Reclaiming the periphery: Automated kinetic perimetry for measuring the peripheral visual field in patients with glaucoma.

Short title Peripheral visual fields in glaucoma.

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Length 4,300 words, 7 figures & 2 tables

Section Code Glaucoma

Keywords glaucoma, visual field, peripheral vision, automated kinetic perimetry

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Support Unrestricted grant from the Investigator-Initiated Studies program of MSD (DPC), Fight for Sight (UK), #1736/37 (PHA)

Disclosures Haag-Streit International (Köniz, Switzerland) provided research support through loan of an Octopus 900 perimeter. None of the authors have a proprietary or financial interest in the subject matter of this paper.

Précis We demonstrate a simple, fully-automated kinetic approach to examine the peripheral visual field. In thirty glaucoma patients, we show that a single peripheral isopter may add important information to threshold perimetry of the central 30°.

Abstract

Purpose: Peripheral vision is important for mobility, balance, and guidance of attention, but standard perimetry examines only <20% of the entire visual field. We report on the relation between central and peripheral visual field damage, and on retest variability, with a simple approach for automated kinetic perimetry (AKP) of the peripheral field.

Methods: Thirty patients with glaucoma (age, median [range] 68 [59-83] y; mean deviation (MD), -8.0 [-16.3, +0.1] dB) performed AKP and static automated perimetry (SAP, GATE strategy, 24-2 test). AKP consisted of a fully automated measurement of a single isopter (III.1.e). Central and peripheral visual fields were measured twice on the same day.

Results: Peripheral and central visual fields were only moderately related (Spearman's rho, 0.51). Approximately 90% of test-retest differences in mean isopter radius (MIR) were <±4°. Relative to the range of measurements in this sample, the retest variability of AKP was similar to that of SAP.

Conclusion: Patients with similar central visual field loss can have strikingly different peripheral visual fields, and therefore measuring the peripheral visual field may add clinically valuable information.

Introduction

Since the advent of computerized visual field testing in the 1970s, almost all innovations in perimetry have focused either on improving the sensitivity to early visual field damage in glaucoma,[1-6] or on increasing either efficiency[7-9] or speed [10] of the tests. This drive towards high diagnostic performance has led to a situation where almost all visual field tests performed in glaucoma patients are confined to the central 25-30 degrees of the visual field, an area that constitutes less than 20% of the entire field of vision.

Peripheral vision contributes to postural stability [11-14] and the guidance of attention,[15] and is important for estimating motion from optical flow.[16-18] In people with normal vision, eliminating clues from the peripheral visual field decreases postural stability,[11] and patients with glaucoma rely more heavily on vestibular and proprioceptive cues to maintain balance than do healthy controls.[12-14] Thus, the central visual field alone does not provide a complete picture of the patients' real-world field of vision, and examinations of the peripheral visual field may help to more fully understand the impact of the disease on individuals.

The peripheral visual field may also add information relevant to clinical decision-making, for example for diagnosis,[19-21] disease phenotyping, and for monitoring progression. For example, peripheral visual field damage has been demonstrated in 15% of glaucoma patients with normal central visual fields.[22] At the other end of the spectrum, in patients with advanced damage in whom much of the central visual field may be damaged beyond the useful dynamic range of static perimetry,[23] tracking peripheral vision may be useful to demonstrate stability or to uncover further deterioration.[24-27]

A key reason for why peripheral visual fields are not measured more often is the lack of fast and efficient automated tests. Static programs that include the periphery are available on the Humphrey Field Analyzer (HFA, Carl Zeiss Meditec) and the Octopus instruments (Haag-Streit, Köniz, Switzerland).[28-32] However, threshold examinations, for example with the 60-4 test of the HFA,[33, 34] usually take more than 10 minutes, in part because they still rely on the classic "Full Threshold" procedures [35] rather than the more efficient techniques for threshold estimation and stimulus pacing introduced by the SITA-Algorithms.[7] Likewise, the suprathreshold tests of these instruments have scarcely changed since the 1980s. Last but not least, statistical tools for interpretation of peripheral perimetry (such as total- and pattern deviation probability maps) have not been made available commercially.

