Point-wise variability of threshold sensitivity of 24-2 and 10-2 visual fields

Aparna Rao1*, Harsha L. Rao2, Debananda Padhy3

Abstract:
PURPOSE: To evaluate point-wise variability of threshold sensitivity at different test locations on 24-2 and 10-2 visual field (VF).

MATERIALS AND METHODS: Electronic medical records of patients seen at a tertiary eye care center were screened to include those with at least 3 reliable VF with glaucomatous defects involving fixation on 24-2 and confirmed on 10-2 test strategy. Ninety eyes of 90 patients were categorized into 3 severity groups based on mean deviation (MD on 24-2) test strategy; MD < -6 dB and > -12 dB, < -12 dB and > -20 dB and > -30 dB. Variability of threshold sensitivity at all topographical test locations in central (ring 1), mid-peripheral (ring 2), peripheral rings on 24-2 VF test strategy (ring 3), and central (ring 4) and paracentral (ring 5) on 10-2 VF test along with variability of visual field index and central field index were calculated by multilevel mixed effects model.

RESULTS: Central ring 1 on 24-2 and ring 4 on 10-2 showed higher variability (> 10 dB) than peripheral ring 2, 3, and 5. Seventy-three eyes were adjudged as stable and 17 as progressing in this cohort. Across severity, variability was seen to decrease with increasing severity with minimal variability in point-wise threshold sensitivity beyond MD < -20 dB.

CONCLUSION: Central test points/ring on 24-2 and 10-2 with greater threshold variability suggests that status of the eye, severity and topographical location of test points should be incorporated into conventional progression algorithms to predict true glaucoma progression.

Keywords: Central field, glaucoma progression, glaucoma, riccos area, threshold sensitivity variability, visual field

Introduction

Glaucoma is a progressive neurodegeneration causing blindness if, left untreated.[1] Visual field (VF) remains the gold standard to monitor glaucoma progression and various algorithms are available to calculate possible or likely progression of glaucoma on VF. Yet, variability of threshold sensitivity at different test locations and different severities of damage limits the utility of VF in predicting true progression in clinical practice.[2-6] Multiple factors such as perimetric test strategy, patient factors, testing condition and the condition of the visual system account for this test-retest variability, the relative differential threshold reserve of retinal ganglion cells (RGC) with different susceptibilities contributes to differences in variability at different topographical VF test locations explaining in part why the central region is affected the last or is least variable.[6] In areas of moderate or severe glaucoma, this fluctuating threshold sensitivity may cause problems in predicting true disease progression using available algorithms. Current algorithms lack the ability to estimate location/area or severity-wise variability which poses a problem for clinicians in...
predicting true progression and differentiating it from fluctuations, especially in patients with advanced glaucoma damage where threshold sensitivities at test locations may be below 10 dB. The 10-2 VF program is usually used for monitoring disease in eyes with advanced glaucoma and in those with central involvement since the 10-2 strategy samples larger number of test points compared to 24-2 strategy. Yet there are regarding the long-term fluctuations of threshold sensitivities on a 10-2 program despite extensive studies on the same on a 24-2 or 30-2 VF program.\[5\-7\]

Earlier studies have reported higher threshold variability at test locations with lower sensitivity with minimal variability beyond-10 dB owing to the “floor effect.” Various studies have evaluated the variability of threshold sensitivity using the frequency of seeing curves or test–retest strategies or least square regression methods.\[13\] The test–retest data assumes the absence of a learning curve effect affecting the threshold variability or variability. One study has reported similar results using linear regression analysis of a large set of longitudinal data.\[5\] Most studies have evaluated the variability of threshold sensitivities on Swedish interactive threshold algorithm (SITA) or full threshold 24-2 strategy or computer simulations.\[6,7,13\] Yet, no study has reported the point-wise variability of threshold sensitivity at different locations on a 10-2 central field. While central field index (CFI) on a 10-2 VF accounts for eccentricity of test locations with a weighting procedure similar to that used for visual field index (VFI) calculations a 24-2 VF program, neither does it account for the severity of damage nor evaluates point-wise variability of threshold sensitivity on a 10-2 program.\[10\] This study aimed to study the point-wise threshold variability on a 24-2 and 10-2 central VF program while studying differences in moderate/severe glaucoma. This may serve as a guide for identifying true glaucoma progression after accounting for the variability of threshold sensitivity at different test locations and severities of damage on a 24-2 or 10-2 VF strategy.

