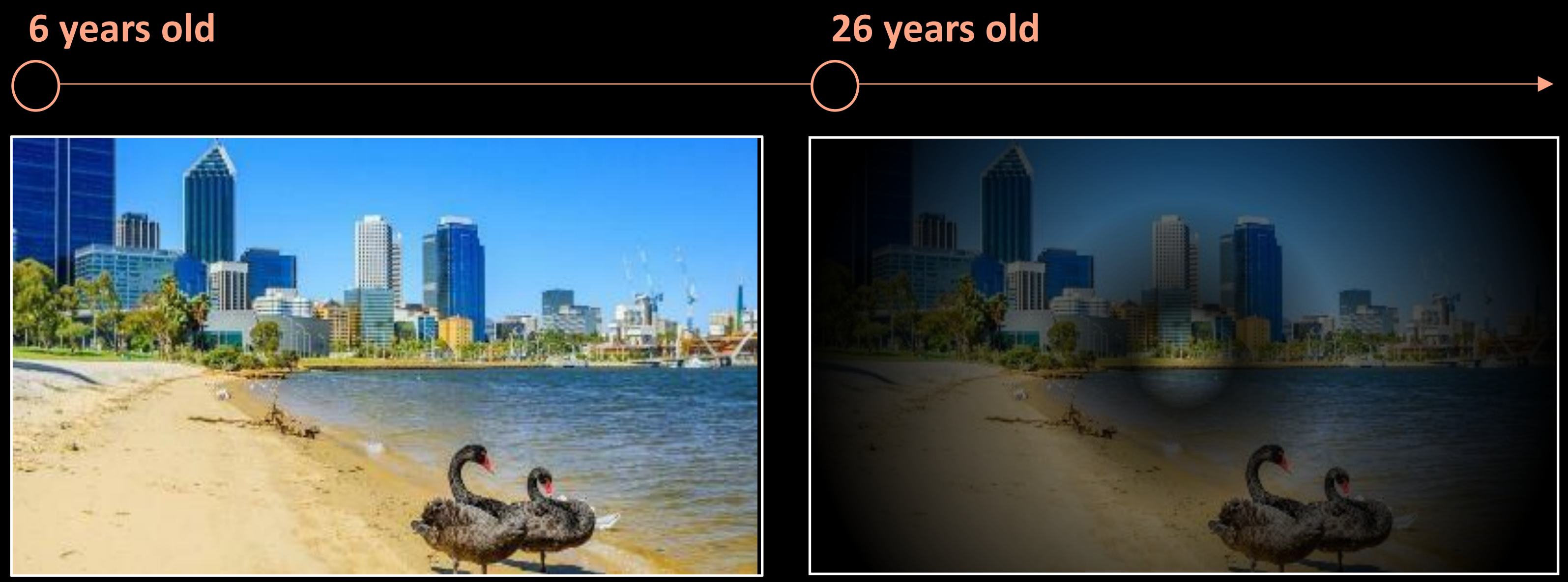
Jing Zhang
Yu You Jiang
Peiluo (Angela) Xu
Nivedhitha Govindasamy
Shaofeng Huang
Raymond L. Warner

Thanks to Alfredo Dubra for sharing the AOSLO optical design and software and Austin Roorda for sharing AO microperimetry technology.

Disclosure: I am an inventor on a patent for optoretinography and receive funding for the lab from PYC Therapeutics and Beacon Therapeutics.

Retinitis Pigmentosa

- Affects 1 in 3,000-5,000 individuals
- Rods degenerate initially with subsequent degeneration of cones and RPE



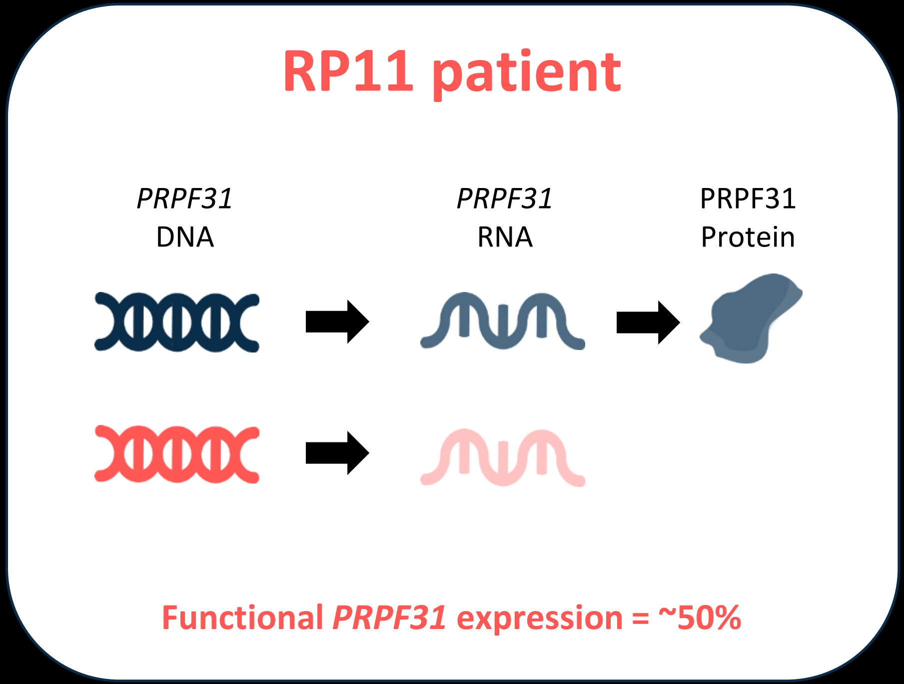
Patients experience night blindness followed by loss of peripheral and then central vision - legal blindness occurs in the 4th or 5th decade of life[1-3]

1. Lisbjerg K, et al. Disease progression of retinitis pigmentosa caused by PRPF31 variants in a Nordic population: a retrospective study with up to 36 years follow-up. Ophthalmic Genet. 2023 Apr;44(2):139-146
2. Daiger S et al. 'Genes and Mutations Causing Autosomal Dominant Retinitis Pigmentosa' Cold Spring Harb. Perspect. Med. 5 (2014)
3. Ellingford J et al. 'Molecular findings from 537 individuals with inherited retinal disease' J Med Genet 53, 761-776 (2016)

Retinitis Pigmentosa type 11

- 1-3% of RP
- Caused by mutations on the *PRPF31* gene
- Autosomal dominant inheritance

- VP-001: a RNA therapeutic that leads to upregulation of *PRPF31*



Experimental treatment of RP11 using VP-001

Progress to date

Phase 1a SAD | Open Label Extension | Phase 1b MAD Study

Platypus | *Wallaby*

- Safety & Tolerability
- Efficacy
  - Low-Luminance Visual Acuity
  - Microperimetry

Phase 2/3 Study[1]

- Safety & Tolerability
- Efficacy
  - **Primary:** Low-Luminance Visual Acuity
  - **Secondary:** Microperimetry

Open-Label Extension Study
Long term (24-month treatment period)[1]

DINGO

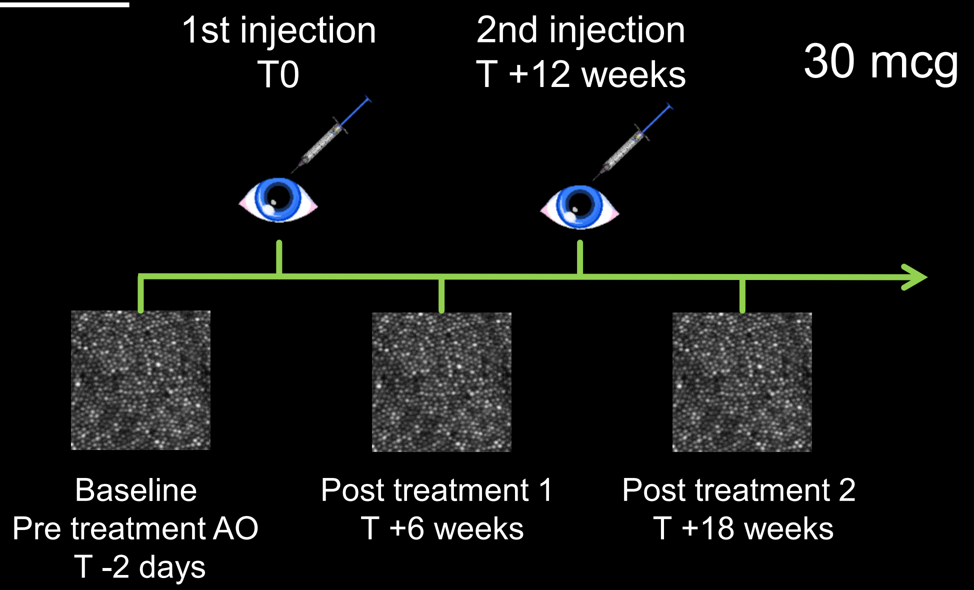
Natural History Study (Quokka)

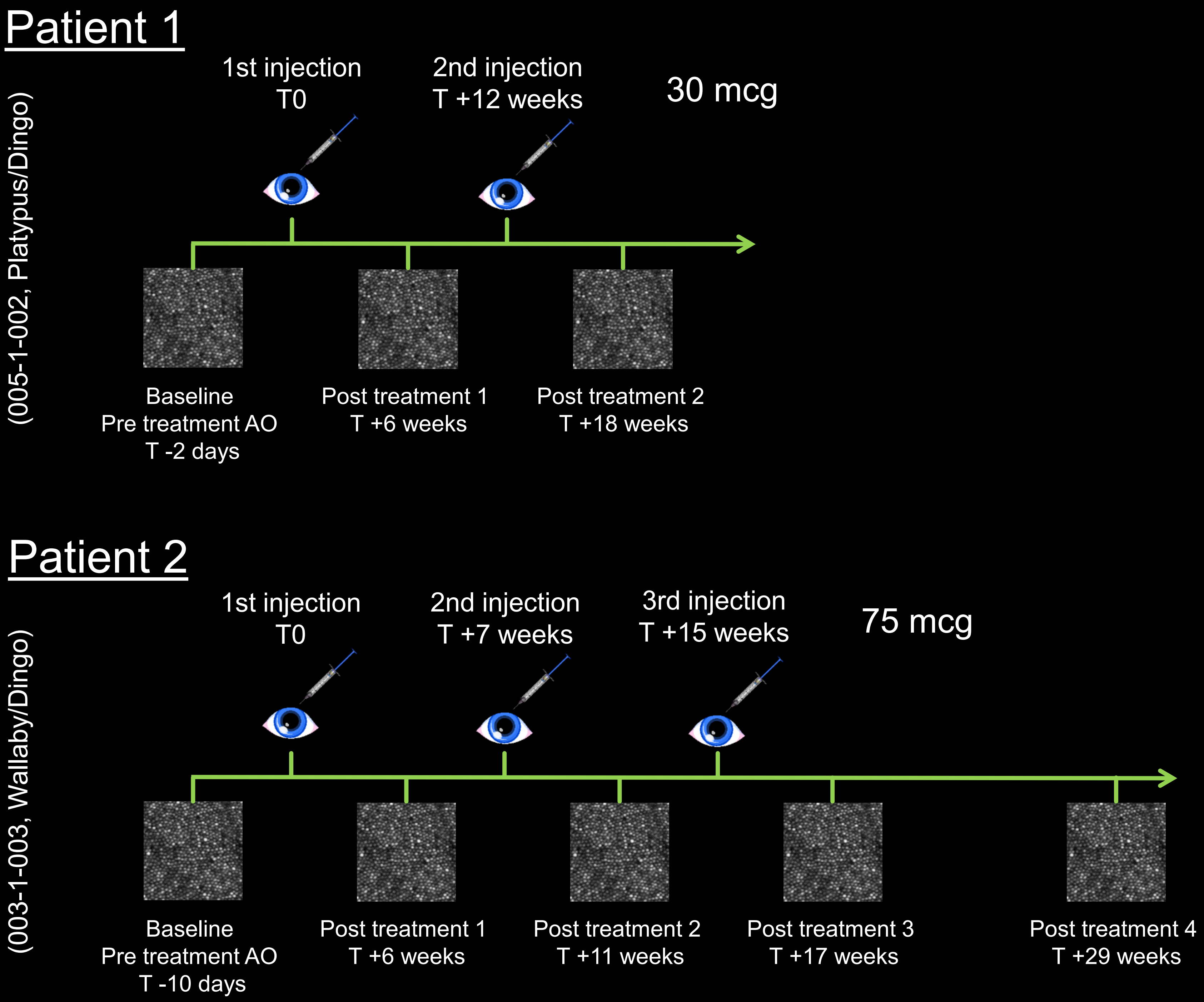
Chen *et al.* Presentation 5499
Thursday, May 7 11:45-12:00
Bluebird Ballroom 1B

1. Subject to the risks and uncertainties outlined in PYC Therapeutics' ASX disclosures of 2 February 2026
2. Based on an analysis of publicly-available information including clinicaltrials.gov
3. See PYC Therapeutics' ASX disclosures of 16 March 2026

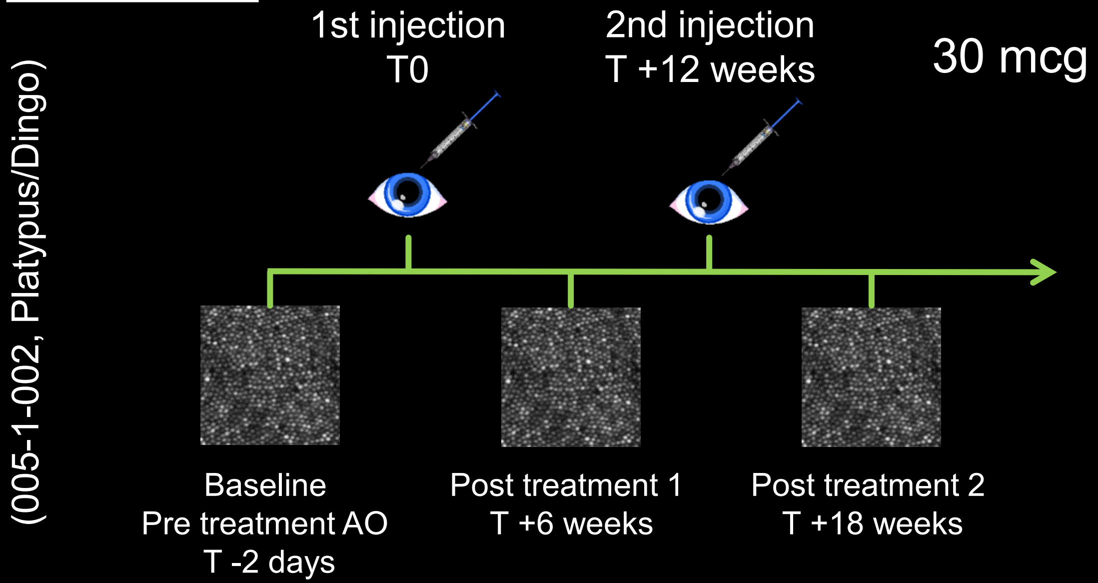
Patient 1

(005-1-002, Platypus/Dingo)



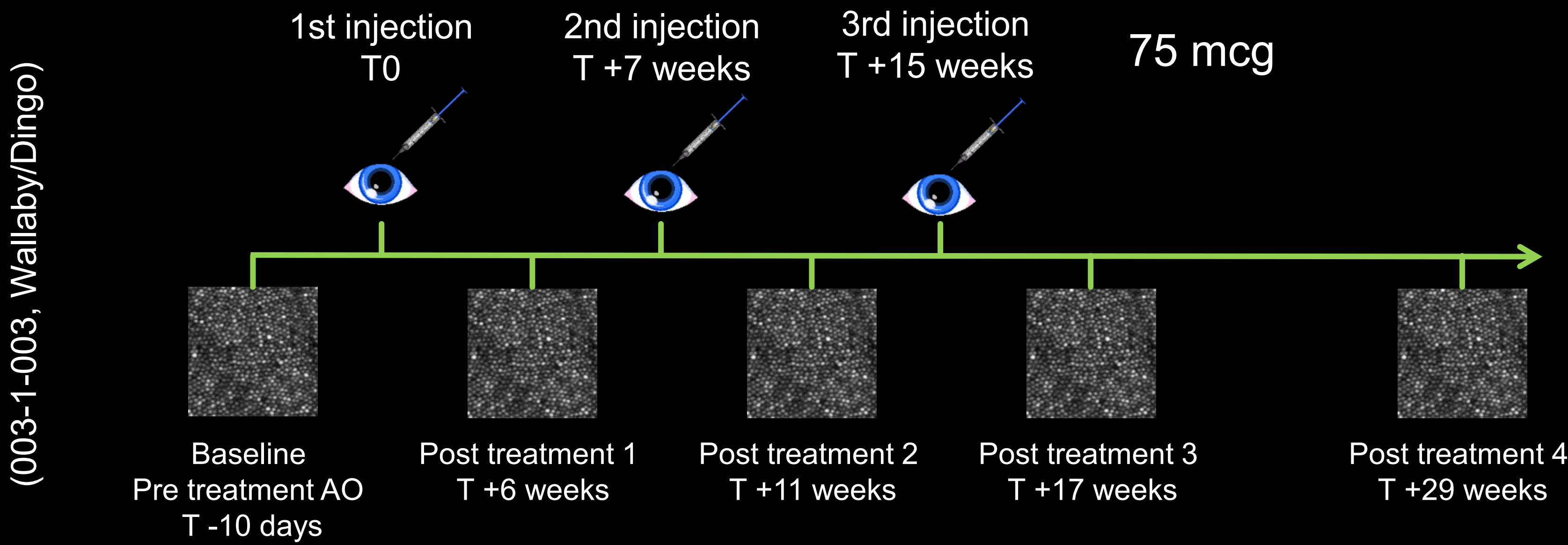

Patient 1
(005-1-002, Platypus/Dingo)
1st injection
T0
2nd injection
T +12 weeks
30 mcg
Baseline
Pre treatment AO
T -2 days
Post treatment 1
T +6 weeks
Post treatment 2
T +18 weeks
Patient 2
(003-1-003, Wallaby/Dingo)
1st injection
T0
2nd injection
T +7 weeks
3rd injection
T +15 weeks
75 mcg
Baseline
Pre treatment AO
T -10 days
Post treatment 1
T +6 weeks
Post treatment 2
T +11 weeks
Post treatment 3
T +17 weeks
Post treatment 4
T +29 weeks

Patient 1



- Adaptive optics scanning light ophthalmoscopy
- Optoretinography
- Adaptive optics microperimetry
- OCT

Patient 2



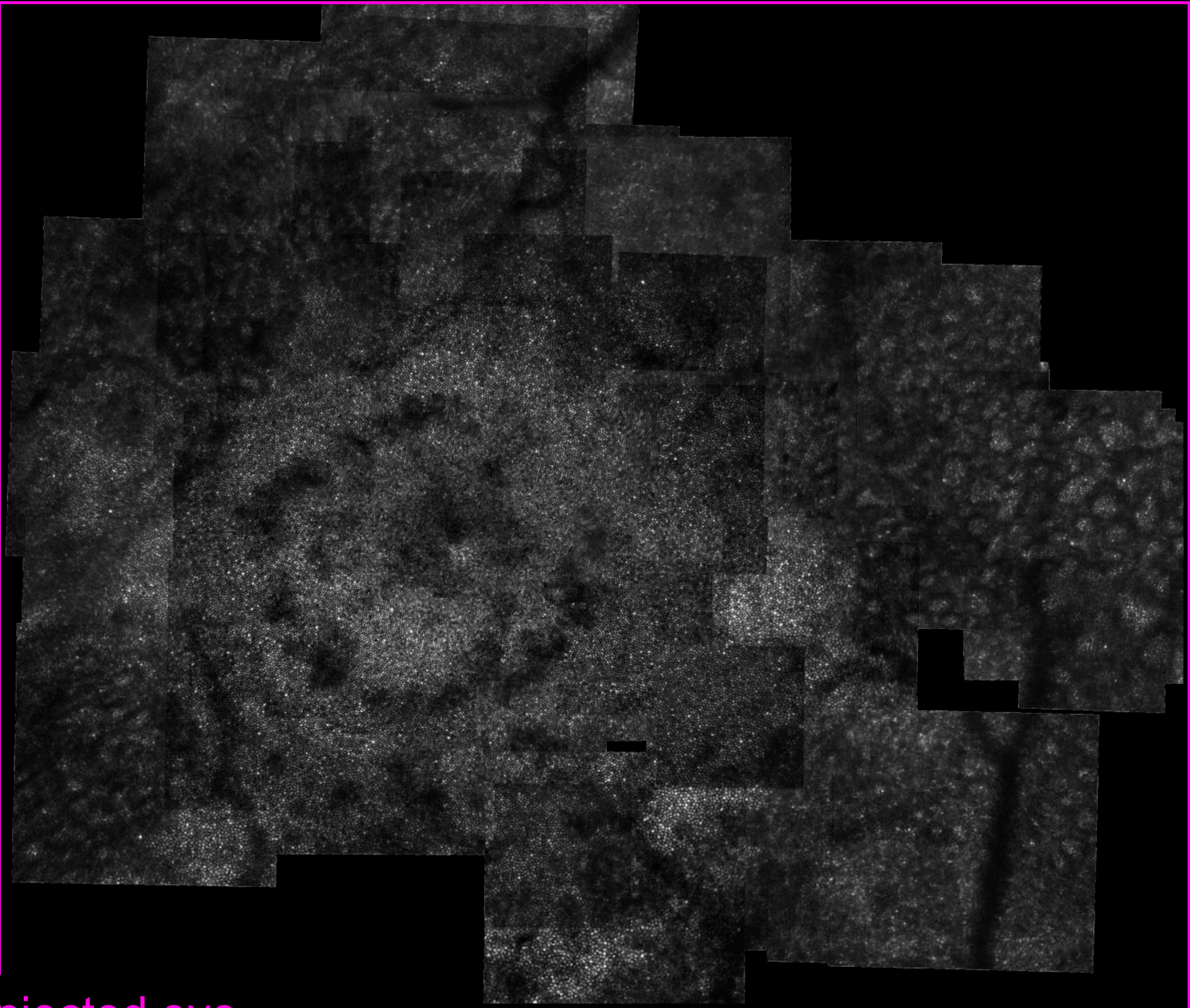
Evaluate retinal structure and function in *PRPF31*-associated retinitis pigmentosa before and after unilateral treatment with experimental VP-001

