PERCEPTUAL FILLING-IN AND READING WITH CENTRAL SCOTOMAS

By

Joshua D. Pratt, OD

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Approved:

____
Harold E. Bedell, PhD (Chair)

____
Yuzo M. Chino, PhD

____
Scott B. Stevenson, PhD

____
George T. Timberlake, PhD

____
Stanley Y. Woo, OD, MS

Committee in Charge

Dedicated to those with vision loss who inspire us to be better through perseverance and hope.

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Abstract

Purpose: Macular degeneration can be severely disabling as patients frequently develop central blind areas (scotomas) which impair their ability to read, drive, and recognize faces. To compensate for the loss of central vision, patients with absolute central scotomas must learn to use their peripheral retina to perform tasks normally performed with the fovea/parafovea. Because of perceptual filling-in, patients perceive characteristics of a scene, such as its color or texture, within the area corresponding to complete vision loss and generally are unaware of the scotoma border and location. I hypothesized that perceptual filling-in makes it more difficult for patients with central scotomas to read effectively using peripheral vision and that making the boundaries of the scotoma visibile would be beneficial as a training mechanism. The specific purpose of this dissertation was to investigate the effects of perceptual filling-in on fixation and reading speed in patients with bilateral central scotomas.

Methods: In experiment 1, I investigated the retinal locus used and the stability of fixation in patients with bilateral central scotomas for six targets, three expected to fill-in and three with letters. In experiments 2 and 3, I examined whether the reading speed of normal subjects is affected by the visibility and information content of a simulated central scotoma. In experiment 4, I tested whether perceptually delineating the visual field location of the scotoma improves reading speed in patients with bilateral central scotomas. A gaze contingent display was used, first to map the scotoma, and then to display the scotoma location continuously as a high-contrast polygon while patients read computer-presented text.

Results: Eleven of twelve subjects in experiment 1 used a retinal location closer to the vestigial fovea to fixate targets expected to fill-in, compared to letters. Target type produced no overall significant difference in fixation stability, which was measured as bivariate contour ellipse area (BCEA). However, for some individual subjects, fixation on letter targets tended to be more stable. In experiments 2 and 3, elapsed reading times were longer for simulated scotomas that were less visible and contained more linguistic information. Subjects adopted different eye-movement strategies for the more and less visible scotoma types, and the improvement in reading speed for the least visible scotoma type was associated with a decrease in saccadic amplitude and an upward shift of the mean fixation locus. Older subjects had more difficulty than younger subjects reading with a simulated central scotoma, especially the scotomas that were less visible and contained more linguistic information. In experiment 4, reading speed improved in all but one of the patients with central field loss after a brief period reading while viewing a polygon that marked the scotoma location. After experience with the overlaid polygon, five of seven patients shifted their fixation location to position the scotoma further from the center of the text, thereby, imaging more of the text on viable retina.

Conclusions: The results of experiment 1 suggest that in patients with central field loss, letter targets generate more consistent fixation behavior than fill-in targets. The results also indicate that fixation using fill-in targets does not allow clinicians to estimate the visual field location of a central scotoma reliably. The data obtained from experiments 2 – 4 suggest that enhancing scotoma visibility has the potential to improve reading speed and to train effective eccentric viewing in patients with central scotomas. The vertical shift of the mean fixation locus demonstrated by normal subjects and by most patients with central field loss suggests that upward eccentric viewing is an adaptive oculomotor strategy in the presence of a central scotoma.

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Chapter 1

General Introduction

In the United States it is estimated that 1.75 million individuals have age-related macular degeneration (AMD) and that AMD is the leading cause of irreversible vision loss among persons more than 65 years of age (Friedman et al. 2004). Macular degeneration can be severely disabling as patients frequently develop central scotomas and lose their ability to read, drive, and recognize faces. To compensate for their loss of central vision, patients with absolute central scotomas must learn to use their peripheral retina to perform tasks normally performed with the fovea/parafovea.

Patients typically adopt one or more specific eccentric retinal loci to track and view objects and to read. These loci have been termed preferred retinal loci (PRLs) and their characteristics have been described (Schuchard 1995; Timberlake et al. 1986). In most patients, the use of a PRL as a pseudofovea is incomplete, as their oculomotor behavior demonstrates a lack of complete re-referencing from the fovea. Some patients may continue to image objects of interest in the scotoma by making foveating saccades (White and Bedell 1990).

Training patients to eccentrically view has been widely implemented as a regular part of low vision services but the benefit of current techniques is debatable (Seiple, Grant, and Szlyk 2011). Perceptual filling-in, the perception of the color and texture of the surrounding visual field within the area of the scotoma, likely complicates training eccentric viewing and oculomotor control and may contribute to the lack of substantial improvement in some patients. Because of perceptual filling-in, patients are generally unaware of their scotoma which makes it difficult for them to understand how they must move and position their eyes to use their remaining peripheral vision (Schuchard 1993). Research evaluating the effect of perceptual filling-in on visual function and the use of techniques that allow patients to visualize their pathological scotomas is needed.

One of the most frequently used techniques for teaching a patient to use his/her remaining functional vision is eccentric viewing training, in which a patient is taught to move his/her eyes or head so that objects are imaged on healthier peripheral retina (Holocomb and Goodrich 1976). A 2004 survey of United States Veterans' Administration (VA) optometrists and visual skills instructors indicates that eccentric viewing training is widely implemented within the VA system with the most commonly used form being the practice of scotoma placement and eye movement control while reading with an optical low vision device or a closed-circuit television (Stelmack, Massof, and Stelmack 2004). In this type of training, a patient is guided to look in the direction thought to be best to position the eye to read. The examiner relies heavily on the patients' ability to recognize where they have remaining vision, as the trainer has no accurate method of monitoring eye position and cannot tell whether the patient is moving his/her eye sufficiently or too much.

The use of a scanning laser ophthalmoscope (SLO) or Nidek MP-1 microperimeter allows the examiner to evaluate eccentric viewing with greater accuracy (Timberlake et al. 1987; Fletcher and Schuchard 1997; Nilsson, Frennesson, and Nilsson 2003; Rohrschneider et al. 2005). With these instruments the examiner is able to observe an image of the patient's fundus while the patient is performing a task such as fixating a target or reading a sentence. The patient is still unable to perceive the location of his/her scotoma, but the examiner can coach the patient to move his/her eye to a more "optimal" location. Use of these instruments has yet to become widely implemented in routine low vision evaluations, possibly because of limited accessibility, high cost, increased time, and the need for greater technical skill.

Much of the current eccentric viewing training is done without the use of fundus imaging devices and focuses on helping the patient recognize where they have to look to perceive objects and perform visual tasks. During such training the specific area on the retina the patient uses to perform tasks is uncertain and the examiner is left to estimate the magnitude of the patient's eye movements, and hence the retinal locus being used, by gross observation. Without dedicated instrumentation, it is not possible to tell if a patient has moved his/her eye sufficiently or too much to perform a certain visual task. It is also unclear where precisely the scotoma is in relation to the targets being viewed and whether the patient's scotoma overlaps the target of interest. Scotoma location relative to the PRL is not clear when performing perimetry using a tangent screen, Humphrey field analyzer or other device that does not image the fundus because the retinal location of fixation is uncertain. A method to predict the retinal location of fixation without fundus imaging would be useful both in training eccentric viewing and in field analysis.

In perceptual filling-in, characteristics of a scene, such as its color or texture, are perceived in an area corresponding to complete vision loss, or as in the case of the physiological blind spot, an area with no photoreceptors. Zur and Ullman demonstrated that gratings, and regular dot patterns that span the scotomatous region of the visual field are nevertheless perceived by patients with AMD to be uniform and continuous (Zur and Ullman 2003). Investigators have also shown that the commonly used Amsler grid is perceived as complete by many patients with dense central scotomas (Schuchard 1993; Achard et al. 1995).

Perceptual filling-in may allow us to elicit fixation using the vestigial fovea in patients who have not shifted their oculocentric visual direction to the PRL. Large targets that extend beyond the central scotoma are expected to perceptually fill-in and patients with absolute scotomas should see these targets as complete and continuous. If a patient perceives a target as filled in, we predict that the patient should position the retinal locus that corresponds to the primary oculocentric visual direction at the center of the target. In contrast the use of small targets that cannot fill-in, such as letters, is expected to elicit the use of the patients' PRL.

A better understanding of the retinal locus patients use to fixate targets that are expected to perceptually fill-in and those that are not may allow us to develop targets that give increased confidence about the retinal location of fixation. These targets may in turn be used for eccentric viewing training and in perimetry. It is also desirable to determine whether fixation stability is better with any one target, as stability frequently limits what tests can be performed.

In experiment 1 we investigate the retinal locus and stability of fixation in patients with bilateral central scotomas for six different targets, three expected to fill-in and three with letters.

The effectiveness of any vision rehabilitation training is likely to be complicated by perceptual filling-in. Based on the observation that perceptual filling-in of text occurs at the physiological blind spot and in artificial scotomas, it is likely that when patients with a central scotoma look at text, they perceive the color, texture, and brightness of the text in the region of their scotoma and the awareness of their scotoma is decreased (Ramachandran and Gregory 1991). It is a common clinical observation that patients with bilateral central scotomas are not fully aware of their scotomas.

Reduced awareness of the scotoma border and location may contribute to ineffective oculomotor control, the placement of text in a non-optimal location relative to the scotoma, and inappropriately directed attention. It can be difficult for patients to understand how they must move and position their eyes to use their remaining peripheral vision. As a result the current methods of eccentric viewing training are likely inadequate in helping patients to correctly position their eye and make useful eye movements especially when viewing paragraph text.

Allowing patients to perceive the specific border and location of their scotoma may be beneficial and has not been explored as a possible training mechanism.

Experiments 2 and 3 examine whether reading speed in normal subjects is affected by the visibility and information content of simulated central scotomas and whether it is feasible to expect reading in patients with central scotomas to be affected by perceptual filling-in.

It is thought that perceptual filling-in is a result of the unmasking of lateral connections within the visual cortex or possibly the result of a top-down effect in which the visual information from the scotoma border is also perceived within the scotoma (Kaas et al. 1990; Chino et al. 1992; Dilks et al. 2009). Because the brain likely uses the information from the retina adjacent to the scotoma border to fill-in the scotoma, we can use this area on the retina and a gaze contingent display to allow patients to perceive their own scotoma.

For example, if a particular color were imaged onto the whole retinal border surrounding the scotoma, the scotoma should fill-in with that color. This is observed to occur at the physiological blind spot and in artificial scotomas, and would be expected to also occur in the pathological scotoma (Spillmann et al. 2006)**.** Using a gaze contingent display, we can continually cover the border of the scotoma, allowing patients to perceive the location and border of their scotoma while performing a task such as reading. Training in which patients can perceive the border and location of their scotoma is expected to help them to learn to better position the scotoma relative to the text or object of interest, appropriately direct their attention, and make more accurate eye movements.

Experiment 4 tests whether perceptually delineating the scotoma location and border using perceptual filling-in improves reading speed in patients with bilateral central scotomas.

It is the purpose of this dissertation to improve our understanding of perceptual filling-in and how it relates to training patients with bilateral central scotomas to eccentrically view.

Chapter 2

Retinal Fixation Locus in Patients with Bilateral Central Scotomas for Targets Expected to Perceptually Fill-in

2.1 Introduction

The purpose of experiment 1 was to determine the retinal locus used by patients with bilateral central scotomas to fixate different target types, and whether fixation stability is better for targets expected to fill-in or letter targets.

For patients who have not experienced a shift in their occulocentric visual direction it was expected that the center of the fill-in targets would be imaged at the vestigial fovea. In contrast the use of small targets that cannot fill-in, such as letters, were expected to elicit the use of the patients' PRL. If targets expected to fill-in are imaged at or near the vestigial fovea, these target types could be used to better approximate the absolute retinal location and scotoma location during eccentric viewing training and visual field testing outside of fundus imaging devices. If on the other hand patients use an alternate retinal locus to view the center of the fill-in targets, it would imply that fill-in targets are unsuited for eliciting fixation at the vestigial fovea and shouldn't be used in eccentric viewing training or perimetry where it often is assumed that patients are fixating with their vestigial fovea.

2.2 Methods

2.2.1 Subjects

Twelve subjects with bilateral central scotomas were recruited from the Center for Sight Enhancement at the University of Houston College of Optometry. Subjects ranged in age from 21 to 88 years old and were previously diagnosed with age-related macular degeneration, Stargardt macular dystrophy or cone-rod dystrophy (Table 1). All subjects had stable vision at the time of the study with no recent gross changes in the state of pathology. Monocular fixation location and stability for different target types was determined for the eye with better letter acuity, which also corresponded to the eye the patient reported they used to read. In subjects whose letter acuity was the same in both eyes and who reported no eye preference, an ocular dominance test similar to the Dolman hole in the card method was used to determine the eye to be tested. The eye not being tested was patched during measurements. Both eyes were dilated with 2.5% phenylephrine to improve retinal image quality.

2.2.2 Stimuli

The subject was presented with 2 groups of custom targets created in Image J software and presented with the Nidek microperimeter's native software. Targets expected to perceptually fill-in consisted of a large filled disk, a large cross, and two superimposed crosses, one with legs along the 90 – 270 and 0 - 180 deg meridians, and the other with legs along the 45 – 225 and 135 – 315 deg meridians (Figure 1). We will call the last type of target a spoke target. The width of the spokes and the legs of the crosses was 1.5 degrees. All targets were black on an illuminated white background of approximately 130 cd/m^2.

The second group of targets consisted of a single letter, and a similar cross and spoke as in the first group of targets, but with a letter in the center. Dark Courier font letters R, S, N, H, K, or Z were used. All of the fixation targets were the same overall diameter of 30 degrees, except for the isolated letter target, which was 0.83 degrees (20/200) for patient's with 20/200 or better acuity, and 1.67 degrees (20/400) for patients with acuity worse than 20/200 but better than 20/400. None of the patients had letter acuity in the better-seeing eye worse than 20/400 (Table 1). The size of the letter stimuli for each patient was based on the visual acuity measured during an eye examination within the previous month.

The patients' instructions depended on target type. For the targets expected to fill-in, the instructions were, "move your eye to the center of the object, and keep your eye as steady as you can while looking at the center of the object." The instructions for the letter targets were, "move your eye to see the letter, and keep your eye as steady as you can while making sure you can see the letter."

Each target was presented twice. Presentation order was randomized and then counterbalanced within each group of targets. The targets expected to perceptually fill in were presented first. Patients indicated with a button push when they were fixating the center of the target or the letter and fixational eye movements were recorded at a rate of 25 samples/s for a period of 30 s using the fixation examination native to the Nidek microperimeter (MP-1).

After each 30 s recording period with the targets expected to fill-in, each subject was asked what the fixation target was and whether it was complete, if there were any broken or missing parts, or if there were any blurry or faint parts of the object. In the trials with letter targets, the patient was asked which letter he or she saw. After the conclusion of the fixation trials, the scotoma in the tested eye was mapped with a custom perimetry program using the Nidek microperimeter software.

2.2.3 Perimetry

Two spoke-like perimetry patterns were used to measure whether the scotomas were absolute and bilateral and whether the fixation targets spanned the scotoma in the study eye. The perimetry programs were designed using the Nidek perimetry software and used Goldman size III stimuli. Tested points were spaced 2 degrees apart over the central 28 degrees with twice the density of points for the study eye along the horizontal and vertical meridians. The automatic threshold strategy was ‘4-2’ for the study eye and ‘fast’ for the non-study eye. Stimulus duration was 200 ms. Sample perimetric results are shown for subject 66 in figure 2. The center of the perimetric array was placed by the examiner at the approximate location used by the patient to fixate the center of the fill-in targets during trials. Patients in whom perimetry results indicated that there was central sparing in either eye were excluded from the study. In all cases but one, subject 44, the 30 degree targets spanned the scotoma of the study eye. The spanning of the scotoma by the target is thought an important prerequisite for the targets to perceptually fill-in (Gerrits and Timmerman 1969; Spillmann et al. 2006).

2.2.4 Eye Position Measurements

Horizontal and vertical eye positions during fixation were recorded for a period of 30 seconds using the fixation examination native to the Nidek microperimeter (MP-1). In the fixation exam, a region of interest (ROI), such as a blood vessel crossing, is chosen from a stationary infrared image of the fundus (Figure 3). The MP-1 then uses a cross correlation of this ROI with images of the fundus sampled at 25 Hz to track the eye position. Because of the instrument’s software design, a separate ROI had to be chosen on each trial but, in general, the same region of the fundus was used to track fixation for all trials for one subject. The tracking algorithm in the Nidek includes a threshold correlation value below which the instrument indicates that it has lost track. A real time image of the region of interest was monitored during each trial to confirm that the MP-1 was accurately tracking. In addition, the recorded eye positions for each trial were analyzed off-line for tracking losses (see below). Because fixation eye movements are not recorded when the tracking algorithm indicates it has lost track, some trials required longer than 30 s to obtain a total of 30 s of fixational eye movements. The length of each trial depended on retinal image quality and whether the MP-1 was able to reliably track the fundus image. Although one patient had one trial that lasted 70 s, the typical duration for a trial including the non-tracked portion was between 30 and 40 seconds. Infrequently, a trial had to be restarted using an alternate region of interest because of poor instrument tracking.

2.2.5 Analyses

Vertical and horizontal eye positions were plotted against time for each trial and a custom MATLAB program was used to detect and remove portions of the data where the MP-1 had lost track but had still recorded fixation values. Tracking loss was evidenced by large upward and downward spikes in the fixation data. The periods of tracking loss demonstrated a high positive velocity coupled with a high negative velocity within two data points or 80 ms. Because two large consecutive saccades cannot occur within this brief time frame, a calculated velocity profile was used to detect these periods of tracking loss and differentiate them from real saccades. After removing the periods of tracking loss the data were analyzed for multiple fixation positions. We classified shifts in fixation as an absolute change in the mean fixation position that is greater than 1.5 degrees as well as greater than two standard deviations of the mean horizontal or vertical eye position before and after the possible shift. We limited our analysis to shifts that were sustained for at least ten percent of the trial or 3 s.

Possible shifts in fixation using the above criteria were detected with a custom MATLAB program and visually confirmed during off-line analysis (Figure 4). Some patients demonstrated rapid back and forth movement between two retinal loci. We did not register these as different fixation positions as we were primarily concerned with the effect that two or more relatively stable fixation loci would have on the bivariate contour ellipse area. This back and forth behavior was interpreted to indicate that fixation was unstable and thus the bivariate contour ellipse area would be descriptive of these data without adjusting for multiple PRLs.

2.2.6 Fixation Stability as Bivariate Contour Ellipse Area

The formula: Area = $\pi\chi^2\sigma_x\sigma_y\sqrt{1-\rho^2}$ was used to calculate the 68% bivariate contour ellipse area (BCEA) for each trial. In the formula, χ^2 is the value that includes 68% of the area of a chi-square distribution with 2 df. The use of the BCEA to describe fixation stability has been described in detail elsewhere (Steinman 1965; Timberlake et al. 2005). Simply put, the BCEA is the area of an ellipse that contains a specific percentage of the horizontal and vertical fixation positions. While this gives us an understanding of overall stability during a trial, care must be taken in its interpretation, as some subjects may shift fixation location during a trial, resulting in an inflated value for the calculated BCEA. This may give the impression that the eye moved around substantially during the trial when, in fact, the subject maintained relatively stable periods of fixation at two or more different retinal loci. In our data, six subjects demonstrated a shift between two loci during 1 to 3 of the 12 trials. This resulted in larger BCEAs for those trials. We analyzed the data with and without accounting for these changes in fixation locus. To calculate an adjusted BCEA for these trials in which a change in fixation was detected, the median of the horizontal and vertical positions before the fixation change were subtracted, respectively, from the horizontal and vertical eye-position data after the fixation change and the adjusted BCEA was calculated from these normalized data.

An alternate method for analyzing fixation stability that accounts for multiple fixation loci based on density plots has been described previously (Crossland et al. 2004). We decided to analyze our data as described above because we were looking to identify clear sustained changes in the fixation locus during a trial, where the overall BCEA was not really descriptive of the subject's fixation stability. The unadjusted BCEAs were preferred to an analysis using density plots, which potentially could have identified multiple PRLs when unstable fixation consisting of quick back and forth movements within an extended PRL moved the image between separated retinal loci. Analysis of fixation across time gave a clearer delineation of whether multiple fixation loci were used. During most of the trials, patients used a single area to view targets, however there were subjects whose fixation position drifted or shifted frequently between two or more points. In these examples the unadjusted BCEA is likely to provide an accurate description of fixation stability.

2.2.7 Fixation Position

For each subject, the fixation data from each trial were registered to a single retinal image to allow for comparison of fixation position between trials. This was necessary as the coordinates of the fixation data for each trial were specified relative to the retinal image that was captured when the ROI was defined for that trial. For each of the subjects trial 1 was used as the image to which all other images were aligned. Alignment was done visually using Image J software and the Align3 TP plugin. Alignment was checked and adjusted using flicker between pairs of images at a frequency of approximately 4 Hz. Images were translated and then rotated until no image motion was apparent with flickering of the images. The amounts of translation and rotation were then used to calculate the offset of each image relative to the image for trial 1 and this offset was applied to the data for that trial. The median horizontal and vertical fixation positions for each trial were then calculated and compared between trials.

The residual foveal pit on a dense macular scan with the Spectralis Optical Coherence Tomographer was used to delineate the approximate retinal location of the vestigial fovea for 9 of the 12 subjects. This location is marked with an F on the images for those 9 subjects. Unfortunately OCT was not a part of the original protocol and was not performed on the first three subjects (10, 11, and 60).

Table 1. Patient characteristics experiment 1

Subject Number	Age (yrs)	Gender	Diagnosis	Study Eye	Visual Acuity (calculated Snellen)	
					OD	OS
59	21	M	Stargardt	OD	20/280	20/400
11	46	F	Cone-Rod	OD	20/60	20/70
39	87	M	AMD	OD	20/80	20/120
66	80	M	AMD	OD	20/200	20/400
60	75	F	AMD	OS	20/240	20/160
10	85	M	AMD	OD	20/80	20/160
44	54	F	Cone-Rod	OS	20/125	20/100
21	84	F	AMD	OS	20/200	20/80
28	26	M	Stargardt	OD	20/320	20/360
37	45	F	Stargardt	OD	20/120	20/120
61	88	M	AMD	OS	NLP	20/100
62	81	F	AMD	OD	20/160	20/120

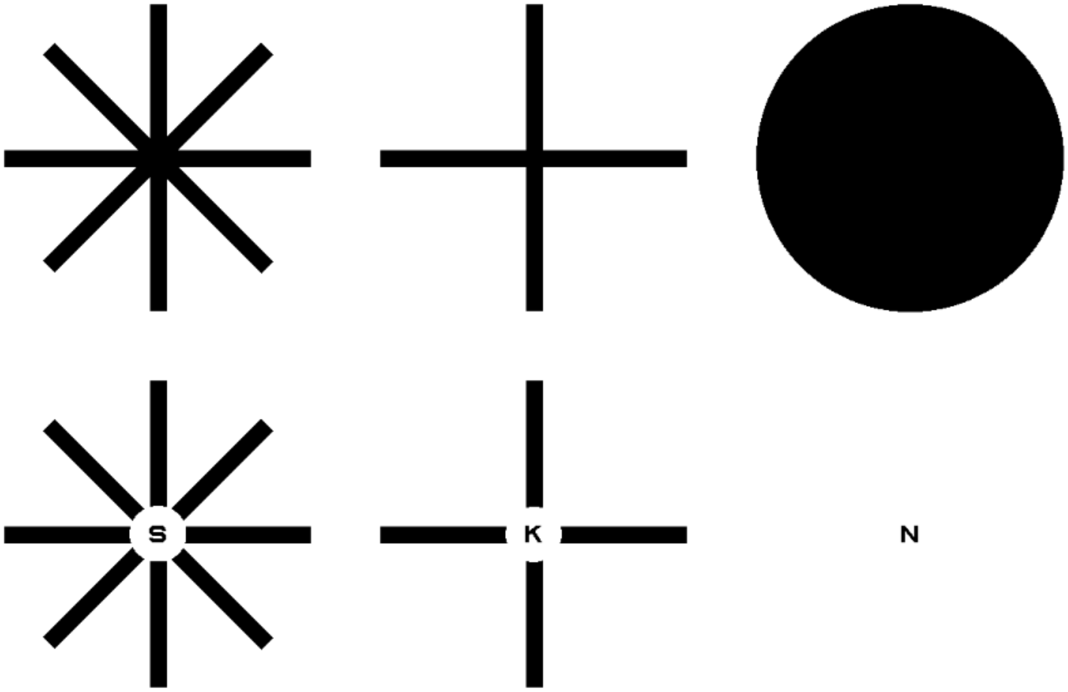


Figure 1. Fixation targets. Targets except for the single letter were 30 degrees in size.

A. **B.**

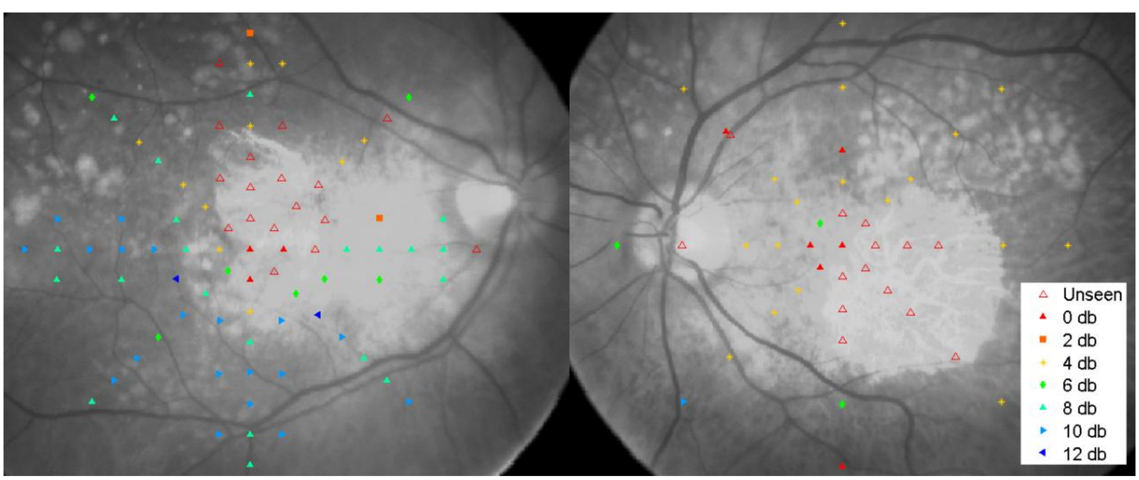


Figure 2. Results of Nidek MP-1 perimetry for the tested (A) and non-tested eye (B) for subject 66. The insert shows the 0-12 decibel scale.

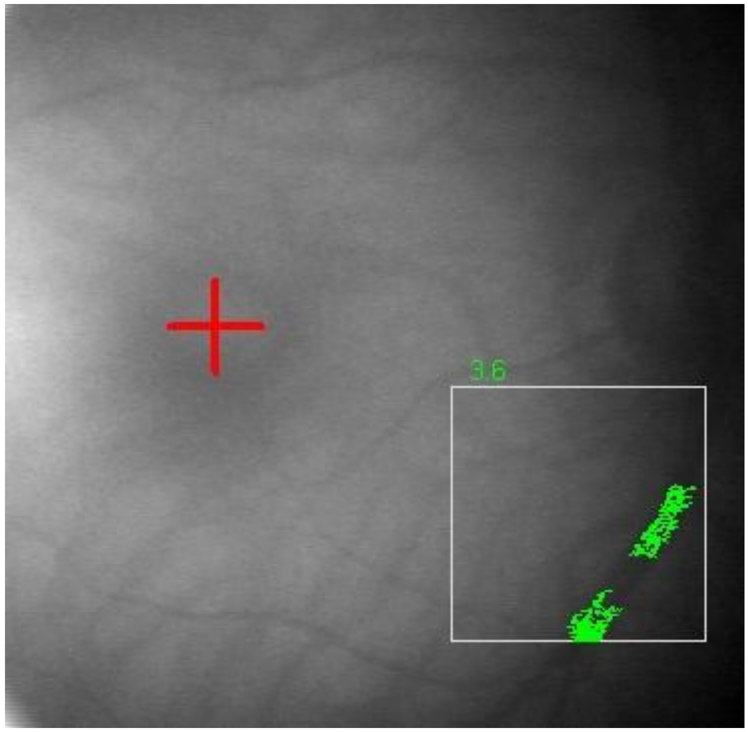
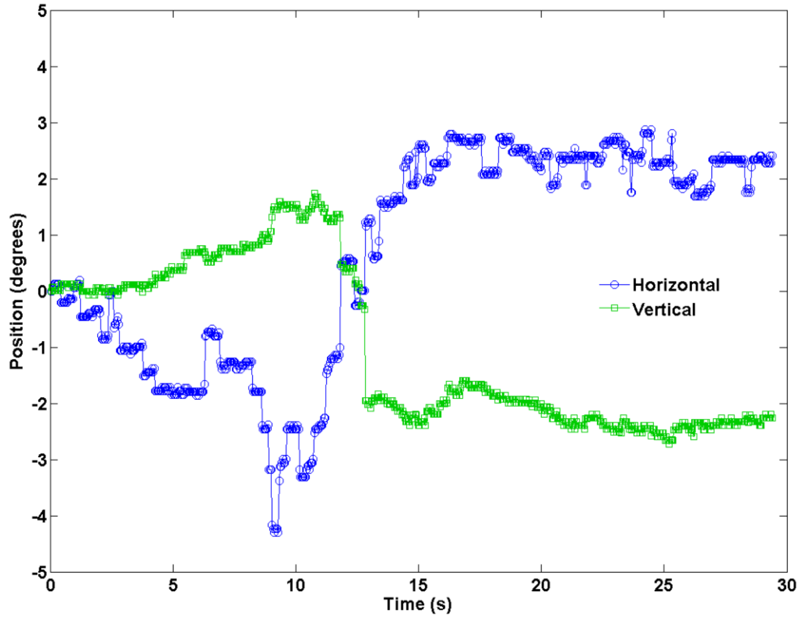


Figure 3. Selection of an ROI in the Nidek MP-1, in a normal subject.

A.



B.

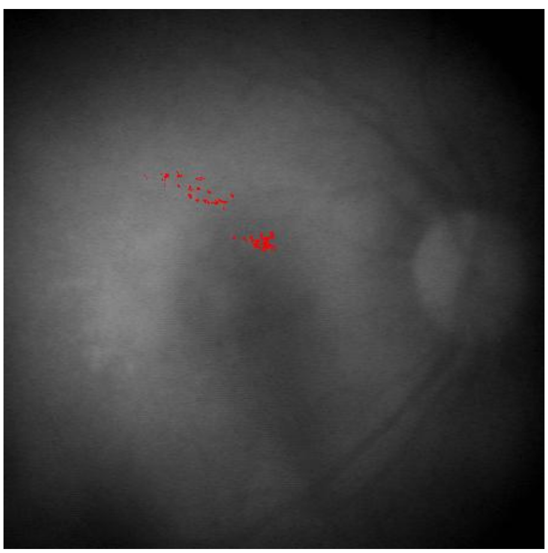


Figure 4. Subject 59 Trial 9, (A) Horizontal and vertical eye position trace during fixation on the spoke-letter target. Left and up are positive on the y-axis. (B) Retinal position of target center plotted on the fundus image. The use of two distinct PRLs is manifest.

2.3 Results

A repeated measures ANOVA was performed on the data for the horizontal and vertical fixation position, separately for each subject. ANOVAs were not performed across all subjects because the horizontal and vertical position is arbitrary and there is no way to relate the position used by one subject to another position used by a different subject. The independent variable was the repeated measures of six target types (cross, spoke, disk, cross-letter, spoke-letter, and letter). The dependent variable was the median horizontal or vertical fixation position for each target type. An alpha level of 0.05 was utilized for this analysis. Post-hoc analysis was carried out and the following comparisons were made: cross and spoke vs. cross-letter and spoke-letter, disk vs. the other 5 target types, disk vs. letter, cross and spoke vs. letter, and cross letter and spoke letter vs. letter. The keep the overall probability of a Type 1 error equal to 0.05, an alpha value of 0.01 was utilized for these analyses.

Eleven out of twelve subjects showed a significant interaction between fixation location and target type in the horizontal or vertical fixation position, or both (Table 2). Nine of these eleven subjects also demonstrated a significant difference in fixation locus for the cross and spoke vs. the cross-letter and spoke-letter, disk vs. the other 5 target types, and disk vs. letter. Seven of these eleven subjects demonstrated a significant difference in the fixation locus for the cross and spoke vs. letter and none of these subjects demonstrated a significant difference between the spoke letter and cross letter vs. the letter.

Fundus plots as well as plots of median horizontal and vertical fixation location demonstrate the difference between the targets that include a letter and the targets that were expected to perceptually fill-in (Figures 5-28). Eleven of the subjects imaged the center of one or more of the fill-in targets within the scotoma while only one subject imaged some of the letter targets within the scotoma. Five of the subjects fixated the fill-in targets and the letter targets with retinal areas within close proximity to one another at the edge of the scotoma. The fill-in targets were imaged closer to the vestigial fovea for all of the subjects but one. Five patients (28, 37, 39, 44, and 62) imaged the fill-in targets at a retinal locus other than the vestigial fovea and four of the patients (11, 21, 61, and 66) imaged the fill-in targets at or near the vestigial fovea. It was not possible to tell without OCT analysis whether the fill-in targets were imaged at the fovea in two of the patients. Nine out of the twelve patients described the large fill-in targets as complete. Seven of these patients reported no broken or missing parts despite much of the target being covered by the scotoma and the center being frequently placed within the scotoma. Many of the patients perceived areas of the targets that appeared faint or blurry or non-uniform.