Manual kinetic Goldmann perimetry[36] as introduced in 1945 is probably still the most extensively used technique for measuring peripheral visual fields. In the hands of a highly trained examiner it is very flexible technique but it is difficult to standardize, difficult to quantify, and difficult to compare between different examiners. Progressively fewer centres possess the resources to perform this technique, and manufacture of the original Goldmann instrument (Haag-Streit, Köniz, Switzerland) has recently been

discontinued. Semi-automated kinetic perimetry (available on the Octopus 900 perimeter, the official successor of the Goldmann instrument) retains much of the flexibility of the manual technique but permits more precise control of stimulus motion. But, since it still requires an interactive examination conducted by an expert examiner with substantial training and experience, the technique is not widely used outside specialist centers.

A key problem in automating kinetic perimetry is that single responses, close to threshold, are highly variable and error-prone. This has previously been pointed out by Lynn et al. who referred to "spurious spikes" in the isopters with an early attempt to automate the technique.[37] In manual Goldmann perimetry, the examiner will seek to confirm responses that are not in keeping with expected values and will disregard implausibly early or late responses. A different solution will need to be established for fully automated kinetic perimetry.

In this paper, we demonstrate the large dissociation between central and peripheral visual fields in a group of patients with moderately advanced glaucoma. We report on a simple approach of repeated kinetic presentations to estimate isopter positions without interactive input from the examiner. We show that the precision of this technique is comparable to that of static perimetry of the central field and suggest further avenues for more efficient perimetry of the peripheral visual field.

Methods

Participants

Thirty patients with open-angle glaucoma were recruited from participants of previous studies at City University, London.[38-40] Patients had been recruited from the glaucoma clinics at Moorfields Eye Hospital, and inclusion criteria were a visual acuity of at least +0.30 log MAR (6/12), ametropia within ±5.00 D equivalent sphere and ±2.50 D cylinder, and no concomitant ocular or systemic disease. Table 1 provides descriptive statistics on the patients' age, visual acuity and contrast sensitivity. All patients were experienced in static perimetry but none had previously performed kinetic perimetry. The study adhered to the Helsinki declaration; the protocol was approved by the School of Health Sciences Research Ethics Committee at City University, and all patients provided written informed consent.

Table 1: Descriptive statistics of the patients' age, visual acuity and contrast sensitivity in the study eye.

	Range	**Mean (SD)**	**Median (IQR)**
Age (years)	59, 83	69 (6)	68 (67, 73)
Visual Acuity (log MAR)	-0.20, +0.30	+0.10 (+0.19)	+0.07 (0.00, +0.14)
Contrast Sensitivity (log)	0.60, 2.05	1.60 (0.30)	1.65 (1.35, 1.95)

Examinations

Of each participant one study eye was randomly selected, and two static examinations were performed of the central visual field, along with two kinetic tests of the peripheral visual field. All tests were carried out during a single session that lasted approximately 2½ hours including breaks. Visual acuity (ETDRS chart, distance 4 m) and contrast sensitivity (Pelli-Robson chart, at 1 m) were measured at the outset of the session.

Visual Field Tests

All visual field tests were performed on an Octopus 900 (serial number 2249, EyeSuite software version 3.0.1, Köniz, Haag-Streit, Switzerland), a projection perimeter with a hemispherical bowl (radius, 300 mm) with a background luminance of 10 cd/m^2. Stimuli were circular luminance increments (Goldmann size III, subtending 0.43°). For kinetic perimetry, the nominal maximum stimulus luminance corresponded to that of the Goldmann perimeter (318 cd/m^2 [1,000 asb]); for static perimetry it was 1,273 cd/m^2 (4,000 asb). Full aperture (38 mm diameter) trial lenses were used to correct refractive errors for static perimetry of the central field. To avoid lens rim artefacts, kinetic perimetry of the peripheral visual field was performed without refractive correction.

Kinetic perimetry of the peripheral visual field

Kinetic perimetry was performed with Goldmann III.1.e stimuli at a speed of 5°/s. According to Goldmann nomenclature, these stimuli are circular spots subtending a visual angle of 0.43° with a luminance of 10 cd/m^2 (ie, a 1.5 log unit attenuation of the 318 cd/m^2 maximum-intensity stimulus of Goldmann perimetry. In terms of contrast, this luminance increment corresponds to a 25 dB stimulus with the Humphrey Field Analyzer [nominal ΔL_{max}=3,183 cd/m^2 = 10,000 asb], and to a 21 dB stimulus with the static programmes of the Octopus 900 [ΔL_{max} =1,273 cd/m^2 = 4,000 asb]).

