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Fixation Stability and Scotoma Mapping for Patients with Low Vision

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Abstract

Purpose—To develop a simplified device that performs fundus perimetry techniques, such as fixation mapping and kinetic perimetry.

Methods—We added visual stimulation to a near infrared retinal imager, the Laser Scanning Digital Camera (LSDC). This device uses slit scanning illumination combined with a 2 dimensional CMOS detector, with continuous viewing of the retina. The CMOS read-out was synchronized with the slit scanning, thereby serving as a confocal aperture to reduce stray light in retinal images. Series of retinal images of 36 deg were automatically aligned to provide data for fixation maps and quantification of fixation stability. The LSDC and alignment techniques also provided fundus viewing with retinal location correction for scotoma mapping.

Results—First, fixation mapping was readily performed in patients with central scotoma or amblyopia. The automatic alignment algorithm allowed quantification of fixation stability in patients with macular pathologies that did not cause scotoma. Second, fixation stability was rapidly and quantitatively assessed by the automatic registration of a series of retina images. There was no significant difference in the fixation stability with automatic vs. manual alignment. Kinetic perimetry demonstrated that fundus imaging helped reduce the variability of perimetric data by identifying and preventing false positives due to eye motion. We found that the size of the blind spot was significantly larger for dark targets on brighter backgrounds than when the contrast was reversed ($p < 0.045$). This is consistent with incremental targets being detected partially or wholly due to scattered light falling on more sensitive retinal locations.

Conclusions—Fundus perimetry with the LSDC allows for a wide range of fixation and perimetry tasks.

Keywords

low vision; fixation stability; scotoma mapping; fundus perimetry; SLO; imaging

Visual function assessment in patients with low vision involves a number of measures beyond visual acuity including fundus perimetry, also known as microperimetry when closely spaced macular targets are presented.^{1,2} Fundus perimetry is a group of techniques, and in each technique a retinal image is obtained while visual stimuli are presented to provide functional information about fixation or retinal sensitivity.^{3–10} Fundus perimetry is used for a variety of purposes, including elucidating disease mechanisms or natural history,

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estimating prognosis for a specific patient, rehabilitating a patient based on his own functional status and goals, or localizing the effects of treatment.^{3–10}

Without fundus perimetry, the measurement of retinal sensitivity can be inaccurate in conditions that affect the fovea or fixation. For example, individuals with macular scotomas may adopt a new area for fixation, a preferred retinal locus (PRL).^{3–4, 9–10} Fixation is displaced, and stability is affected, relative to the target size and resolution. Subsequently, visual sensitivity measurements are potentially inaccurate, since the PRL displaces the retina away from the expected locations at which normative values for perimetry would provide an accurate basis of comparison. The PRL may differ in size, shape, and orientation, and depends not only upon retinal status but also task or experimental condition, such as light level.¹¹

While a PRL that develops outside the foveal region can be a useful adaptation to central visual loss, the resulting visual function is better quantified if the PRL is stable. One method of assessing the PRL, as well as fixation with the functioning fovea, is to measure fixation stability. Fixation stability has been studied with methods ranging from categorical analysis to quantitative metrics that include both magnitude of variation and direction, such as the bivariate contour ellipse area (BCEA).^{3–4, 9–10, 12–14} A recently developed classification method assigns patients to three groups or categories by the counting of the proportion of fixation samples that fall within a 2 deg diameter circle centered on the fovea.^{15–16} For the number (#) of fixation points within this circle, # > 50% is defined as predominantly central fixation, 25% < # < 50% is poor central fixation, and # < 25% is predominantly eccentric fixation. While this classification provides the advantage of an easily understood categorization, one disadvantage is that it does not provide a quantitative outcome that is a continuous variable for analysis, which might be required in a treatment trial or for better assessment with vision training. Another disadvantage is that the method lacks further detail about different aspects of fixation ability, such as the direction that the patient is likely to look. A final disadvantage of the classification method is that it does not readily distinguish among the very good fixation abilities found in young, normal subjects or the very poor fixation often found in patients with extremely poor vision or poor control of gaze. In contrast, the BCEA method provides a quantitative metric that has variables that are continuous, not categorical, and can be used to distinguish among the fixation abilities and preferences of subjects by means of a wide range of statistics. The BCEA provides the advantage of the directional component of fixation, but has the disadvantage of being more complicated than just a single continuous variable. In this study, we propose an intermediate method that is quantitative but provides a readily understood continuous variable, the standard deviation of the Euclidean distance from fixation errors. We provide measurements, and highlight the comparison of this method and the BCEA.