A repeated measures ANOVA was also performed on the fixation stability, measured as BCEA, for the group as a whole and for each individual subject. The log BCEA was used for analysis to better approximate a normal distribution of BCEA values. No significant difference in BCEA between the target types was found for the group $F(11,55) = 2.511$, $p = 0.0646$. Only two of the subjects showed a significant difference in the BCEA with target type (Table 3). Post-hoc analysis was carried out for the two subjects who had significant differences in BCEA. BCEA values were compared for cross and spoke vs. cross-letter and spoke-letter, disk vs. the other 5 target types, and cross-letter and spoke-letter vs. letter. The disk had a significantly larger BCEA for these two subjects. The cross-letter and spoke-letter targets had a significantly smaller BCEA than the cross and spoke targets for subject 37 and approached significance for subject 10. There was no significant difference between the cross-letter and spoke-letter targets vs. the letter target for either subject.

Significance did not change when accounting for multiple fixation loci within a trial for either the group or individual comparisons. A change in fixation during one to three of the trials was found for subjects 11, 21, 39, 59, 62, and 66. The change in calculated BCEA for these trials can be found in the appendix in Table 13.

While most of the subjects demonstrated no significant difference in BCEA values between target types, four of the subjects showed a trend for fixation to be more stable for targets containing a letter. This agrees with the results for the two subjects who exhibited a significant difference in BCEA between target types.

Table 2. Comparison of fixation location across target types for individual subjects. The significant values are highlighted in green. c = cross, s = spoke, cl = cross-letter, sl = spoke-letter, d = disk, l = letter

		Overall			c/s vs. cl/sl			disk vs. all	
Subject		F(5)	*p*		F(5)	*p*		F(5)	*p*
10	x	74.106	0.0001		68.026	0.0002		294.265	0.0001
	y	7.244	0.0159		0.066	0.8053		36.066	0.001
11	x	0.855	0.559		--	--		--	--
	y	64.56	0.0001		194.122	0.0001		67.533	0.0002
21	x	5.303	0.033		0.519	0.4982		24.838	0.0025
	y	1.643	0.2803		--	--		--	--
28	x	1.329	0.3652		--	--		--	--
	y	10.004	0.0071		19.739	0.0044		19.033	0.0048
37	x	2.239	0.1774		--	--		--	--
	y	4.162	0.0559		--	--		--	--
39	x	8.14	0.012		1.756	0.2334		8.699	0.0256
	y	7.102	0.167		32.63	0.0012		0.238	0.6432
44	x	3.605	0.075		--	--		--	--
	y	13.358	0.0033		9.26	0.0227		49.945	0.0004
59	x	3.262	0.0912		--	--		--	--
	y	7.563	0.0143		23.954	0.0027		0.9	0.3795
60	x	134.616	0.0001		507.982	0.0001		63.416	0.0002
	y	3.582	0.0759		--	--		--	--
61	x	12.187	0.0043		29.271	0.0016		20.964	0.0038
	y	0.0514	0.7592		--	--		--	--
62	x	13.725	0.0031		1.942	0.2129		66.105	0.0002
	y	21.262	0.0009		18.661	0.005		75.43	0.0001
66	x	30.748	0.0003		89.233	0.0001		54.247	0.0003
	y	7.305	0.156		0.951	0.3671		35.017	0.001

Table 2 cont.

		cl/sl vs. l			c/s vs. l			d vs. l	
Subject		F(5)	*p*		F(5)	*p*		F(5)	*p*
10	x	0.742	0.422		34.489	0.0011		225.705	0.0001
	y	<0.001	0.9879		0.051	0.8286		22.426	0.0032
11	x	--	--		--	--		--	--
	y	2.097	0.1977		164.461	0.0001		127.908	0.0001
21	x	1.009	0.354		0.173	0.692		11.346	0.0151
	y	--	--		--	--		--	--
28	x	--	--		--	--		--	--
	y	0.669	0.4445		19.765	0.0043		27.069	0.002
37	x	--	--		--	--		--	--
	y	--	--		--	--		--	--
39	x	4.502	0.0781		10.264	0.0185		17.053	0.0062
	y	3.355	0.1167		8.022	0.299		0.001	0.9763
44	x	--	--		--	--		--	--
	y	0.4243	0.735		11.167	0.0156		48.007	0.0004
59	x	--	--		--	--		--	--
	y	1.589	0.2543		27.633	0.0019		8.954	0.0242
60	x	<0.001	0.9989		338.707	0.0001		157.358	0.0001
	y	--	--		--	--		--	--
61	x	0.597	0.4692		26.935	0.002		31.495	0.0014
	y	--	--		--	--		--	--
62	x	0.002	0.9651		1.401	0.2814		45.207	0.0005
	y	0.002	0.9687		12.731	0.0118		63.642	0.0002
66	x	1.907	0.2165		40.091	0.0007		55.058	0.0003
	y	0.005	0.9464		0.751	0.4195		18.141	0.0053

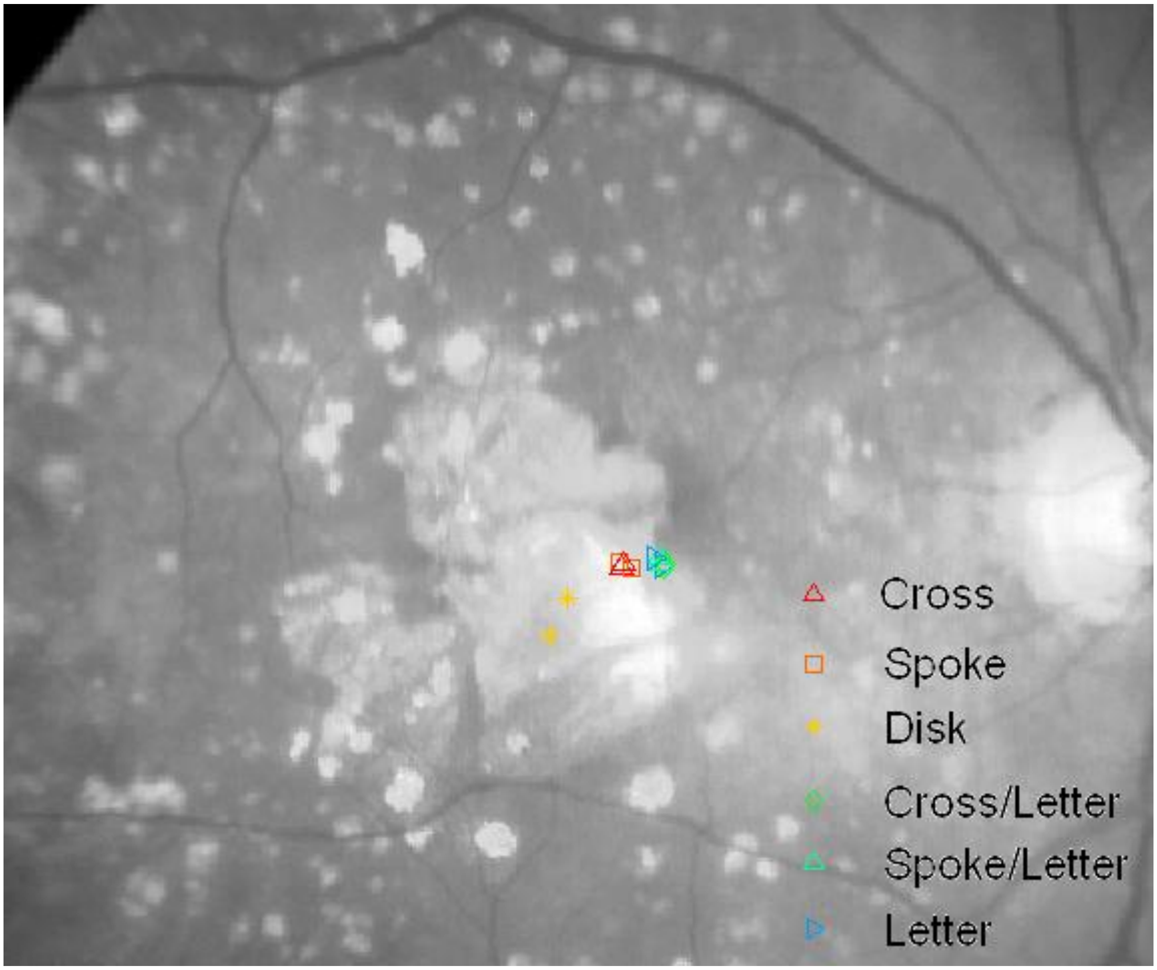
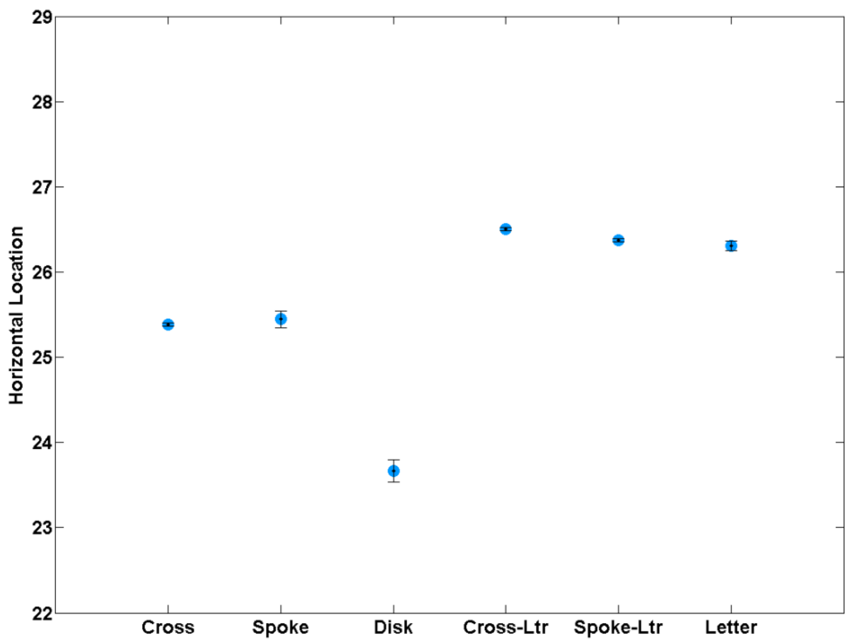


Figure 5. Subject 10's median fixation location for 6 target types. Each target was presented twice. The optic nerve is on the right of this image. The width of the image is approximately 38 deg and the height is approximately 32 deg. Each of the subsequent images is the same size and an effort was made to position the center of the optic nerve on either the right or left edge of the image as a reference.



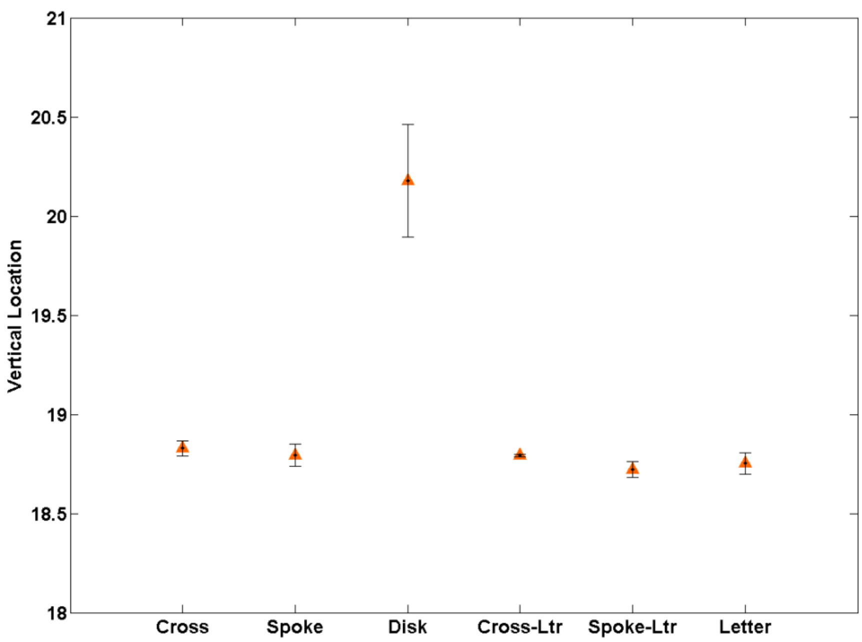


Figure 6. Subject 10’s median horizontal and vertical fixation location for six target types. Each target was presented twice. The plotted symbols represent the average of the medians for the two trials. Standard error is represented by error bars. Position (in deg) is measured from top left of image.

Figure 7. Subject 11's median fixation location for 6 target types. Each target was presented twice.

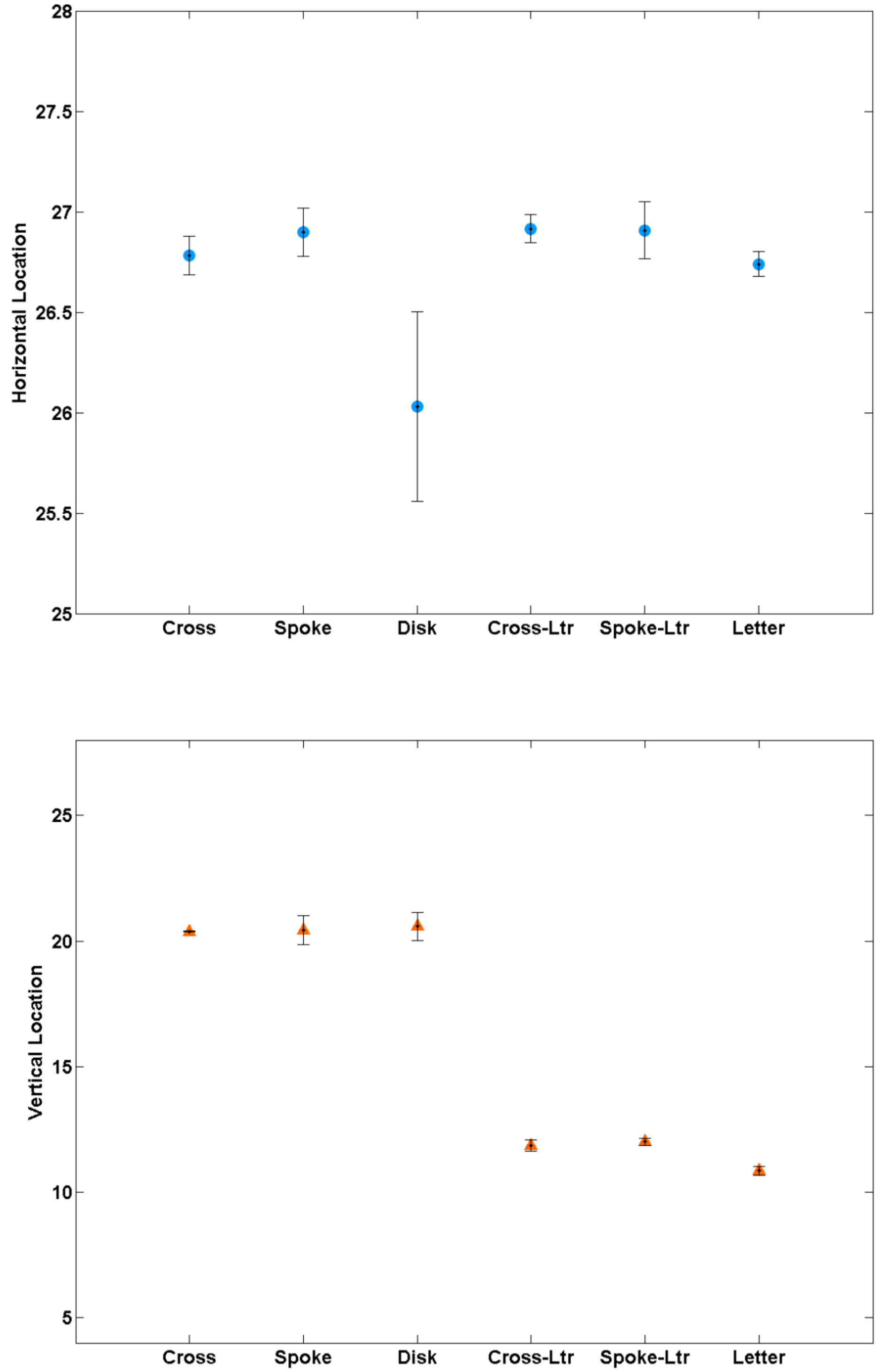


Figure 8. Subject 11's median horizontal and vertical fixation location for six target types. Position (in deg) is measured from top left of image.

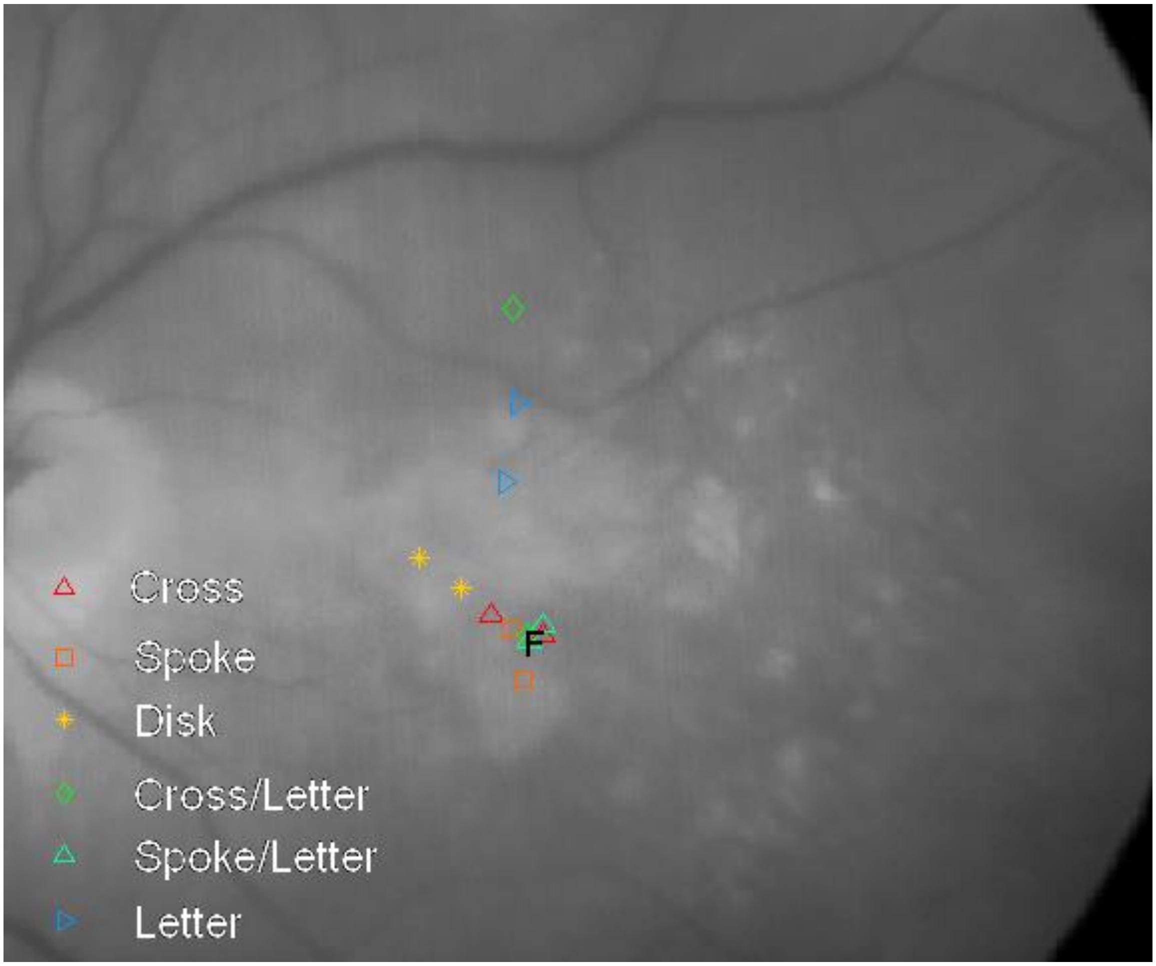


Figure 9. Subject 21's median fixation location for 6 target types. Each target was presented twice. The approximate position of the fovea as determined from OCT images is labeled with an F.

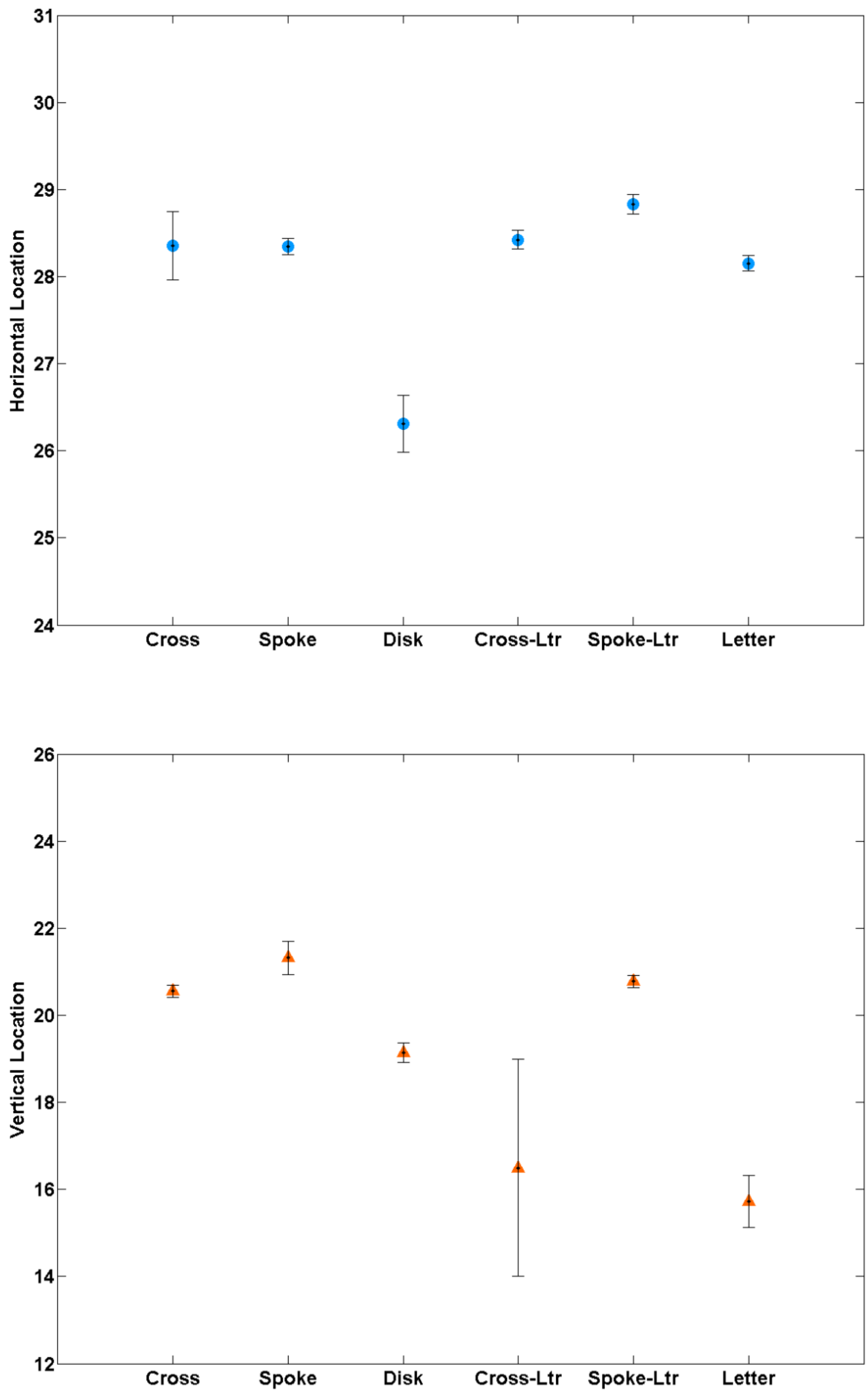


Figure 10. Subject 21's median horizontal and vertical fixation location for six target types. Position (in deg) is measured from top left of image.

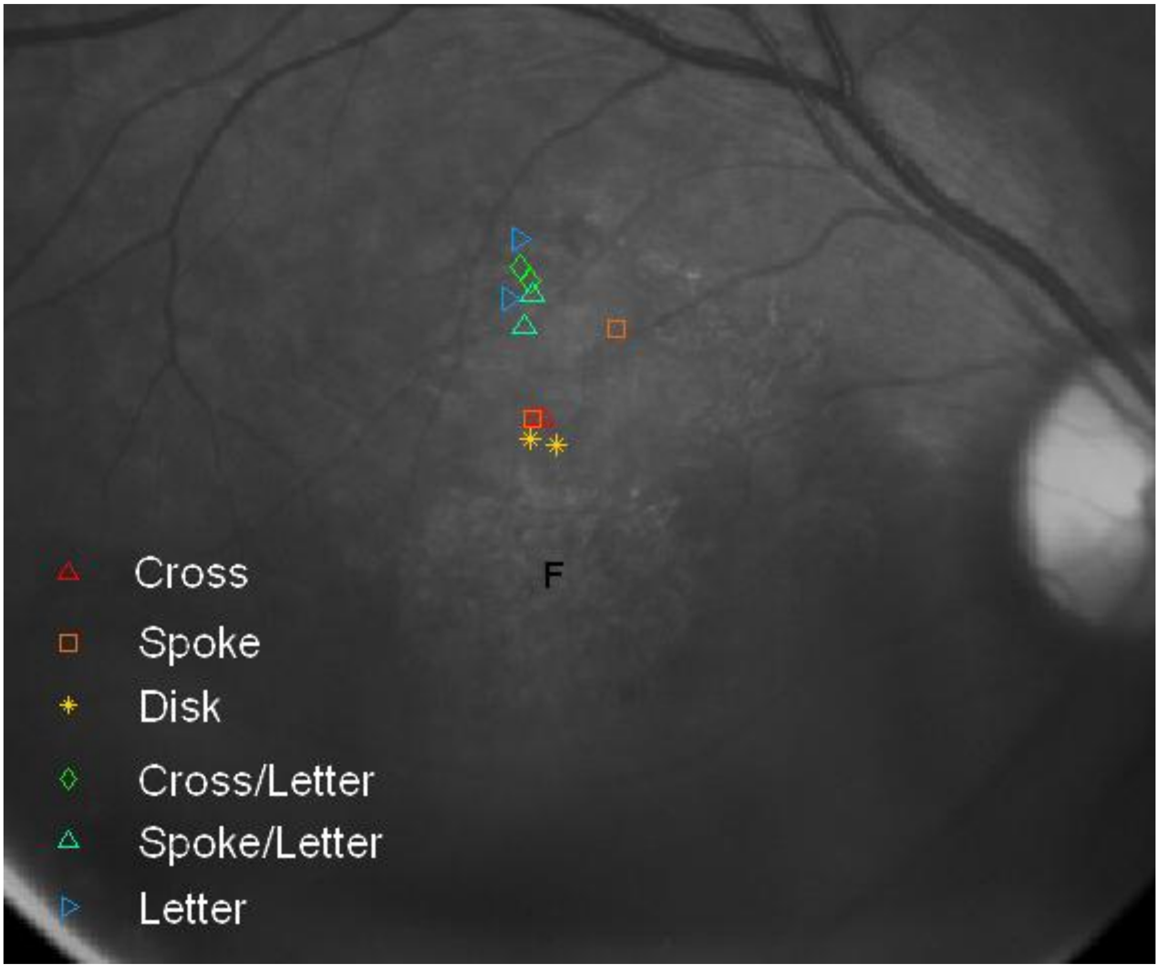


Figure 11. Subject 28's median fixation location for 6 target types. Each target was presented twice. The approximate position of the fovea as determined from OCT images is labeled with an F.

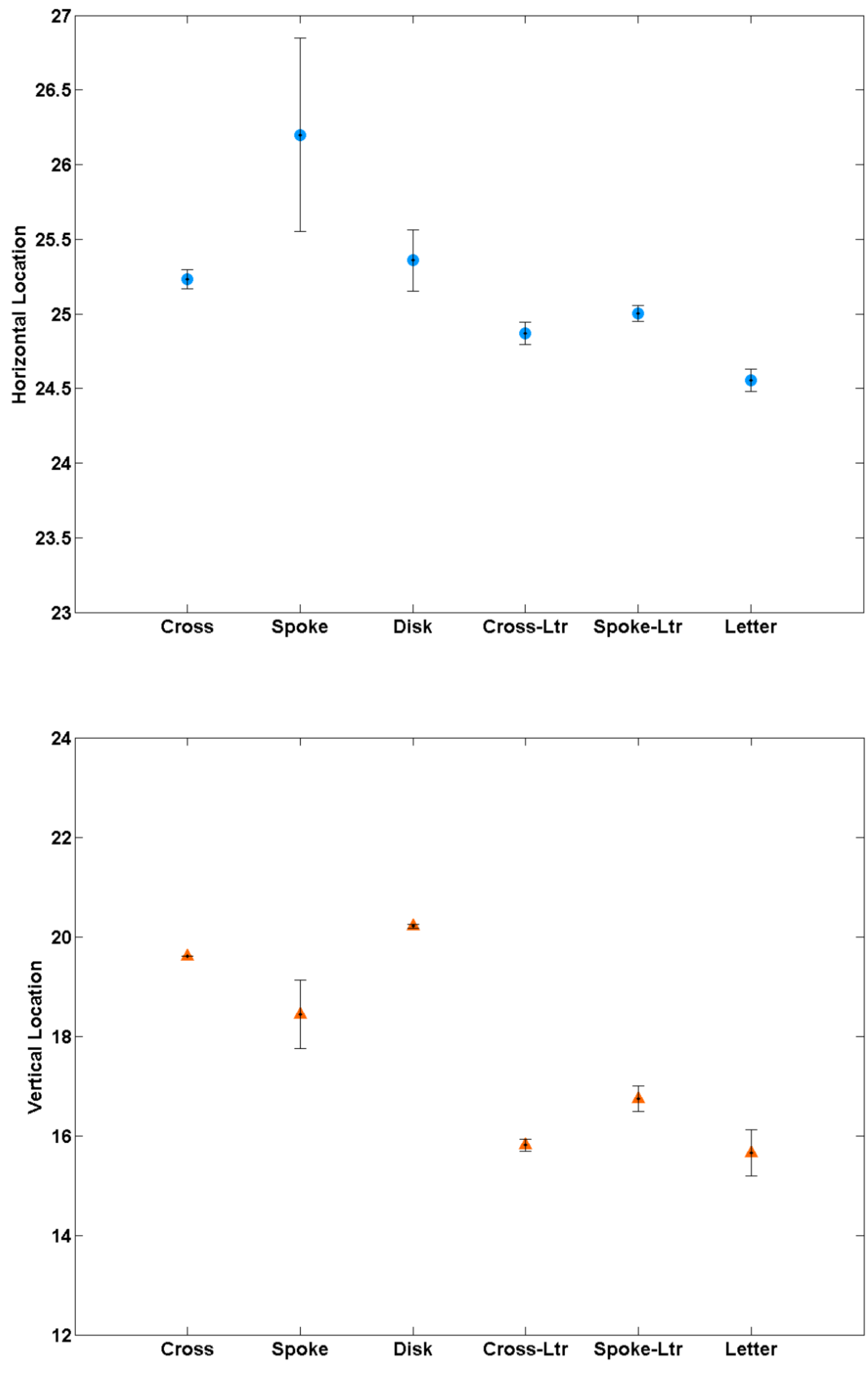


Figure 12. Subject 28's median horizontal and vertical fixation location for six target types. Position (in deg) is measured from top left of image.

Figure 13. Subject 37’s median fixation location for 6 target types. Each target was presented twice. The approximate position of the fovea as determined from OCT images is labeled with an F.

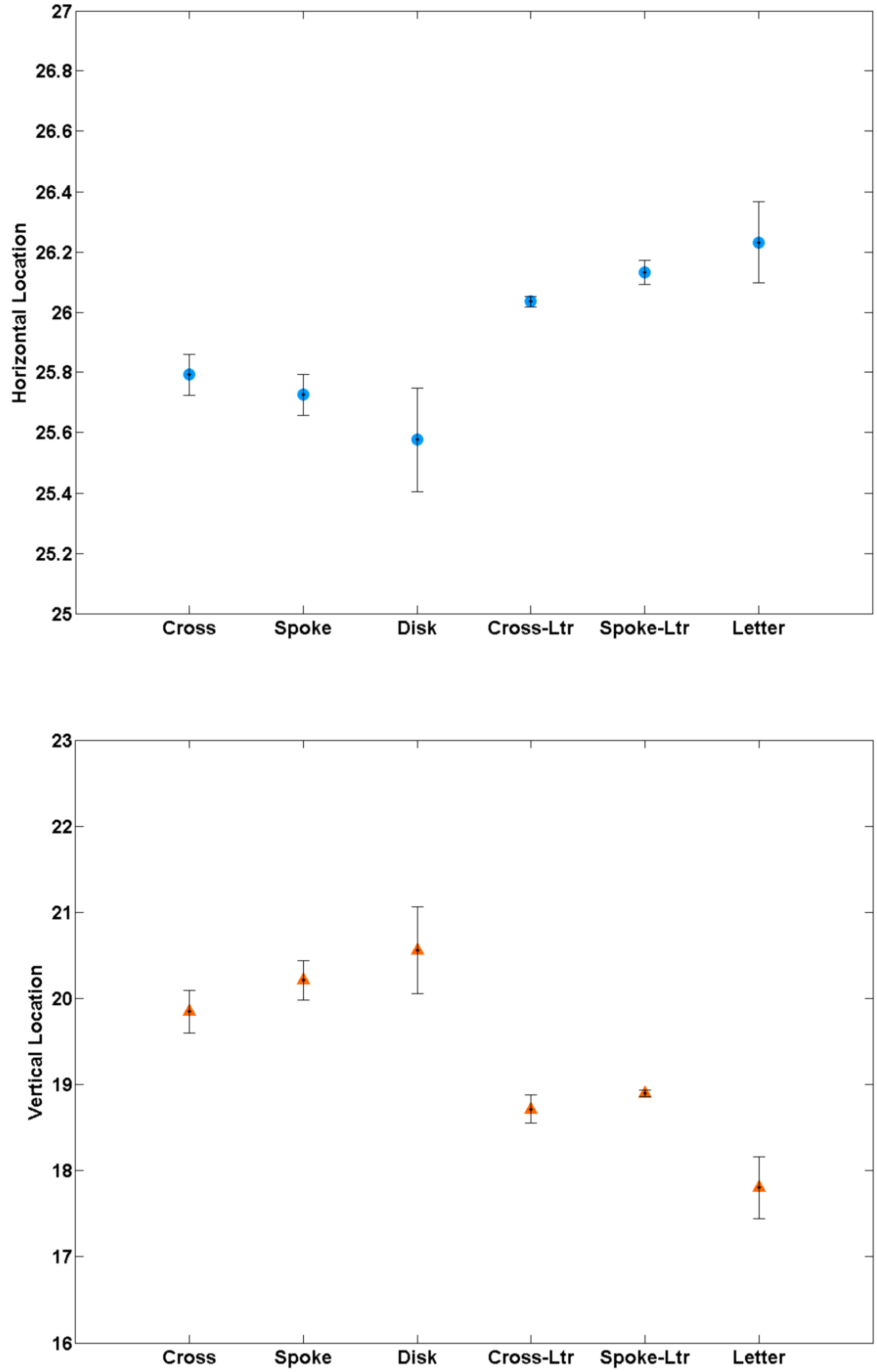


Figure 14. Subject 37's median horizontal and vertical fixation location for six target types. Position (in deg) is measured from top left of image.

