Fixation Stability, Fixation Location, and Visual Acuity after Successful Macular Hole Surgery

Luminita Tarita-Nistor,1,2 Esther G. González,1,2,3 Mark S. Mandelcorn,5 Linda Lillakas,1,2 and Martin J. Steinbach1,2,5

PURPOSE. This study examined whether changes in fixation stability and fixation location are good predictors of visual acuity after successful macular hole surgery.

METHODS. Ten patients with macular hole were tested before surgery and at 1 and 3 months after surgery. Visual acuity was measured with the ETDRS; fixation stability and fixation location were assessed with the MP-1 Micropimeter (Nidek Technologies Srl, Vigonza, PD, Italy). The quantitative measure of fixation stability was calculated with a bivariate contour ellipse area (BCEA). Fixation location shift was evaluated using the differential map analysis feature of the MP-1 Micropimeter.

RESULTS. There was a significant improvement in visual acuity after macular hole closure. Fixation location shifted an average of 0.55 deg and 0.87 deg at 1 month and 3 months after surgery, respectively. The fixation shift was not a good predictor of visual outcome. Fixation stability improved from an average of 0.35 deg2 before surgery to 0.29 deg2 at 3 months after surgery. The change in fixation stability (ΔBCEA = BCEA before − BCEA after surgery) correlated highly with visual outcome. The regression model showed that ΔBCEA accounted for a significant proportion of the variance in visual acuity both 1 and 3 months after surgery.

CONCLUSIONS. Some changes in ocular motor function explain the visual outcome after the anatomic success of macular hole surgery. Fixation location shift has no influence on visual acuity post-operatively; however, change in fixation stability is a strong predictor of visual outcome after successful closure of the macular hole. (Invest Ophthalmol Vis Sci. 2009;50:84 – 89) DOI:10.1167/iovs.08-2342

Diopathic macular hole is a degenerative defect of the central retina that leads to a displacement of photoreceptors in the fovea. Patients affected by this disease usually experience metamorphopsia and a sharp drop in visual acuity.1 Macular hole is age related and more prevalent in elderly women.2 Previously considered an untreatable disease, macular hole is now correctable with a surgical procedure (pars plana vitrectomy) that has been continuously refined since its introduction in 1991.3 Surgery results in closure of the macular hole in a high proportion of patients, leading to an improvement in visual acuity and contrast sensitivity, and to an increase in the subjective perception of visual function and visual quality of life.4–10 However, despite surgical anatomic success, visual outcome (i.e., visual acuity) is below expectation in many cases.2,6,11 For example, Haritoglou et al.12 reported a high rate of macular hole closure post-operatively (96%), but acuity improved from a median of 20/100 to a median of 20/40 three years after surgery. This means that half of the patients still had low vision (worse than 20/40) in the operated eye.

These reports suggest that other factors may influence the visual outcome after macular hole closure. It has been shown that the size and duration of symptoms pre-operatively do not influence the development of visual acuity post-operatively.2,6,11 Moreover, examination of retinal anatomy using optical coherence tomography (OCT) after full macular closure shows abnormalities of the intraretinal architectural morphology such as foveal photoreceptor abnormalities, foveal detachment, foveal lesions, external limiting membrane, and/or retinal nerve fiber layer defects in many cases.3–15 Yet, some studies have found that abnormalities in the morphology of the macular area, as revealed by OCT examination, are not very good predictors of post-operative visual function.16,17 For example, Miura et al.16 examined visual outcome and macular morphology in the early stages after successful macular hole surgery. They divided their sample into a normal morphology group (patients who had a normal foveal contour after surgery) and an abnormal morphology group (patients whose holes were closed after surgery, but presented abnormalities such as intraretinal cysts or subretinal fluid), and found no difference in visual acuity between the two groups, both pre- and post-operatively.

Changes in ocular motor function—gaze selection and control—may explain the relatively moderate visual acuity improvement in some cases after anatomic closure of macular hole. Because macular hole leads to loss of central vision, patients affected by this disease use other parts of their retina for fixation. These “new foveae” are called preferred retinal loci (PRls).

