VFMA: Topographic Analysis of Sensitivity Data From Full-Field Static Perimetry

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Purpose: To analyze static visual field sensitivity with topographic models of the hill of vision (HOV), and to characterize several visual function indices derived from the HOV volume.

Methods: A software application, Visual Field Modeling and Analysis (VFMA), was developed for static perimetry data visualization and analysis. Three-dimensional HOV models were generated for 16 healthy subjects and 82 retinitis pigmentosa patients. Volumetric visual function indices, which are measures of quantity and comparable regardless of perimeter test pattern, were investigated. Cross-validation, reliability, and cross-sectional analyses were performed to assess this methodology and compare the volumetric indices to conventional mean sensitivity and mean deviation. Floor effects were evaluated by computer simulation.

Results: Cross-validation yielded an overall $R^2$ of 0.68 and index of agreement of 0.89, which were consistent among subject groups, indicating good accuracy. Volumetric and conventional indices were comparable in terms of test–retest variability and discriminability among subject groups. Simulated floor effects did not negatively impact the repeatability of any index, but large floor changes altered the discriminability for regional volumetric indices.

Conclusions: VFMA is an effective tool for clinical and research analyses of static perimetry data. Topographic models of the HOV aid the visualization of field defects, and topographically derived indices quantify the magnitude and extent of visual field sensitivity.

Translational Relevance: VFMA assists with the interpretation of visual field data from any perimetric device and any test location pattern. Topographic models and volumetric indices are suitable for diagnosis, monitoring of field loss, patient counseling, and endpoints in therapeutic trials.
levels, and detect subtle sensitivity gradients and emerging scotomas. In the absence of a fast, full-thresholding algorithm, previous full-field static perimetry studies have used the standard full-threshold staircase strategy and limited the number of test points to avoid long exam durations. A new, fast full-threshold algorithm, GATE-i7, has enabled full-field static perimetry with more test locations and practical test durations (Weleber RG, et al. IOVS 2009;50:ARVO E-Abstract 3813; Schiefer U, et al. IOVS 2009;50:ARVO E-Abstract 5354).

Clinicians currently have several options to aid in the assessment of static visual field tests. Among them are visual appraisals of the test results for emerging scotomas and disease regionality, and the quantification of defects and the remaining field by performance metrics or indices. Current visualization techniques include charts of individual sensitivity levels, grayscale and color representations in which the spatial distribution of the sensitivity levels are quantized with large interval, and deviation plots showing comparisons with average age-matched healthy normal controls. These display methods typically generate flat, 2-D illustrations where the spatial and sensitivity dimensions can appear pixelated. An early form of 3-D display of sensitivity has been used to illustrate the progression of field loss in patients with retinitis pigmentosa from mutation of RP1. Other mathematical models have been developed to study the effects on the visual field of neurological disease, trauma, retinal degenerations, and glaucoma. These display methods typically generate 3-D illustrations where the spatial and sensitivity dimensions can appear pixelated. An early form of 3-D display of sensitivity has been used to illustrate the progression of field loss in patients with retinitis pigmentosa from mutation of RP1. Other mathematical models have been developed to study the effects on the visual field of neurological disease, trauma, retinal degenerations, and glaucoma.

Perimetry data can be condensed into global indices of visual function. These indices quantify and distill trends in the visual field into simple numerical summary measures, and are important as endpoints in therapeutic trials, longitudinal analyses, and patient assessments. Conventional indices include mean sensitivity (MS) and mean deviation (MD), which are based on the average sensitivity value. These indices are appropriate for rectilinear grids with uniform spacing; however, for grids with radial patterns, central condensation, and unequal spacing, these indices become weighted averages. The weighting biases the indices to the regions of higher sampling density, which alters their interpretation and limits their comparison among grids with different sampling patterns. Furthermore, these indices are global measures and can be insensitive to local spatial or regional behavior.