Materials and Methods

The study included patients attending glaucoma service at a tertiary center in East India from 2011 to 2018. Inclusion criteria for the study were primary adult glaucoma (primary open-angle, primary open-angle glaucoma, or angle-closure glaucoma, primary angle-closure glaucoma) with established disc and corresponding glaucomatous VF damage. Patients with any neurological deficits or associated retinal diseases (vein occlusive disease or retinopathy), were excluded. Data for all selected patients were collected from the hospital electronic database to retrieve demographic and clinical variables such as best-corrected visual acuity, intraocular pressure (IOP) by Goldman applanation tonometry, and cup disc ratio. The study was approved by the institutional review board and adhered to the tenets of the declaration of Helsinki. (IRB number: 2014-16-IM-3.), written consent forms were obtained from patients.

The VF of each patient were screened to include only those with at least 3 reliable (with <15% false positives or <20% fixation losses) tests which were reproducible on 24-2 and 10-2 test strategies (Humphrey VF analyzer, Carl Zeiss Meditec, USA). Only the worst eye in each patient was selected for the study and correlated to the topographical region of optic nerve (ON) damage. A glaucomatous VF defect was defined by a glaucoma hemifield test outside normal limits, the presence of at least three nonedge test points in the same hemifield on the pattern deviation probability plot at P <5% with at least one point at P <1% and excluding points directly above or below the blind spot. Fixation involvement was confirmed when at least one test point of P <5% was seen in any hemifield within the central 10 degree with at least one point with P <1% within the innermost central 4 points on a SITA 24-2 program, confirmed on 10-2 program.

As protocol, the VF at the institute is done annually with repeat VF advised in the event of unreliable field at any visit as defined above. The baseline best field of the patient was taken for comparison with subsequent 2 visits in this study with exclusion of baseline fields reflecting learning effects. The baseline fields were used to stratify the VFs into three groups based on severity, namely mean deviation on 24-2 (hereby defined as MD), MD<6 dB and >-12 dB, MD>-12 dB and >-20 dB and MD>-20 dB and >-30 dB while eyes with MD >6 dB and <30 dB were excluded. The EMR hospital database was used to stratify eyes into stable or progressing eyes based on clinical judgment by the treating clinician. Patients with indeterminate status or incomplete database record where clinical stability or progression could not be retrieved were excluded. Clinical stability was ascertained in the absence of any fresh changes like fresh retinal nerve fiber layer defects, increase in focal neuroretinal rim changes or new disc hemorrhage, adjudged by the treating clinician during any visit (mandating augmentation of therapy or surgery). Clinical disc progression was ascertained in the event of increase in cup disc ratio or increased focal neuroretinal thinning, disc hemorrhage or widening of existing/ occurrence of new nerve fiber layer defects (with or without raised IOP) mandating augmentation of therapy.

The VFI and CFI were calculated as published previously, Figure 1, see supplemental methods.\[10,14\] Point-wise threshold differences in the same individual between visits at each test location were calculated using multilevel mixed effects model and each eye was considered an independent unit, Figure S1.
All statistical analysis was performed using STATA (Statacorp, Version 10, USA) with residuals or variability, see supplemental methods for detailed statistical analysis.

**Results**

Of 1287 patients attending our glaucoma service during the study period, 90 eyes of 90 patients (M: F = 66:24) fulfilling the inclusion criteria were included for the study. Table 1 gives the demographic and clinical characteristics of these patients.