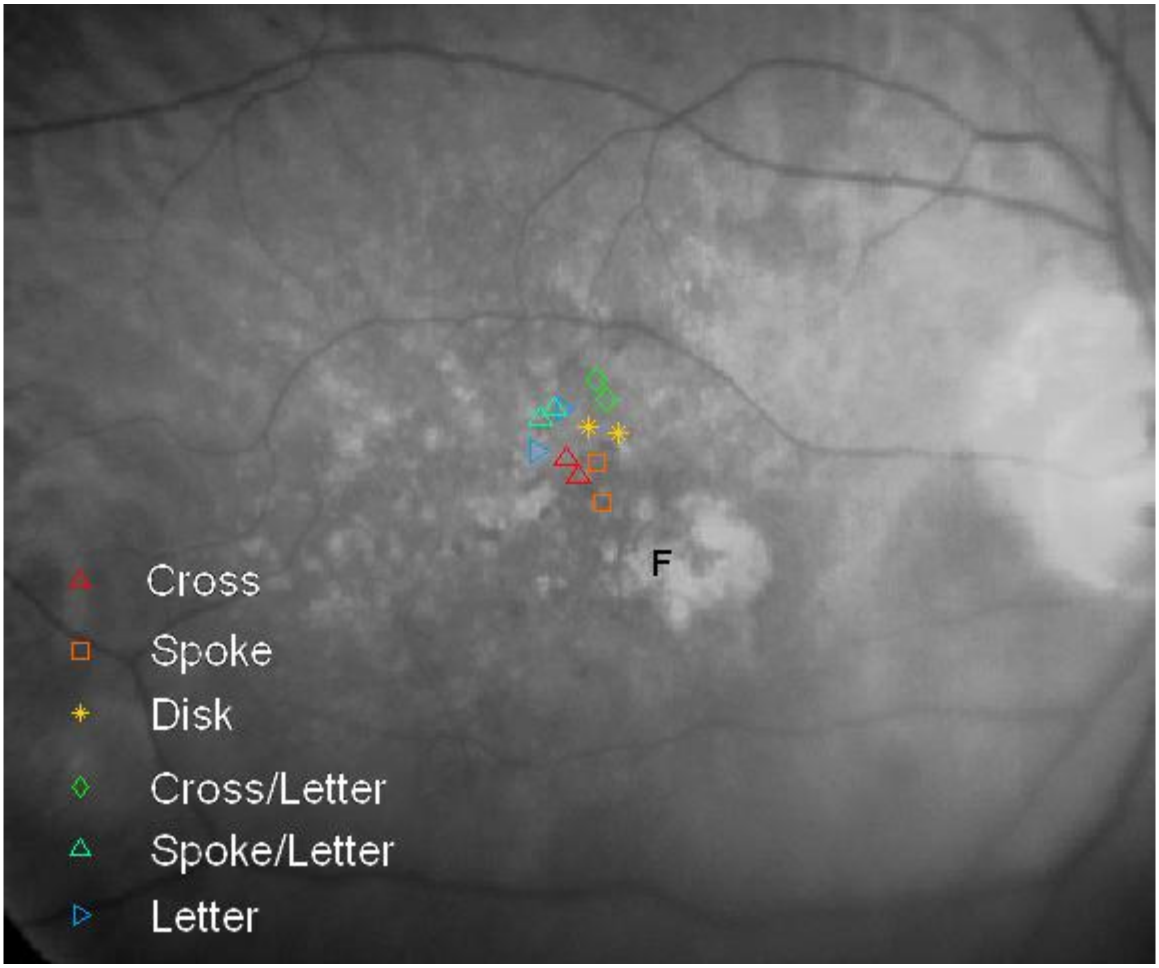


Figure 15. Subject 39's median fixation location for 6 target types. Each target was presented twice. The approximate position of the fovea as determined from OCT images is labeled with an F.

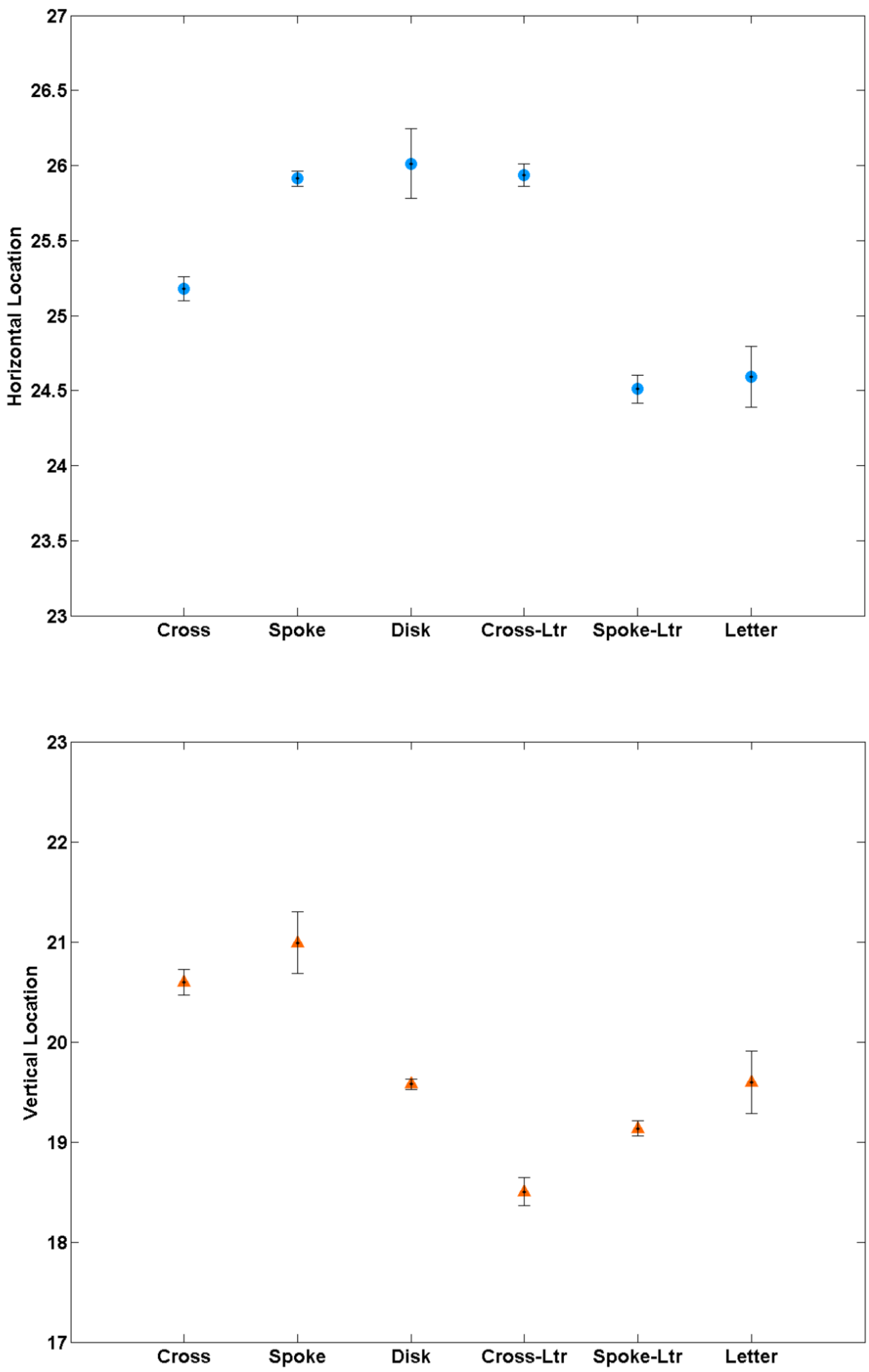


Figure 16. Subject 39's median horizontal and vertical fixation location for six target types. Position (in deg) is measured from top left of image.

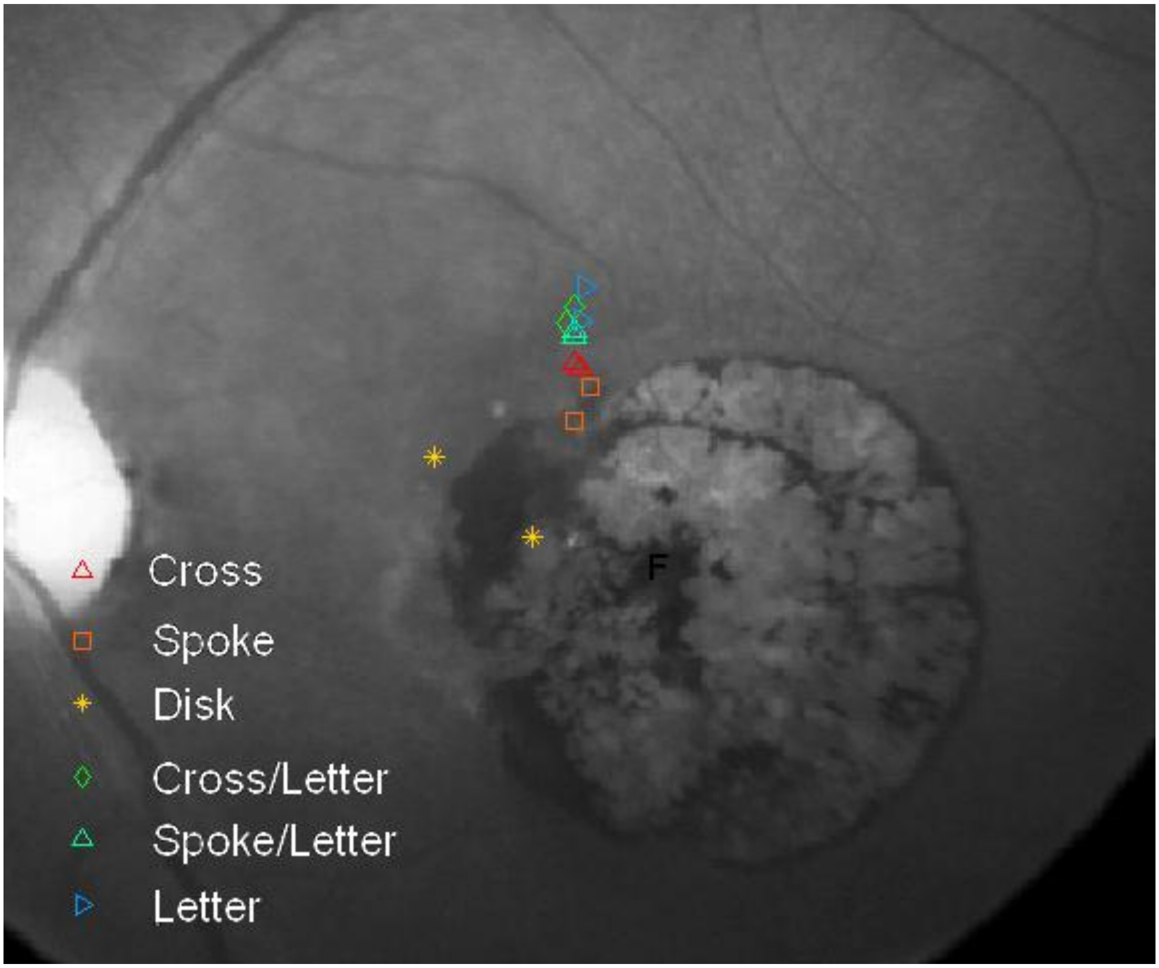


Figure 17. Subject 44's median fixation location for 6 target types. Each target was presented twice. The approximate position of the fovea as determined from OCT images is labeled with an F.

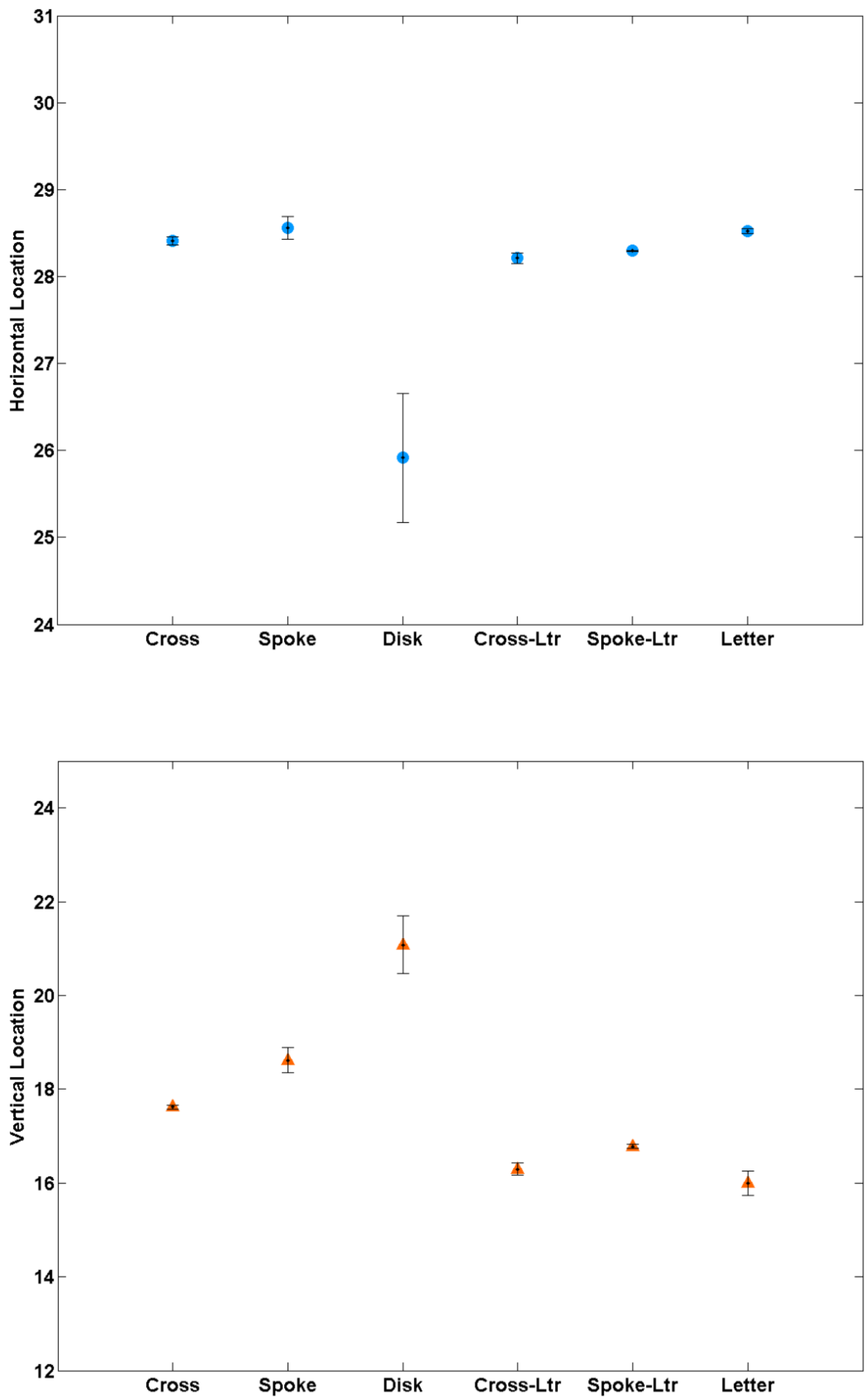


Figure 18. Subject 44's median horizontal and vertical fixation location for six target types. Position (in deg) is measured from top left of image.

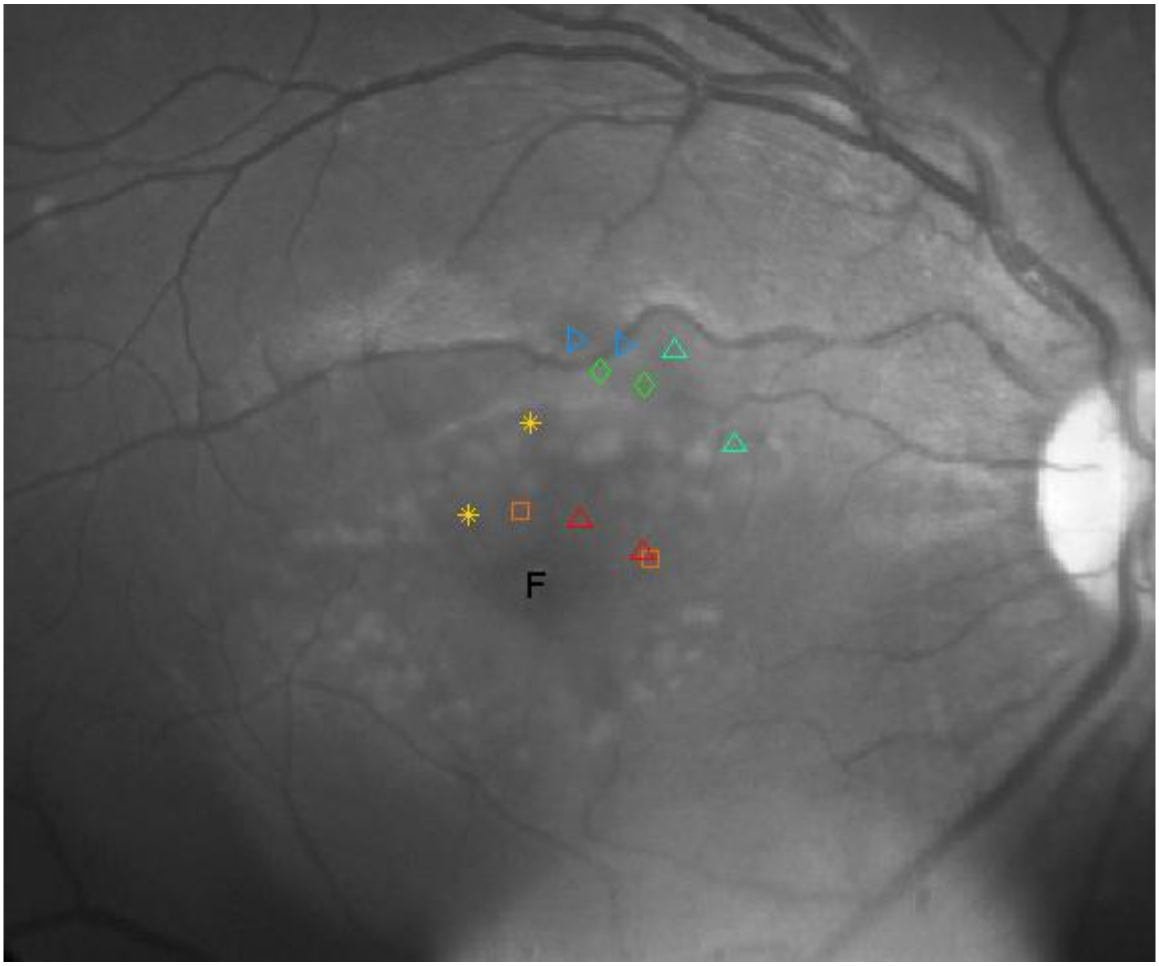


Figure 19. Subject 59’s median fixation location for 6 target types. Each target was presented twice. The approximate position of the fovea as determined from OCT images is labeled with an F.

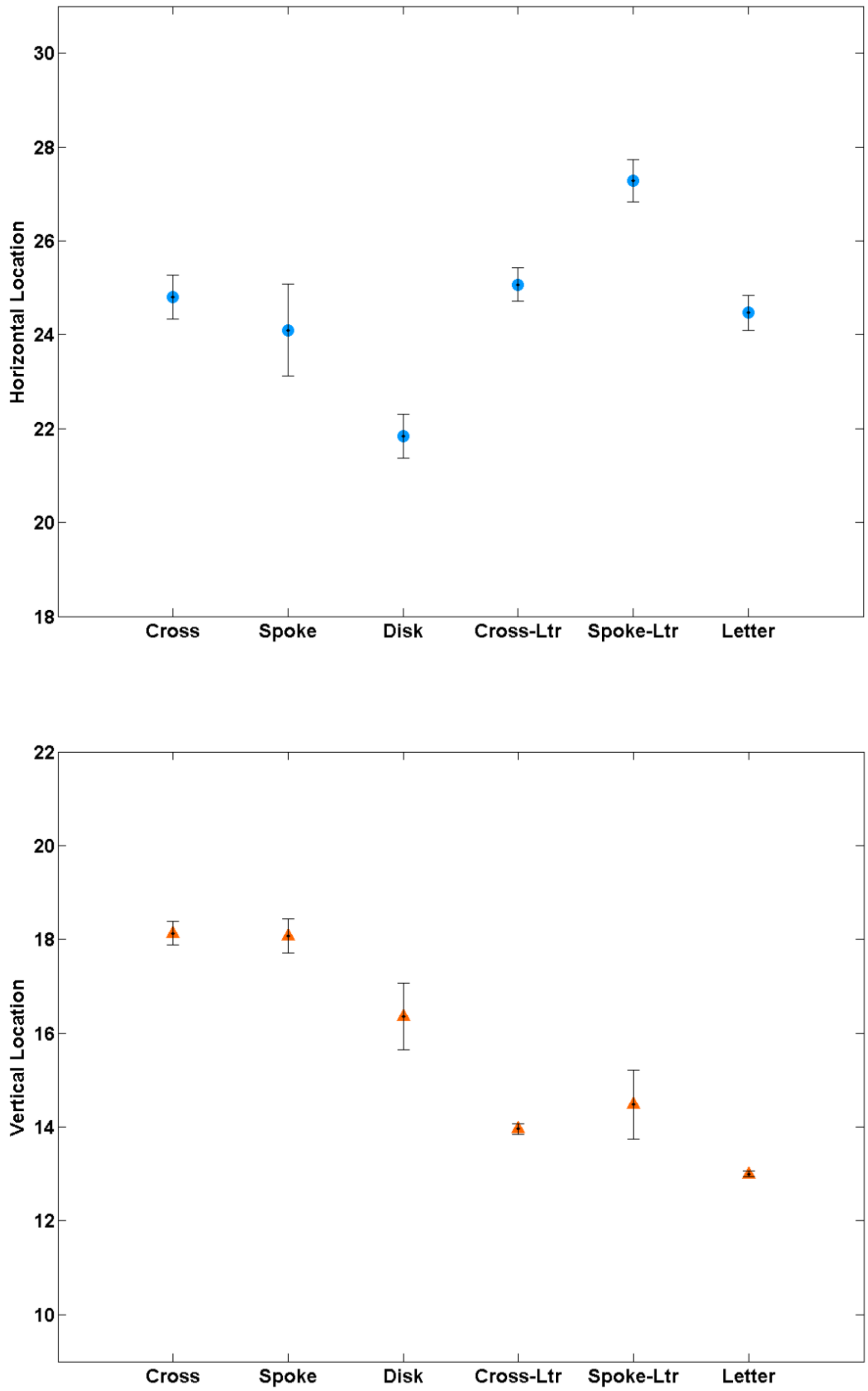


Figure 20. Subject 59's median horizontal and vertical fixation location for six target types. Position (in deg) is measured from top left of image.

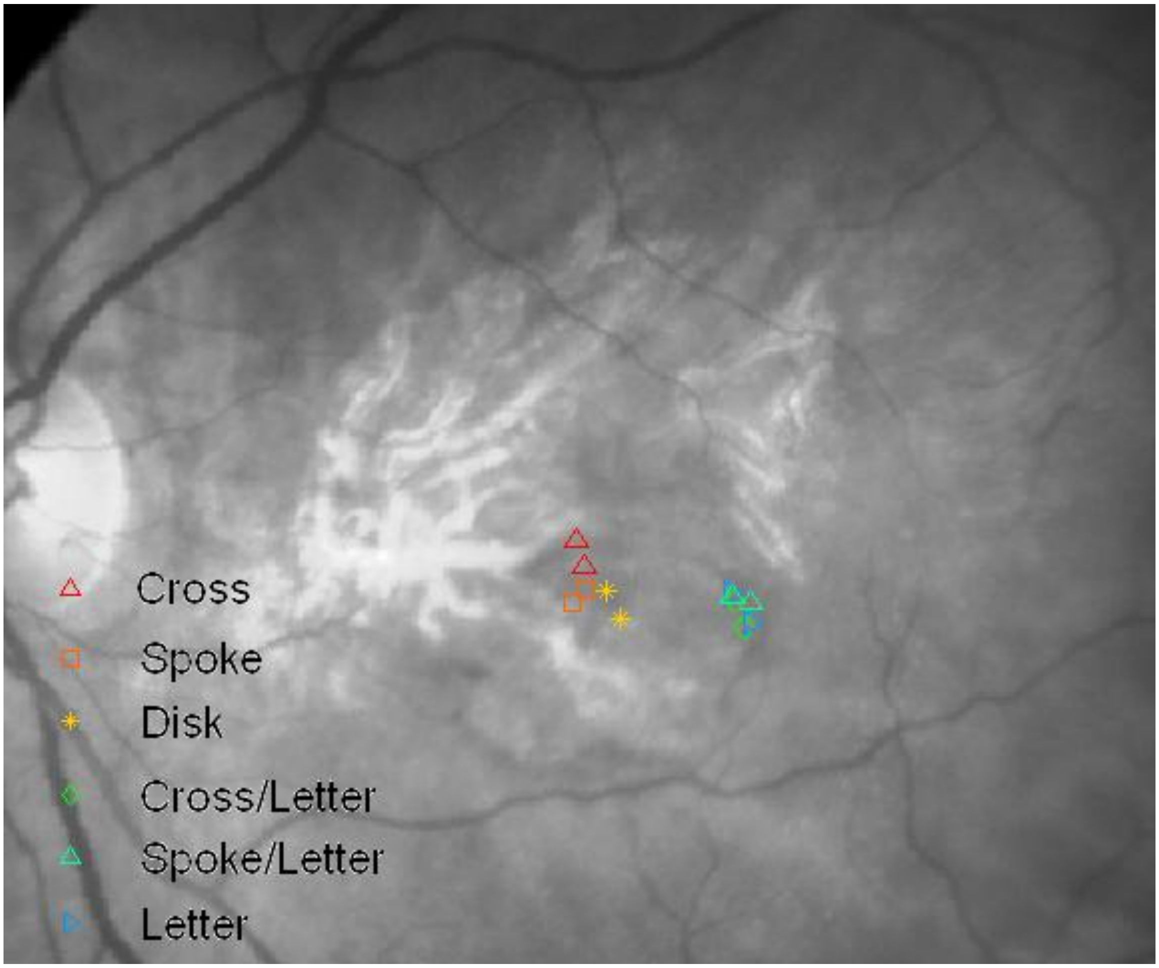
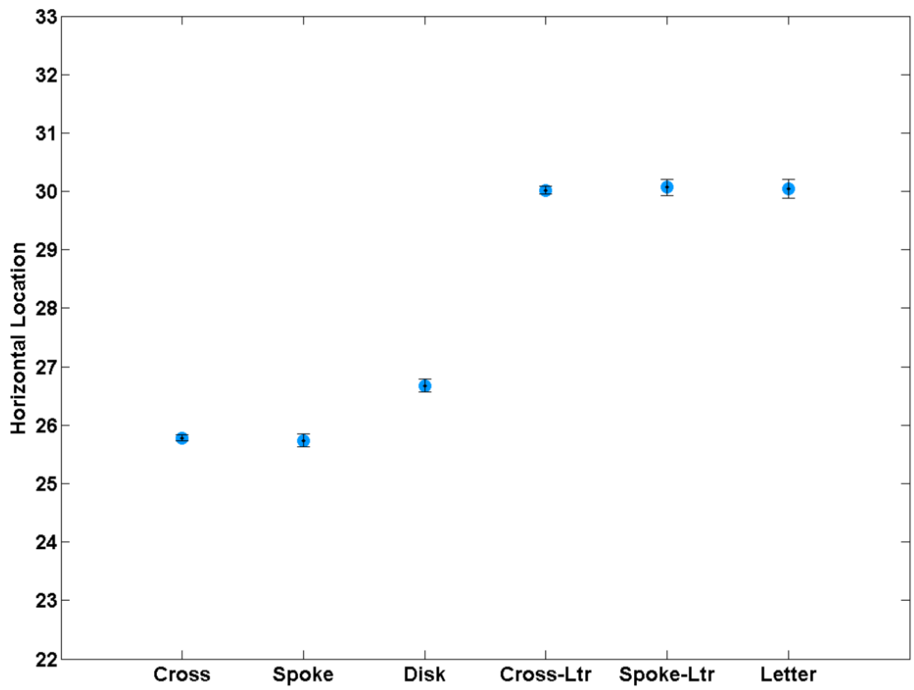


Figure 21. Subject 60’s median fixation location for 6 target types. Each target was presented twice.



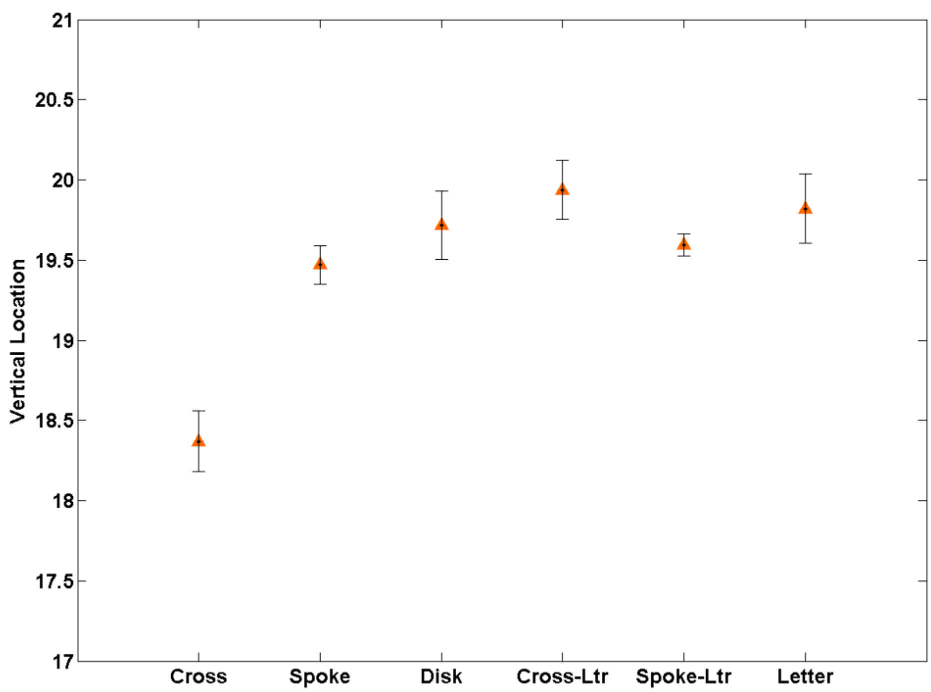


Figure 22. Subject 60's median horizontal and vertical fixation location for six target types. Position (in deg) is measured from top left of image.

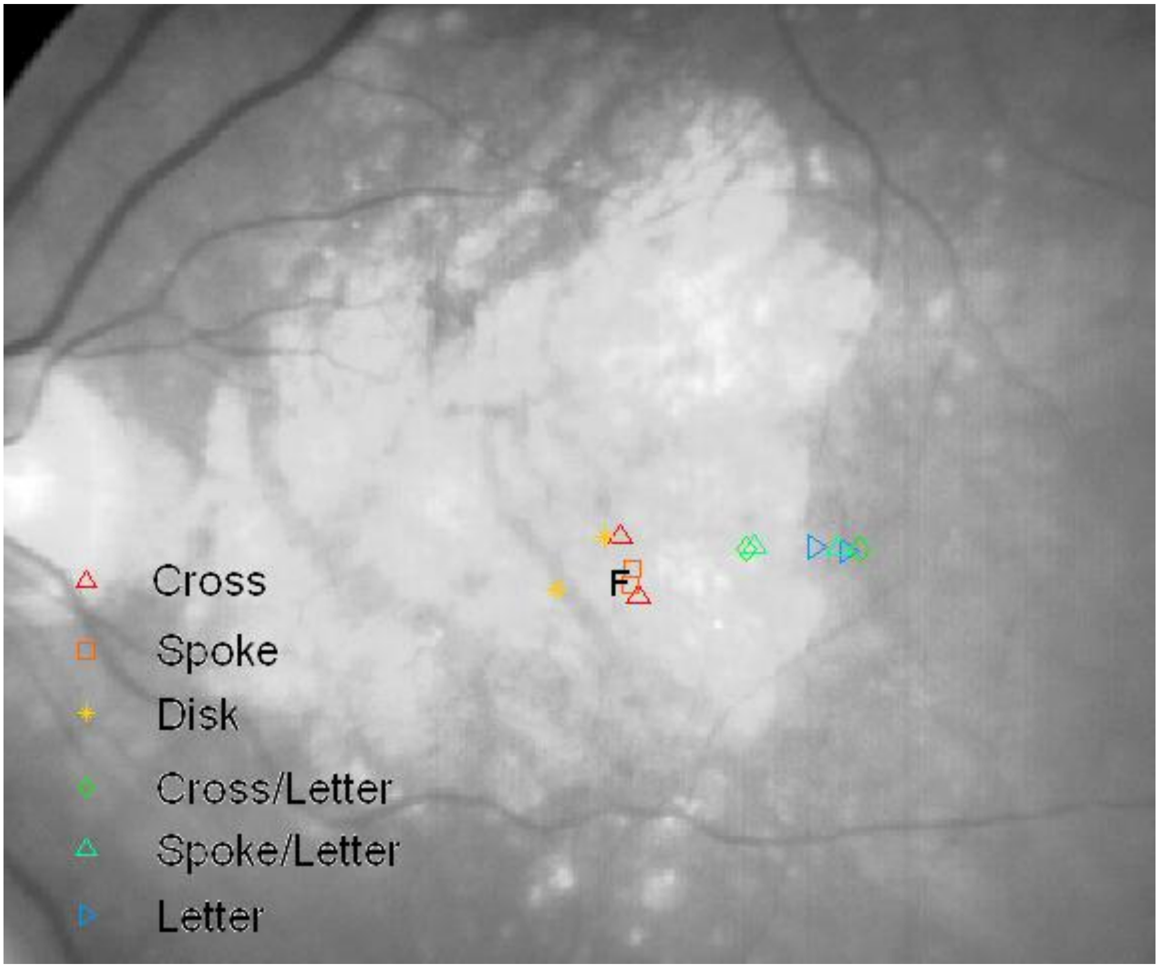


Figure 23. Subject 61's median fixation location for 6 target types. Each target was presented twice. The approximate position of the fovea as determined from OCT images is labeled with an F.