We demonstrate the use of a novel fundus imaging device, the Laser Scanning Digital Camera (LSDC), for studying fixation and mapping scotomata.^{17–19} This device provides a simplified apparatus that builds upon the previous fundus perimetry techniques developed for the Scanning Laser Ophthalmoscope (SLO).^{3–10} The original SLO techniques used the same laser for providing the image and the visual stimuli, so that the light reflecting off the retina demonstrated the location of the stimuli direction.^{3,4} The light was imaged onto the retina using the equivalent of Maxwellian view, so that it was readily determined that the light intended to pass through the pupil did so. If the subject's pupil is misaligned with respect to the pupil of the instrument, then the retinal image is dark or vignetted. Similarly, the raster was focused on the retina, producing the potential for high contrast stimuli. When a single laser was used, dark targets on the bright background used for retinal imaging were typical.

We later developed SLO fundus imaging using near infrared illumination,^{5–8,20} which provided retinal imaging at a comfortable light level and with reduced effect on the visual stimuli, but required calibration of the stimuli to the retinal image. Visual stimuli are presented under either manual or computer control, and the location of the resulting stimulus location on the retina can be determined by landmark selection in real time. Mapping retinal sensitivity immediately occurs without the need for videotape and post processing. A selection of visible wavelengths provides RGB or monochrome stimuli over a several log unit intensity range.^{5–8,20}

Further development led to combining a retinal image from an SLO with a choice of arbitrary stimuli such as digits,²¹ using a beam splitter to add the visual channel information to the fundus image, but requiring calibration of the positions of the retina to the target. Once computers readily supported two monitors, the SLO raster has been used as one monitor, i.e. to present the visual stimuli, and the experimental program is displayed on the other monitor. Later fundus imaging devices, such as the MP-1, the Opko, and the MAIA, use similar techniques to the SLO, with the parameters available for visual stimuli dependent upon the choice of both hardware and software.^{13–16,22–25} The MP-1 provides a wide field image, but does not use scanning laser technology, resulting in a lower contrast image that does not reveal drusen with the same clarity that an SLO does.^{8,26–28} The MP-1 visual stimuli lack sufficient dynamic range to provide sufficiently bright stimuli for some patients, which creates a ceiling effect in the data collection. Further, the lack of uniformity of the background has led to spurious visual defects when compared with standardized perimetry results.²⁹ The MAIA has an increased dynamic range, compared with the original MP-1. The Opko device provides a variety of visual stimuli such as targets for static perimetry of Goldmann size III, and also features optical coherence tomography structural assessment of the retina for comparison.²⁴

The LSDC uses near infrared illumination for fundus imaging and a choice of visual display technologies for stimulus presentation.^{17–19} It differs from the original SLO in that it illuminates the fundus by scanning a slit, in one dimension to produce a square raster, instead of scanning a single point of light in two dimensions. Further, the light returning from the eye is not descanned, or built up with additional circuitry or computer software over time, but rather is led to a 2 dimensional CMOS detector that directly reads images, line-by-line in synchronization with the laser scanning. This simplifies the optical, mechanical, and electronic design. In addition, like the SLO, there is the possibility for indirect imaging, also known as dark field imaging, in which the multiply scattered light from the eye is preferentially detected by displacing in time the readout of the sensor with respect to the laser scan. This is similar to increasing the distance between a confocal aperture and the center of the optical path of the returning light.^{27,28} The indirect mode of detection enhances the visibility of certain structures, particularly deeper ones such as the choroidal rim of the optic nerve head, which are normally obscured by the highly reflective, overlying retina.^{28,30}

