Sampling the Visual Field Based on Individual Retinal Nerve Fiber Layer Thickness Profile

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**Purpose.** Current perimeters use fixed grid patterns. We test whether a grid based on an individual’s retinal nerve fiber layer (RNFL) thickness profile would find more visual field (VF) defects.

**Methods.** We describe the defect-based method for choosing test locations. First, the VF locations with the highest positive predictive value to detect glaucoma from the 24-2 pattern are chosen. An additional 26 locations are chosen from a 2 × 2 degree grid based on RNFL thickness. An individualized map was used to relate VF locations to peripapillary RNFL thickness.

To test whether the 52 locations chosen by the defect-based method find more defects than other test grids, we collected a 386-location (2 × 2 degree grid) VF measurement on 23 glaucoma participants and classed each location in the dataset as either abnormal or normal using a suprathreshold test. Using this data, defect-based sampling was compared to: a method that sampled VF locations uniformly around the optic nerve head (ONH); the 24-2 pattern; a polar pattern; and a reduced polar pattern. The outcome measure was the number of abnormal points that were selected as test locations.

**Results.** For 8 eyes, no method found more abnormal points than would be expected by chance (hyppergeometric distribution, P < 0.05). Of the remaining 15 eyes, the defect-based method identified more abnormal locations on nine eyes, which was significantly better than the other three sampling schemes (24-2: 2 eyes, P < 0.001; polar: 2 eyes, P < 0.001; reduced polar: 2 eyes, P < 0.004; and uniform: 1 eye, P < 0.001).

**Conclusions.** Using structural information to choose locations to test in a VF for individual patients identifies more abnormal locations than using existing grid patterns and uniform sampling based on structure.

Keywords: automated perimetry, visual fields, glaucoma, optical coherence tomography
collected “ground truth” visual fields as input data for comparing the sampling models using a high resolution 2° rectangular grid. In this section, first we describe this empirical data collection which was used as data to test the sampling schemes, and then the sampling schemes themselves.

Data Collection for Testing Schemes

In order to collect high resolution visual fields, 23 participants with clinically diagnosed and currently treated primary-open angle glaucoma were included in the study. All participants had characteristic glaucomatous optic disc features along with VF changes typical of glaucoma (grayscale visual fields are provided as Supplementary material). The median age of participants was 70 (range, 59–85 years). Participants were recruited from a database of previous participants in research studies that had provided consent to be subsequently contacted. This study was approved by the Human Research Ethics Committee of the University of Melbourne. All participants provided written informed consent in accordance with the tenets of the Declaration of Helsinki. Participants with visual acuity less than 6/12, refractive error greater than 6 diopters (D) spherical equivalent, astigmatism greater than 1.5 D, tilted optic disc, or any other ocular disease other than glaucoma were excluded. Systemic disease known to be associated with visual disorder (e.g., diabetes, migraine) was also a criterion for exclusion. Only one eye was tested for each participant, if both eyes were eligible then one was chosen randomly. Each participant underwent a VF examination using the high resolution grid, a Humphrey 24-2 Swedish Interactive Test Algorithm (SITA) standard VF test, optical coherence tomography (OCT), and axial length measurements.

High resolution visual fields were collected using a rectangular grid with 2° spacing on a perimeter (Octopus 900; Haag-Streit AG) controlled via the Open Perimetry Interface.8 The square grid was displaced 1° from both the horizontal and the vertical meridian. To further sample the nasal visual field, additional test locations were added at 23, 25, and 27° eccentricity nasally. Figure 1 shows the customized grid with 386 locations for the left eye. The commercial perimeter (Haag-Streit AG) contains a small mirror at 13° eccentricity directly below fixation which is used for an infrared camera to monitor eye movements. To avoid interference with this mirror, stimulus placement at 1° either side of this mirror was avoided. The customized grid contains approximately 7 times more test locations than the 24-2 test pattern (marked as black dots in Fig. 1).

In order to test the sampling strategies in this study, we only need to classify all 386 locations as either normal or abnormal, hence a multisampling suprathreshold test strategy was used. This also had the side effect of keeping test times to an acceptable level, given the large number of test locations. The multisampling test procedure9 presents two stimuli per location and required two “seen” or two “not seen” to terminate. If the two stimulus presentations gave opposing responses, then a third stimulus was presented and the majority response taken as output.

