Repeatability of Nidek MP-1 Fixation Measurements in Patients With Bilateral Central Field Loss

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Purpose. Visual performance in patients with bilateral central field loss is related to fixation stability. This study evaluated the repeatability of visual-fixation parameters in patients with bilateral central field loss, measured with the MP-1 microperimeter for fixation durations on the order of 15 to 30 seconds.

Methods. Bivariate contour ellipse area (BCEA), and the eccentricity and meridian of the preferred retinal locus (PRL) were determined in 56 eyes of 56 patients, sampled at two investigational sites. Repeatability and agreement were assessed by estimating 95% limits of agreement for each parameter from two fixation examinations conducted on the same day.

Results. The 95% confidence intervals (CI) for log BCEA and for PRL eccentricity and meridian were ±0.67 log deg^2, ±2.0°, and ±65.9°, respectively. Each CI decreased substantially if a small number of outlying data points were excluded. For all parameters, the mean difference between the two fixation examinations was close to zero.

Conclusions. For most patients with bilateral central field loss, the repeatability of estimated BCEA and PRL eccentricity and meridian is good. When repeated estimates of fixation parameters do not agree, the absence of a well-developed PRL or the use of multiple PRLs may be suspected.

Keywords: central field loss, fixation stability, preferred retinal locus, repeatability, microperimeter

It is assumed commonly that efficient oculomotor and visual performance in patients with bilateral central field loss are associated with the use of a stable extrafoveal preferred retinal locus (PRL). In particular, visual acuity,[1–3] reading performance,[2,4–7] and visual search[8] are reported to be better in patients with more stable fixation. Recently, Mandelcorn et al.[9] recommended including fixation stability as an outcome measure in studies that assess treatments for macular disease.

The locus and stability of fixation can be described in terms of the position and size of a bivariate contour ellipse, the area (BCEA) of which includes a specific percentage of the retinal locations during a period of fixation.[10,11] The Nidek MP-1 microperimeter (Fremont, CA, USA) performs 'fixation examinations' and reports the BCEAs that include 68.2%, 95.4%, and 99.6% of the recorded fixation samples, corresponding to ±1, ±2, and ±3 SD around the mean fixation locus. In the literature, a 68.2% bivariate contour ellipse is the most commonly used.

Although repeatability of retinal sensitivity measurements using the MP-1 and MAIA microperimeters has been reported[12–17] the repeatability of measured fixation steadiness, as determined using the MP-1 in patients with bilateral central field loss, has been assessed only once.[18] In the study by Chen et al.,[18] fixation on a 2° cross was measured during perimetric testing for an average duration of approximately 12 minutes. This duration greatly exceeds the duration of most naturally occurring fixation tasks and is likely to overestimate the variability of fixation when the duration is briefer.[19] In addition, Morales et al.[20] reported that, in the majority of their patients with AMD, a shift occurred between the location of the PRL determined from 10 seconds versus 6 minute samples of fixation. Elsner et al.[21] compared the BCEAs determined from a single fixation examination using a scanning laser ophthalmoscope but computed using an automatic versus a manual algorithm. The 95% confidence interval (CI) for agreement between the two algorithms was approximately ±0.6 log min arc^2 in their sample of 27 patients without macular scotomas.

The aim of this study was to assess the repeatability of fixation parameters in patients with bilateral macular disease, when measured using the Nidek MP-1 microperimeter for a duration of fixation equal to 15 to 30 seconds.

