

Evaluation of Central and Peripheral Visual Field Concordance in Glaucoma

Jamie L. Odden,^{1,2} Aleksandra Mihailovic,^{3,4} Michael V. Boland,³ David S. Friedman,^{3,4} Sheila K. West,^{3,4} and Pradeep Y. Ramulu^{3,4}

¹Department of Epidemiology and Biostatistics, Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland, United States

²University of North Dakota, School of Medicine and Health Sciences, Grand Forks, North Dakota, United States

³Wilmer Eye Institute, Johns Hopkins University, Baltimore, Maryland, United States

⁴Dana Center for Preventive Ophthalmology, Johns Hopkins University, Baltimore, Maryland, United States

Correspondence: Pradeep Y. Ramulu, The Wilmer Eye Institute, Woods 327, 600 North Wolfe Street, Baltimore, MD 21287, USA; pramulu@jhmi.edu.

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PURPOSE. The purpose of this study was to characterize the extent to which central visual field (VF) loss reflects peripheral VF loss in patients with varying degrees of glaucoma severity.

METHODS. A total of 232 patients with glaucoma or suspect glaucoma completed static central VF testing using the 24-2 pattern and peripheral VF testing using the suprathreshold 30-60 pattern. Points from 24-2 tests were reclassified as normal/abnormal based on pattern deviation values.

RESULTS. Strong positive correlations ($r \geq 0.7$) were observed between the proportion of abnormal central and peripheral points for the full VF, superior hemifield, and inferior hemifield, although the percentage of total central and peripheral abnormal points differed by $\geq 10\%$ in 45% of eyes. In eyes with an average of 10%–40% abnormal points in the central and peripheral VFs, 12.0% more abnormal peripheral points were noted compared with the percentage of abnormal central points ($P < 0.001$; SD, 16.7%; range, 61% more to 37% less). In eyes with an average of 60%–90% abnormal points in the central and peripheral VFs, 16.4% fewer abnormal peripheral points were noted compared with the percentage of abnormal central points ($P = 0.04$; SD, 20.9%; range, 19% more to 49% less).

CONCLUSIONS. Central 24-2 testing generally reflects the extent of damage to the more peripheral VF in glaucoma, although significant disagreement exists for individual eyes. Further work is needed to determine whether integration of peripheral test points can improve detection of true VF loss in early glaucoma or be useful in monitoring progressive glaucomatous damage to areas of preserved VF in advanced glaucoma.

Keywords: glaucoma, peripheral visual field, central visual field, static perimetry, automated perimetry

Visual fields (VFs) in glaucoma are used to assess both the presence and worsening of glaucomatous damage. Furthermore, the results of VF testing, along with other metrics such as visual acuity and contrast sensitivity, have been used to define the visual impact of glaucoma. Visual field testing, however, offers unique insights into the impact of glaucoma on the individual as it combines information on detection ability (sensitivity) and location. Glaucomatous VF defects occur throughout the field of vision, including the central 10°, the mid-periphery (as measured in standard tests over the central 24–30°), and the far periphery, although they are most frequently tested over the central 24–30° of vision.

Far peripheral testing is rarely used in the routine clinical assessment of glaucoma, although previous studies suggest that it provides relevant information independent of that gained from central testing.¹ For example, Freeman et al.¹ demonstrated that peripheral VF abnormal points were associated with greater odds of falling, whereas central VF abnormal points were not. Along the same lines, peripheral vision may play a particularly important functional role in balance, with some studies suggesting that it has a dominant role over central vision with regard to maintaining postural stability.^{2,3} One justification

for the testing of central VFs alone is that more pointwise variability exists at more peripheral points so it is difficult to determine what is normal vs. abnormal in peripheral testing, although some peripheral tests adjust for peripheral variability by tailoring testing to each individual's expected hill of vision.⁴

Another reason for focusing on central testing is that information captured in the more central VF may reflect the results of more peripheral testing. Indeed, prior work has demonstrated that peripheral VFs are rarely abnormal in the context of a normal central VF, although these studies did not include subjects with moderate to severe glaucoma.⁵⁻⁷ Additionally, the peripheral and central VFs have typically been assessed using different perimetric techniques (i.e., kinetic and static perimetry), limiting the ability of prior studies to compare results in different VF regions. Finally, previous studies generally categorized central and peripheral VF loss as either "present" or "absent," even though standardized criteria for documenting glaucomatous peripheral VF loss have not been validated.

Here, we determine the relationship between static perimetry results obtained from central and peripheral testing by comparing the percent of abnormal points in each region and eschewing classification of VF loss as either "absent" or

“present.” Although past studies focused primarily on early or suspect glaucoma, we analyzed how central and peripheral VF results differed over a wide spectrum of glaucoma severity. Given the potential for lid and/or nose artifacts in peripheral testing, we also compared central versus peripheral VF loss over the superior and inferior hemifields, and the temporal and nasal hemifields, to ensure that observed differences were not the result of artifacts caused by the eyelids or nose.

METHODS

The study protocol was approved by Johns Hopkins University School of Medicine Institutional Review Board and followed the principles of the Declaration of Helsinki. Written informed consent was obtained from all patients.