The stimulus intensity for the suprathreshold stimulus was chosen from a hill of vision (HoV) model,7 since there is no empirical normative data available for a 2° grid. The HoV model gives normal threshold values for size III white-on-white targets for a given participant age and location in the field (assuming that 0 dB is 1273 cd/m²). A frequency of seeing (FoS) curve8 was drawn aligning the 50% probability of seeing the size III target with the HoV model estimated sensitivity value. The FoS curve was modeled as a cumulative Gaussian with a mean at the HoV value, and a standard deviation obtained from Henson et al.8 Note that in the Henson et al. study they measured standard deviation of FoS in normal, glaucoma, ocular hypertension, and optic neuritis on a dB scale that had 0 dB equal to 3183 cd/m², and so we converted this to the Octopus 900 dB scale that has 0 dB equal to 1273 cd/m² using a nonlinear curve fit. This resulted in log (FoS standard deviation) = 2.896 − 0.079 × threshold. The decibel value closest to the 99% probability of seeing on this FoS curve minus 2 dB to compensate for generalized reduced sensitivity9 was taken as the suprathreshold stimulus intensity value.

To make the test easier for participants, the VF test was broken up into four runs, each testing approximately 96 VF locations. Each run sampled locations from all four VF quadrants and from a range of eccentricities in order to create similar cognitive demands to a standard VF test. The same four test grids were used for all participants but the order of testing using each grid was randomized between participants and adequate breaks were given between each run.

In addition to the customized VF testing, each participant also underwent standard clinical VF testing using the HFA II (Carl Zeiss Meditec). The SITA standard test strategy was used and visual fields were collected using the 24-2 and 10-2 test pattern.

Optical Coherence Tomography

All participants underwent OCT to measure peripapillary RNFL thickness. The spectral domain OCT (Spectralis; Heidelberg Engineering GmbH, Heidelberg, Germany) was used to measure a high resolution circular scan of radius 3.6 mm centered on the ONH. All images were obtained using an automatic retinal tracker (ART; Heidelberg Engineering GmbH). With the ART mode activated, the OCT device (Heidelberg Engineering GmbH) takes a fixed number of B-scans per location during the scanning process and averages them for noise reduction. The ART mode was set to take the maximum 100 B-scans per location (default is nine). All images were obtained well above the manufacturer’s recommended minimum signal-to-noise ratio of 20 dB.

Figure 1. Customized two degree grid used to collect visual field data for a left eye. Filled circles are the 24-2 locations that were included in the test.
The inbuilt image processing software of the OCT device (Heidelberg Engineering GmBH) was used to segment the RNFL thickness and this was subsequently manually cross-checked and corrected where necessary by one of the authors (SBG). Blood vessels were removed from RNFL profiles using the method described as in Ballae Ganeshrao et al., which was based on Patel et al. Briefly, custom software written in R (version 3.1.1) was used to extract blood vessel edges. The software reads the raw format (.vol) images exported from the OCT device (Heidelberg Engineering GmBH) and allows users to manually identify blood vessel edges from B-scan images as they cast shadows. After the user identifies all blood vessel edges, the height of the blood vessel was subtracted from the RNFL thickness profile, assuming vessels are circular.

**Individualized Spatial Map**

An individualized spatial map was used to connect locations in the visual field with locations on the circular scan of the ONH. The individualized spatial map takes into account ONH position relative to the fovea, axial length, and macular retinal ganglion cell body displacement based on the Turpin et al. implementation of Drasdo et al. The position of horizontal raphe used in the individualized maps was 170° from the fovea-disc angle.

**Spatial Sampling Methods**

We now describe the two new sampling methods used for choosing VF test locations: the defect-based method and the uniform method.

**Defect-Based Method of Choosing VF locations**

The defect-based method keeps 26 fixed locations from the 24-2 pattern (filled circled locations in Fig. 2), and allocates an additional 26 variable locations based on an individual’s RNFL thickness as measured by their OCT scan. The 26 variable locations were either chosen from the 2° grid or the 4° grid as shown in Figure 2. Since there is a considerable amount of variability in the structure-function relationship in individuals with glaucoma, sampling a visual field entirely based on structural damage may not be a sensible thing to do, hence the decision to only move half the 24-2 locations based on structure, and keep half fixed independent of structure.

The fixed VF locations were selected based on the positive predictive value of a VF location in detecting early to moderate glaucomatous VF defects, the first 26 VF locations (Fig. 2, shown in filled circles) ranked based on the positive predictive value formed the fixed locations. The remaining 26 variable locations were allocated according to the scheme presented in Figure 3, which requires selection of ONH sectors, and then selection of locations that map to those sectors.