Methods

Data were obtained from the preferred or better-seeing eye of 56 patients with bilateral central field loss, collected at two sites. In patients whose eye preference was unknown and who had equal visual acuity in the two eyes, one eye was selected at random. The complete sample included 26 patients from the

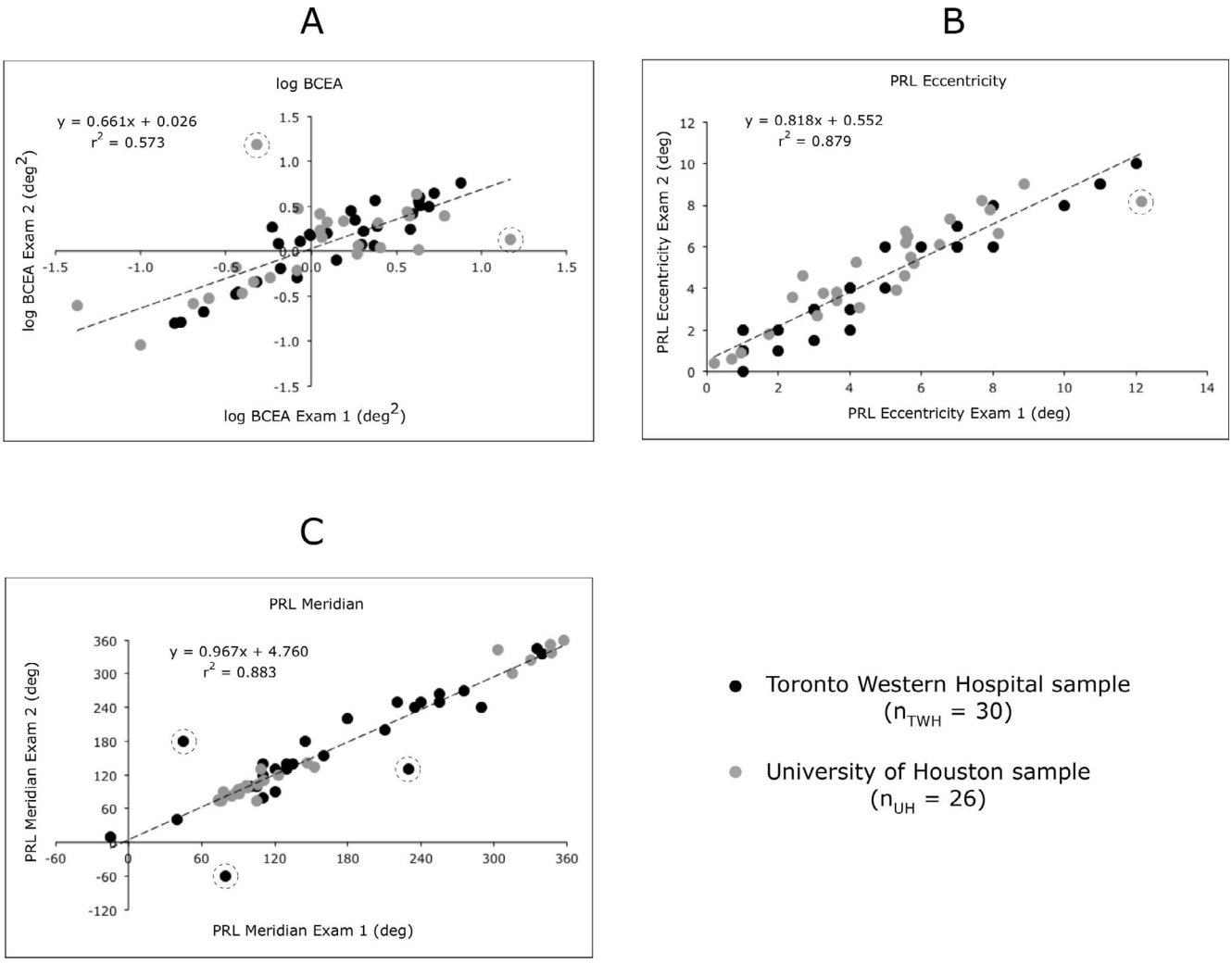

Figure 1. First- versus second-examination measures of log BCEA (in log deg^2, *panel A*), estimated PRL eccentricity (in deg, *panel B*), and estimated PRL meridian with respect to the foveal location (in deg, *panel C*). The *gray* and *black symbols* indicate data from UH and TWH, respectively. In each panel, *dotted circles* surround data points that are outliers (≥3 SD). In *panel C*, the data points with negative x or y values represent patients whose PRL meridians fell in quadrants 1 and 4 on the two fixation examinations, for example, 80° on examination 1° and 300° (equal to –60°) on examination 2.