METHODS

Subjects were recruited from the Indiana University School of Optometry (Bloomington, IN, USA) following approved human subjects protocol procedures. We selected subjects for fixation stability analysis from those tested with the LSDC, including the widest available range in our sample for age and retinal status, i.e. normal control subjects and patients with diabetes, glaucoma, age-related macular degeneration, auto-immune disease, epiretinal membrane, amblyopia, high myopia, or other conditions. Informed consent was obtained from all subjects after explanation of the nature and possible consequences of the study. The research followed the tenets of the Declaration of Helsinki.

Equipment and Procedure: All Experiments

The LSDC used a Vertical Cavity Surface Emitting Laser (VCSEL), 850 nm, 2 mW maximum at the cornea, as the illumination source for fundus imaging. The VCSEL was turned on only during active imaging. This method eliminated raster flyback lines from the visual stimulus background. The illumination was formed into a slit, and then scanned by a galvanometer across the retina to make a 36×36 deg raster. The galvanometer speeds allowed for quiet operation. The input/exit pupil of the LSDC was only 2.5 mm, so that the light level was similar across subjects despite senile miosis. The appearance of the raster was a dim red without clearly visible raster lines, which was comfortable but nevertheless capable of slightly changing the hue of the background in perimetry for the dimmest background such as those used in standard Goldmann stimuli.

Image acquisition was performed with a monochrome CMOS sensor, which had 1024×1024 pixels of digital resolution. The image acquisition rate could be varied from 1 – 36 Hz for 1 Mpixel images without loss of data, but the images appeared noisy at the higher end of this range. For smaller regions of interest, up to 250 fps could be acquired. Typical full frame rates were 11 – 17 Hz. Given the value of 1024 pixels of digital resolution and a raster of 36 deg visual angle, and assuming that 1 deg visual angle retina would subtend 290 microns of retina, we arrive at the following calculations: 2.1 min arc/pixel and 10.2 microns of retina/pixel. With hyperopia or myopia, of instrument defocus, these figures will be less accurate.

Subjects, Equipment, and Procedure Experiment 1: Locus of Fixation in Patients with Central Vision Loss

We mapped the locus of fixation in 10 subjects with retinal disease selected to provide a spectrum of fixation abilities: 7 with central scotoma concomitant with macular degeneration, 2 with milder central vision loss associated with diabetic retinopathy, and 1 with high myopia and amblyopia in the fellow eye. The fixation target was a single, bright red light emitting diode (LED) of 3 deg visual angle, selected from an array of 5×5 LEDs within the enclosure of the LSDC. Although the light level was variable via a pulse width modulation circuit, all tests were performed at a constant level. The LEDs were projected in Maxwellian view through the same entrance pupil as the imaging illumination, and was focused by the same optics onto the retina. This provided stimuli that were in focus on the retina, regardless of the patient's central vision. Further, the entrance/exit pupil was 2.5 mm. Therefore, the light level was similar for all subjects and all retinal locations, and effects of age or status of pupil dilation were minimal.

The use of red fixation targets reduced the effects of absorption or scatter by the aged lens, and reduced individual differences in fixation target brightness due to macular pigment absorption.^{3–6} The subject's task was to look at the fixation LED that was straight ahead and inside the LSDC. A series of 20 fovea-centered retinal images were acquired in 20-frame ring buffers in < 2 sec. The right eye and left eye were imaged sequentially. Fixation mapping was performed by registering the images from a buffer, with 11 fps used as the image acquisition frame rate for this study. We developed an automatic image registration method, with versions in both Matlab (Mathworks, Natick, MA) and the C programming language, which runs in real time. First, a suitable region of interest for registration was found automatically by performing a zero-lag cross-correlation between the base image with and without median filtering. The remaining 19 images were registered by cross-correlation, providing the coordinates that defined the image displacements. Images that did not reach a criterion cross-correlation coefficient were excluded from further analysis. Once the alignment algorithm was applied to individual frames of an image series with respect to the

first one, the number of pixels of fixation shift in the x and y direction was automatically obtained.

