Characterization of Retinal Function using Microperimetry-Derived Metrics in both Adults and Children with \textit{RPGR}-Associated Retinopathy

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Running (Short) Title: Microperimetry in \textit{RPGR}-Retinopathy

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Highlights

- *RPGR*-associated retinopathy is a predominantly symmetric test.
- Microperimetry has a good test-retest reliability for the disease and can track progression of retinal functional loss.
- The high degree of reproducibility of results, good interocular correlation, and accurate tracking of change over time lends this modality well to assessing the outcomes of gene therapy trials.

Abstract

**Purpose:** To investigate microperimetry testing of *RPGR*-associated retinopathy in a cohort of children and adults.

**Study design:** Prospective observational case series.

**Methods:** The coefficient of repeatability and intraclass correlation coefficient (ICC) of mean sensitivity (MS) were calculated for mesopic microperimetry. Best-corrected visual acuity (BCVA), contrast sensitivity (CS), MS, total volume (*V_{TOT})*, and central 3-degree field volume (*V_{3})* from volumetric and topographic analyses were acquired.

**Results:** Seventy-six *RPGR* subjects (53 adults, 23 children) were recruited. The mean follow-up period was 2.8 years. The ICC values for MS, *V_{TOT}*, and *V_{3}*, were 0.982 dB (95% confidence intervals, CI 0.969 to 0.989), 0.970 dB-sr (95% CI -0.02658 to 0.03691) and 0.986 dB-sr (95% CI 0.978 to 0.991), respectively. The r values for interocular MS, *V_{TOT}*, and *V_{3}*, were 0.97 (P<0.01), 0.97 (P<0.01) and 0.98 (P<0.01) respectively, indicating strong inter-ocular correlation. The interocular correlation of
progression for MS, $V_{TOT}$ and $V_3$ was 0.81 (P<0.01), 0.64 (P<0.01) and 0.81 (P<0.01), respectively. There was no statistically significant difference in the interocular progression rates for MS or $V_{TOT}$. $V_3$ did show a statistically significant difference. Most patients lost retinal sensitivity rapidly during their second and third decades of life.

**Conclusions:** The high degree of reproducibility of results and the good interocular correlation lends this modality to accurately monitoring disease progression, as well as supporting validation of the use of MP in assessing the outcomes of gene therapy clinical treatment trials.

**Introduction**

X-linked retinitis pigmentosa (XLRP) is a subset of genetically heterogenous conditions that fall under the broad phenotypic group of retinitis pigmentosa (RP). Affected individuals typically present with nyctalopia and progressive peripheral visual loss. In the later stages of the condition, central vision becomes affected, resulting in severe visual impairment.\(^1\)

XLRP accounts for 5-15\% of all RP cases.\(^2, 3\) Pathogenic sequence variants in the RP GTPase regulator gene ($RPGR$) have been shown to be responsible for 75\% of cases of XLRP. $RPGR$ variants have also been associated with cone dystrophy (COD),
cone-rod dystrophy (CORD), and sector RP. (4-6) RPGR-associated RP (XLRP-RPGR) has a particularly severe phenotype, characterised by early onset of symptoms, usually in early childhood and particularly rapid progression of visual loss. It is currently the target of several gene therapy trials (NCT04671433, NCT03252847, NCT03116113, NCT03316560, NCT04517149) that aim to arrest progression and improve retinal function. A recent publication of the initial results of a gene therapy trial for XLRP-RPGR included microperimetry (MP) testing as part of the secondary outcomes. (7) This trial used the mesopic Macular Integrity Assessment (MAIA) MP assessment (CenterVue MP Systems, Padova, Italy), which was central to achieving an objective assessment of both retinal sensitivity changes after treatment and for the monitoring of inflammatory complications of gene therapy and documenting their resolution.

