The RUSH2A Study: Dark-Adapted Visual Fields in Patients With Retinal Degeneration Associated With Biallelic Variants in the USH2A Gene

David G. Birch,1 Lassana Samarakoon,2 Michele Melia,2 Jacque L. Duncan,3 Allison R. Ayala,2 Isabelle Audo,4,5 Janet K. Cheetham,6 Todd A. Durham,6 Alessandro Iannaccone,7 Mark E. Pennesi,8 and Katarina Stingl9,10; for the Foundation Fighting Blindness Consortium Investigator Group

1Retina Foundation of the Southwest, Dallas, Texas, United States
2Jaeb Center for Health Research, Tampa, Florida, United States
3University of California, San Francisco, San Francisco, California, United States
4Institut de la Vision, Sorbonne Université, INSERM, CNRS, Paris, France
5Centre Hospitalier National d’Ophthalmologie des Quinze-Vingts, INSERM-DGOS CIC1423, Paris, France
6Foundation Fighting Blindness, Columbia, Maryland, United States
7Duke University Medical School, Duke Eye Center, Department of Ophthalmology, Durham, North Carolina, United States
8Casey Eye Institute - Oregon Health & Science University, Portland, Oregon, United States
9University Eye Hospital, Center for Ophthalmology, University of Tübingen, Tübingen, Germany
10Center for Rare Eye Diseases, University of Tübingen, Tübingen, Germany

Correspondence: Allison R. Ayala, Jaeb Center for Health Research, 15310 Amberly Dr, Tampa, FL 33647, USA; fbcresponsauth@jaeb.org.

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Purpose. To measure visual fields using two-color dark-adapted chromatic perimetry in a subset of participants in the Rate of Progression of USH2A-related Retinal Degeneration (RUSH2A), a study of USH2A-mediated syndromic (USH2) and autosomal recessive nonsyndromic retinitis pigmentosa, determine percentage retaining rod function, and explore relationships between dark-adapted visual fields (DAVF) and rod function from ERG and full-field stimulus thresholds (FST).

Methods. Full-field rod mean sensitivity, number of rod loci, maximum sensitivity, DAVF full-field hill of vision (DAVF VTOT), and 30° hill of vision (DAVF V30) were measured in one eye for DAVF ancillary study participants (n = 49). Loci where cyan relative to red sensitivity was more than 5 dB on dark-adapted chromatic perimetry were considered rod mediated. Correlation coefficients between the DAVF measures and standard clinical measures were estimated, as were kappa statistics (κ) for agreement between DAVF and other measures of rod function.

Results. Of 49 participants tested with DAVF, 38 (78%) had evidence of rod function, whereas 15 (31%) had measurable rod ERGs. DAVF maximum sensitivity was highly correlated with FST white thresholds (r = −0.80; P < .001). Although not statistically significant, the number of rod loci and DAVF VTOT were lower in eyes with longer disease duration by 0.82 (95% confidence interval, −1.76, 0.12) loci/year and 0.59 (95% confidence interval, −1.82, 0.64) dB-steradians/year, respectively.

Conclusions. Rod-mediated function on FST and DAVF is present in many patients with symptomatic USH2A-related retinal degeneration, including some without measurable rod ERGs. RUSH2A longitudinal data will determine how these measures change with disease progression and whether they are useful for longitudinal studies in inherited retinal degenerations.

Keywords: visual fields, dark adaptation, autosomal recessive retinitis pigmentosa, Usher syndrome type 2, full-field stimulus test

The Rate of Progression of USH2A-related Retinal Degeneration (RUSH2A) 4-year natural history study of Usher syndrome type 2 (USH2) and nonsyndromic autosomal recessive retinitis pigmentosa (ARRP) was initiated in 2017 to estimate annual change in state-of-the-art outcome measures in patients with USH2A-related retinal degenera-
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METHODS

Study Design

The RUSH2A multicenter, international, longitudinal natural history study has enrolled participants at 16 clinical sites in North America, South America, and Europe.