**FIGURE 2.** (A) Two-degree grid and (B) four-degree grid derived from the 2° grid. Filled circles were fixed VF locations and open circles were locations available for variable VF location selection. Fixed locations were selected based on the 24-2 6° grid.
As required by the first part of the process, to identify the most abnormal 30° sectors of the ONH, the RNFL thickness profile was first normalized to be a percentage difference from the mean normal RNFL thickness (obtained from Heidelberg Engineering GmBH). The profile was then divided into twenty-four 30° sectors (each sector overlapped with the two adjacent sectors by 15°). For each of the sectors, the lowest 5th percentile of the normalized RNFL thickness was chosen to represent the minimum RNFL thickness of that sector. We did not take the actual minimum because segmentation and/or imaging errors might give unusually low values. Figure 4 shows this process for one subject. Sectors were ranked in ascending order according to these minimums. These sectors are chosen in turn, and whenever one sector is used it, and the two sectors that overlap it, are no longer considered in the process. Once a sector is chosen, the second part of the process is to find all the possible locations in the VF that map back into that ONH sector. For this we use the map of Denniss et al., examples of which are shown in Figure 5. We take as many locations in the mapped area as possible, and continue until all 26 variable locations are allocated.

### Uniform Method

The defect-based method will cluster VF locations in areas of decreased RNFL thickness, while the 24-2 pattern samples the visual field uniformly in visual space. An alternative approach is to choose VF locations uniformly in structural space. To achieve this, we used the same mapping from ONH to VF as in the defect-based method, but attempted to allocate one location to every 360°/52 ≈ 7 degree sector. If there was more than one VF location mapping to a 7° sector, then the specific VF location within the sector was chosen randomly. If there

![Figure 4](http://arvojournals.org/)  
**FIGURE 4.** Top: displays an RNFL profile of a subject (black line) with blood vessels removed (RNFL-noBV: dashed line) and the population mean (mean normal: green line) and confidence intervals in shaded areas with red indicating $P < 1\%$ and yellow indicating $P < 5\%$. Bottom: shows the same RNFL as a percentage difference from the population mean, and the minimum (lowest 5th percentile) for each 30° sector whose boundaries are shown as ticks on the top and bottom axis. The red area shows the sector with the lowest 5th percentile that would be chosen first by the defect-based method.

![Figure 5](http://arvojournals.org/)  
**FIGURE 5.** Areas of the 2° VF mapped to the sector beginning at 270° for two different eyes (red and blue) with the same axial length. The purple area indicates the overlap between the two regions. The ellipse shows the location of the blind spot (ONH) for each eye.
were no locations mapping into a 7\(^\circ\) sector, as will be the case in the temporal VF; then the closest location was chosen.

Fixed Radial Patterns

The 24-2 pattern is a uniform rectangular grid. There are other patterns in commercial perimeters that follow a radial or polar pattern. One such is the G pattern of the commercial perimeters (Heidelberg Engineering GmBH). We include a polar sampling scheme (P59) similar to the G pattern in our analysis for comparison to the rectangular grid patterns. Note that the G pattern has 59 locations, giving it more of an opportunity to find abnormalities in the visual field than the procedures that only use 52 locations. The G pattern coordinates are offset by 1\(^\circ\) from our baseline 2\(^\circ\) grid. Therefore, our polar pattern (P59) was shifted from the G pattern by 1\(^\circ\) both horizontally and vertically so that most of the locations aligned with our high density 2\(^\circ\) grid; for these locations we choose the closest point in the 2\(^\circ\) grid. We also include this modified polar pattern with the 10 outermost locations removed, giving a pattern with 49 locations (P49 grid).

Analysis

Sampling methods are compared by the number of abnormal locations they identify in either the 2\(^\circ\) or 4\(^\circ\) baseline visual fields collected on the 23 participants. In order to compare the number of abnormal locations identified in any one field by a procedure to that expected by chance, we use the hypergeometric distribution. We flag procedures where the probability of finding the observed number of abnormal locations is less than 0.05, determined for each individual patient given the number of abnormal locations found in their baseline field.

RESULTS

Figure 6 shows an example of defect-based and uniform sampling method compared to other procedures, a paired t-test was used to compare the number of abnormal points identified in the 23 participants.

Figure 6. An example of (A) the defect-based sampling method and (B) the uniform sampling method using a 2\(^\circ\) grid for an individual. (C) RNFL thickness for the individual with VF points shown along the top positioned horizontally according to their mapped 1\(^\circ\) ONH sector.
significant higher than all other methods except for the P49 method, as shown in Figure 7 (using a significance level of 0.05/8 = 0.006). The defect-based method had 36% precision for the 4" grid. Overall, the closest method was at least 5% less effective; that is, the defect-based method identified about three more abnormal locations on average than the other methods across all 23 patients.