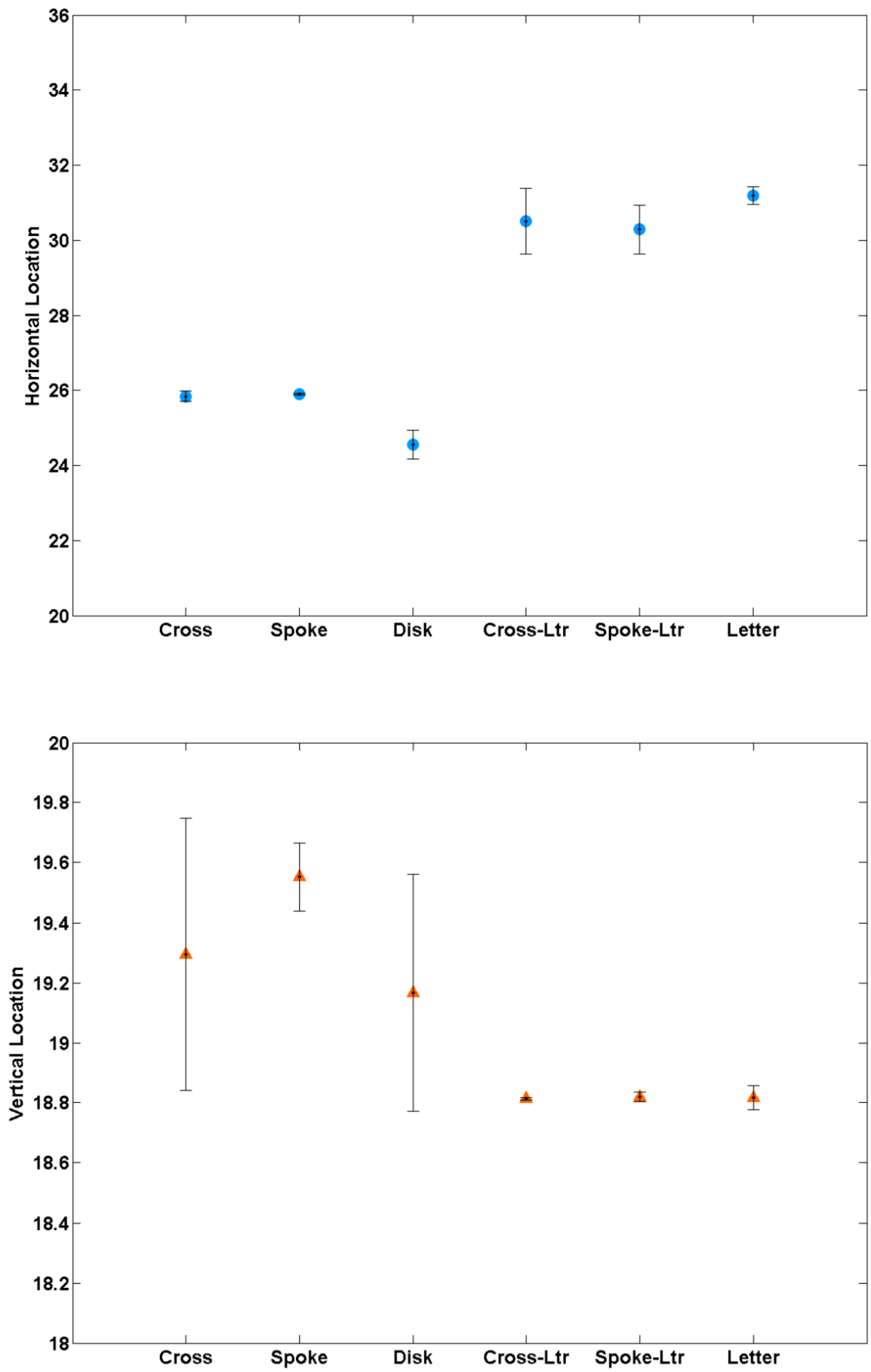


Figure 24. Subject 61's median horizontal and vertical fixation location for six target types. Position (in deg) is measured from top left of image.

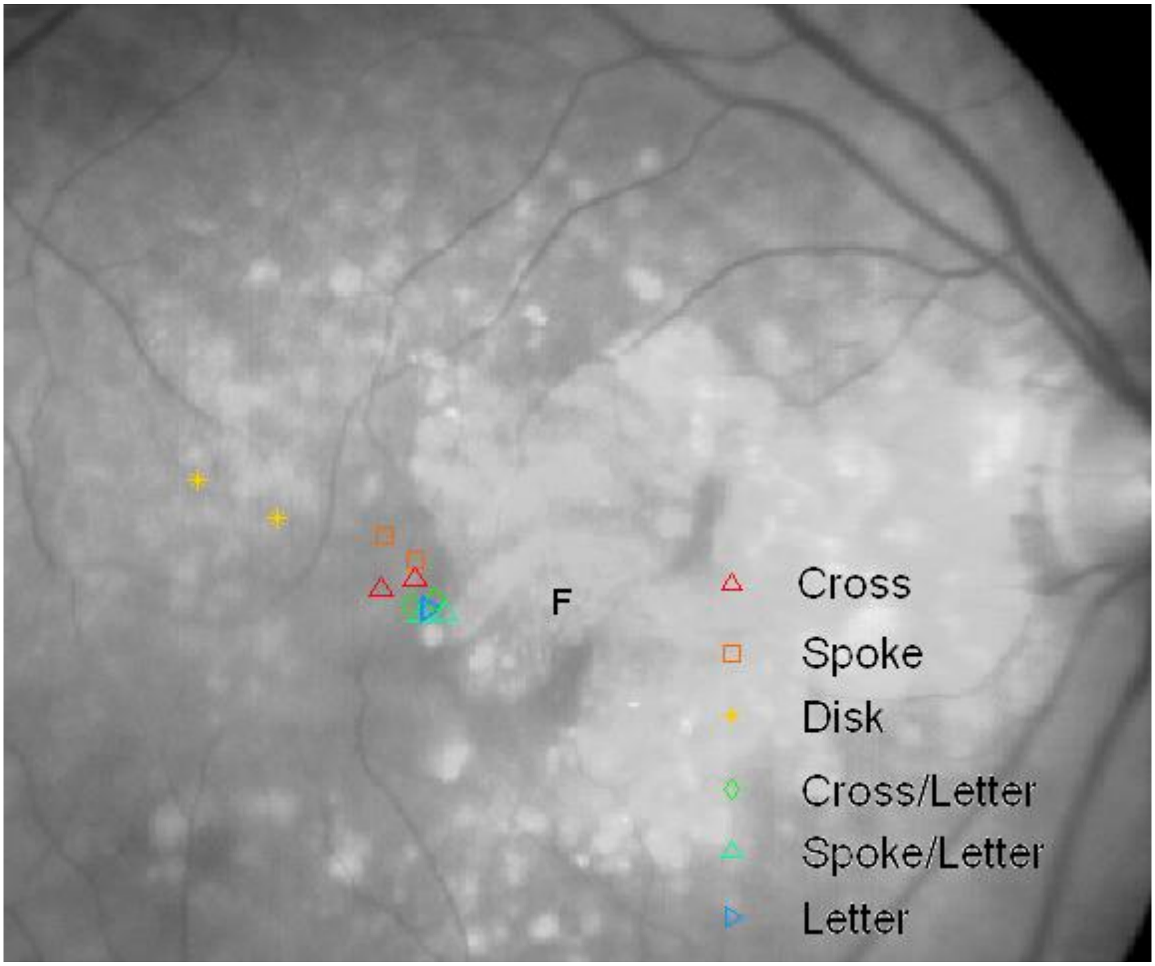
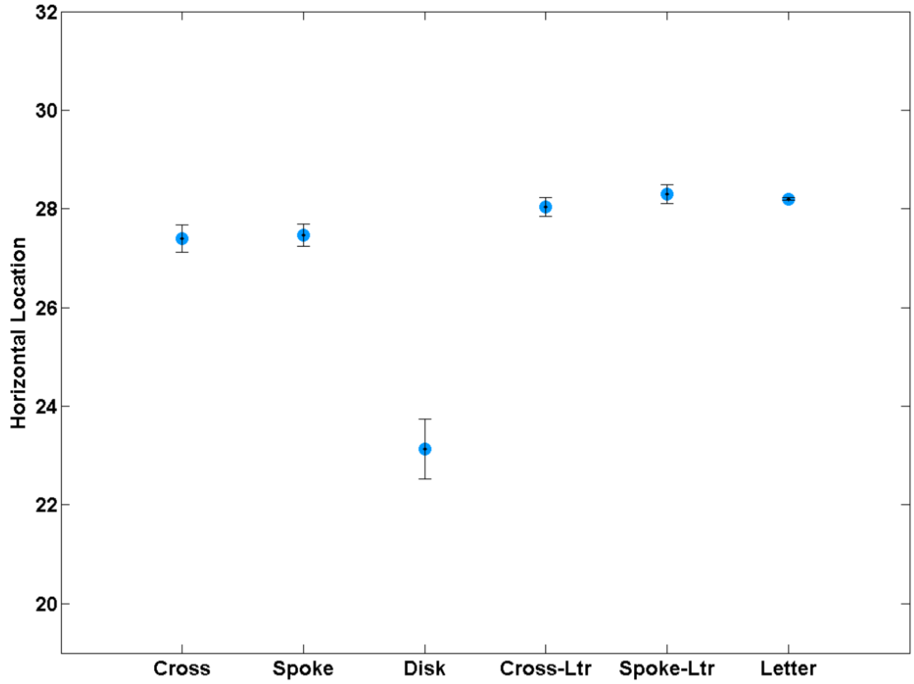


Figure 25. Subject 62’s median fixation location for 6 target types. Each target was presented twice.



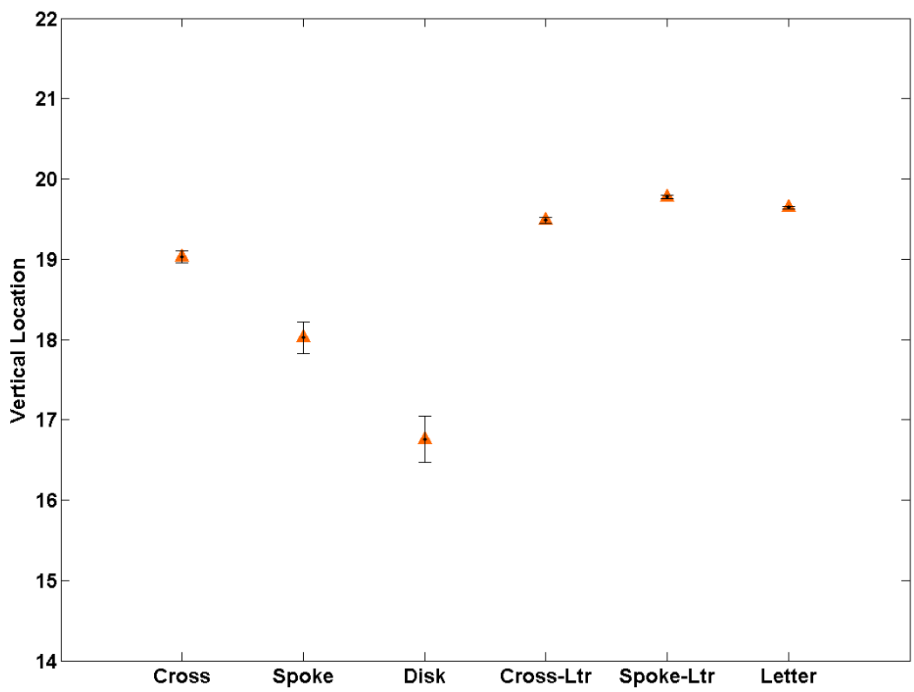


Figure 26. Subject 62's median horizontal and vertical fixation location for six target types. Position (in deg) is measured from top left of image.

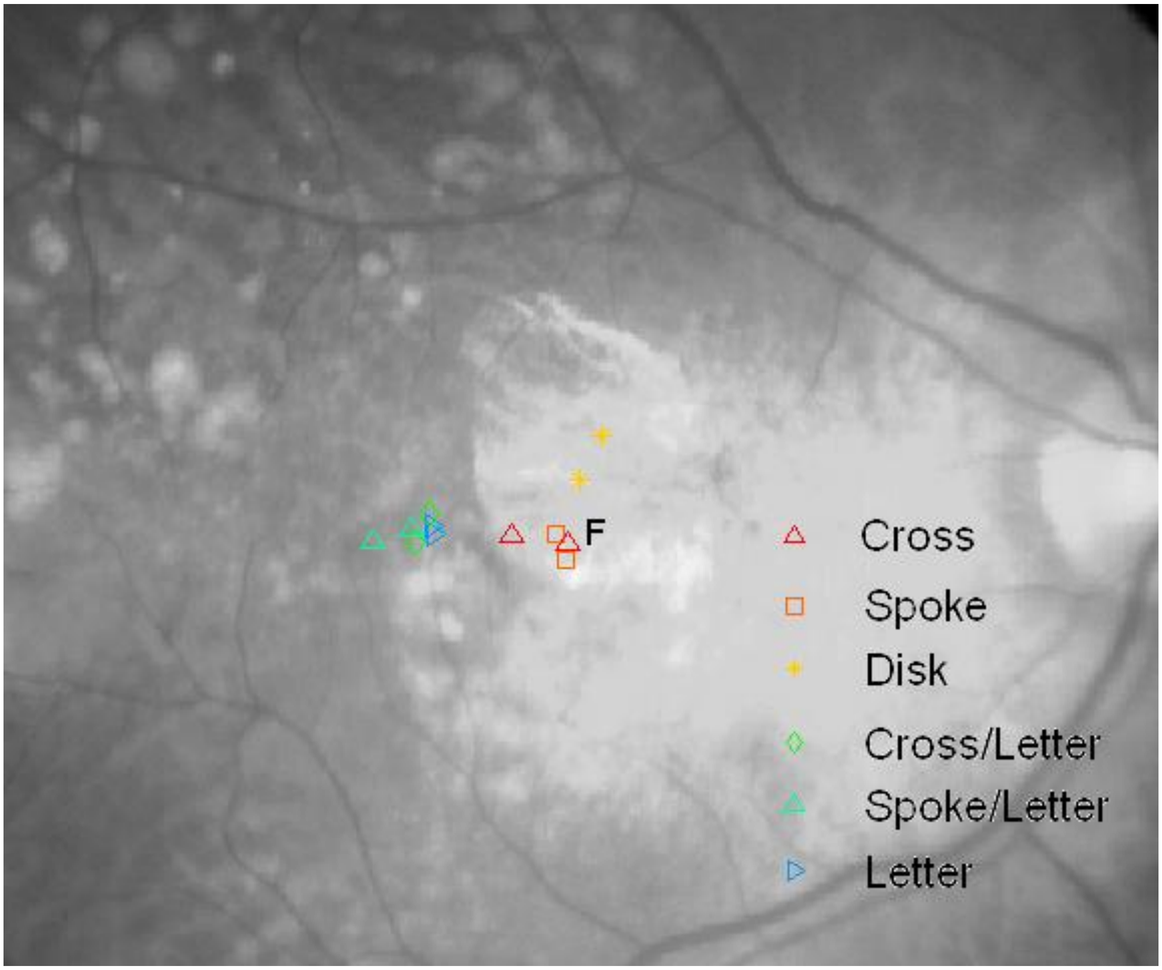


Figure 27. Subject 66’s median fixation location for 6 target types. Each target was presented twice. The approximate position of the fovea as determined from OCT images is labeled with an F.

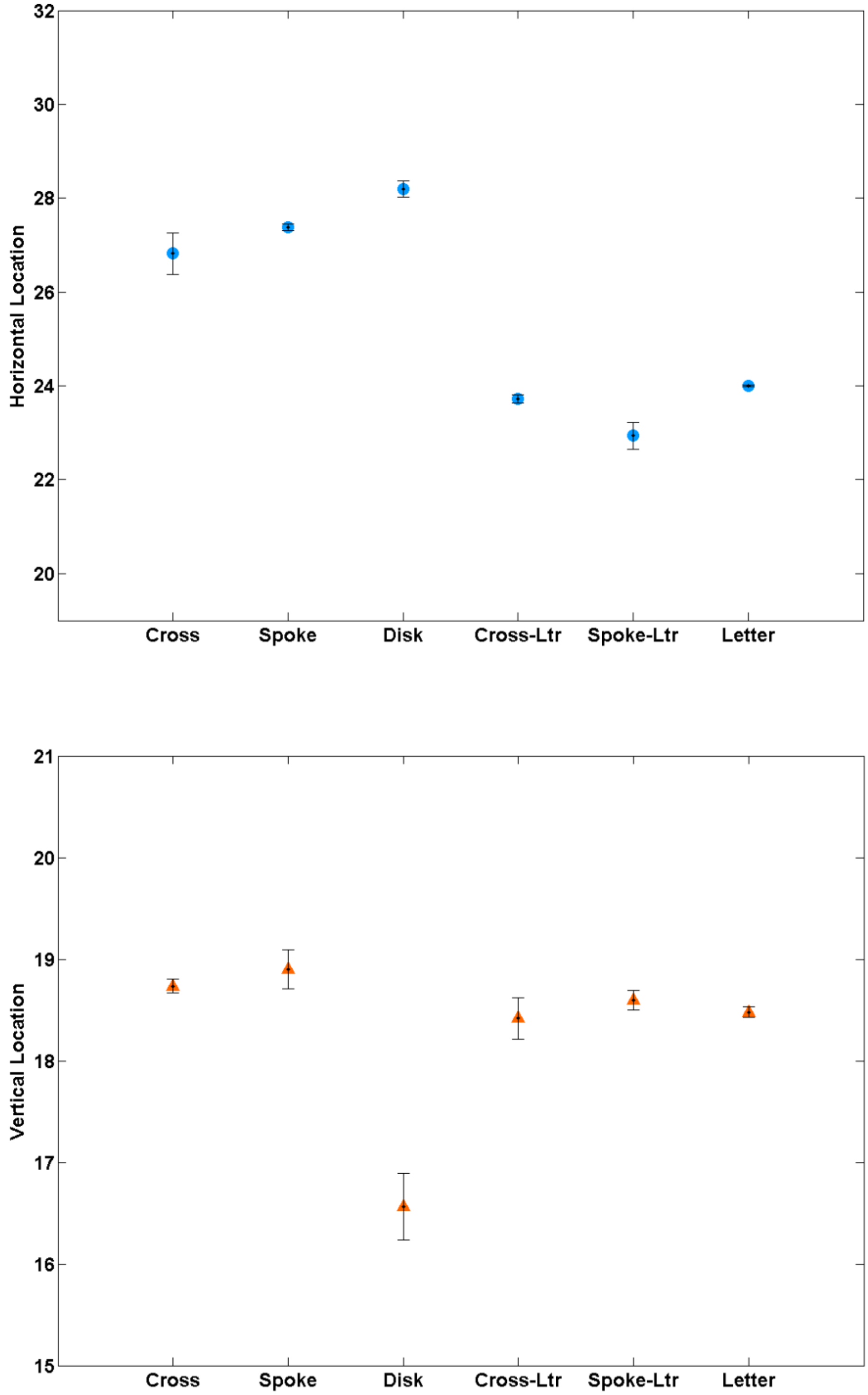


Figure 28. Subject 66’s median horizontal and vertical fixation location for six target types. Position (in deg) is measured from top left of image.

Table 3. Comparison of BCEA between target types for individual subjects. c = cross, s = spoke, cl = cross-letter, sl = spoke-letter, d = disk, l = letter

	Overall		c/s vs. cl/sl		d vs. all		cl/sl vs. l	
Subject	*F*	*p*	*F*	*p*	*F*	*p*	*F*	*p*
10	4.926	0.0389	5.002	0.0667	18.906	0.0048	0.108	0.7536
11	0.744	0.6183						
21	2.256	0.1753						
28	2.184	0.1846						
37	8.583	0.0105	22.796	0.0031	14.278	0.0092	0.014	0.9107
39	0.661	0.6667						
44	2.003	0.2111						
59	1.668	0.2746						
60	2.815	0.12						
61	1.324	0.3666						
62	1.897	0.2291						
66	4.21	0.546						

2.4 Discussion

The difference in fixation location for large targets that span the scotoma and are expected to fill-in from those targets with letters suggests that the occulocentric visual direction has not completely shifted to the PRL. Many of the patients also imaged the center of the fill-in targets within the scotomatous region and four of the patients imaged the center at the vestigial fovea, further demonstrating the lack of complete re-referencing of the oculomotor system and providing evidence for perceptual filling-in of large targets. However, six patients demonstrated the use of a retinal locus not at the vestigial fovea and in the direction of the PRL to view the large fill-in targets suggesting a partial shift in occulocentric visual direction toward the PRL.

A study by Schuchard and Raasch looked at fixation location with pericentral targets in which they expected to find a difference in fixation locus based on instructions (Schuchard and Raasch 1992). They believed that patients would fixate with their vestigial fovea if asked to move their eye to point directly at the center of the target, whereas the patient would use their PRL if asked to move their eye to best see the target. This was similar to the expectations in our experiment except we expected subjects to use different retinal loci based on target type as opposed to solely instructions. Our results concur with those found by Schuchard and Raasch. Although they weren't specifically looking for it, Schuchard and Raasch found a difference in fixation location for large pericentral targets and a smaller cross. Unlike their results, however, we had multiple individuals image the large fill-in targets within the scotoma and close to the vestigial fovea. Also, all but one of our subjects imaged the large targets closer to the fovea. Scuchard and Raasch had one individual (the younger patient with Stargardts) image the pericentral targets at the fovea. Both of our studies indicate that large pericentral or fill-in targets are unsuited for predicting the fixation location, as different subjects did not consistently use the vestigial fovea to image the larger targets.

The observation that subjects imaged one or more of the fill-in targets within the scotoma indicates that these target types cannot be used for eccentric viewing training if the examiner wants the patient to fixate with the PRL. We could not make a precise determination of whether subjects were using the vestigial fovea to fixate the center of the fill-in targets because of pathological changes in retinal morphology. However, it appeared from OCT scans or the fundus image that patients 11, 21, 61 and 66 were using an area relatively close to the vestigial fovea to view the fill-in targets while with subjects 28, 37, 39, 44, and 62 it was apparent they were using an alternate locus. Therefore, the large fill-in targets appear unsuited for eliciting “fixation” at the vestigial fovea in all patients. Therefore, care should be taken in clinical practice as well as research studies in which it is sometimes assumed that a patient will place the vestigial fovea or scotoma over the center of a large pattern such as the radial pattern used in tangent-screen perimetry.

Letter targets appear best suited for eccentric viewing training or for mapping the scotoma location relative to the PRL as they elicit fixation at the location of the PRL and rarely do patients image them within the scotoma (Timberlake et al. 1987). A letter target also gives the examiner and the patient feedback as to whether the patient is maintaining fixation outside the scotoma as the letter will disappear if imaged within the scotoma. Fixation stability was also found to be better for the letter targets. Better fixation stability will result in better test reliability.

The majority of the patients reported the large targets to be perceptually complete, despite much of the target being covered by the scotoma and the center of the target frequently being placed near the center of the scotoma (see appendix Table 14). This result agrees with prior research demonstrating perceptual fill-in at the pathological blind spot and provides evidence for filling-in of additional target types. Zur and Ullman (2003) demonstrated filling-in of gratings and uniform dot patterns. Filling-in of a single 0.73 deg wide line also occurred for one of the three subjects in their study. The two other subjects perceived a gap in the line and reported it as incomplete, demonstrating a lack of complete fill-in of single lines.

Why subjects may perceive a uniform pattern as complete but not a line is unclear but may be related to the amount of visual information received from a stimulus. In our study the target that was most similar to a line was the cross, which was perceived as complete by most subjects. The perceptual filling-in of the cross target may have been secondary to the increase in information provided by two lines or from a larger line thickness than in the Zur and Ullman study (1.5 deg vs. 0.73 deg). In addition, our target presentation was different than that used by Zur and Ullman, who limited the stimulus duration to 400 ms. We asked the subject what they perceived after they had fixated the target for at least 30 s. The additional time would allow for greater visual information from exposures at multiple retinal image locations. Despite this additional information, many of the patients reported areas of the target that appeared faint or blurry, indicating that the filling-in process was not always complete and that there may be varying levels of perceptual filling-in.

Chapter 3

Reading Speed and Reading Eye Movements with Simulated Central Scotomas of Varying Visibility and Linguistic Content

3.1 Introduction

It is a common clinical observation that patients with bilateral central scotomas are not fully aware of their scotomas. Reduced awareness of the scotoma border and location may contribute to ineffective oculomotor control, the placement of text in a non-optimal location relative to the scotoma, and inappropriately directed attention. It can be difficult for patients to understand how they must move and position their eyes to use their remaining peripheral vision. As a result the current methods of eccentric viewing training are likely inadequate in helping patients to correctly position their eye and make useful eye movements especially when viewing paragraph text.

Experiments 2 and 3 examined whether reading speed in normal subjects is affected by the visibility and information content of simulated central scotomas. In experiment 2 reading speed was expected to be slower with a less visible simulated scotoma composed of random letters (mixed-text) than with a more visible random-dot scotoma. If reading rate is slower with the less visible scotoma, it is feasible to expect reading in patients with central scotomas to be affected by perceptual filling-in. In experiment 3 two additional scotomas that were variations of the mixed-text scotoma were used to delineate whether the linguistic information or the visibility of the simulated scotomas resulted in an observed difference in reading rates between scotoma types. It was expected that reading rates with the two additional scotoma types would each be slower than with the random-dot scotoma but faster than the mixed-text scotoma. This would indicate that both information content and scotoma visibility contribute to slower reading rates with simulated scotomas in normal subjects. If both visibility and linguistic information contribute to decreased reading rates, reading speed in patients with bilateral central scotomas is likely to improve if both the scotoma location is made more visible and the information content of the scotoma is decreased.

3.2 Methods Experiment 2

3.2.1 Subjects

Seven students and three faculty members from the University of Houston College of Optometry as well as two additional middle-aged adults participated in the study. All twelve subjects had normal visual acuity and no ocular pathology except for mild cataracts in one individual. All subjects had a basic knowledge of macular degeneration and the visual changes that accompany this disease but none had previous experience with a simulated scotoma. Five of the twelve subjects had a basic knowledge of eccentric viewing and two of the twelve subjects had advanced knowledge of eccentric viewing and had administered eccentric viewing training to patients.

3.2.2 Simulated Scotoma

Subjects read aloud a series of 40 – 60 MNRead style sentences, which they viewed monocularly with one of two simulated central scotomas. One scotoma (random-dot scotoma) was composed of random dark and light squares twelve minutes by twelve minutes, the stroke width of a one degree letter. The random-dot scotoma was highly visible. The other, less visible scotoma (mixed-text scotoma) was composed of random letters with the same background luminance and word spacing as the text (Figure 29). The background luminance of the monitor outside the lens system was 430 cd/m^2. Each sentence was checked to ensure that the words aligned in both the mixed-text and normal sentences and that there were no words spelled in the mixed-text 'sentences'. If a word was encountered, the first letter of the word was changed to the next letter in the alphabet that did not spell a word.

Two display pages were used during each trial to create the simulated scotoma. The first page consisted of the MNRead sentence to be read and the second page was composed of the simulated scotoma image (Figure 30). The first page was displayed at every location on the screen except for a four-by-four degree square window through which the second page was displayed. Horizontal and vertical eye movement signals sampled at 120 Hz from a dual-Purkinje eyetracker (Crane and Steele 1985) were used to move the simulated scotoma window with the center of gaze.

The delay of scotoma update was measured with a UDT PIN 10DP photocell placed over a uniformly black simulated scotoma on the display screen. A model eye was mounted on a galvanometer in the dual-Purkinje eyetracker and driven with a square wave signal from a function generator to generate simulated oblique saccades. The simulated scotoma moved back and forth on the display screen during the simulated eye movements. The change in luminance registered by the photocell was compared to the position signals from the galvanometer to measure the delay between saccade onset and movement of the scotoma. Delay of scotoma update was no greater than one frame or 8 ms.

3.2.3 Dual-Purkinje Eyetracker Calibration and Set-up

Subjects were positioned with a mouth bite and a head rest to minimize head movements. They were required to keep their upper teeth in the mouth bite while dropping their lower jaw to read aloud. The right eye was patched and the experiment carried out with the left eye for each subject.

During calibration, subjects were asked to fixate a small laser spot which was moved to the edge of displayable text while the position of a uniformly black square, the size of the simulated scotoma used in the experiment, was continuously displayed on the monitor. The horizontal and vertical dc position and the gain of eye movement signals were adjusted so the location of the black square remained centered on the laser spot in all directions of gaze. This allowed the simulated scotoma to be accurately updated and displayed continuously at the fovea, covering the central four degrees of the visual field during the experiment. The screen was immediately blanked whenever the eye tracker signaled that the eye-position signal was lost, including during blinks, which prevented the subjects from accidentally viewing the text with the fovea.

Sentences were 60 characters in length and comprised four lines of fixed-width dark courier text (Mansfield, Legge, and Bane 1996) with a lower-case ‘x’ height of one degree and a spacing between the center of adjacent letters of 1.4 degrees. A one degree letter was used based on the critical print size for normal subjects at 3-4 degrees eccentricity (Chung, Mansfield, and Legge 1998). The text was presented as black letters on a bright background on a 19 inch monochromatic Image Systems monitor, viewed at optical infinity through a visual stimulus deflector (Crane and Clark 1978). The field of view was limited by the lens system of the stimulus deflector to thirty degrees. Contrast was approximately 95%. Sentence sequences were randomly generated from a set of 271 sentences and no sentence was repeated within a sequence. Half of the subjects started reading with the random-dot scotoma; the other half started with the mixed-text scotoma and scotoma type was alternated in blocks of 10 trials.

Subjects were instructed that one of two simulated scotomas would obstruct their central vision and they would have to use their peripheral vision to the left, right, above or below the scotoma to read. Before each sentence the subject was cued and the trial was stopped when the subject read the last word of the sentence correctly. For the purpose of recording and storing the eye movement data, each trial was limited to a maximum length of 64 seconds. Some of the subjects were not able to read the first few sentences with the mixed-text scotoma within 64 seconds. However, in general, subjects were able to accurately read the sentences within the allotted time.

3.2.4 Eye Movement Analyses

Vertical and horizontal eye-position records during each trial were analyzed using custom Matlab programs. Horizontal and vertical eye velocity was calculated by dividing the angular difference between adjacent eye-position samples by the time between samples (8.33 ms). A velocity greater than 15 deg/s in absolute magnitude was used to identify the onset and completion of saccades. Velocity noise was less than a third of the chosen saccade threshold, corresponding to approximately 4 deg/s. Eye-position data for the beginning and end of each saccade were used to calculate saccadic amplitude and direction. Only saccades with amplitude greater than one degree (1 letter size) were included in subsequent analyses to limit the influence of fixation eye movements within the same letter.

The average amplitude of saccades was calculated for each reading trial. Saccades per second were determined by dividing the number of saccades by the elapsed time for each trial. Saccades were categorized as horizontal (orientations between 330 – 30 and 150 – 210 deg), vertical (60 – 120 and 240 – 300 deg), or oblique (30 – 60, 120 – 150, 210 – 240, and 300 – 330 deg). Saccadic refixations were identified when the end of one saccade fell within 1.4 deg (the center-to-center distance between two adjacent letters) of the starting position of the previous saccade. The average vertical and horizontal eye position for each trial was determined from the median location during fixations, defined as the intervals between saccades.

3.3 Methods Experiment 3

3.3.1 Subjects

Six students, average age 25, and six UHCO staff, average age 61, with normal visual acuity and no ocular pathology read aloud a series of 64 sets of random words with one of four types of superimposed simulated central scotoma. None of the subjects took part in experiment two or either of the preliminary experiments that are described below. The experimental set up was similar to that in experiment two except that four instead of two scotoma types were used and sets of eight random words were substituted for the MNRead style sentences. Random words were used in an effort to increase the difference between the reading speed with the mixed text and random dot scotomas. With a larger difference between these two scotoma types, we hoped it would be easier to measure a difference between the additional scotoma types and the mixed text and random dot scotomas. The elapsed time to read each set of 8 words and eye movement data were recorded as before. The four scotoma types were presented in random order within each block of four trials.

3.3.2 Simulated Scotoma

To differentiate the effect on reading speed of scotoma visibility vs. information content of the artificial scotoma pattern, we altered the characteristics of the mixed-text scotoma to produce a third and fourth scotoma type. The low-luminance scotoma was composed of random letters with the same spacing as the text but with a decreased background luminance (low-luminance scotoma). This scotoma type retained the spurious information content provided by the random letters but made the location and extent of the scotoma more visible.

The flipped-letter scotoma was created by disrupting normal letter orientation. A custom Matlab program flipped each random letter both upside down and left to right while maintaining the same spacing and background luminance as the original text. For those letters that resembled another letter after misorienting them, an additional manipulation of the letter was performed. For example a letter ‘g’ in the dark courier font when flipped and rotated resembled a letter ‘b’, so the leg was cut and displaced centrally (Figure 31). The flipped-letter scotoma was less visible than the random-dot or low-luminance scotomas, but had decreased linguistic information content compared to the mixed-text and low-luminance scotomas because it contained no normal letters.