Eligibility and Enrollment

Participants in the RUSH2A study had USH2 or nonsyndromic ARRP with at least two homozygous or heterozygous disease-causing variants in USH2A, based on a genetic report from a CLIA-certified laboratory or the equivalent in non-US countries. Participants with USH2 who had at least two disease-causing mutations and participants with homozygous disease-causing mutations did not undergo segregation analysis, but segregation studies were performed to confirm inheritance of all compound heterozygous pathogenic variants in participants with ARRP. A patient-reported history of hearing loss and review of the baseline audiology examination by an independent audiologist determined the diagnosis of USH2 (vs. ARRP). Additional criteria for the RUSH2A study were baseline ETDRS visual acuity letter score of 54 or more (approximately 20/80 or better), stable fixation, and clinically determined kinetic visual field III/IV diameter of 10° or more in every meridian of the central field of the study eye (defined as the eye with better BCVA and determined at investigator discretion if both eyes had the same BCVA) using the Octopus 900 Pro (Haag-Streit, Mason, OH) as described previously.

Defining Rod-Mediated Stimulus Detection

Two-color perimetry was used to determine whether rods or cones were mediating detection at each location. Under dark-adapted conditions, mean normal sensitivity values are 20 to 25 dB higher to cyan (505 nm) than to red (625 nm). This finding is consistent with the scotopic luminosity curve, where the rods are approximately 2.5 log units more sensitive to 505 nm than to 625 nm. As the rods degenerate, sensitivity to cyan decreases, whereas sensitivity to red decreases slightly, but is then mediated by cones. Sensitivity to cyan continues to decrease as rods degenerate until it, too, is mediated by cones. The cyan stimulus is 4 dB brighter than the red stimulus in cd/m², which is consistent with the mean normal sensitivity to cyan being approximately 4 dB greater than to the red under light-adapted conditions. Thus, the spectral sensitivity difference (cyan – red) at each point stipulated whether rods were mediating the detection of the stimulus. Participants were considered to have evidence of rod function if the
cyan–red difference was more than 5 dB for at least one cluster of three or more locations within the field. This criterion of three or more points in a cluster was adopted to avoid a spurious high cyan value, leading to a participant being considered to have rod function. Topographic analysis of cyan values for all rod-mediated locations was provided by visual field modeling and analysis, which produces three-dimensional surface models of the hill of vision (HOV). The total volume \(V_{TOT}\) in decibels-steradians beneath the surface of the thin plate spline representation of the HOV and within the external boundary of the grid was quantified, as was the volume within the central 30° of the field \(V_{30}\). Participants with evidence of rod function at the DAVF initial visit (RUSH2A 12-month visit) will complete additional DAVF testing at 12, 24, and 36 months (RUSH2A 24-, 36-, and 48-month visits) subsequent to the initial visit.

**Statistical Analysis**

Forty-nine participants were tested for DAVF rod function (Fig. 1). Logistic regression was used to test for differences in the proportion with rod function on DAVF among the USH2 and ARRP groups, adjusted for disease duration (the difference between participant age and the self-reported age of symptom onset). Differences in the proportion with rod function on DAVF among age and disease duration groups were tested using Fisher’s exact test. Linear regression was carried out to estimate the rate of decline and 95% confidence interval (CI) of the DAVF continuous measures as a function of disease duration. Spearman correlation coefficients were estimated between DAVF measures \(V_{TOT}, V_{30}, \) maximum/mean sensitivity, and full-field rod mean sensitivity treated as continuous variables for analysis) and standard summary measures of visual field obtained using Octopus 900 Pro. Spearman correlation coefficients were also estimated between DAVF initial visit measures (at RUSH2A 12-month visit) and clinical measures obtained at the same visit from the FST white stimulus and FST blue stimulus. ERG data (the amplitude of the b-wave from the dark adapted dim-flash 0.01 cd.s/m² ERG response) obtained at RUSH2A baseline was used to obtain correlations with DAVF measures, because ERG testing was not performed at the initial DAVF visit. Bias-corrected accelerated bootstrap method was used to get 95% CIs for the correlation coefficients. ANOVA was used to evaluate the relationship between maximum DAVF sensitivity

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**Figure 1.** DAVF ancillary study enrollment flow chart.