Two aspects of the PRL are of interest: stability of fixation and retinal location. First, fixation stability refers to the precision of eye fixation or the variability of fixation when one fixates intently on a stimulus for a certain period.18 The quantitative measurement of fixation stability is expressed with the bivariate contour ellipse area (BCEA); it represents the area on which the eyes fixate for a certain proportion of time, and its calculation is based on the SD of the horizontal and vertical eye movements during fixation.18–22 Thus, good fixation is revealed by a small BCEA. Unfortunately, to our knowledge, only qualitative measures have been used in studying the fixation stability of patients with macular hole23; however, quantitative measures of fixation stability of patients with age-related macular degeneration—an eye disease that leads to a more severe central vision loss—show that these people have impaired fixation stability which may contribute to their poor visual function.21–22

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Supported by the Natural Sciences and Engineering Research Council of Canada (NSERC) Grant A7664 (MJS); the Sir Jules Thorn Charitable Trust (MJS); the Kembil Family Foundation (MJS); the Vision Science Research Program; the CNIB EA Baker Applied Research Grant (EGG), and an anonymous donor.

Submitted for publication May 27, 2008; revised July 28, 2008; accepted October 29, 2008.

Disclosure: L. Tarita-Nistor, None; E.G. González, None; M.S. Mandelcorn, None; L. Lillakas, None; M.J. Steinbach, None

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Second, PRL location may play an important role in visual performance. After the anatomic success of surgery, one might expect a great deal of recovery in visual function and a shift of the PRL location back toward its former location. It has been shown that retinal sensitivity as revealed by microperimetry increases significantly, and the absolute scotoma produced by the hole disappears in a large proportion of patients after successful closure of the hole. Studies using a scanning laser ophthalmoscope (SLO) also show that the PRLs are located at or near the upper margin of the macular hole before the surgery and that they shift toward the fovea after surgery. But precise measurements of the PRL shift after surgery have not been published, nor has the relationship between the PRL shift and visual performance after surgery been explored.

The development of new technology in the past few years (MP-1 Microperimeter, Nidek Technologies Srl., Vigonza, PD, Italy) allows us to record the exact location of PRLs, and to do a differential analysis of two fixation tests performed on the same eye. Differences in degrees between PRL locations before and after surgery can be accurately displayed, if proper calibration is performed. In addition, eye movements during fixation can be registered and the BCEA calculated from the raw data provided by the microperimeter. Therefore, this new technology permits us to track changes in PRL location and fixation stability after successful macular hole surgery. Since the discrepancy between anatomic and functional success is not well explained by factors such as abnormalities in the morphology of the macular area, the primary purpose of this study was to identify ocular motor changes that may predict visual function after successful closure of macular hole. Specifically, we studied changes in fixation stability and PRL location 1 month and 3 months after successful macular hole surgery, and how these adjustments related to visual outcome. We hypothesized that changes in fixation stability and PRL location would be good predictors of visual acuity after macular hole closure.

### Methods

#### Participants

Thirteen consecutive patients with a diagnosis of nontraumatic, degenerative macular hole with vitreous detachment scheduled for surgery and who met our inclusion criteria were initially enrolled in the study. Three patients were excluded from analysis because of unrelated medical complications after surgery (1 case) and unsuccessful macular hole closure (2 cases). Therefore, this study is based on data from ten patients (3 males and 7 females; mean age, 64 years; SD, 8.9). There were 4 left and 6 right eyes. The holes were designated as stage 4 according to Gass’s classification system. The hole diameter ranged from approximately 420 to 870 μm as measured with the OCT (Stratus OCT Model 3000; Carl Zeiss Meditec Inc., Dublin, CA). Duration of symptoms ranged from 2 to 10 months. The patients’ pre-operative baseline characteristics are shown in Table 1.

Patients with macular hole were recruited from referrals to the surgical retina practice of one of the authors (MSM) at the Toronto Western Hospital. Each patient underwent a complete ophthalmologic examination that confirmed the diagnosis of macular hole. No patient had any history of neurologic diseases or cognitive impairment, or any coexisting ocular pathology. Informed consent was obtained from all participants. The research was conducted in the Ocular Motor Laboratory at the Toronto Western Hospital, approved by the University Health Network Research Ethics Board and conducted in accordance with the tenets of the Declaration of Helsinki.