Design, Setting, and Participants

All subjects in this study were enrolled as part of a larger, longitudinal study to determine risk factors for falls among glaucoma patients. Subjects were recruited between September 2013 and March 2015 at the glaucoma clinic at the Johns Hopkins Wilmer Eye Institute. Subjects 57 years and older were eligible for study participation if they had a physician diagnosis of primary open angle, primary angle closure, pseudoexfoliative, or pigmentary glaucoma. Because we were interested in studying the differences in central and peripheral VF loss across the full spectrum of glaucomatous disease, glaucoma suspects based on intraocular pressure elevation, family history, narrow angles, presence of pseudoexfoliative material, or pigment dispersion syndrome were also included. Subjects with any concurrent eye disease resulting in visual acuity worse than 20/40 in the better eye were excluded. In particular, subjects were excluded if they had a diagnosis of AMD, uveitis, a neurologic disorder resulting in VF loss, or a history of pan-retinal photocoagulation or retinal detachment. Other exclusion criteria included (1) any laser eye treatment or surgery (ocular or nonocular) in the last 2 months, (2) any hospitalization in the last month, (3) bed or wheelchair confinement, and (4) an inability to complete VF testing.

Central and Peripheral Testing of the VF

Study participants performed VF testing using two algorithms, both of which were conducted on a single Humphrey Field Analyzer II (Carl Zeiss Meditec, Inc., Dublin, CA, USA): (1) the 24-2 Swedish interactive thresholding algorithm (SITA) standard test (reflecting central testing), with 52 test points tested with stimulus eccentricities ranging out to 21° in all directions except nasally (where stimuli ranged out to 27°) and (2) the peripheral 60 screening test pattern (reflecting peripheral testing) with 60 test points displayed between 30° and 60° eccentricity from fixation. Tests were done on different days, with the central test preceding the peripheral test (median, 2.0 months; interquartile range, 0.6–6.7 months).

For the peripheral 60 screening test pattern, points were classified as seen or not seen using a standard suprathresholding algorithm with a stimulus 6 dB brighter than the expected sensitivity at a given test location. The subject's expected sensitivity at each location is extrapolated from four fully thresholded values (one obtained from each quadrant) along with the expected decline of sensitivity with eccentricity (hill of vision), patient age, and pupil size (written communication, Carl Gagnon, Technical Support Engineer, Carl Zeiss Meditec, 2015). Eyelids were taped open for 24-2 testing to receive a true measure of glaucoma severity, whereas eyelids were not taped open for peripheral testing to receive a functional

measure. Corrective lenses were used for 24-2 testing; however, no corrective lenses were used for peripheral testing per manufacturer recommendations.

Evaluation of VF Results

For both tests, abnormal points were deemed to be those with a sensitivity at least 6 dB below the expected value for that location, given that in the peripheral 60 screening test, points are inherently tested with stimulus 6 dB brighter than the expected sensitivity at that location. Central test points were classified as abnormal if the value on the pattern deviation plot was ≤ -6 dB at a given test location and classified as normal if the value was > -6 dB. For peripheral testing, points were concluded to be abnormal when not seen, in line with the test algorithm described above. Pattern deviation values were used to classify central points (as opposed to mean deviation values) as pattern deviation adjusts for individual variations in the hill of vision, just as peripheral testing individualizes stimulus intensities to each person's expected hill of vision. Peripheral testing accounts for the possibility of diffuse, severe loss by limiting the degree to which the expected sensitivity is shifted.⁸ To account for severe diffuse loss in central points, pattern deviation values were recalculated for 8% of central VFs to allow a maximum of 5 dB added to total deviation values.

Selection of Study Eyes

All analyses focused on one eye per subject ($N = 232$). Given the strong association of better-eye VF results and functional outcomes, the eye with the better (less negative) mean deviation (MD) on 24-2 testing was defined as the study eye in primary analyses and was then compared with peripheral testing for the corresponding eye.⁹ If a subject did not have peripheral testing performed for the chosen eye, then the subject was dropped from analysis (one subject). Sensitivity analyses were also performed in which the worse eye was selected based on 24-2 MD results.

Statistical Analysis

Correlation analyses were performed using Pearson's correlation coefficient to compare the percentage of peripheral and central abnormal points (calculated from the ratio of abnormal points to total tested points) of the entire VF or a specific VF region. To analyze the difference in peripheral and central VF loss by glaucoma severity, plots were constructed demonstrating the difference between the percentage of abnormal central and peripheral points over the range of disease severity (defined via the average percentage of abnormal central and peripheral points) for both the total central and peripheral VFs, as well as specific visual VF regions (i.e., superior and inferior hemifields). Paired *t*-tests were used to test for statistical significance of the mean difference between the percentage of abnormal central and peripheral points.