Retinal sensitivity measures are widely used as part of retinal functional assessment and often constitute key metrics for monitoring disease progression. Common modalities for measuring retinal sensitivity include either full field dynamic and static perimetry or MP (fundus guided perimetry). Test-retest repeatability of MP in an RPGR patient cohort using the MAIA system has been reported. (8) Previously published data from our group explored repeatability, interocular symmetry and rate of progression using full-field static perimetry in XLRP-RPGR. (9) We have developed a customised testing protocol for RPGR-associated retinopathy using the Nidek MP1, aiming for a standardised and reproducible assessment of point-by-point retinal sensitivity, as surrogate measures of retinal function and disease progression. Further analysis of retinal sensitivity was undertaken using the Visual Field Monitoring and Analysis software (VFMA: Office of Technology Transfer & Business Development, Portland, OR). (10-12) This utilises all the point-by-point retinal sensitivity measures obtained from the MP testing grid to generate a comprehensive volume plot of retinal sensitivity, which is also a more sensitive measure of change over time. A total hill of vision (V Tot) can be generated or any other volumetric measure of sensitivity within defined retinal areas e.g. within the central 3 degrees (V3).
We aimed to characterize retinal function in detail, including disease symmetry and natural history, in a large molecularly confirmed cohort of *RPGR*-associated retinopathy, employing a range of MP derived metrics. The correlation of MP metrics with contrast sensitivity (CS) and best corrected visual acuity (BCVA), was investigated. This study also provides data to support the validation of MP derived metrics as clinically meaningful endpoints for patient stratification and monitoring of treatment effect in both on-going and future gene therapy trials.
Methods

Ethical approval was received from the ethics committee at Moorfields Eye Hospital (London, UK) for this study. The study adhered to the Declaration of Helsinki.

Subjects

All subjects were affected males, with molecular genetic confirmation of disease-causing variants in RPGR. Subjects younger than 18 years of age were classified as children and those older than 18 were classified as adults.

Molecular Genetics

All patients were recruited from the MEH retinal genetics service. Patients were genetically screened by variable protocols as previously described. (13)

Assessment of Visual Function

Patients attended research appointments at 6-monthly intervals for two years and consequently for annual visits. Visual function assessments included BCVA at 4m, using the Early Treatment Diabetic Retinopathy Study (ETDRS) chart, followed by CS testing at a distance of 1m with the Pelli-Robson chart. BCVA was recorded in logarithm of the minimum angle of resolution (logMAR) units and CS as logCS units.

Assessment of Retinal Function

Mesopic fundus-guided perimetry was performed using the Nidek MP-1. Pupils were dilated using 2.5% phenylephrine hydrochloride solution (Bausch & Lomb, Inc., Tampa, FL) and 1% tropicamide ophthalmic solution (Akorn, Inc., Lake Forest, IL). Fixation was monitored by a dedicated ophthalmic technician throughout each assessment. A single horizontal trans-foveal optical coherence tomography (OCT) scan performed on a Spectralis OCT (Heidelberg Engineering, Heidelberg, Germany), was imported into the perimeter to facilitate the accurate centration of the testing grid over the anatomical fovea. The radial pattern 44-point testing grid developed for these assessments is shown as supplementary material (Supplementary Figure 1). Background illumination was set to 4 apostilbs (1.27 cd/m2) and a Goldmann size III stimulus was
presented for 200ms. The testing protocol used a 4 to 2 dB full-threshold bracketing test strategy. A mean sensitivity (MS) value was automatically computed by the manufacturer’s software. The intrinsic reliability reports from the device were collected, however, in the absence of robust evidence of their value they were not used as an exclusion criterion. Fixation stability within 4 degrees was used as a primary reliability assessment and tests falling below 90% had testing repeated. Those with fixation stability less than 90% were included in the analysis only if repeat testing remained consistent in terms of MS and the volumetric sensitivity indices. Subjects with sensitivities below the testing threshold (recorded sensitivity of 0) were also excluded from further testing or analysis.

Volumetric indices of retinal function
Test data were exported from the software as comma-separated value (csv) files for analysis in the VFMA software. This software generates a 3-dimensional hill-of-vision (HOV) model of the visual field and allows the calculation of a volume of sensitivity beneath the surface of the model, based upon the total sensitivity across the solid angle of the base of the test grid, in decibel-steradian (dB-sr) units. (14) This is an objective numerical measure of the total sensitivity of the examined retinal area (termed $V_{\text{total}}/V_{\text{TOT}}$) and it can be sub-analysed by area. In our study, we also analysed the visual field contained within a central circle of 3 degrees radius (termed $V_3$), based upon the total sensitivity across the solid angle of a central 6 degrees, to reflect the function of the central visual field.