Patient 2

Baseline, Pre-treatment

Patient 2: Degenerative microcysts over time

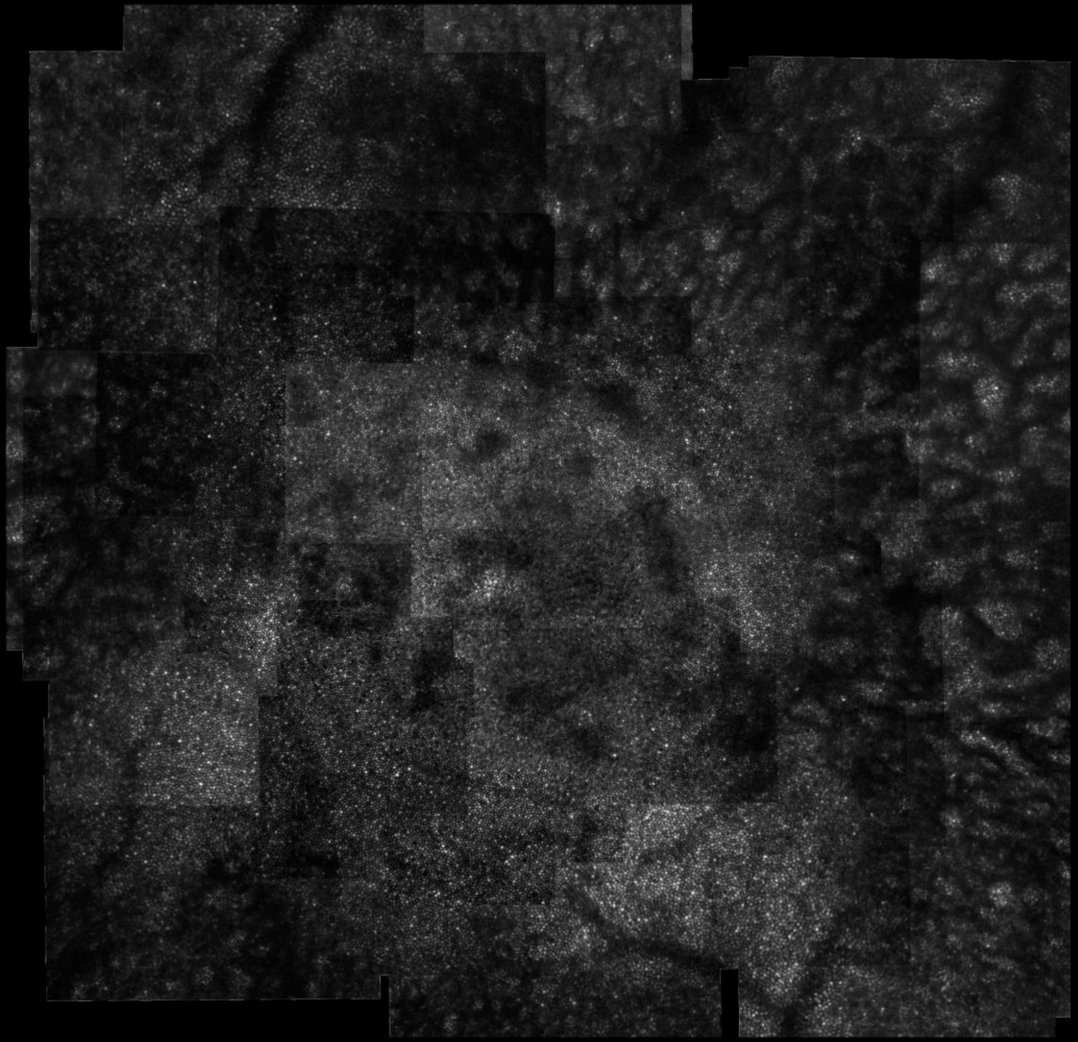
Baseline, Pre-treatment



Injected eye

Patient 2: Degenerative microcysts over time

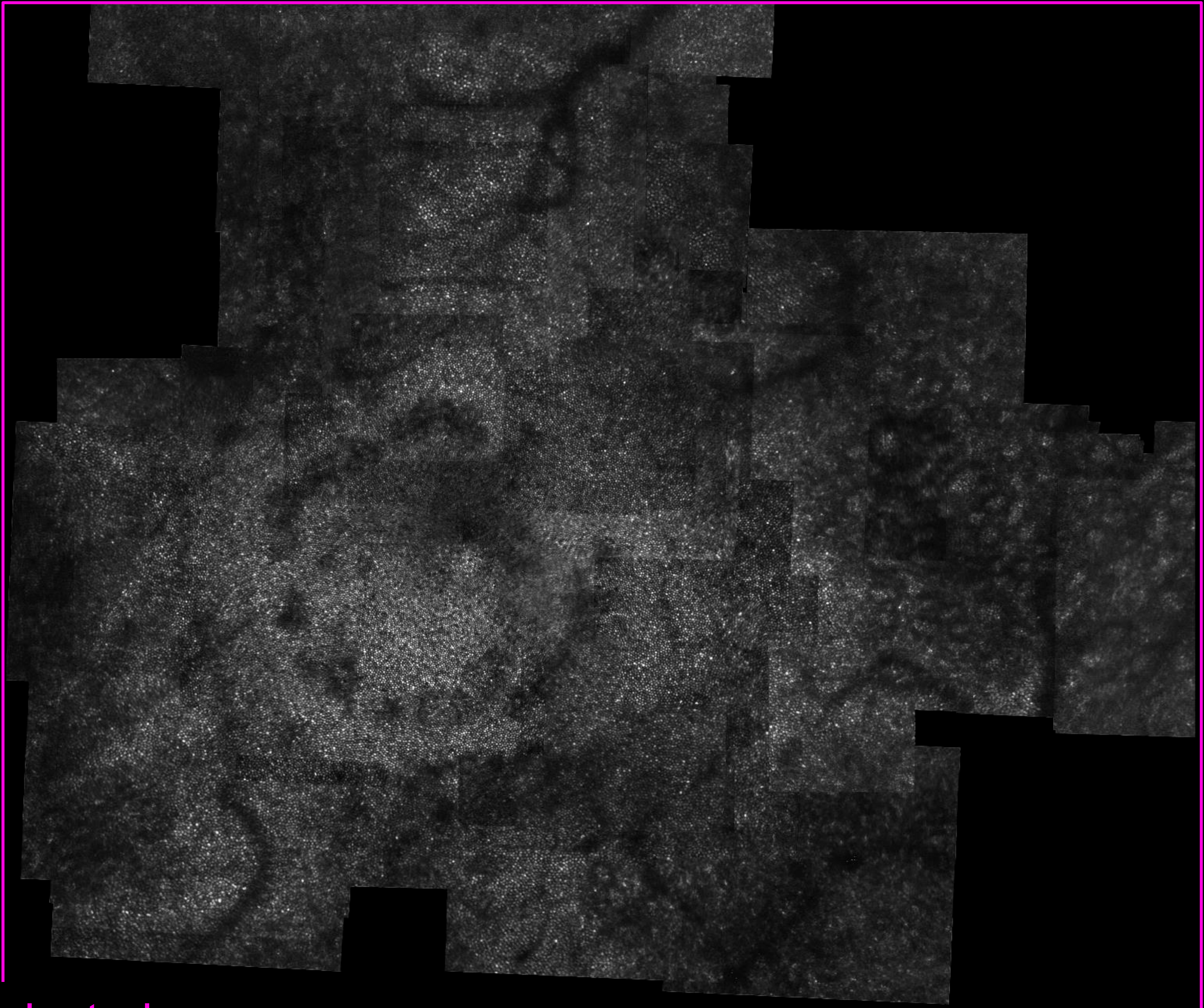
Baseline, Pre-treatment



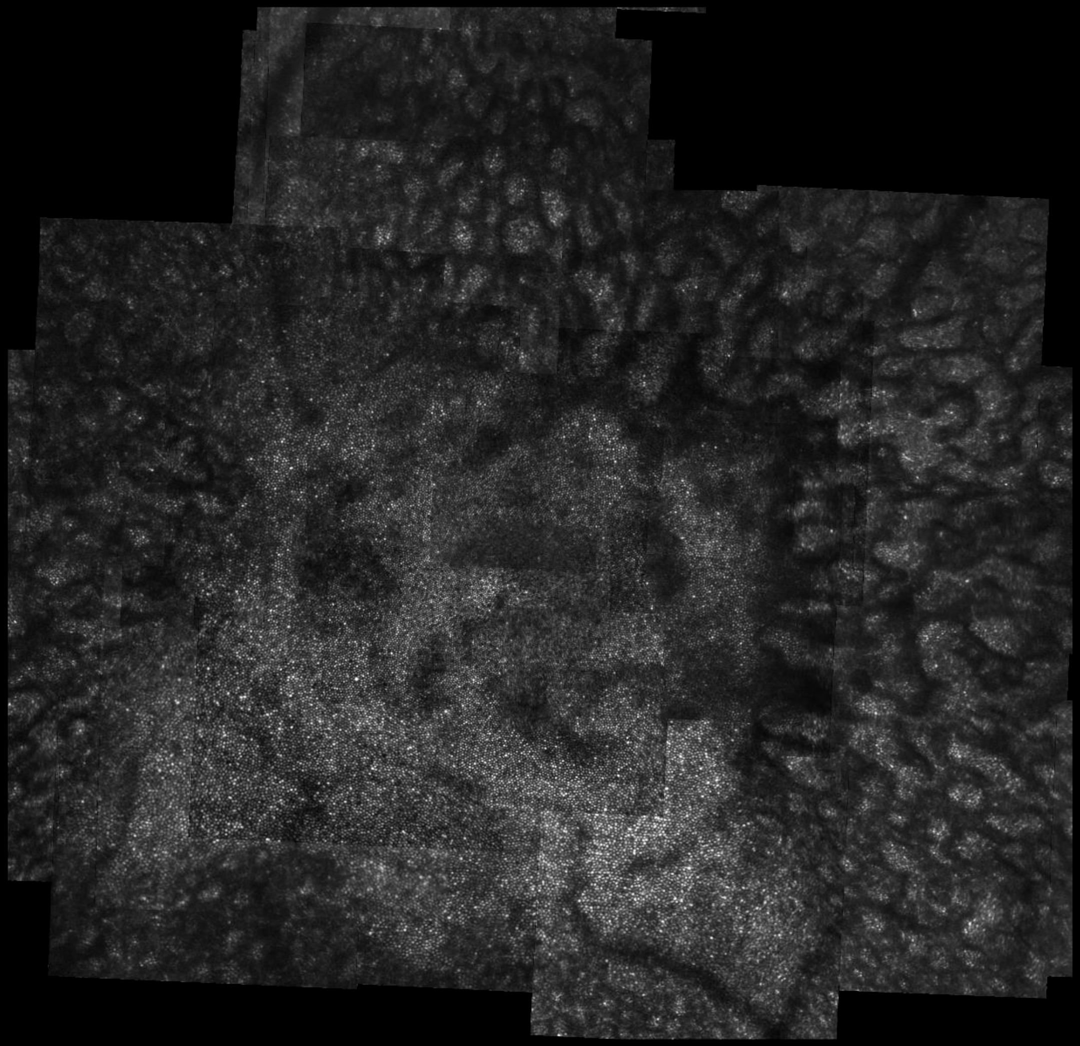
Control eye

Patient 2: Degenerative microcysts over time

Post-injection 3, 17 weeks

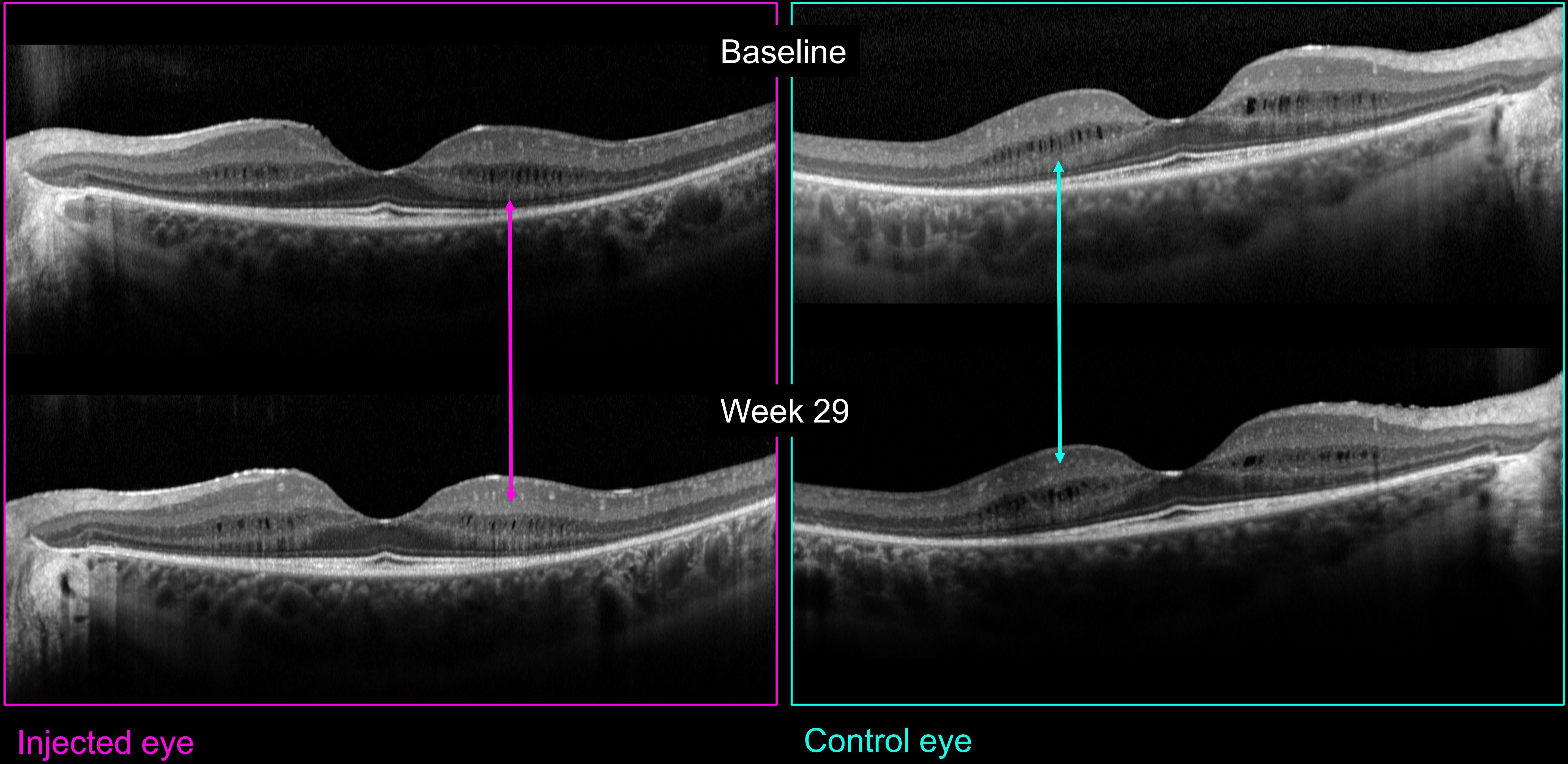


Injected eye

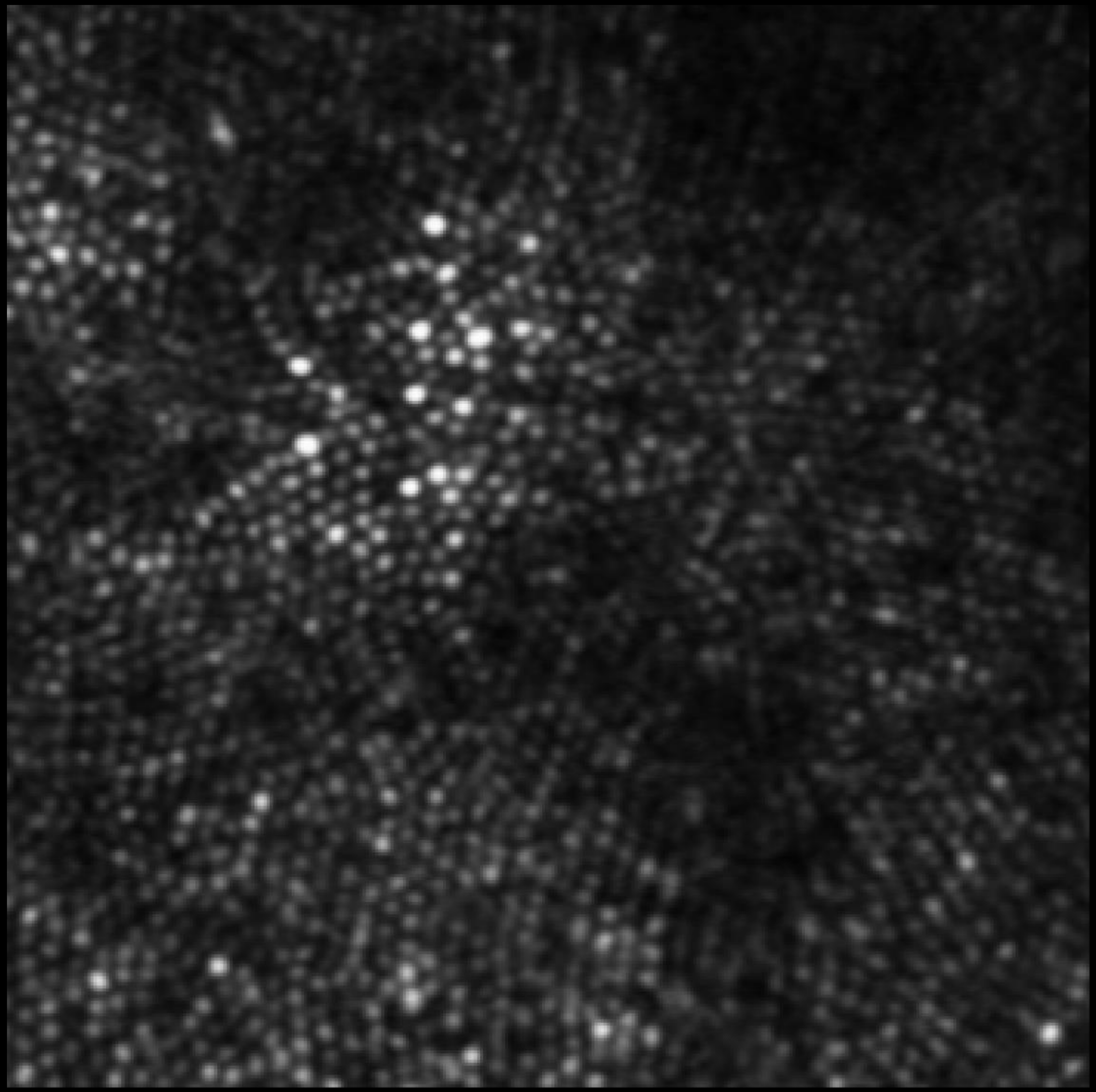


Control eye

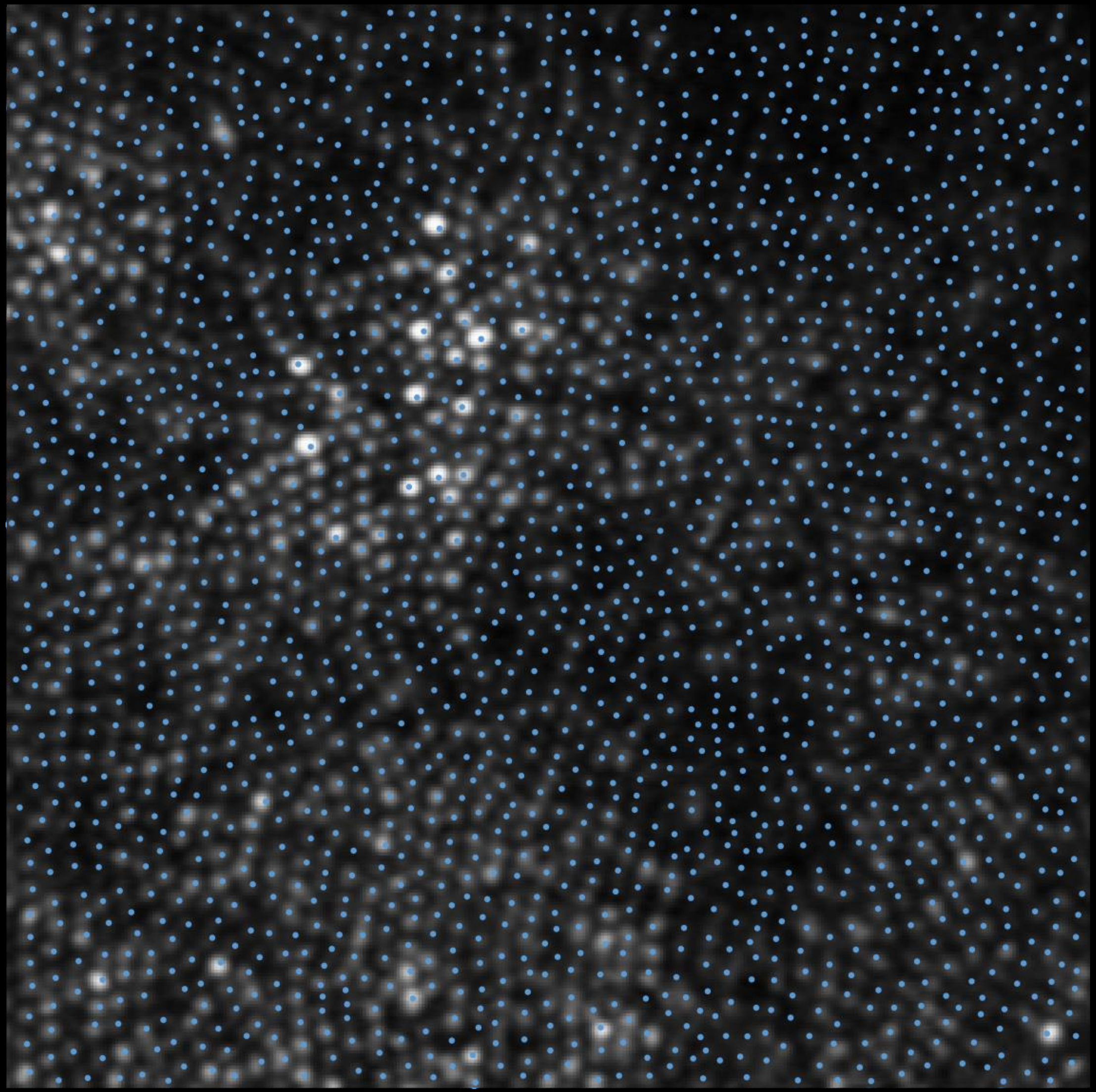
Patient 2: Degenerative microcysts over time



