Increased Detection Rate of Glaucomatous Visual Field Damage With Locally Condensed Grids

A Comparison Between Fundus-Oriented Perimetry and Conventional Visual Field Examination

Ulrich Schiefer, MD; Mark Flad, PJ; Florian Stumpp, AiP; Alexander Malsam, AiP; Jens Paetzold, Dr rer nat; Reinhard Vonthein, Dr rer pol; P. Oliver Denk, MD; Pamela A. Sample, PhD

Objective: To compare detection rates of glaucomatous visual field defects (VFDs) between the conventional 6° × 6° stimulus grid and locally condensed target arrangements in morphologically suspicious regions.

Methods: A total of 66 eyes of 66 patients with glaucoma or patients suspected of having glaucoma (34 females and 32 males; age range, 14-85 years) were enrolled in this study. Individual, local target condensation was realized by fundus-oriented perimetry (FOP) using a campimeter and compared with the results of conventional automated perimetry (CAP), obtained with the Humphrey Field Analyzer (30-2 grid).

Results: Twenty-three of the 66 patients showed normal findings with both methods; 27 had concordantly pathological results. In 15 patients we obtained normal findings with CAP, whereas FOP revealed early glaucomatous VFDs. Only one patient showed VFDs with CAP, whereas FOP results were normal. Scotoma detection rates significantly differed between the 2 methods (P<.001, sign test). Test duration with FOP was more than doubled compared with CAP. When considering only FOP points coinciding with the 6° spacing of the 30-2 grid, there was no longer a significant difference between FOP and CAP (P>.25, sign test). This indicated that the target pattern, rather than the perimetric device, was most relevant for detecting glaucomatous VFDs. Follow-up throughout a series of 3 subsequent sessions at 6-month intervals revealed repeatable results in more than two thirds of all eyes for both FOP and CAP.

Conclusions: Fundus-oriented perimetry that uses individually condensed test grids significantly increases the detection rate of glaucomatous VFDs in morphologically conspicuous areas compared with CAP using equidistant (6° × 6°) target arrangements. Repeatability is comparable between both methods.


PERIMETRIC characterization of functional change may be more important than mere detection of functional loss. Nevertheless, reliable detection of a glaucomatous field defect is an essential prerequisite and baseline for evaluation of functional changes that manifest themselves in variation of scotoma depth and/or size. Whereas defect depth should be assessed by a sophisticated thresholding algorithm, quantification of scotoma size demands an adequate target density. Due to limitations in test duration, condensation of test points restricted to those visual field areas that correspond to morphologically suspicious regions (optic disc notching, splinter hemorrhages, retinal nerve fiber layer defects) would be ideal. This is realized in fundus-oriented perimetry (FOP) using the Tuebingen Computer Campimeter (TCC), with optic disc and foveola serving as morphologic landmarks for adjustment of their psychophysically measured counterparts (ie, blind spot and visual field center). The Humphrey Field Analyzer model 630 (HFA, 30-2 grid) (Humphrey Instruments, San Leandro, Calif) served as the conventional perimetric control.

This study compares detection rates of glaucomatous visual field defects (VFDs) in patients with circumscribed morphologic lesions between a local evidence-based condensation of perimetric test locations in morphologically conspicuous areas using FOP with detection rates of conventional perimetry. Finally, stability (ie, repeatability of scotomata detection over time) was analyzed, comparing FOP with conventional perimetry.

METHODS

Fundus-oriented perimetry or campimetry has been described elsewhere in detail. This new concept (Figure 1) uses a digitized fundus image of the patient as a basis for constructing an individual grid of perimetric stimuli. The
fundus image is downloaded from a data carrier (disk or photo CD) or digitized by a slide scanner, depicted on a control monitor and mirrored, if necessary, with the help of software, which was especially designed for this purpose. Assuming central fixation, the foveola of the fundus image is aligned to the center of the perimetric field using a cross hair. In a second step, the blind spot, which has been previously determined by means of kinetic perimetry, is interactively superimposed onto the optic disc of the fundus image by automatic activation of rotary and zoom routines. Thus, the method allows a direct adaptation of the perimetric procedure to the individual fundus structure. It is capable of detecting even minute VFDs, such as angioscotomata or shallow nerve fiber bundle defects.4-7

The FOP operators based generating of the individualized grids on the fundus image: morphologic damage (eg, circumscribed cupping of the optic disc, retinal nerve fiber layer defects, peripapillary splinter hemorrhages) was identified and located directly on the digitized fundus images. Assumed scotoma borders were outlined according to the course of the retinal nerve fibers up to the horizontal raphe.