Subjects, Equipment, and Procedure Experiment 2: Quantifying Fixation Stability in Patients without Central Scotoma

We quantified fixation stability in 27 patients, 18 males, 9 females, age 61 ± 13 yr (mean $\pm$ standard deviation; range 38 – 83 yr). The patients had diabetes or other documented macular pathology that did not lead to central scotoma. We performed the statistics on each eye analyzed separately. The visual stimulus was a single, bright red light emitting diode (LED). Three fields of view were collected for each eye of each patient, a foveal-centered, a slightly nasal, and a disc-centered view. We report data from the foveal-centered field of view for two reasons. First, the foveal-centered field of view provides the most conservative test of our method, since this field of view provides the fewest large landmarks for image alignment. Second, many methods of visual function testing and imaging require a foveal centered view, for example visual fields. Results for the other fields of view are similar or better, due to the inclusion of major retinal vessels and optic nerve head landmarks from a larger portion of the images.

We compared the measurements for fixation stability that were obtained with the automatic alignment method described in Experiment 1 to fixation stability from manual alignment. In the manual image registration method, which was performed on the saved data, the experimenter manually selected the same feature in each image series. Only frames with blinks or large intra-frame motion were excluded from further analysis.

We compared the results with two methods. For the manual and the automatic methods separately, the Euclidean distances between the same location in each frame and the centroid were calculated. The standard deviation of the Euclidean distance was taken as a metric for fixation stability. The standard deviation method provides a readily analyzed parameter, which may then be assigned to a category that is useful for a given study rather than being a predetermined distance from the fovea. In addition, the BCEA was also computed, which provides a metric that we anticipated to be less influenced by outliers when this is desirable. Bland-Altman analysis was also performed to evaluate the agreement of the fixation stability metrics, standard deviation automatic vs. manual method, BCEA automatic vs. manual method, and standard deviation vs. BCEA. For these comparisons the BCEA metric, which is based on units of pixels², was converted to linear pixels by a square-root transformation, since the standard deviation is given in linear pixels. As the underlying difference in metric requires assumptions about how to match results from the two techniques, the cross technique comparisons should be considered qualitative. In contrast, the regression analysis that we used for automatic vs. manual methods within provides a quantitative comparison.

Subjects, Equipment, and Procedure Experiment 3: Mapping the Blind Spot with Stimuli with Bright Backgrounds and Dark Targets

We investigated whether dark targets on bright backgrounds have the potential to reduce the artifact from the light scattering, as has been reported previously.³¹ Light from bright targets on a dark background can scatter light to other retinal locations that would not support detection, for example targets presented on and near to the optic nerve head or a scotoma. In this experiment, the usual parameters for Goldmann perimetry were reversed, with the background set to the intensity of the usual Goldmann target, 1000 Apostilbs, and the dark targets about 1.5 log units dimmer. Although an additional 1.4 log unit decrement was possible with the LSDC visual display, the stimuli were matched to the Goldmann light levels. Kinetic visual stimuli were presented along meridians centered on the optic nerve head, with targets presented as dark circles on a brighter background or bright circles on a

darker background, with the incremental and decremental stimuli presented in separate sessions. The results for incremental vs. decremental targets were compared for 6 volunteers, aged 33 – 61 years, 5 M, 1 F. During the kinetic perimetry test with the LSDC-S, non-mydratic near-infrared retinal images were acquired to provide information on retinal location and false alarms.

A RGB visual stimulus was provided by a Digital Light Projector (DLP), optically integrated into an LSDC. The DLP (Optoma, Freemont, CA) was operated in VGA mode, 640×480 pixels. The DLP graphics were produced by treating this display as the second monitor of a Windows computer. The dynamic range when all color channels were manipulated together was 2.92 log units, or 29.2 dB, as measured at the exit pupil of the LSDC (EG&G, San Diego, CA) and was displayed using 8 bit resolution of intensity. The DLP provides brighter or dimmer setting selections, but this does not increase the dynamic range of the background with respect to the target or fixation stimulus. We set the background light level using both the digital input to the DLP and neutral density filters. The display was projected in Maxwellian view through the same entrance pupil as the imaging illumination, and was focused by the same optics onto the retina. The LSDC provided spherical correction. Thus, visual stimuli could be projected approximately in focus for the region of retina under test of each subject, despite the poor visual acuity in the region of the optic nerve head.