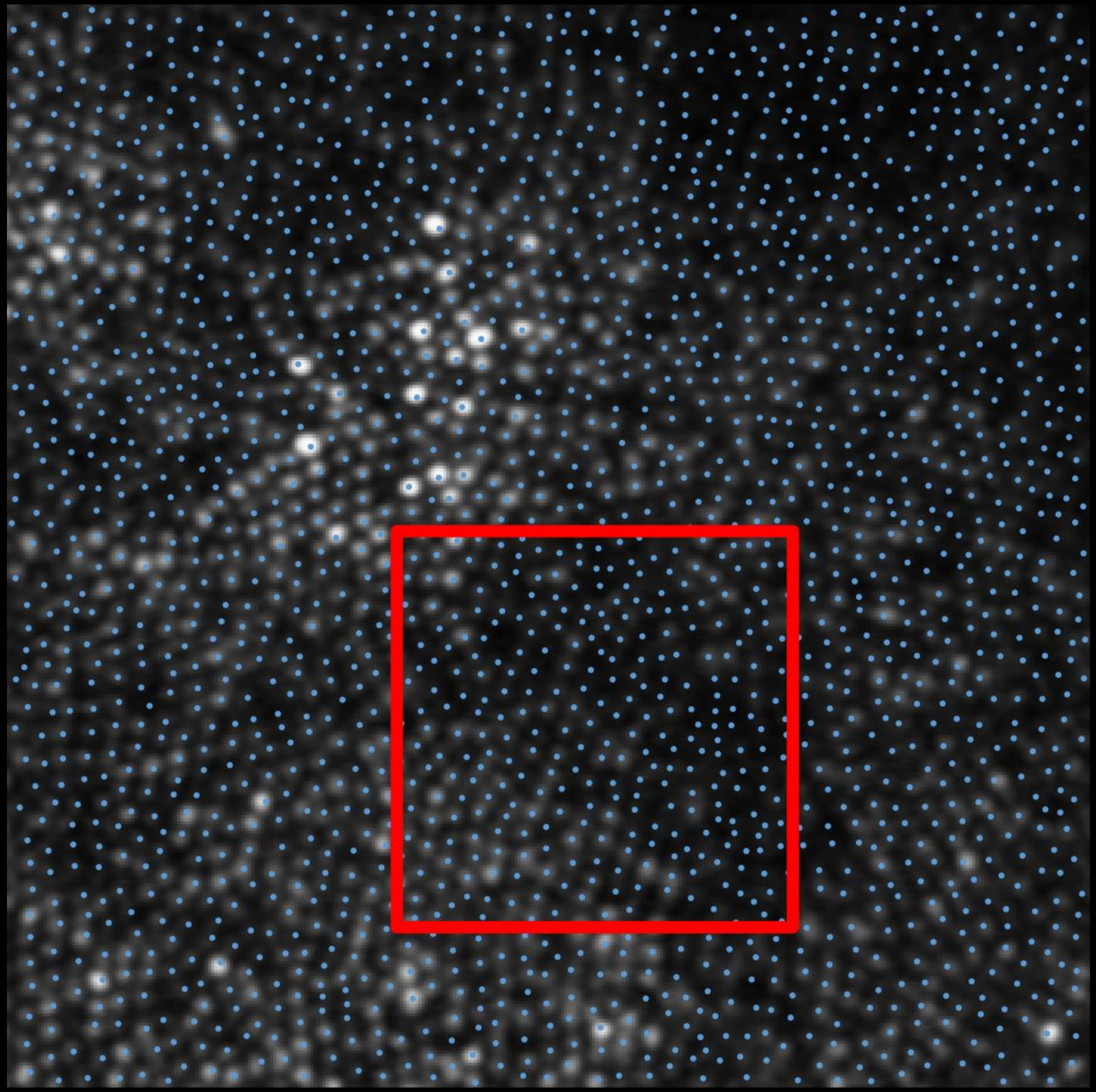
Patient 2: Peak cone density over time



Patient 2: Peak cone density over time

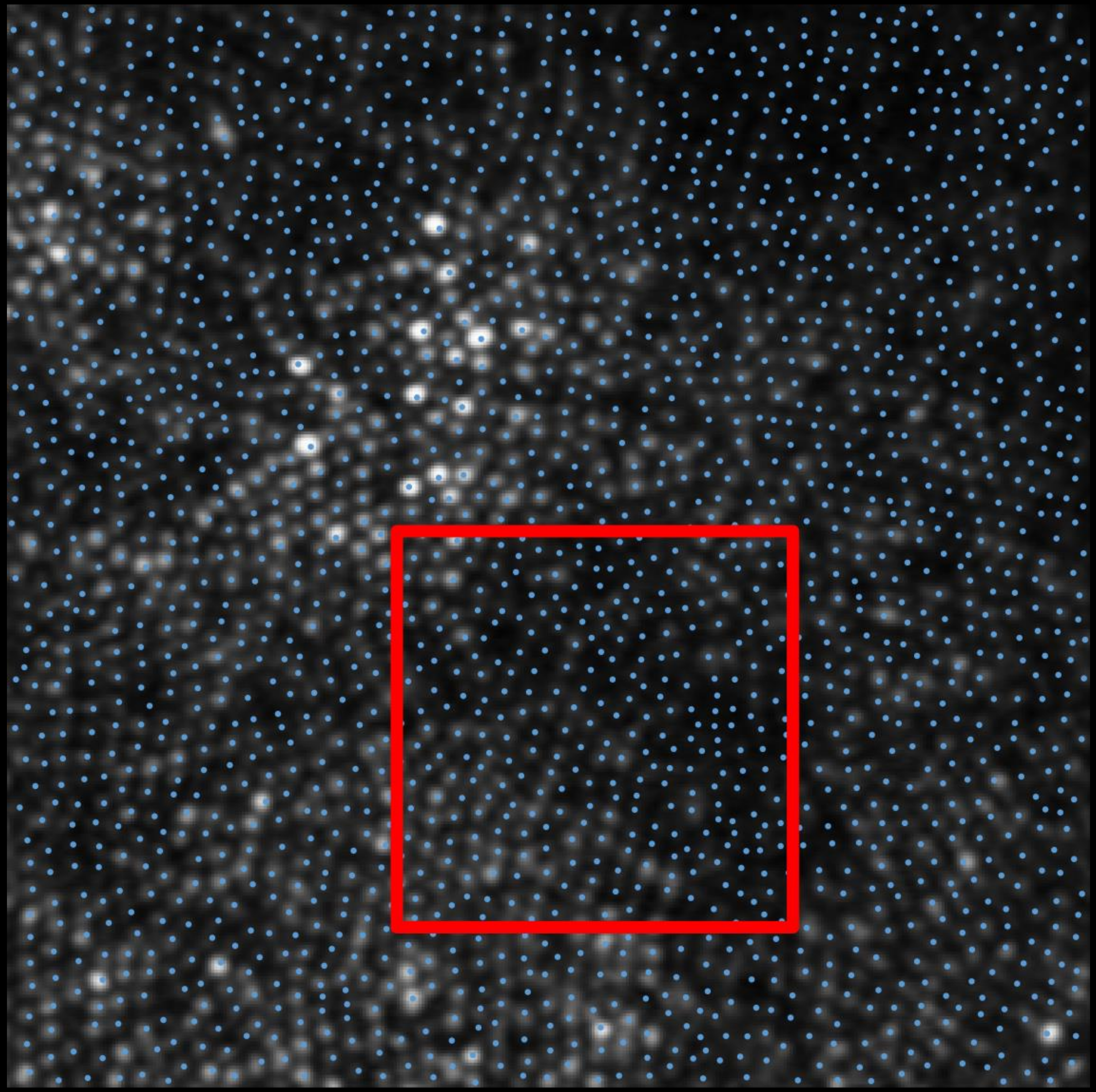


Patient 2: Peak cone density over time

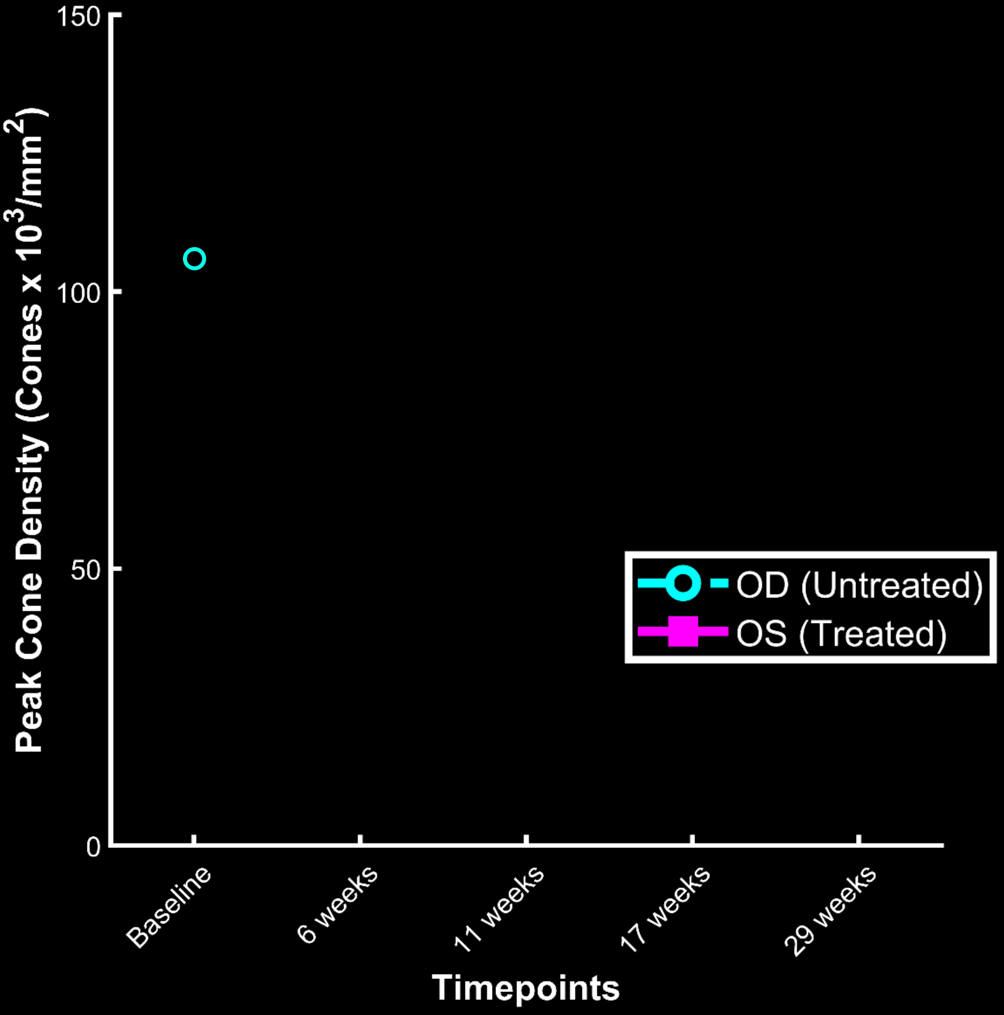


106,039 cones/mm^2

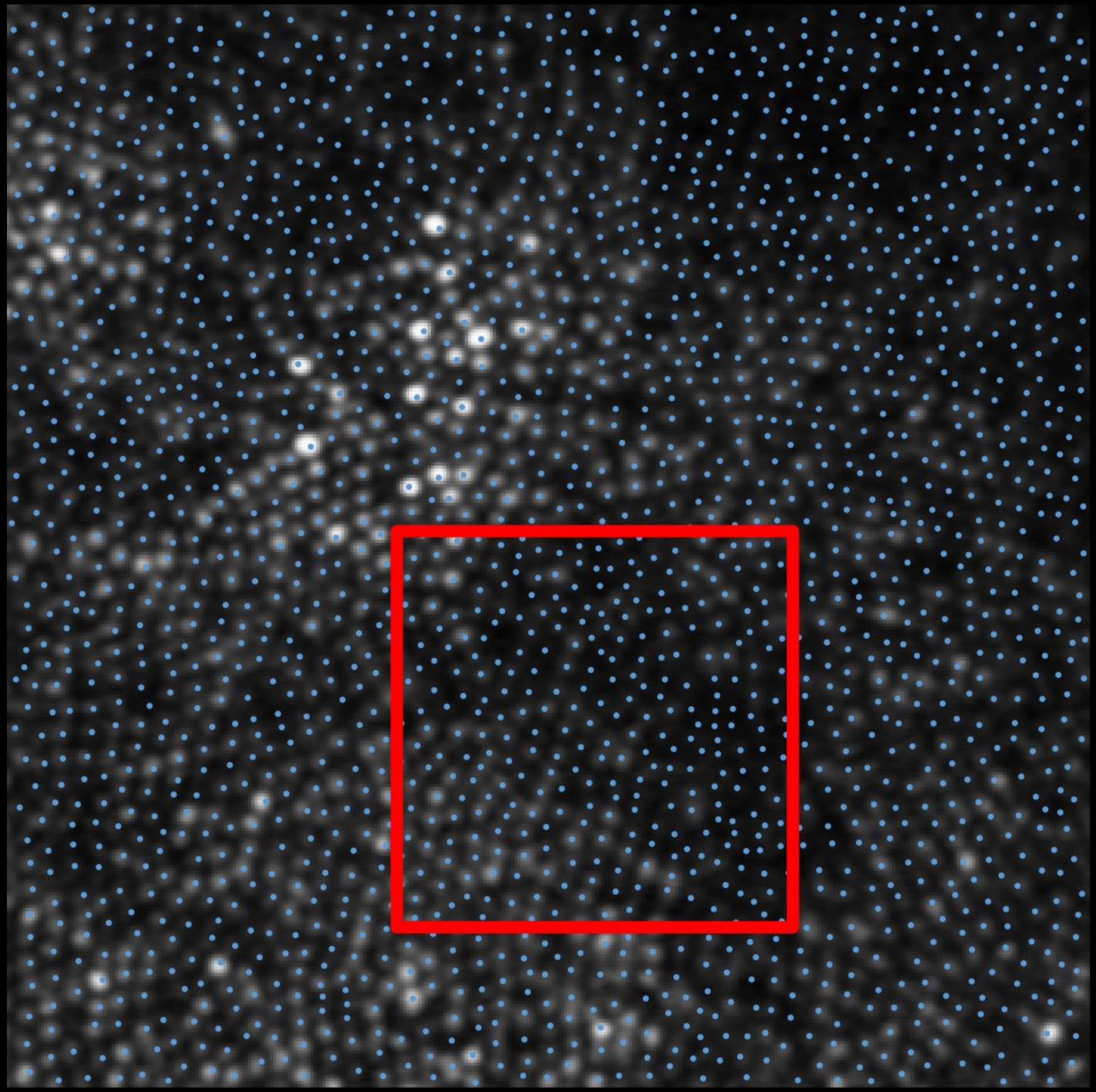
Patient 2: Peak cone density over time



106,039 cones/mm^2

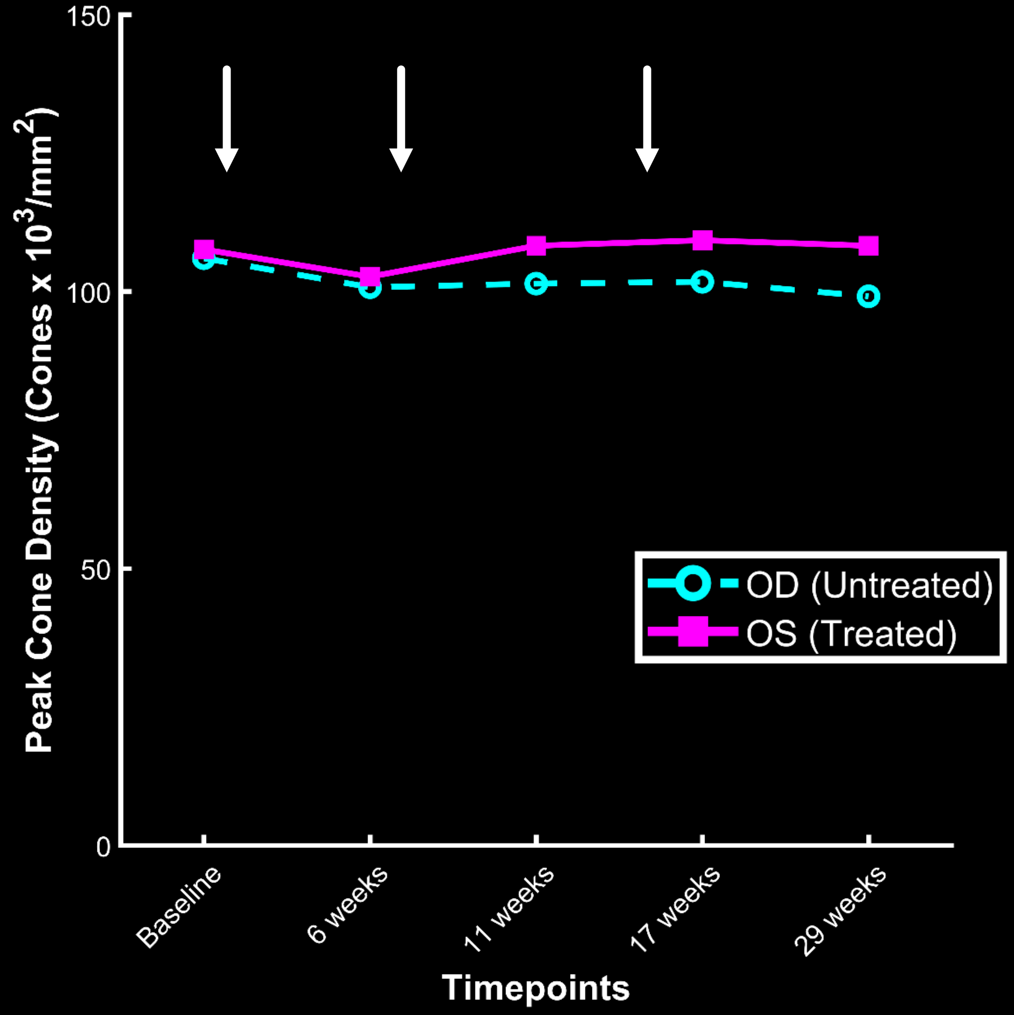


Patient 2: Peak cone density over time



106,039 cones/mm^2

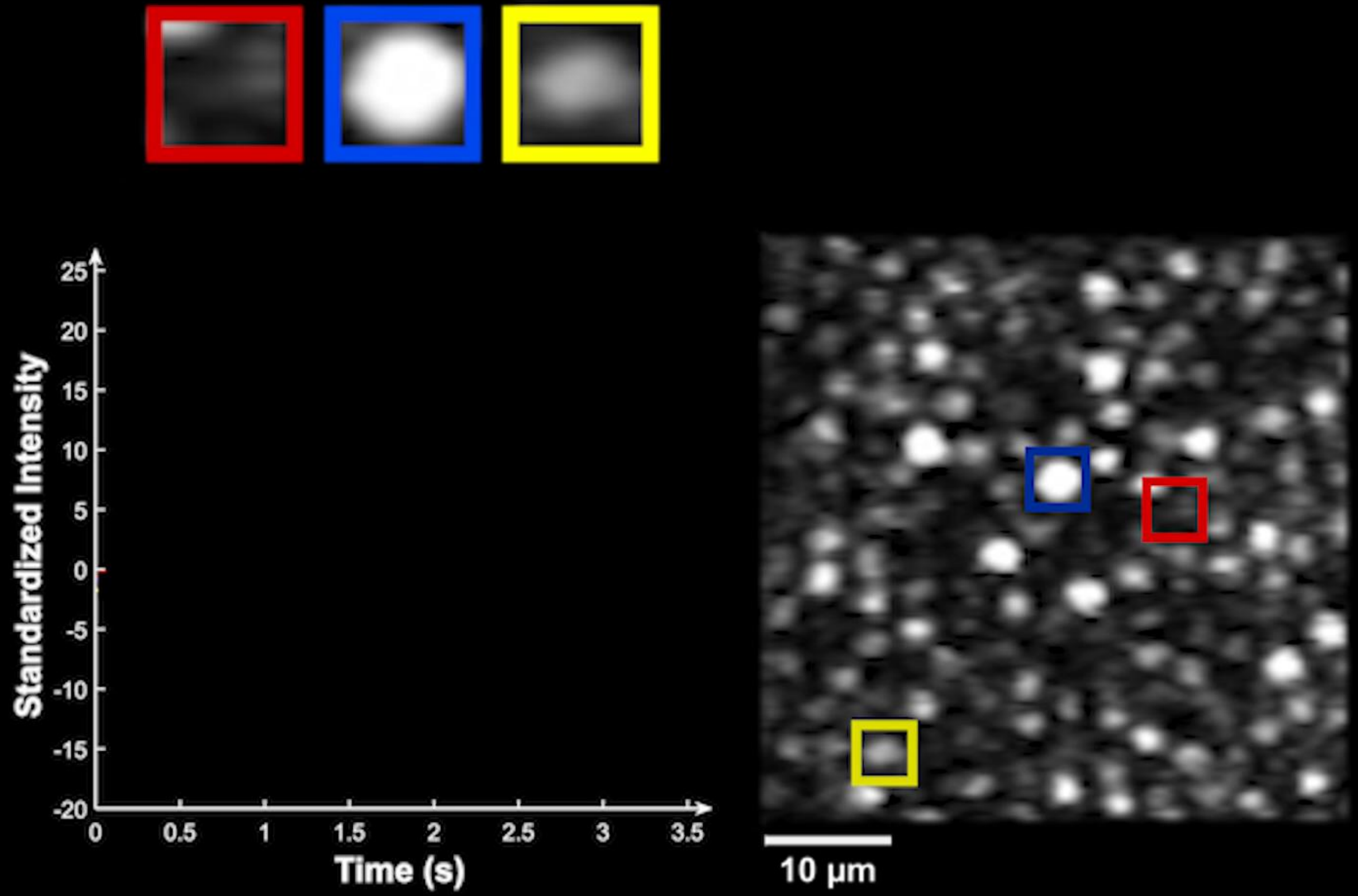
*Arrows depict VP-001 injections



Optoretinography

- Objective measure of photoreceptor function.
- An optical signal that occurs in response to a visible stimulus.

Optoretinography



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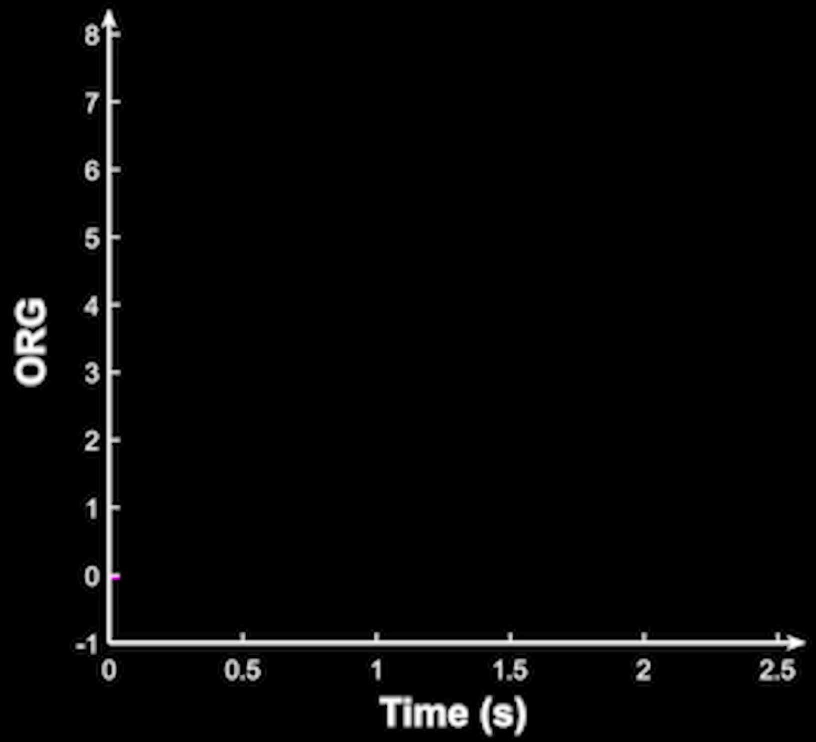

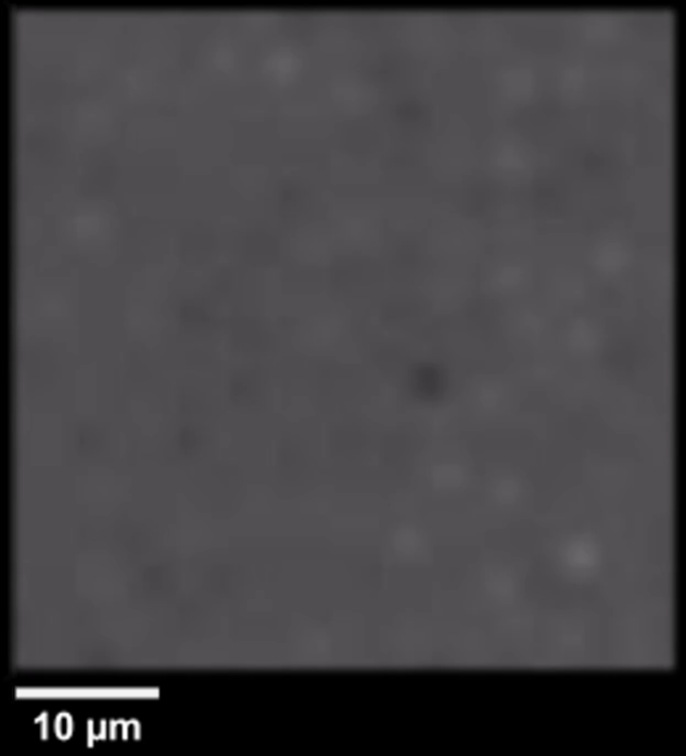

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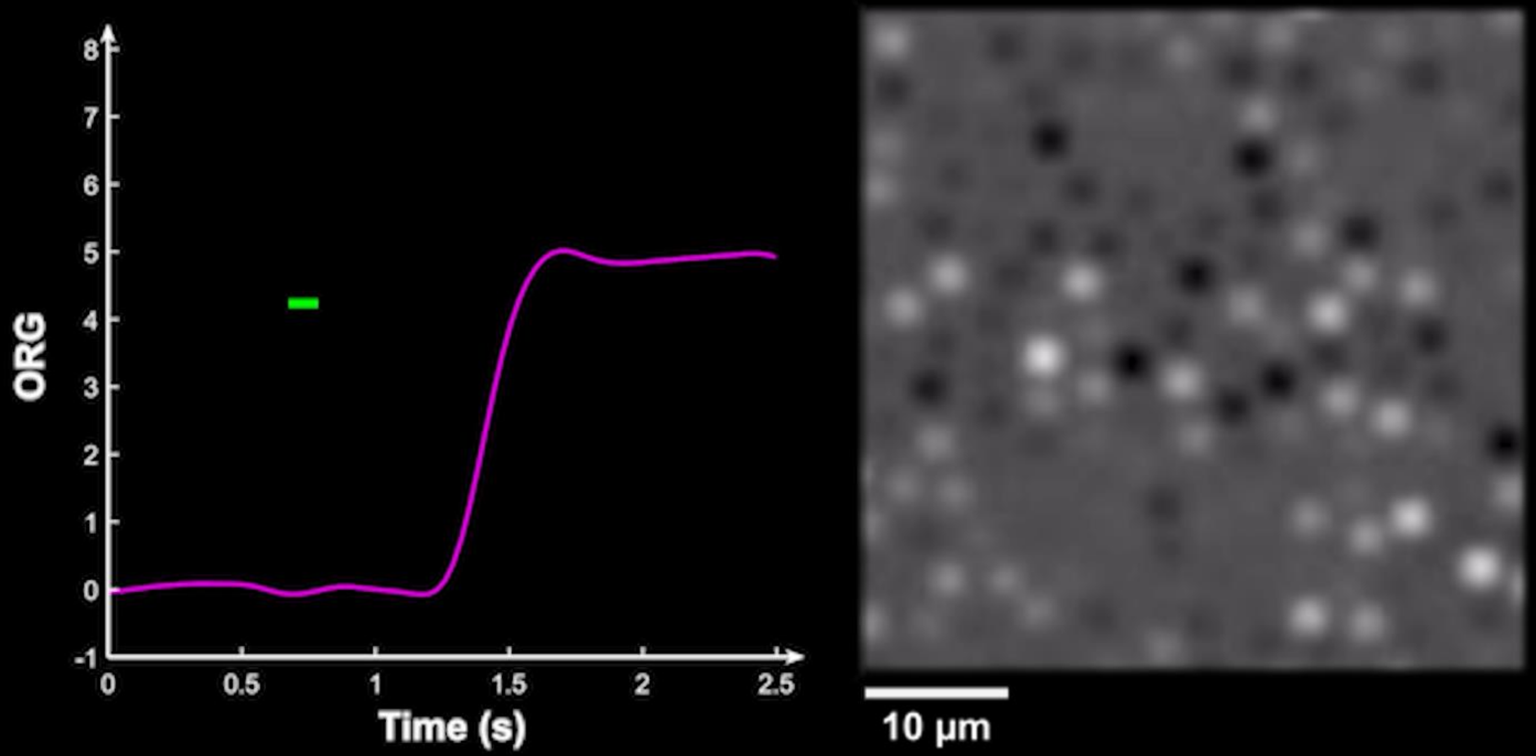
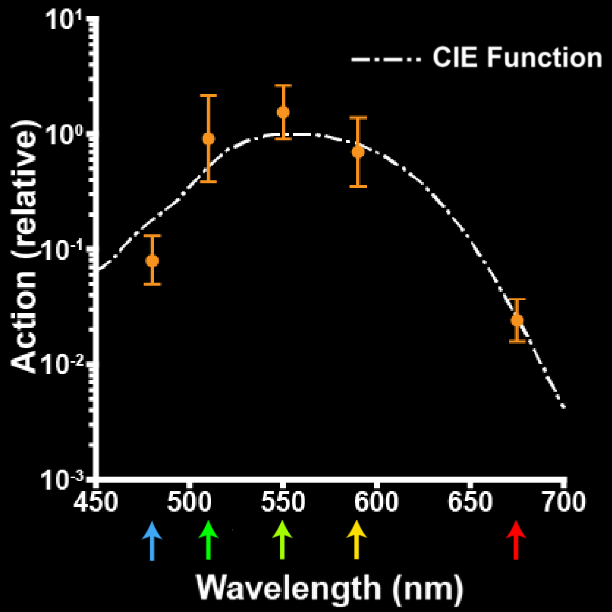