In the actual set-up, a calibrated, high-resolution video display unit10 is used instead of a cupola. The 20-in monitor covers a visual field of approximately 35° horizontally and approximately 24° vertically (radius) in an examination distance of 30 cm. Stimuli were scaled to maintain the same visual angle as Goldmann size III. The set-up additionally renders a conical nerve fibers up to the horizontal raphe.

The FOP grid is split into 2 complementary randomization subsets of an approximately equal number of test points, which are presented in 2 subsequent sessions (Figure 2). The test point grid exceeds any scotoma border by at least 5° in each direction. The maximum number of stimulus locations is 152. The FOP grid is split into 2 complementary randomized subsets of an approximately equal number of test points, which are presented in 2 subsequent sessions (Figure 2). Thus, no more than 76 locations are examined in each perimetric subset. The time span between the subsessions is normally a few hours at maximum; it did not exceed 24 hours in this study.

A modified 4-/2-/1-dB strategy with 3 reversals is applied with FOP. Each perimetric grid is adapted according to the individual fundus findings. Additional test points are inserted between the original 30-2 stimulus locations. Mesh density of the stimulus grid within the scotoma area is at least 3° × 3°, and minimum scaling is restricted only to the pixel size of the monitor. The test point grid exceeds any scotoma border by at least 5° in each direction. The maximum number of stimulus locations is 152. The FOP grid is split into 2 complementary randomized subsets of an approximately equal number of test points, which are presented in 2 subsequent sessions (Figure 2). Thus, no more than 76 locations are examined in each perimetric subset.

To de-
Comparison of Detection Rates of Humphrey Field Analyzer (HFA) and Fundus-Oriented Perimetry (FOP) Using the Tuebingen Computer Campimeter (TCC)

<table>
<thead>
<tr>
<th>Normal</th>
<th>Pathological</th>
<th>Sum</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>HFA 30-2</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TCC-FOP</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>23</td>
<td>1</td>
</tr>
<tr>
<td>Pathological</td>
<td>15</td>
<td>27</td>
</tr>
<tr>
<td>Sum</td>
<td>38</td>
<td>28</td>
</tr>
<tr>
<td><strong>TCC-FOP 30-2</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TCC-FOP</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>24</td>
<td>0</td>
</tr>
<tr>
<td>Pathological</td>
<td>11</td>
<td>31</td>
</tr>
<tr>
<td>Sum</td>
<td>35</td>
<td>31</td>
</tr>
<tr>
<td><strong>HFA 30-2</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TCC-FOP 30-2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>34</td>
<td>1</td>
</tr>
<tr>
<td>Pathological</td>
<td>4</td>
<td>27</td>
</tr>
<tr>
<td>Sum</td>
<td>38</td>
<td>28</td>
</tr>
</tbody>
</table>

*Abnormal visual field was defined as 3 or more contiguous nonedge points with P<.05 or 1 of 3 with P<.01, P<.001 (sign test) for HFA 30-2 compared with TCC-FOP and TCC-FOP 30-2 compared with TCC-FOP, respectively. P>.25 (sign test) for HFA 30-2 compared with TCC-FOP 30-2.

OPHTHALMOLOGIC EXAMINATION

Each patient underwent a complete ophthalmologic examination, including subjective and objective refraction (retinoscopy), visual acuity (distant, near), orthopic examination, examination of efferent and afferent pupil reaction, slitlamp examination, intraocular pressure (IOP) measurement (non-contact tonometer, additional IOP dates from reliable records), gonioscopy, and fundus examination (dilated pupils: direct and indirect binocular ophthalmoscopy, 78-diopter [D] lens).

PHOTODOCUMENTATION

Stereophotography of the optic disc, photography of posterior pole, and photography of the nerve fiber layer (no more than 2 months before first and after last perimetric session) were also performed.

PARTICIPANTS

We enrolled 66 eyes of 66 patients with glaucoma or patients suspected of having glaucoma (34 females, 32 males). The age range of the patients was 14 to 85 years. A written informed consent of each patient was obtained, and the examinations were performed according to the Declaration of Helsinki. The study was approved by the local ethics committee.