Progression Analysis
Progression rates for each individual eye were obtained from gradients of linear trend lines fitted to data points using the least squares method. Photoreceptor degeneration and the decline of visual function in RP, both in animal models and humans follows an exponential pattern over an extended time period. (15-20) Nevertheless, shorter follow up periods can be successfully modelled using a linear best-fit line to capture a short-range progression snap shot. (9) Only eyes with a minimum of three data points, and a minimum follow-up of 1 year were included.
Disease Symmetry
The Bland-Altman analysis was used to assess interocular differences in MS, $V_{TOT}$ and $V_3$ at baseline and for the interocular progression rates. Spearman’s correlation coefficient was used to investigate interocular correlation between baseline MS, $V_{TOT}$ and $V_3$, and progression rates for $V_{TOT}$ and $V_3$.

Statistical analysis
Statistical analysis was carried out using SPSS Statistics (Chicago, Illinois). Significance for all statistical tests was set at $P < 0.05$. The Shapiro-Wilk test was used to test for normality for all variables. Test–retest reliability was investigated with the intraclass correlation coefficient (ICC) based on absolute agreement and a 2-way mixed-effects model using results from the right eye to minimize the clustering effect.
Results

Demographics and Genetics
Seventy-six subjects with *RPGR*-retinopathy underwent MP testing (53 adults, 23 children). The age range of patients was 6.9-55.8 (mean 25, median 24) at baseline testing. The mean follow-up period was 2.8 years (range 1.2-5.3). The flowchart of subject participation is given in Figure 1.

All subjects had disease-causing variants in *RPGR*, either in the open reading frame 15 (ORF15, 64%) or in exons 1-14 (36%). Of those with variants in the ORF15 region, there were two patients expressing a cone dystrophy (COD) phenotype, one patient with cone-rod dystrophy (CORD), and one patient with sectoral RP. All other patients had XLRP.

Functional assessment
The baseline BCVA, CS, MS, V_{TOT} and V_{3} metrics are presented in Table 1. Annual progression rates for these parameters are also reported.

Test-retest reliability
After exclusions for sub-threshold sensitivity (MS value of 0dB), 135 pairs of tests were analysed. All paired same-day tests passing the exclusion criteria were included, not only those at baseline. The ICC values in this sub-group for MS, V_{TOT} and V_{3} were 0.982 (95% confidence intervals, CI 0.969 to 0.989), 0.970 (95% CI -0.02658 to 0.03691) and 0.986 (95% CI 0.978 to 0.991), respectively. This indicates a strong correlation between separate consecutive tests and a high test-retest reliability for this modality. Bland-Altman plots for the test-retest reliability of right eye MS, V_{TOT} and V_{3} are presented in Figure 2.

Interocular symmetry
Data from 190 test pairs for right and left eyes at baseline were analysed following the application of the aforementioned exclusion criteria. The r values (Pearson’s correlation coefficient) for interocular MS, V_{TOT} and V_{3}, were 0.97 (P<0.01), 0.97 (P<0.01) and 0.98
(P<0.01), respectively; indicating strong interocular correlation of all metrics. The interocular correlation (Spearman’s correlation coefficient) of progression for MS, $V_{TOT}$ and $V_3$ were 0.81 (P<0.01), 0.64 (P<0.01) and 0.81 (P<0.01), respectively. The Bland-Altman plots for the interocular MS and $V_{TOT}$ are presented in Figure 3. There was no statistically significant difference in the interocular progression rates for MS or $V_{TOT}$ (P = 0.26 and 0.70 respectively, paired t-test). $V_3$ did show a statistically significant difference at P = 0.01.

Rate of Progression

As there was a strong interocular correlation at baseline, only right eye (OD) data was selected for analysis of progression as being representative of the cohort. The mean rates of annual progression of MS, $V_{TOT}$ and $V_3$ were 0.82 dB/year, 0.04 dB-sr/year and 0.01 dB-sr/year respectively. (Table 1). Figure 4 shows the progression plots for MS, $V_{TOT}$ and $V_3$.

The rate of progression in the ORF15 genotype sub-group was comparable to that of the sub-group with disease-causing variants in Exons 1-14 (MS 0.81 dB/year in both sub-groups; $V_{TOT}$ 0.042 and 0.039 dB-sr/year respectively; $V_3$ 0.009 and 0.013 dB-sr/year respectively). None of the differences reached statistical significance (p= 0.667 for MS, p = 0.535 for $V_{TOT}$ and p = 0.395 for $V_3$).