To determine the change in background luminance needed to render the low-luminance scotoma more visible, contrast thresholds were determined for three subjects. Subjects were asked to view a set of random words while horizontal and vertical eye movement signals were used to impose a change in background luminance on the central four degrees of visual field. The luminance of this region was varied until the subject reported that they could detect a luminance decrement. A Weber contrast of minus 15%, equal to three times the highest contrast threshold of the three subjects, was used to create the background luminance for all subjects.

To verify that the flipped-letter scotoma was less visible than the random-dot and low-luminance scotomas, four other subjects judged the size of each scotoma type compared to a filled square standard. The point of subjective equality for all four scotoma types was similar but the standard deviation of the point of subjective equality, derived from a bootstrap procedure, for the mixed-text and flipped-letter scotomas was 4-5 times larger than the random-dot and low-luminance scotomas. We interpret this outcome to indicate that the boundaries of the flipped-letter scotoma and mixed-text scotomas were less defined than the other two scotoma types. (See appendix Table 15).

3.3.3 Word Sets

Word sets containing eight frequently used English words were generated using a word frequency list from the Corpus of Contemporary American English (Davies). The word sets were composed of four lines of two word pairs; five and six letter pairs formed two of the lines and four and seven letter pairs formed the other two lines for a total of 48 characters. The four and seven letter words were randomly paired as were the six and five letter words. These pairs were then used to generate 120 word sets by randomly choosing two six/five letter pairs and two seven/four letter pairs and randomly assigning the order of the pairs.

A. B.

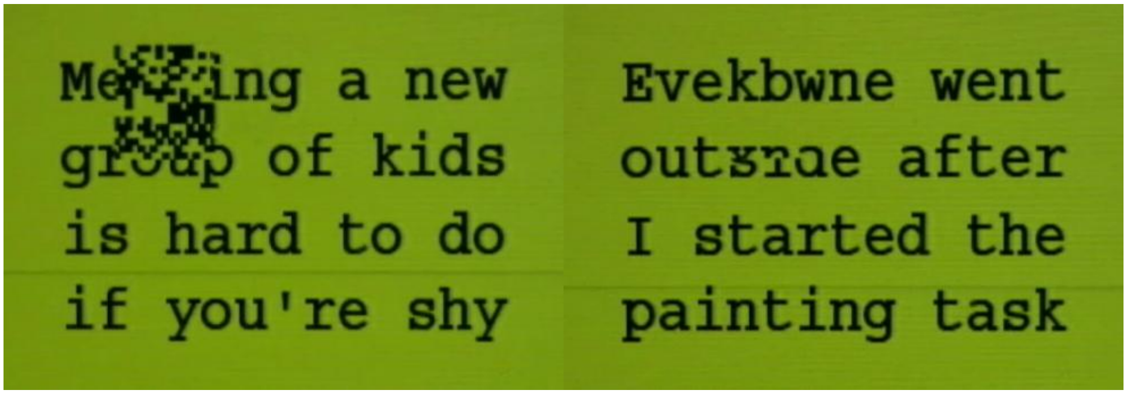


Figure 29. Simulated Scotoma Types. Random-dot scotoma (A) and mixed-text scotoma (B, upper left region of the text).

Figure 30. Display pages used to create the simulated scotoma demonstrating the window through to the scotoma page. The location of this window on the display was moved with the measured horizontal and vertical eye position.

A. B.

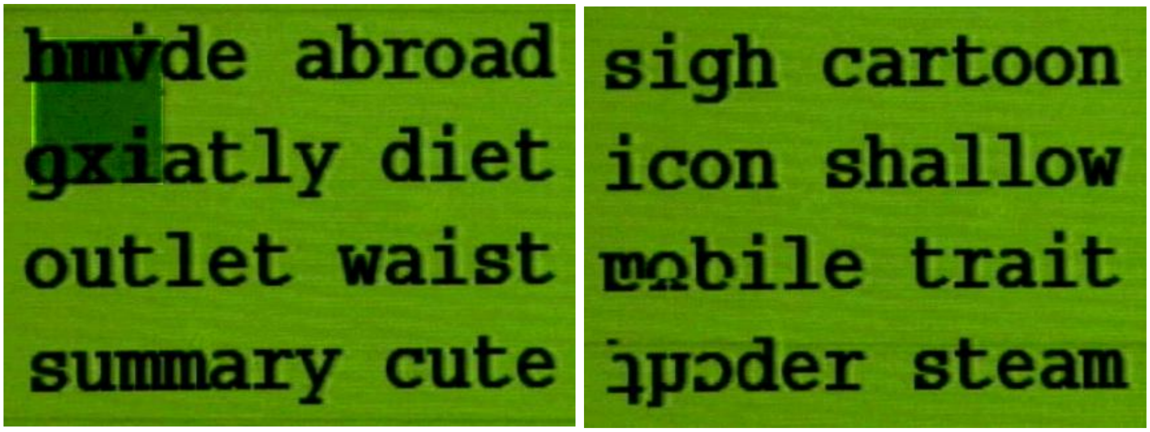


Figure 31. Two additional scotoma types used in Experiment 3. Low-luminance (A) and flipped-letter (B, lower left region of the text) scotomas.

3.4 Results Experiment 2

Elapsed reading times were longer for the mixed-text than for the random-dot scotoma, although the difference decreased over trials for most subjects (Figures 32 and 33). Median elapsed reading time determined for blocks of 10 trials was consistently longer for the mixed-text than the random-dot scotoma, except in one subject for whom the elapsed times were equivalent in the final block of trials (Figure 34).

Subjects adopted different eye-movement strategies for the two types of scotomas. The number of saccades per second was greater for the random-dot scotoma (Figure 35). The proportion of refixation saccades was greater for the random-dot scotoma (Figure 36). The proportion of non-horizontal (vertical + oblique) saccades was greater for the mixed-text scotoma (Figure 37). The average vertical position of fixation during trials was higher for the mixed-text scotoma. For the mixed-text scotoma, most subjects demonstrated an elevation of the vertical fixation location with an increase in the trial number (Figures 38, 39).

In some subjects, changes in the eye-movement characteristics with trial number indicated a change in strategy when reading with the mixed-text scotoma. Saccadic amplitude tended to decrease in subjects who exhibited greater improvement in the mixed-text reading rate (r= 0.68; p = 0.014, Figure 40). The fixation locus tended to shift upward in subjects who exhibited greater improvement in the mixed-text reading rate (r = 0.56; p = 0.057, Figure 11). No significant changes occurred in the number of saccades per second, the proportion of refixation saccades, or the proportion of non-horizontal saccades in association with improvement of the mixed-text reading rate (Figures 41, 42).

Scanpaths from subject 193 illustrate most of the differences between the eye movements with the two types of scotoma and the changes in eye-movement strategy with number of trials (Figure 43).

3.5 Results Experiment 3

Three additional older subjects besides the six included in the analyses below were unable to read while viewing with the mixed text scotoma within the 60 s allotted time period. About a half an hour was spent with each of these subjects coaching them and allowing them to practice reading with the scotomas. Reading ability improved with the random-dot scotoma for 2/3 of these subjects. They were still unable to read with the mixed-text, low-luminance, or flipped scotomas and thus were unable to complete the study.

A factorial repeated measures ANOVA was performed on the data from experiment 3. The independent variable included a between subject variable, the age group, and a within-subject variable, the four simulated scotoma types (flipped, low-luminance, mixed-text, and random-dot). The dependent variable was the median elapsed reading time for each scotoma type. An alpha level of 0.05 was utilized for this analysis. Sphericity was not assumed and the Huynh-Feldt correction for non-sphericity of variances was utilized.

As in experiment 2, there was a significant effect of scotoma type $F(3,30) = 17.49$, $p < 0.001$ and reading speed with the random-dot scotoma was the fastest. There was also a positive interaction in the elapsed reading time between the age group and the simulated scotoma type $F(3,30) = 5.55$, $p = 0.01$. Post-hoc analysis revealed a significant difference between low-luminance and random-dot scotomas $F(1,30) = 23.34$, $p < 0.001$, flipped and random-dot scotomas $F(1,30) = 23.59$, $p < 0.001$, and mixed-text and random-dot scotomas $F(1,30) = 48.82$, $p < 0.001$. The difference between the mixed-text and low-luminance scotomas as well as the difference between the mixed-text and flipped scotomas were barely not significant ($F(1,30) = 4.65$, $p = 0.053$ and $F(1,30) = 4.65$, $p = 0.055$ respectively). The elapsed times for the flipped and low-luminance scotomas were similar, and when the results of the two scotoma types were grouped, were found to be significantly faster than the mixed-text scotoma $F(1,30) = 6.12$, $p = 0.03$.

From plots of the mean elapsed reading time, it appeared that the positive interaction between age group and simulated scotoma type was caused by the greater difference in elapsed time between the random dot scotoma and the other scotoma types in the older age group (Figure 44). An analysis of the data without the random-dot scotoma confirmed this observation $F(3,30) = 0.976$, $p = 0.347$. The average elapsed time for the non-random-dot scotomas for the older subjects was 37 s and for the younger subjects it was 19 s. For the random-dot scotoma, the average elapsed time for the older subjects was 26 s and for the younger subjects it was 16 s (Figure 44).

As in experiment 2 the average vertical position of fixation was different for the different scotoma types. The scotomas containing text (mixed-text, low-luminance, and flipped) had a higher vertical fixation position than the random-dot scotoma both in the older and the younger subjects $t(11) = 4.47$, $p < 0.001$. It was thought that the observed difference in reading speed between the older and the younger subjects may have been explained by a difference in vertical fixation position. However, there was no significant difference in the average vertical fixation position between the older and younger subjects ($t(10) = 1.42$, $p = 0.187$). On the other hand, in older subjects there was a correlation between vertical fixation position and the median reading speed of trials with scotomas containing text ($F(1, 4) = 37.36$, $p = 0.004$), with those subjects that did not adopt a more vertical fixation position having poorer reading rates. These results imply that while adoption of optimal eye movement strategies are important, there are likely other factors, such as a possible decrease in pericentral retinal function with age, that contribute to decreased reading rates in older individuals.

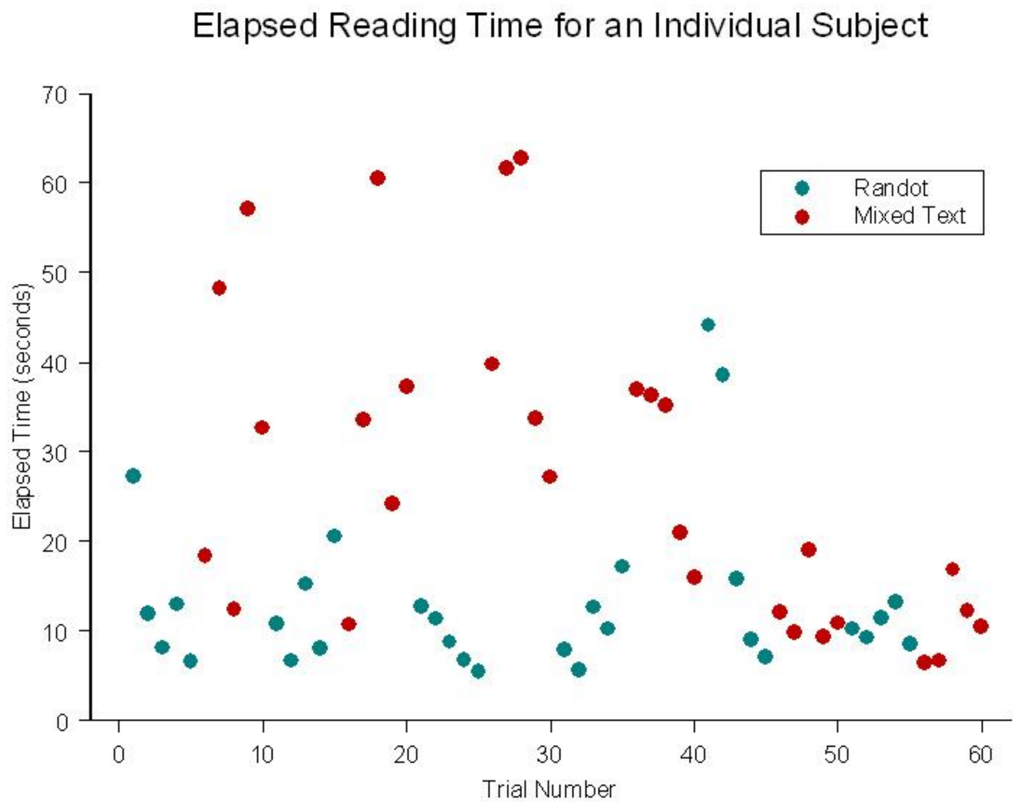


Figure 32. Elapsed reading time for single MNRead sentences is plotted against trial number for subject 193. The red and blue symbols denote trials with the mixed-text and random-dot scotoma respectively.

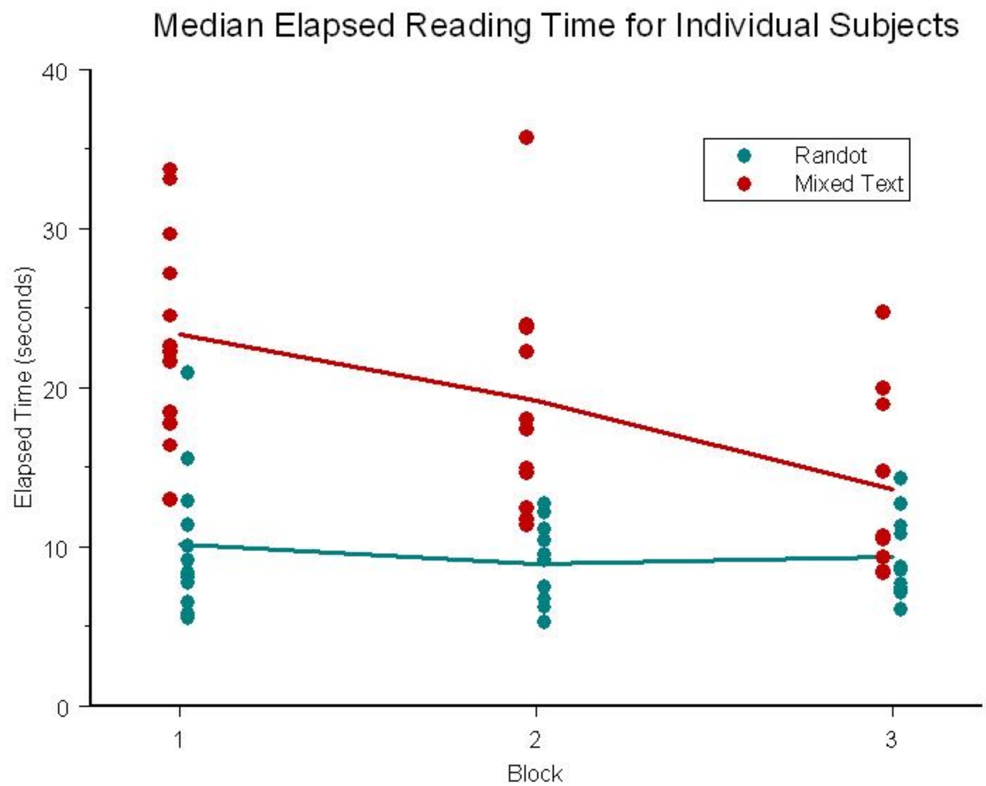


Figure 33. The median elapsed reading time for individual subjects (symbols) and mean time across subjects (lines) are shown for successive blocks of 10 trials of the mixed-text and random-dot scotoma conditions.

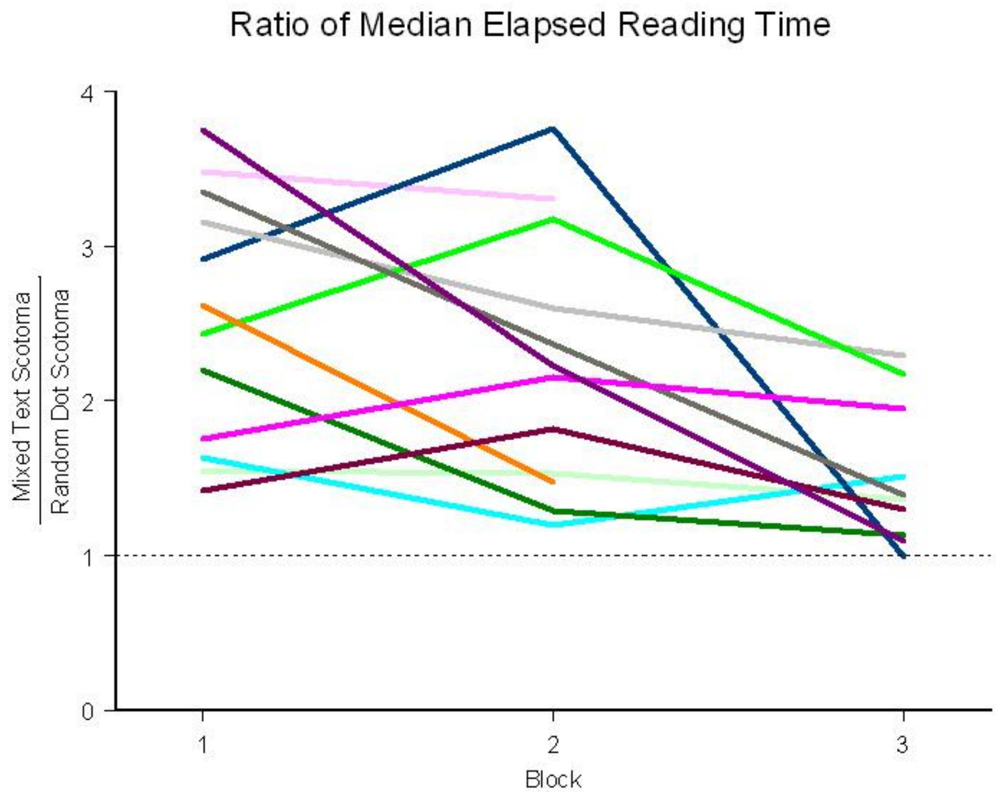


Figure 34. The ratio of elapsed reading time for successive blocks of 10 trials of the mixed-text and random-dot scotoma conditions is shown separately for each subject. Two subjects completed only two blocks of trials per scotoma type.

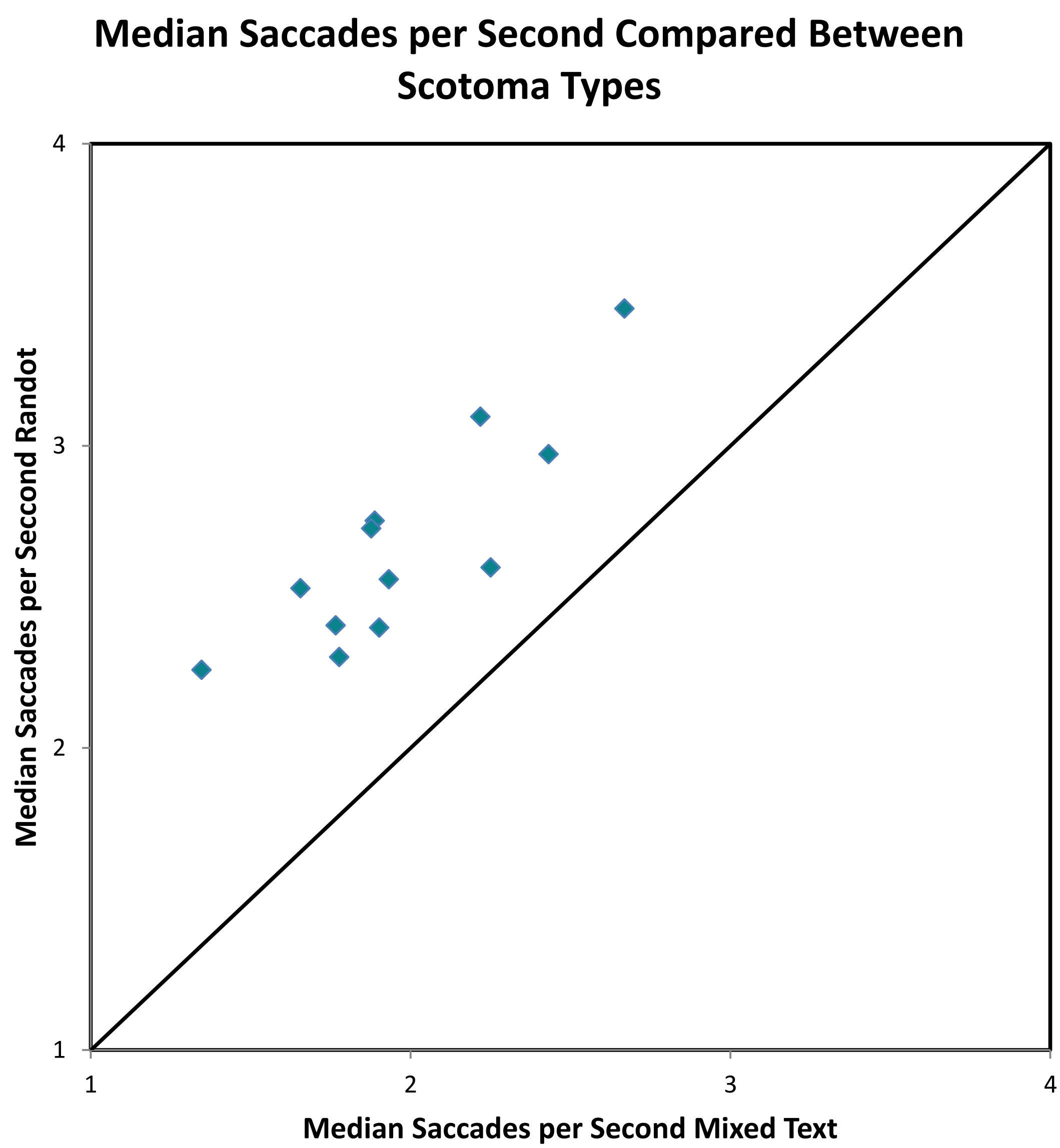


Figure 35. Median saccades per second averaged across all trials for the mixed-text and random-dot scotomas. Each dot represents the data for a single subject.

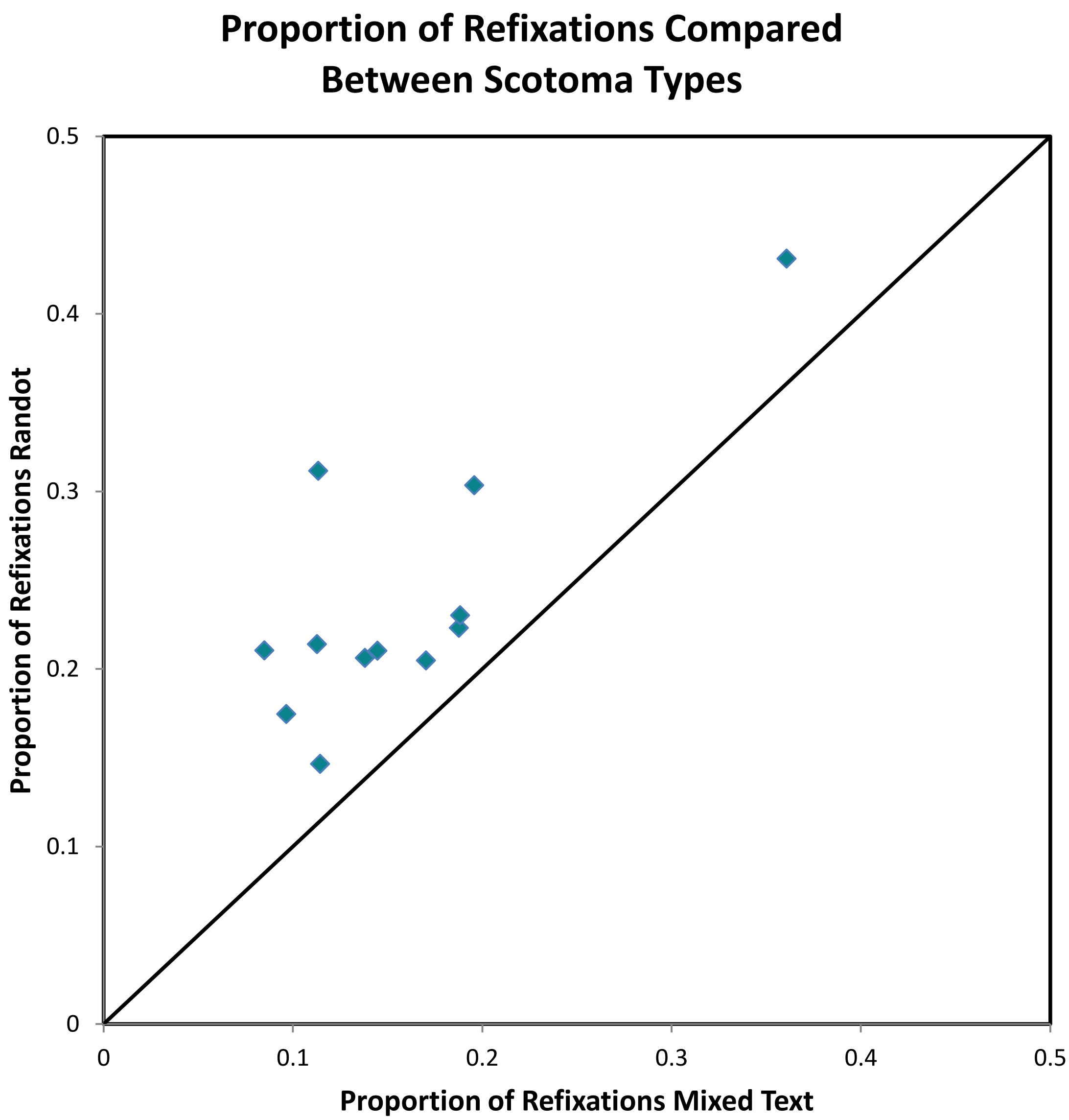


Figure 36. Proportion of all saccades that were refixations averaged across all trials for the mixed-text and random-dot scotomas.

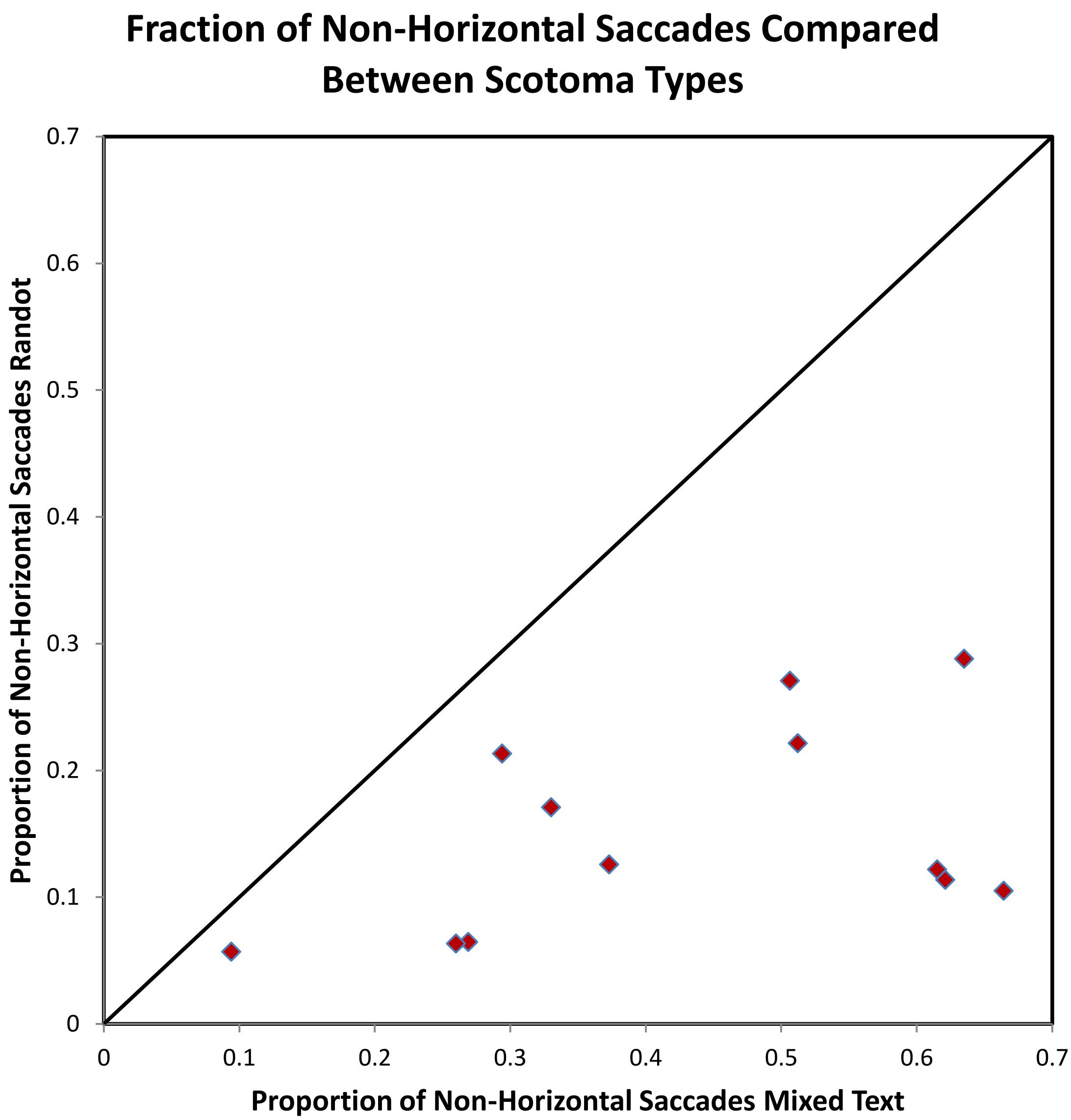


Figure 37. Median fraction of non-horizontal saccades averaged across all trials for the mixed-text and random-dot scotomas.

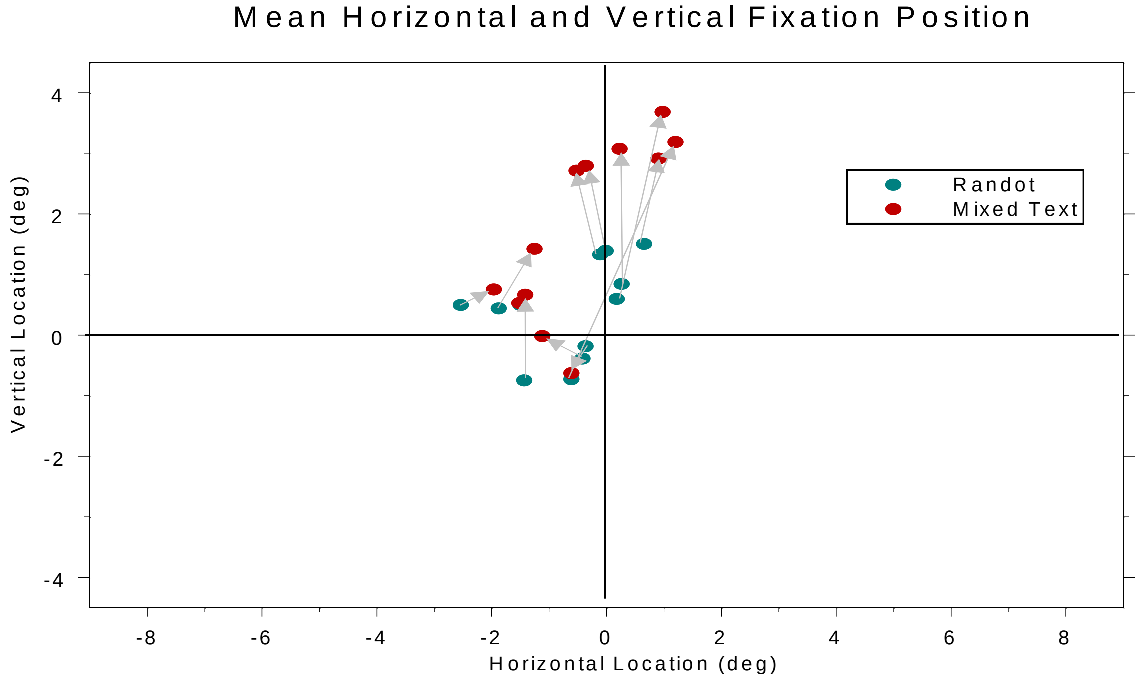


Figure 38. Mean horizontal and vertical fixation position averaged across all trials for the mixed-text and random-dot scotomas. The mean locations for the two scotoma types for each subject are connected with an arrow.

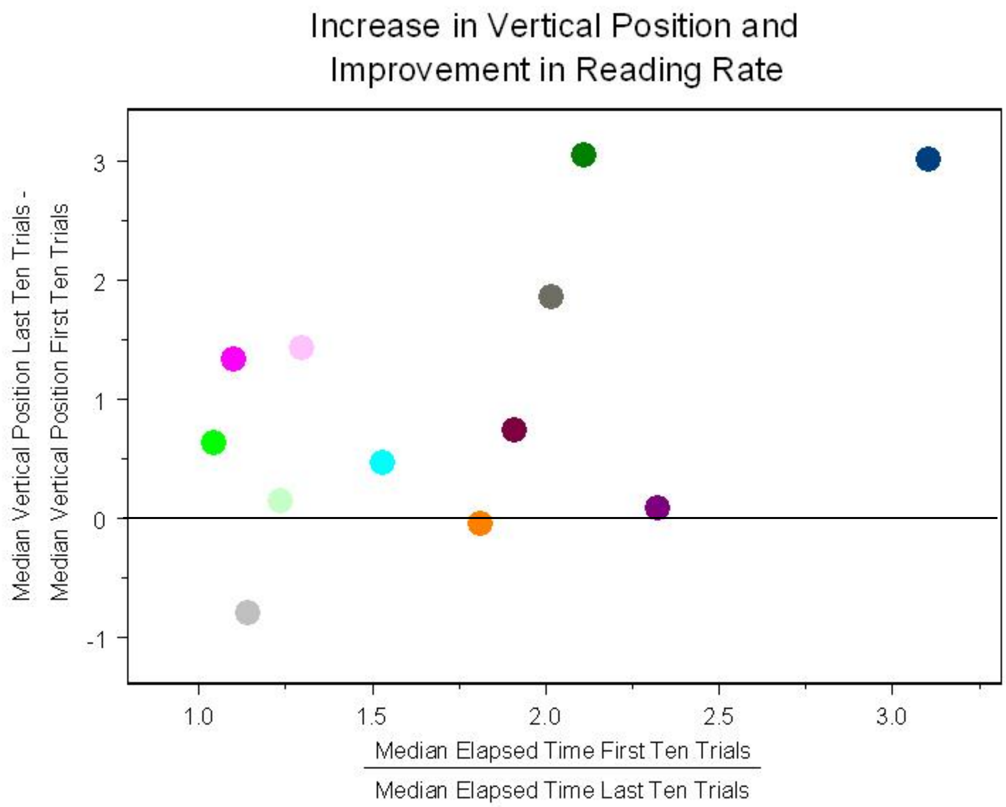


Figure 39. Comparison of median vertical eye position vs. the ratio of elapsed reading times during the first and last ten trials for the mixed-text scotoma. Each dot is representative of an individual subject.