University Eye Institute, University of Houston College of Optometry (UH) and 30 patients from the Toronto Western Hospital (TWH). The research protocols used at UH and TWH were approved by local ethics committees and, in accordance with the tenets of the Helsinki declaration, all patients provided voluntary written informed consent before undergoing testing.

In the UH sample, the patients' ages ranged from 20 to 88 years, with a median of 54 years. The majority of patients were diagnosed with AMD ($N = 11$) or Stargardt disease ($N = 10$). Three patients had cone or cone–rod dystrophy, one had bilateral macular holes, and one had macular loss secondary to Plaquenil toxicity. Best corrected visual acuity in the tested eye ranged from 20/30 to 20/320 with a median value of 20/125.

The patients from TWH had a median age of 82, with a range from 34 to 95 years old. Twenty-six of the 30 patients had a diagnosis of AMD. Two of the remaining patients had cone dystrophy, one had Stargardt disease, and one had bilateral myopic macular degeneration. The range of best-corrected visual acuity in the tested eyes was 20/35 to 20/250, with a median of 20/100.

In the UH sample, perimetric testing performed with the MP-1 confirmed the presence of a dense central scotoma in both eyes of each patient. Nevertheless, three of the patients in the UH sample used a PRL during fixation that was within 1° of the estimated foveal location (Fig. 1B). Perimetric testing was not performed routinely on the patients in the TWH sample.

Both in Houston and Toronto, the patients underwent two 'fixation examinations' on the same day using the Nidek MP-1 microperimeter. An infrared camera in the MP-1 captures the black and white image of the fundus, which is used to evaluate the patients' fixation in real time. Eye position is recorded by tracking an anatomical landmark in a 128 × 128 pixel window (approximately 8° × 8°) of the retinal image that is selected by the operator. Fundus movements are recorded while the patient fixates on a target projected on a graphics screen. The MP-1 automatically compensates for stimulus projection location and calculates the horizontal and vertical eye locations relative to a reference frame at a sampling rate of 25 Hz. During the examination, the head is stabilized by a chin and forehead rest. In this study, the nonviewing eye was patched.