Of these, 17 eyes were classified clinically as progressing with progression seen over a mean of 16 ± 6.7 months. There was no significant difference in the age (58 ± 15.3 vs. 59 ± 14.7 years) though the baseline IOP was significantly higher in the progressing eyes (30 ± 13.8 vs. 20 ± 6.9 mm Hg, \( P = 0.0005 \)) with worse baseline MD (stable 11.9 ± 9.5 dB, progressing...
eyes −22 ± 6.7 dB, \( P = 0.002 \), Table S1). The change in MD over the study period was significantly higher (\( P = 0.03 \)) in the progressing eyes (−2.1 ± 0.8 dB) than stable eyes (−1 ± 1.2 dB). The global indices like CFI or VFI at baseline did not vary significantly between the stable and progressing eyes, [Table 2]. Global indices like MD (on 24-2 and 10-2 VF) were significantly different between eyes with different glaucoma severities [Table 2]. While VFI progressively decreased with increasing severity, the CFI varied minimally between MD > and <−20 dB. The ring averages on 24-2 followed a similar pattern of VFI with decrease seen with increasing severity while ring 4 averages on 10-2 changed minimally with increasing glaucoma severity in contrast to ring 5 [Table 2].

Point wise variability on 24-2 and 10-2

Figure 2 shows the variability at all test locations on 24-2 and 10-2 in the patients included in the study. The central ring 4 on 10-2 VF showed higher variability than paracentral ring 5 which paralleled higher variability of test points in ring 1 than Ring 2/3 on 24-2, Figure 2 and Tables 2 and 3. Point-wise variability showed >6 dB changes in test points located within 3 degrees of fixation in ring 1 (P1 and P2 as shown) on 24-2 and ring 4 on 10-2 (Point 2, 3 and 4). This was paralleled with a >3 dB variability of the mean ring averages with maximal variability seen for central ring 4 on 10-2 VF. While central test points in ring 1 on 24-2 and ring 4 on 10-2 showed maximal variability of threshold sensitivity, other test points in ring 2, 3, and 5 also showed >3 dB fluctuations.

Table 1: Demographic and clinical characteristics of patients included in the study

| Variables           | Distribution |
|---------------------|--------------|
| Male: female        | 66:24        |
| Stable/progressing  | 73:17        |
| Right eye/left eye  | 46:44        |
| Number of fields    | 5±2.3        |
| Diagnosis           |              |
| POAG                | 53           |
| PACG                | 37           |
| Age (years)         | 59±13.9      |
| IOP (mm Hg)         | 22±10.7      |

IOP=Intraocular pressure, POAG=Primary open angle glaucoma, PACG=Primary angle closure glaucoma

Table 2: Threshold sensitivities at baseline of rings in the periphery and center on 10-2 and 24-2 visual fields compared to global visual field index and central field index in eyes with varying glaucoma severity

|                      | MD<−6 dB and ≥−12 dB (n=12) | MD<−12 and ≥−20 dB (n=17) | MD<−20 dB and ≥−30 dB (n=61) | \( P \) |
|----------------------|-----------------------------|-----------------------------|--------------------------------|-------|
| Ring 4 average on 10-2 (dB) | 23±5.7                      | 22±6.6                      | 19±8.9                        | 0.03  |
| Ring 5 average (dB)     | 18±6.8                      | 15±5.1                      | 13±7.02                       | 0.02  |
| Ring 1 on 24-2 (dB)     | 18±7.5                      | 15±7.2                      | 14±8.4                        | 0.07  |
| Ring 2 on 24-2 (dB)     | 14±8.9                      | 11±6.2                      | 9±7.4                         | 0.03  |
| Ring 3 on 24-2 (dB)     | 12±10.03                    | 9±6.9                       | 6±4.9                         | 0.02  |
| VFI (%)                | 51±31.07                    | 38±21.9                     | 26±24.1                       | 0.007 |
| CFI (%)                | 74±12.5                     | 66±17.3                     | 66±10.7                       | 0.04  |