Kinetic stimuli started well outside the normal range of visibility[41] and moved at a speed of 5°/s from the periphery towards the centre. The entire visual field was sampled along 16 meridians (Figure 1). Three repetitions were performed for each vector, and the final isopter was defined by the median (middle) of the three responses. Stimuli were presented in random order. The mean radius of the isopter (MIR) was used as a global summary measure, and the reproducibility of an individual patient's answers was summarised as the median absolute deviation (MAD) of individual responses from the final isopter.

Unlike in manual kinetic Goldmann perimetry where perimetrists add additional stimuli to define the shape of isopters in areas of visual field damage, estimates that that fell within the central 10° of fixation were treated as missing data and would appear as a gap in the isopter (see

[patient *n*] for example).

False positives catch trials (n=6) were stimuli presented in the far nasal periphery where they were invisible while the sound associated with the movement of the perimeter's projection system was audible. To acquaint patients with the procedure three training stimuli were presented at the outset of the tests. The entire examination was programmed as a custom test in the XML language of the EyeSuite software. Altogether, each test consisted of a total of ~60 presentations (3 training stimuli, 48 kinetic stimuli, and 6 false-positive catch trials) and took approximately 11 minutes.

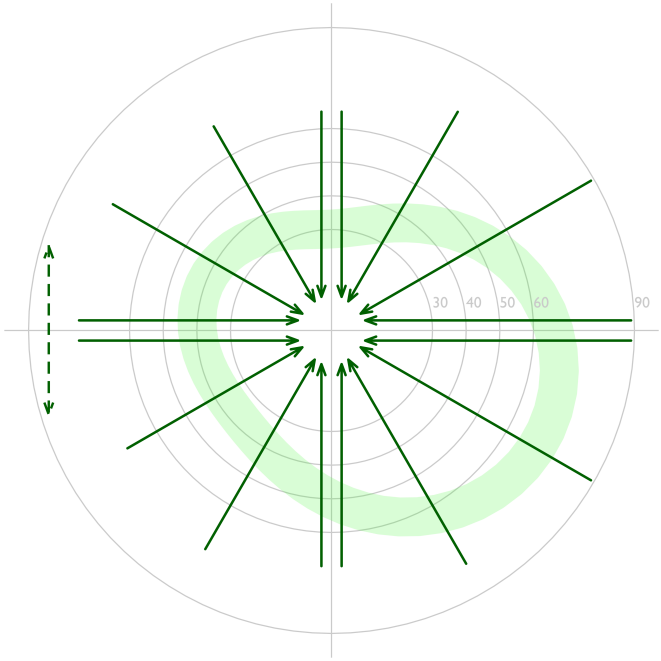

Figure 1:
Kinetic automated perimetry: Goldmann III1e stimuli were moved along sixteen meridians (green arrows) at a speed of 5°/sec. Three stimuli were shown on each meridian. Starting points of the arrows represent the start location of the stimuli. If not detected they moved to within 3 degrees of the fixation point. The dashed arrow represents the location of the 6 false positive catch trials. The light shaded region indicates the normative response range according to Vonthein et al. [42].

Static automated perimetry of the central visual field

Static perimetry of the central visual field was performed with the German Adaptive Threshold Estimation (GATE) strategy with a 24-2 test pattern and a stimulus duration of 200 ms. The GATE strategy has been described previously.[42, 43] At the outset of the initial test, thresholds are determined at four seed locations, and start intensities at other locations are then adjusted accordingly. In subsequent tests the GATE strategy starts with stimuli slightly brighter than the thresholds estimated during the previous test and varies stimulus intensities according to a 4-2 dB staircase that normally terminates after two response reversals. In contrast to the classic full threshold strategy,[35] however, a maximum-intensity stimulus (0 dB) is shown if the initial stimulus had not been seen. If this stimulus is not seen the procedure terminates, otherwise a stimulus 4 dB brighter than the initial intensity is presented next. Finally, the threshold is estimated as the intensity midway between the brightest stimulus not seen and the dimmest stimulus seen.

As a summary measure we used the mean deviation (MD), the average difference of all 54 threshold estimates from their age-corrected expected values. During the test ~10 false positive and ~10 false negative catch trials were presented to estimate the observer's reliability. GATE tests involved ~200 stimulus presentations and took ~6 minutes.