Most patients lost retinal sensitivity rapidly during their second and third decades of life. Patients with COD, CORD and sectoral RP phenotypes were outliers as would be anticipated. For example, the patient with sectoral RP demonstrated a similar characteristic rapid decline in MS, $V_{TOT}$ and $V_3$, however, this was noted later in life. One of the two COD patients and the CORD patient demonstrated unique relative preservation of $V_{TOT}$ into later life, however, with characteristic reductions in MS and $V_3$.

Correlation with BCVA and CS

The correlation between baseline BCVA and CS, and the MS, $V_{TOT}$ and $V_3$ metrics was tested using the Spearman correlation coefficient. There was a positive statistically significant correlation between baseline BCVA and CS, BCVA and MS, BCVA and $V_{TOT}$, and BCVA and $V_3$ (0.80, 0.62, 0.58, 0.77 respectively). There was also a positive
statistically significant correlation between baseline CS and MS, CS and $V_{TOT}$, and CS and $V_3$ (0.70, 0.65, 0.85 respectively).

The correlation between progression rates of BCVA and CS, and the MS, $V_{TOT}$ and $V_3$ metrics was also investigated. There was a weak positive correlation between annual progression rates of BCVA and CS (0.14) and weak positive correlations between the progression rates of BCVA and the MS, $V_{TOT}$ and $V_3$ metrics (0.06, 0.14 and 0.03 respectively). There was also a weak positive correlation between the annual progression rates of CS and MS, $V_{TOT}$ and $V_3$ (0.21, 0.29 and 0.26 respectively). These were not found to be statistically significant.
Discussion

To our knowledge, this is the largest prospective report on retinal sensitivity using microperimetry in a large molecularly confirmed group of RPGR subjects including both adults and children. Traditional assessments of visual function such as visual acuity and contrast sensitivity are not ideal for monitoring disease progression in RPGR, as most changes occur outside of the fovea until late on in the disease course. This means that relative preservation of the VA and CS parameters does not reflect the rapid progressive changes in visual function that occurs. Furthermore, clinical treatment trials need to review the response to treatment over relatively short time periods, over which VA and CS have been observed to remain largely stable. Hence surrogate markers of retinal function need to be employed for accurate monitoring.

Interocular Symmetry

There was good overall symmetry in the MS and the volumetric indices of retinal function, $V_{TOT}$ and $V_3$ at baseline, as demonstrated by the $r$ values of the interocular correlation coefficient.

Interocular symmetry of visual function has previously been demonstrated in RPGR subjects.\(^{(9, 21)}\) The interocular correlation of progression of the MS, $V_{TOT}$ and $V_3$ metrics was more variable. However, for MS and $V_{TOT}$ the variability did not reach statistical significance ($p = 0.264$ and $p = 0.705$, paired t-test). Interocular variability in progression of $V_3$ was statistically significant at $p = 0.01$. It is not clear what this signifies clinically, however, we postulate that the absolute values of retinal sensitivity are so small for the $V_3$ metric, that the effect of small differences and any outlying values is magnified and can skew the analysis.

Clinical trials of treatment frequently utilise fellow eyes as controls and hence good interocular correlation is useful in monitoring treatment response versus control progression. We believe adequate interocular symmetry is demonstrated in our subjects to facilitate this; however, we would recommend acquiring sufficient baseline testing to establish a reliable and robust starting point and focusing assessments on the MS and $V_{TOT}$ metrics. Furthermore, with high levels of interocular disease symmetry...
demonstrated, the advent of approved gene therapy in the future promises potentially similar benefit to both eyes from receiving treatment.

Test-Retest Reliability
The ICC results for MS, $V_{TOT}$ and $V_3$ indicate strong test-retest reliability. The MS is a traditional measure of visual function, however, because it is a mathematical average, it lacks the precision necessary to distinguish point-by-point sensitivity and does not possess the comprehensive reflection of total retinal sensitivity such as that achieved by the volumetric indices $V_{TOT}$ and $V_3$. Good test-retest reliability of these metrics lends support to their use in monitoring visual function progression in this cohort of patients.

MP is a faster test to perform compared to full field perimetry such as the Octopus900 (Haag-Streit AG, Koniz, Switzerland) and hence may be easier to include in testing regimens for both monitoring of progression and recording the response to treatment trials. It was also reasonably well tolerated by children in our study, with subjects as young as 8 being able to reliably perform testing on the Nidek MP-1 in this cohort. Given the early onset of visual loss in XLRP, this lends it well to detect changes in childhood. A recent report(8) utilising the MAIA perimeter reported good test-retest reliability for testing in an XLRP-RPGR cohort (with no data provided on the age of these subjects - but likely to have been adults only). They found greater variability between the first two tests a subject performs than between tests 2 and 3, indicating a learning phenomenon, resulting in the recommendation to perform three baseline assessments in cases of clinical trials and use the final macular sensitivity result as baseline. The ICC results for MS and the volumetric indices in our study confirms high levels of test-retest reliability for MP measurements on the Nidek MP-1 perimeter. This further supports the potential use of this device to monitor progression and treatment effect in XLRP-RPGR.