1. Not consented: 1 declined, 1 machine not available, 1 discontinued due to death
2. Not screened for rod function: 1 withdrew consent, 4 errors resulting in testing not done or too far out of visit window
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(highest sensitivity value within the testing field) and FST threshold, and residuals were regressed on FST threshold to determine whether the variance of maximum sensitivity increased with FST thresholds. Evidence for rod function by FST was defined as a threshold of less than −30 dB. ERG rod function was defined as a b-wave amplitude of greater than 0. Kappa statistics (κ) were calculated to measure agreement between evidence of rod function by DAVF versus other modalities. Owing to the small sample size, the bias-corrected percentile bootstrap method was used to get 95% CIs for kappa estimates. Analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC).

RESULTS

The enrollment flow chart for the study is shown in Figure 1. Forty-nine of 105 participants in the primary RUSH2A cohort were tested for DAVF rod function. The baseline characteristics of this subset of participants at the DAVF initial visit are shown in Table 1. Of the screened participants, 29 (59%) were female, 44 (90%) identified themselves as White, and 31 (63%) were enrolled from the United States or Canada. The median age of participants was 37 years (interquartile range [IQR], 14–27), and the median disease duration was 14 years [IQR, 7–28].

Forty-nine of 105 participants in the primary RUSH2A cohort were tested for DAVF rod function. The baseline characteristics of this subset of participants at the DAVF initial visit are shown in Table 1. Of the screened participants, 29 (59%) were female, 44 (90%) identified themselves as White, and 31 (63%) were enrolled from the United States or Canada. The median age of participants was 37 years (interquartile range [IQR], 14–27), and the median disease duration was 14 years (IQR, 7–21).

Thirty-eight of the 49 screened participants (78%) had evidence of rod function. As shown in Table 1, the age of the reported onset of disease and the age at DAVF initial visit was comparable in those with and without DAVF evidence of rod function. Median disease duration for participants with rod function was 13 years (IQR, 7–20 years) vs. 18 years (IQR, 13–28 years) for participants with no evidence of DAVF rod function.

The clinical diagnosis was USH2 in 28 participants and ARRP in 21 participants; evidence of rod function was found in 19 (68%) of USH2-diagnosed participants and 19 (90%) of ARRP-diagnosed participants (P = 0.09, adjusted for disease duration) (Fig. 4). For USH2-diagnosed participants in the less than 40-year and 40-year and older age groups, evidence of rod function was seen in 15 (75%) patients and 4 (50%) patients, respectively (P = 0.37); for ARRP-diagnosed participants, evidence was seen in 8 (100%) and 11 (85%) participants, respectively (P = 0.50) (Table 2). For USH2-diagnosed participants in the less than 15-year and 15-year and more disease duration groups, evidence of rod function was seen in 10 (77%) and 9 (60%) participants, respectively (P = 0.43); for ARRP-diagnosed participants evidence was seen in 12 (100%) and 7 (78%) participants, respectively (P = 0.17) (Table 3).

Of the 49 participants, 15 (31%) had measurable rod ERGs. Of the 15 participants with measurable rod ERGs, 14 (93%) showed evidence of DAVF rod function. Of the 34 with unmeasurable rod ERGs, 24 (71%) showed evidence of rod function on DAVF. Agreement as measured by the kappa statistic regarding evidence of rod function by DAVF versus FST white, FST blue, and rod ERG was 0.38 (95% CI, 0.18 to 0.58), 0.40 (95% CI, 0.08 to 0.72), and 0.16 (95% CI, 0.005 to 0.31), respectively. In USH2 participants alone, agreement regarding evidence of rod function by DAVF versus FST white, FST blue, and rod ERG was 0.25 (95% CI, 0.04 to 0.46), 0.40 (95% CI, 0.03–0.77), and 0.07 (95% CI, −0.13 to 0.27), respectively. In ARRP-diagnosed participants evidence was seen in 12 (100%) and 7 (78%) participants, respectively (P = 0.17) (Table 3).