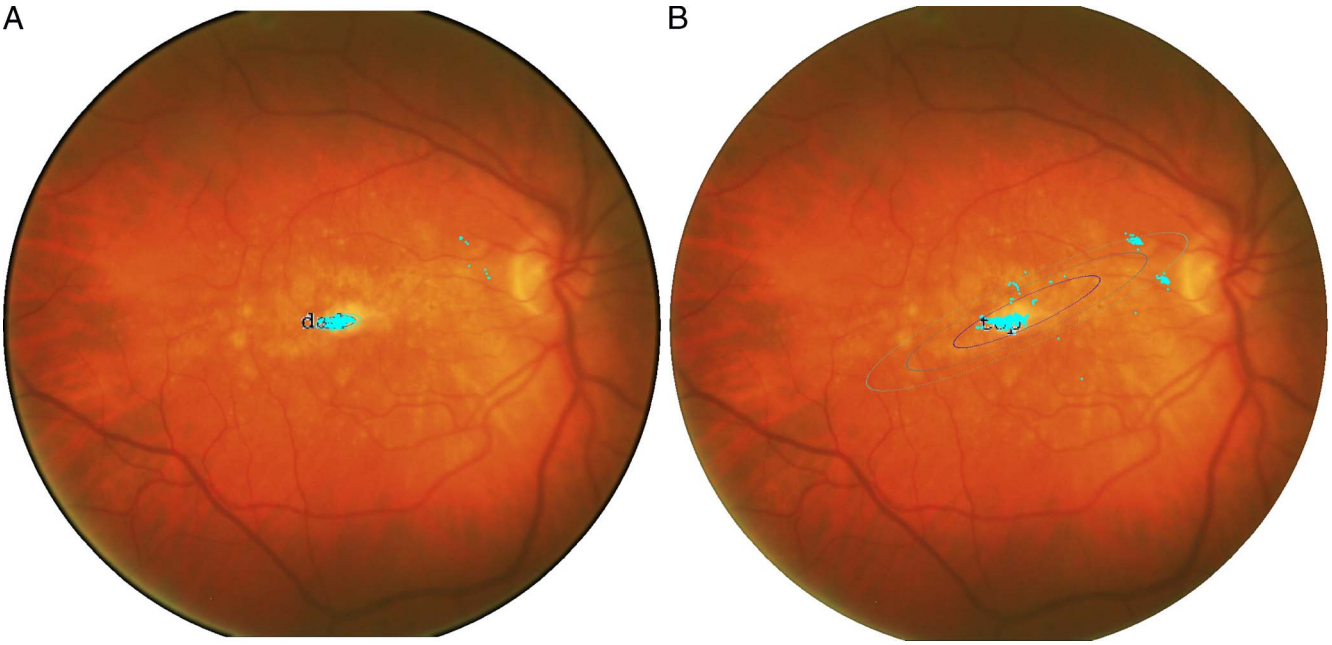

Figure 2. Color fundus images showing the distribution of fixation locations (*light blue dots*) for UH patient K3 during fixation examinations 1 (*left panel*) and 2 (*right panel*). The patient was instructed to fixate the central letter of the 3-letter word. The 68.2%, 95.4%, and 99.6% bivariate contour ellipses determined by Nidek MP-1 software are represented by the *dark*, *medium*, and *light blue figures* (partially obscured in the *left panel*), respectively. In both panels, note the distinct cluster of fixation samples close to the optic disk (*up* and *right* in each image). For examination 1 only, the MP-1 treated these fixation locations as outliers and excluded them when calculating BCEA.

The average duration of the fixation examinations at UH was 33 seconds. At TWH, the duration of the fixation examinations averaged 15.5 seconds. During the examination, blink detection derives from the requirement for the instrument to have a view of the fundus to perform recording. Other nontracking events are detected by the MP-1′s proprietary software. Although the manufacturer does not provide information about measurement precision, Midena et al.[22] reported the mean tracking accuracy of the MP-1 is approximately 5 min arc both in the horizontal and vertical directions.

The fixation target used for the UH sample of patients was a single capital letter for 12 patients[23] and the central letter of a lower case 3-letter word for 14 patients. The angular size of single-letter fixation targets was larger than the patient's measured visual acuity. The size of the word fixation targets was equal to the critical print size, determined beforehand using hand-held MNRead charts.[24] Patients were instructed to look at the center of the single letter or at the middle letter of the 3-letter word, while ensuring that the entire target remained visible. The patients in the TWH sample viewed a bright red cross and were instructed to fixate its center, except for one patient who was asked to fixate on the middle of a 3-letter word composed of 20/200 letters. The cross target subtended 3° for 26 of the patients, but was increased in size to 6° for one patient and to 7° for another two patients who had poor visual acuity.

A 68.2% bivariate contour ellipse, extending ±1 SD from the mean fixation locus, was calculated by the MP-1 from the fixation locations recorded during intervals of valid tracking. Off-line calculation of the BCEAs using the fixation data exported from the MP-1, after excluding points more than ±3 SD from the mean fixation position, confirmed the calculated BCEA values. We did not attempt to correct the calculated BCEA value[23,25] for the one patient who exhibited multiple PRLs (see below). The log BCEAs were transformed logarithmically to reduce positive skew and produce an approximately normal distribution of the data.[7,11,26]