### Apparatus and Stimuli

The affected eye’s best corrected visual acuity at 2 m was recorded using the ETDRS chart (Lighthouse Int., NY). The MP-1 Microperimeter (MP-1) was used to record fixation location and eye movements during fixation, to take fundus photographs, and to perform differential map analyses of fixation locations. This instrument records the fixation location and eye movements during fixation in people with central vision loss, using an auto eye-tracking system that registers eye positions relative to an anatomic landmark and compensates for stimulus projection location. The fundus movements are recorded while the patient fixates on a target projected on a graphics screen. During this procedure the auto-tracking system calculates horizontal and vertical eye movements relative to a reference frame at a rate of 25 Hz. In addition, an OCT (Carl Zeiss Meditec Inc.) was used to examine the thickness of different intraretinal layers, to measure the hole size, and to confirm the successful closure of the hole.

### Procedure

All patients underwent the same surgical procedure (pars plana vitrectomy with internal limiting membrane peeling) performed by the same retinal surgeon (MSM). The surgical procedure consisted of a standard 3-port pars plana vitrectomy, removal of posterior cortical vitreous, staining of the internal limiting membrane with indocyanine green (ICG), and removal of internal limiting membrane in the macular area within the temporal vessels, followed by total fluid-gas exchange with sulfur hexafluoride (SF6). Post-operatively, patients maintained a face-down position for at least 7 days.

Three sets of tests were performed on each patient scheduled for surgery: The first, one week prior surgery (pre-op); the second, 1 month after surgery (1 month post-op); and the third, 3 months after surgery (3 months post-op). Only the affected eye was tested. Each set of tests consisted of: 1) measurements of best-corrected visual acuity; 2) fixation stability; fixation location and fundus photograph recordings with the MP-1; 3) OCT examination. All tests were done monocularly while the non-affected eye was patched. To record fixation location and eye movements during fixation, patients were seated with their head in the headrest of the MP-1. A 3-degree red cross was projected in the middle of the viewing area, and participants were asked to look at the stimulus at all times. The fixation test lasted less than one minute, after all setup adjustments were made. A fundus photograph was obtained at the end of each fixation test. No mydriatic drops were used. The differential analysis of the fixation locations before and after surgery, and the analysis of fixation stability were done off-line. After all these tests were completed, an OCT examination was performed. A fast macular thickness map scan was used, with a scan length of 6 mm.

### Data Analysis

The calculation of the global BCEA is described in Timberlake et al.21 The BCEA (expressed in deg²) is given by the formula:

\[
\text{BCEA} = \pi \chi^2 \sigma_x \sigma_y \sqrt{1 - \rho^2}
\]

where \( \chi^2 \) is the chi-squared value (2df) corresponding to a probability value of \( P = 0.682 \) (\( \approx 1 \) SD), \( \sigma_x \) and \( \sigma_y \) are standard deviations of the horizontal and vertical eye movements, and \( \rho \) is the Pearson product-moment correlation coefficient of the horizontal and vertical eye movements.21

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**Table 1. The Patients’ Pre-operative Baseline Characteristics**

<table>
<thead>
<tr>
<th>Patients’ Characteristics</th>
<th>Range</th>
<th>Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>45-77</td>
<td>64 ± 8.9</td>
</tr>
<tr>
<td>Acuity, logMar</td>
<td>0.44-0.88</td>
<td>0.69 ± 0.13</td>
</tr>
<tr>
<td>Duration of symptoms, mo</td>
<td>2-10</td>
<td>4.8 ± 2.3</td>
</tr>
<tr>
<td>Hole size, μm</td>
<td>423-869</td>
<td>561 ± 168</td>
</tr>
</tbody>
</table>

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*Downloaded From: http://iovs.arvojournals.org/pdfaccess.ashx?url=/data/journals/iovs/932956/ on 06/22/2017*
The computation of each BCEA was based on >700 fixation points. In comparison, the BCEA calculations coming from data recorded with the SLO and reported in the literature are based on approximately 100 data points.\textsuperscript{21} Fixation points falling outside ±3 SD of each distribution were removed\textsuperscript{27} and analysis was carried out in accordance with the guidelines described in Tarita-Nistor et al.\textsuperscript{22} to reduce the instrument errors.

