The Usefulness of Gaze Tracking as an Index of Visual Field Reliability in Glaucoma Patients

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Submitted: July 9, 2015
Accepted: August 18, 2015

Citation: Ishiyama Y, Murata H, Asaoka R. The usefulness of gaze tracking as an index of visual field reliability in glaucoma patients. Invest Ophthalmol Vis Sci. 2015;56:6233–6236. DOI:10.1167/iovs.15-17661

Purpose. We evaluated the usefulness of gaze tracking (GT) results as an index of visual field reliability in glaucoma.

Methods. The study population consisted of 631 eyes of 400 patients with open angle glaucoma in an institutional practice, with 10 visual fields (VFs). For the observational procedure, visual fixation was assessed using the gaze fixation chart at the bottom of the VF (Humphrey Field Analyzer, 30-2 SITA standard) printout. Average frequency of eye movement between 1’ and 2’ (move1–2), 3’ and 5’ (move3–5), and greater than or equal to 6’ (move>6) were calculated. In addition, average tracking failure frequency (TFF) and average blinking frequency (BF) were calculated. The relationship between mean deviation (MD), fixation losses (FLs), false-positives (FPs), false-negatives (FNs), move1–2, move3–5, move>6, TFF, BF, and pattern standard deviation (PSD) were evaluated using linear modeling. Main outcome measures included parameters related to over- or underestimation of MD values.

Results. Patients’ mean MD progression rate was \(-0.23\) dB/y. The best model to predict MD values included FL rate, FP rate, move1–2, move3–5, move>6, TFF, BF, and PSD as dependent variables with coefficients of 0.90, 9.2, −0.57, −0.52, −2.2, −1.1, and −0.56, respectively (\(P < 0.001\)).

Conclusions. High FL and FP rates tend to raise MD values. By contrast, high values of move1–2, move3–5, move>6, TFF, BF, and PSD tend to lower MD values. Thus, GT parameters can be used as new indices of VF reliability through the prediction of over- or underestimation of VF results.

Keywords: gaze tracking, glaucoma, visual field

Assessing the reliability of visual field (VF) results is very important at clinical settings, because the time it takes to detect progression is largely influenced by the variability of VFs, which impedes clinicians when making medical and surgical treatment decisions. In the Humphrey Field Analyzer (HFA; Carl Zeiss Meditec, Dublin, CA, USA), several methods have been used to estimate the reliability of VF tests. Fixation loss (FL) is recorded when a stimulus projected onto the area of the blind spot is perceived, and it indicates test reliability and vision fixation. Elevated FLs can mask the presence of early scotoma. False-positive (FP) rate is estimated by the number of positive answers that occur during a “listen time,” which starts shortly after the end of the response window and ends 180 ms after the onset of the next stimulus. False-negatives (FNs) mainly occur when a patient fails to respond to a stimulus that is more intense than that to which the patient had responded previously. A high rate of FP answers is thought to indicate “trigger-happy” patients and a high rate of FN responses is thought to represent inattention during an examination.

While some past studies have reported on the usefulness of these indices, more recent studies have pointed out their limitations; FLs also can result from the mislocalization of the blind spot and fixational instability can be found even in well trained observers. A high FN rate is reported to be associated with the amount of field loss as well as threshold reproducibility.

Gaze tracking (GT) is a record of eye movement monitored during the actual sensitivity measurement. Its use in clinical practice has been somewhat limited, since results are merely represented as a printed line diagram at the bottom of the VF printout, and, as a result, can only be evaluated subjectively by clinicians. Nonetheless, it has been reported that GT is useful for evaluating the quality of fixation, particularly when VF defects surround the blind spot, and indeed, we have recently reported the usefulness of GT parameters for VF reliability as measured by test–retest reproducibility. In the study, GT results were evaluated objectively and quantitatively, and GT parameters were closely related to test–retest reproducibility; the FN rate also was significantly related to test–retest reproducibility, but the FP rate and FL rate were not. Nevertheless, the results do not deny the usefulness of the FP and FL indices, because they may be related to over- or underestimation of VF sensitivity. Indeed, Junoy Montolfo et al. investigated the residuals from a mean deviation (MD) trend analysis and reported that high FP rates increase MD values. Thus, the objective of the current study was to investigate the usefulness of GT parameters, in addition to classic reliability indices, in the over- and underestimations of VF results.