In the UH sample, the retinal eccentricity and the meridian of the PRL were calculated from the results of each examination by assuming a foveal location that is 15.5° temporal and 1.5° below the center of each patient's optic disc.[27] For the TWH sample, the assumed foveal location was 15.5° temporal and 1.3° below the center of the optic disc.[1] A PRL to the right of the estimated foveal location (i.e., nasal retina in the right eye and temporal retina in the left eye) was designated as having a meridian of zero. Superior and inferior on the retina were designated as the 90° and 270° meridians, respectively. Repeatability of the 68.2% BCEA, PRL eccentricity, and PRL meridian were assessed from the two measurements performed on each patient. Ninety-five percent limits of agreement between the repeated measurements were determined using Bland-Altman analyses.[28] Because of differences in the details of the testing and analysis procedures at the two institutions, the data for each sample are first considered separately and then in combination.

Results

UH Sample

Averaged across the two examinations, the log BCEA ranged from −1.02 to 0.65 (0.1–4.5 deg^2) with a mean value of 0.03 (1.08 deg^2). The median log BCEA was 0.18 (1.5 deg^2). The estimated eccentricity of the PRL ranged from 0.3° to 10.1° with a mean distance of 4.9° (median distance also = 4.9°). In 16 of 26 patients the PRL was in the superior retina, within ±22.5° of the vertical meridian. Three patients had PRLs within ±22.5° of the horizontal meridian and seven patients had PRLs along an oblique meridian.

Figure 1A plots the log BCEAs measured during examination 1 versus examination 2. Two outlying data points (≥3 SDs) are

surrounded by dotted circles. As illustrated in Figures 2A and 2B, one of these patients consistently used more than one PRL, which strongly influenced the calculated BCEA for one of the fixation examinations but not the other. Specifically, the MP-1 software categorized the small number of samples at this patient's second PRL near the optic disk as statistical outliers (Fig. 2), and did not include them when calculating the BCEA for the first fixation examination (confirmed by off-line analysis of the exported data). The second patient whose data are marked in Figure 1A as an outlier had no well-defined PRL and fixated in a long arc along the nasal and superior margins of the central scotoma during one, but not the other, of the two examinations.

Figure 1B plots the estimated eccentricity of the PRL on examination 1 versus examination 2. With the exception of one patient, indicated by the dotted circle, the estimated PRL eccentricity was similar for the two examinations. Figure 1C shows the PRL meridians with respect to the estimated foveal location on examination 1 versus 2. The estimated meridians were similar on the two examinations for all of the patients.

Bland-Altman analyses indicated the limits of agreement for log BCEA, estimated PRL eccentricity and estimated PRL meridian for the two fixation examinations. For each of these parameters, the mean difference between examinations 1 and 2 is close to zero: 0.03 log deg^2 for log BCEA, 0.13° for PRL eccentricity, and 1.90° for PRL meridian. The calculated 95% limits of agreement are ±0.71 log deg^2 for BCEA, ±2.23° for the estimated eccentricity of the PRL, and ±21.8° for the meridian of the PRL with respect to the estimated foveal location.

TWH Sample

Log BCEA ranged from –0.80 to 0.82 (0.16–6.6 deg^2) with a mean value of 0.11, equivalent to 1.3 deg^2. The median log BCEA was 0.16, or 1.5 deg^2. The estimated eccentricity of the PRL ranged from 0.5° to 11° with a mean of 4.2° (median = 2.8°). In 12 of 30 patients the average PRL was displaced vertically (±22.5°) from the estimated foveal location, in eight patients in the superior retina and in four patients in the inferior retina. In eight patients the PRL was within ± 22.5° of the horizontal meridian and in the remaining 10 patients the PRL was displaced along an oblique meridian from the estimated foveal location.

Figure 1A shows that log BCEAs for the patients in the TWH sample were similar on examinations 1 and 2. Figure 1B plots the estimated eccentricities of the PRL on examination 1 versus examination 2, which also were similar. Figure 1C shows the PRL meridians with respect to the estimated foveal location on examination 1 versus 2. The estimated meridians were similar during the two examinations for 27 of the 30 patients. For the remaining three patients (dotted circles) the mean location of the PRL was between 0.5° and 2.25° from the estimated foveal location, such that relatively small differences in the position of the PRL on the two examinations produced large differences in the calculated meridian.