The assessment of fixation shift was done with the differential map analysis feature of the MP-1. When proper calibration is used,\textsuperscript{22} this feature shows the distance in degrees between the centroids of two fixation stability examinations. An example of a differential map analysis is shown in Figure 1.

In cases where one-way repeated-measures analyses of variance were performed, the familywise error rate across the pairwise comparisons was controlled with the Bonferroni approach. Alpha level was set at 0.05 for all tests. Acuity values were expressed in logMAR units. Data were checked for multivariate (where applicable) and univariate outliers.

**RESULTS**

**Acuity**

A one-way repeated-measures analysis of variance was conducted with the factor being the time of testing (pre-op, 1 month post-op, and 3 months post-op) and the dependent variable being the best corrected visual acuity measured with the ETDRS. The results showed a significant time effect $F_{(2,8)} = 10.08, P < 0.01$. The observed power (power, 0.91) and the effect size ($\eta^2$, 0.72) were large, despite the small sample size. The pairwise comparisons showed that there was a significant difference between pre-op acuity (mean, 0.69 logMAR; SD, 0.13) and post-op acuity at both post-op testing times (1 month post-op: mean, 0.49 logMAR; SD, 0.16; 3 months post-op: mean, 0.46 logMAR; SD, 0.17). These differences were of clinical significance as well (two acuity lines different). There was a significant difference between acuity measured at 1 month and that measured at 3 months post-operatively ($P < 0.05$). However, the significant difference between acuity measured at 1 month and at 3 months post-operatively was too small to be of clinical significance. The acuity measurements are plotted in Figure 2. Duration of symptoms and hole size did not correlate with acuity pre- or post-operatively.

**BCEA Analysis**

Mean pre-op BCEA was 0.35 deg$^2$ (SD, 0.18), 1 month post-op was 0.31 deg$^2$ (SD, 0.16), and 3 months post-op was 0.29 deg$^2$ (SD, 0.17). The BCEA improved after surgery, but a one-way repeated measures analysis of variance showed that this improvement was not large enough to reach significance, probably due to the small sample size. We would need a sample size of 28 to obtain a power of 0.8 with a medium effect size. The results are shown in Figure 3.

**Fixation Shift Analysis**

Two differential analyses were performed for each patient: one between the centroids of the pre-op and 1 month post-op fixation stability examinations, and one between the centroids of the pre-op and 3 months post-op fixation stability examinations. The mean fixation shift 1 month post-op was 0.55 deg (SD, 0.25) and the mean fixation shift 3 months post-op was 0.87 deg (SD, 0.44). A paired-sample $t$-test showed that the differences between the fixation shifts at 1 month and at 3 months post-op were statistically significant ($t_{(9)} = 2.78, P < 0.05$). The results are illustrated in Figure 4.

**Relationships among Variables**

**Pre-op.** The relationships between acuity and BCEA pre-operatively were examined using a Pearson product-moment correlation. Acuity did not correlate with BCEA pre-operatively.

**One Month Post-op.** The relationships among a few variables were of interest: acuity, fixation shift, and BCEA measured 1 month post-operatively. In addition, since the fixation shift provided information only about the distance between the centroids of the pre-op and post-op fixation examinations, a new variable was created to see the change in BCEA after the...
surgery. This variable was called ΔBCEA and was defined as the difference between BCEA pre- and 1 month post-op. The Pearson product-moment correlation coefficients among all these variables are shown in Table 2.

A multiple regression analysis was conducted to determine what amount of variance in visual acuity is predicted by the ΔBCEA and fixation shift 1 month post-op. BCEA was excluded from the regression model because it correlated highly with ΔBCEA; thus, it could have created problems such as redundancy or multicollinearity.