The location of the DLP projection was co-registered to the imaging illumination prior to the experiment. The spatial extent of the DLP window was controlled via software. Thus, the location and size of pixels of the visual display, i.e. the DLP, being a lower resolution and not necessarily having the same native aspect ratio was adjusted to the desired the field of view but not inherently related to the resolution of the LSDC or the sensor. The resolution and size of the display window was set according to the experimental task, providing sufficient spatial resolution to obtain Goldmann III, IV, and V target sizes and smooth motion for kinetic perimetry to map the blind spot. Prior to initiating the stimuli, the fixation position of the subject was adjusted to place the optic nerve head and surrounding retina in clear view for the operator.

Subjects were instructed to stare at a red fixation target on a 36 deg diameter gray background, while a series of white 0.14 degree stimuli were presented near the optic nerve head. The path taken by the stimulus was one of eight meridians that converged at a point on the optic nerve head. The meridians were separated by 45 deg, and 7 deg long. During the first half of the perimetry session, the stimuli moved incrementally inwards, i.e. from “seen” to “not seen”, with each retinal frame acquired. The subject responded by pressing a button when the stimulus disappeared. Following two measurements at each meridian, the stimuli then moved outwards, i.e. from “not seen” to “seen.” For these stimuli, the subject pressed the button when the stimulus appeared. The stimulus velocity was constant at 0.88 deg per sec, with 40 frames acquired per meridian. While larger stimuli and faster speeds were available, pilot data indicated that the borders of the blind spot were less accurately mapped with larger targets or faster speeds. The meridians were presented in pseudo-random order twice for each condition.

To obtain the location of the isopters around the optic nerve head, we averaged the locations of target relative to the retina at the time that the subject indicated the change from “seen” to “not seen” or from “not seen” to “seen.” These locations were computed from the x and y coordinates needed to shift the images to register with the starting position. The images for each meridian were then automatically aligned to create a map of the blind spot on the screen. The distance from the center of the optic nerve head where the decremental targets were detected was compared to that for incremental targets. If intraocular light scatter leads

to a false positive response, even if the retinal position is accurate, then the blind spot for the decremental targets will be larger. Data from the subjects and all meridians were pooled for a repeat measures ANOVA.

RESULTS

Experiment 1: Locus of Fixation in Patients with Central Vision Loss

The automatic image registration algorithm reduced the appearance of noise in the average images (Fig. 1) and provided maps of the locus of fixation over time (Figs. 2,3). Large individual differences in fixation ability were demonstrated. For instance, in a young, normal subject the fixation was consistent across images (Fig. 2). However, the 3 deg diameter LED, which was selected to be visible for patients with low vision, did not allow the demonstration of the tightest possible locus of fixation. The highly reflective young fundus has the bright ring around the fovea, typical of a confocal image of a young eye. A snapshot of only 2 sec of images demonstrates high quality fixation in the normal subject.

In contrast, in an older subject with age-related macular degeneration, the fixation varies from frame to frame (Fig. 3) and is readily visualized with respect to the geographic atrophy. The standard deviation of the fixation was 161 microns with respect to the central locus of fixation, 33 min arc. For a subject with high myopia in both eyes, and amblyopia in the eye with the higher refractive error, the fixation was worse, a standard deviation of 234 microns, or 48 min arc. The retinal image clearly demonstrates the pathologically large optic nerve head, extensive peripapillary atrophy, and fundus reflectivity changes that were shown to be small breaks in Bruch's membrane on OCT.