Methods

The study was approved by the Research Ethics Committee of the Graduate School of Medicine and Faculty of Medicine at The
which is FP
high FL or FP values were not excluded using the HFA criteria,
current study was to evaluate the influence of reliability
clinically insignificant senile cataract. As the purpose of the
disease that could affect the VF, including cataract other than
except for cataract extraction and intraocular lens implanta-
examined were equal to or better than 6/12. Eyes with the
(quoted move
1–2
A
short downward bar
represents tracking failure, while a long downward bar
indicates eyelid closure. Gaze tracking parameters were calculated as follows: average TFF, average BF, the
average frequency of eye movement per stimulus between 1° and 2°
(denoted move
1–2
), 3° and 5° (denoted move
3–5
), and more than 6°
(denoted move
6–8
).

University of Tokyo. Written consent was taken by patients for
their information to be stored in the hospital database and used
for research. This study was performed according to the tenets
of the Declaration of Helsinki.

Subjects

We included in the study 631 eyes of 400 open angle
glaucoma patients at the glaucoma clinic in The University
of Tokyo Hospital. Each patient had at least 10 VFs with the
HFA (30-2 Swedish Interactive Threshold Algorithm, SITA,
standard program). A patient’s most recent 10 VFs were
used in the analysis when more than 10 VFs had been
recorded.

All patients enrolled in the study fulfilled the following
criteria: (1) glaucoma was the only disease causing VF damage,
(2) patients were followed for at least 6 months at The
University of Tokyo Hospital and had undergone at least two
VF measurements before this study, and (3) all patients had
glaucomatous VF defects in at least one eye defined as three or
more contiguous total deviation points at \( P \geq 0.05 \), or two or
more contiguous points at \( P < 0.01 \), or a 10 dB difference
across the nasal horizontal midline at two or more adjacent
points, or MD worse than \(-5 \) dB. All visual acuities of the
eyes examined were equal to or better than 6/12. Eyes with the
following conditions were excluded: previous ocular surgery
except for cataract extraction and intraocular lens implanta-
tion, and other anterior and posterior segment of the eye
disease that could affect the VF, including cataract other than
clinically insignificant senile cataract. As the purpose of the
current study was to evaluate the influence of reliability
indices on over- or underestimation of VF results, VFs with
high FL or FP values were not excluded using the HFA criteria,
which is FP < 20% or FL < 15%. However VFs with FL, FP, or

<table>
<thead>
<tr>
<th>TABLE 1. Investigated Parameters</th>
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<tbody>
<tr>
<td><strong>Analyzed Parameters</strong></td>
</tr>
<tr>
<td>FL</td>
</tr>
<tr>
<td>FP</td>
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<td>FN</td>
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</table>
| move
1–2                            |
| move
3–5                            |
| move
6–8                            |
| TFF                             |
| BF                              |
| PSD                             |

\( \text{PSD, pattern standard deviation.} \)

\( \text{TABLE 2. Patient Demographics} \)

<table>
<thead>
<tr>
<th>Demographics</th>
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<tbody>
<tr>
<td>Age, mean ± SD</td>
<td>56.5 ± 12.6</td>
</tr>
<tr>
<td>Sex, male/female</td>
<td>222/178</td>
</tr>
<tr>
<td>MD in the initial VF dB, mean ± SD (range)</td>
<td>-7.3 ± 5.9 (-27.0 to 2.7)</td>
</tr>
<tr>
<td>PSD in the initial VF dB, mean ± SD (range)</td>
<td>8.8 ± 5.0 (1.2 to 19.0)</td>
</tr>
<tr>
<td>MD in the last VF dB, mean ± SD (range)</td>
<td>-8.7 ± 6.5 (-28.1 to 2.7)</td>
</tr>
<tr>
<td>PSD in the last VF dB, mean ± SD (range)</td>
<td>9.9 ± 4.8 (1.2 to 18.6)</td>
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\( \text{FN > 50% were excluded, to avoid the influence of extremely unreliable VF tests.} \)

Gaze Tracking Measurements

The GT system monitors patients’ gaze position at each
stimulus presentation (Fig.). An upward bar in the chart
indicates fixation disparity and the length of the bar represents
the magnitude of disparity, from 1° to a maximum of 10°.