Initially, the predictive variables were entered into the model simultaneously. The result of this analysis indicated that the ΔBCEA and fixation shift accounted for a significant amount of variance in visual acuity, \( R^2 = 0.74, F_{(2,7)} = 10.03, P < 0.05 \). A post-hoc power calculation for multiple regression revealed a very large effect size (\( f^2 = 2.85 \)) and power (power, 0.97). The intercept was 0.54 and the standardized regression coefficients were -0.55 for the ΔBCEA and -0.05 for the fixation shift. Only the first regression coefficient was significant (\( P < 0.05 \)). Squared semi-partial correlation for fixation shift (which shows the unique variance explained by this measure) was extremely low (0.002). Indeed, a hierarchical regression showed that with only ΔBCEA in the model, the relationship between visual acuity and fixation shift did not result in a significant increment in \( R^2 \). Based on these results we concluded that fixation shift has little predictive power beyond that contributed by the ΔBCEA. Thus, we retained only the ΔBCEA in the regression model and reduced our analysis to a simple bivariate regression. The regression equation for the 1 month post-op case is

\[
\text{Acuity} = -0.56 \times \Delta \text{BCEA} + 0.52
\]

The relationship between acuity and ΔBCEA is plotted in Figure 5.

**Three Months Post-op.** An analysis similar to the previous one was performed to examine the relationships among variables at 3 months post-op. The measures were repeated 3 months after the surgery. The ΔBCEA was defined this time as the difference between BCEA pre- and 3 months post-op. The Pearson product-moment correlation coefficients among all these variables are shown in Table 3.

### Table 2. Correlations among Variables One Month Post-op

<table>
<thead>
<tr>
<th></th>
<th>Acuity</th>
<th>Fixation Shift</th>
<th>BCEA</th>
<th>ΔBCEA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acuity</td>
<td>1</td>
<td>-0.46</td>
<td>0.38</td>
<td>-0.86*</td>
</tr>
<tr>
<td>Fixation shift</td>
<td>1</td>
<td>-0.46</td>
<td>0.49</td>
<td></td>
</tr>
<tr>
<td>BCEA</td>
<td>1</td>
<td>-0.68†</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>ΔBCEA</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* \( P < 0.01 \), †\( P < 0.05 \) (2-tailed).

### Table 3. Correlations among Variables Three Months Post-op

<table>
<thead>
<tr>
<th></th>
<th>Acuity</th>
<th>Fixation Shift</th>
<th>BCEA</th>
<th>ΔBCEA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acuity</td>
<td>1</td>
<td>0.25</td>
<td>0.15</td>
<td>-0.78*</td>
</tr>
<tr>
<td>Fixation shift</td>
<td>1</td>
<td>-0.47</td>
<td>-0.05</td>
<td></td>
</tr>
<tr>
<td>BCEA</td>
<td>1</td>
<td>-0.62†</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>ΔBCEA</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* \( P < .01 \) (2-tailed), †\( P < .05 \) (1-tailed).

A regression analysis was performed in a manner similar to that in the previous section. The results indicated that the ΔBCEA and fixation shift accounted for a significant amount of variance in visual acuity, \( R^2 = 0.65, F_{(2,7)} = 6.54, P < 0.05 \). Similarly to the previous analysis, the post-hoc power calculation for multiple regression revealed a very large effect size (\( f^2 = 1.86 \)) and power (power, 0.87). The intercept was 0.42 and the standardized regression coefficients were -0.77 for the ΔBCEA and 0.21 for the fixation shift. Once again, only the first regression coefficient was significant (\( P < 0.05 \)). A hierarchical regression showed that with only ΔBCEA in the equation, \( R^2 = 0.61, F_{(1,8)} = 12.34, P < 0.01 \). The addition of the fixation shift did not result in a significant increment in \( R^2 \) (change, 0.045). Therefore, with only ΔBCEA in the model, the regression equation for the 3 months post-op case is

\[
\text{Acuity} = -0.58 \times \Delta \text{BCEA} + 0.49
\]

The relationship between the two variables is plotted in Figure 6.