**Table 1.** Characteristics of Study Participants at the DAVF Initial Visit

| DAVF Initial Visit Characteristics | No Evidence | Evidence |
|-----------------------------------|-------------|----------|
| Gender                            |             |          |
| Female                            | 8 (28%)     | 21 (72%) |
| Male                              | 3 (15%)     | 17 (85%) |
| Clinical diagnosis                |             |          |
| USH2                              | 9 (32%)     | 19 (68%) |
| ARRP                              | 2 (10%)     | 19 (90%) |
| Race/ethnicity                    |             |          |
| White                             | 8 (18%)     | 36 (82%) |
| Hispanic                          | 2 (67%)     | 1 (33%)  |
| Asian                             | 1 (50%)     | 1 (50%)  |
| Enrollment area                   |             |          |
| United States/Canada              | 5 (16%)     | 26 (84%) |
| Europe/UK                         | 6 (33%)     | 12 (67%) |
| Age at visit, years               |             |          |
| Median (IQR)                      | 40.5 (31.0, 45.8) | 37.2 (28.0, 48.8) |
| [Min, Max]                        | [26.4, 64.1] | [17.8, 69.7] |
| <40                               | 5 (18%)     | 23 (82%) |
| ≥40                               | 6 (29%)     | 15 (71%) |
| Age at onset, years               |             |          |
| Median (IQR)                      | 19.0 (13.0, 24.0) | 19.5 (14.0, 37.0) |
| [Min, Max]                        | [12.0, 27.0] | [7.0, 56.0] |
| <16                               | 3 (19%)     | 13 (81%) |
| ≥16                               | 6 (35%)     | 11 (65%) |
| ≥25                               | 2 (13%)     | 14 (88%) |
| Duration of disease, years        |             |          |
| Median (IQR)                      | 17.7 (12.8, 27.9) | 13.1 (7.1, 20.3) |
| [Min, Max]                        | [7.0, 45.1] | [2.0, 37.4] |
| <10                               | 2 (13%)     | 14 (88%) |
| ≥10                               | 5 (28%)     | 13 (72%) |
| ≥20                               | 4 (27%)     | 11 (73%) |

DAVF results from an eye retaining evidence of rod function are shown in Figure 2. Sensitivity at most field locations is higher for cyan than for red (Fig. 2a). The HOV model for rod-mediated sensitivity is shown in Figure 2b. This participant eye showed minimal rod-mediated function in the central retina, but retained high rod sensitivity in the periphery. Other patterns of rod visual field are shown in Figure 3, with top-down views shown in the left column and side views shown in the right column. Row A shows a participant with preserved rod function throughout the periphery and peaks in the central 30°, row B shows a participant with a deep mid peripheral scotoma and row C shows a participant with residual rod function only in the far periphery.

**Table 2.** Characteristics of Study Participants at the DAVF Initial Visit

| Evidence of Rod Function at DAVF Initial Visit |
|-----------------------------------------------|
| No Evidence | Evidence |
| N (11) | (N = 38) |
| Gender |             |
| Female | 8 (28%) | 21 (72%) |
| Male | 3 (15%) | 17 (85%) |
| Clinical diagnosis |             |
| USH2 | 9 (32%) | 19 (68%) |
| ARRP | 2 (10%) | 19 (90%) |
| Race/ethnicity |             |
| White | 8 (18%) | 36 (82%) |
| Hispanic | 2 (67%) | 1 (33%) |
| Asian | 1 (50%) | 1 (50%) |
| Enrollment area |             |
| United States/Canada | 5 (16%) | 26 (84%) |
| Europe/UK | 6 (33%) | 12 (67%) |
| Age at visit, years |             |
| Median (IQR) | 40.5 (31.0, 45.8) | 37.2 (28.0, 48.8) |
| [Min, Max] | [26.4, 64.1] | [17.8, 69.7] |
| <40 | 5 (18%) | 23 (82%) |
| ≥40 | 6 (29%) | 15 (71%) |
| Age at onset, years |             |
| Median (IQR) | 19.0 (13.0, 24.0) | 19.5 (14.0, 37.0) |
| [Min, Max] | [12.0, 27.0] | [7.0, 56.0] |
| <16 | 3 (19%) | 13 (81%) |
| ≥16 | 6 (35%) | 11 (65%) |
| ≥25 | 2 (13%) | 14 (88%) |
| Duration of disease, years |             |
| Median (IQR) | 17.7 (12.8, 27.9) | 13.1 (7.1, 20.3) |
| [Min, Max] | [7.0, 45.1] | [2.0, 37.4] |
| <10 | 2 (13%) | 14 (88%) |
| ≥10 | 5 (28%) | 13 (72%) |
| ≥20 | 4 (27%) | 11 (73%) |
FIGURE 2. Derivation of rod visual fields in a participant with ARRP. Fields were obtained twice, once with a cyan test and once with a red test (a). Not seen points are indicated with NO. Locations where the cyan-red difference was greater than 5 dB were considered rod mediated. Topographic analysis of cyan values for all rod-mediated locations was provided by visual field modeling and analysis (b).