In the current study, GT data were exported as JPEG images
from the Beeline (Tokyo, Japan) data filing system. Then
the frequency of the upward and downward bars with each length
in the GT records were simply calculated as follows: average
frequency of eye movement per stimulus between 1° and 2°
(denoted move
1–2
), 3° and 5° (denoted move
3–5
), and greater
than or equal to 6° (denoted move
6–8
), average tracking failure
frequency (denoted TFF), and average blinking frequency
(denoted BF). The three levels of move
1–2
, move
3–5
, and
move
6–8
 were chosen following the approach in our recent
study.

Statistical Analysis

The relationship between MD values, and FL, FP, FN, move
1–2
, move
3–5
, move
6–8
, TFF, BF, and pattern standard deviation (PSD)
was analyzed using the linear mixed model in which each eye
was treated as a random effect, as shown in Table 1. The linear
mixed model is equivalent to ordinary linear regression in that
the model describes the relationship between the predictor
variables and a single outcome variable. However, standard
linear regression analysis makes the assumption that all
observations are independent of each other. In the current
study, measurements are nested within subjects and, thus,
dependent of each other. Ignoring this grouping of the
measurements will result in the underestimation of standard
effects of regression coefficients. The linear mixed model
adjusts for the hierarchical structure of the data, modeling in a
way in which measurements are grouped within subjects. In
the model selection, PSD was included as one of the possible
parameters because the purpose of the current study was to
decide the parameters related to over- or underestimation of
MD values among all possible parameters, not to predict MD
values from other measurements.

The best linear model was selected among all possible
combinations of predictors: 2\(^6\) patterns based on the second
order bias corrected Akaike Information Criterion (AICc)
index. The AIC is a well-known statistical measure used in
model selection, and the AICc is a corrected version of the AIC,
which provides an accurate estimation even when the sample
size is small. All analyses were performed using the statistical
programming language ‘R’ (R version 2.15.1; The Foundation
for Statistical Computing, Vienna, Austria).

\( \text{Figure. An example of a GT figure with GT parameters superim-_posed. An upward bar in the chart indicates fixation disparity and the length of the bar represents the magnitude of disparity, from 1° to a maximum of 10°. A short downward bar represents tracking failure, while a long downward bar indicates eyelid closure. Gaze tracking parameters were calculated as follows: average TFF, average BF, the average frequency of eye movement per stimulus between 1° and 2° (denoted move}_1–2, 3° and 5° (denoted move}_3–5, and more than 6° (denoted move}_6–8).} \)
The results of the study subjects are summarized in Table 2. Subjects comprised 222 males and 178 females. The mean age of the patients was 55.6 ± 12.6 (mean ± SD) years. Ten VFs were obtained in 5.8 ± 1.3 years. The mean MD value of the initial VFs was −7.5 ± 5.9 dB and in the last VFs it was −8.7 ± 6.5 dB. The mean PSD value of the initial VFs was 8.8 ± 5.0 dB and in the last VFs, it was 9.9 ± 4.8 dB. The MD progression rate was −0.23 ± 0.039 dB/y on average.

As shown in Table 3, average rates (mean ± SD [range]) of FL, FP, and FN were 6.9 ± 8.6 [0–48]%], 2.9 ± 3.8 [0–43]%, and 3.6 ± 5.2 [0–46]%, respectively.

The average eccentricity of eye movement throughout the VF test was 1.9 ± 1.5 [0–12]° per stimulus (mean ± SD [range]). As shown in Table 4, average values of move_12, move_35, move_60, TFF, BF were 0.65 ± 0.17 [0.00–0.97] per stimulus, 0.10 ± 0.12 [0.00–0.96] per stimulus, 0.070 ± 0.15 [0.00–1.00] per stimulus, 0.037 ± 0.095 [0.00–0.90], 0.045 ± 0.086 [0.00–0.99] per stimulus, respectively.