Rate of Progression
The mean rates of annual progression of MS, $V_{TOT}$ and $V_3$ were 0.82 dB/year, 0.04 dB-sr/year and 0.01 dB-sr/year, respectively, in our cohort. This is comparable to the progression rates previously reported by Tee at al based on full-field static perimetry
using the Octopus 900 perimeter, with the V\textsubscript{30} and V\textsubscript{5} mean annual rates of progression of right eyes being reported as 0.6819 and 0.0056 dB-sr, respectively (8). Together, these findings support the anticipated progression of the natural history of XLRP-RPGR and lend weight to prognostic information that can be imparted to patients.

The correlation of the baseline BCVA and CS with the MS and the volumetric indices is robust and statistically significant. The greatest correlation was observed between baseline BCVA and CS, with the second strongest correlation being noted between both BCVA and V\textsubscript{3}, and CS and V\textsubscript{3}. This implies that baseline BCVA, CS and V\textsubscript{3} may be useful as surrogate markers for disease severity at baseline. However, there was only a weak, not statistically significant correlation, between the progression rates of BCVA and CS, and the MS and V\textsubscript{TOT}. This supports the observation that progression rates of central visual loss can differ significantly from full visual field loss in this primarily rod-centric phenotype, with central macular function remaining relatively preserved until the latest stages of disease.

It is notable that the progression rates of loss of retinal sensitivity are comparable between the molecularly heterogeneous cohort of XLRP patients, with similar progression rates being recorded between the ORF15 and the Exons 1-14 sub-groups. A previous study investigating progression rates using full-field Octopus perimetry found an increased rate of progression (although not statistically significant) in the Exon 1-14 sub-group, although their findings may have been confounded by an age disparity between the two molecularly distinct cohorts. (8) Another study in the Asian population, also supported that patients with variants in exons 1-14 retained less visual acuity than patients with ORF15 variants and deteriorated faster. (22) Similar findings were identified in a cohort of Japanese patient (n=14). (23)

Limitations
There are several limitations of the study. For evaluating progression rates, a longer time period would be desirable, which would allow modelling of progression according to established exponential models. In our study, with shorter follow-up, a linear trend line fit was more appropriate for estimating progression rates. The Nidek-MP-1 has a relatively narrow dynamic range of 0 to 20 dB and this meant that in our cohort, younger
subjects were sometimes able to reach the ceiling of sensitivity and maximum sensitivity values were recorded for sequential tests. Similarly, older patients frequently fell below the sensitivity threshold and values of zero were generated for their retinal sensitivity results, despite some preserved level of retinal function (BCVA and CS). These floor and ceiling effects could be addressed with wider bracketing strategies for the testing protocol, which is not possible to achieve on the Nidek MP-1. Newer MP devices have a wider dynamic range of stimuli intensities. It is nevertheless useful to analyse the data acquired on the Nidek MP-1, as the majority of our cohort of patients fell well within its sensitivity brackets and so useful progression data was collected.

Furthermore, the testing protocol utilised only a mesopic testing strategy. Latest MP devices can perform across a range of illuminations and record sensitivities under photopic, mesopic and dark-adapted scotopic conditions, as well as utilising rod and cone-specific colour stimuli (cyan and red, respectively). XLRP-RPGR is a condition affecting the rod then cone system. It is therefore of interest to specifically probe the rod system in XLRP-RPGR to more fully assess disease progression particularly in the early stages, and directly probe the cone system for later disease stages. The Nidek-MP-1 tests a mixture of rod and cone function under standard mesopic protocol conditions. An alternative to the latest MP devices may be the dark-adapted chromatic Medmont M700 perimeter (Medmont International Pty Ltd; Victoria, Australia) which has been designed to probe different photoreceptor mechanisms,(24, 25) but requires further investigation. Further exploration of retinal function in affected females with RPGR retinopathy will be of value,(26) as well as correlation of MP with advanced cellular imaging techniques.(27, 28)