Experiment 2: Quantifying Fixation Stability in Patients without Central Scotoma

The difference between automatic and manual fixation stability assessment was not statistically significant for either eye (ANOVA, $p=0.98$, 0.093 , for OD and OS, respectively). The comparisons for automatic and manual alignment for both the standard deviation and the BCEA metrics indicate that manual alignment statistics are acceptably characterized by the automatic methods (Fig. 4). The difference between left and right eye was not statistically significant (matched sample t-test, $p=0.198$), and therefore we do not illustrate OD vs. OS. As seen in Fig. 4A, the automatic method gave slightly lower average values for the standard deviation of the Euclidean distance than did the manual method (54 vs. 61 microns, 11 and 13 min arc, respectively). This is in the range of only 4 – 6 pixels on the image for most subjects. This difference and outliers on Bland-Altman analysis were driven by data sets with the fewest images successfully aligned or large mean errors (Fig. 4B).

The linear regression line was closer to the unity line for the BCEA metric ($y = 0.59 + 0.85 * x$; $r^2 = 0.57$) than the standard deviation metric ($y = 3.5 + 0.43 * x$; $r^2 = 0.12$) (Figs. 4C vs. 4A). This result was due to 2 extreme outliers with the standard deviation metric, which included image series where less than 10 of 20 images could be aligned due to extreme deviations from fixation by a few patients. The Bland-Altman analysis had a slope of $+0.14$ for BCEA ($r^2 = 0.03$) and -0.29 for the standard deviation method ($r^2 = 0.04$), but neither was statistically significant from a slope of 0 (Figs. 4D vs. 4B). The slope of the long axis of the ellipse varied from 1 to 89 deg. The ratio of the long-to-short axis for BCEA was on average 3.2 ± 2 (range: 1.1 – 9.6 and 2.8 ± 1.6 (range: 1.2 – 9.9) for automatic and manual alignment, respectively.

The standard deviation method provides a simple, rapid and automatic qualitative classification, distinguishing poor from good fixation in the majority of patients. The BCEA method is well suited for strongly directional fixation patterns and reduces the influence of

outliers (Figs. 4E and 4F). The asymmetry of the fixation patterns found in our group of patients was more than twice the value of 1.2 reported for normal eyes.⁹

Experiment 3: Mapping the Blind Spot with Stimuli with Bright Backgrounds and Dark Targets

In the kinetic perimetry test, the operator was able to monitor the retinal position as the subject responded to the visual stimuli (Fig. 5). As expected, most subjects' data indicated a larger blind spot when the kinetic target moved from "not seen" to "seen," i.e. outwards. There were false positives in naïve subjects, even when the eye was appropriately positioned. Nevertheless, when the speed of the target motion was sufficiently reduced to overcome reaction time variability, the visual function map formed by the radial mid-point between the inward-moving stimuli agreed well with the boundaries of the optic nerve head shown in the subjects' images.

The blind spot for the decremental targets (dark target on light background) was larger than for the incremental targets, $p < 0.045$ (Fig. 6). This supports the hypothesis that intraocular light scatter can lead to false positive responses when high contrast targets are needed due to a scotoma, despite focusing the targets being in focus on the retina.

General Discussion

In these three types of data analysis, we demonstrated that image registration and averaging not only provide enhanced image contrast in the LSDC but also quantified fixation stability. As with many methods of fundus perimetry, there is the potential of reducing inter-individual differences, due to the Maxwellian view presentation that ensures that light from the stimulus enters the eye and is focused on the retina. Fixation mapping and stability, as well as scotoma mapping using the blind spot, were performed in normal subjects and in patients with a wide variety of retinal and systemic conditions. The results of our automated method of assessment of fixation stability were comparable to manual assessment. The key advantages of the automatic method are that it requires no additional hardware and is available almost immediately after data acquisition. Patients with poor vs. good fixation are readily identified within seconds. None of the subjects required mydriasis.

A wide variety of target sizes and speeds were presented for fixation or detection in kinetic perimetry. The potential for removing false positives and false negatives based on retinal location and lid closure can lead to improved accuracy. Further, the test times for visual function tests may be shortened if a significant proportion of the variability is due to these errors.

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Figure 1.