PATIENTS WITH GLAUCOMA: INCLUSION CRITERIA

In case of advanced visual field loss, automated static grid perimetry using thresholding strategies is not the method of choice; this holds even more true for FOP. For that reason, patients with advanced optic disc cupping that exceeded 2 clock hours were excluded from this study. Inclusion criteria were circumscribed glaucomatous morphologic lesions (retinal nerve fiber layer defect, cupping of optic disc, n=55) with or without corresponding localized glaucomatous VFDs (Aulhorn stage I-III), no history or signs of other neurophthalmologic diseases, spherical ametropia below 8 D, cylindrical ametropia below 3 D, central visual acuity equal to or better than 10/20, no relevant opacities of central refractive media (cornea, lens, vitreous body), and not receiving miotic drugs. Patients suspected of having glaucoma were defined as individuals with subtle morphologic changes related to glaucoma without VFDs on conventional perimetry (n=11). Only one eye of each patient was examined in the study. If both eyes showed a localized retinal nerve fiber layer defect, one was selected at random.

EVALUATION OF BASELINE PERIMETRIC RESULTS

Perimetric results within the morphologically conspicuous areas were evaluated according to the following criteria: 3 contiguous nonedge points with P<.05, with at least 1 of the 3 with P<.01. The evaluation was based on the analysis of the total deviation probability plots. Visual field areas with already known advanced visual field loss (exceeding Aulhorn stage III) were not included.

EVALUATION OF PERIMETRIC FOLLOW-UP RESULTS

Perimetric examinations were repeated at least 3 times at 6-month intervals for each patient. The criteria described herein were applied in an identical manner for all perimetric follow-up results to evaluate whether a change from pathologic to normal or vice versa occurred during the observation period.

FOP OBTAINED WITH TCC VS CONVENTIONAL HFA 30-2

The Table gives the comparison of detection rates of HFA 30-2 and TCC-FOP, according to the described evaluation criteria. In 23 patients, both methods showed normal findings. Twenty-seven individuals had pathological findings with both methods. In 15 patients we found normal visual fields with HFA 30-2, whereas FOP revealed early glaucomatous functional damage.

Figure 4 shows a typical result: neither the HFA 30-2 gray-scale plot nor the total pattern deviation probability plot revealed a typical glaucomatous field defect, which clearly shows up on FOP with a locally enhanced grid density.

Only one patient had pathological HFA results, whereas FOP results were normal (Figure 5). Detection rates of VFDs significantly differed between the 2 methods (P<.001, sign test).

FOP OBTAINED WITH TCC VS TCC 30-2

Comparison of scotoma detection rates was made between FOP with a locally condensed stimulus grid (TCC-FOP) and with the equidistant, 6°×6° grid (TCC 30-2) on the same instrument (TCC) to rule out instrumentation differences as the cause for the results. Twenty-four patients with glaucoma or patients suspected of having glaucoma concordantly showed normal results, and 31 demonstrated pathological results in both methods. In 11 patients, TCC-FOP was able to demonstrate visual field loss, with the FOP 30-2 results still being normal (Figure 6). The opposite constellation did not occur. Thus, FOP-TCC with local grid condensation was
able to pick up VFDs in morphologically conspicuous regions, which could not be detected by the conventional 6° × 6° grid using the same instrument (P < .001, sign test).

CONVENTIONAL HFA 30-2 VS TCC 30-2: 6° × 6° GRID

Detection rates of conventional HFA 30-2 compared with those of TCC 30-2 with identical (6° × 6°) grid are given in the Table. Based on the described criteria characterizing glaucomatous visual field loss, 34 patients showed concordantly normal and 27 showed concordantly pathological results in both methods. Four patients demonstrated pathological perimetric results with TCC 30-2, with the HFA 30-2 results being normal. The opposite constellation occurred in one patient. Detection rates did not differ significantly between the 2 perimeters (P > .25, sign test).

EXAMINATION DURATION: CONVENTIONAL HFA 30-2 VS FOP-TCC

Most probably due to its 3 reversals, examination duration of a single session is somewhat longer in the FOP-TCC technique (median, 21.3 minutes; interquartile range, 2.8 minutes; minimum, 15.9 minutes; maximum, 34.8 minutes) than in HFA (median, 15.2 minutes; interquartile range, 2.1 minutes; minimum, 11.7 minutes; maximum, 19.9 minutes). In contrast to FOP with TCC, breaks within one HFA session were not recorded. In all, FOP, which is based on 2 sessions, takes approximately more than twice as long as the single-session HFA 30-2 examination.