To improve the interpretation and assessment of static perimetry data, we introduce a topographic approach to Visual Field Modeling and Analysis (VFMA). Topographic methods are currently used in photokeratoscopy to map the surface of the cornea and in the analysis of retinal layers with optical coherence tomography. A similar approach has been used to present topographic assessment of the optic disc. In this study, we perform topographic modeling, interactive visualization, and data distillation of visual field sensitivity data using a custom software application we developed called VFMA. VFMA renders 3-D surface models of the hill of vision (HOV) and its defects, and also provides quantitative functional measures. We focus on several visual function indices that are derived from the HOV volume, or the volume beneath the sensitivity surface. These indices capture the visual field magnitude and extent at all states of disease without weighting bias, and are more meaningful when comparing exams acquired with different grids than indices based on simple averaging, such as MS and MD. The volumetric indices are conceptually similar to the kinetic visual field global volume, but VFMA allows measurements from the entire visual field as well as specific regions of interest. Furthermore, VFMA provides contour analysis and comparisons with normative data, supports perimeter test grids of any size and arrangement, and performs peripheral field modeling with minimal cartographic distortion. In this study, we used VFMA to demonstrate the clinical use of HOV volume analysis in patients with retinitis pigmentosa.

We also investigated the effects of perimeter hardware limitations on the visual function indices. The maximum luminance for a stimulus, which is set by the perimeter manufacturer, determines the minimum sensitivity value (MSV) measurable. In this work, the term “floor effect” is used to describe sensitivity values that are near the MSV or are clipped by the MSV, which occurs when the subject cannot detect the perimeter’s maximum intensity stimulus. Floor effects can have a significant influence on the outcome and interpretation of a perimetry exam. We performed a post hoc analysis of floor effects and their impact on the visual function indices. Progressively larger MSVs were imposed on the perimeter data we collected to simulate the floor effects induced by perimeters with smaller maximum stimuli.

**Methods**

**Subjects**

The 98 subjects in this study, summarized in the first row of Table 1, included 16 normal volunteers (age range, 18.5–62.7 years) and 82 patients with...
informed consent was provided by all subjects. Approval adhering to the tenets of the Declaration of Helsinki was obtained from the Oregon Health and Science University (OHSU) Institutional Review Board, and written, informed consent was provided by all subjects with either an Octopus 101 or an Octopus 900 perimeter (Haag-Streit AG, Köniz, Switzerland) using a 10 cd/m² (31.5 apostilbs) background, the GATE-i strategy, and Goldmann stimulus size V. Fixation was monitored by the technician during the entire testing session. Subjects were tested with the radially oriented, centrally condensed, binocularly symmetric grid pattern shown in Figure 1. This grid consisted of 164 points spanning a solid angle, or angular footprint, of 3.69 steradians (sr). Measured threshold values from the Octopus 101 were exported and converted to differential luminance sensitivity (DLS) in decibels (dB); for the Octopus 900, this conversion was performed automatically by the manufacturer’s EyeSuite software. The quality of each subject’s exam was assessed by a reliability factor (RF), defined as the percentage of total catch trials resulting in either a false-positive or false-negative. Any exam with an RF > 15% for normal subjects or 25% for patients was excluded; based on this criterion, three normal and nine patient exams were excluded.

Table 1. Summary of the Data Used in Each Analysis

<table>
<thead>
<tr>
<th># Normal Subjects</th>
<th># Normal Exams</th>
<th># RP Patients</th>
<th># RP Exams</th>
<th># PCRP Patients</th>
<th># PCRP Exams</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>16</td>
<td>61</td>
<td>76</td>
<td>344</td>
<td>6</td>
</tr>
<tr>
<td>Age: 37.2 ± 13.8</td>
<td>OD: 31</td>
<td>Age: 42.1 ± 16.5</td>
<td>OD: 171</td>
<td>Age: 44.3 ± 18.7</td>
<td>OD: 19</td>
</tr>
<tr>
<td>OS: 30</td>
<td></td>
<td></td>
<td>OS: 173</td>
<td></td>
<td>OS: 19</td>
</tr>
<tr>
<td>LOOCV</td>
<td>16</td>
<td>61</td>
<td>76</td>
<td>344</td>
<td>6</td>
</tr>
<tr>
<td>Age: 37.2 ± 13.8</td>
<td>OD: 31</td>
<td>Age: 42.1 ± 16.5</td>
<td>OD: 171</td>
<td>Age: 44.3 ± 18.7</td>
<td>OD: 19</td>
</tr>
<tr>
<td>OS: 30</td>
<td></td>
<td></td>
<td>OS: 173</td>
<td></td>
<td>OS: 19</td>
</tr>
<tr>
<td>Test-retest</td>
<td>10</td>
<td>46</td>
<td>10</td>
<td>76</td>
<td>NA</td>
</tr>
<tr>
<td>Age: 37.1 ± 13.5</td>
<td>OD: 23</td>
<td>Age: 42.1 ± 11.7</td>
<td>OD: 38</td>
<td></td>
<td></td>
</tr>
<tr>
<td>OS: 23</td>
<td></td>
<td></td>
<td>OS: 38</td>
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<tr>
<td>Cross-sectional</td>
<td>16</td>
<td>31</td>
<td>76</td>
<td>150</td>
<td>6</td>
</tr>
<tr>
<td>Age: 37.2 ± 13.8</td>
<td>OD: 16</td>
<td>Age: 42.1 ± 16.5</td>
<td>OD: 74</td>
<td>Age: 44.3 ± 18.7</td>
<td>OD: 6</td>
</tr>
<tr>
<td>OS: 15</td>
<td></td>
<td></td>
<td>OS: 76</td>
<td></td>
<td>OS: 6</td>
</tr>
</tbody>
</table>