To determine whether nose/upper eyelid artifacts might be responsible for disagreement between central and peripheral testing, the mean difference in central and peripheral abnormal points was also calculated for each hemifield (superior, inferior, nasal, and temporal) in the full population. To see whether peripheral defects more commonly occurred in the superior or nasal hemifield during a specific disease stage, which would imply that stage-specific differences may be the result of artifacts, we plotted the difference in the percentage of peripheral abnormal points by hemifield (superior hemifield minus inferior hemifield, or temporal minus nasal hemifield) versus MD. To explore the possibility of confounding by

TABLE 1. Characteristics of 231 Study Subjects and Better Eyes Based on MD

Subjects	Percentage
Age (mean, IQR), y	70.5 (11)
Sex, Male	50.0
Race, African American	28.0
Employed	36.6
Years of education (mean, IQR)	17 (3)
Married	64.2
Lives alone	19.8
Better eye	
Mean deviation (mean, IQR)	-4.7 (4.7)
Percentage abnormal central points (mean, IQR)	17.6 (21.2)
Percentage abnormal peripheral points (mean, IQR)	24.2 (23.3)
Percentage superior abnormal central points (mean, IQR)	19.6 (26.9)
Percentage inferior abnormal central points (mean, IQR)	15.6 (15.4)
Percentage superior abnormal peripheral points (mean, IQR)	28.6 (32.1)
Percentage inferior abnormal peripheral points (mean, IQR)	20.4 (18.8)
Spherical equivalent (mean, IQR)	-1.34 (2.75)
Axis (mean, IQR)	120.6 (123)

IQR, interquartile range.

corrective lens use in central and peripheral testing, respectively, the percent difference in abnormal points between central and peripheral testing for the entire VF was plotted against spherical equivalent.

Data were analyzed using STATA v 13 (Stata Statistical Software: Release 13; StataCorp LP, College Station, TX, USA).

RESULTS

Eyes of 232 patients were analyzed, and general characteristics of study participants are provided in Table 1.

Strong correlations ($r \geq 0.7$) were noted between the percentage of abnormal points on central and peripheral tests for the full VF, superior hemifield, and inferior hemifield (Table 2; Fig. 1).¹⁰

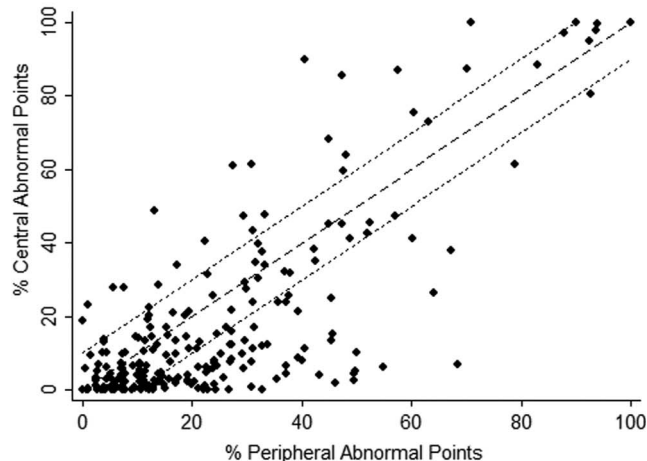
The strongest correlations were demonstrated when comparing the percentage of abnormal points across the full central and peripheral regions ($r = 0.77$), with slightly lower correlations noted when only points in the superior ($r = 0.70$) or inferior ($r = 0.76$) hemifields were assessed. Weaker correlations were noted when comparing the percentage of abnormal superior peripheral points and inferior central points ($r = 0.57$) or inferior peripheral points and superior central points ($r = 0.57$). Similar values for these correlations, as well

TABLE 2. Correlations of the Various Portions of the Central and Peripheral VF

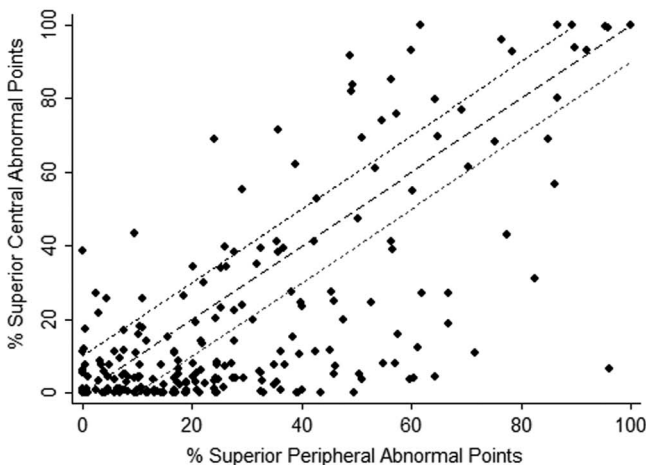
Region of the Peripheral VF	Region of the Central VF		
	All	Superior	Inferior
All	0.77	0.69	0.72
Superior	0.70	0.70	0.57
Inferior	0.72	0.57	0.76

Values in each cell represent the correlation coefficients of the percent of points abnormal in the corresponding regions.