Bland-Altman analyses of log BCEA, estimated PRL eccentricity, and estimated PRL meridian for this sample of patients indicate that mean differences between the two fixation examinations again are close to zero (0.021 log deg^2 for log BCEA, 0.48° for PRL eccentricity, and 0.67° for PRL meridian). The 95% limits of agreement are ±0.37 log deg^2 for BCEA, ±1.79° for the estimated eccentricity of the PRL, and ±87.8° for the meridian of the PRL with respect to the estimated foveal location. When the three outliers who fixated near the estimated foveal location are removed, the confidence limits for the meridian of the PRL decrease to ±38.7°.

Combined Samples

After pooling the data from the UH and TWH samples, the average log BCEA for the two examinations was 0.08 log deg^2, corresponding to 1.2 deg^2 (median = 0.18 log deg^2, equal to 1.5 deg^2). The mean difference in log BCEA from examination 1 to examination 2 was 0.0 log deg^2 and the 95% limits of agreement ranged from –0.67 to 0.67 log deg^2 (Fig. 3). If the two outliers from the UH sample are removed, the range of the 95% limits of agreement for log BCEA is reduced to –0.47 to 0.49 (±0.48 log deg^2). The mean difference in the eccentricity of the PRL between examinations 1 and 2 was 0.30°, with 95% limits of agreement that ranged from –1.74 to 2.33 deg (±2.03°). Removing one outlier from the UH sample reduced the range of the 95% limits of agreement for PRL eccentricity to –1.56° to 2.02° (±1.79°). Finally, the mean difference in the meridian of the PRL from examination 1 to examination 2 was 0.50°, with 95% limits of agreement that ranged from –65.4° to 66.4°. After eliminating the three outliers from the TWH sample, the 95% limits of agreement decreased to between –33.6° and 29.4° (±31.5°).

In the combined sample, the log BCEA, averaged for the two examinations, exhibited a moderate positive correlation (r = 0.38; $t_{df=54}$ = 2.99, P = 0.0042) with the average estimated eccentricity of the PRL (Fig. 4). A positive correlation was observed also in each of the two subsamples (UH sample, r = 0.32; TWH sample, r = 0.45), although only the correlation in the TWH sample achieved statistical significance ($t_{df=28}$ = 2.64, P = 0.014). In agreement with a previous report on fixation in healthy subjects,[29] there was no significant change in log BCEA with age (r = –0.24, $t_{df=54}$ = 1.84, P = 0.072).

Discussion

A preliminary communication by Rigoni et al.[30] reported an average log BCEA during fixation in 100 healthy observers of –0.35 log deg^2 and characterized the test–retest reliability of the MP-1 as 'good.' Other studies[19,31,32] reported mean values of log BCEA during fixation by healthy observers between –0.7 and –1.0 log deg^2. On the other hand, Chen et al.[18] reported a mean BCEA for their 50 patients with central field loss of 4.26 log min arc^2, corresponding to 0.70 log deg^2, or 5.0 deg^2. Using patients with similar characteristics, the mean log BCEA of 0.08 log deg^2 that we measured is nearly 0.6 log units (4 times) smaller. Other studies that assessed the fixation of patients with central field loss reported mean values of log BCEA range from 0.34 to 0.60, for testing durations between 30 and 60 seconds.[7,19,33]

Part of the difference between the log BCEA values reported by Chen et al.[18] and the current study may be attributable to the substantially longer fixation intervals that were sampled by Chen et al. In a group of 60 patients with early or advanced AMD, Longhin et al.[19] found that the mean BCEA during the initial 10 seconds of fixation was 2.5 times (~0.4 log deg^2) smaller than the mean BCEA determined during the entire (unspecified) duration of microperimetric testing. In addition, some of the variation in the mean log BCEA values reported by different authors is likely to reflect the characteristics of the patients with central field loss that were sampled in each study.