Ages are at the time of most recent testing, and are listed as mean ± SD. NA indicates data was not analyzed.

Among the patients, 76 (range, 12.6–75.6 years) had inherited forms of typical RP and six (range, 22.4–70.3 years) had pericentral RP (PCRP). For normal subjects, the exclusion criteria were history of migraines, uveitis, glaucoma, retinal, or other disease that would influence visual field testing; ocular surgery for reasons other than cataracts (a minimum of 6 months following cataract surgery was required); medication known to affect vision; or refractive error > ±6 diopters (spherical) or > 2 diopters (cylindrical). One control required a +4.75 sphere and 4 RP patients required spherical corrections for the more hyperopic eye of +3.25, +4.00, +4.50, and +6.00. Approval adhering to the tenets of the Declaration of Helsinki was obtained from the Oregon Health and Science University (OHSU) Institutional Review Board, and written, informed consent was provided by all subjects.

**Visual Field Testing**

Full-field automated static testing was performed on all subjects with either an Octopus 101 or an Octopus 900 perimeter (Haag-Streit AG, Kòniz, Switzerland) using a 10 cd/m² (31.5 apostilbs) background, the GATE-i strategy, and Goldmann stimulus size V. Fixation was monitored by the technician during the entire testing session. Subjects were tested with the radially oriented, centrally condensed, binocularly symmetric grid pattern shown in Figure 1. This grid consisted of 164 points spanning a solid angle, or angular footprint, of 3.69 steradians (sr). Measured threshold values from the Octopus 101 were exported and converted to differential luminance sensitivity (DLS) in decibels (dB); for the Octopus 900, this conversion was performed automatically by the manufacturer’s EyeSuite software. The quality of each subject’s exam was assessed by a reliability factor (RF), defined as the percentage of total catch trials resulting in either a false-positive or false-negative. Any exam with an RF > 15% for normal subjects or 25% for patients was excluded; based on this criterion, three normal and nine patient exams were excluded.

**HOV Modeling With Thin Plate Spline (TPS) Interpolation**

Topographic surface models of the HOV were created for each exam with TPS interpolation of the perimetry data. The surface was constrained outside the subject’s field-of-view by adding $N_z = 60$ artificial points with zero sensitivity along a circle with radius 120°, as shown in Figure 1b. The set of points $\{(x_i, y_i, z_i)\}_{i=1}^N$ defined the data from one static visual field exam, where $N = N_x + N_y = 224$, $(x_i, y_i)$ is location of the $i$th grid point in angular coordinates and $z_i$ is the corresponding DLS value in dB. The HOV surface model was defined at location $(x, y)$ by

$$\hat{z}(x, y) = w^T d,$$

where $w = [w_x \ w_y\ w_0\ w_1 \ w_2 \ldots w_N]^T$ and $d = [x\ y\ 1\ \phi(|x-x_i|)\ldots\phi(|x-x_N|)]^T$ are $(N+3) \times 1$ vectors of weights and displacements, respectively. Here, $\phi(r) = r^2 \log(r)$ is the infinitely differentiable TPS radial basis function, and $x = [x\ y]^T$ and $x_i = [x_i\ y_i]^T$ are $2 \times 1$ coordinate vectors. The weight vector was found by solving the
matrix equation

\[ Aw = b, \text{where} \ b = [z_1z_2 \ldots z_N 0 0 0]^T \]

and

\[ A = \begin{bmatrix} \Phi & C \\ C^T & 0 \end{bmatrix} \]

The \( i^{th} \) element of the \( N \times N \) submatrix \( \Phi \) is \( \Phi_{ij} = \phi(||x_i - x_j||) \), and the \( j^{th} \) row of the \( N \times 3 \) submatrix \( C \) is \([1 \ x_i \ y_i]\). Once the weight vector \( w \) was calculated, the surface was interpolated at an arbitrary location \((x, y)\) by updating \( d \) with the location coordinates and evaluating Equation 1. In this study, we interpolated the data from each exam onto a dense 501 \( \times \) 501 point rectilinear grid with 0.36° spacing along each dimension, which is outlined in Figure 1b.