Analyses

The relation between central and peripheral visual field damage was examined via Spearman rank order correlation between MD (central field) and MIR (peripheral field).

Retest variability was estimated with a modified version of Bland-Altman analysis[44] which relates the differences between repeated tests to the best available estimate of the underlying "true" value (the mean of the repeated tests). The median of the retest differences indicates systematic changes between the first and second test that can arise from learning effects, and the retest variability is estimated from the dispersion of the differences. Because the standard deviation of the differences is highly affected by outliers, we used the median absolute deviation (MAD) of the retest differences to estimate the limits of agreement. We defined these as the median difference $\pm 2.2 * MAD$, which estimates the range in which 9 out of 10 observations would be expected to fall if the data were normally distributed.

Graphical representations of the visual fields and statistical analyses were performed in R (version 2.15.1, R Development Core Team (2012)).

Results

Most patients in this sample had moderate to moderately advanced damage in the central visual field, and only one patient had an MD better than -3.0 dB (Table 2).

Table 2: Summary statistics of the central and peripheral visual field tests.

	Mean (SD)	**Median (IQR)**	**Range**
Central visual field (GATE)			
Mean Deviation (dB)	-8.4 (4.4)	-8.1 (-11.9, -5.1)	-16.3, +0.1
False-negative response error rate	0.09 (0.12)	0.08 (0, 0.19)	0, 0.63
False-positive response error rate	0.06 (0.11)	0 (0, 0.12)	0, 0.54
Test duration (min:sec)	6:13 (0:58)	6:03 (5:30, 6:45)	4:44, 9:30
Peripheral visual field (AKP)			
Mean Isopter Radius, °	33.2 (7.9)	31.7 (29.8, 38.1)	11.5, 48.1
Isopter confidence band, °	2.7 (1.4)	2.2 (1.6, 3.3)	1.1, 7.4
False-positive response error rate	0.08 (0.13)	0 (0, 0.16)	0, 0.5
Test duration (min:sec)	11:30 (1:45)	11:30 (10:15, 12:30)	8:00, 16:30

Relationship between peripheral and central visual fields.

Our results demonstrated the large dispersion between peripheral and central visual fields (Figure 2). For example, some patients with deep central losses showed a nearly normal peripheral isopter (see patient *e* in Case Examples, Figure 6) while others with similar or less marked central damage showed a much more constricted peripheral isopter (see patient *z*, Figure 7). In particular in patients with severe central damage, the position of the peripheral isopters varied substantially (see patients *B* and *f* in the supplementary material).

The Spearman rank order correlation coefficient of MIR and MD was ρ=0.51 (95% CI: 0.18, 0.74; Fig 2). This correlation is considerably lower than the correlations between the test and retest values of MD (ρ=0.89, 95% CI: [0.78, 0.95]) and MIR (ρ=0.92, 95% CI: [0.84, 0.96]). This means that the lack of a close relationship between central and peripheral visual field estimates in our data is a true finding and not caused by poor precision of individual examinations.

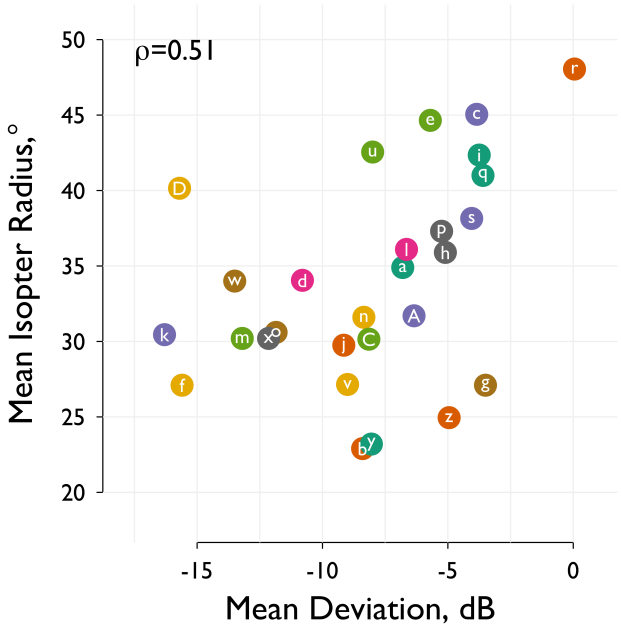

Figure 2:

Relationship between global summary measures of peripheral visual field (mean radius of isopter, MIR) and central visual field damage (mean deviation, MD). Each data point shows the mean of the 2 repeated tests. The Spearman rank order correlation coefficient was 0.51 (95% CI, 0.18, 0.74).