**DISCUSSION**

Macular hole surgery yields excellent anatomic results, but the functional outcome is not always as good.\(^2,6,11\) Numerous studies have shown significant improvements in acuity (two lines or better) after macular hole closure\(^3–10; \) yet, at least half of the patients still have low visual acuity after surgery.\(^12\) It has been difficult to explain the discrepancy between the anatomic and functional results. Attempts have been made to explain this finding by examining the residual abnormalities found in the macular morphology as revealed by the OCT,\(^1,3–15\) but this explanation has not been always supported by other studies: only a very small number of morphologic macular defects could predict visual outcome after surgery.\(^16,17\)

Changes in ocular motor functions and their role in visual outcome post-operatively have not been properly explored. It is reasonable to assume that closure of the macular hole would lead to a recalibration of the visual system producing changes
in fixation location and stability. Thus, we hypothesized that changes in ocular motor functions would predict the visual outcome after successful closure of the macular hole. Specifically, we thought that changes in fixation stability and in PRL location would be good predictors of visual acuity after surgery; our hypothesis has been only partially confirmed.

The success rate of the surgery was 85% after one operation and this is consistent with the values reported in the literature, which vary from 73% to almost 100% for small macular holes.1,4,6,9,12,17 For example Haritoglou et al.4 reported a success rate of 87% by one surgery and 96% after two operations; these results were replicated in their long-term follow up study.12

As expected, visual acuity improved significantly—both statistically and clinically—even in the first post-operative stages. But the anatomic success of the surgery did not restore normal visual acuity and this result is in agreement with past research. Hole size and duration of symptoms pre-operatively did not correlate with acuity at any point in time.

Our two predictors of visual outcome were changes in PRL location and in fixation stability after surgery. First, we found that the PRL shifted about half a degree 1 month post-op and almost 0.9 degrees 3 months post-op. The differences in fixation shift were statistically significant. This means that fixation shifts after 1 month and continues to do so after 3 months post-operatively. Theoretically, the ideal result after successful closure of the hole would be for the macula to recover its function and the PRL to move back to its former location. But this may not be the case. Guez et al.,25 who visually inspected the PRL shift using an SLO, also found that the PRL location shifted after successful surgery, but that the direction of shift varied: the new location tended to be near the opposite side of the hole. The regression analysis showed that ΔBCEA accounted for a high amount of variance in acuity. This result further explains the discrepancy between the anatomic and functional outcomes: this discrepancy is due in part to abnormalities of intraretinal architectural morphology, but mainly because fixation stability fails to improve significantly after macular closure and fixation relocation in many patients. Those patients whose fixation stability improved the most showed the best visual acuity, whereas patients with poorer acuity had the least improvement in fixation stability.

One may argue that this finding is limited by our small sample size. Interestingly, despite the fact that two of the variables—acuity and fixation shift—changed significantly between the two testing times, the same pattern of results was obtained from the multiple regression analyses. The post-hoc power analyses revealed a very large effect size and power in both regression models. We also collapsed the two sets of data and re-did the analysis with a sample size of 20 and, once again, obtained the same outcome. The effect size of the collapsed model was very strong ($F^2$, 1.08) and the post-hoc statistical power was 0.96, much larger than the typically desired power level of 0.8.

The large, replicable effect size comes from both our strong experimental manipulation and our precise measures.26 For instance, the calculation of each BCEA is based on >700 data points recorded for the vertical and horizontal fixation eye movements. Each of these large fixation data sets was checked for outliers; points falling outside $±3$ SD of the distribution were removed. Only after the fixation raw data had been cleaned were the BCEAs computed. This very accurate analysis of raw data highly increased the precision (BCEA) and the accuracy (BCEA centroid location) of the fixation stability measurements. In addition, care was taken to avoid instrument errors when measuring the fixation location shift, in accordance with the guidelines described in Tarita-Nistor et al.25 Moreover, both sets of data used for the multiple regression analyses were cleared from univariate and multivariate outliers. One patient, who suffered an unrelated medical complication after the surgery, was eliminated from our analysis because the obtained data were outliers.

In summary, we conclude that closure of the macular hole leads to a recalibration of the visual system and that the changes in ocular motor function may help to explain the visual outcome after surgical closure of macular hole. Surprisingly, the PRL location shift has no influence on visual acuity post-operatively. However, the change in fixation stability is a very good predictor of visual outcome after successful closure of macular hole.
References