The blind spot was detected automatically from a group of candidate locations in the testing grid, shown in red in Figure 1. These seven points were separated into two clusters with combinatorial optimization by maximizing the separation between the mean DLS values in each cluster. The grid locations belonging to the cluster with the smaller mean were labeled as the blind spot. To mitigate the clustering error caused by a large spurious DLS value, the blind spot cluster was constrained to a maximum of five samples.

For visualization and interactive examination, VFMA generated a 3-D rendering of the interpolated HOV surface color-coded by DLS value. User-controllable rotation, panning, and zooming operations enabled interactive inspection of the HOV surface model. In addition, geographic and topographic selections of the HOV were made through the VFMA interface. For example, region-of-interest (ROI) analyses were possible by defining boundaries, such as a circle centered at the origin or an iso-sensitivity contour around the base of a scotoma.

Volumetric Visual Function Indices

We developed a class of visual function indices based on the volume within the interpolated HOV surface. Whereas a conventional index like mean sensitivity conveys only visual sensitivity information, a volumetric measure is more general, and captures the sensitivity and the topographic footprint over which the sensitivity is assessed. This makes it more appropriate for comparisons among irregular grids and grids of different sizes and topographic footprints. It also represents the visual field function with a unit of quantity, the volume of sensitivity, which can be useful when describing how much sensitivity has been lost or gained over time.

The volume represents the total sensitivity across solid angle, and is reported in units of decibel-stereadians (dB-sr). The decibel was chosen to indicate the magnitude of sensitivity because it is a logarithmic
unit and corresponds well to perceptual differences. The steradian was chosen to define the angular extent because it is the International System of Units (SI) measure of solid angle. To minimize cartographic distortions, especially in the peripheral visual field, all mathematical operations are executed on a spherical surface representing the interior of the perimeter cupola. In spherical coordinates, the volume is

\[ V = \iiint_{\mathcal{S}} \hat{z}(\theta, \phi) \sin(\theta) d\theta d\phi \] (3)

where \( \theta \) is the co-latitude angle, \( \phi \) is the azimuth angle, and \( \mathcal{S} \) is the selection region defined by the user. Here, \( V \) represents the volume of the solid defined by \( \hat{z}(\theta, \phi) \) and \( \hat{z} = 0 \) over the angular region \( \mathcal{S} \). The VFMA calculates volumes by the midpoint integration rule wherein the finely interpolated surface is summed and scaled by the pixel extent.\(^{22} \)

The volume can be customized according to what region \( \mathcal{S} \) is selected for investigation. When the selection region is the entire grid, the result is the total volume, \( V_{\text{TOT}} \). In this study, we analyzed \( V_{\text{TOT}} \) and the central field volume, \( V_{30'} \), defined by a setting the selection region \( \mathcal{S} \) to be a circle with a radius of \( 30' \) centered on the point of fixation. The footprints of these volumes are depicted in Figure 1. We also examined the normalized index \( V_{30'}/V_{\text{TOT}} \), which approaches zero as central sensitivity is lost and approaches one as peripheral sensitivity is lost. The blind spot was not removed before surface fitting and calculation of these volumes.

We also analyzed topographic surface models of visual field defect. Because Equation 2 is linear in the \( z_i \) sensitivity values, an HOV model of the defect was created by replacing each \( z_i \) value with the DLS difference between the subject and an age-adjusted normal.\(^{23} \) The resulting interpolated surface depicts the visual field in defect space, as opposed to the native DLS space. The defect space surface models are three-dimensional, finely sampled analogues of total deviation plots, and are useful for quantifying patterns for field loss. For example, a scotoma appears as a recession in the DLS surface and as an elevated ridge in the defect surface. In defect space, the volume is

\[ D = \iiint_{\mathcal{S}} (z_i(\theta, \phi) - \hat{z}(\theta, \phi)) \sin(\theta) d\theta d\phi \] (4)

where \( z_i \) is the age-adjusted normative DLS. These volumes measure the net defect volume in the selection region. In this study, we analyzed the defect space volumes \( D_{\text{TOT}} \) and \( D_{30'} \). For defect space measures, the blind spot was removed before volume calculation.