Test-retest variability of static and kinetic perimetry

There were no clinically meaningful differences between the results of the two sessions, in either the central or the peripheral visual field (median test-retest difference, 0.25° and -0.1 dB, p=0.28 and 0.78, respectively). The median absolute differences between test and retest were 1.3° with MIR and 0.9 dB with MD, and approximately 90% of test-retest differences were within ±4° (MIR) with kinetic perimetry, and within ±2.5 dB (MD) with static perimetry.

A formal comparison of retest variability between SAP and AKP is problematic – after all, different regions of the visual field are measured with different estimation techniques and with different units of measurement. We therefore related the spread of the retest differences to the range of measures obtained in this sample (Figure 2 for peripheral kinetic visual field tests, Figure 3 for central static visual field tests). The ratio between the ranges of the data (width of the grey rectangle) to the spread of test-retest differences (height of the rectangle) was similar for central and peripheral examinations. Thus, the precision of AKP of the peripheral field is similar compared to that of SAP of the central visual field.

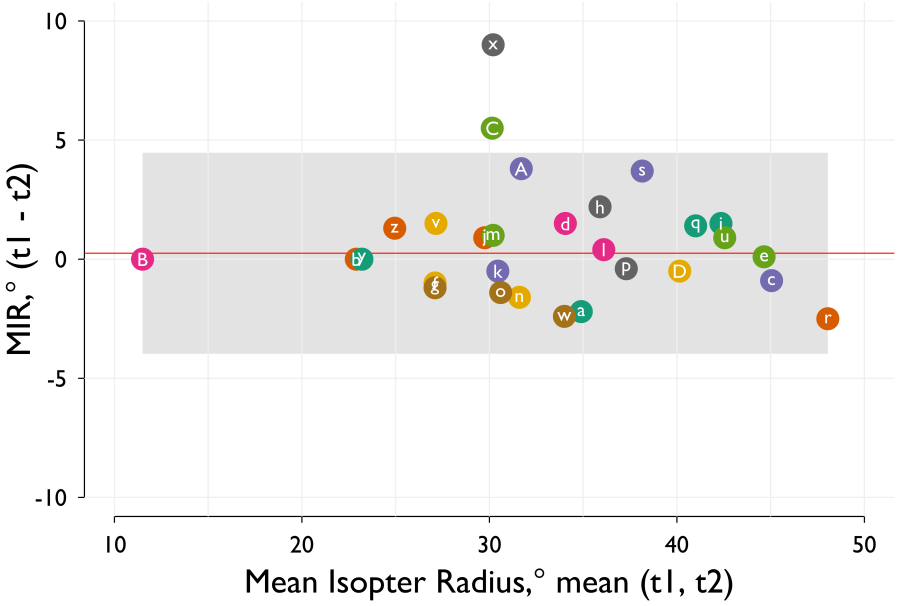

Figure 3:

Relationship between test-retest differences in mean isopter radius (MIR) and the range of peripheral visual field damage (mean of MIRs of 2 repeated tests). The height and width of the grey rectangle indicate the 90% retest interval of the Mean Isopter Radius ±4°, height of the rectangle) and the range of estimates in this sample (12° to 48°, width of rectangle). The red line indicates the median of the test-retest difference.