Comparison of a single image frame (left) from the LSDC and 20-frame averaged image (right) of an undilated 75 year old white female with central scotoma concomitant to age-related macular degeneration. Visualization of small retinal vessels is noticeably improved with the reduction of the salt and pepper noise present in the single frame by averaging. Images are aligned automatically before averaging. There are significant fundus changes due to AMD, including geographic atrophy, a large central scar, and hyperpigmentation.

Figure 2. Fixation location as a function of time in OS of a 29 year old normal male subject with a dark fundus. The color bar encodes the acquisition time of each fixation point from blue (first) to red (last).

Figure 3. Fixation location as a function of time in the undilated subject of Fig. 1. The color bar encodes the acquisition time of each fixation point from blue (first) to red (last). The standard deviation of fixation errors was 33 min arc.

Figure 4.

Comparison of the fixation results as computed by different methods, with data from the automatic vs. manual alignment of images in 27 diabetic subjects in Experiment 2. Most of these subjects had much better fixation than subjects with macular disease that were described in Experiment 1, and had better fixation than the subject shown in Figure 3. Two methods for quantifying the fixation stability were used, the standard deviation (SD) of Euclidean distance and the bivariate contour ellipse area (BCEA). The dashed line in A, C, & E are the linear regression lines. Dashed and dash-dotted lines in B, D, and F are the means and limits of agreement (± 2 standard deviations from mean), respectively. (A) SD for manual alignment plotted vs. automatic alignment ($y = 7.38 + 0.43 * x$; $r^2 = 0.12$, $p = 0.074$). (B) Bland-Altman plot of the comparison of the SD for automatic and manual

alignment ($y = 1.76 - 0.29 * x$; $r^2 = 0.04$, indicating no significant difference from 0 in the slope). The mean and 95% limits of agreement were -1.43 and between 11.6 to -14.5 min arc, respectively. **(C)** BCEA for manual alignment plotted vs. automatic alignment ($y = 0.59 + 0.85 * x$; $r^2 = 0.57$). The units of C and D are min arc² because an ellipse, not a single vector, is being used to describe the fixation data. Note the decreased impact of outliers on the data, as compared with panel A, with a significant association $p < 0.0001$ for BCEA. However, the quantitative difference between the two methods was insufficient to misclassify subjects as having fixation that would fall outside of a 2 deg diameter circle, since the mean error was < 1 deg or 60 min arc for all subjects in this experiment. **(D)** Bland-Altman plot of the comparison of the BCEA for manual and automatic alignment ($y = 0.26 - 0.14 * x$; $r^2 = 0.03$ with $p = 0.369$, indicating no significant difference in the slope). The mean and 95% limits of agreement were 0.15 and 0.7 to -0.4 min arc². **(E)** Comparison of the automatic alignment values for the SD vs. BCEA method ($y = 3.37 + 0.19 * x$; $r^2 = 0.10$ and $p = 0.114$). **(F)** Bland-Altman plot of SD vs. BCEA method ($y = 1.09 - 0.69 * x$; $r^2 = 0.21$, and $p = 0.016$ indicating that the slope of -0.69 was different from 0. The mean and limits of agreement were -3.6 and between 4.5 and -11.7 pixels. The plot shows the outliers mainly occurred for the larger eye movements in this sample, and while the Bland-Altman slope is < 0 , the fixation stability would still be classified in the best category.

Figure 5. LSDC-S sample retinal image with responses plotted for kinetic perimetry targets that were displayed while the operator viewed the retinal image in real time. Targets moved along one of the eight meridians, shown as the red lines. Each meridian was tested twice. Each green circle represents one response from seeing to non-seeing for a meridian. This example used decremental targets.

Figure 6. Kinetic Perimetry Data Using Decrements vs. Increments to map the Optic Nerve Head. The thick gray lines represent black targets on a white background, background for 8 data points around the optic nerve head. The thick black lines represent white targets on black. White targets, on average, resulted in a smaller area optic nerve head map, which was significant using repeat measures ANOVA ($P = 0.045$.) Radial lines represent stimulus meridian, and concentric lines show degrees.