**Validation and Analyses**

The accuracy of the HOV modeling was assessed using leave-one-out cross-validation (LOOCV).\(^{20,24} \) LOOCV measures the residual DLS error at each of the test locations by reinterpolating the surface using all data except that location, and then accumulates the errors from all test locations. The error for the \( k \)th location is \( e_k = \hat{z}_k (x_k, y_k) - z_k \), where \( \hat{z}_k (x_k, y_k) \) is the HOV surface interpolated at location \((x_k,y_k)\) using the set of points \( \{(x_i,y_i,z_i)\}_{i=1,i\neq k}^N \) in Equation 2. Errors are measured only at the locations of the 164 test points and not at the 60 boundary constraints. Table 1 provides a summary of the data used in the LOOCV analysis. Only the most recent perimetry exam for each subject’s eye was used. For comparison with the TPS interpolation in VFMA, we also performed LOOCV on HOV models generated with nearest-neighbor (NN) interpolation. Being a zeroth-order approach, NN interpolation served as a reference for benchmarking the higher-order TPS method. Performance was assessed by the coefficient of determination \( (R^2)^{24} \) and the index of agreement \( (d) \),\(^{25,26} \) as given by

\[ R^2 = \frac{\sum_{k=0}^{N_t} (z_k - \bar{z})(\hat{z}_k - \bar{\hat{z}})^2}{\sum_{k=0}^{N_t} (z_k - \bar{z})^2 \sum_{k=0}^{N_t} (\hat{z}_k - \bar{\hat{z}})^2} \] (5)

and

\[ d = 1 - \frac{\sum_{k=0}^{N_t} c_k^2}{\sum_{k=0}^{N_t} [\hat{z}_k - \bar{\hat{z}}] + [\hat{z}_k - \bar{\hat{z}}]^2} \] (6)

Here, \( \bar{\hat{z}} = \sum_{k=0}^{N_t} \hat{z}_k \) is the mean sensitivity and \( \bar{\hat{z}} = \sum_{k=0}^{N_t} \hat{z}_k \) is the mean interpolated value during LOOCV. Better performance is indicated by larger \( R^2 \) and \( d \). The \( R^2 \), which specifies the proportion of the data variation captured by the topographic model, is commonly used as a goodness-of-fit metric. The \( d \) is an alternative metric ranging from 0.0 (no agreement between the model and observation) and 1.0 (perfect agreement).

Repeatability analysis was performed on the visual function indices derived from test–retest data from 10 normals and 10 RP patients. All subjects had an initial visual field test and between 1 and 5 additional tests. Repeated tests were included only if obtained...
within 90 days of the initial test. Table 1 summarizes the data used for this analysis. We analyzed the volumetric measures $V_{TOT}$, $V_{30'}$, $V_{30'}/V_{TOT}$, $D_{TOT}$, and $D_{30'}$ from VFMA as well as the conventional indices MS and MD. Repeatibility performance was assessed by the coefficient of variation (CV), where $CV = \sigma/\mu$, $\sigma$ is the within-subject deviation estimated via 1-way ANOVA and $\mu$ is the corresponding mean. We also estimated the repeatability coefficient (RC) = $1.96/\sqrt{2}\sigma^2$, which is the value below which lies with 95% probability the difference between any two measures from the same subject. Smaller values for CV and RC indicate higher reliability.

A cross-sectional analysis was performed to obtain descriptive information for each visual function index for the three subject groups. Groups were compared with a linear mixed-effects model, allowing for unequal variances in different groups, and adjusting for age at exam and the perimeter device used. The outcome variable was the average of each index over all recorded measurements from each patient’s visual field exam also are depicted using conventional display methods. The conventional indices MS and MD, the volumetric indices $V_{TOT}$, $V_{30'}$, $D_{TOT}$, $D_{30'}$, and the ratio $V_{30'}/V_{TOT}$ are presented in Figures 2 and 3, and a volumetric measurement of the ring scotoma is presented for the field in Figure 3. The 3-D topographic representations generated by VFMA show the HOV contours and enhance the subtle variations in the visual fields.