See text for full description of ring1-5, *Kruskal–Wallis test. MD=Mean deviation, VFI=Visual field index, CFI=Central field index
Table 3 and Figure 3. It was also observed that the variability decreased with increasing glaucoma severity in both stable and progressing eyes with minimal variability of threshold sensitivity seen in progressing eyes with severe glaucoma. This may be attributed to the floor effect with decreased threshold reserves in eyes with

| Visual field parameter | MD <–6 and ≥–12dB* | MD <–12 and ≥–20dB* | MD <–20dB and ≥–30dB* |
|------------------------|---------------------|----------------------|------------------------|
| VFI (%)                | Stable | Progressing | Stable | Progressing | Stable | Progressing |
| 12.3                   | 14.2   | 7.2       | 3.3    | 8.1          | 6.8    |
| 9.5-16.7               | 6.3-19.1 | 6.04-8.6 | 2.2-3.5 | 5.6-11.8   | 3.1-10.1 |
| CFI (%)                | 12.3   | 2.03     | 5.9    | 5.1          | 5.4    | 6.8    |
| 9.09-16.6              | 0.7-5.3 | 4.9-7.04 | 3.5-7.6 | 3.7-7.8     | 3.1-10.9 |

10-2 point-wise and ring-wise variability

| Ring 4 (dB)           | Stable | Progressing | Stable | Progressing | Stable | Progressing |
|-----------------------|--------|--------------|--------|-------------|--------|--------------|
| 4.5                   | 4.4    | 4.01         | 4.9    | 4.7         | 3.6    |
| 3.2-6.1               | 2.6-7.3 | 3.3-4.7     | 3.3-7.1 | 3.4-6.7     | 1.6-7.9 |
| 3.8                   | 1.7    | 3.5          | 2.1    | 2.4         | 0.6    |
| 2.8-5.2               | 0.4-6.6 | 3.01-4.2    | 1.4-3.1 | 1.6-3.5     | 0.2-1.4 |
| 5.8                   | 1.2    | 6.5          | 5.4    | 8.8         | 7.06   |
| 4.2-7.8               | 0.4-3.5 | 5.5-7.7     | 3.4-7.4 | 6.1-12.6    | 3.2-11.4 |
| 7.4                   | 5.4    | 6.7          | 5.1    | 6.8         | 8.05   |
| 5.5-9.9               | 2.2-13.5 | 5.6-8.03    | 3.4-7.5 | 4.7-9.9     | 3.8-12.01 |
| 6.6                   | 5.6    | 5.9          | 4.4    | 6.4         | 0.2    |
| 4.8-8.9               | 2.1-15.07 | 4.9-7.07    | 3.01-6.3 | 4.4-9.3     | 0.1-1.4 |
| 5.9                   | 4.9    | 6.5          | 3.7    | 6.4         | 0.3    |
| 4.1-7.5               | 2.9-8.2 | 5.4-7.7     | 2.5-5.4 | 4.1-8.6     | 0.1-0.8 |
| 6.7                   | 7.9    | 6.00         | 6.5    | 4.8         | 3.2    |
| 5.2-9.1               | 4.2-11.9 | 5.2-7.7     | 4.9-9.5 | 4.1-9.5     | 1.4-7.1 |
| 6.04                  | 5.3    | 6.3          | 4.1    | 3.8         | 6.4    |
| 4.4-8.2               | 2.4-11.4 | 1.3-7.0     | 2.7-6.1 | 2.4-5.08    | 2.8-14.5 |
| 6.1                   | 6.8    | 6.6          | 5.3    | 5.7         | 9.5    |
| 4.5-8.3               | 4.8-12.04 | 5.5-7.9     | 3.6-7.7 | 3.9-8.3     | 3.9-21.05 |
| 4.3                   | 7.1    | 6.09         | 7.7    | 1.8         | 1.8    |
| 1.2-14.6              | 6.01-8.1 | 4.1-8.9     | 5.4-11 | 0.7-5.6     | 0.7-5.00 |
| 8.7                   | 6.9    | 9.2          | 3.06   | 6.2         | 1.3    |
| 6.5-11.6              | 3.2-15.7 | 6.8-12.4    | 2.03-4.4 | 4.3-8.8     | 0.5-2.8 |
| 9.2                   | 10.4   | 6.1          | 7.9    | 4.8         | 7.2    |
| 6.7-12.1              | 14.7-23.3 | 5.1-7.3     | 2.9-7.7 | 3.3-7.07    | 5.5-12.6 |
| 10.1                  | 11.4   | 9.9          | 9.05   | 10.8        | 2.9    |
| 7.2-14.07             | 5.1-25.4 | 8.4-11.7    | 4.1-19.8 | 7.8-14.9    | 1.3-6.5 |
| 6.7                   | 1.7    | 6.6          | 7.4    | 3.7         | 5.8    |
| 5.05-9.0              | 0.6-4.6 | 5.5-7.9     | 4.9-11.1 | 2.5-5.3     | 2.3-12.3 |