The 95% interval of agreement for log BCEA that we calculated from the pooled data set is ±0.67 log deg^2, which is similar to the value of ±0.62 reported by Chen et al.[18] In our sample of patients with bilateral central field loss, the 95% intervals of agreement are inflated by a small number of outliers. Specifically, the 95% interval of agreement for log BCEA decreases to ±0.48 log deg^2 if the data from two outliers from the UH sample (one with multiple PRLs) are excluded

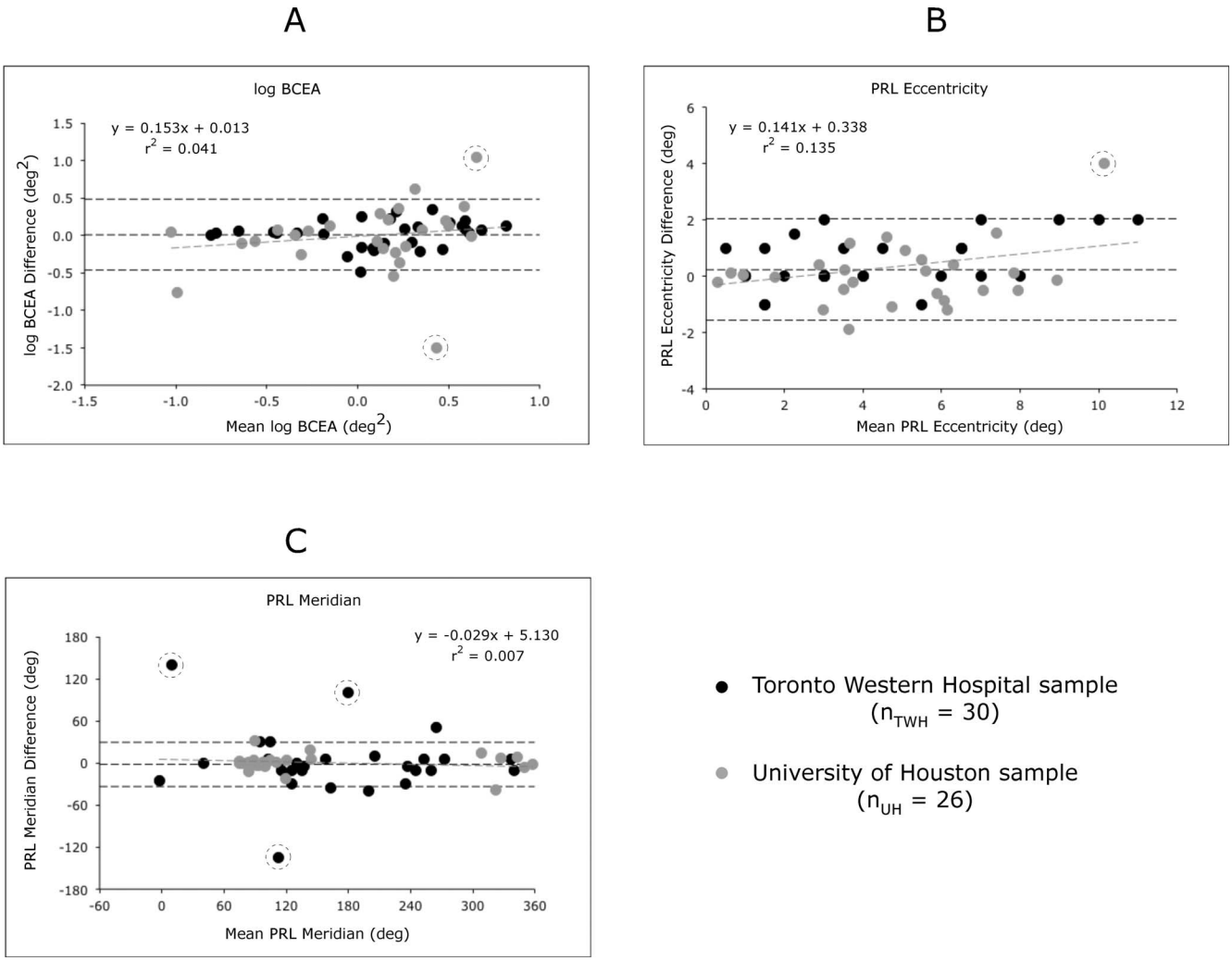

Figure 3. Bland-Altman plots indicate the repeatability of measured log BCEA (*panel A*), estimated PRL eccentricity (*panel B*), and estimated PRL meridian (*panel C*) for 26 patients from UH (*gray symbols*) and 30 patients from TWH (*black symbols*). In each panel, the equation is given for the *light gray line* fit to data. The *middle horizontal dashed line* represents the mean difference between the estimates for examinations 1 and 2 and the *two straddling lines* indicate the upper and lower limits of the 95% interval of agreement. *Circled outliers* were excluded when calculating the indicated intervals of agreement.

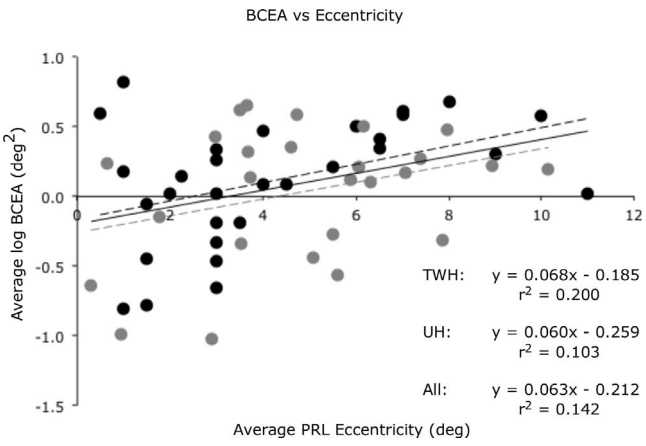

Figure 4. Average log BCEA (in log deg^2) is plotted against the average estimated PRL eccentricity (in degrees) for 26 patients from UH (*gray symbols*) and 30 patients from TWH (*black symbols*). *Best fit regression lines* are shown for each sample separately, and for the combined sample of 56 patients.

from the analysis. Similar reductions occur in the 95% intervals of agreement for the eccentricity and the meridian of the PRL if between one and three outliers are removed from each calculation.