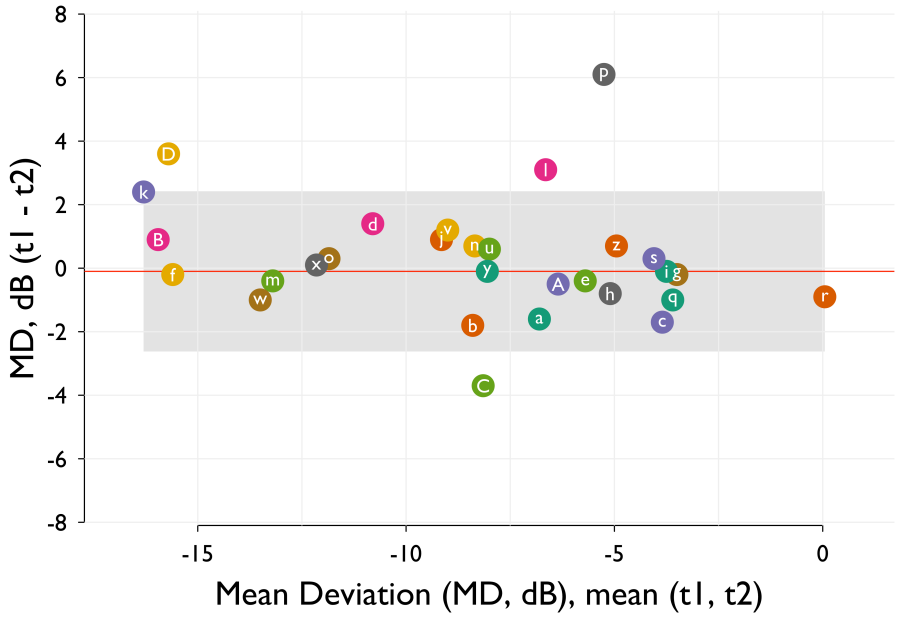

Figure 4:

Relationship between test-retest differences in mean deviation (MD) and the range of central visual field damage (mean of MDs of 2 repeated tests). The grey rectangle indicates the 90% retest interval (±2.5 dB, height of the rectangle) and the range of mean MDs in this sample (-16.1 dB to +0.1 dB, width of rectangle).

Most patients completed the session without any problems, but in two patients the initial kinetic tests had to be interrupted to instruct the patients to avoid false-positive responses. Obviously erratic "outlier" responses occurred in about two thirds of tests (see single responses in case examples, Figure 6-8, and in supplementary material). This confirmed the need to obtain several responses to achieve a precise estimate of isopter position. The width of the confidence interval around the isopters, derived from the MAD of repeated responses, varied by a factor of >5 between patients (Table 2).

In 19 patients (65%) our technique resulted in gaps in the isopter (see patients *u* and *z* in Figures 5 and 7), because some stimuli could not be detected until they were close to fixation. In one patient with deep and widespread visual field damage, no useful isopter could be estimated with the III.1.e stimulus because more than 75% of responses were located within the central 10° (patient *B* in supplementary material).

Case examples

Examples of three individual patients illustrate the relationship between peripheral and central visual fields and the repeatability of the tests (Figure 5-7). Both central and peripheral visual field examinations are shown by overlaying the greyscale representation of the central visual field with a plot of the kinetic isopter. Single kinetic responses are shown as red dots, and the final isopter is plotted in dark green. Median responses < 10° were treated as "missing data" and appear as gaps in the isopter. The MAD measuring the scatter of single responses is shown as a green band surrounding the isopter, and normative values[41] are represented as the light green band.