A: Total central vs. Total peripheral



B: Superior central vs. Superior peripheral



C: Inferior central vs. inferior peripheral

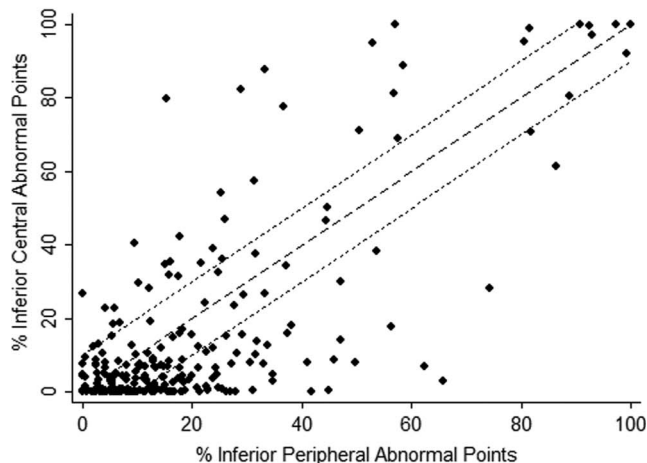
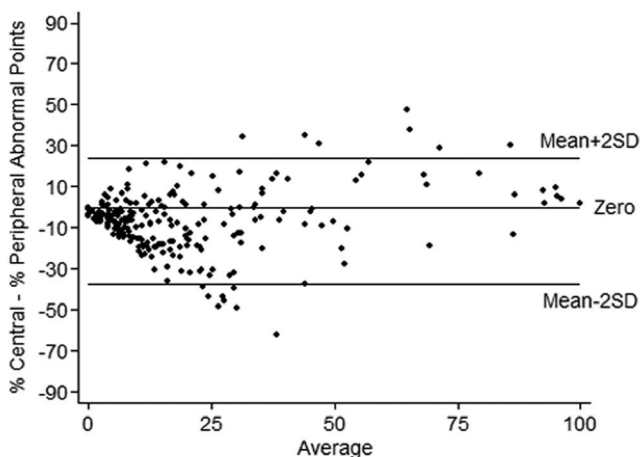
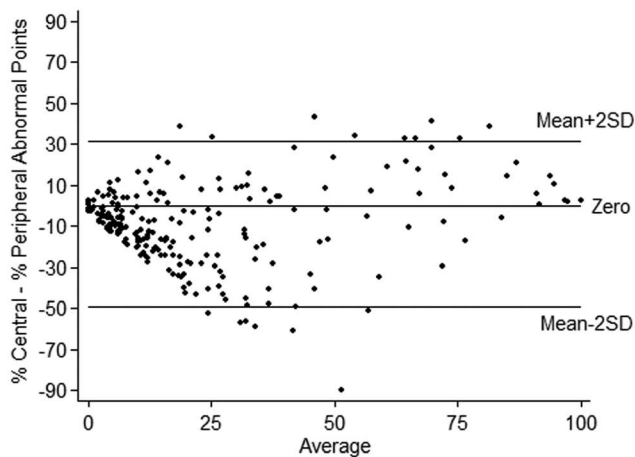


FIGURE 1. Percentage of abnormal points in the central versus peripheral visual field. (A) Total central versus total peripheral. (B) Superior central versus superior peripheral. (C) Inferior central versus inferior peripheral. *Dashed line* represents $x = y$. Points within *dotted lines* represent eyes with $\leq 10\%$ disagreement between percent central and peripheral abnormal points.