Optoretinography



Research Article
Vol. 8, No. 11 | 1 Nov 2017 | BIOMEDICAL OPTICS EXPRESS 5098
Biomedical Optics EXPRESS

Non-invasive assessment of human cone photoreceptor function

ROBERT F. COOPER,[1,2] WILLIAM S. TUTEN,[1,2] ALFREDO DUBRA,[3] DAVID H. BRAINARD,[2] AND JESSICA I. W. MORGAN[1,4,*]

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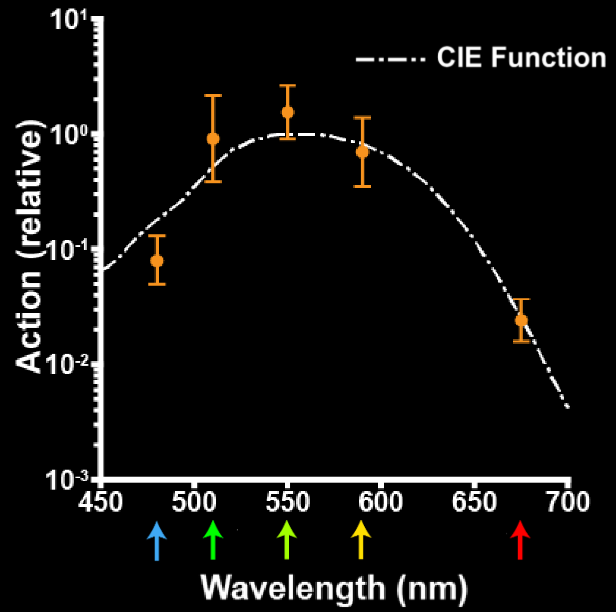

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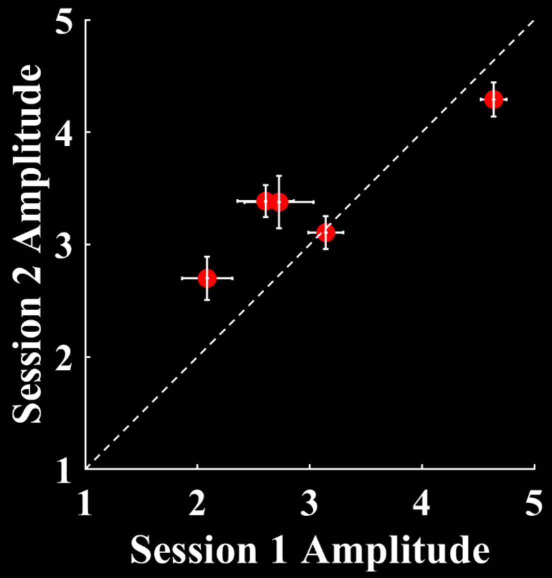

Research Article
Vol. 13, No. 12 / 1 Dec 2022 / Biomedical Optics Express 6561
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Repeatability and reciprocity of the cone optoretinogram

R. L. WARNER,[1] D. H. BRAINARD,[2] AND J. I. W. MORGAN[1,3,*]

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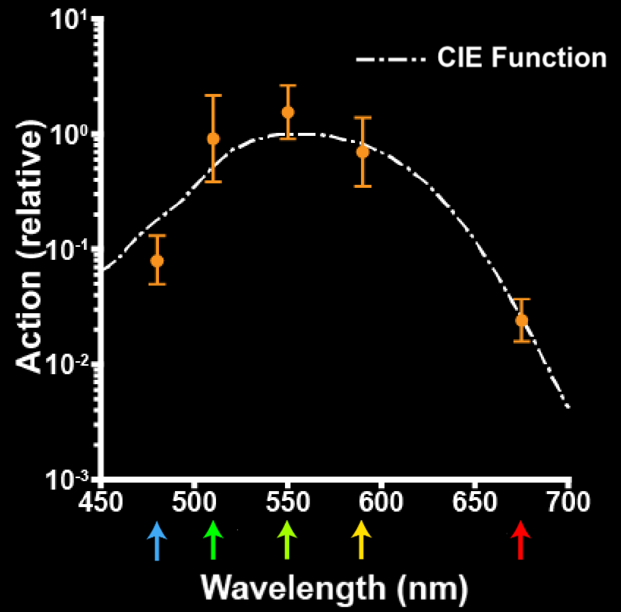

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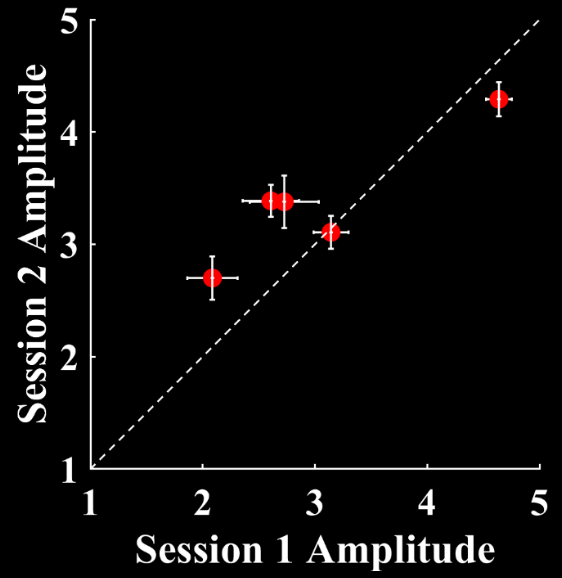

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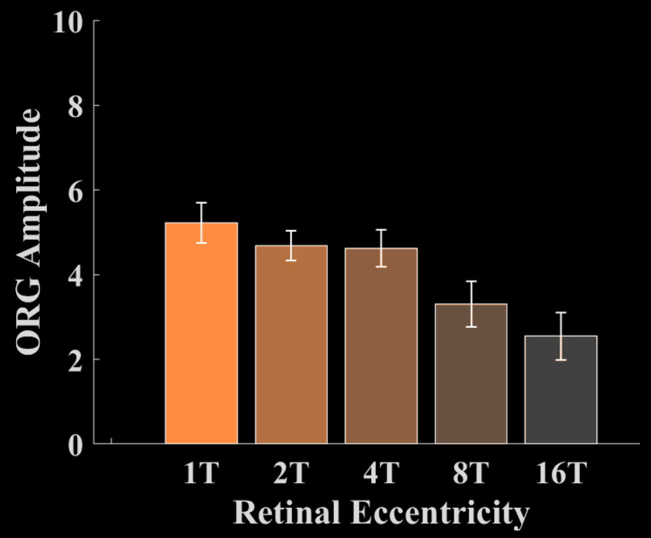
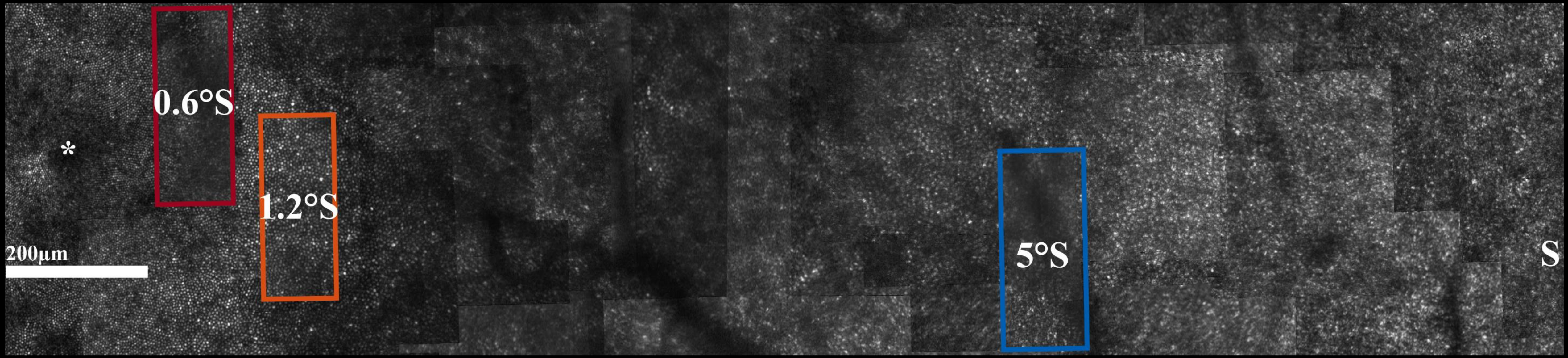


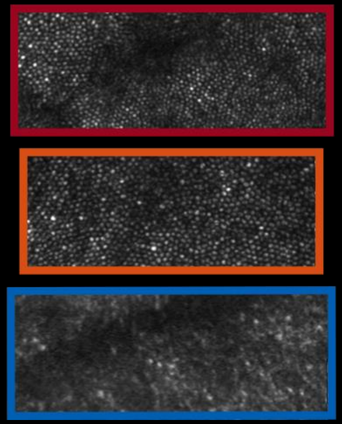
photonics
MDPI
Article

The Cone Optoretinogram as a Function of Retinal Eccentricity †

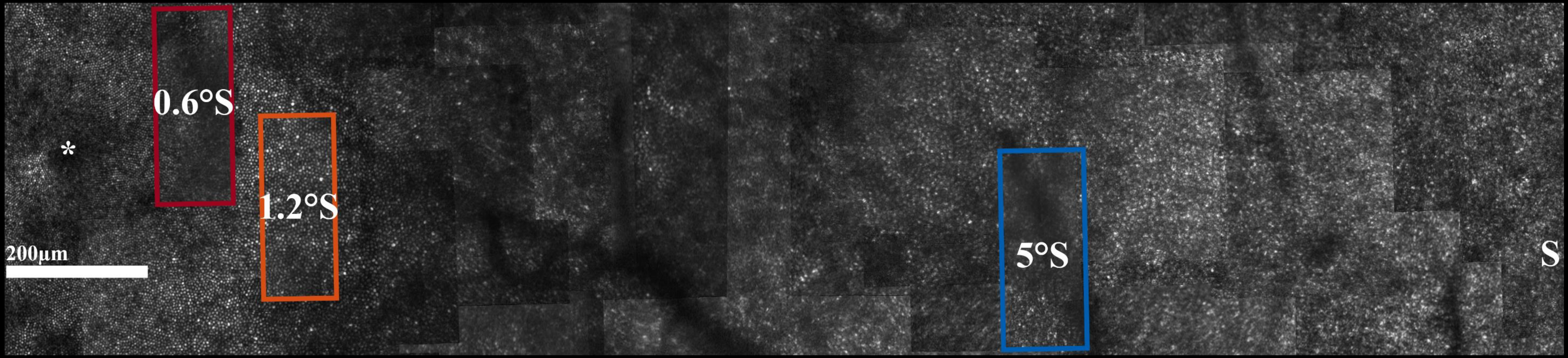
Raymond L. Warner [1], Peiluo Xu [2], David H. Brainard [3] and Jessica I. W. Morgan [1,4,*]

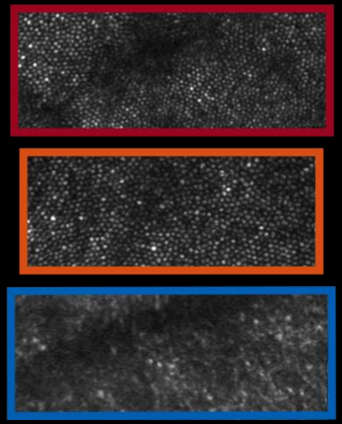
Optoretinography, Patient 2 Baseline, OS

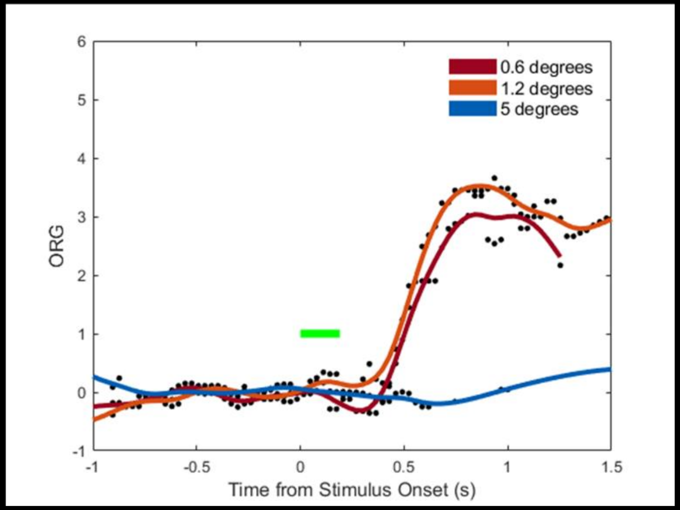


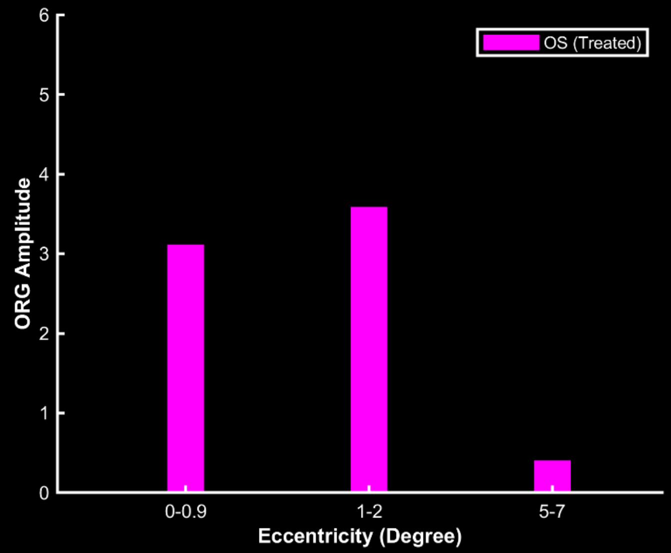


Optoretinography, Patient 2 Baseline, OS

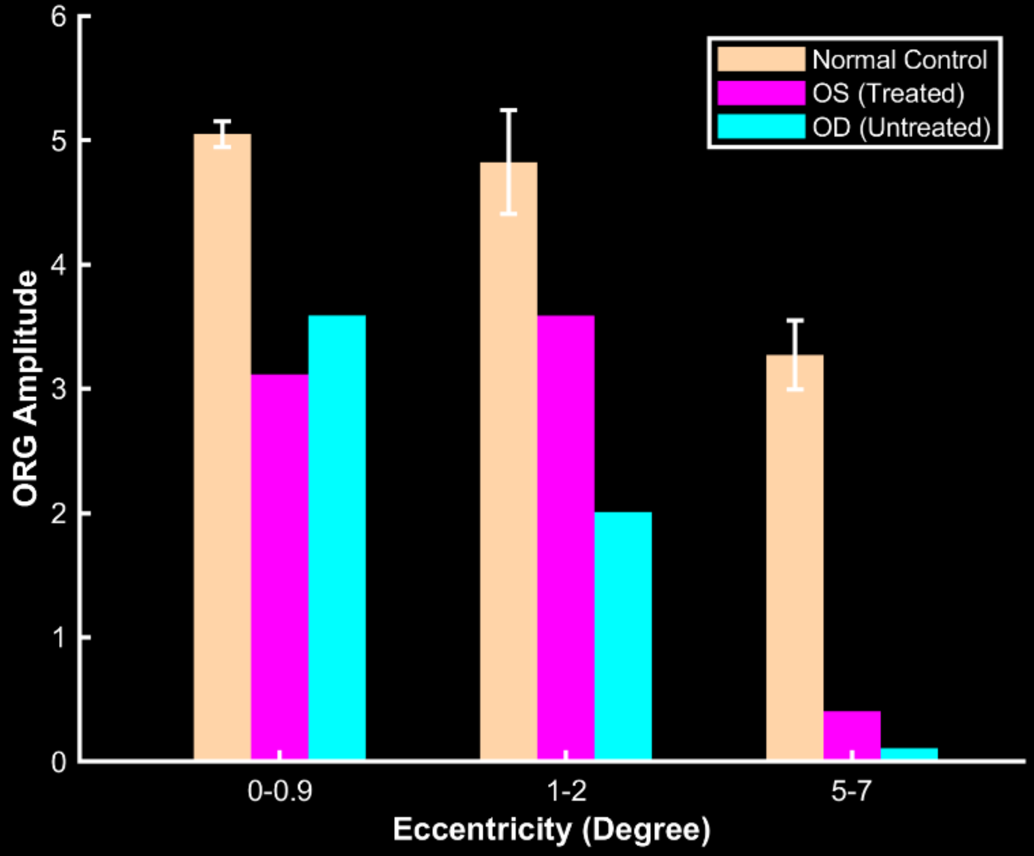






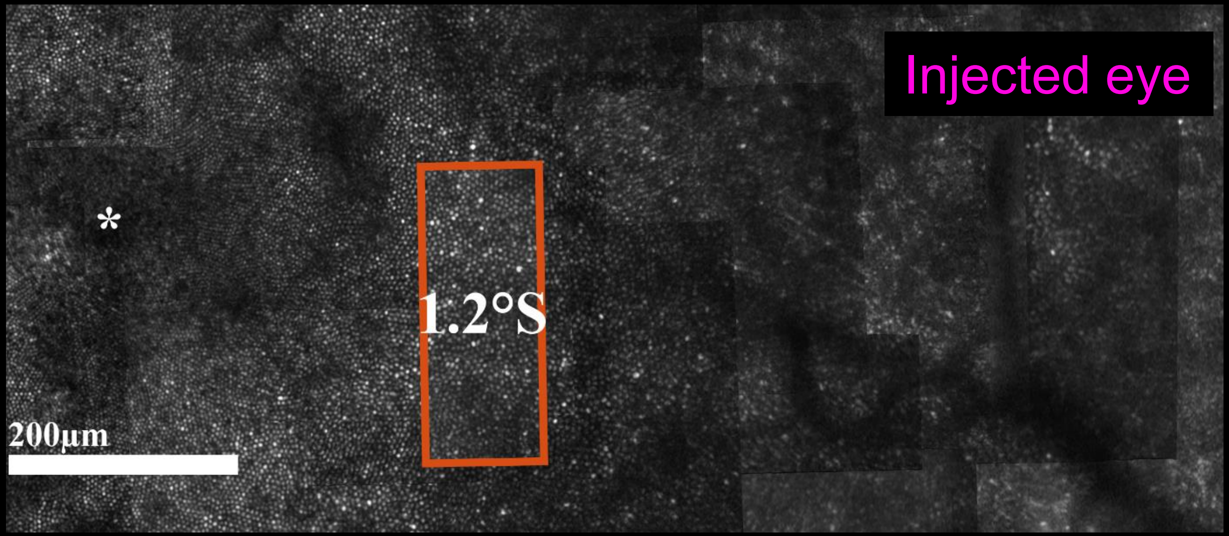


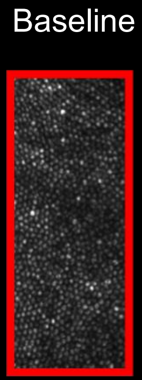
Optoretinography, Patient 2 Baseline

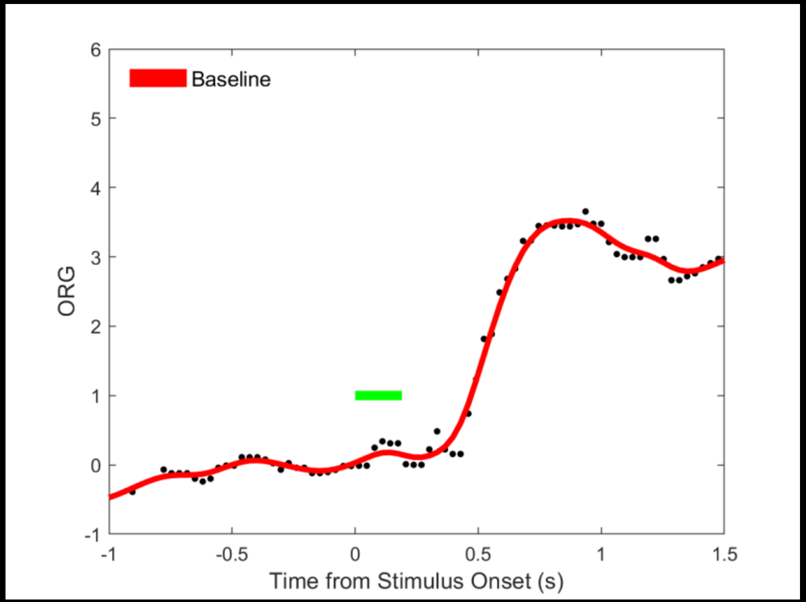


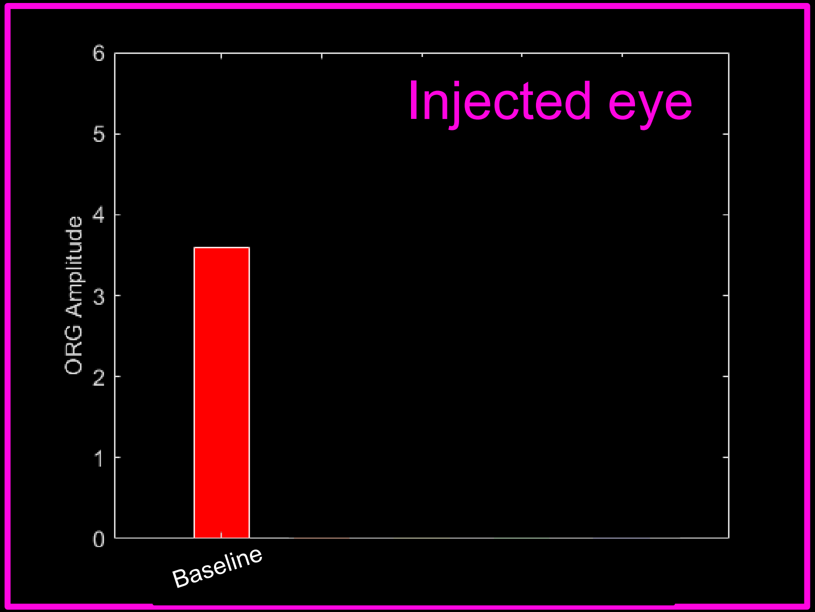
Baseline ORG amplitude is reduced from normal.