The cross-validation results are presented in Table 2. The TPS interpolator showed good performance with large $d$ values indicating high accuracy, and also good consistency with similar $R^2$ values and similar $d$ values in each subject group. By comparison, the performance of the NN interpolator was lower and less consistent among groups. The $R^2$ and $d$ values from the VFMA TPS interpolator were significantly larger than those from the NN interpolator, overall ($P < 0.001$) and within each subject group ($P < 0.001$ in each case). The standard deviations for $R^2$ and $d$ were largest in the RP group, which is likely a reflection of the diversity of visual field patterns within this group.

The complete cross-validation results for each simulated MSV are presented in Supplementary Tables S1 through S6. As the simulated MSV increases and floor effects become more pronounced, the $R^2$ and $d$ values changed only slightly, getting worse in the RP and PCRP groups and better in the normal group. The improvement in the normal group is due to the increased uniformity and spatial autocorrelation of the far peripheral fields where the floor effects are more likely to occur. The worsening in the patient groups is a result of the floor effects causing abruptly increased sensitivity values at isolated test locations, which reduces the local autocorrelation and the accuracy of any neighborhood-based interpolation scheme. At every simulated MSV, the $R^2$ and $d$ values from VFMA remained significantly larger than the NN interpolator.
Figure 2. Comparison of different visualizations and indices of a static perimetry exam from a 63-year-old patient with mild autosomal dominant retinitis pigmentosa from the frameshift mutation, NM_006,269.1:c.3157delT(P.Tyr1053ThrfsX4) of RP1 in association with a second, novel heterozygous mutation in RP9, NM_203,288.1:c664delT, which is predicted to eliminate a stop codon and add 28 amino acids.
Volumetric indices were generally smaller, and hence the mean differences between the RP and PCRP group were significantly different for every index. Compared to the original, unadjusted values in Table 4, the mean differences between the RP and normal groups were smaller, and hence the P values comparing these groups tended to be larger. This impact is most apparent in comparisons of the regional volumetric measures $V_{30^\circ}$ and $D_{30^\circ}$, since these are the indices for which the original P values in Table 4 were substantially larger than 0.0001. When more severe floor effects are simulated at an MSV of 18 dB, as shown in Supplementary Table S16, the mean differences between groups decreased for all indices, which impacted the statistical comparisons between the subject groups. Again, this is most apparent when comparing $V_{30^\circ}$ and $D_{30^\circ}$ to the RP and PCRP groups.

**Discussion**

**HOV Analysis With VFMA**

The LOOCV results demonstrate that the choice of interpolator is important. A higher-order method
Figure 3. Comparison from a patient with autosomal dominant pericentral retinitis pigmentosa in association with a reported heterozygous mutation in NR2E3, NM_014249.2: c.166G>A(P.G56R), and a second heterozygous variation, NM_005802.3:c.2643C>G(P.H881Q), of unknown significance in TOPORS. (a) Scaled-point plot of DLS values. (b) Incremental color-scale plot generated by the
with smooth kernels like TPS interpolation is more accurate than a piecewise constant method when interpolating static visual field data.

The volumetric visual function indices tested in this study are comparable in performance to the conventional indices mean sensitivity and mean deviation. The test–retest analysis indicates that the volumetric indices have similar reliability as the conventional ones, and the cross-sectional analysis confirms that the volumetric indices are as discriminative among subject groups.

The volumetric measurements from the visual field in Figure 2 are consistent with the visual field phenotype reported in autosomal dominant RP from mutation of RP1 and are in agreement with a prior report of the central visual field in RP being more robust and intact compared to that of the periphery. The visual field loss with a pericentral distribution seen in Figure 3 is consistent with autosomal dominant RP associated with a heterozygous mutation of NR2E3 and an autosomal dominant mutation of TOPORS.

The magnitudes of the volumetric visual function indices depend on the topographic angular footprint of the testing grid and the stimulus size. The total volume $V_{\text{TOT}}$ is a function of the grid extent and, because DLS values are non-negative, is monotonically nondecreasing with grid solid angle. Regional indices like $V_{30^\circ}$ have a fixed topographic footprint and do not have this dependency. Depending on the grid extent, the field may be truncated, especially in normal subjects. Compared to stimulus size III, size V has been shown to have a larger dynamic range and smaller variability in glaucoma patients. In RP patients, use of stimulus size V yields more seeing locations whereas use of size III has been suggested for early disease to allow access to statistical analyses of progression that are not available for size V. Based on the concept of spatial summation, we predict that stimulus size is positively correlated with volume. Studies are currently underway to characterize the sensitivity of the volumetric measures to these factors.