24-2 program point-wise and ring-wise variability

| Ring 1 (dB)           | Stable | Progressing | Stable | Progressing | Stable | Progressing |
|-----------------------|--------|--------------|--------|-------------|--------|--------------|
| 5.5                   | 5.6    | 4.4          | 2.3    | 3.1         | 3.2    |
| 4.07-7.4              | 3.3-9.5 | 3.3-4.8     | 1.5-3.4 | 2.2-4.5     | 1.5-7.06 |
| 6.1                   | 6.1    | 6.2          | 5.9    | 7.1         | 6.6    |
| 4.5-8.3               | 4.1-11.6 | 5.2-7.5     | 4.1-8.8 | 4.9-10.3    | 3.06-14.5 |
| 8.4                   | 9.08   | 4.9          | 7.4    | 5.1         | 3.09   |
| 5.4-11.09             | 5.3-15.3 | 4.1-5.8     | 5.1-10.8 | 3.4-7.3     | 1.3-6.9 |
| 8.5                   | 11.3   | 6.08         | 5.4    | 4.8         | 7.8    |
| 6.2-11.5              | 6.7-19.1 | 5.09-7.2    | 3.7-8.07 | 3.3-7.03    | 3.7-16.5 |
| 4.7                   | 11.5   | 5.7          | 5.2    | 7.3         | 7.7    |
| 3.5-6.3               | 5.8-19.5 | 4.8-6.8     | 3.4-7.5 | 5.4-10.6    | 2.9-9.7 |
| 5.2                   | 5.3    | 4.8          | 4.1    | 2.9         | 1.1    |
| 3.8-7.04              | 2.1-13.1 | 4.04-5.7    | 2.8-6.2 | 2.04-4.6    | 0.5-2.4 |
| 6.5                   | 12.2   | 6.1          | 3.2    | 5.6         | 5.3    |
| 4.8-8.8               | 7.2-12.06 | 5.1-7.3     | 2.2-4.7 | 3.8-8.1     | 2.4-11.4 |

*All values represent residuals (minimum–maximum)—See text for full description of ring 1-5 and statistical method for residual calculation. MD=Mean deviation.
Correlating the variability in CFI (ΔCFI) and VFI (ΔVFI) with the variability of threshold sensitivities of all ring averages, MD (on 24-2 or 10-2), age and IOP, maximal correlation of Δ CFI was seen with the change in ring 4 threshold averages suggesting that the central VF test locations contribute to the CFI variability maximally than peripheral test points on 10-2 VF ($R^2 = 32.7\%$, $\beta = 0.2$, $P < 0.001$). Similarly, ΔVFI correlated maximally with threshold variability of ring 1 and 2 on 24-2 ($R^2 = 58.7\%$, $P = 0.01$ and 0.02 for ring 1 and ring 2, respectively). This correlates with increased weightage of central points on 24-2 and 10-2 compared to peripheral points while calculating VFI or CFI. Both Δ CFI and Δ VFI did not correlate with age, IOP, or ring threshold averages. There was no correlation between variability on ring averages with the age, diagnosis, or baseline MD in stable or progressing eyes.