Optoretinography, Patient 2 over time

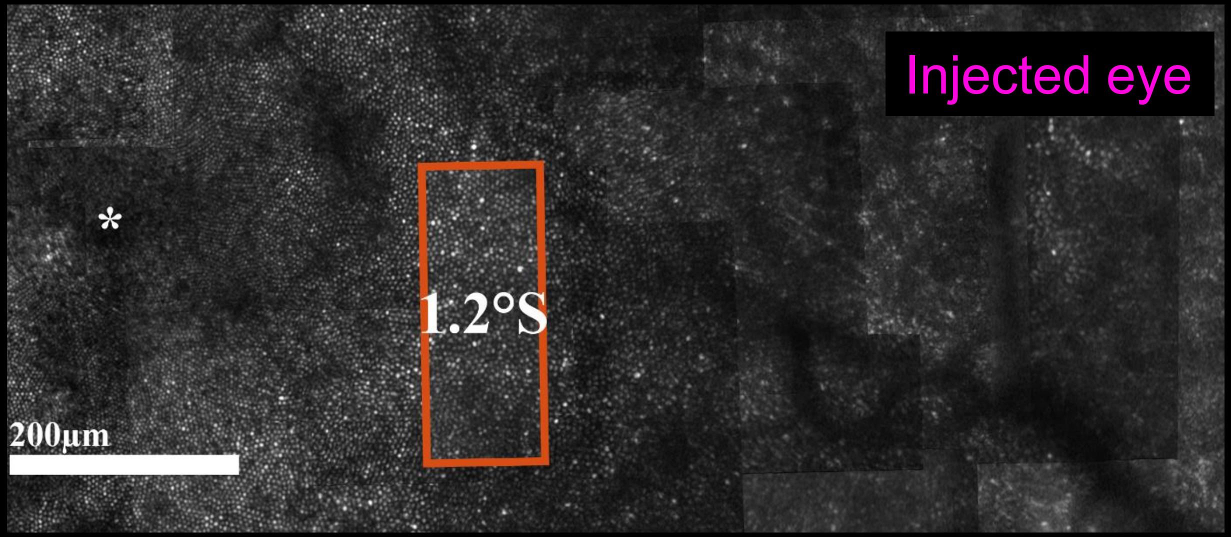


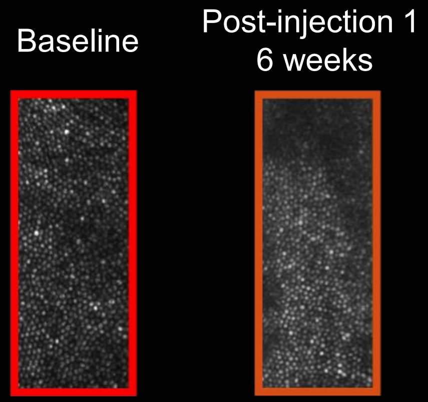


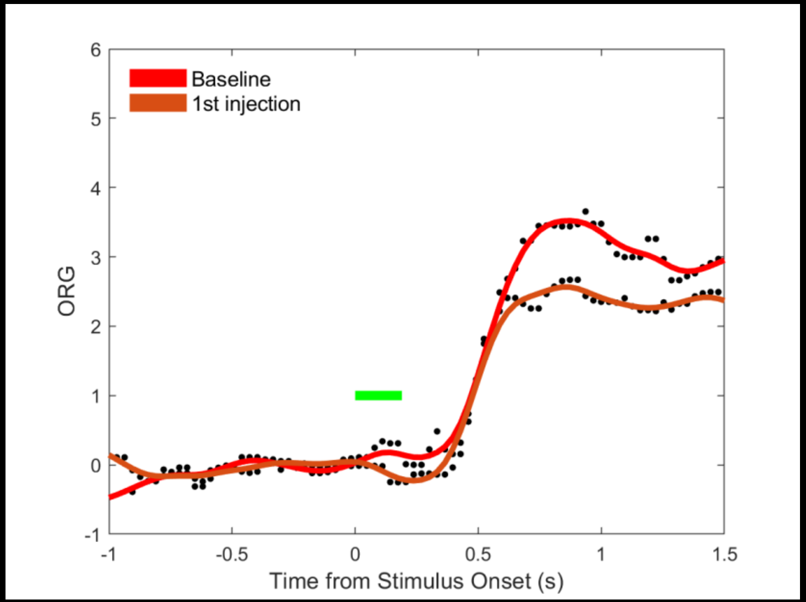


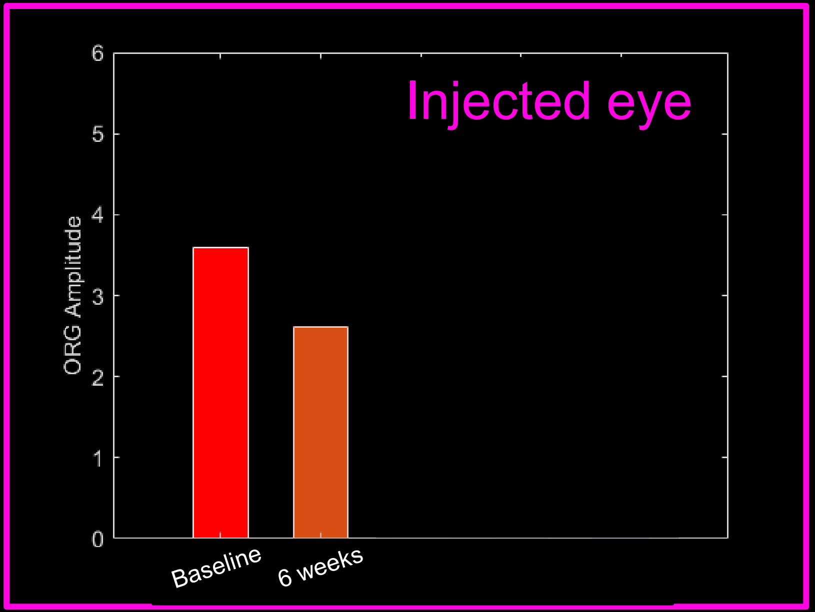


Optoretinography, Patient 2 over time

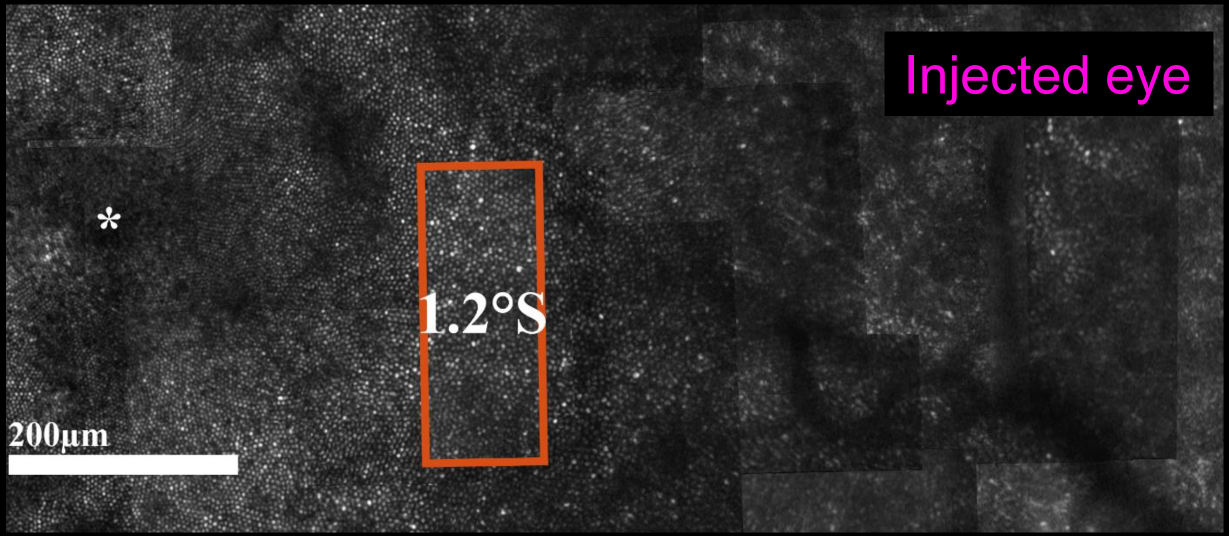


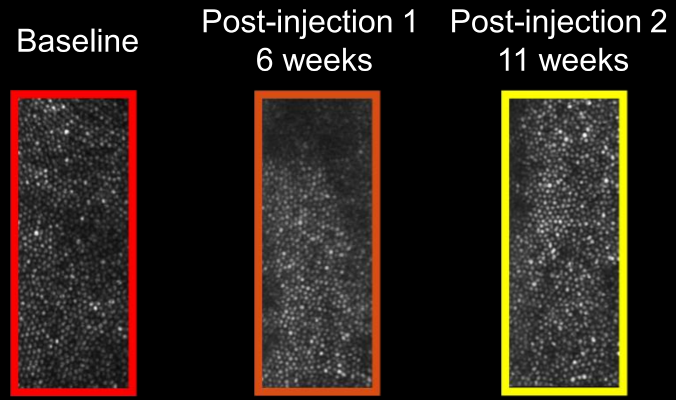


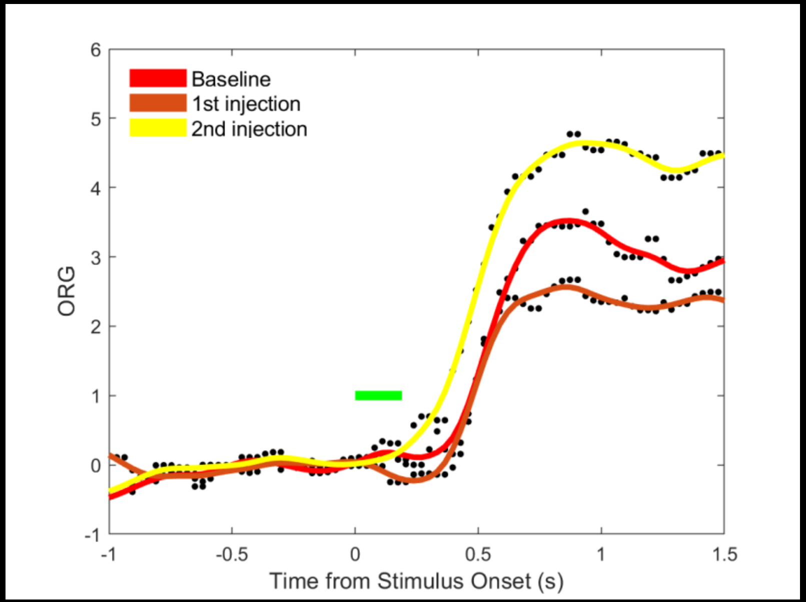


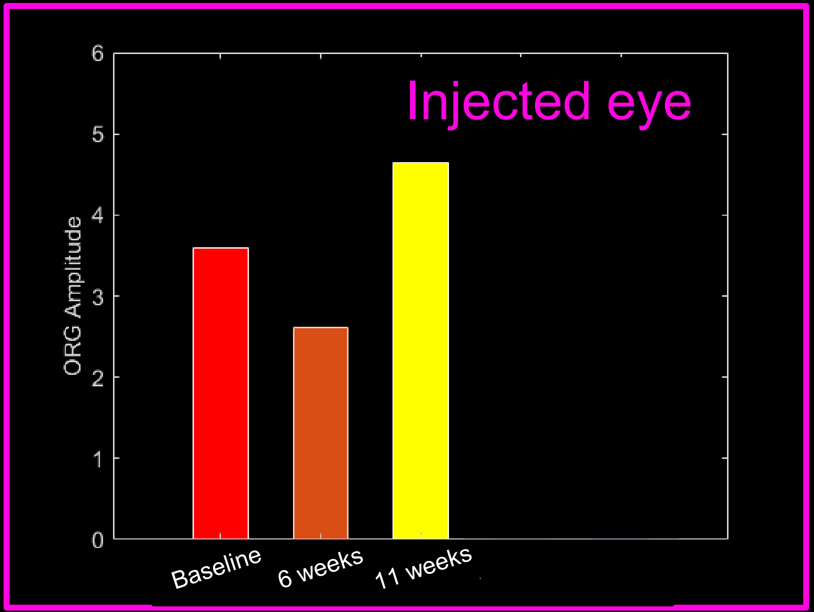


Optoretinography, Patient 2 over time

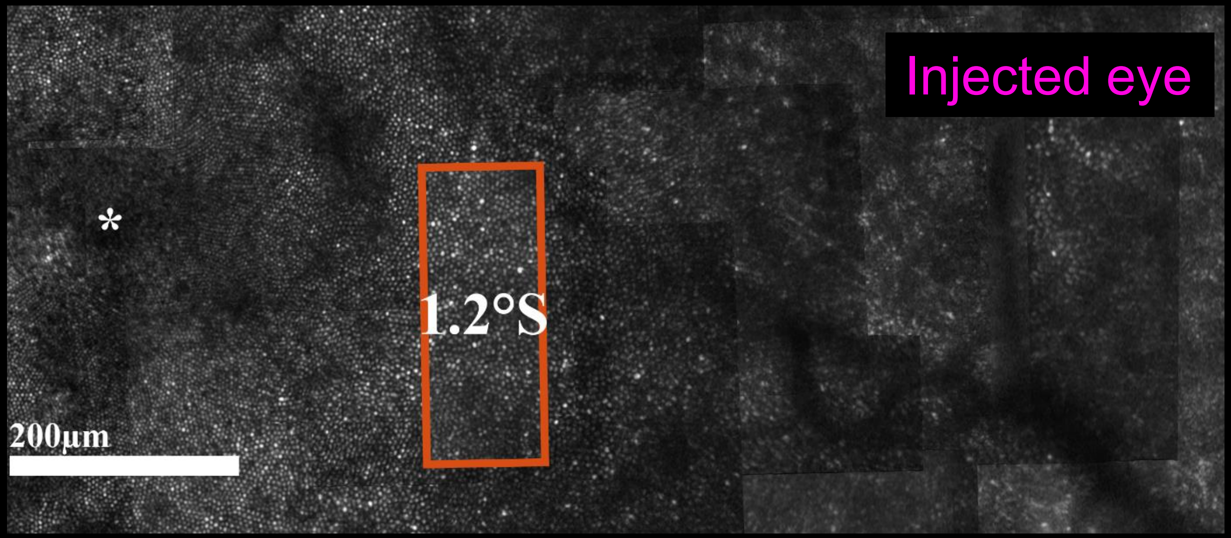


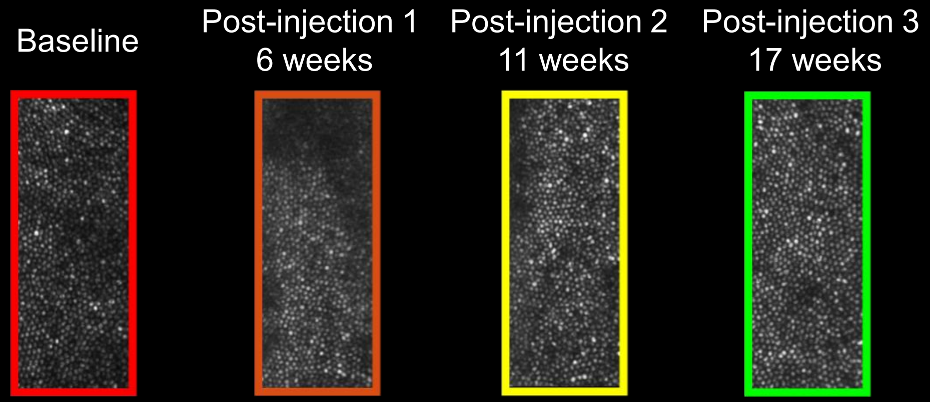


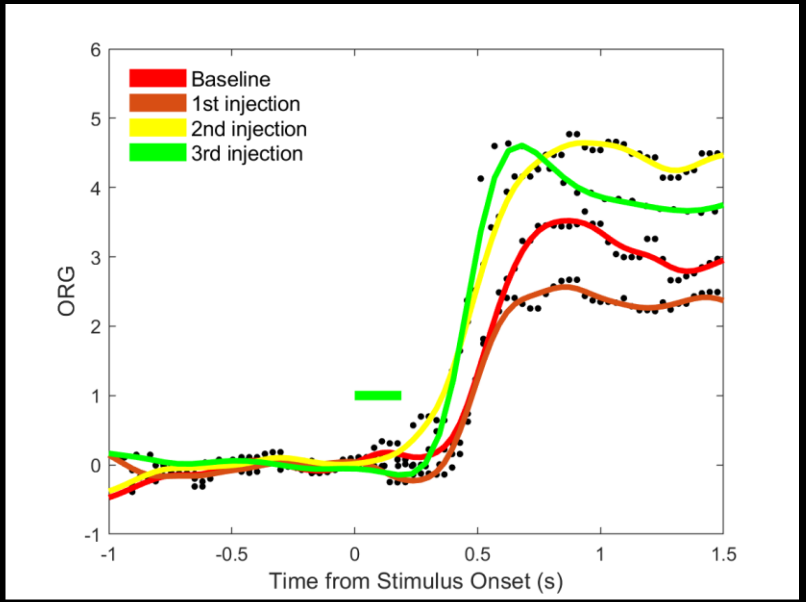


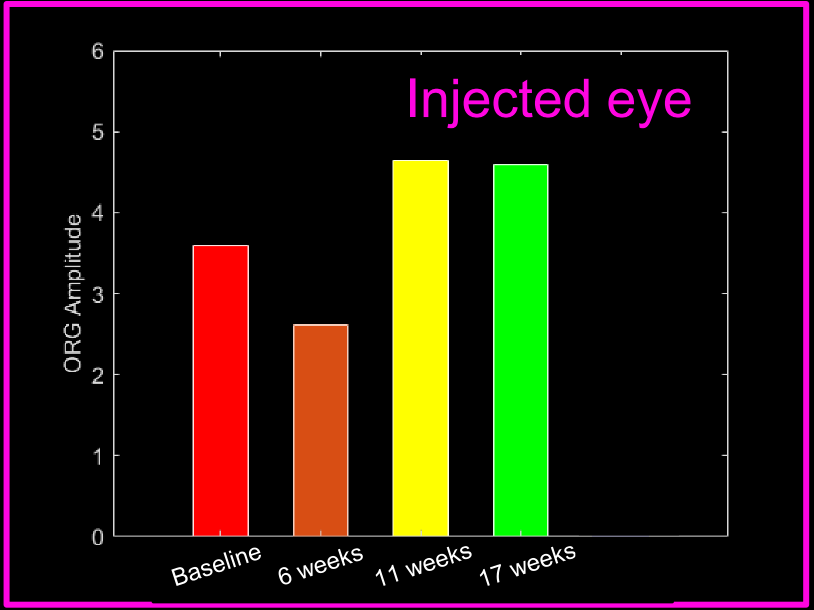


Optoretinography, Patient 2 over time

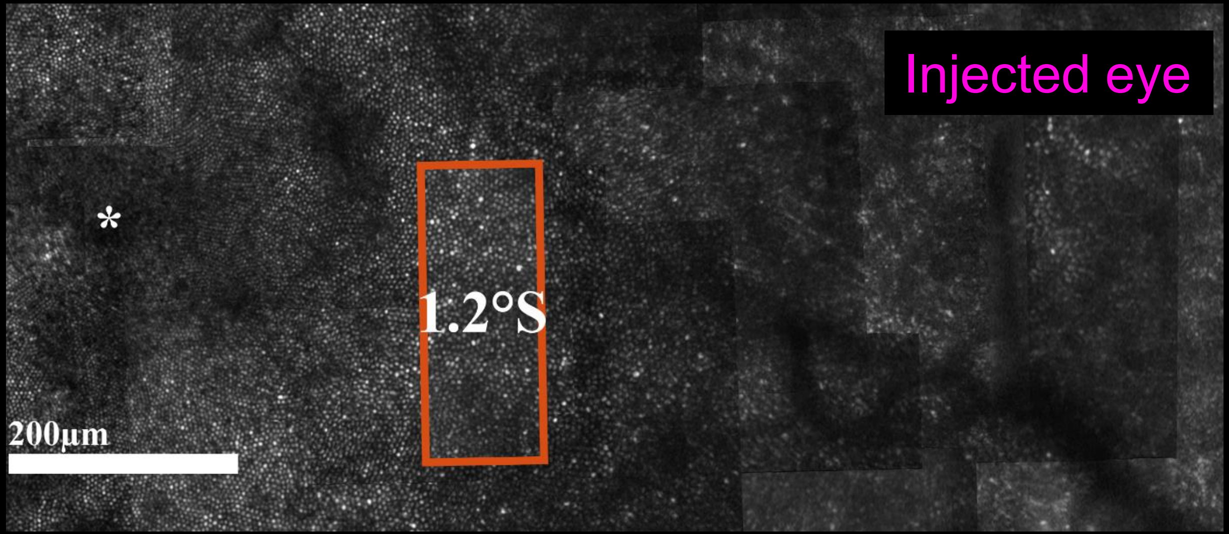


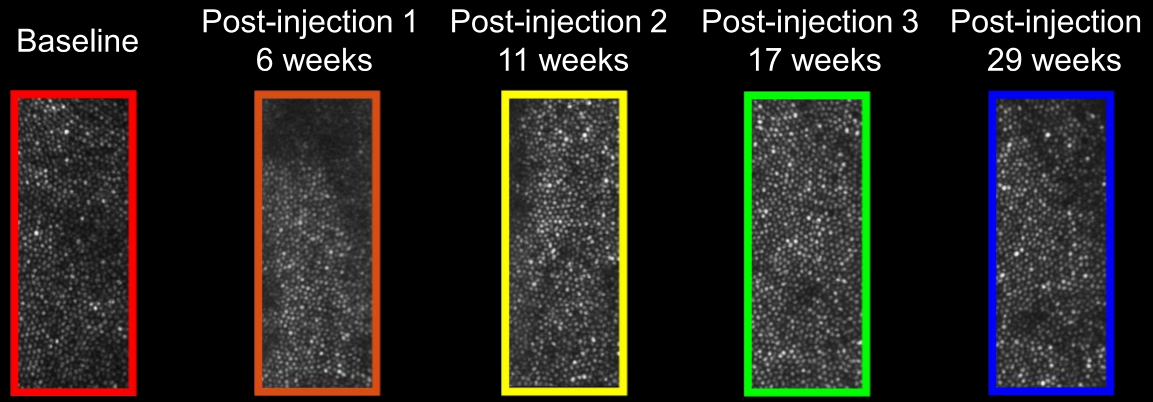


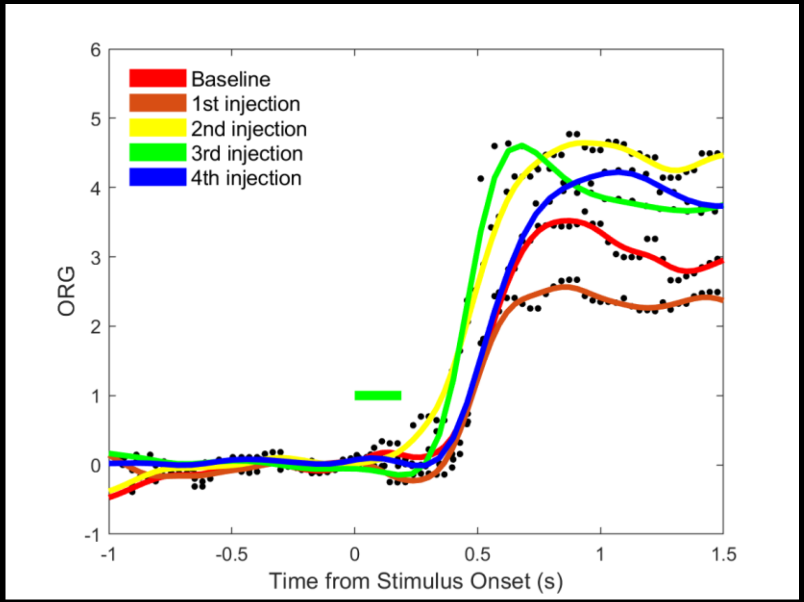


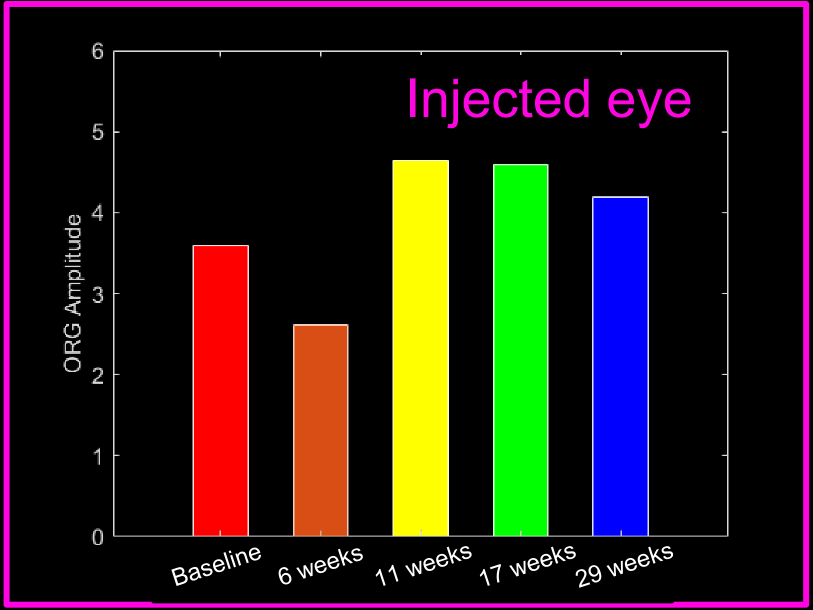


Optoretinography, Patient 2 over time

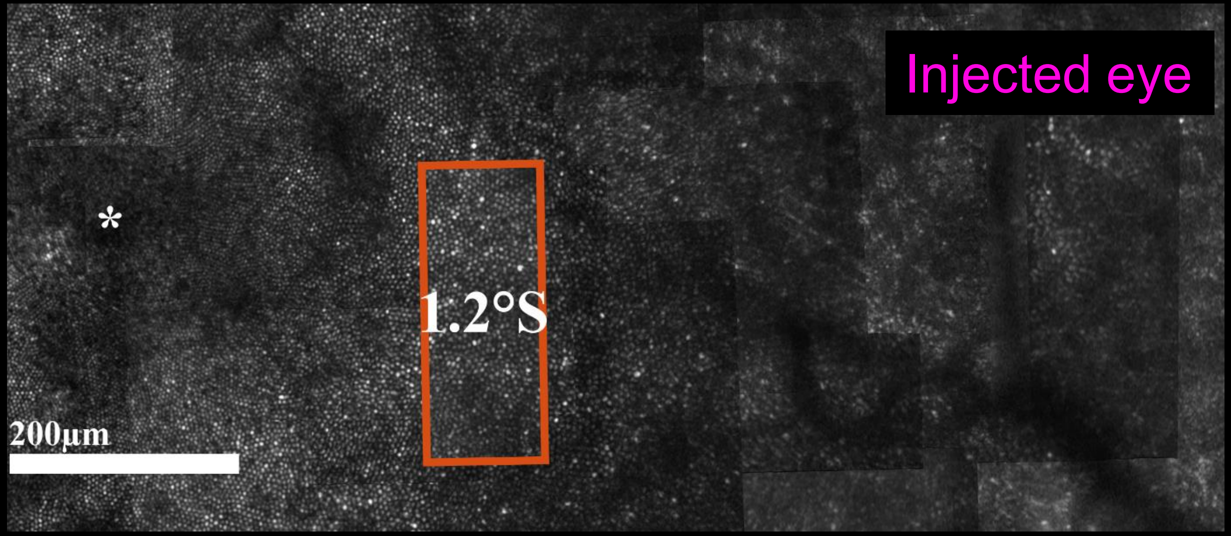


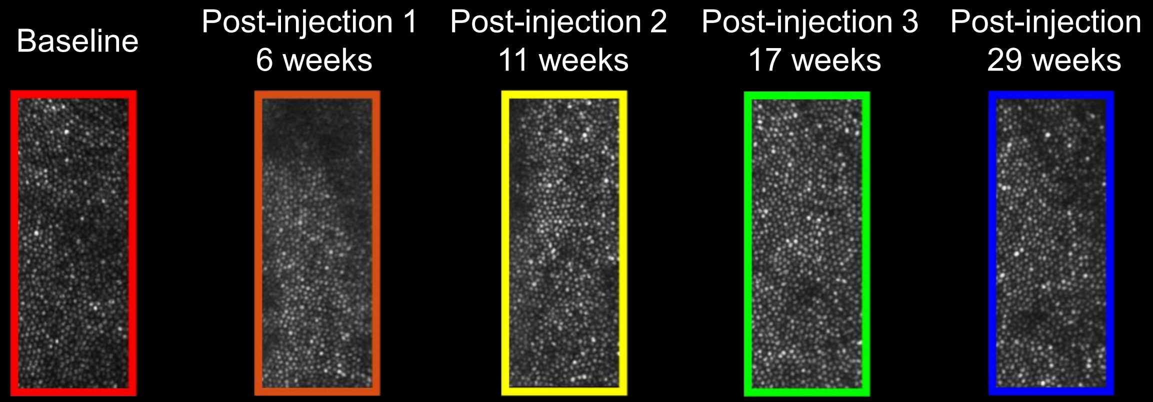