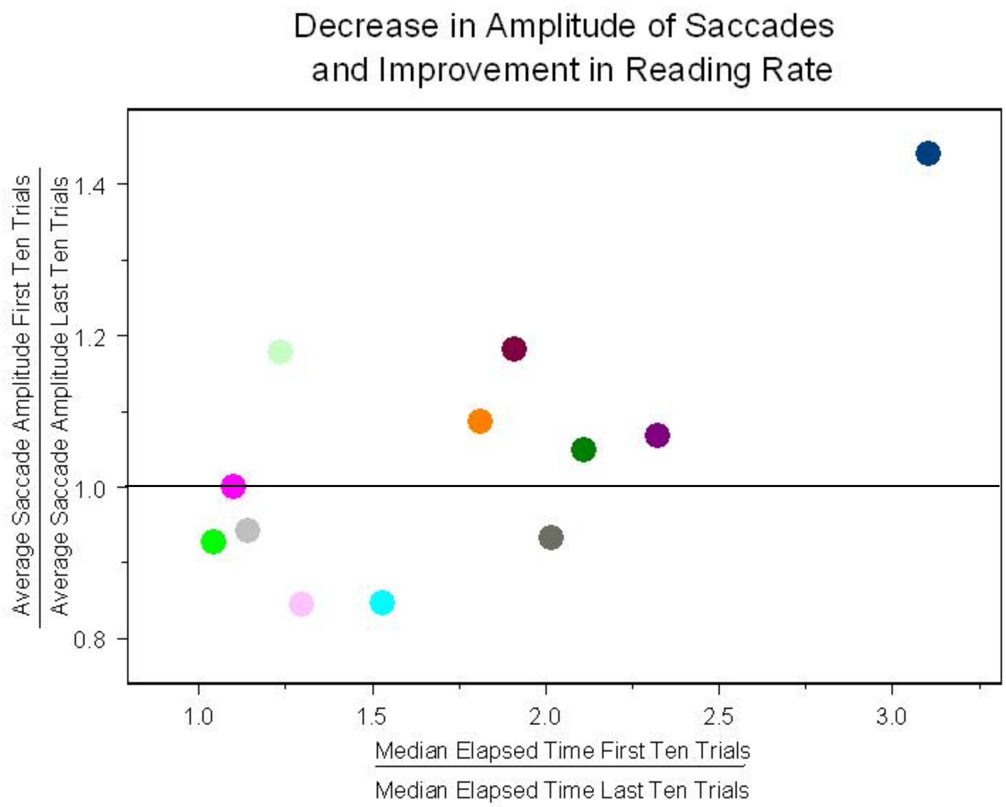


Figure 40. Ratio of the mean saccade amplitude and the ratio of the median elapsed time for the first and last ten trials for the mixed-text scotoma condition.

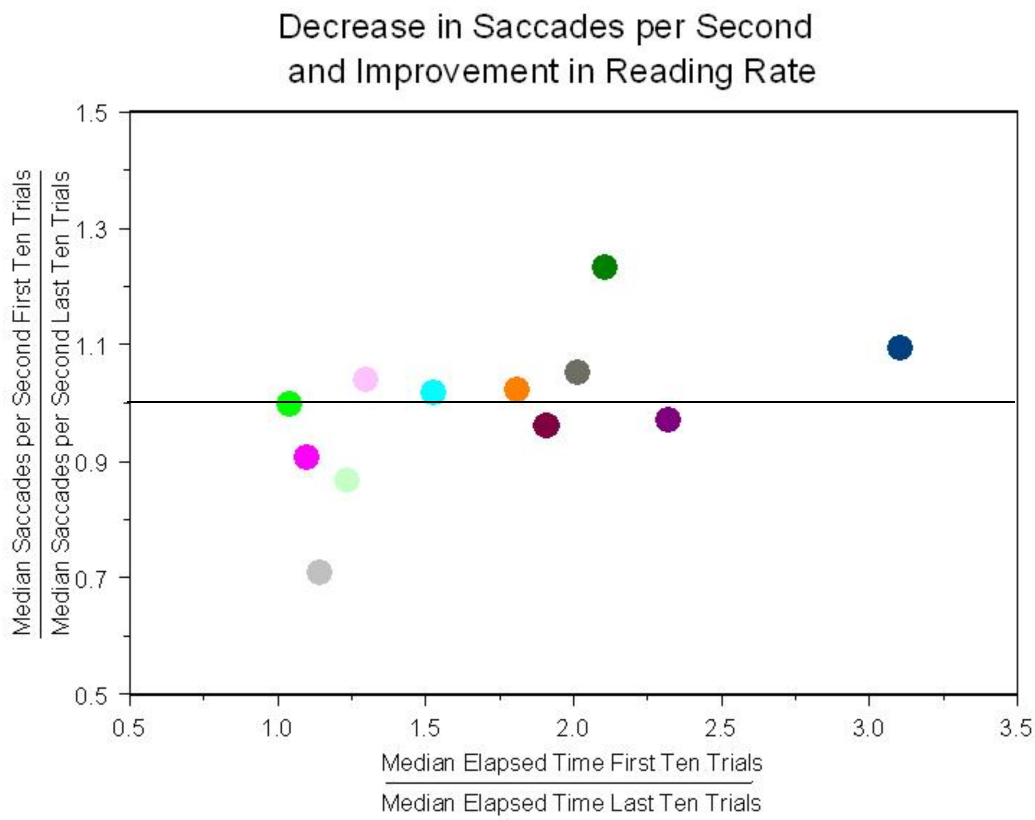


Figure 41. Ratio of the number of saccades per second and median elapsed time compared between the first and last ten trials for the mixed-text scotoma.

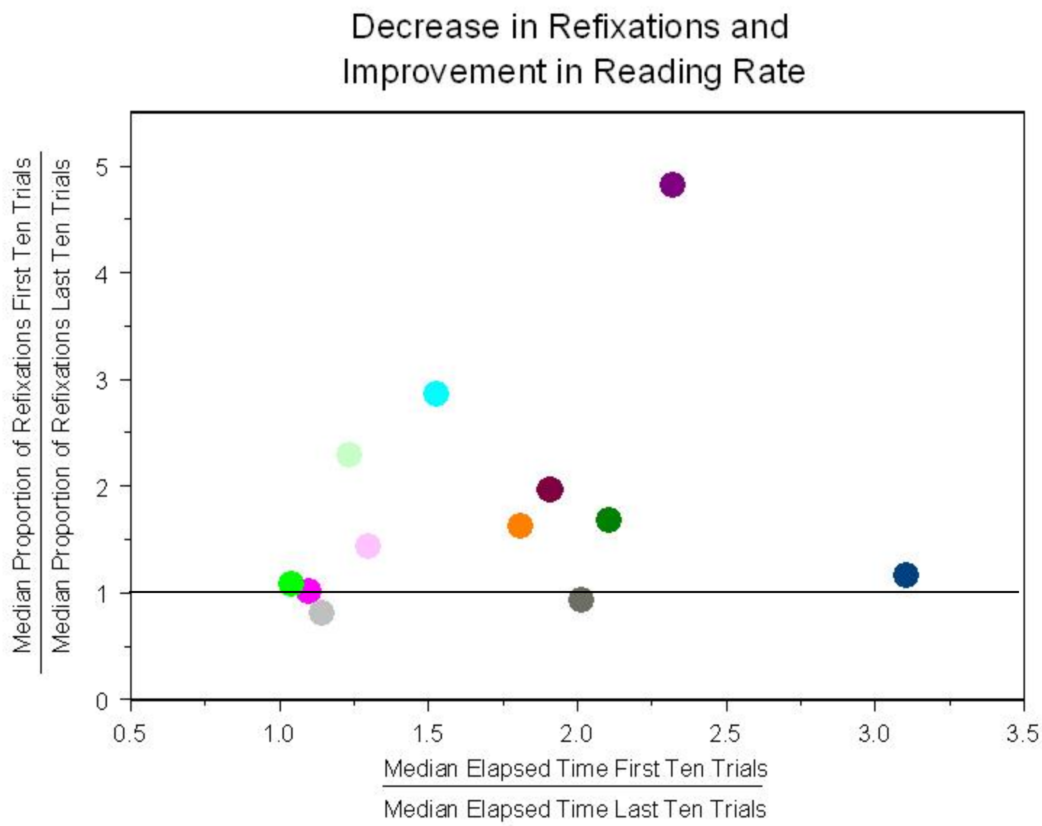


Figure 42. Ratio of the number of refixations and median elapsed time compared between the first and last ten trials for the mixed-text scotoma.

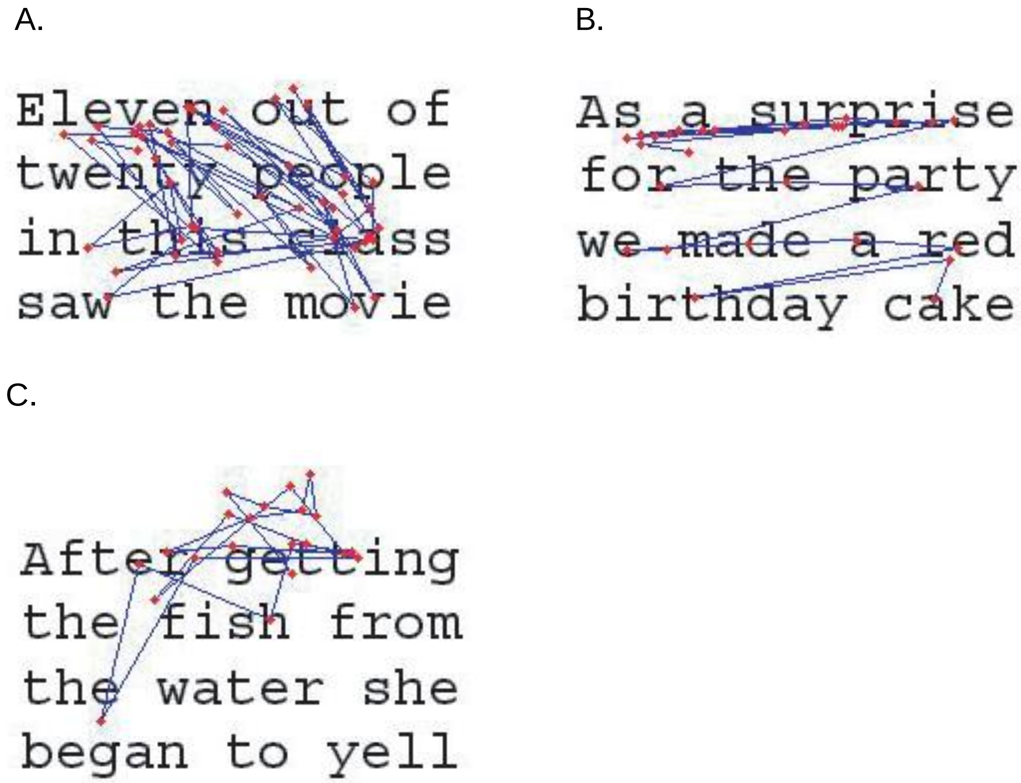


Figure 43. Scanpaths for subject 193 near the start of a session during reading with the mixed-text (A) and random-dot (B) scotomas. A scanpath obtained while the subject read with the mixed-text scotoma toward the end of trials appears in panel (C).

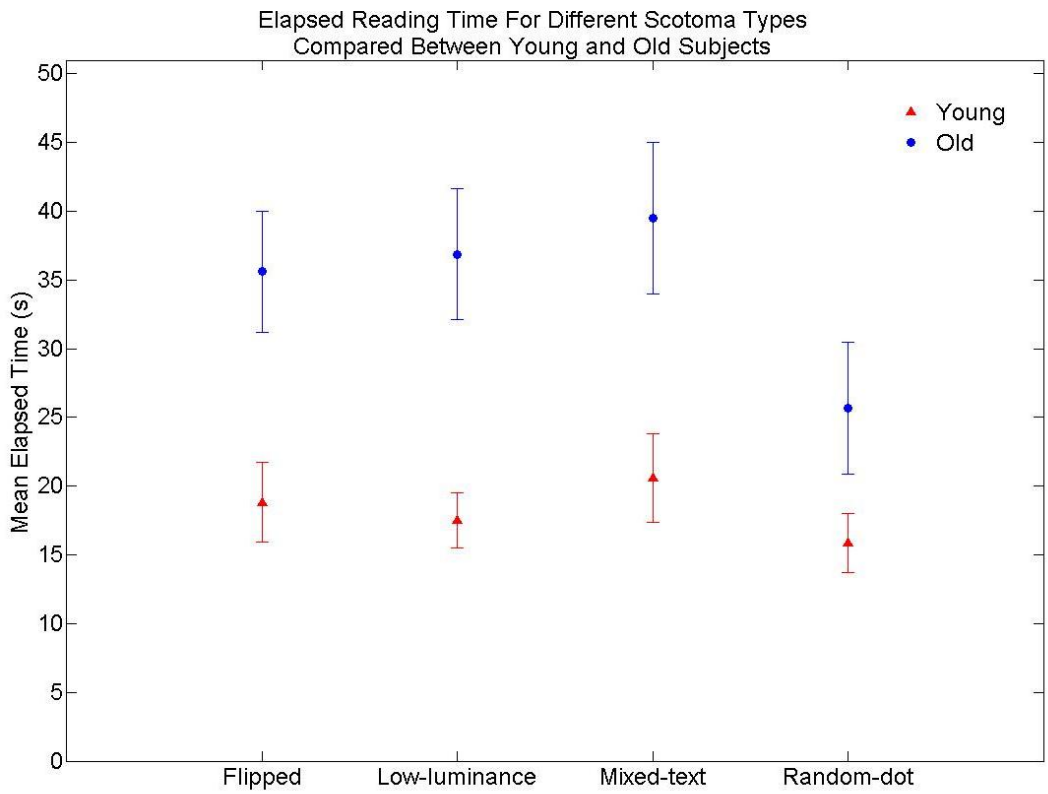


Figure 44. Elapsed reading time for different scotoma types compared between young and old subjects. Mean for each group is plotted with the standard error.

3.6 Discussion

Reading in patients with central scotomas is likely affected by perceptual filling-in, at least in the initial stages of adaptation. Both experiments 2 and 3 demonstrated that reading speed is better for a more visible scotoma with less linguistic content.

Experiment 2 also demonstrated that different reading strategies are employed by subjects for the two scotoma types. Subjects demonstrated a pattern of rapid horizontal back and forth movements with the random-dot scotoma, and they appeared to piece together words by using information to the left and right of the scotoma. Despite these back and forth movements, the eye movements with the random-dot scotoma appeared more like normal reading eye movements in the absence of a scotoma than the eye movements with the mixed-text scotoma.

The improvement in reading speed with the mixed-text scotoma for most subjects over the length of the study session is likely secondary to a change in eye movement strategy, in which subjects positioned the simulated scotoma above the text to read. The fact that the reading speed with the mixed-text scotoma remained slower than with the random-dot scotoma over the length of the experimental session for most subjects indicates that adaptation was not fully complete by the end of the session and/or that the adoption of an alternate eye movement strategy did not fully compensate for the poor visibility of the scotomatous region and/or the presence of spurious linguistic content.

Older subjects overall had greater difficulty than younger subjects when reading with a simulated central scotoma. The older subjects had particular difficulty with the scotomas that were less visible and contained spurious information. This indicates that defeating perceptual filling-in is likely to be most beneficial to older patients with central field loss. However, older patients may not achieve the reading rates of younger individuals with similar pathology even when information about the location of the scotoma is provided artificially.

Chapter 4

Reading Speed and Reading Eye Movements in Patients with Central Scotomas When the Scotoma Location is Made Perceptually More Visible

4.1 Introduction

Experiment 4 tested whether perceptually delineating the scotoma location and border using perceptual filling-in improves reading speed in patients with bilateral central scotomas. It was expected that reading speeds would improve after patients practiced reading with the scotoma location and border delineated with a gaze contingent polygon overlay. It was also expected that reading speed would be faster for those trials in which the scotoma location and border were delineated. If reading speed improves with delineation of the scotoma location and border, patients are likely to benefit long-term from similar training and additional research looking at efficacy of such training would be warranted.

4.2 Methods

4.2.1 Subjects

Nineteen subjects with bilateral central scotomas were recruited from the UHCO Center for Sight Enhancement. Testing was performed monocularly and the better seeing and preferred eye of the subject was used. An eye dominance test using a trial frame with +10 diopter lenses in front of both eyes was used to confirm the preferred eye in those subjects with similar acuities in both eyes and in those subjects reporting no eye preference. When using a +10 diopter microscope, subjects are forced to choose one eye to use for reading as it is not possible to sustain fusion comfortably at 10 cm. The non-tested eye was patched during testing.

Eight of the subjects provided usable data (Table 4). The other subjects either demonstrated relative scotomas during the experiment with a high contrast target (despite an absolute scotoma on the Nidek MP-1), central sparing, or we could not present a letter size large enough on our monitor to assess the critical print size for the experiment.

4.2.2 Perimetry

The Nidek MP-1 microperimeter was used initially to confirm bilateral central scotomas and to assess whether subjects had central sparing or a ring scotoma. A custom perimetry program was designed using the Nidek perimetry software using Goldmann size III stimuli. Tested points were spaced at half degree intervals over the central eight degrees. Eight points were also placed 15 degrees from center along the 90 – 270, 0 - 180 deg, 45 – 225, and 135 – 315 deg meridians to probe whether subjects were responsive and attentive during testing. The raw automatic threshold strategy was used with a step size of 10 dB. Stimulus duration was 200 ms. The center of the perimetric array was placed by the examiner at the approximate location of the vestigial fovea while the fundus was viewed in the MP-1 instrument. In addition to the perimetry performed with the Nidek MP-1, a custom Matlab program was used to perform gaze contingent perimetry and map out the scotoma edge on the CRT monitor prior to presenting sentences for the reading trials.

4.2.3 Critical Print Size

A CRT monitor was placed 57 cm from the subjects' tested eye. Cheek rests and an adjustable strap behind the head were used to stabilize head position. The cheek rests were curved and positioned to sit under the zygomatic bones. This allowed good control of lateral and forward head movement. Vertical head movement was still possible but subjects were instructed to not move their heads and were able to keep their heads relatively stable during trials. Cheek rests were used instead of a mouth bite or head rest and chin cup to allow subjects to read aloud and to avoid possible dental concerns.

The EyeLink II eyetracker was positioned firmly on the subject's head and the camera and forehead band heights were adjusted so the top and bottom of the CRT monitor were visible to the subject. The refraction from the latest exam was refined and used to calculate the power of a 70 mm lens blank mounted on the forehead band of the EyeLink. For example, for a subject with a -1.00 D refractive error, a +0.75 D lens blank was used. The bottom was cut off the lens blanks used in the experiment so that the lens did not interfere with the EyeLink II camera adjustment but still allowed the subject to view the whole screen.

To determine the critical print size, subjects read aloud MNRead style sentences composed of 4 rows of text with 13 characters per row (Mansfield, Legge, and Bane 1996). A set of 271 sentences were randomly ordered for each subject and this order was used for all sentence presentations during the study session. No sentence was presented twice during a study session. Some subjects were not able to complete the study in one visit. The sentence order was randomized again at the second visit and occasionally a sentence that was used in the first visit was presented during trials at the second visit. Elapsed time and number of correct words was used to calculate reading speed. Initial letter size was 1.3 logMAR and descended in 0.2 logMAR steps until a decrease in reading speed greater than twenty percent of the maximum was found. The critical print size was further refined using ascending steps of 0.1 logMAR. The best bilinear fit of reading speed versus logMAR was used to determine critical print size (Figure 45). The experiment was not conducted for individuals whose critical print size appeared to be greater than 1.3 logMAR.

Subjects, when allowed to more readily perceive the location of their scotoma, may adapt a strategy in which they move their scotoma out of the way and use a slightly more peripheral locus for reading. To account for a possible more peripheral reading locus, a text size equal to 0.2 logMAR above the critical print size was used in the main experiment to measure reading speed with and without the scotoma visible.

4.2.4 EyeLink II Calibration

A Rodenstock Scanning Laser Ophthalmoscope (SLO) was fitted with a 4f relay lens system to allow for imaging of the retina after reflection from a dichroic mirror. The SLO images were used to verify that subjects viewed each of the nine calibration points used in a modified version of the Eye Link calibration program with the same retinal locus during calibration. The dichroic mirror reflected infrared light from the SLO while passing visible light from the monitor to the subjects' eye. Subjects were thus able to view the monitor through the dichroic mirror while the SLO was used to image the retina from the side (Figures 46 and 47).

A nine point calibration was used. To allow for SLO imaging during calibration of the EyeLink II, the locations of the calibration targets were adjusted inward toward the center of the screen from EyeLink default positions. The resultant nine point calibration had target positions in a grid pattern. Non-central calibration points were +/- 7.3 deg horizontally and +/- 5.5 deg vertically from center. Screen dimensions were 36.4 x 27.3 cm or 35.4 x 26.9 deg. Each of the non-central targets could be moved on the monitor by the experimenter using the computer keyboard during the calibration process in case a subject did not use the same retinal locus to view one or more of the calibration targets.

To register the position within the SLO raster with locations on the CRT monitor, five normal subjects successively fixated each of the nine fixation targets while their fundi were viewed with the SLO. The position of the foveal pit seen in the SLO image was marked with an indelible pen on a transparency fixed on the SLO monitor screen for each of the nine calibration points. The location of the foveal pit for the calibration positions was similar for all of the subjects and the average position was used as a reference for subjects with macular degeneration. A laser pointer mounted on the rail that held the SLO relay-lens system was used to ensure that the SLO raster center was aligned with the CRT monitor center prior to calibration.

Pupils were dilated with 2.5% phenylephrine if smaller than about 4 mm in the light. Each subject was calibrated in the following manner: The EyeLink eyetracker was mounted on the head, and the non-viewing eye was patched. The camera in front of the viewing eye was adjusted. Cheek rests and a strap behind the head were used to stabilize the head.

The subject was asked to keep his or her head as still as possible and to look at the center of the central calibration target presented at the center of the screen. An image of the subject’s fundus was viewed on the SLO monitor. The retinal locus used by the subject to view the central calibration target was determined and each of the remaining eight calibration points were then presented in a random sequence. Calibration points were manually accepted using the EyeLink II software after it was confirmed from the SLO image that the fixation target was imaged with the same retinal locus as the first, central target. If the subject used a different locus for one of the calibration targets, he or she was coached to look at the center of the ‘x’ and hold his/her eye still. If the subject still didn’t image the ‘x’ using the same retinal locus, the ‘x’ was moved on the monitor until the initially used retinal locus lined up with the calibration mark made for normal subjects.

4.2.5 Gaze-Contingent Display

Eye position data from the EyeLink II eye tracker and a custom Matlab program were used to create a gaze contingent display. The eyetracker was used in the 250 Hz pupil-corneal reflex mode with headtracking engaged. Because of physical interference from the components of the relay optical system of the SLO, the markers used for headtracking were shifted horizontally to be visible to the head mounted camera on the Eyelink. Two of the markers were placed above and below the horizontal center of the display screen and two were mounted 37.9 cm to the right of center when imaging the left eye and 37.9 cm to the left of center when imaging the right eye. The non-central markers were mounted on a board attached to the monitor. The normal horizontal separation and vertical heights of the markers were conserved.

After calibration of the eyetracker, stabilized kinetic perimetry was performed from non-seeing to seeing along eight meridians (0 deg to 315 deg, in 45 deg increments) from the center of the scotoma. The approximate center of the scotoma in the SLO image was determined using retinal landmarks from the MP-1. The subjects were asked to fixate a letter which was moved on the display screen until the scotoma center was positioned near the center of the SLO raster. A continuously presented square black probe, two times the stroke width of the letter size to be used during the experiment, was positioned at the center of the screen, inside the scotoma. The probe was moved from center in 2 deg increments along one of the eight meridians until the subject reported seeing the probe. The probe was then stepped back toward the center of the scotoma in 1 deg increments until the subject reported it disappeared. The probe was then again stepped outward in 0.5 degree increments until the subject reported it was visible. This position at which the probe was just visible was recorded and the probe was returned to the screen center. Testing was then conducted along the next meridian until all 8 meridians had been tested and transition points from non-seeing to seeing recorded. These transition points were connected and the resulting polygon was filled to form a gaze contingent black polygon at the location of the subject's scotoma (Figure 48). Stabilization of the black polygon was not absolute as no subject reported that the polygon faded.

After mapping the location of the scotoma, subjects were asked to look at the center of a letter 'x' positioned at the center of the screen while the fundus image was viewed in the SLO. To ensure that the polygon indicating the location of the scotoma did not cover viable retina near the PRL, the border of the polygon was adjusted inward if it covered any part of the letter 'x' while it was determined from the SLO image that the subject was not positioning the scotoma on the letter (Figure 48). Only the border near the 'x' was adjusted inward.

The measures of horizontal and vertical eye position from the Eye Link II were used to update the location of the polygon on the monitor. The innate noise of the Eye Link II eye tracker prevented fading of the polygon overlay. The usable range of the Eye Link is estimated to be +/- 20 degrees horizontally and +/-18 degrees vertically in the 250 Hz tracking mode. With thirteen characters per line, this limits maximum displayable letter size to 2.3 degrees, equivalent to 1.44 logMAR. Our display screen and experimental setup limited the maximum displayable letter size to 1.3 logMAR, with a 1.66 deg 'x' letter height. This resulted in a horizontal line length of 28 degrees and a total vertical height of 14.6 degrees, which are within the trackable range of the EyeLink eyetracker.

4.2.6 Reading Speed with and without Scotoma Visibility

Subjects read aloud sentences with and without the superimposed black polygon that marked the location of their scotoma. The same sentence order used to determine the critical print size was maintained so that none of the sentences were presented twice during a study session. Blocks of 6 trials with the superimposed polygon were alternated with blocks of 6 trials without the polygon. There were a total of 42 trials (7 blocks) for each subject. The first block was without the superimposed polygon and used to determine baseline reading rates and reading eye-movements. A drift correction of the Eye Link was performed before each of the blocks with the superimposed polygon. Occasionally the nine-point calibration had to be repeated when the EyeLink II camera accidentally bumped against the cheek rests or if the patient needed to take an extended break.

4.3 Analyses

Maximum initial and final reading speeds at the print size used during the experiment were calculated from the median value for the first six and the last six trials. Initial reading speed was compared to the maximum reading speed for trials conducted during calculation of the critical print size.

Saccades that achieved a velocity greater than 15 deg/s and resulted in a shift in fixation greater than 0.5 deg were identified and counted. The angle and size of each identified saccade were calculated using a custom Matlab program.

The average amplitude of saccades was calculated for each reading trial. Saccades per second were determined by dividing the number of saccades by the elapsed time for each trial. Saccades were categorized as horizontal (orientations between 330 – 30 and 150 – 210 deg), vertical (60 – 120 and 240 – 300 deg), or oblique (30 – 60, 120 – 150, 210 – 240, and 300 – 330 deg). The average vertical and horizontal eye position for each trial was determined from the median location during fixations, defined as the intervals between saccades.

To further analyze the patients' reading eye movements, two experienced eye movement researchers ranked the eye movement traces for the first and last 6 trials for each subject from 1 to 12, with a rank of 1 corresponding to the trial that most resembled normal reading eye movements. The researchers were masked to trial order and the trials were randomized for each researcher. Figure 49 is the vertical and horizontal eye movement trace for a beginning trial for patient 13 with an average rank of 9. Figure 50 is the vertical and horizontal eye movement trace for an ending trial for patient 13 with an average rank of 3.

Table 4. Patient characteristics experiment 4

Subject Number	Age (yrs)	Gender	Diagnosis	Study Eye	Critical Print Size logMAR
64	76	F	Exudative AMD	OS	0.7
55	74	M	Exudative AMD	OS	1.0
78	84	M	Non-exudative AMD	OD	1.0
31	88	M	Non-exudative AMD	OD	0.9
51	82	M	Non-exudative AMD	OD	1.0
13	81	F	Non-exudative AMD	OS	0.7
96	78	F	Exudative AMD	OS	1.0
39	81	M	Myopic Chorioretinal Degeneration + Non-exudative AMD	OS	0.7

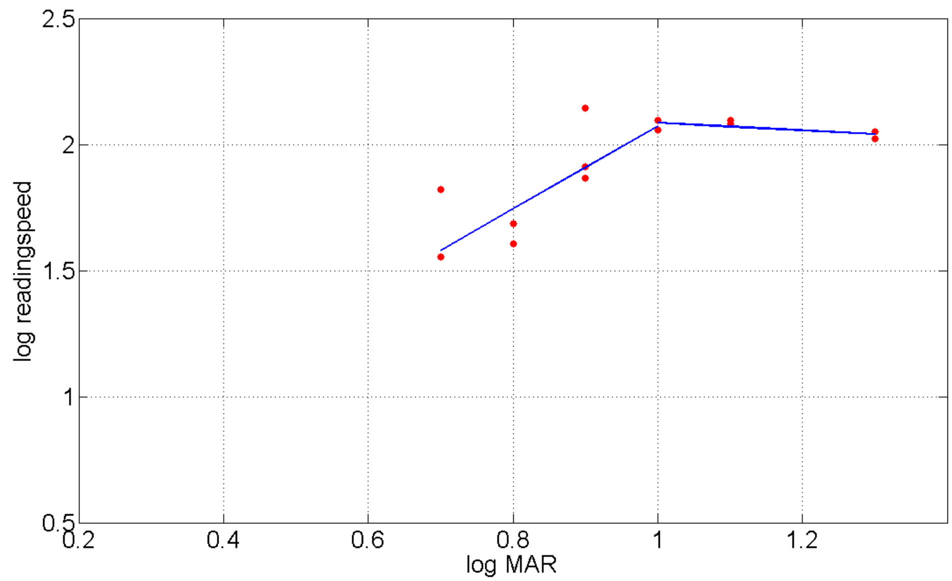


Figure 45. Bilinear fit of MNRead data for subject 78 demonstrating a critical print size of 1.0 logMAR. Reading trials with and without a visible polygon that marked the subject's scotoma were performed using a print size equivalent to 1.2 logMAR for this subject.

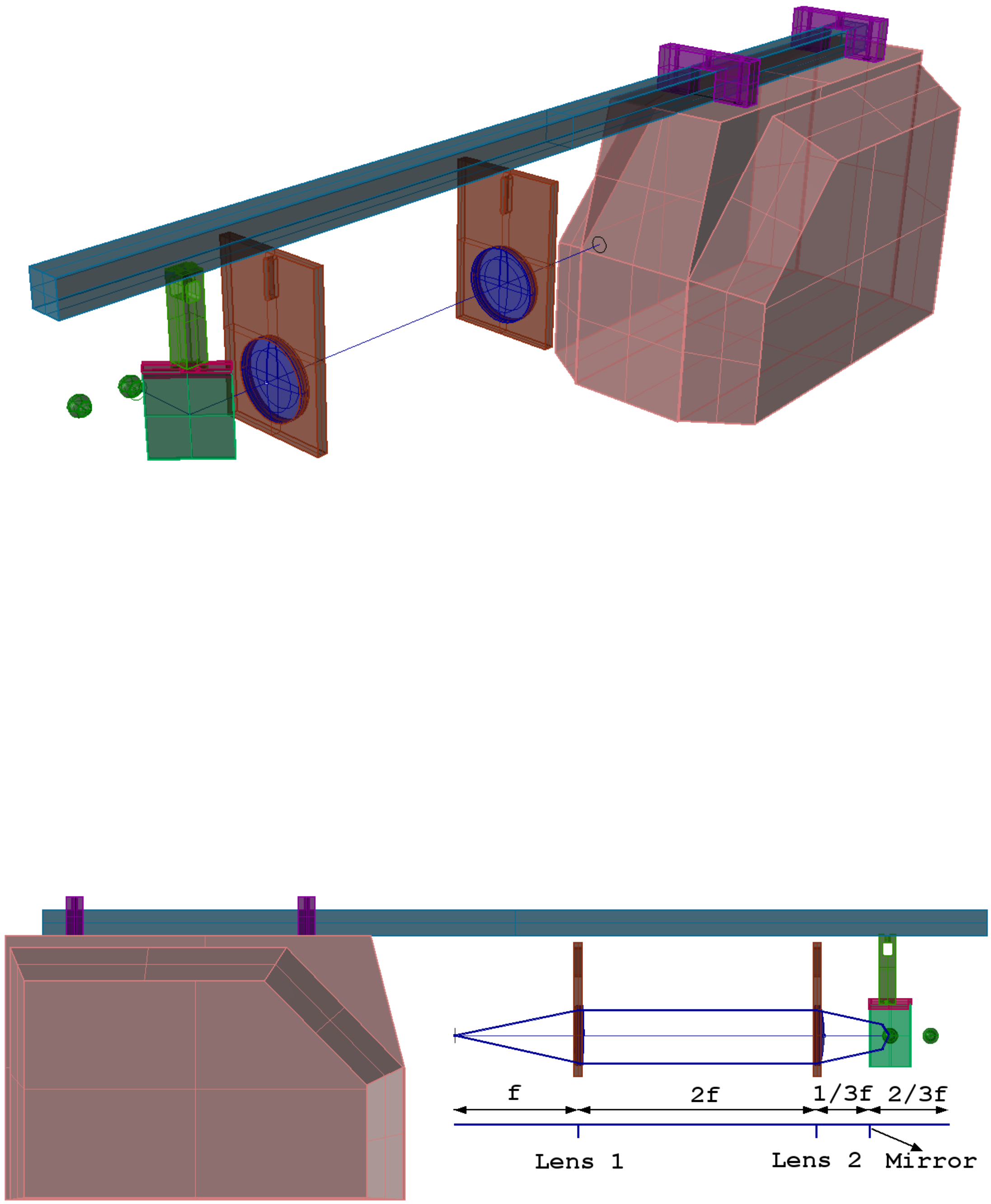


Figure 46. Schematic representation of the SLO setup with imaging of subjects' fundus from the side. The configuration shown was used to test a subject with a preferred left eye. The orientation of the dichroic mirror that allowed the SLO to view the subject's fundus could be flipped to permit testing of a subject with a preferred right eye.