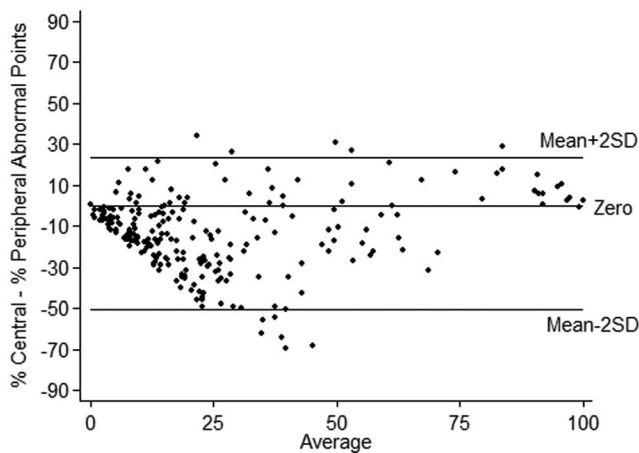
A: Global



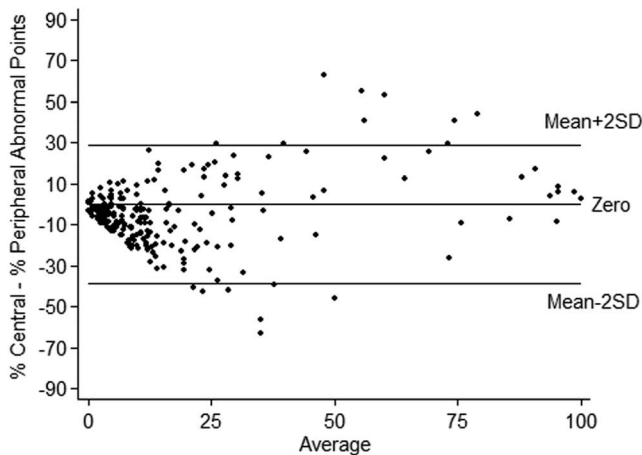
B: Superior Hemifield



C: Nasal Hemifield



D: Inferior Hemifield



E: Temporal Hemifield

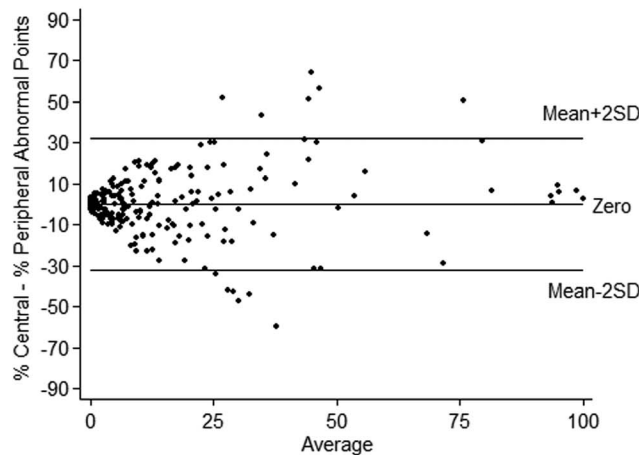


FIGURE 2. Difference between the percentage of total abnormal central and peripheral points and the average percentage of abnormal central and peripheral points. (A) Global, (B) superior hemifield, (C) nasal hemifield, (D) inferior hemifield, and (E) temporal hemifield. Zero lines and 95% confidence intervals (mean \pm 2 SD) are illustrated with *solid lines*.

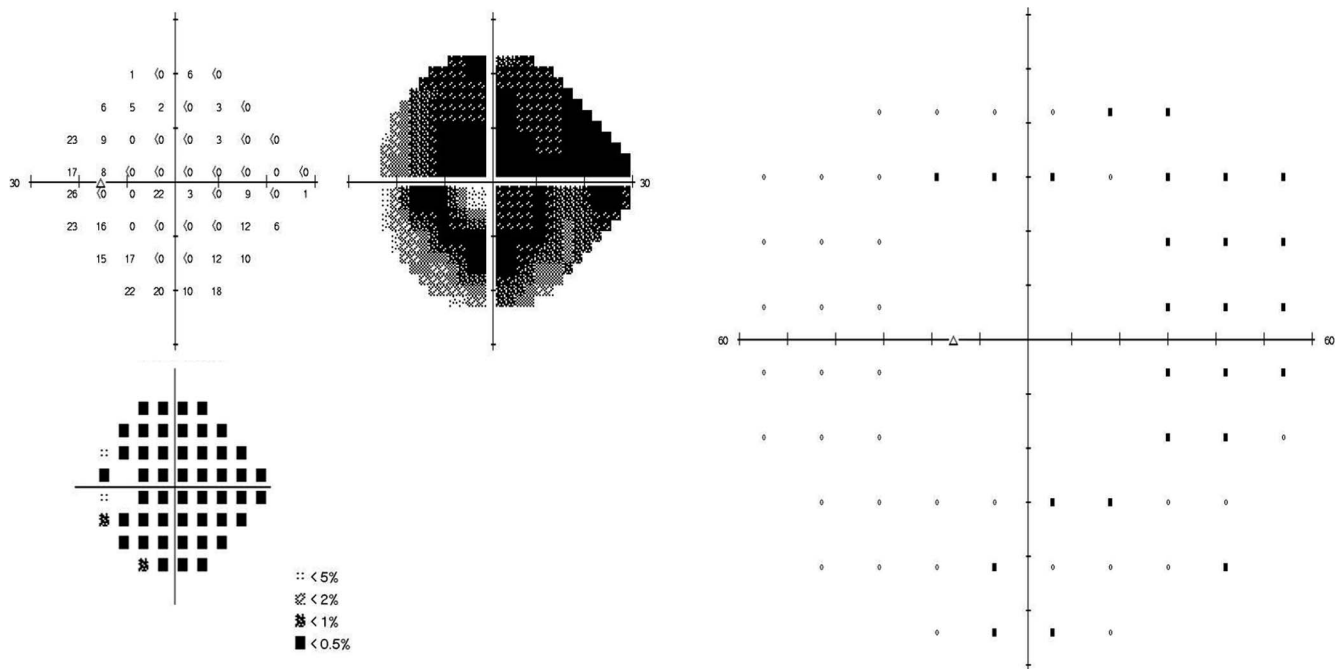


FIGURE 3. Example of patient with diffuse, advanced central loss (*left*) and significant peripheral sparing of the temporal hemifield (*right*). On the total deviation plot from static central 24-2 testing, *four dots* indicate total deviation probability < 5%; *lighter gray* < 2%; *darker gray* < 1%; *black square* < 0.5%. On the static peripheral 60 screening test pattern, *darker rectangles* are points not seen, and the *triangle* indicates the blind spot.

as the analyses below, were found when analyses were performed on (1) eyes with at least moderate VF loss (defined as a VF mean deviation of -5 dB or worse; $n = 65$); (2) eyes with fewer than 33% false positives on both central and peripheral testing (13 excluded), and (3) worse eyes (selected based on having a more negative MD on central 24-2 testing).