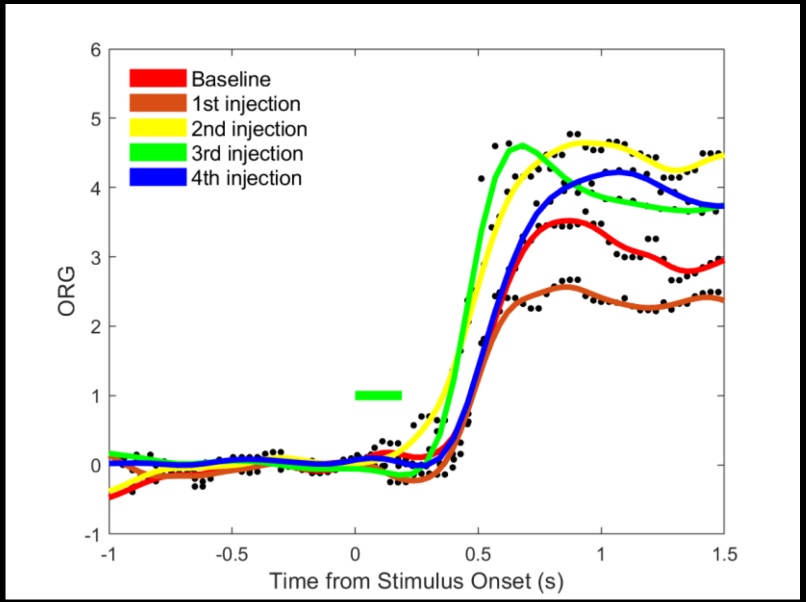


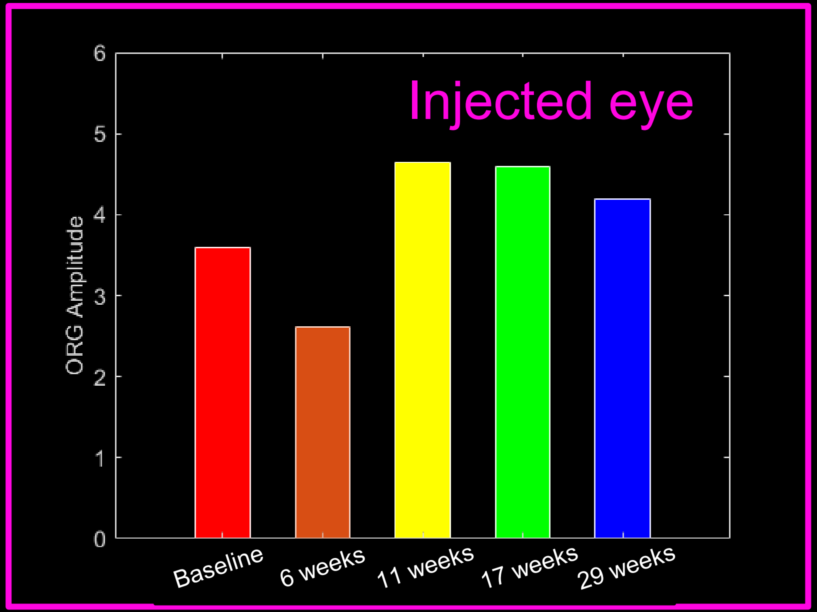


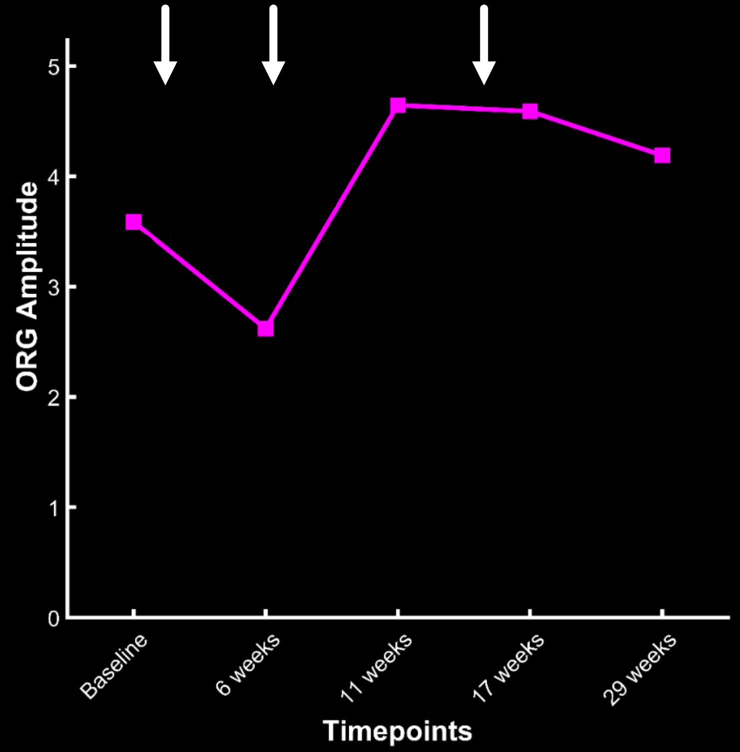
Optoretinography, Patient 2 over time



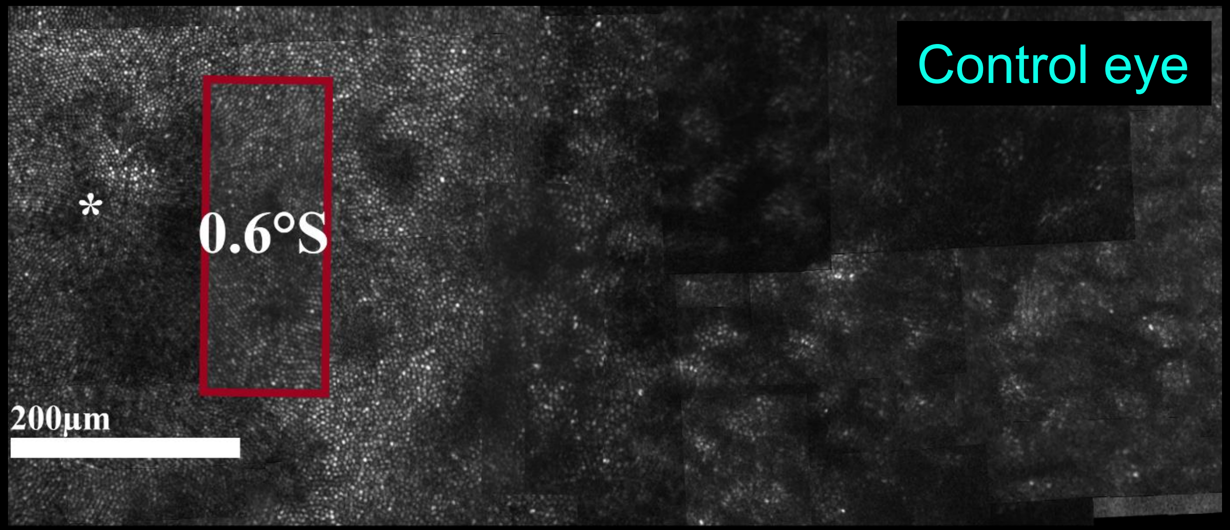


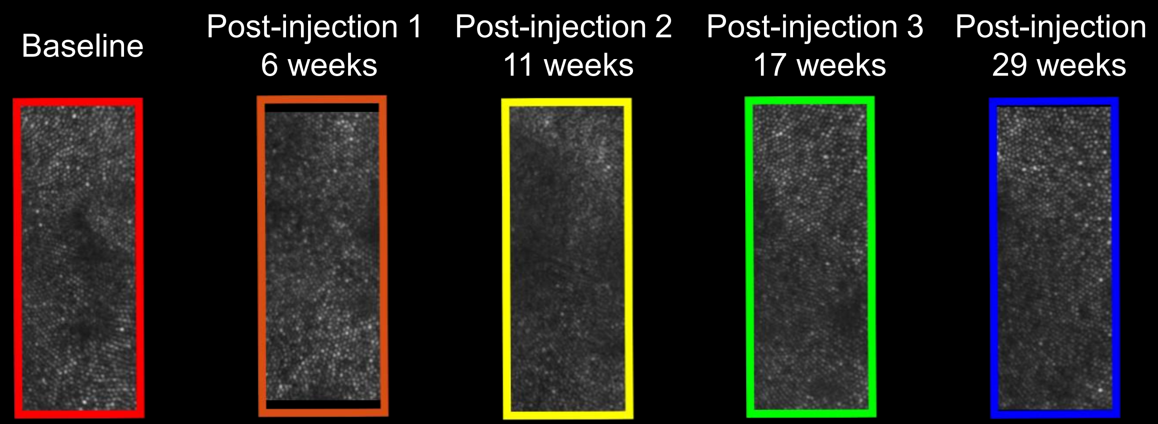


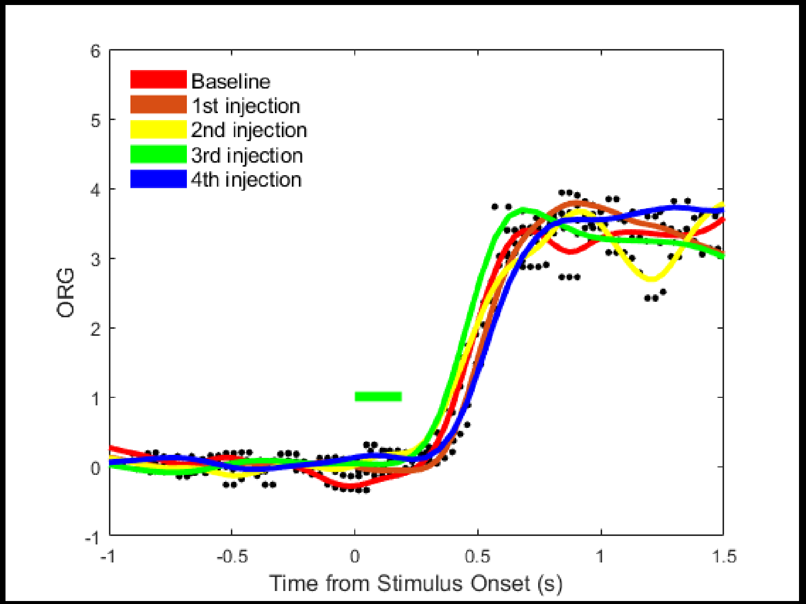


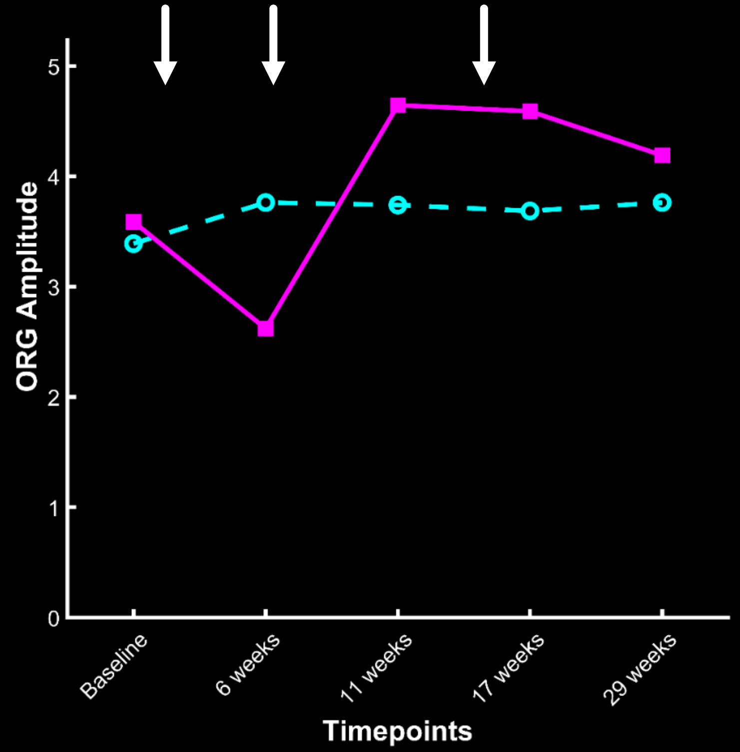


Optoretinography, Patient 2 over time

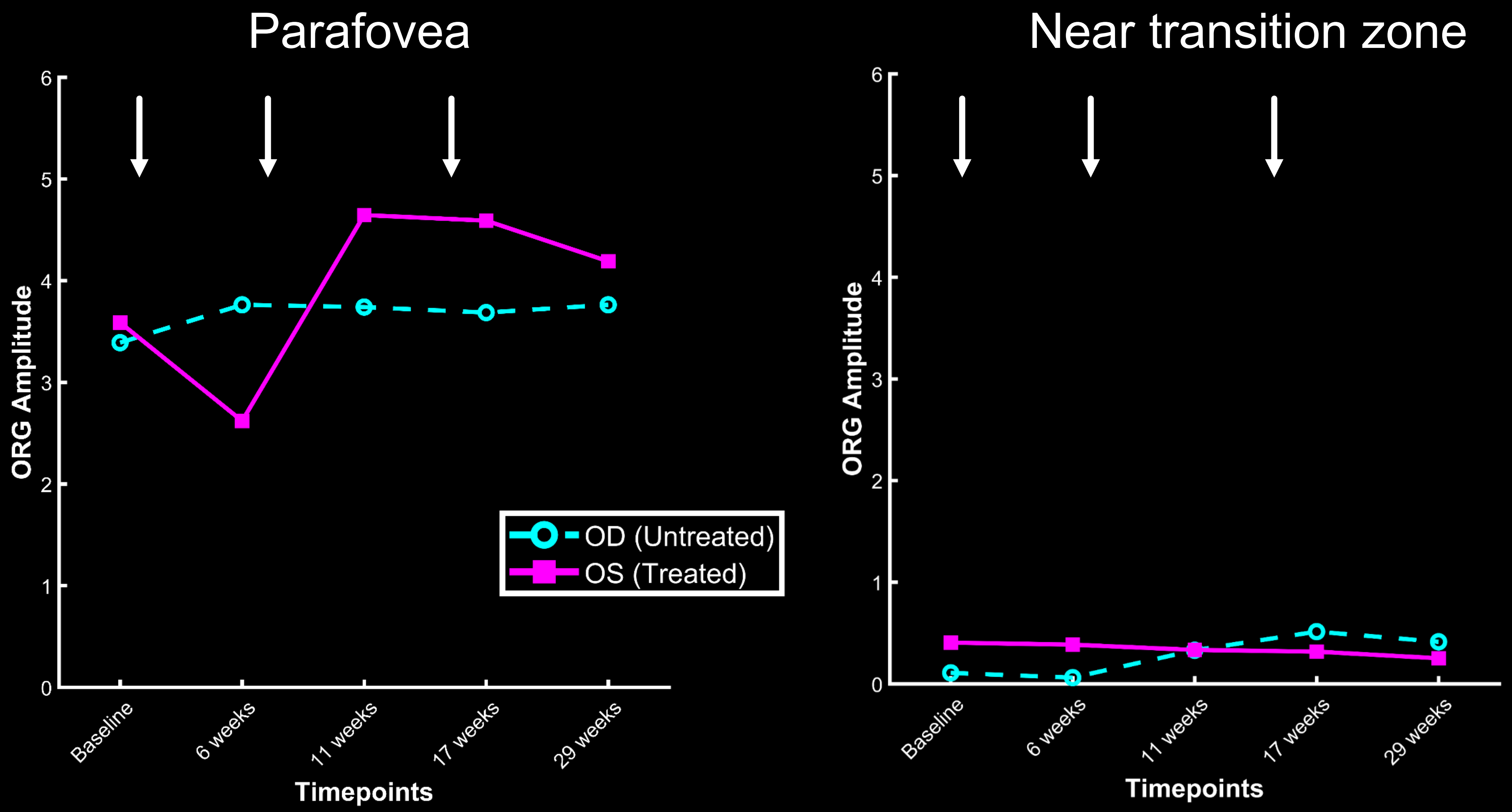






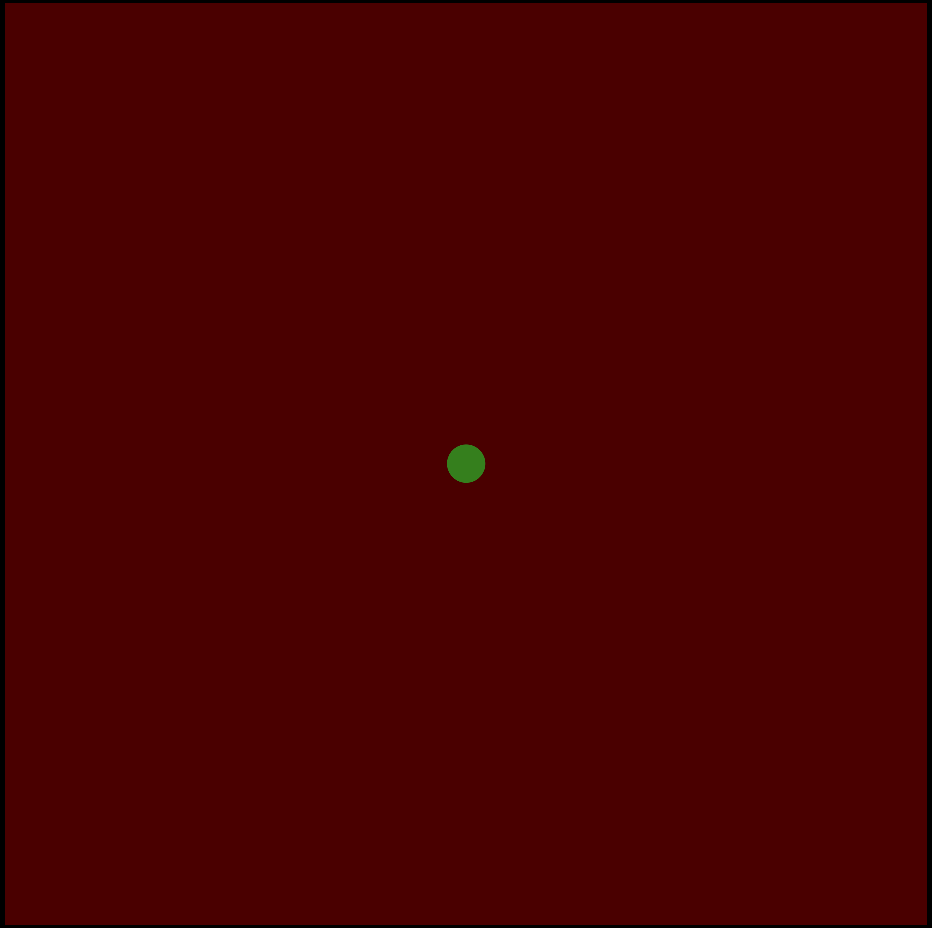


Optoretinography, Patient 2 over time



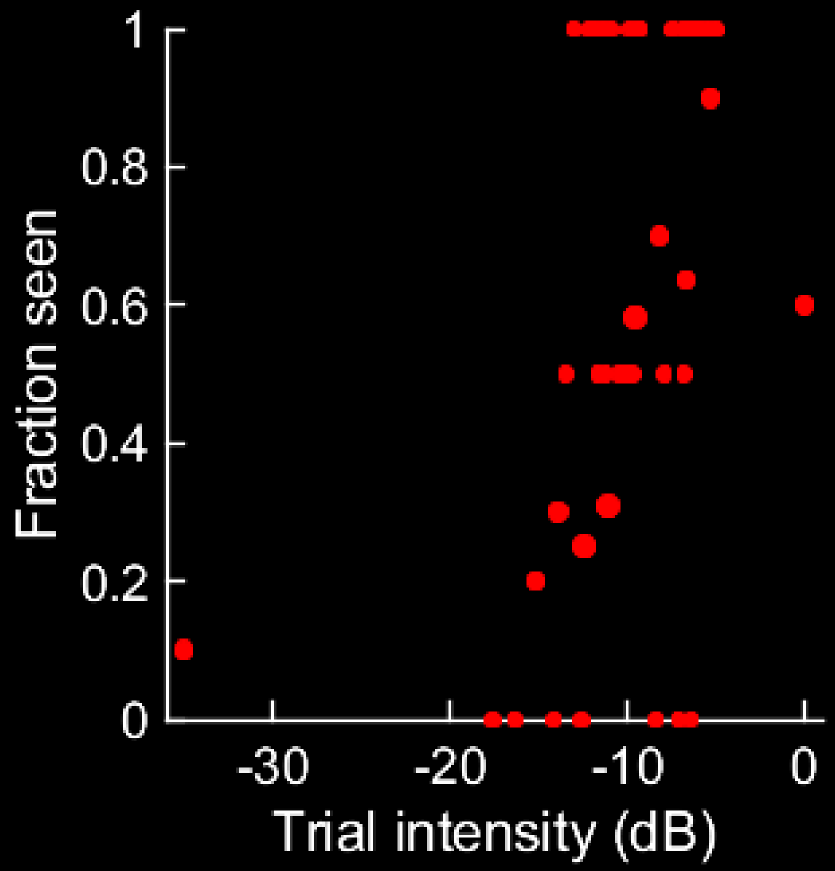
AO microperimetry

AO microperimetry



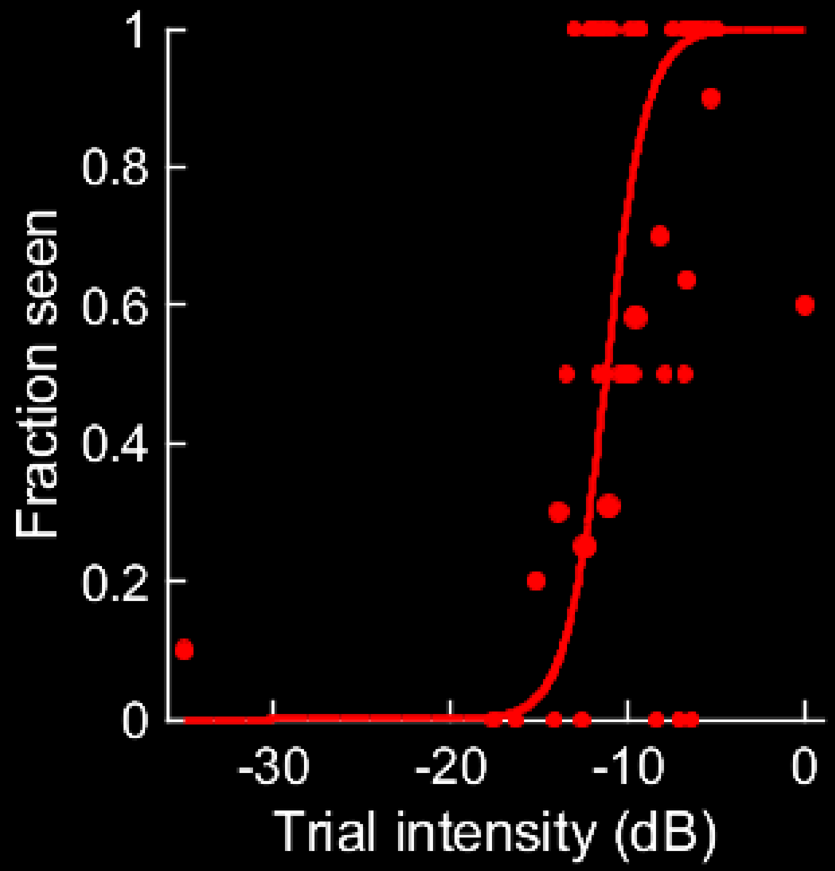
- Image the retina with infrared illumination with AOSLO.
- Deliver a 550 nm stimulus to targeted locations, repeatedly.
- Stimulus size varied by eccentricity but remained the same across time points for all locations.
- Yes/No response for each trial.
- QUEST adaptive staircase of 20 trials, 3 times.
- 100 trials using MOCS for intensities around the expected sensitivity.