As shown in Table 5, FL, FP, move_35, move_60, TFF, BF, and PSD were selected as significant predictors of MD. The coefficients of FL, FP, move_35, move_60, TFF, BF, and PSD were 0.90, 9.2, −0.57, −0.52, −2.2, −1.1, and −0.56, respectively (linear mixed model, P < 0.001).

### DISCUSSION

In the current study GT results from 30-2 HFA VFs were evaluated quantitatively and objectively. The influence of GT results, FLs, FPs, FNs, and PSD on MD values was then investigated. It was suggested that high FL and FP rates tend to raise MD values. Misfixation of more than 3° during the sensitivity measurement, as represented by move_35 and move_60, was significantly related to low MD values. Misfixation of less than 3° did not have a significant effect on MD values.

With regard to standard reliability indices, FL measures visual fixation during VF tests and is recorded when a patient is not well-fixated and could not see the target stimulus during blinking, as suggested in a previous report.20 On the other hand, move_12 was not significantly related with MD values. This is unsurprising given the 6° spacing of VF test points in the 30-2 VF. Moreover, a previous study has reported that eye movement of less than 3° are commonly observed in VF tests, even in well-trained healthy observers.4,21

The relationship between PSD and MD can be explained using a quadratic linear regression model16,22 where PSD decreases in the moderate to advanced stages of the disease.7 PSD was included as a predictor of MD in the best linear model in the current study. This may be because the progression of MD, in our study patients, was slow in general (~0.23 dB/y on average) and so the relationship between PSD and MD was linear in this narrow range of progression.

One caveat of the current investigation is the limited information derived from the GT record. Gaze tracking parameters were merely extracted as the average frequency throughout the VF measurement. A more detailed investigation could be carried out if the “real-time” GT tracking results were available to researchers, thus making it possible to analyze fixation status at each sensitivity measurement. A further caveat is that GT results can be related to dry eye,23 hence, further investigation is needed to shed light on this issue.

<table>
<thead>
<tr>
<th>TABLE 3. Results of Classic Parameters</th>
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<tr>
<td><strong>Classic Parameters</strong></td>
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<tr>
<td>FL, %, mean ± SD (range, per stimulus)</td>
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<tr>
<td>FP, %, mean ± SD (range, per stimulus)</td>
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<td>FN, %, mean ± SD (range, per stimulus)</td>
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<th>TABLE 4. Frequency of Gaze Tracking Parameters</th>
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<tr>
<td><strong>GT Parameters</strong></td>
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<tr>
<td>move_12, mean ± SD (range, per stimulus)</td>
</tr>
<tr>
<td>move_35, mean ± SD (range, per stimulus)</td>
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<tr>
<td>move_60, mean ± SD (range, per stimulus)</td>
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<tr>
<td>TFF, mean ± SD (range, per stimulus)</td>
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<td>BF, mean ± SD (range, per stimulus)</td>
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<th>TABLE 5. Selected Parameters</th>
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<tr>
<td><strong>Selected Parameters</strong></td>
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<tr>
<td>Coefficient</td>
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the current study, GT data were exported as JPEG images from the Beeline data filing system and various GT parameters were simply calculated by reading the JPEG image. Thus, GT parameters can be obtained on a personal computer; simple software could be built to give clinicians access to this GT information to estimate the reliability of patients’ VFs at clinical settings.

In conclusion, we analyzed the influence of eye movements derived from the GT record on HFA VF tests. Gaze tracking parameters are significantly related to the underestimation of sensitivity in 30-2 VF tests.

Acknowledgments

Supported in part by Grant 26462679 (RA) from the Ministry of Education, Culture, Sports, Science, and Technology of Japan and Supported in part by Grant 26462679 (RA) from the Ministry of Education, Culture, Sports, Science, and Technology of Japan and Supported in part by Grant 26462679 (RA) from the Ministry of Education, Culture, Sports, Science, and Technology of Japan and Supported in part by Grant 26462679 (RA) from the Ministry of Education, Culture, Sports, Science, and Technology of Japan.

Disclosure: Y. Ishiyama, None; H. Murata, None; R. Asaoka, None

References