(kappa = 0.01–0.20) with DAVF regarding evidence of rod function. There was some evidence agreement varied with age and diagnosis groups. However, the sample sizes were too small to make a definitive conclusion.

Along with mean sensitivity and maximum sensitivity, an HOV analysis of the DAVF results provided volumetric measures of total field (VTOTAL) and the volume of the central 30° (V30). The correlations among DAVF measures of rod visual field and light adapted static HOV parameters were low, ranging from 0.31 to 0.40 (Table 5). However, DAVF measures were highly correlated with FST measures of rod function in these participants. DAVF maximum sensitivity decreased with higher FST white stimulus intensity (r = −0.80; *P < .001; 95% CI, −0.92 to −0.59); the variance in the maximum sensitivity increased as the FST stimulus intensity increased (P = 0.05), especially above the −30 dB level, where FST thresholds may be influenced by cones (area to the right of the vertical red line). DAVF mean sensitivity, DAVF VTOTAL, and DAVF V30 were moderately correlated with FST white thresholds (r = −0.71 [95% CI, −0.86 to −0.50], r = −0.72 [95% CI, −0.87 to −0.51], and r = −0.61 [95% CI, −0.81 to −0.31]), respectively; all *P < .001). Correlations with FST blue thresholds were similar to those with FST white thresholds (Table 5). Among participants with evidence of rod function, the number of rod loci and the DAVF VTOTAL were lower in participants with longer disease duration by −0.82 loci per year (95% CI, −1.76 to 0.12) and −0.59 decibels-steradians per year (95% CI, −1.82 to 0.64) of disease duration, respectively (Figs. 6 & 7). The number of rod loci and DAVF VTOTAL also were lower in USH2 than ARRP participants (mean difference, −16; 95% CI, −33 to −0.3; *P = 0.046; and mean difference, −20; 95% CI, −41 to 0.7; *P = 0.058, respectively).

DISCUSSION

The inclusion criteria for the primary cohort of the RUSH2A trial included BCVA letter score of 54 or more (approximate Snellen equivalent of 20/80 or better) and a visual field diameter of 10° or more in every meridian of the central
FIGURE 3. Representative rod visual fields, with top-down views shown in the left column and side views shown in the right column. Row A shows a participant with preserved rod function in the central 30°. Row B shows a participant with a deep mid peripheral scotoma, and row C shows a participant with only residual rod function in the far periphery.

FIGURE 4. DAVF evidence of rod function by clinical diagnosis.

* $P=0.09$ for comparison of presence of rod function between the USH2 and ARRP groups, adjusted for disease duration, using logistic regression.
field, resulting in a population of syndromic (USH2) and nonsyndromic (ARRP) participants with intermediate stage disease. We showed that the rod ERG was not useful for following these participants, with approximately 50% in RUSH2A showing unmeasurable responses, whereas FST seemed promising as a reliable measure of rod function. However, because the FST only measures the most sensitive region, there could be large changes elsewhere that go undetected.