**Discussion**

This study found higher variability of the central than paracentral test points on 24-2 and 10-2 VF with higher variability in stable eyes than progressing eyes. The variability was seen to be minimal in severe glaucoma (MD beyond -20 dB), with <5 dB change seen in stable or progressing severe glaucoma eyes. Progressing...
eyes showed <5 dB change in points in the center with corresponding change in global VF indices reflecting that the cut-off of 10 dB signifying progression by automated software algorithms need to be redefined. The current study showed that glaucoma severity, region of the test points, and status of the eye (stable or progressing with stable eyes having a larger cut off >10 dB for flagging progression) need to be considered while analyzing progression.

The VF test points in the center on the VF assume utmost importance because of larger cortical representation of the fovea, the region with maximal visual acuity in the retina, and the last to be involved in glaucoma.\cite{7,10,11,14} Several studies have reported the variability of threshold sensitivity to be maximal in peripheral regions of the 24-2 VF where the receptive fields of RGC are larger.\cite{15} Yet a descriptive segmentation of RGC at the center as in 10-2 central/paracentral and peripheral regions is not included in current algorithms. In our earlier study, we found that the central VF test points on 10-2 VF program are more variable than the peripheral, suggesting that the CFI variability or stability is explained by other factors like threshold reserve of ganglion cells.\cite{14}

The short-term and long-term variability of VF test points has been reported in several studies.\cite{5-8,14-19} Gardiner et al. reported that relation between threshold sensitivity and variability on 24-2 changed with eccentricity with central areas being less variable in healthy regions owing to larger stimulus size for central region greater than Ricco’s area.\cite{5} They observed minimal changes with eccentricity in damaged portions of the VF. Parrish and co-workers also observed increasing inter-test variability with eccentricity on static perimetry along the 45° meridian similar to other studies reporting variability and long-term variations in threshold sensitivity on 24-2 VF.\cite{4} Surprisingly, the threshold variability in central 10-2 VF has not been studied earlier. This study identified greater variability in central points on 10-2 with lesser variability in progressing eyes with severe glaucoma. This is similar to Gardiner’s observation; however, we used multilevel random effects regression analysis and stringent stratification into groups depending on status of the eye and glaucoma severity.

This study found <5 dB change in threshold sensitivity in progressing eyes. Test points near the fovea have maximal threshold reserves and therefore represent the last ones to be involved in glaucoma.\cite{7,11,15} These regions of RGC therefore need a greater cut off beyond which the RGC dysfunction may happen nonlinearly across disease severity. Current event and trend-based progression software do not adjust for severity of glaucoma or expected variability across regions or test locations. This study found several eyes with >10 dB change in stable group suggesting automated algorithms need to incorporate expected threshold variability across test locations and severity for flagging disease progression.

The progression criteria for VF differ in different studies.\cite{20-29} Yet, an important caveat is that these criteria are defined for full threshold program while most clinicians use SITA program, where the threshold cut off may not be similar.\cite{25} The glaucoma progression analysis program allows comparison of SITA fields with follow-up full threshold fields though requires clinical overview to differentiate from nonclinical causes of worsening of points. The glaucoma change probability (GCP) analysis takes into account the “noise” or variability in eccentric locations of the VF and if there is a change in threshold greater than the test-retest variability found for a group of stable glaucoma patients at a probability of $P < 5\%$, the program flags it by a triangle on the GCP printout. This study found a <5 dB change may be statistically significant in eyes with severe glaucoma with decreasing variability across glaucoma severity. This suggests that location of points, severity and status of the eye needs to be incorporated into software algorithm to accurately calculate progression analysis in routine clinical practice.