Table 2. Cross-Validation Results Showing the Coefficient of Determination ($R^2$) and Index of Agreement ($d$), Listed as Mean $\pm$ SD, for the Two Interpolation Methods Tested in This Study

<table>
<thead>
<tr>
<th></th>
<th>Overall</th>
<th>Normal Subjects</th>
<th>RP Patients</th>
<th>PCR Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>$R^2$: VFMA (TPS)</td>
<td>0.68 $\pm$ 0.16</td>
<td>0.66 $\pm$ 0.11</td>
<td>0.69 $\pm$ 0.19</td>
<td>0.63 $\pm$ 0.13</td>
</tr>
<tr>
<td>$R^2$: NN</td>
<td>0.48 $\pm$ 0.20</td>
<td>0.37 $\pm$ 0.11</td>
<td>0.51 $\pm$ 0.20</td>
<td>0.28 $\pm$ 0.09</td>
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<tr>
<td>$d$: VFMA (TPS)</td>
<td>0.89 $\pm$ 0.09</td>
<td>0.89 $\pm$ 0.04</td>
<td>0.89 $\pm$ 0.10</td>
<td>0.88 $\pm$ 0.05</td>
</tr>
<tr>
<td>$d$: NN</td>
<td>0.79 $\pm$ 0.12</td>
<td>0.72 $\pm$ 0.08</td>
<td>0.82 $\pm$ 0.12</td>
<td>0.71 $\pm$ 0.06</td>
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</table>

In each subject and overall, the performance of the TPS interpolator was significantly better than the NN interpolator for $R^2$ and $d$. 

http://tvstjournal.org/doi/full/10.1167/tvst.4.2.14
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increasing the MSV will artificially improve the sensitivities in the central fields of typical RP and PCRP patients, making them appear more similar and more difficult to discriminate.

### Translation to the Clinic

In a clinical setting, VFMA has been a useful tool for illustrating to the patient the appearance of his/her visual fields.

### Table 3. Repeatability Results Showing the Repeatability Coefficient (RC) and the Coefficient of Variation (CV) for the Conventional and Volumetric Visual Function Indices

<table>
<thead>
<tr>
<th></th>
<th>Normal Subjects</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th>RP Patients</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RC</td>
<td>SD_w</td>
<td>Mean</td>
<td>CV</td>
<td>RC</td>
<td>SD_w</td>
<td>Mean</td>
<td>CV</td>
<td></td>
</tr>
<tr>
<td>$V_{TOT}$ (dB-sr)</td>
<td>9.81</td>
<td>3.54</td>
<td>103</td>
<td>0.03</td>
<td>6.29</td>
<td>2.27</td>
<td>30.1</td>
<td>0.08</td>
<td></td>
</tr>
<tr>
<td>$V_{30^\circ}$ (dB-sr)</td>
<td>1.08</td>
<td>0.39</td>
<td>27.4</td>
<td>0.01</td>
<td>2.19</td>
<td>0.79</td>
<td>11.0</td>
<td>0.07</td>
<td></td>
</tr>
<tr>
<td>$V_{30^\circ}/V_{TOT}$</td>
<td>0.03</td>
<td>0.01</td>
<td>0.27</td>
<td>0.04</td>
<td>0.28</td>
<td>0.10</td>
<td>0.40</td>
<td>0.25</td>
<td></td>
</tr>
<tr>
<td>MS (dB)</td>
<td>1.91</td>
<td>0.69</td>
<td>29.4</td>
<td>0.02</td>
<td>1.75</td>
<td>0.63</td>
<td>11.0</td>
<td>0.06</td>
<td></td>
</tr>
<tr>
<td>$D_{TOT}$ (dB-sr)</td>
<td>9.81</td>
<td>3.54</td>
<td>9.28</td>
<td>0.38</td>
<td>6.26</td>
<td>2.26</td>
<td>82.3</td>
<td>0.03</td>
<td></td>
</tr>
<tr>
<td>$D_{30^\circ}$ (dB-sr)</td>
<td>1.08</td>
<td>0.39</td>
<td>0.97</td>
<td>0.40</td>
<td>2.25</td>
<td>0.81</td>
<td>17.3</td>
<td>0.05</td>
<td></td>
</tr>
<tr>
<td>MD (dB)</td>
<td>1.91</td>
<td>0.69</td>
<td>2.46</td>
<td>0.28</td>
<td>1.75</td>
<td>0.63</td>
<td>20.9</td>
<td>0.03</td>
<td></td>
</tr>
</tbody>
</table>