The ancillary study reported here uses two-color DAC perimetry to derive rod visual fields. Two-color perimetry, originally pioneered by Wald and Zeavin, has long been used to map rod and cone sensitivity. With this technique, the sensitivity difference (cyan–red) to chromatic test stimuli can be used to determine whether rods, cones or both photoreceptor systems mediate the threshold at a given location in the retina. Two-color perimetry has been performed using a variety of modified perimeters.

### Table 2. Proportion with DAVF Rod Function by Clinical Diagnosis and Age Group

| Clinical Diagnosis | Evidence of Rod Function | Age Group (Years) | All N (%) | P   |
|--------------------|--------------------------|------------------|-----------|-----|
|                    |                          | <40 N (%)        | ≥40 N (%) |     |
| DAVF               | No                       | 5 (25%)          | 4 (50%)   | 9 (32%) | 0.37 |
|                    | Yes                      | 15 (75%)         | 4 (50%)   | 19 (68%) | 0 (0%) | 0.0 (15%) | 2 (10%) |
|                    | All                      | 20 (100%)        | 8 (100%)  | 28 (100%) | 8 (100%) | 15 (100%) | 21 (100%) |

### Table 3. Proportion With DAVF Rod Function by Clinical Diagnosis and Disease Duration

| Clinical Diagnosis | Evidence of Rod Function | Disease Duration (Years) | All N (%) | P   |
|--------------------|--------------------------|--------------------------|-----------|-----|
|                    |                          | <15 N (%)                | ≥15 N (%) |     |
| DAVF               | No                       | 3 (23%)                  | 6 (40%)   | 9 (32%) | 0.17 |
|                    | Yes                      | 10 (77%)                 | 9 (60%)   | 19 (68%)| 0 (0%) | 0 (0%) | 2 (22%) | 2 (10%) |
|                    | All                      | 13 (100%)                | 15 (100%) | 28 (100%) | 12 (100%) | 7 (78%) | 19 (90%) |

### Table 4. Agreement of Evidence of Rod Function by DAVF Versus Other Modalities (Stratified by Clinical Diagnosis and Age Group); All (N = 49)

| Evidence of Rod Function Other Modalities | DAVF | FST White Stimulus† | FST Blue Stimulus‡ | ERG Rod B-Wave§ |
|------------------------------------------|------|---------------------|--------------------|-----------------|
|                                           | No N (%) | Yes N (%) | κ (95% CI) | No N (%) | Yes N (%) | κ (95% CI) | No N (%) | Yes N (%) | κ (95% CI) |
| All                                      | 10 (22%) | 0 (0%)   | 0.38      | 4 (9%)    | 5 (11%)   | 0.40      | 10 (20%) | 1 (2%)    | 0.16      |
| <40 years                                | 15 (33%) | 21 (46%) | (0.18, 0.58)| 3 (6%)    | 4 (9%)    | (0.08, 0.72)| 24 (49%) | 14 (29%)  | (0.005, 0.31) |
| ≥40 years                                | 5 (19%)  | 0 (0%)   | 0.31      | 2 (7%)    | 3 (11%)   | 0.26      | 2 (1%)   | 7 (17%)   | 0.03      |
| USH2                                     | 12 (31%) | 14 (44%) | (0.06, 0.55)| 3 (11%)   | 9 (31%)   | (−0.18, 0.71)| 3 (11%)   | 1 (4%)    | 0.03      |
| AARRP                                    | 3 (15%)  | 12 (42%) | (0.15, 0.82)| 1 (5%)    | 4 (15%)   | (0.13, 1.00)| 7 (33%)  | 2 (6%)    | 0.04      |