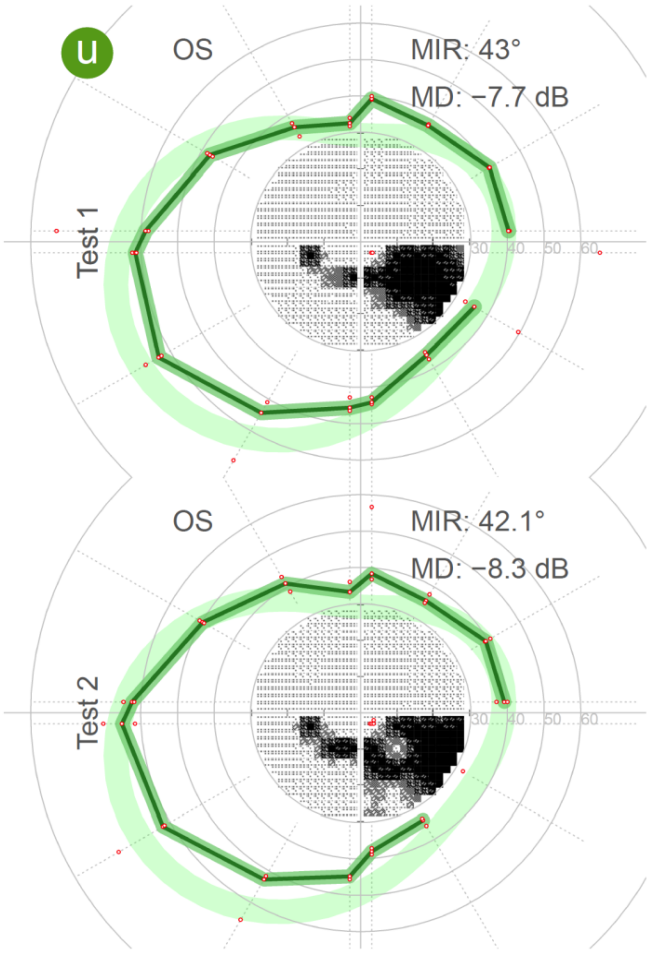

Figure 5:
Patient u's central field showed a dense inferior arcuate scotoma with a nasal step. The III.1.e isopter (dark green) showed that the nasal step extended far into the periphery. Elsewhere the isopter was close to the expected values of Vonthein [41] (light green band). Most responses (red dots) were tightly clustered and the confidence interval around the isopter was narrow (MAD test 1, 1.3°; test 2, 1.2°; medium dark green band). Both peripheral and central visual field test results appeared rather similar in the first and second examinations.

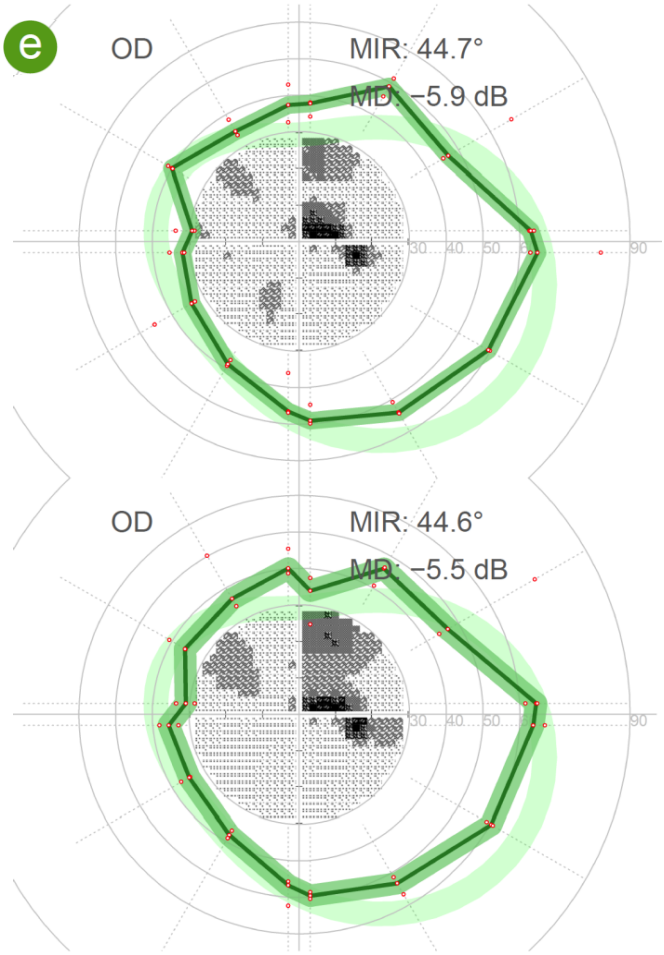

Figure 6:

Patient e had deep focal damage in the central superior visual field, but a substantially preserved peripheral III.1.e isopter. Retest variability was low with both central static and peripheral kinetic techniques.