We also chose to include only a short follow-up to evaluate variability over time rather than a follow-up...
of 5 years or 10 years which may bring in variability because of progression in cataract or surgery. We also did not include other varieties of glaucoma nor eyes with significant cataract where these cut-offs may be more variable. In summary, our study found that point-wise variability of threshold sensitivities increased with increasing glaucoma severity with a plateau effect occurring at -20 dB. Long-term fluctuations in central test points in eyes with early damage may not necessarily signify progression while progressing eyes in severe glaucoma may show <5 dB changes in center and peripheral test locations which have to be individually screened for accurately monitoring progression in these eyes. Such differences in variability of threshold sensitivities mandates incorporation of separate weightages to points of specific test locations (central or peripheral), severity of damage and disease status for accurately prognosticating and predicting progression on VFs.

Acknowledgment
Electronic medical records institute team of LV Prasad Eye Institute for collecting details and data.

Financial support and sponsorship
Nil.

Conflicts of interest
The authors declare that there are no conflicts of interests of this paper.

References
1. Coleman AL. Glaucoma. Lancet 1999;354:1803-10.
2. Heijl A, Leske MC, Bengtsson B, Hyman L, Bengtsson B, Hussein M, et al. Reduction of intraocular pressure and glaucoma progression: Results from the Early Manifest Glaucoma Trial. Arch Ophthalmol 2002;120:1268‑79.
3. Diaz‑Aleman VT, Anton A, de la Rosa MG, Johnson ZK, McLeod S, Azuara‑Blanco A. Detection of visual‑field deterioration by Glaucoma Progression Analysis and Threshold Noiseless Trend programs. Br J Ophthalmol 2009;93:322‑8.
4. Parrish RK 2nd, Schiffman J, Anderson DR. Static and kinetic visual field testing. Reproducibility in normal volunteers. Arch Ophthalmol 1984;102:1497‑502.
5. Gardiner SK, Demirel S, Johnson CA. Modeling the sensitivity to variability relationship in perimetry. Vision Res 2006;46:1732‑45.
6. Russell RA, Crabb DP, Malik R, Garway‑Heath DF. The relationship between variability and sensitivity in large‑scale longitudinal visual field data. Invest Ophthalmol Vis Sci 2012;53:5985‑90.
7. Heijl A, Lindgren G, Olsson J. Normal variability of static perimetric threshold values across the central visual field. Arch Ophthalmol 1987;105:1544‑9.
8. Heijl A, Lindgren A, Lindgren G. Test‑retest variability in glaucomatosus visual fields. Am J Ophthalmol 1989;108:130‑5.
9. Bengtsson B, Heijl A. A visual field index for calculation of glaucoma rate of progression. Am J Ophthalmol 2008;145:345‑53.
10. de Moraes CG, Furlanetto RL, Ritch R, Liebmann JM. A new index to monitor central visual field progression in glaucoma. Ophthalmology 2014;121:1531‑8.
11. Hood DC, Raza AS, de Moraes CG, Liebmann JM, Ritch R. Glaucomatous damage of the macula. Prog Retin Eye Res 2013;32:1‑21.
12. Drance SM, Berry V, Hughes A. Studies on the effects of age on the central and peripheral isopters of the visual field in normal subjects. Am J Ophthalmol 1967;63:1667‑72.
13. Spry PG, Johnson CA, McKendrick AM, Turpin A. Variability components of standard automated perimetry and frequency‑doubling technology perimetry. Invest Ophthalmol Vis Sci 2001;42:1404‑10.
14. Rao A, Padhy D, Mudunuri H, Roy AK, Sarangi SP, Das G. Central field index versus visual field index for central visual function in stable glaucoma. J Glaucoma 2017;26:1‑7.
15. Park SC, Kung Y, Su D, Simonson JL, Furlanetto RL, Liebmann JM, et al. Parafoveal scotoma progression in glaucoma: Humphrey 10‑2 versus 24‑2 visual field analysis. Ophthalmology 2013;120:1546‑50.