Although overall correlations between the percentages of central and peripheral points were strong, greater than 10% disagreement in the percentage of abnormal central and peripheral points was noted in 45%, 61%, and 45% of the total VF, superior hemifield, and inferior hemifield, respectively (Fig. 1).

To determine whether the proportion of central vs. peripheral VF loss varied by glaucoma severity, the difference between the percentage of abnormal central and peripheral points was plotted against the average percentage of abnormal central and peripheral points (Fig. 2). For the total VF region, peripheral points were more often abnormal compared with central points (6.6% more abnormal peripheral than central points; SD, 15.5%; $P < 0.001$; Fig. 2A). At earlier stages of VF loss, the percentage of peripheral VF loss generally exceeded the percentage of central VF loss, whereas at later stages of VF loss, the percentage of central VF loss generally exceeded percentage peripheral VF loss. Specifically, eyes with 10%–40% abnormal points averaged across the whole VF demonstrated 12.0% more (SD, 16.7%; range, 61% more to 37% less) abnormal peripheral points ($P < 0.001$), whereas eyes with 60%–90% abnormal points averaged across the whole VF demonstrated 16.4% fewer (SD, 20.9%; range, 19% more to 49% less) abnormal peripheral points ($P = 0.035$). When restricting the analysis to either the superior or the inferior hemisphere, similar patterns of change across disease stage persisted (Figs. 2B, 2C). Examples of eyes with greater central than peripheral VF loss at an advanced stage of VF loss and greater peripheral than central VF loss at an early stage of VF loss are shown in Figures 3 and 4, respectively.

The percentage of peripheral VF loss exceeded the percentage of central VF loss more in the superior hemifield

compared with the inferior hemifield and more in the nasal hemifield compared with the temporal hemifield (Table 3). To explore whether these peripheral defects were more frequently located in the superior or nasal regions during a particular disease stage, we looked at the peripheral testing results alone and regional differences across disease severity. The tendency toward more abnormal superior (versus inferior) or nasal (versus temporal) peripheral points did not vary with disease severity (Figs. 5A, 5B).

We speculated that central versus peripheral differences may vary more with greater refractive error given that peripheral testing was done without a corrective lens. To investigate this, the percent difference in abnormal points between central and peripheral testing was plotted across refractive error, demonstrating no observable trend (Pearson's correlation coefficient [r] = 0.03).

DISCUSSION

In our sample of glaucoma patients and glaucoma suspects, central and peripheral testing results were strongly correlated, although our results reveal several limitations with the idea that the extent of peripheral VF loss can be inferred from central testing. Specifically, there can be significant loss in the peripheral VF that is not reflected by the extent of central VF loss, particularly in early disease as a result of perimetric damage manifesting only in the periphery. In advanced disease, eyes may have relative peripheral sparing (particularly in the temporal VF) despite advanced central loss. Defects likely reflecting nose/eyelid artifacts were observed in peripheral testing; although these defects did not seem to account for the differences in central and peripheral VF loss noted across disease stage. The potential for significant disagreement between central and peripheral tests suggests that the central 24-2 test results may be an imperfect measure of disability in some persons and suggests possible benefits for testing the VF outside the central 24° – 30° in some eyes.