† Defined as at least one cluster of rod-mediated points in visual field where cyan relative to red sensitivity is >5 dB.
‡ Defined as a white threshold of less than −30. Three participants missing data for FST White
§ Defined as a blue threshold of less than −25. Three participants missing data for FST Blue.
§§ Defined as ERG rod function b-wave amplitude of >0.
|| Bias-corrected percentile bootstrap method used to get 95% CIs for Kappa estimate.
Table 5. Correlation of DAVF Measures With Standard Measures

| DAVF Measures          | Full Field Rod Mean Sensitivity | Maximum Sensitivity | Mean Sensitivity | Standard (non-DAVF) Measures |
|------------------------|--------------------------------|---------------------|-----------------|-----------------------------|
|                        | Correlation Coefficient 95% CI | Correlation Coefficient 95% CI | Correlation Coefficient 95% CI | Correlation Coefficient 95% CI |
| Mean sensitivity       | 0.37 (0.04 to 0.66)            | 0.35 (0.07 to 0.64)  | 0.37 (0.16 to 0.56) | 0.38 (0.07 to 0.66)         |
| Octopus-VTOT           | 0.40 (0.04 to 0.71)            | 0.38 (0.07 to 0.65)  | 0.37 (0.04 to 0.64) | 0.38 (0.04 to 0.66)         |
| Octopus-V30            | 0.35 (0.01 to 0.67)            | 0.33 (0.05 to 0.64)  | 0.33 (0.04 to 0.64) | 0.33 (0.04 to 0.66)         |
| FST White              | 0.43 (0.01 to 0.69)            | 0.43 (0.02 to 0.68)  | 0.43 (0.04 to 0.71) | 0.43 (0.04 to 0.66)         |
| FST Blue               | 0.40 (0.01 to 0.66)            | 0.39 (0.04 to 0.65)  | 0.39 (0.04 to 0.65) | 0.39 (0.04 to 0.66)         |

* Bias-corrected accelerated bootstrap method used to get 95% CIs for spearman correlation coefficient.

Figure 5. Maximum rod field sensitivity was inversely correlated with FST white thresholds. FST thresholds are mediated by rods for points to the left of the red vertical line.

Figure 6. The number of rod-mediated loci with the DAVF decreased with increasing duration of disease.

including the Goldmann–Weekers, Tubingen, Octopus, and Humphrey instruments. Although they provide useful data for single-site studies, these custom devices are not readily adaptable to multicenter trials. The Medmont DAC perimeter is commercially available and in use at six of the sites participating in RUSH2A, allowing us to conduct an ancillary study in approximately half of the enrolled RUSH2A participants.

The majority of participants in the ancillary study showed evidence of rod-mediated detection in at least one cluster of points in the field. This included 14 of 15 patients (93%) retaining measurable rod ERGs, but more importantly 24 of 34 patients (71%) with unmeasurable rod ERGs. This finding is consistent with data in autosomal dominant RP, including the Goldmann–Weekers, Tubingen, Octopus, and Humphrey instruments. Although they provide useful data for single-site studies, these custom devices are not readily adaptable to multicenter trials. The Medmont DAC perimeter is commercially available and in use at six of the sites participating in RUSH2A, allowing us to conduct an ancillary study in approximately half of the enrolled RUSH2A participants.

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The intertest and intratest variability in DAVF measured in the majority of participants tested in the RUSH2A study was found to be substantial, with values greater than 0.01 cd.s/m² flash. Although the RUSH2A study has shown that USH2 participants tend to be more severely affected than ARRP participants at a similar age, our sample size was too small to establish a difference based on diagnosis. The correlations between DAVF parameters and light-adapted static perimetric parameters ranged from 0.31 to 0.4. This outcome suggests that DAVF is capturing a dimension of visual experience that is distinct from the standard visual field. It will be interesting in the future to compare the topography of rod and cone fields to determine possible relationships between regional rod and cone loss. The value at the most sensitive region within the rod visual field (maximum sensitivity) was highly (inversely) correlated with FST white or blue thresholds. This finding is reassuring, because it has been shown in previous studies that FST measures the volume of VTOT tended to decrease with increasing disease duration, but examples of substantial rod function were found at all durations.

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The correlation is greatest over the region where the FST white threshold is extremely subjective and USH2 patients may be more attentive to vision problems than patients with ARRP. But although not significant, these trends in the cross-sectional data suggest that longitudinal measures in patients may be sensitive to disease progression.

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