AO microperimetry



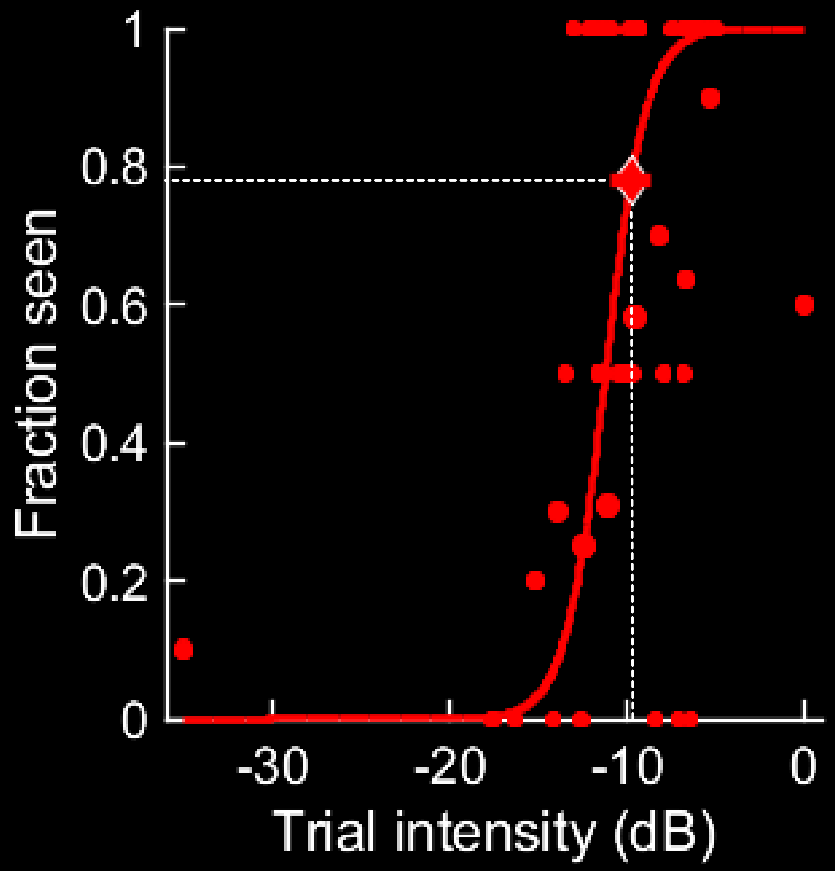
Baseline

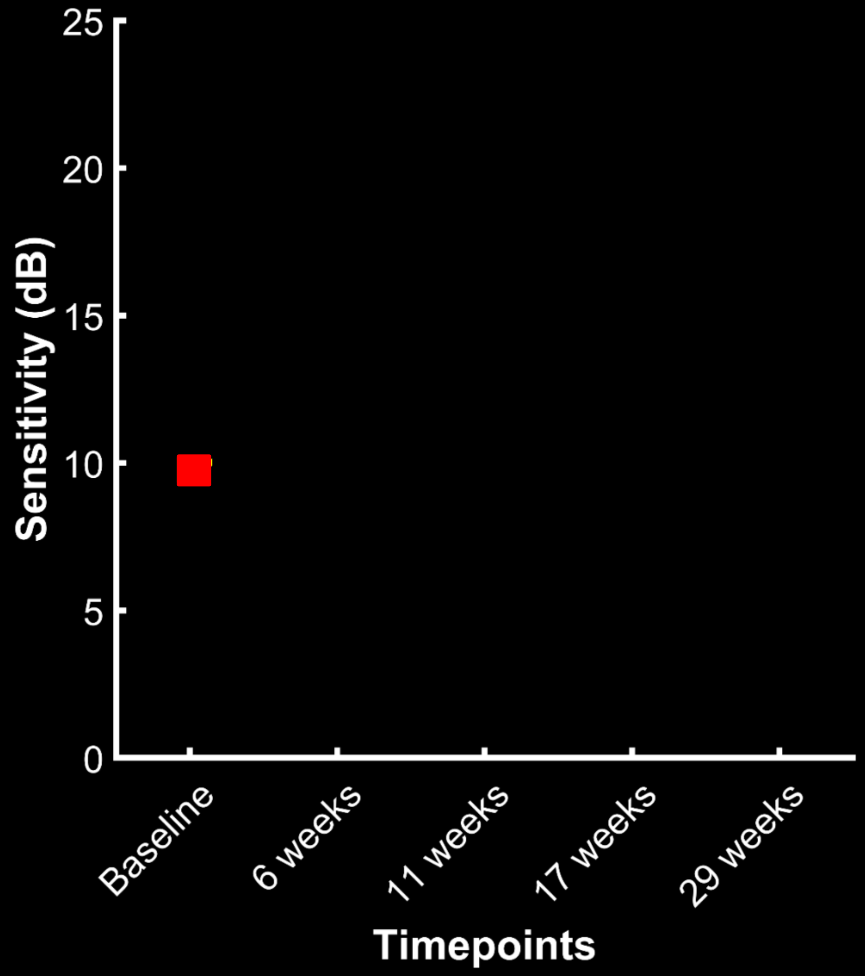
AO microperimetry



Baseline

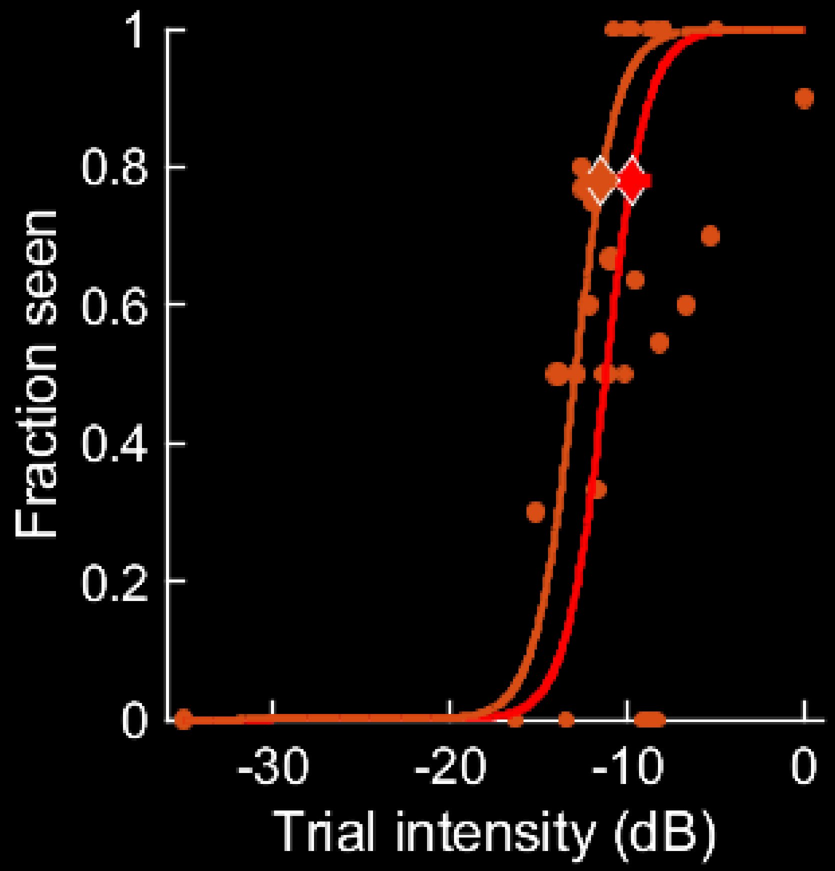
AO microperimetry

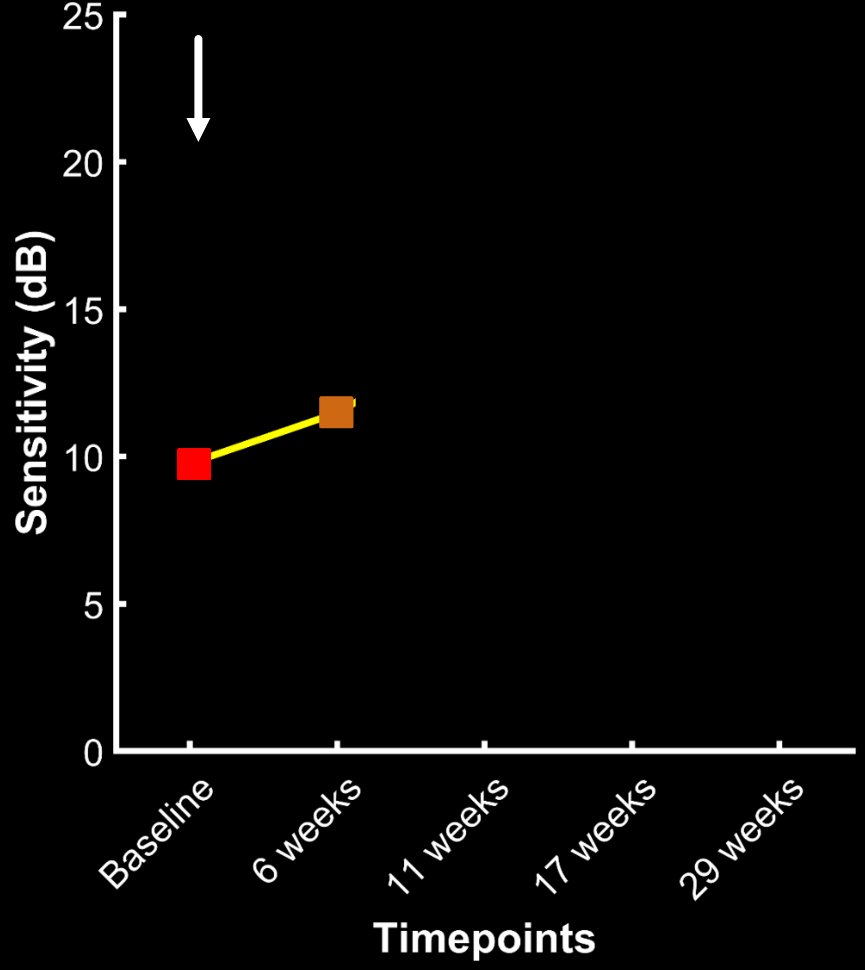




Baseline

AO microperimetry – sensitivity over time

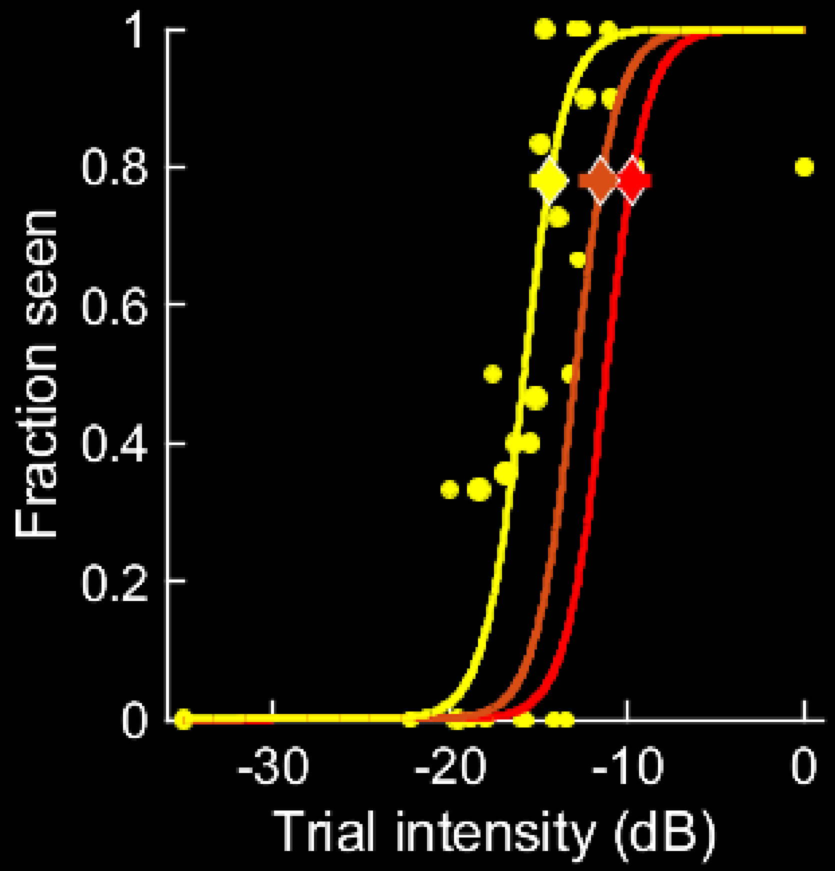


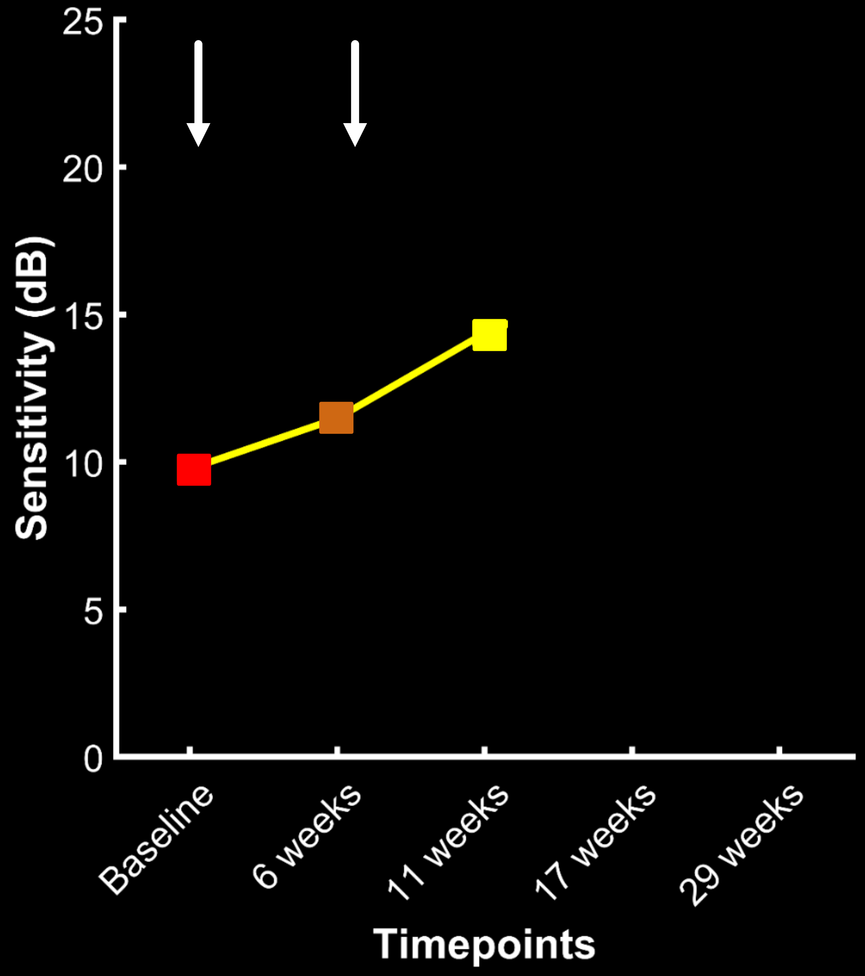


Baseline

Post-injection 1
6 weeks

AO microperimetry – sensitivity over time



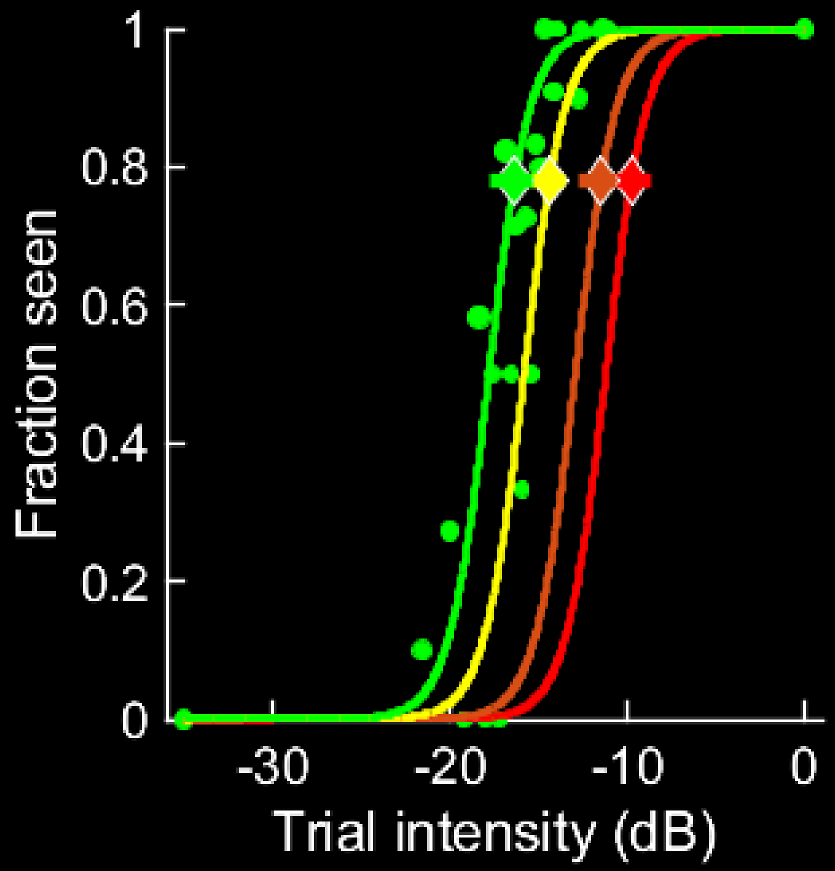


Baseline

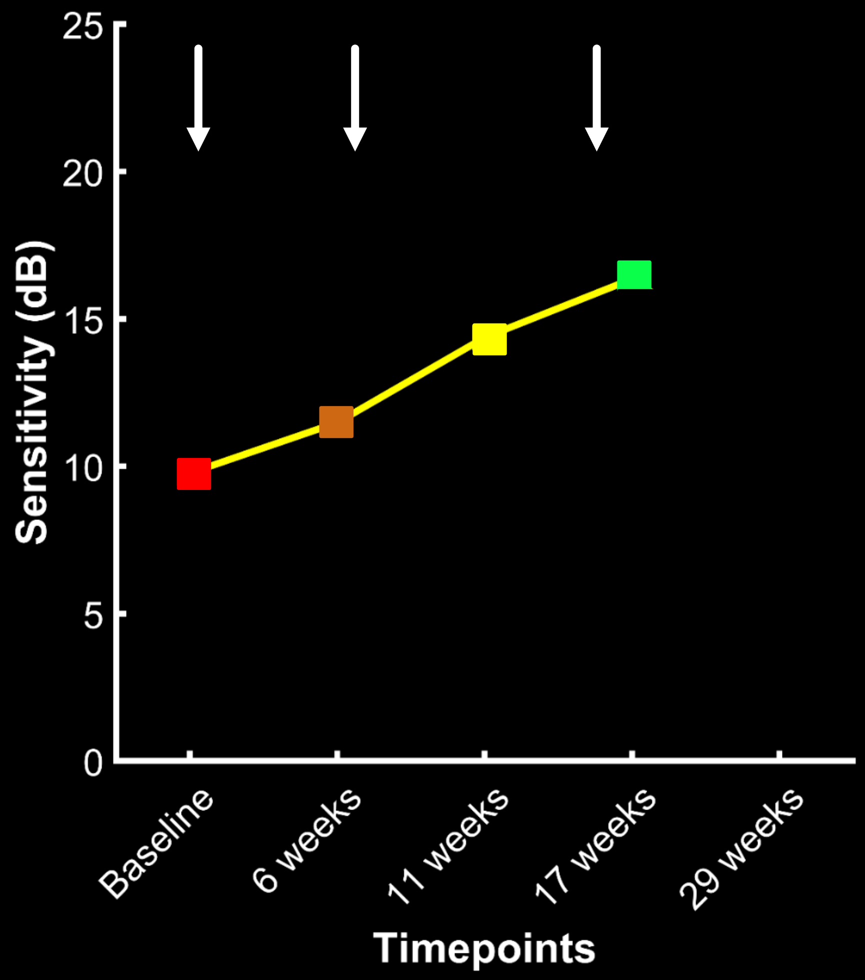
Post-injection 1
6 weeks

Post-injection 2
11 weeks

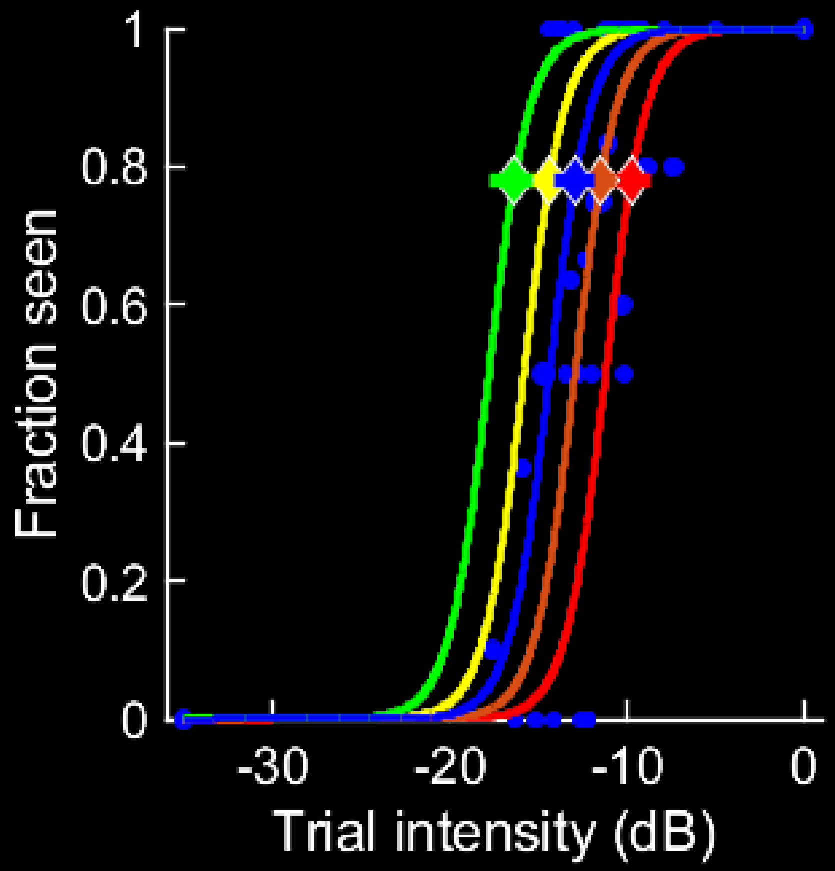
AO microperimetry – sensitivity over time