16. Katz J, Sommer A. Asymmetry and variation in the normal hill of vision. Arch Ophthalmol 1986;104:65‑8.
17. Gardiner SK. Differences in the relation between perimetric sensitivity and variability between locations across the visual field. Invest Ophthalmol Vis Sci 2018;59:3667‑74.
18. Wilensky JT, Joondeph BC. Variation in visual field measurements with an automated perimeter. Am J Ophthalmol 1984;97:328‑31.
19. Flammer J, Drance SM, Zulauf M. Differential light threshold. Short‑ and long‑term fluctuation in patients with glaucoma, normal controls, and patients with suspected glaucoma. Arch Ophthalmol 1984;102:704‑6.
20. The effectiveness of intraocular pressure reduction in the treatment of normal‑tension glaucoma. Collaborative Normal‑Tension Glaucoma Study Group. Am J Ophthalmol 1998;126:498‑505.
21. Boden C, Blumenthal EZ, Pascual J, McEwan G, Weinreb RN, Medeiros F, et al. Patterns of glaucomatous visual field progression identified by three progression criteria. Am J Ophthalmol 2004;138:1029‑36.
22. Nouri‑Mahdavi K, Hoffman D, Coleman AL, Liu G, Li G, Gaasterland D, et al. Predictive factors for glaucomatous visual field progression in the Advanced Glaucoma Intervention Study. Ophthalmology 2004;111:1627‑35.
23. Manassakorn A, Nouri‑Mahdavi K, Koucheki B, Law SK, Caprioli J. Pointwise linear regression analysis for detection of visual field progression with absolute versus corrected threshold sensitivities. Invest Ophthalmol Vis Sci 2006;47:2896‑903.
24. Bengtsson B, Olsson J, Heijl A, Rootzén H. A new generation of algorithms for computerized threshold perimetry, SITA. Acta Ophthalmol Scand 1997;75:368‑75.
25. Artes PH, Iwase A, Ohno Y, Kitazawa Y, Chauhan BC. Properties of perimetric threshold estimates from Full Threshold, SITA Standard, and SITA Fast strategies. Invest Ophthalmol Vis Sci 2002;43:2654‑9.
26. Chakravarti T. Assessing precision of Hodapp‑Parish‑Anderson criteria for staging early glaucomatous damage in an ocular hypertension cohort: A retrospective study. Asia Pac J Ophthalmol (Phila) 2017;6:21‑7.
27. Tanna AP, Budenz DL, Bandi J, Feuer WJ, Feldman RM, Herndon LW, et al. Glaucoma progression analysis software compared with expert consensus opinion in the detection of visual field progression in glaucoma. Ophthalmology 2012;119:468‑73.
28. Katz J. A comparison of the pattern‑ and total deviation‑based Glaucoma Change Probability programs. Invest Ophthalmol Vis Sci 2000;41:1012‑6.
29. Heijl A, Leske MC, Bengtsson B, Bengtsson B, Hussein M; Early Manifest Glaucoma Trial Group. Measuring visual field progression in the Early Manifest Glaucoma Trial. Acta Ophthalmol Scand 2003;81:286‑93.
Supplemental Table S1: Baseline visual field parameters in stable and progressing eyes in patients included in the study

| Visual field parameter | Stable eyes  | Progressing eyes | P   |
|------------------------|--------------|------------------|-----|
| CFI (%)                | 70±12.5      | 64±10.2          | 0.9 |
| VFI (%)                | 37±24.7      | 30.6±24.4        | 0.9 |
| IOP (mm Hg)            | 20±9.6       | 30±13.5          | 0.0005 |
| Ring 1 average (dB)    | 16±7.5       | 15±6.8           | 0.8 |
| Ring 2 average (dB)    | 10±7.5       | 9±6.0            | 0.9 |
| Ring 3 average (dB)    | 8±5.9        | 6±6.6            | 0.9 |
| Ring 4 average (dB)    | 21±7.08      | 20±8.2           | 0.8 |
| Ring 5 average (dB)    | 15±6.9       | 15±6.1           | 0.7 |

See text for full description of ring 1-5. VFI=Visual field index, CFI=Central field index, IOP=Intraocular pressure

Supplemental Figure 1: Levels of analysis for mixed effect model for evaluating threshold variability of points in each location/rings of 24-2 and 10-2 visual fields