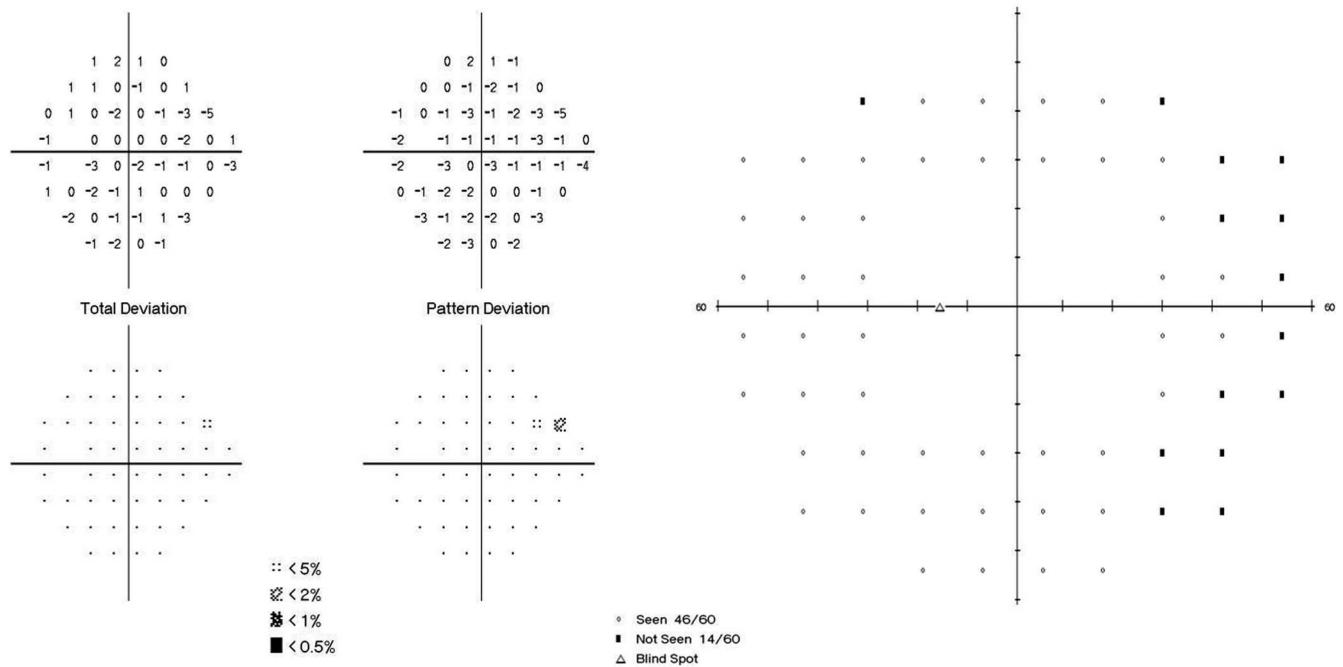


FIGURE 4. Example of patient with less central loss compared with peripheral loss. See Figure 3 legend for description of plots. Dots for pattern deviation probabilities represent similar cutoffs as those for total deviation probabilities.

Our finding that individuals with normal VFs over the central 24°–30° could manifest abnormalities in their more peripheral VF is consistent with prior work revealing that roughly 11%–17% of eyes with a diagnosis of glaucoma or suspect glaucoma and a “normal” central VF demonstrate defects outside the central 30°.^{5,6,11,12} Most peripheral defects have been noted in the nasal VF in these prior studies, mirroring our findings (Table 3). Although previous work examined the peripheral VF through kinetic perimetry or static perimetry performed only in the nasal quadrant, our work examined the full static peripheral VF between 30° and 60°.^{5,6,11} Reporting the percentage of subjects with normal central VFs who have peripheral VF defects is complicated by the fact that completely normal central VFs (VFs with no abnormal points on either the total or pattern deviation plot) are rare, and formal criteria for identifying “true” peripheral defects are not available. Therefore, we chose to compare the percentage of abnormal points in peripheral and central VFs across the spectrum of disease severity and found that peripheral loss, on average, exceeded central loss at early stages of the disease. This pattern persisted even when only superior points were considered, suggesting that our finding was not the result of nose artifacts.

Although peripheral testing can be associated with greater variability/unreliability of test points, these facts do not completely explain our findings of more frequent peripheral defects in early to moderate VF loss. First, the peripheral test that we used is an individualized suprathreshold test as it adjusts for peripheral variability by tailoring stimuli intensity to the individual’s expected hill of vision after thresholding sensitivity in four cardinal points. Second, our findings are consistent across region, with findings persisting even after restricting analyses to specific hemifields where interference from artifacts is unlikely. Peripheral testing can also be associated with a higher potential for false positives. Previous work noted an average false-positive rate of 12% when testing the far nasal peripheral VF with static perimetry, suggesting that there may be error introduced because of inconsistent

responses.¹¹ However, more peripheral than central loss was still observed in early-moderate VF loss when subjects with greater than 33% peripheral false positives were excluded.

At more advanced stages of disease, we found that the percentage of abnormal central points exceeded the percentage of abnormal peripheral points, suggesting relative peripheral sparing. Again, findings persisted even when VFs with high false positives were excluded. This finding is consistent with prior evidence for a “temporal island” of spared vision among patients with advanced glaucoma.¹³ Previous longitudinal work by Brais et al. further demonstrated that progression in advanced disease most often occurred in the temporal VF, suggesting that peripheral testing could be used to monitor disease progression in late disease for patients with extensive central loss.¹⁴

Several practical limitations remain with regard to evaluation of the peripheral VF. Normal subjects have greater variability at more peripheral points, likely reflecting variations in the normal hill of vision, and pointwise variability in the peripheral VF is believed to be greater in the superior and nasal quadrants, regions frequently affected by early glaucoma.^{4,15} Additionally, central 24-2 testing takes less time, leading to decreased patient fatigue, and has been shown to pick up a reasonable amount of early disease by itself.^{16–19} Finally, more false positives may occur in testing of the far peripheral VF, leading to more spurious defects.¹¹ Ideal algorithms to test the

TABLE 3. Mean Difference Between Percentage of Central and Peripheral Abnormal Points by Region

VF Region	Mean	SD
Total region	−6.6*	15.5
Superior	−9.0*	20.2
Inferior	−4.8*	16.9
Temporal	0.1	16.0
Nasal	−13.7*	18.5

* Paired *t*-test reveals *P* < 0.05.