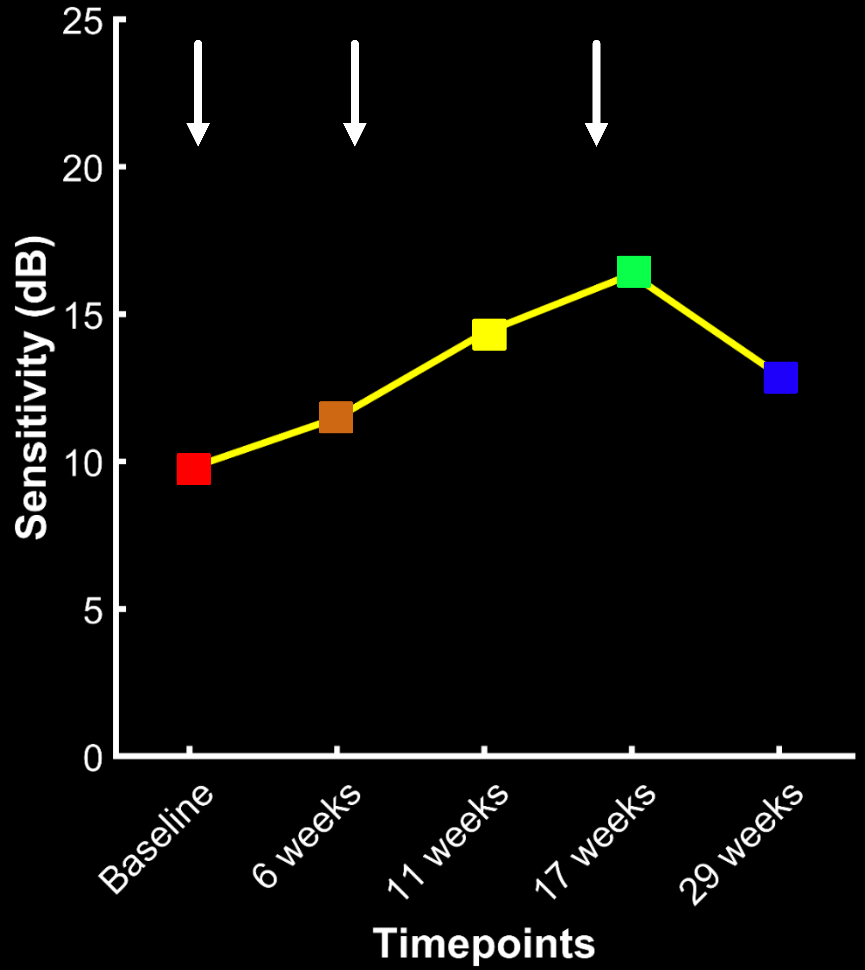


Baseline
Post-injection 1
6 weeks
Post-injection 2
11 weeks
Post-injection 3
17 weeks



AO microperimetry – sensitivity over time





Baseline

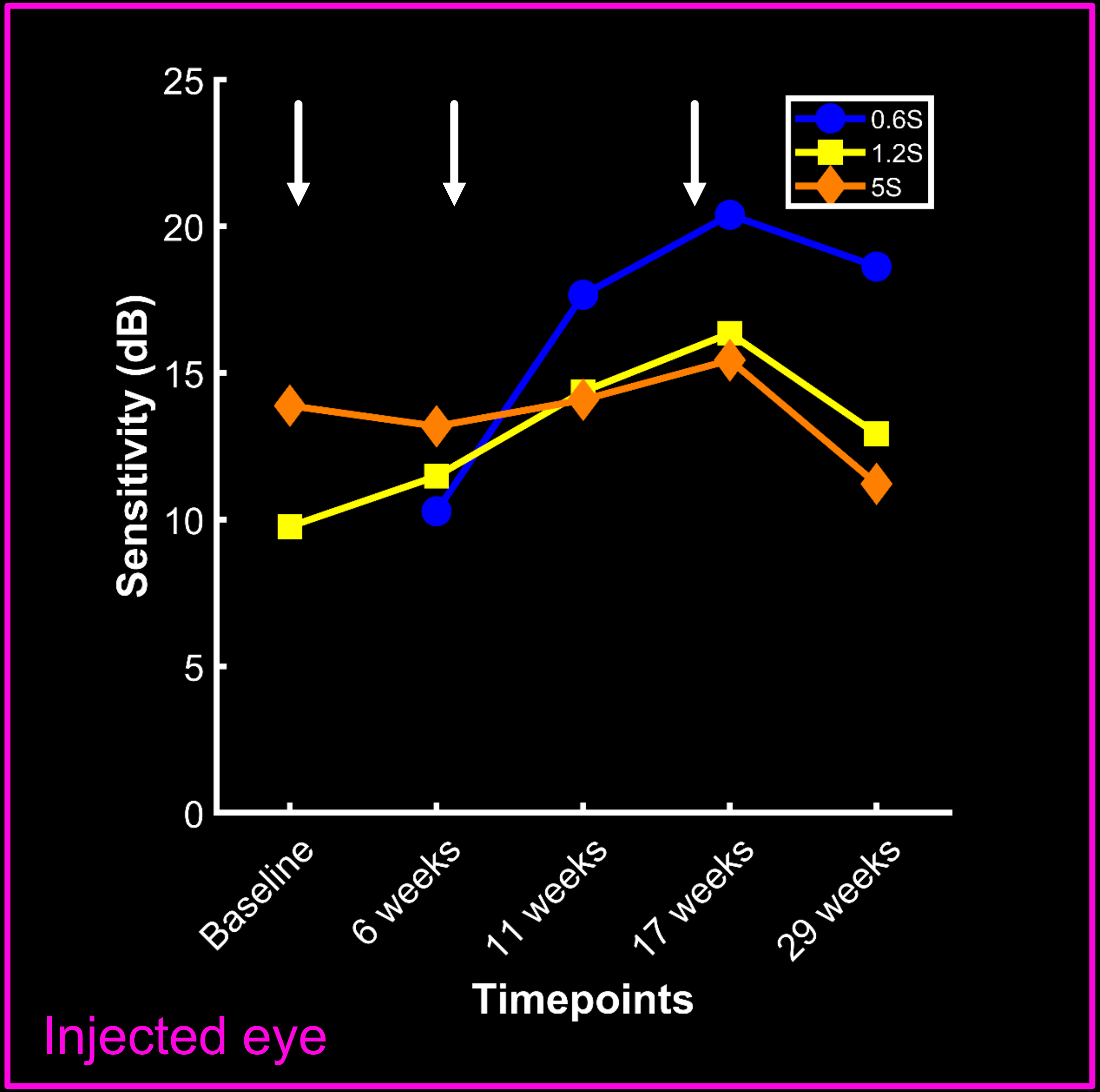
Post-injection 1
6 weeks

Post-injection 2
11 weeks

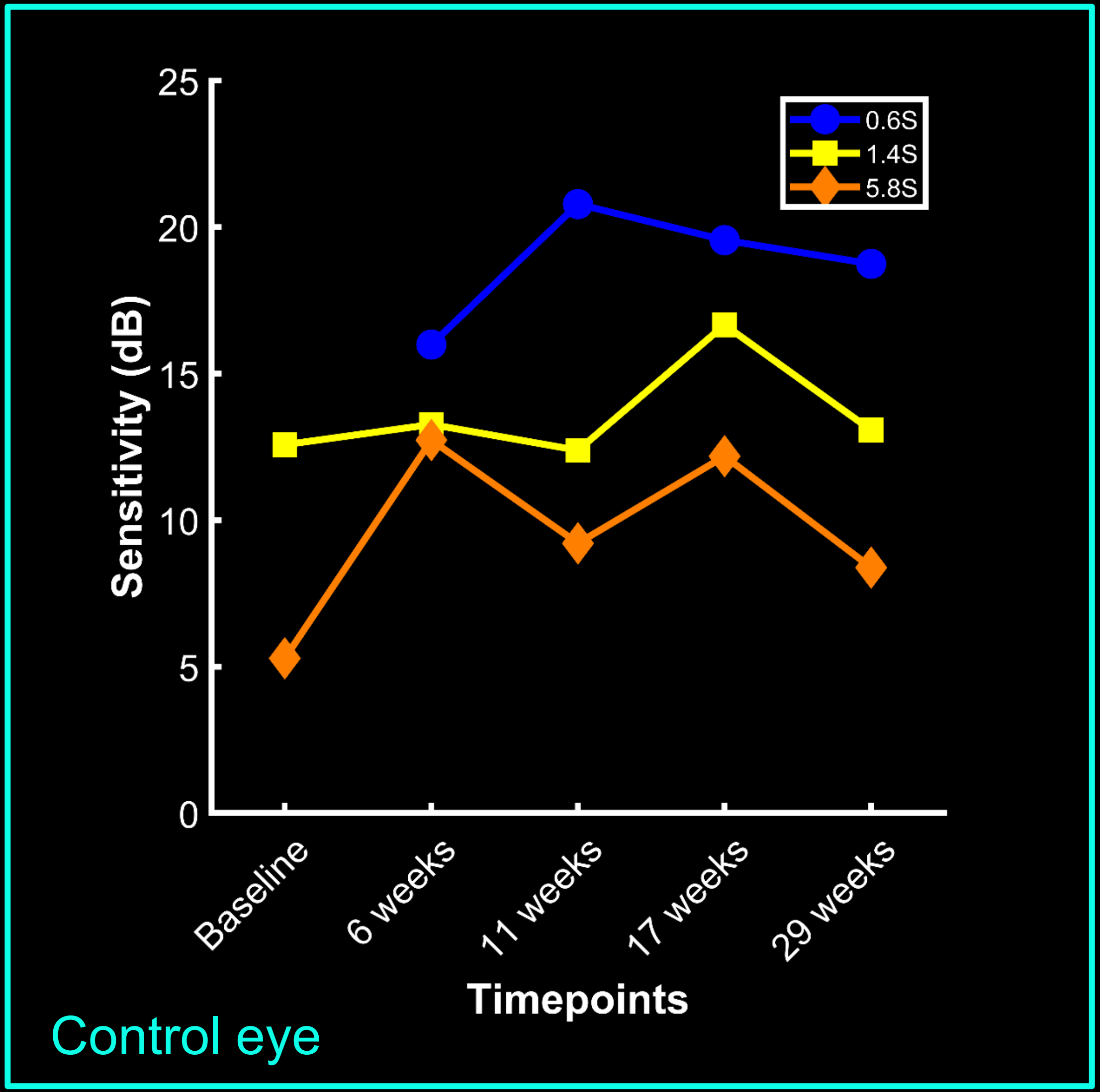
Post-injection 3
17 weeks

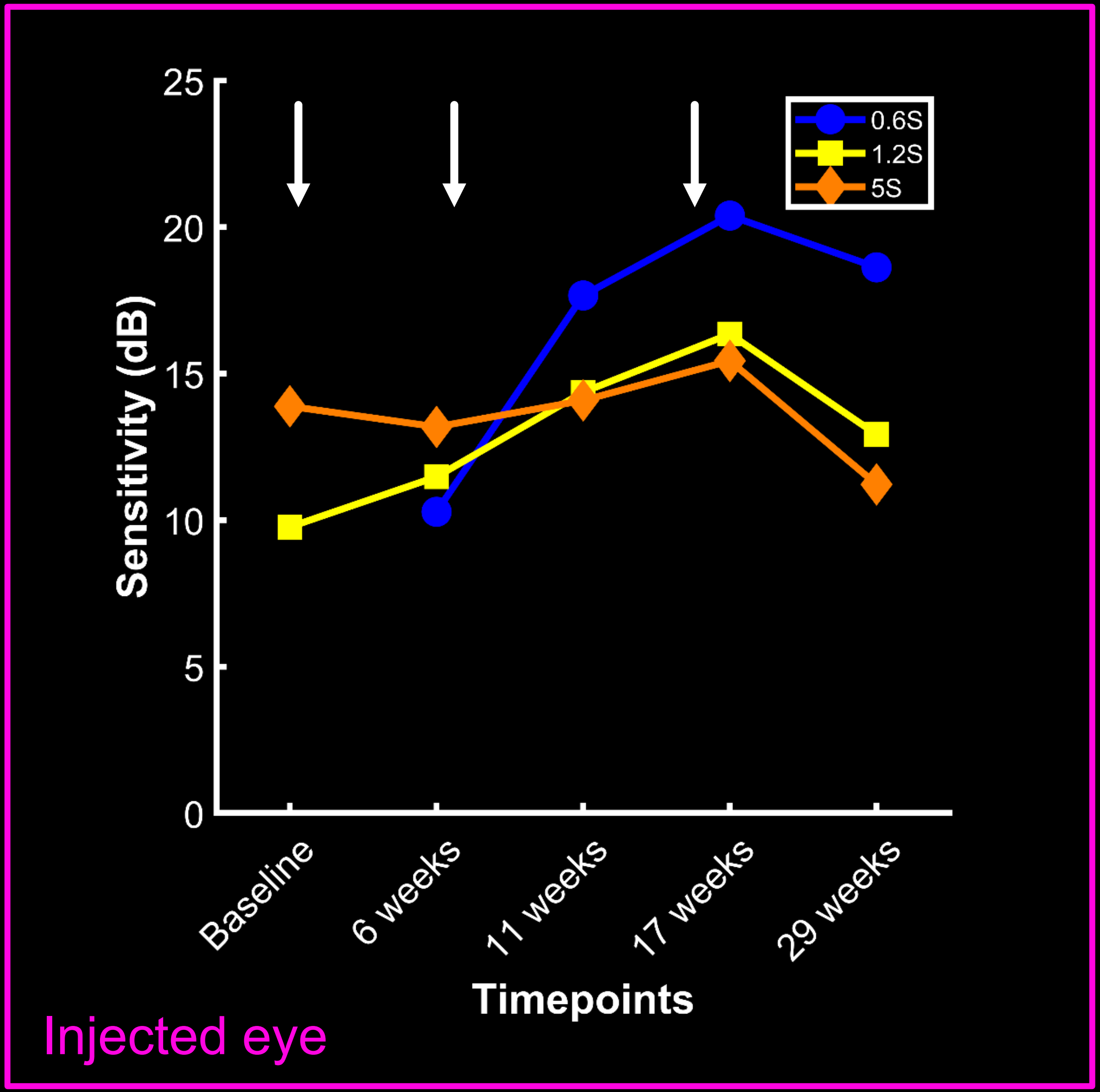
Post-injection
29 weeks

Sensitivity over time, Patient 2



Sensitivity over time, Patient 2

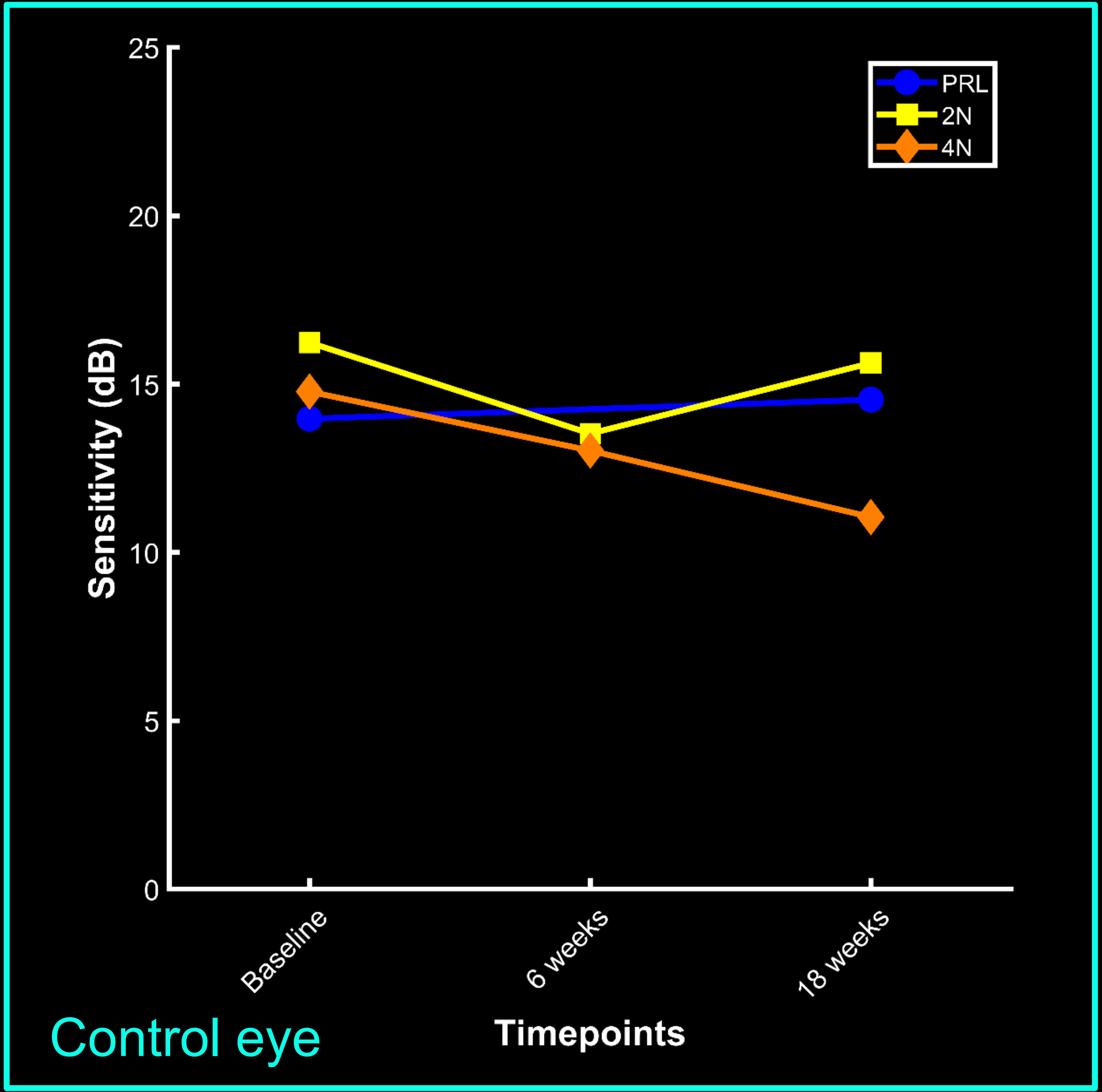


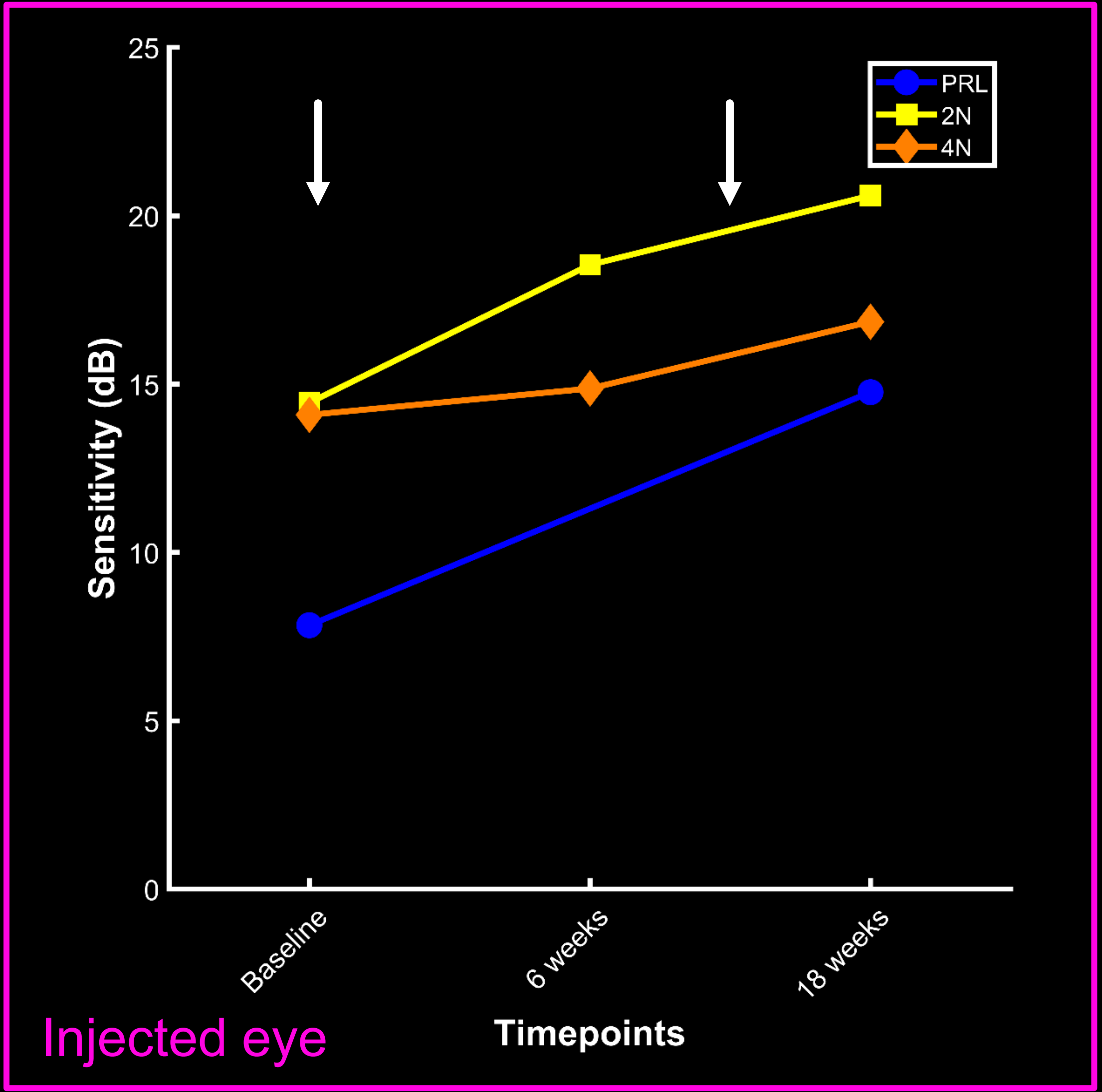


Patient 1

Patient 1

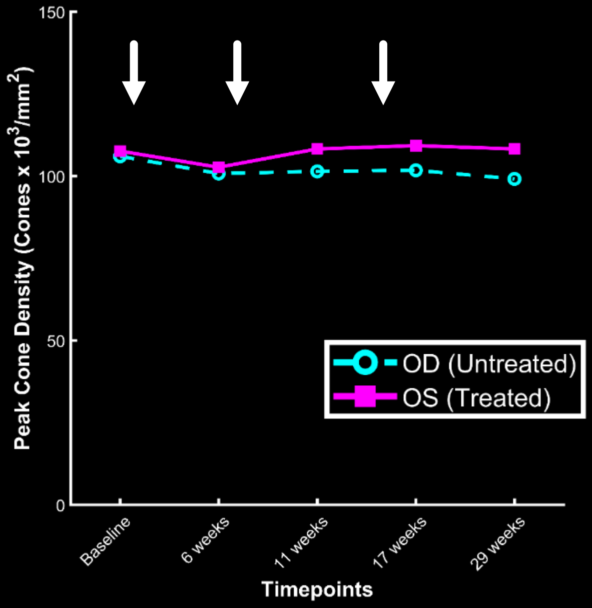
Sensitivity over time, Patient 1



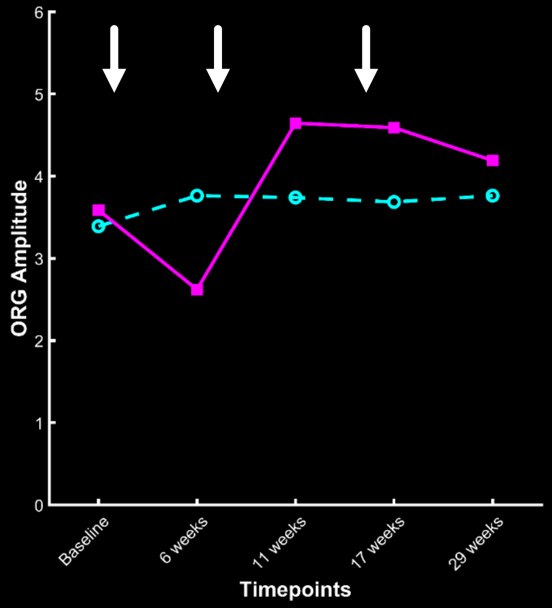


Summary

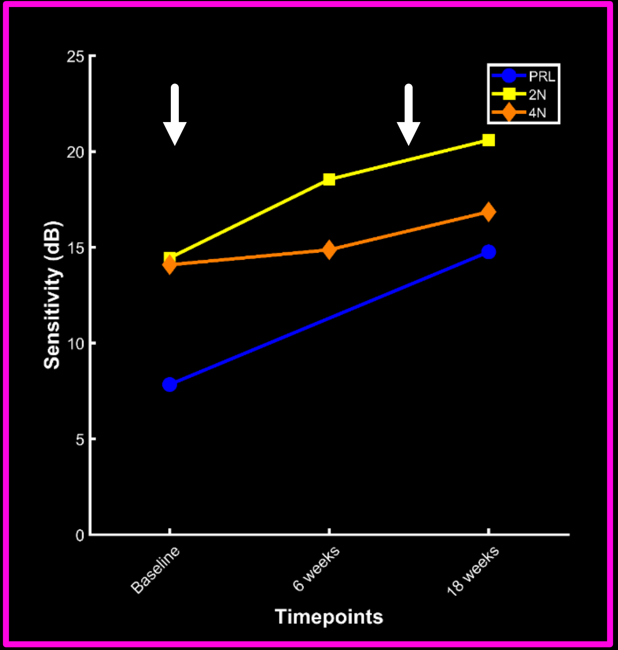
Cone density



ORG amplitude



AO sensitivity



- Cone density, ORG amplitude, and AO sensitivity can be used to assess experimental therapies for retinal disease.
- Cone structure and function were maintained or improved following treatment with VP-001.
- The data support future studies to assess VP-001 efficacy in additional RP11 patients.