PERIMETRIC FOLLOW-UP

In 62 of the 66 eyes, stability (ie, repeatability of scotoma detection over time for at least 3 subsequent follow-up sessions at 6-month intervals) could be analyzed. In 27 patients, FOP and HFA 30-2 both showed pathological results (p) in all 3 sessions (Figure 7), whereas in 17 eyes, both methods yielded normal outcomes (n) in all 3 examinations. A change of status during the 3 sessions occurred rarely. The HFA 30-2 flagged a change in classification (n → n − p, n − p → p) in 2 patients, whereas FOP revealed pathological results in all 3 sessions. Also, FOP indicated a change in classification in 2 eyes (n − p → p), one of which showed pathological results in all 3 HFA 30-2 sessions and the other of which revealed normal visual fields in all HFA 30-2 examinations. Improvements (p → p − n, p − n → n) rarely occurred (2 patients exclusively in FOP, 1 patient exclusively in HFA 30-2, and 1 patient in both methods). Unstable results (n − p → n, p − n → p) were also rarely observed in both methods (3 patients exclusively in FOP; 1 patient exclusively in HFA 30-2).

Reduction of examination duration is currently one of the major issues in glaucoma perimetry. On the one hand, this is achieved by modifying the perimetric strategy and/or the thresholding algorithm, such as in the tendency-oriented perimetry (TOP) or the Swedish interactive thresholding algorithm (SITA) procedures. By this means, the number of questions asked and therefore the patient’s fatigue can be reduced. However, the widely used, equally spaced, 6° × 6° Humphrey Field Analyzer 30-2 grid (Humphrey Instruments, San Leandro, Calif) (A, gray-scale plot [left] and uncorrected total deviation probability plot [right]); see also the Table.

Recent results indicate that glaucomatous progression occurs in the vicinity of already affected visual neurons, suggesting that a local progression of scotoma depth and/or size may be the first signs of change. As a logical consequence, perimetric techniques should enhance resolution in areas where a defect has already been identified. Langerhorst et al demonstrated that higher test point density within the central 10° visual field enhanced scotoma detection. Westcott et al showed a similar effect by adding test locations within the region of the nasal step. In contrast to FOP, both methods did not adapt stimulus
arrangements according to the individual morphologic findings but used default grids, thereby eventually wasting time with additional test points in obviously normal regions. In a recent publication,29 local condensation of perimetric grids with FOP, considering morphologic abnormalities structurally such as optic disc notching and/or retinal nerve fiber defects, could be proven to increase the scotoma detection rate compared with conventional, equidistant, 6° perimetric grids.

With the help of fundus-controlled perimetry, targets can be presented via a scanning laser ophthalmoscope or fundus camera directly onto the retina under observation of the examiner.30-32 However, the examination area is comparatively small (<20° radius), especially with a scanning laser ophthalmoscope, and thus this technique is not able to detect changes within the nasal step region. Glaucomatous alteration of the retinal nerve fiber layer does not exclusively affect just the morphologically visible area but predominantly affects more peripheral regions, corresponding to the course of the nerve fibers. This further reduces the value of the direct fundus-controlled perimetric methods. Furthermore, these methods require real-time autotracking algorithms, which are currently available in prototype models only.33

Figure 5. Representative visual field results of 3 subsequent perimetric sessions: (1) initial session, (2) approximately 6 months after session 1, and (3) approximately 12 months after session 1. B, The gray-scale plot with superimposed total pattern deviation plot of fundus-oriented perimetry within sessions 1 and 3 only shows an equivocal glaucomatous visual field defect within the locally condensed test point arrangement and therefore was rated as normal (see also the Table). A, Conventional Humphrey Field Analyzer (HFA) 30-2 (Humphrey Instruments, San Leandro, Calif) (gray-scale plot [B] and uncorrected total deviation probability plot [A]) clearly demonstrates pathological results in all 3 sessions and therefore was classified as pathological. However, note the considerable positional instability of scotoma during the HFA 30-2 follow-up period. LA indicates left eye; PSD, pattern SD.
The individually tailored arrangement of test points, as realized in FOP, requires an age-related smooth normative model of the entire 30° hill of vision, since a considerable number of stimulus locations cannot be (directly) referred to a rigid set of normative test points. Recent strategies with reduced test times may be even more efficient when integrating this smooth model for enhancing spatial resolution in regions of interest.