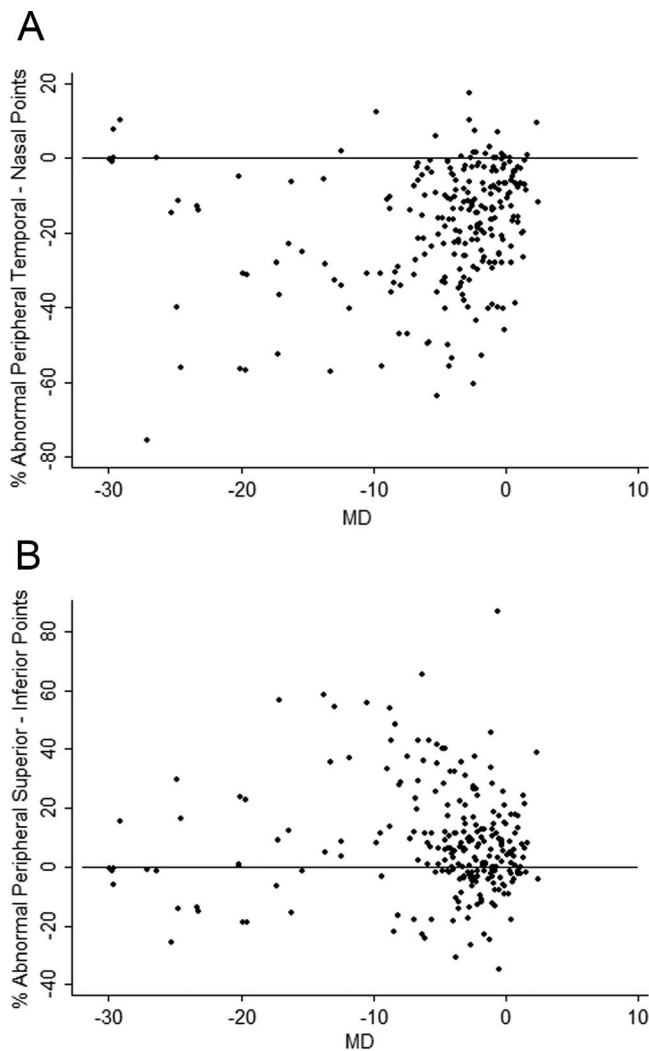


FIGURE 5. Regional difference in percent peripheral abnormal points versus MD. (A) Difference between temporal and nasal versus MD. (B) Difference between superior and inferior versus MD.

far peripheral VF would initially test only a few peripheral points in eyes with little or no central defects and then perform further testing of the peripheral VF if abnormal points are observed. Considerations should also be given to peripheral testing in patients with advanced central loss in whom standard 24-2 or 10-2 tests are unlikely to detect further progression.¹⁴

Several limitations of this study merit further discussion. Peripheral defects in our study were most frequently located superior or nasal, the most common regions of glaucomatous change, but also where VF defects could arise in patients with large noses and/or deep-set orbits.¹⁷ Indeed, we noted that peripheral loss exceeded central loss more in the superior (versus inferior) and nasal (versus temporal) hemifields (Table 3), and lower correlations between the central and peripheral and central VFs were noted superiorly compared with inferiorly (Table 2; $r = 0.70$ and 0.76 , respectively). However, the tendency toward more abnormal peripheral points superiorly did not vary across the spectrum of disease severity (Fig. 5). Thus, nose/eyelid artifacts seem to result in global differences between central and peripheral VF loss but are unlikely to account for differences in central and peripheral VF loss across disease severity. Indeed, our study findings were consistent when restricted to hemifields that are less subject to

nose and lid artifacts. Another potential issue with peripheral testing is that it is performed without refraction and may lead to false peripheral defects due to refractive error. However, central versus peripheral differences did not vary with greater refractive error, meaning that the corrective lenses are not likely to have globally impacted comparisons between the two tests (Pearson's correlation coefficient [r] = 0.03). Also, a learning effect has been documented in peripheral testing, which is greater than the learning curve with central 24-2 testing, and some abnormal peripheral defects may have normalized on repeat testing.¹⁵ Finally, a better study design would have been to compare the variability between central and peripheral results to repeated central or peripheral tests to better understand how much of our observed differences were due to differences in VF sensitivity over the tested regions as opposed to variability inherent in repeat testing. Such an approach would have also helped to establish if greater test-to-test variability is indeed observed with more peripheral testing.

To our knowledge, ours is the first study to compare static perimetry results in central and peripheral VFs across a broad spectrum of disease severity. Furthermore, we compared the two tests in a manner that does not force us to define an abnormal defect in both peripheral and central testing. Additional work is necessary to define the separate contributions of central and peripheral VF loss to disability and to determine whether peripheral VF testing can be consistently applied in clinical situations. Further studies are also needed to determine whether algorithms that combine peripheral monocular test results outside the central 30° might be more relevant to functional ability than monocular visual field tests,^{20,21} although one study comparing better-eye and integrated central visual field results showed minimal differences in the degree of VF loss calculated by each method and also noted very similar relationships between the degree of VF damage estimated by each method and functional measures.²¹

CONCLUSIONS

Central 24-2 testing generally reflects the extent of damage to the more peripheral VF in glaucoma, although significant disagreement can exist at the individual level. In particular, patients with early disease manifest more peripheral than central damage, and more study is required to determine whether thoughtful integration of more peripheral test points using novel or previously described methods^{22,23} may increase the detection of true VF loss in patients with early disease. In later disease, central damage exceeds peripheral damage, and testing of the peripheral VF may be useful to identify progressive damage to the areas of remaining vision.

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