Conclusions
We report detailed findings on interocular symmetry, test-retest reliability, and progression of retinal functional loss, using mesopic MP in the largest molecularly confirmed RPGR cohort to date, including both adults and children. The high degree of reproducibility of results, good interocular correlation, and accurate tracking of change over time lends this modality well to monitoring disease progression, as well as
supporting the validation of the use of MP in assessing the outcomes of gene therapy trials.
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b. Financial Disclosures:

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c. Other Acknowledgments:

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Legends

Figure 1: Flow chart of subject recruitment and participation in testing

![Flow chart image]

- 76 RPGR subjects underwent MP 2once (53 adults, 23 children)
- 180 repeat tests (twice on same visit)
  - Exclusions:
    - Retinal sensitivity below threshold: 45 tests
- 41 patients completed a minimum of three visits over a minimum of 1 year (OU data for all)
  - Exclusions:
    - Retinal sensitivity below threshold: 16 eyes of 10 patients
- 135 tests for test-retest variability analysis
- 249 patient visits with OU data
  - Exclusions:
    - Retinal sensitivity below threshold: 59
- 66 eyes for rate of progression analysis
- 190 tests for interocular variability analysis of progression

Figure 2: Test-retest reliability assessment. Bland-Altmann plots of the test-retest reliability of the mean sensitivity measurements (MS, dB), the volumetric measurement of total retinal sensitivity ($V_{TOT}$, dB-sr), and the volumetric measurement of the fovea-centred area of radius 3 degrees ($V_3$, dB-sr).
Figure 3: Interocular symmetry assessment. Bland-Altmann plots of the interocular symmetry of the mean sensitivity (MS, dB) and the volumetric measurement of total retinal sensitivity ($V_{TOT}$, dB-sr).
Figure 4: Progression of retinal functional loss. Plots with best-fit lines of all individual subjects (XLRP = 27, COD = 2; CORD = 1; Sector RP = 1) in the cohort who possessed three or more consecutive retinal sensitivity measurements. (A) The mean sensitivity (MS, dB), (B) the volumetric measurement of total retinal sensitivity ($V_{TOT}$, dB-sr), and (C) the volumetric measurement of the fovea-centred area of radius 3 degrees ($V_3$, dB-sr) are presented for the analyzed right eyes.
### Table 1: Functional Assessment of Progression

| Metric    | OD Baseline Mean (SD) | OD Baseline Median (IQR) | OD Progression Rate Mean (SD) | OD Progression Rate Median (IQR) | OS Baseline Mean (SD) | OS Baseline Median (IQR) | OS Progression Rate Mean (SD) | OS Progression Rate Median (IQR) |
|-----------|-----------------------|--------------------------|-------------------------------|-----------------------------------|-----------------------|--------------------------|-------------------------------|---------------------------------|
| BCVA, LogMAR | 0.41 (0.34) | 0.34 (0.34) | 0.00 (0.05) | 0.00 (0.04) | 0.44 (0.40) | 0.39 (0.28) | 0.03 (0.07) | 0.0 (0.0) |
| CS, logCS | 1.19 (0.45) | 1.30 (0.63) | 0.02 (0.09) | 0.02 (0.08) | 1.15 (0.42) | 1.23 (0.56) | 0.00 (0.08) | 0.0 (0.0) |
| MS, dB | 6.75 (6.47) | 3.9 (10.0) | 0.82 (0.87) | 0.74 (1.10) | 6.75 (6.84) | 3.30 (10.96) | 0.67 (0.86) | 0.5 (1.0) |
| V TOT, dB-sr | 0.30 (0.36) | 0.12 (0.54) | 0.04 (0.06) | 0.0289 (0.069) | 0.31 (0.39) | 0.10 (0.53) | 0.04 (0.06) | 0.0 (0.0) |
| V 3, dB-sr | 0.06 (0.06) | 0.04 (0.11) | 0.01 (0.01) | 0.01 (0.01) | 0.05 (0.06) | 0.04 (0.08) | 0.01 (0.01) | 0.0 (0.0) |

Mean and median best-corrected visual acuity (BCVA) in LogMAR units, mean sensitivity (MS) in decibels (dB) and the volumetric indices $V_{TOT}$ and $V_3$ in decibel-steradians (dB-sr) for the right eye (OD) and left eye (OS). Progression rates calculated per year. SD = standard deviation, IQR = interquartile range.