Listed next to each index is the unit, if applicable, for the RC, mean, and within-subject SD (SD_w). The CV is dimensionless.

Table 4. Cross-Sectional Results Comparing the Mean Visual Function Indices in Each Subject Group Based on Regression Models

<table>
<thead>
<tr>
<th></th>
<th>Estimated Mean ± SEM</th>
<th>Estimated Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Normal Subjects</td>
<td>RP Patients</td>
</tr>
<tr>
<td>$V_{TOT}$ (dB-sr)</td>
<td>103.1 ± 2.0</td>
<td>30.7 ± 2.3</td>
</tr>
<tr>
<td>$V_{30^\circ}$ (dB-sr)</td>
<td>27.6 ± 0.1</td>
<td>9.7 ± 0.8</td>
</tr>
<tr>
<td>$V_{30^\circ}/V_{TOT}$</td>
<td>0.27 ± 0.01</td>
<td>0.38 ± 0.02</td>
</tr>
<tr>
<td>MS (dB)</td>
<td>29.7 ± 0.4</td>
<td>10.2 ± 0.7</td>
</tr>
<tr>
<td>$D_{TOT}$ (dB-sr)</td>
<td>9.1 ± 2.0</td>
<td>81.4 ± 2.3</td>
</tr>
<tr>
<td>$D_{30^\circ}$ (dB-sr)</td>
<td>0.8 ± 0.1</td>
<td>18.6 ± 0.8</td>
</tr>
<tr>
<td>MD (dB)</td>
<td>2.2 ± 0.4</td>
<td>21.6 ± 0.7</td>
</tr>
</tbody>
</table>

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visual fields and comparisons with expected results for normals. With a binocularly symmetric test grid, the visual fields for each eye can be fused using best location or spatial probability summation to simulate vision with binocular viewing for the patient. Demonstrating the effects of visual field loss on how one sees, monocularly and with binocular viewing, has become an integral part of the care of patients with retinitis pigmentosa and allied disorders at the Oregon Retinal Degeneration Center. Such visual presentations are very helpful when explaining how field loss creates impairment, the concept of compensation of seeing field between the two eyes, and in discussing issues surrounding driving and disability. The conventional global visual function indices of mean sensitivity and mean defect are valuable to clinicians, particularly for standard rectilinear grids, but can present difficult concepts for patients to understand. In our experience with patients, we have found that describing the visual field as a hill of vision in the literal sense facilitates their comprehension, and the volume of the hill is a more intuitive functional measure than indices based on the average hill height such as mean sensitivity.

VFMA also enables localized volumetric measurements that quantify visual function in specific regions of the hill of vision, which otherwise could not be achieved easily with currently available techniques. Of importance is the ability to measure volumetric visual function indices correlating to a specific area of retina undergoing genetic or stem cell therapy intervention. Repeated measurements in this same area provide a functional assessment of the effects, positive and negative, of regional therapeutic interventions, measurements that are difficult to obtain in any other manner.

The defect space is useful for volumetric measurement of central, pericentral, or regional scotomas, particularly for follow-up test sessions and comparisons among patient cohorts. Defect space volumes also are useful for measuring field loss in patients with retinal degenerations, macular dystrophies, including Stargardt disease, optic atrophies, and other causes of central or paracentral scotomas.

Summary

We have developed a topographic methodology and software application, VFMA, for processing and visualizing static perimetry data. It is applicable to any static perimetric sensitivity data, including standard automated perimetry and microperimetry. VFMA generates a 3-D model of the hill of vision, allowing detailed topographic examinations of visual fields in DLS and defect spaces, and the creation of global and regional visual function indices for quantitative assessments. We believe this new methodology will aid examinations of pathologic changes in macular degenerations and other diseases of the visual system, improve the analysis of structure-function relationships, and provide more refined outcome measures for clinical trials.

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