Figure 47. Experimental set-up with head-mounted EyeLink II and head stabilization with cheek rests.

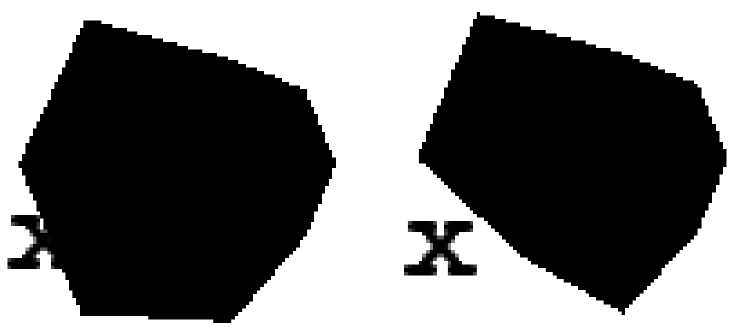


Figure 48. Black polygon (left panel) constructed from modified kinetic perimetry, not-seeing to seeing along 8 meridians, starting at the scotoma center. Adjustment of the polygon edge inward (right panel) so it does not cover the retinal locus used by the patient to fixate the letter x.

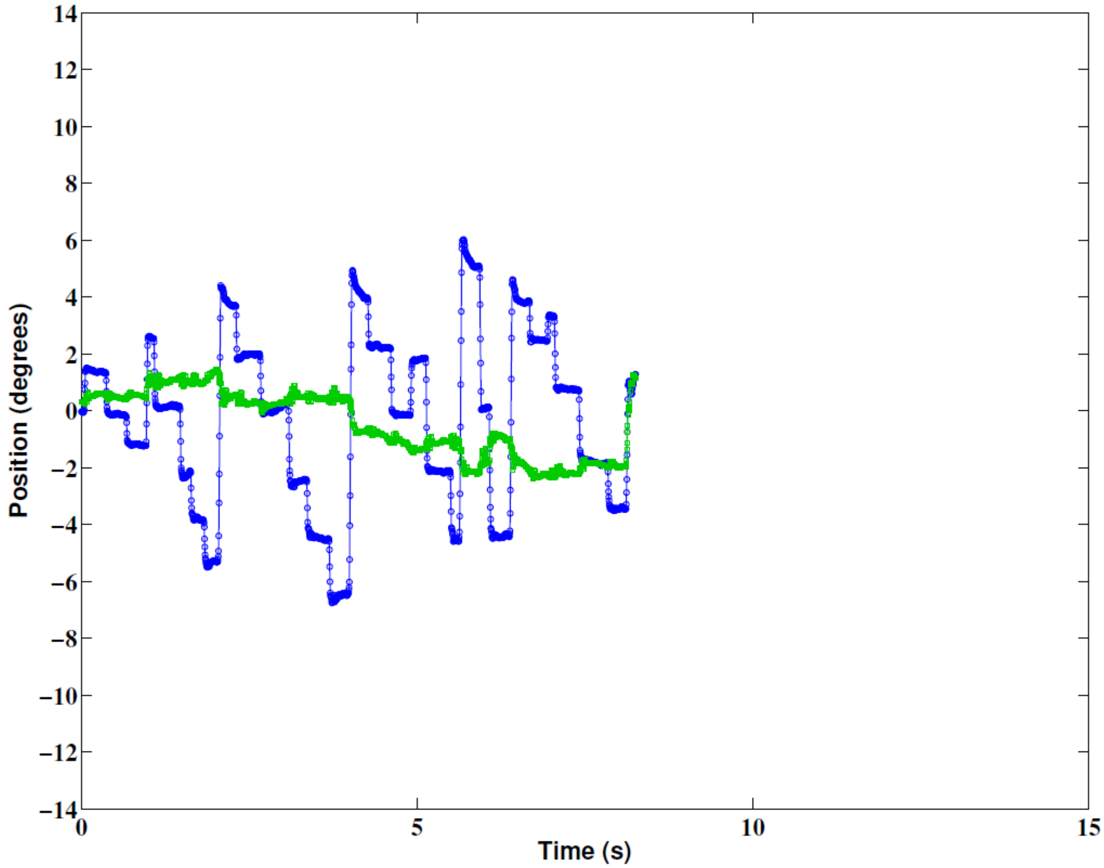


Figure 49. Horizontal (blue) and vertical (green) eye trace for a trial at the beginning of the study session for patient 13. The average rank for this trial was a 9.

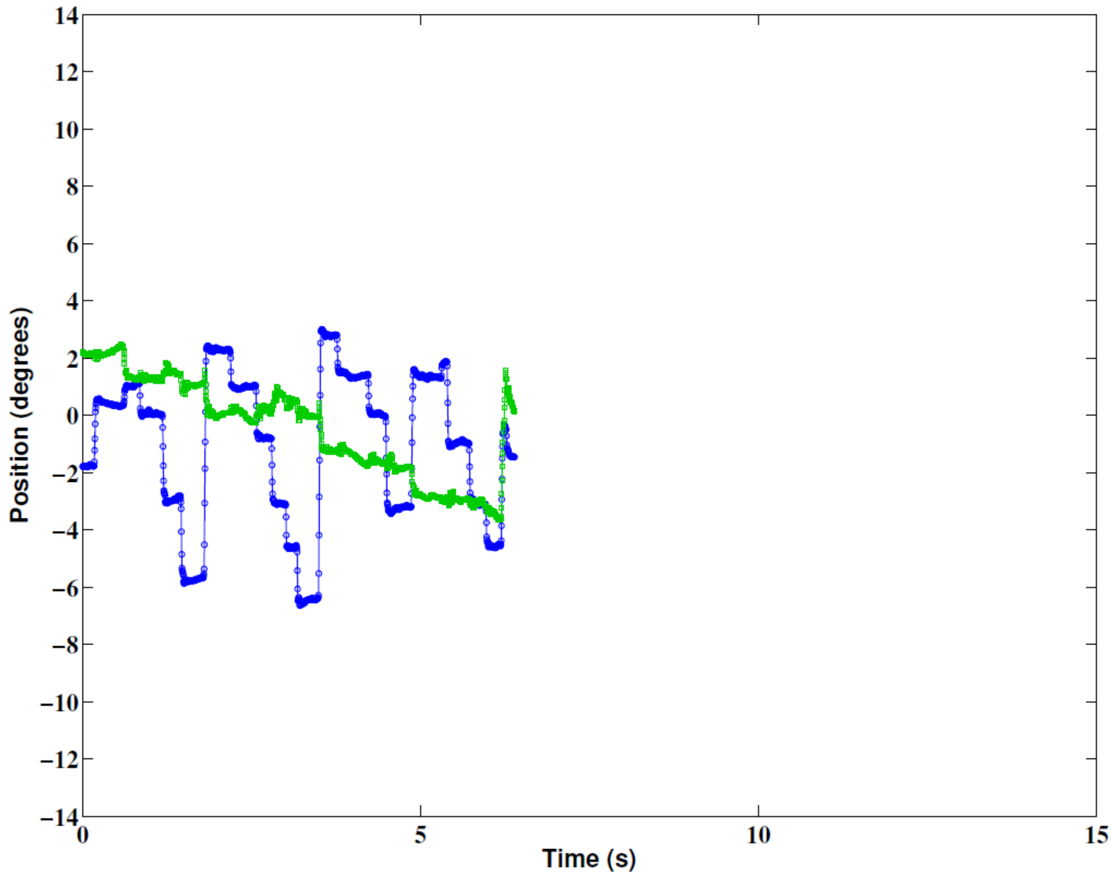


Figure 50. Horizontal (blue) and vertical (green) eye trace for a trial at the end of the study session for patient 13. The average rank for this trial was a 3.

4.4 Results

The mean reading speed of the initial six trials without the superimposed polygon and the mean reading speed of the last six trials without the superimposed polygon were compared for each individual subject. All of the subjects but one showed an increase in reading speed. The individual that showed no improvement (Subject 78) had the smallest scotoma and was also the fastest reader with an initial mean reading speed of 113 words per minute. The improvement in reading speed was statistically significant for only two of the subjects when a paired *t* test was performed on each of the individual data sets (Table 5). However, a paired-samples *t* test for the group as a whole revealed a statistically significant increase in reading speed of 0.075 ± 0.060 (SD) log wpm after reading with the superimposed polygon, $t(7) = 3.53$, $p = 0.01$ (Figure 51).

The mean log reading speed for all trials without and with the superimposed polygon for each subject were also analyzed. A paired-samples *t* test revealed that the mean log reading speed was significantly faster without (1.89 ± 0.13 log wpm) than with (1.82 ± 0.16 log wpm) the superimposed polygon, $t(7) = -3.360$, $p = 0.012$ (Figure 52).

The initial reading speed and eye movement data for subject 39 were lost during the experiment due to a program crash. Therefore, the reading speeds for the reading trials that determined the critical print size were used to calculate the initial reading speed for this subject. Trials for letter sizes at or above the critical print size were used. Because eye movements were not recorded during the assessment of the critical print size, analyses comparing initial to final eye movement data could not be performed for this subject.

The following eye movement parameters appeared to change across reading trials and were further analyzed with statistical tests of significance: the mean vertical and horizontal position of the fixation locus, the number of saccades/s, the median fixation duration, the mean amplitude of saccades, and the number of non-horizontal saccades. For each of these parameters, a t-test was used to compare the first six and last six reading trials *without* the superimposed polygon for each individual subject. The data are included in Tables 6-11. Individual subjects demonstrated significant changes in reading eye movements, with the greatest number of subjects demonstrating a shift in the average vertical fixation locus.

The difference between the average of the initial 6 and last 6 trials for each subject comprised the group data used to analyze the group as a whole. One sample *t* tests were performed for changes in saccades/s, average fixation duration, average amplitude of saccades, and proportion of non-horizontal saccades. There was no significant difference between the initial and final reading eye movements across subjects for any of these parameters (Table 12). There were nonsignificant trends for an *increase* in the average amplitude of saccades (6/7 subjects) and for a decrease in the number of saccades per second (5/7 subjects).

To compare the rank given by each researcher to the patients' reading eye movements, linear regressions were performed for the rankings of each individual patient. For four of the patients the rankings correlated very well (R^2 = 0.814, 0.891, 0.865, 0.945, Figure 54); for one patient the rankings correlated well (R^2 = 0.681); and for the other two patients the correlation was not as good (R^2 = 0.247, 0.290, Figure 55). Overall the rankings of the two researchers agreed quite well and an additional analysis to evaluate the improvement in reading speed and reading eye movements was performed. The average rank given to a trial by the two researchers for the end trials was subtracted from the average rank of the beginning trials. A more positive difference indicated eye movements were judged more similar to normal reading eye movements toward the end of trials. Difference in average reading speed was also calculated with a more positive number corresponding to a greater improvement in reading speed. Regression analysis of the average of the ranking by the researchers demonstrated a highly significant relationship between improvement in reading speed and eye movements judged to be more similar to normal reading eye movements ($F(1,5) = 20.44$, $p = 0.006$, Figure 56).

The position of the scotoma relative to the text was also analyzed across trials. After reading with the superimposed polygon it was thought that subjects may shift their position of gaze to move their scotoma out of the way and better position the area near the PRL to read text. For example the initial fixation locus or single-letter PRL is shown in Figure 53 for subject 55, demonstrating a PRL that is down and to the left of the scotoma in visual space. During reading this subject's scotoma would be expected to cover part of a word to the right of the PRL. However the whole word should become visible if the subject moved his eye to shift the scotoma further up.

An alternative possibility is that the scotoma becomes more centered on the text as the patient learns to read around the scotoma. Most normal subjects in experiment 2 demonstrated the ability to read around the random-dot scotoma without changing their average horizontal or vertical fixation position. If this were the case in subjects with macular degeneration, we would have expected to see an increased number of saccades per second similar to that seen with the random-dot scotoma in experiment 2.

Some patients may understand that they need to view words eccentrically, but may not be able to judge how far to the side to position their eye and may use a retinal locus too far off the scotoma. By using the polygonal overlay to make the scotoma location more visible, patients might position their eyes more effectively. This would result in the patient positioning the scotoma closer to the text of interest.

After experience in reading with the overlaid polygon, five of the seven patients showed a shift that positioned the scotoma further from the text (Figures 57, 59-62). Two of the subjects who had large scotomas that were initially positioned above the center of text re-positioned the scotoma closer to the center of the text in the final reading trials.

Four of the subjects who moved the scotoma to be further out of the way while reading, shifted the scotoma upward. One subject positioned the scotoma further down and right to move it out of the way while reading.

Five of the seven subjects used a PRL that projects in visual space inferior and to the left of the scotoma. This is consistent with past findings that many patients place their scotoma up and to the right when they eccentrically view (Guez et al. 1993; Sunness et al. 1996; George T Timberlake et al. 2005; Verezen et al. 2011). This preference is interesting in that it doesn't appear to depend on which eye is used, as is the case for the patients reported here.

All patients reported that the polygon overlay looked completely filled in, was uniform in color (black) and had sharp borders. After the experiment, the subjects were asked what they perceived in the area of the scotoma without the polygon overlay. The subjects were instructed to hold their eye still while viewing the center of a MNRead sentence. The eye not tested during the experiment remained patched. All patients reported a blank white area with the same color and luminance as the background. None of the patients reported perceiving letters or other information content within the scotoma.

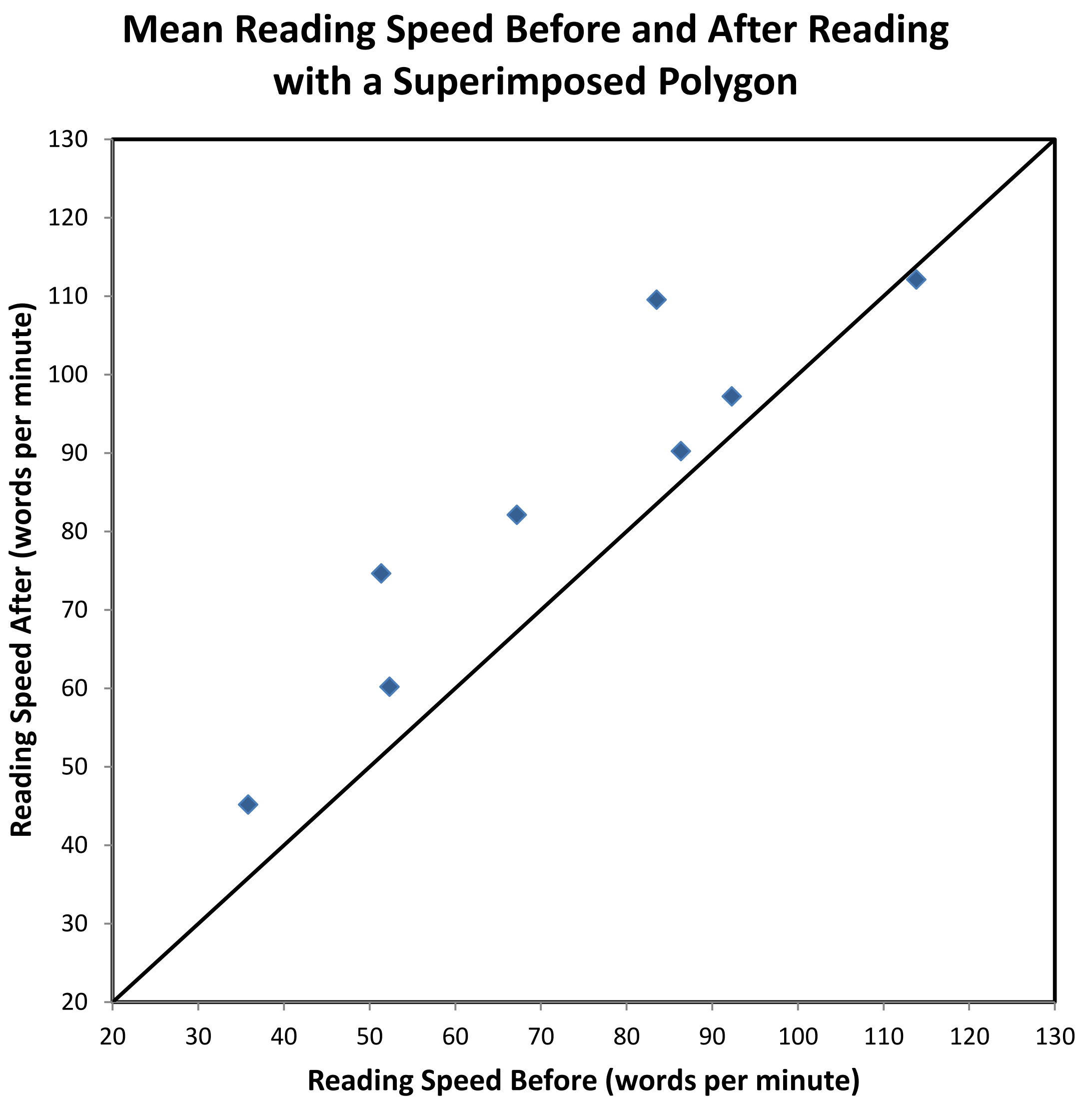


Figure 51. Reading speed in words per minute for 8 subjects compared before and after reading with a polygon overlay at the position of the central scotoma.

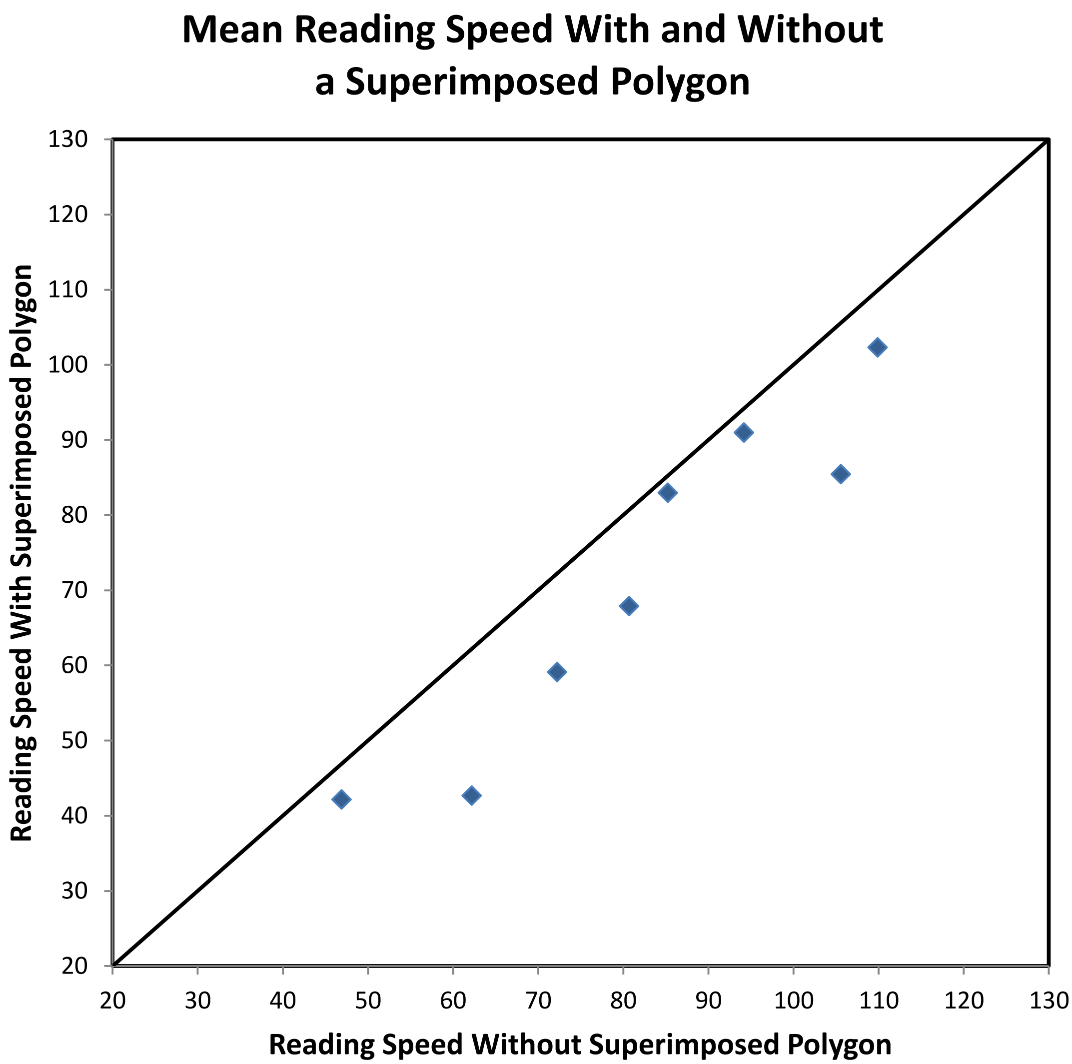


Figure 52. Mean reading speed compared for trials with a superimposed polygon and trials with no superimposed polygon.

Table 5. Average reading speed (wpm) for the initial 6 and last 6 trials for each patient

Patient	Initial 6 Trials	Last 6 Trials	*t*(5)	*p*
64	51	75	3.960	0.011
55	84	110	3.652	0.015
78	114	112	-0.167	0.874
31	86	90	0.828	0.446
51	36	45	1.584	0.174
13	67	82	1.916	0.114
96	92	97	0.930	0.395
39	52	60	1.088	0.326

Table 6. Average vertical fixation locus before and after reading with a polygon overlay at the position of the central scotoma (degrees from center of the screen, up is positive)

Subject Number	Before	After	*t*	*p*
64	1.76	1.15	-2.450	0.058
55	-1.19	3.31	7.599	0.001
78	-1.70	-0.42	2.247	0.075
31	0.83	3.13	5.055	0.004
51	1.16	-1.02	-6.330	0.001
13	-0.17	0.92	5.493	0.003
96	7.86	6.33	-3.190	0.024

Table 7. Average horizontal fixation locus before and after reading with a polygon overlay at the position of the central scotoma (degrees from center, left is positive)

Subject Number	Before	After	*t*	*p*
64	-0.07	0.20	0.669	0.533
55	6.70	7.26	1.353	0.234
78	1.58	-0.09	-5.341	0.003
31	0.89	0.23	-1.217	0.278
51	3.34	0.83	-3.827	0.012
13	1.75	1.77	0.027	0.980
96	6.24	6.72	0.452	0.670

Table 8. Average number of saccades per second before and after reading with a polygon overlay at the position of the central scotoma

Subject Number	Before	After	*t*	*p*
64	2.41	2.62	-1.547	0.182
55	3.83	3.69	1.069	0.334
78	3.16	2.79	3.301	0.021
31	2.67	2.00	4.959	0.004
51	2.31	2.46	-1.435	0.211
13	3.18	3.02	1.717	0.147
96	3.96	3.18	5.699	0.002

Table 9. Average fixation duration (s) before and after reading with a polygon overlay at the position of the central scotoma

Subject Number	Before	After	*t*	*p*
64	0.29	0.25	-2.494	0.055
55	0.17	0.16	-0.216	0.837
78	0.22	0.23	0.419	0.692
31	0.30	0.30	0.084	0.936
51	0.25	0.24	0.548	0.607
13	0.24	0.24	-0.72	0.946
96	0.13	0.18	10.616	<0.001

Table 10. Average amplitude of saccades (deg) before and after reading with a polygon overlay at the position of the central scotoma

Subject Number	Before	After	*t*	*p*
64	3.26	3.28	0.110	0.917
55	3.83	4.69	3.410	0.019
78	6.55	7.44	4.470	0.007
31	4.83	4.26	-3.726	0.014
51	4.02	4.12	0.356	0.736
13	2.74	2.83	0.878	0.420
96	5.63	5.94	0.875	0.422

Table 11. Proportion of non-horizontal saccades before and after reading with a polygon overlay at the position of the central scotoma

Subject Number	Before	After	*t*	*p*
64	0.03	0.06	-1.118	0.314
55	0.13	0.09	1.147	0.303
78	0.06	0.24	-3.842	0.012
31	0.20	0.22	-0.343	0.746
51	0.05	0.03	0.921	0.399
13	0.04	0.02	1.354	0.234
96	0.51	0.25	10.616	<0.001

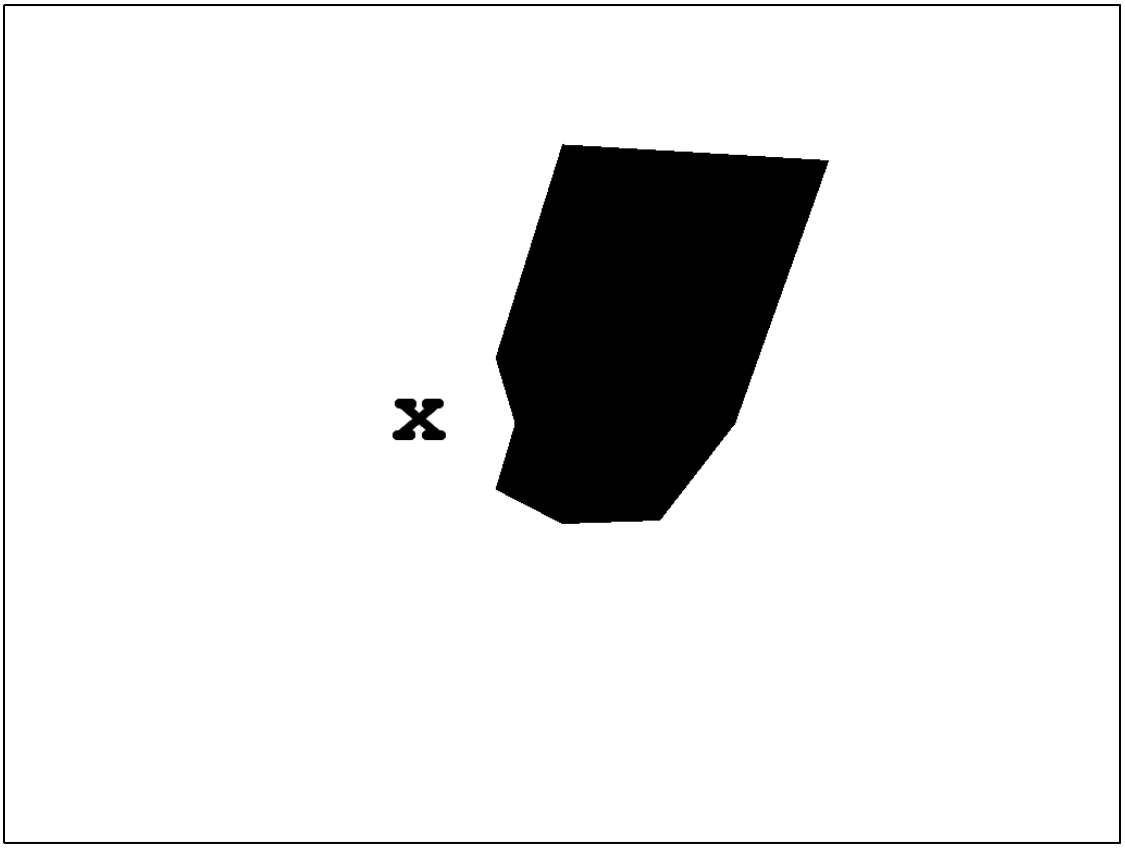


Figure 53. The initial fixation locus or single-letter PRL for subject 55. This is the location of the mapped polygon when the patient is viewing a single letter. The letter is the same size as the text used during reading for this subject.

Table 12. Change in reading eye movements compared between initial and final trials averaged across all subjects. Statistics are from the comparison of the grouped mean difference between initial and final trials for individual subjects.

	Initial Mean	Final Mean	*t*	*p*
sac/s	3.08	2.82	-1.767	0.128
amplitude of saccades (deg)	4.41	4.65	1.270	0.251
fixation duration (s)	0.23	0.23	0.058	0.956
proportion of non-horizontal saccades	0.15	0.13	-0.307	0.769

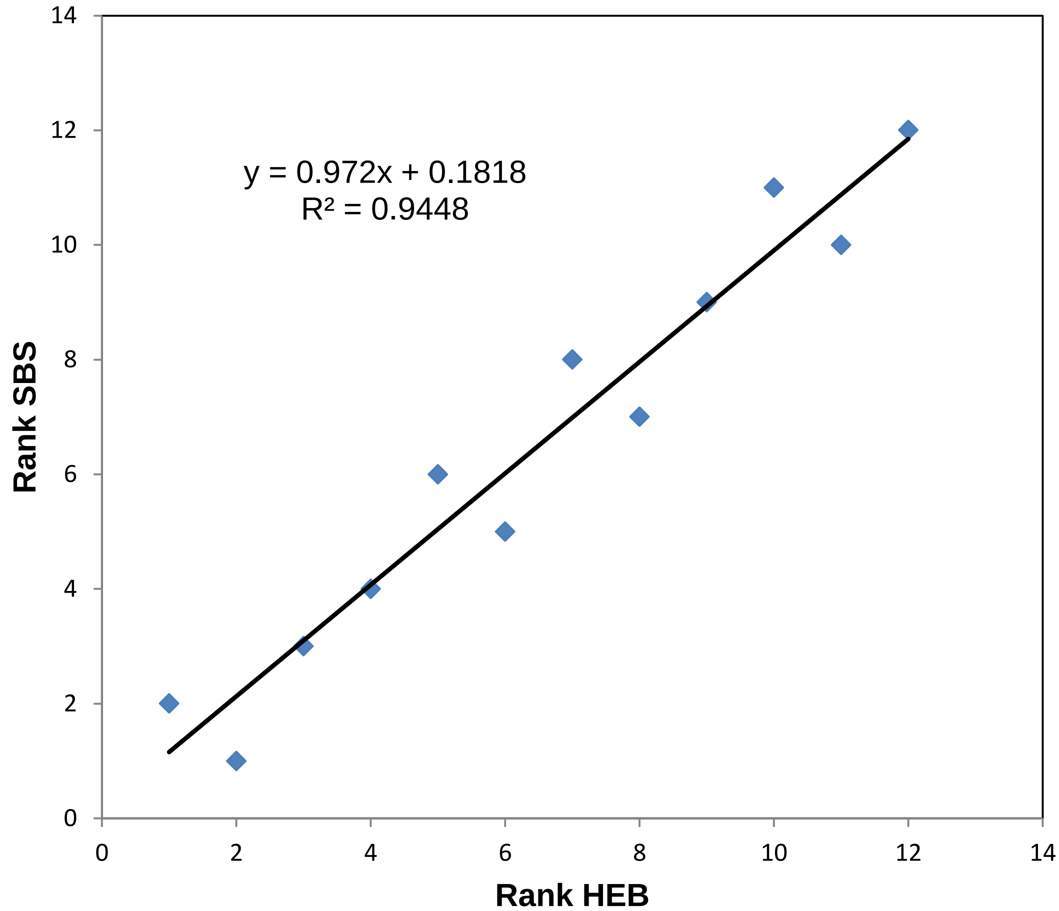


Figure 54. Correlation of ranking of reading eye movements between researchers for patient 13.

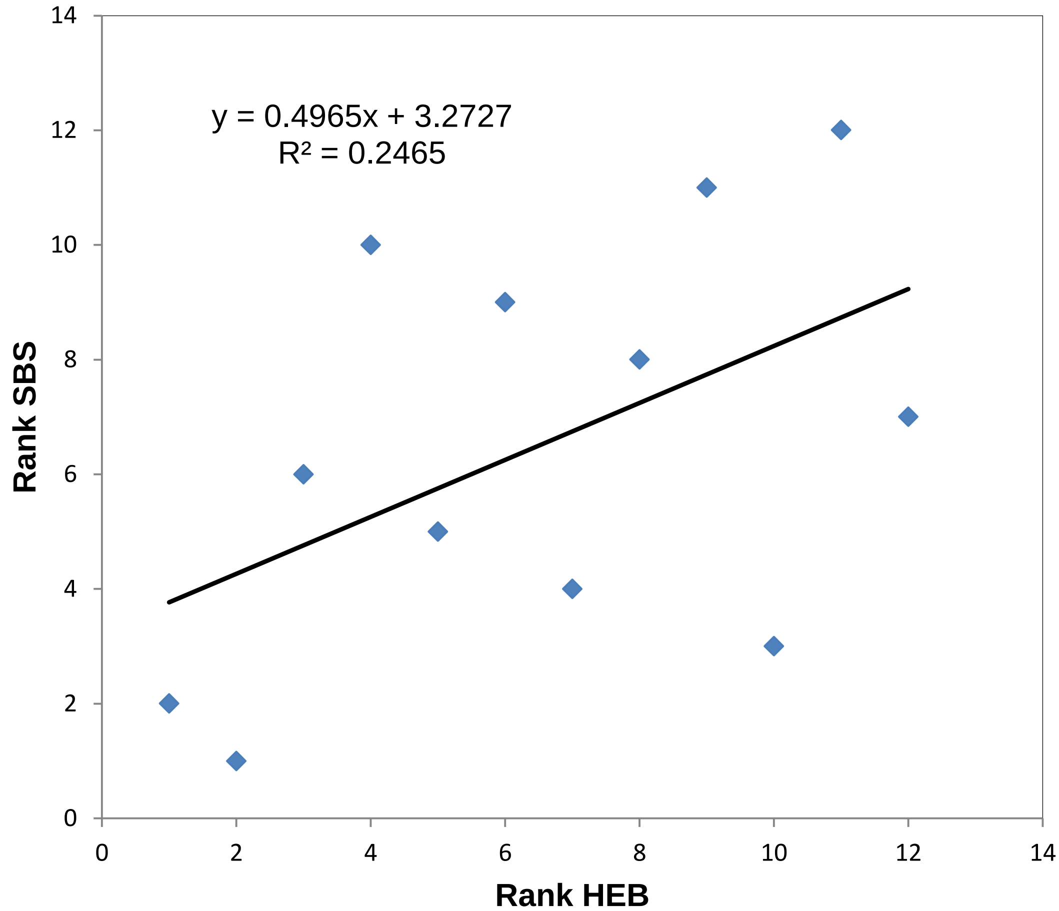


Figure 55. Correlation of ranking of reading eye movements between researchers for patient 96.