**Discussion**

We have shown that using OCT information to automatically choose half of the locations in the visual field for testing, while leaving the other half fixed, identifies more abnormal points in the visual field than using a fixed pattern (either rectangular or polar).

Using structural information to determine the placement of VF stimuli is not a new idea. Previously, in the FOP scheme, locations were added to a standard test grid manually by the examiner based on retinal photos. We purport that our method has two advantages: first, it is fully automatic, requiring no manual location selection; and second, we do not increase the number of test points relative to a standard grid approach.

An alternative approach to FOP for choosing VF locations based on structural damage could be to predict the visual field using OCT information to automatically choose variable location points in the superior (based on the most damaged OCT sector) and so had none left to allocate into the inferior field. However, the schemes that sampled the field on a regular grid had locations in both scotomas. Increasing the number of variable locations allowed would work well for this participant; however, in this study, we chose our parameters a perimetric test. This could be a fruitful area of investigation, and may improve upon our simple heuristics based on OCT sectors used in the defect-based method.

The individualized map between OCT and VF locations used in this study is developed based on a computational model. In order to validate the individualized map, we need to physically measure and observe an individual's retinal nerve fiber (RNFL) arrangements in the retina. However, using current imaging technologies, it is not feasible to directly observe an individual's RNFL arrangement. Although, there are several recent advancements in adaptive optics imaging technologies that enable in vivo imaging of RNFL arrangements that present using adaptive optics-scanning light ophthalmoscopy is only possible to measure superficial RNFL arrangements and it takes about 40 minutes (including short breaks) to image a 20° × 1° rectangular portion of retina. Therefore, the individualized map used in this study has been shown to have good agreement with maps derived from visual inspection and subsequent hand tracing of RNFL trajectories and unlike other maps, the individualized map enables customization for each individual using an individual's biometric data. Improvements in mapping between clinical structural measures and VF space should only improve our defect-based method.

In this dataset, for patient 15 (Table) the fixed grids (24-2, P59 and P49) found more abnormal locations than the defect-based method. This individual had both a superior and inferior RNFL defect. The defect-based method placed all of its 26 sectors used in the defect-based method.
priori rather than finding the best fit for our dataset. It would be ideal to have a dataset against which we could optimize the various heuristics and parameters chosen here, and another dataset to validate these choices. Collecting visual fields at a resolution of 2° is laborious and demanding on the volunteers; therefore, this ideal situation may not be possible.

Participant 1 had an early macular defect that was not detected by the peripapillary RNFL scan, but did show up on a 10-2 field and the suprathreshold tests. Because the peripapillary RNFL scan was normal, the defect-based method failed to allocate additional VF locations in the macula region. Evidence for an inability to detect the macular RNFL thinning by peripapillary RNFL scans is scattered throughout the literature. Tan et al. studied the diagnostic ability of peripapillary RNFL and macular scans to identify macular defects. They found in 78 glaucoma eyes with central perimetric defects, both peripapillary RNFL and macular scans identified a macular defect on 65% of eyes, 13% of eyes had macular defects identified only by peripapillary RNFL scans and 9% of eyes had macular defects only on macular scans (Fig. 7 in Tan et al.). Based on this, the defect-based method will fail to allocate VF locations to the macular region in the 9% of cases with macular defects (those with normal peripapillary scans). In order to avoid this scenario, a future defect-based method may be feasible that is based on a combination of macular thickness scans and peripapillary scans, possibly with higher weighting given to macular thickness scans to detect central VF defects.

Participant 3 had a superior RNFL defect but their suprathreshold visual field and HFA visual fields did not show any corresponding inferior VF defect. There is apparent structure-function discordance in this individual. There are several reasons for the structure-function discordance, which includes variability associated with structure and functional measures, individual differences in structure-function mapping, using fixed ONH sector sizes, the dynamic range of structural and functional instruments, instrument floor effect, etc. (for detailed review, please see Refs. 17, 30, and 31). The defect-based method depends on the existence of a predictable structure-function relationship in glaucoma. If there is significant discordance between structure and function like in participant 1 and 3, then the defect-based method will break down. Perhaps in these cases, regular test patterns that sample the visual field uniformly in VF space have an advantage, although in our data, that is not obvious as the regular patterns generally fail to do better than random patterns (P < 0.05).

While in this manuscript we are not proposing a specific perimetric thresholding procedure that would make use of the locations identified by defect-based sampling, there are at least three areas of consideration for the development of such a procedure. First, any VF procedure that tests at locations that may differ from patient to patient increases the burden of clinical interpretation of the VF output over the current “one size fits all” situation. The 24-2 and G patterns are well established in clinical practice, allowing experienced clinicians to quickly glean information from their display. There is an extra burden on clinicians to interpret VF data with varying locations for different patients. This might be overcome by presenting data in a standard format using interpolation, or 3D displays, but this requires further work specific to different tests.