The results presented in this article clearly demonstrate that individual condensation of test points by FOP-TCC significantly increases detection of glaucomatous VFDs compared with a conventional HFA 30-2 technique. These results are consistent with the expectation that early glaucomatous visual field loss usually is not characterized by scattered single locations of reduced differential luminance sensitivity but already in this stage affects the immediate surrounding area (Figure 7). Naturally, these local changes are only detectable with an adequate stimulus arrangement and therefore can be missed by the routinely used 6° × 6° stimulus grids. Basically, there is a simple and readily available option for refining this relatively coarse type of grid, namely combining (overlapping) two 6° × 6° grids (eg, HFA 30-2 and 30-1 or Octopus 32 and 31; Interzeag, Bern, Switzerland), which are characterized by 3° offset in regard to the horizontal and vertical axes. However, these kinds of equally spaced grids adequately represent neither the retinotopic arrangement of retinal receptive elements nor the course of retinal nerve fibers and therefore seem to be suboptimal for detecting early glaucomatous loss. Adequately spaced and locally condensed test point arrangements, as used in this study, turn out to be more appropriate to pick up subtle defects according to the standard criteria of glaucomatous visual field loss.

Since not only the test point arrangement but also instrumentation and examination technique were changed in these experiments, these differences may have been of decisive influence on this results. As mentioned in the “Methods” section, the test point arrangement in the FOP-TCC procedure was interwoven with an original 30-2 grid. Comparison between the entire TCC-FOP grid and a TCC 30-2 grid that mimicked the 6° × 6° spacing (Table) again showed a significant difference favoring FOP between these 2 grids for the same instrument.

Of course, this positive effect demonstrated with FOP is purchased at the expense of examination duration, taking about twice as long as conventional 30-2 full-threshold examination. Since FOP can be subdivided into several sessions, this procedure may be reasonable in inpatient situations or in combination with other time-consuming examinations, such as diurnal IOP recordings. Intersession variability (medium-term fluctuation) of the 9 reference points, presented in fixed locations at all sessions, turned out to be in the range of 1% of the total variation (F.S., unpublished data).

These statements, of course, do not only hold true for scotoma detection or follow-up for progression. Keltner et al recently published disappointing results in regard to repeatability when analyzing follow-up examinations in patients enrolled in the Ocular Hypertension Treatment Study. In the case of change to a pathological visual field test, no more than 13% stayed pathological throughout a series of 3 subsequent perimetric examinations.

In this study, follow-up examinations (3 perimetric sessions in 6-month intervals) were able to confirm more than 43% of the initially pathological results for both methods (ie, FOP and HFA 30-2). This may be due to the fact that patients with manifest glaucomatous optic neuropathies were enrolled in this study.

This technique has to be modified for routine perimetric evaluation and follow-up of patients with glau-
This can be done by additional implementation of fast thresholding strategies, considering previous perimetric results and neighborhood threshold values within the actual session. Furthermore, the grid can be made coarser within areas of morphologically normal regions and in regions with established absolute visual field loss.
If these cover a considerable area, computer-assisted automated kinetic perimetry or screening algorithms may help to reduce examination time.\textsuperscript{39,40} Analysis of perimetric results obtained with spatial high-resolution techniques and/or special thresholding algorithms using neural network technology is currently under way.\textsuperscript{41-44} These data may help to establish adaptive, computer-assisted generation of optimized target locations and luminance levels in real time (ie, during the session). Target density enhancement should particularly consider the region of the scotoma border, which is of special importance for follow-up purposes.\textsuperscript{45} This kind of local progression of functional defects has recently been established also by morphometric and histologic observation.\textsuperscript{22-24}

The goal of our study was to identify morphologically conspicuous areas, take into account the physiologic pattern of receptor and ganglion cell distribution, and adapt the target arrangement to assess the psychophysically measured sensitivity within the corresponding visual field locations for each individual. With this approach, we were able to more adequately characterize functional field loss in glaucoma using FOP than we could with the conventional, comparatively coarse, equidistant, 6° perimetric grids.

Submitted for publication June 17, 2002; final revision received November 27, 2002; accepted December 20, 2002.

The corresponding author had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

This study was supported by MSD Sharp & Dohme GmbH, Haar, Germany, and Allergan Inc, Irvine, Calif. We are grateful indebted to the reviewer’s valuable, constructive comments.

Corresponding author and reprints: Ulrich Schiefer, MD, Department II, University Eye Hospital Tuebingen, Schleichstr 12-16, D-72076 Tuebingen, Germany (e-mail: ulrich.schiefer@uni-tuebingen.de).

REFERENCES