It is not surprising that the observed values of log BCEA correlate with the retinal eccentricity of the PRL. A similar relationship between fixation stability and the eccentricity of the PRL was reported by several previous investigators.[1,2,11,34,35] White and Bedell[36] noted that fixation stability worsens in subjects with healthy vision according to the retinal eccentricity of the fixation stimuli and found a similar, albeit statistically nonsignificant relationship in their sample of patients with central field loss.

Some of the patients in our samples used a PRL that was very close to the estimated foveal position. There are three possible, nonmutually exclusive reasons for this apparently incongruous behavior, which was observed even in some of the UH sample of patients, all of whom demonstrated bilateral central field loss during microperimetric testing. First, some patients may have small islands of residual vision near the fovea that were not sampled by the relatively coarse array of perimetric test locations. Second, foveal or parafoveal sensitiv-

ity in some of the patients may have been insufficient to detect the brightest test spots presented by the MP-1 during microperimetric testing, but still adequate to perceive and fixate the large, high-contrast letter or cross targets that were used for the fixation examination. And, finally, in some of the patients the foveal scotoma may have been smaller than the size of the fixation target, which would have allowed these patients to fixate using the fovea on a target that was perceptually filled-in.[23]

We suggest that estimates of fixation parameters, such as log BCEA, PRL eccentricity, and PRL meridian, in patients with bilateral central field loss might best be determined from two or more successive brief examinations and examined for concordance. When repeated estimates do not agree, the examiners should be alert to the possibility that the patients either do not have a firmly established PRL or switch between multiple PRLs.

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