Second, the defect-based sampling method is designed to increase the likelihood of spatial sampling damaged locations in the visual field, and these areas of the visual field have high variability when tested with existing thresholding algorithms. Testing in these regions should increase the sensitivity of a test in detecting glaucoma compared with one that tests on a fixed grid. However, it is not clear if testing in these regions, instead of testing in regions that do not have a corresponding RNFL deficit, will increase sensitivity for monitoring glaucomatous

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**Figure 7.** Difference in the proportion of locations identified that are abnormal out of all locations between the defect-based method and other methods as shown on the x-axis for all 23 patients. P values shown under each box are from a paired Wilcoxon-test (R version 3.3.0).
change. Perhaps getting more reliable threshold estimates in areas of the visual field that are deteriorating but have higher dB values than those obtained in a damaged area would be preferable. Determining how to use the locations identified by the defect-based method in a VF test requires further study. Third, the magnitude of test-retest variability in the selection of locations that may arise from variability in OCT parameters from one visit to the next is not entirely clear, and may vary between instruments and will depend upon the use of follow-up image alignment features within individual OCT platforms. Various parameters like low signal strength, sample density, low RNFL thickness, media opacity, pupil size, OCT segmentation errors, eye movements, and position of scan circle are known to affect the RNFL thickness measurement.33–36

The uniform sampling method does not improve the number of abnormal VF locations identified compared to the other methods. The uniform method proposed in this experiment samples the visual field as evenly as possible around the ONH within the constraints of these visual fields. Note: to truly sample evenly around the ONH requires stimulus placement in areas quite dissimilar to the most common way of sampling the visual field using a rectangular grid, in which stimulus placement extends only six degrees temporal to the blind spot. We similarly collected our ground truth visual fields without these locations; hence there are not adequate VF locations in the temporal VF region to map evenly around the ONH.

The visual fields that were used to test our VF sampling models were collected using a suprathreshold test strategy for several reasons. First, in order to assess the utility of the spatial sampling strategies, only a classification of “normal” or “abnormal” is required for each VF location. We could have measured fields using a threshold approach, but for the purpose of evaluating the sampling methods, would then have reduced the dataset to normal/abnormal using a total deviation classification or similar approach anyhow. Given the large amount of data that needed to be collected (the 2° grid has approximately 7 times the VF locations as a standard 24-2 pattern), the use of a suprathreshold approach was most pragmatic. The total test visit time was approximately 2 hours (customized VF test, Humphrey VF test, imaging, and axial length measurements), with the customized VF test containing 386 locations taking on average 29 ± 3 minutes (excluding breaks) to complete. It should be noted that the suprathreshold visual field is not the part of the defect-based sampling method, but was measured to provide test data to enable the main study (analysis of different sampling strategies) to be performed. The defect-based method described in this study is relevant to any test strategy/algorithm (e.g., SITA, Zippy Estimation of Sequential Testing [ZEST], staircase, screening procedures etc.).

We evaluated the defect-based method on 23 subjects. Although the number of participants is not large, the amount of VF information collected in each participant was almost seven times more than that collected in regular clinics. In addition to this, the 23 participants used in our study represented a substantial variety of spatial patterns of glaucomatous VF loss ranging from minimal damage to extensive loss (Supplementary Fig. S1, 24-2 grayscale ordered by MD). We deliberately selected patients with a range of VF defects that could arise due to RNFL thickness loss. A limitation of the defect-based sampling method is that it ignores some regions of the visual field that are not associated with an OCT deficit. Figure 6A shows the locations that are definitely chosen (black dots), but it is feasible that there might be large areas not sampled. This should not be a problem for diagnosis of glaucoma, as the defect-based method generally finds abnormal VF locations; but it may be a problem for monitoring the progressive deterioration of normal points. Whether the information lost in not testing the OCT-normal regions of a fixed grid is compensated by the information gained by testing abnormal locations chosen by the defect-based method for determining glaucomatous progression requires further investigation. A second limitation of the defect-based sampling method is that locations are chosen based on individual RNFL thickness, so any VF defects that do not involve RNFL thickness loss may not be selected as a region of interest. Therefore, this approach is really targeted toward glaucomatous VF damage.

In conclusion, structural information can be used to locate more abnormal points in an individual’s visual field than current fixed-grid patterns in common use without increasing the number of locations examined.

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References