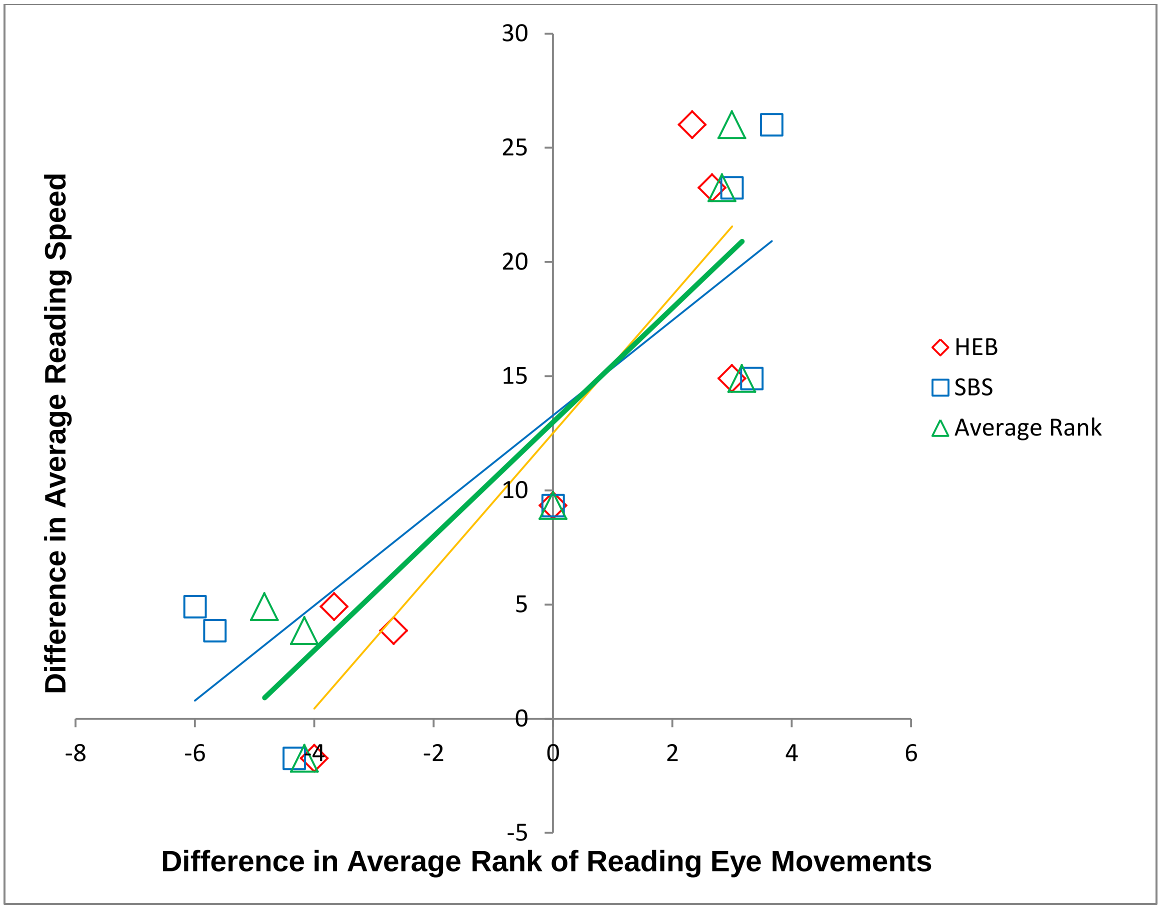


Figure 56. Improvement in reading speed with eye movements judged more similar to normal reading eye movements.

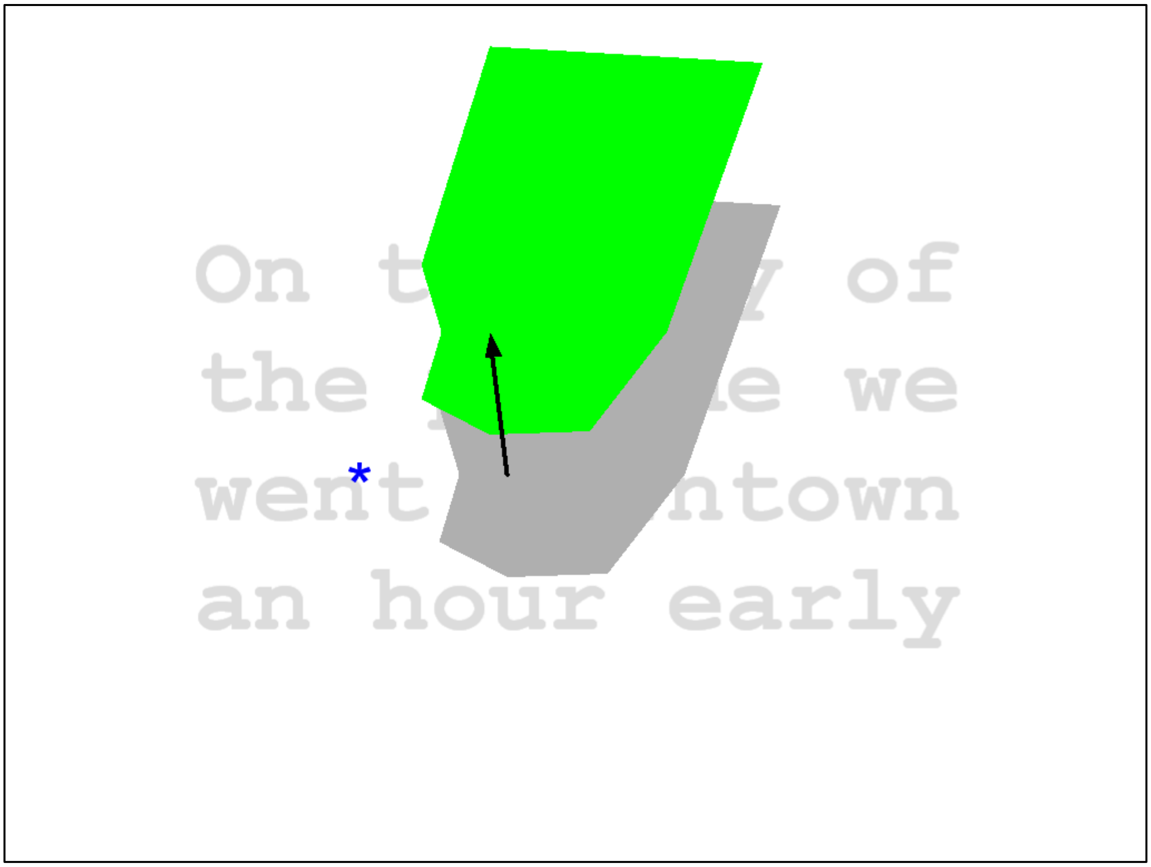


Figure 57. Horizontal and vertical shift in fixation locus for subject 55. The average position of the scotoma location for the initial 6 trials is drawn in gray and the average position for the final 6 trials is drawn in green. The polygon used to represent scotoma location in this image is the actual polygon overlay used during alternate sets of reading trials for this subject. However the polygon overlay was not visible during the trials compared in this analysis. The polygon overlay is used here solely to approximate the position and size of the patient's actual scotoma. The patient's actual scotoma was slightly smaller than that displayed here, as the polygon is based on the locations where the patient was just able to see the test probe. The length of the black arrow is scaled to represent the shift in fixation locus from the first to the last 6 trials and represents a 4.5 degree change. Letter size is 1.2 logMAR, such that a lower case x subtends 1.3 degrees. The dimensions of the monitor, as represented by the rectangular outline, were

35 deg by 27 deg. An asterisk marks the location of the single-letter PRL in relation to the position of the initial scotoma.

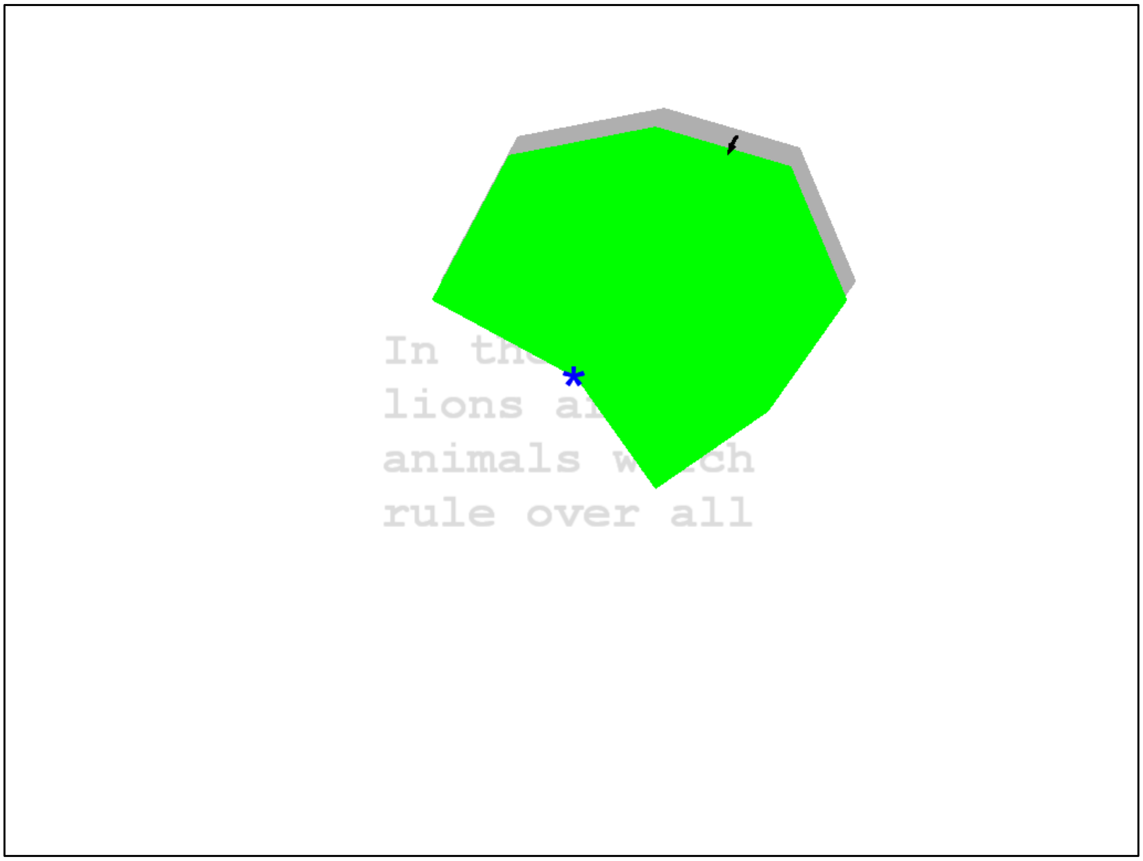


Figure 58. Horizontal and vertical shift in fixation locus between the first and last 6 reading trials without the polygon overlay for subject 64. The length of the black arrow is scaled to represent the shift in fixation locus from the first to the last 6 trials and represents a 0.67 degree change. Letter size is 0.9 logMAR and a lower case x subtends 0.67 degrees.

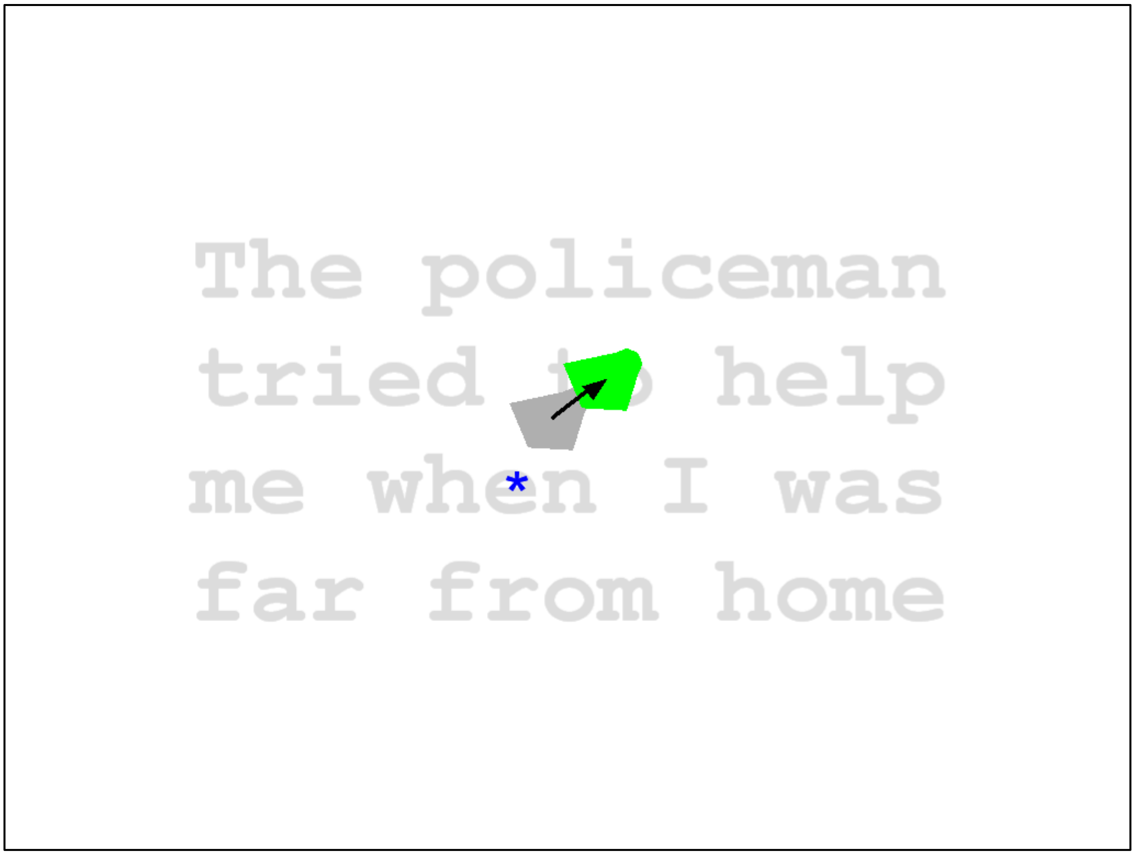


Figure 59. Horizontal and vertical shift in fixation locus between the first and last 6 reading trials without the polygon overlay for subject 78. The length of the black arrow is scaled to represent the shift in fixation locus from the first to the last 6 trials and represents a 2.1 degree change. Letter size is 1.2 logMAR and a lower case x subtends 1.3 degrees.

Figure 60. Horizontal and vertical shift in fixation locus between the first and last 6 reading trials without the polygon overlay for subject 31. The length of the black arrow is scaled to represent the shift in fixation locus from the first to the last 6 trials and represents a 2.4 degree change. Letter size is 1.1 logMAR and a lower case x subtends 1 degree.

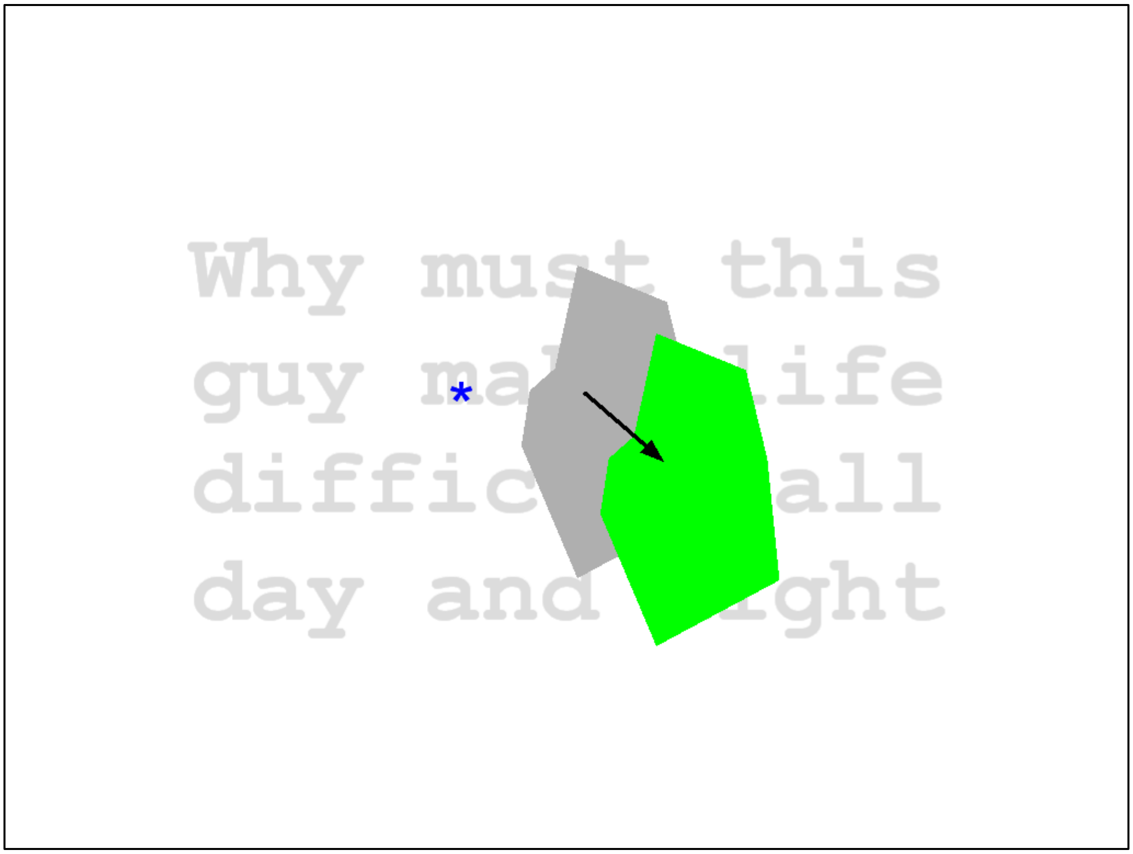


Figure 61. Horizontal and vertical shift in fixation locus between the first and last 6 reading trials without the polygon overlay for subject 51. The length of the black arrow is scaled to represent the shift in fixation locus from the first to the last 6 trials and represents a 3.3 degree change. Letter size is 1.2 logMAR and a lower case x subtends 1.3 degrees.

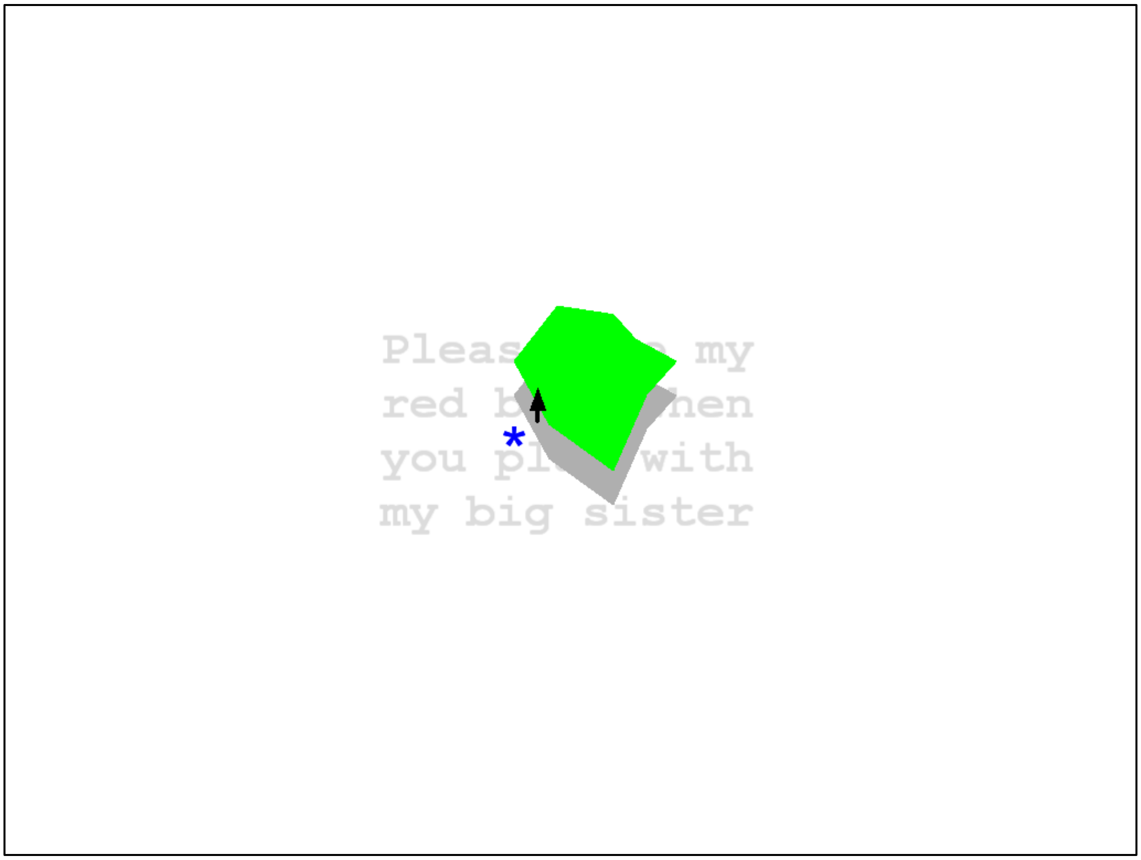


Figure 62. Horizontal and vertical shift in fixation locus between the first and last 6 reading trials without the polygon overlay for subject 13. The length of the black arrow is scaled to represent the shift in fixation locus from the first to the last 6 trials and represents a 1.1 degree change. Letter size is 0.9 logMAR and a lower case x subtends 0.67 degrees.

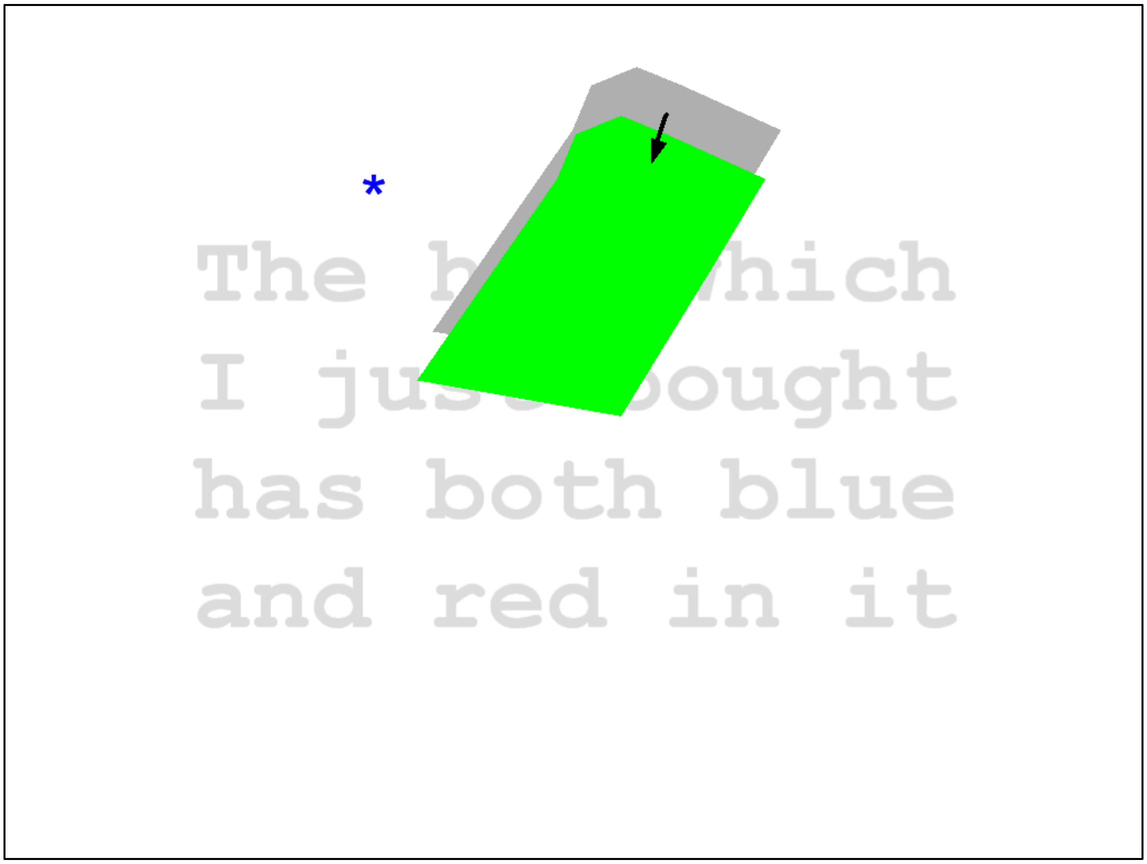


Figure 63. Horizontal and vertical shift in fixation locus between the first and last 6 reading trials without the polygon overlay for subject 96. The length of the black arrow is scaled to represent the shift in fixation locus from the first to the last 6 trials and represents a 1.6 degree change. Letter size is 1.2 logMAR and a lower case x subtends 1.3 degrees.

4.5 Discussion

The improvement in reading speed (average 0.075 log wpm or 19%) over the short experimental session for all subjects but one indicates that making the scotoma location more visible is potentially beneficial to improving reading speed. It is possible but unlikely that the observed improvement in reading speed was a result of learning the specific reading task instead of the influence of the polygon overlay. Three reasons that it is unlikely that the results simply reflect learning of the experimental task are: 1. The fixation location changed over the study session and resulted in a shift of the scotoma away from the center of text for five of the seven subjects, indicating that the patients were either adopting an alternate eye movement strategy or shifting their PRL, 2. Reading is an overlearned task and most of the subjects reported being avid readers even after the onset of their central scotomas, 3. The subjects were allowed to practice the experimental paradigm during the trials used to calculate the critical print size and generally showed the same reading speed for the critical print size and the initial reading speed before introduction of the polygon to mark the scotoma location. Eye movements were also ranked to be more consistent with normal reading eye movements toward the end of trials in subjects who showed the most improvement in reading speed.

The fact that all of the subjects read slower when the polygon overlay was visible argues against the polygon overlay resulting in the observed improvement in reading speed. Subjects may have read slower with the polygon overlay because the polygon was slightly larger than the actual scotoma and may have covered part of the area used normally by the patient to read. The EyeLink II does not provide perfect image stabilization as indicated, for example, by an absence of image fading, and may result in small shifts in the retinal area covered by the polygon, disrupting the patient's "normal" reading pattern. The polygon overlay may have also caused attention to be allocated to the region of the scotoma resulting in less sustained attention on the text.

After patients had experience with the polygon overlay, during subsequent reading without the polygon the PRL typically (5 out of 7) shifted further from the scotoma. This shift presumably allows more of the fixated word to be imaged on seeing retina. The PRL is frequently located at or very near the border of the scotoma which may be problematic for efficient reading. In normal reading, the letters to the right, and to a lesser extent the letters to the left, of fixation are important to achieving optimal reading speed (Rayner et al. 1981). For this reason, it is likely that the amount of a word that a patient with central vision loss can see during one fixation will exert an influence on reading speed.

Chapter 5

General Conclusions

The results of this dissertation have important implications for low vision examinations and for research conducted with patients with macular degeneration or central scotomas. In Experiment 1 we hoped to show that patients with central scotomas image targets that are expected to fill-in at the vestigial fovea or near the center of the scotoma, which would allow the examiner to use these target types to better approximate the location of the scotoma in visual space and the eccentricity and direction at which eccentric viewing training may be beneficial. What we found however, was that although 11 of 12 patients used a retinal locus different than the single-letter PRL to image fill-in targets, the location of this PRL was not consistent with the location of the vestigial fovea in all patients and some patients used an area at the edge of the scotoma near the single-letter PRL. However, some patients did place the fill-in target within the scotoma. The between subject variability in placement of the fill-in targets relative to the scotoma and the vestigial fovea indicates that fill-in targets are not a good stimulus to approximate the scotoma location or to assess the magnitude of eccentric viewing. This variability also suggests that fill-in targets are not optimal for fixation during vision testing, including visual field tests. There was also a trend among six of the subjects for the BCEA to be smaller for a letter target, indicating that it is likely a better target for fixation.

One common test employed by many occupational therapists is the use of a clock dial to approximate the direction that patients should eccentrically view during visual tasks. Patients are asked to look at the center of a clock dial and to report which numbers appear the clearest. This information is then used to coach the patient to eccentrically view. A macular mapping test using a similar but more elaborate paradigm has been developed to more accurately plot remaining functional vision (Hahn et al.

2009). This test uses a large spoke like target that is supposed to stimulate foveal fixation and the surrounding letter targets are scaled for eccentricity based on this assumption. The results of this test and as well as the clock dial test become less interpretable when the retinal location of fixation is unknown. As the results of Experiment 1 indicate that a large fixation target does not assure foveal fixation, these and similar tests may be improved if a letter fixation target is used. This would allow the location of reduced vision relative to the PRL to be mapped. It is likely that by incorporating targets with letters, examiners will achieve more consistent and accurate results when they test the visual function of patients with macular scotomas.

Experiment 2, 3, and 4 all indicate that patients with central scotomas will potentially benefit from training that delineates the location of the scotoma. Changes in the mean vertical fixation location in both experiments 2 and 4 suggest that reading speed with central scotomas should improve when patients learn to position the scotoma out of the way. The preferred direction that was found for moving the scotoma out of the way is consistent with the most commonly observed location of the PRL in patients with central scotomas.

Future research evaluating the efficacy of training involving delineation of the scotoma location is necessary. A larger sample size with better established baseline reading speeds and longer training periods will allow more certainty that reading speed improves with this training. Research comparing improvement in reading with training between patients who have recently developed central scotomas and patients who have long-standing central scotomas, and patients with poor reading speed and patients with relatively good reading speed, as well as in patients with different scotoma characteristics, will allow us to evaluate which patients are most likely to benefit from training.

Research evaluating alternate methods of delineating the location of the scotoma could also lead to more practical and less technically demanding approaches to training. Flickering random dot patterns have been explored as a means of scotoma detection as flicker appears to temporarily defeat perceptual filling-in (Aulhorn and Köst 1988). Research comparing the eye movement strategies of patients with central scotomas who are good readers to similar patients that are poor readers will allow us to see if there are any strategies that can be beneficial to training reading in this patient population.

Future research also needs to address patient perception within the scotoma. In our last study we asked patients what they perceived in the location of their scotoma after trials with the polygon overlay. Patients stated that they perceived a white area with the same luminance as the background in the location of their scotoma. It will be important to measure whether patients perceive this white area without steady fixation on text and whether the polygon overlay increases awareness of the scotoma location and content.

Appendices

Table 13. Effect of correcting for multiple fixations on BCEA

		Target Type					
		cross	spoke	disk	cross-letter	spoke-letter	letter
Subject							
11	Uncorrected	5.91					
	Corrected	1.30					
	Uncorrected	22.63					
	Corrected	2.08					
21	Uncorrected					5.40	4.19
	Corrected					0.65	2.17
39	Uncorrected		4.18		12.72		
	Corrected		2.91		6.39		
59	Uncorrected			3.48		6.20	
	Corrected			1.93		0.98	
62	Uncorrected		38.86				
	Corrected		21.15				
66	Uncorrected	2.08				1.07	
	Corrected	0.81				0.66	
	Uncorrected	3.98					
	Corrected	0.74					

Table 14. Phenomenological data from Experiment 1. Whether patients reported the large fill-in targets to appear complete, broken or missing, or blurry or faint.

Patient	Target Type	Appears Complete	Broken or Missing Portion	Blurry or Faint Portion
10	Cross	Y	N	N
	Spoke	Y	N	N
	Disk	Y	N	N
11	Cross	N	Y	Y
	Spoke	N	Y	Y
	Disk	N	Y	Y
21	Cross	Y	N	Y
	Spoke	Y	N	Y
	Disk	N	N	N
28	Cross	Y	N	N
	Spoke	Y	N	N
	Disk	Y	N	N
37	Cross	Y	N	N
	Spoke	Y	N	N
	Disk	Y	N	N
39	Cross	Y	N	N
	Spoke	Y	N	N
	Disk	Y	N	N
44	Cross	Y	Y	N
	Spoke	Y	Y	Y

	Disk	Y	Y	Y
59	Cross	Y	Y	Y
	Spoke	N	Y	Y
	Disk	Y	Y	Y
60	Cross	N	N	Y
	Spoke	Y	N	Y
	Disk	N	Y	Y
61	Cross	Y	N	Y
	Spoke	Y	N	Y
	Disk	Y	N	Y
62	Cross	Y	N	Y
	Spoke	Y	N	Y
	Disk	Y	N	Y
66	Cross	N	Y	N
	Spoke	N	Y	N
	Disk	N	Y	Y

Table 15. Standard deviation of size comparison to a black 4 degree scotoma calculated for different scotoma types from point of subjective equality (PSE) data.

Scotoma Type	Subject	Sigma	PSE
Flipped	1	0.459	4.141
	2	0.447	3.906
	3	0.486	3.813
	4	0.498	3.766
Low-luminance	1	0.341	4.070
	2	0.176	3.930
	3	0.183	4.035
	4	0.296	3.891
Mixed-text	1	0.938	4.188
	2	0.692	3.813
	3	0.396	3.734
	4	0.626	3.906
Random-dot	1	0.182	3.945
	2	0.190	3.949
	3	0.109	3.848
	4	0.096	4.023

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