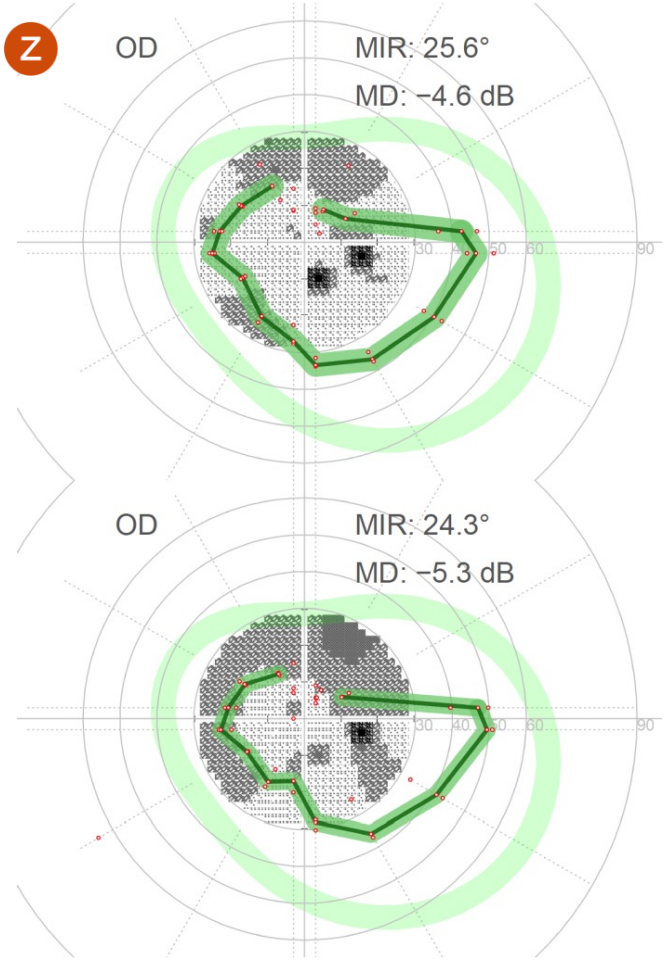

Figure 7:

Patient z had moderate diffuse central visual field damage with static perimetry and a substantially constricted III.1.e isopter (mean MIR 25°. In comparison, an MIR ~47° would be expected in a healthy person of the same age).

Discussion

The objective of this study was to explore differences between central and peripheral visual field damage in glaucoma, and to investigate the precision of isopters that are estimated from repeated kinetic stimulus presentations. Our results show that patients with similar central visual field loss may have strikingly different peripheral visual fields, and this suggests that peripheral perimetry may provide an important component of a more complete assessment of patients' visual field-related functional impairment. Further, our results demonstrate that kinetic perimetry of a single isopter can provide a global estimate of peripheral visual field with similar precision to that of the MD of static perimetry in the central visual field. In contrast to other approaches to automate kinetic perimetry[45] the simple approach reported here does not aim to reproduce the often complex isopter shapes of manual Goldmann perimetry in damaged visual fields. Rather, it aims to provide a clinically useful summary measure of peripheral visual field extent that can be used to complement information available from static perimetry of the central visual field.

Lynn et al. have previously described "spurious spikes" in isopters from automated kinetic perimetry.[37] As in Lynn's data, our results revealed obvious "outlier" responses in most of the automated kinetic exams. One obvious approach to reducing the impact of such outliers is to increase the number of obtained responses. Nowomiejska et al., for example, measured along 24 instead of the traditionally recommended 12 meridians.[46] In contrast, we increased the sampling by *repeating* presentations at the same meridians. By pooling this information on the reproducibility of responses at each position of the visual field, this approach allowed us to estimate a confidence interval for the isopter for each individual patient. The ±4° retest interval of the III.1.e isopter compares favourably to data reported previously.[24, 46-55]

With manual Goldmann perimetry, the peripheral borders of the visual field are traditionally determined with the I.4.e stimulus in healthy visual fields, or with the III.4.e or V.4.e stimuli when visual fields have already sustained some damage. In this study, we used the III.1.e stimulus (approximately equivalent to the I.3.e isopter which is the largest Goldmann isopter not constrained by facial features, in healthy eyes), to keep stimulus size similar to that most often used in static perimetry (0.43°). Given that our technique will almost always be applied to patients with moderate and advanced visual field damage, more intense (larger and/or brighter) stimuli must be considered for future work. However, this does not change our principal conclusion that, with a fully automated kinetic technique, isopters are best derived from repeated rather than single stimulus presentations.

The kinetic approach used in this study was designed for currently available commercial equipment (Octopus 900, with tests fully pre-specified in an EyeSuite XML file). The long test times (~11 min, on

average) would make its clinical application challenging. With the Open Perimetry Interface (OPI),[56] it will now be possible to reduce test time through more efficient sampling strategies. For example, stimulus presentations should start closer to the expected isopter locations, and, when two closely spaced responses have already been obtained on a particular vector, a third presentation may not be needed. It may also be useful to confine kinetic perimetry to those parts of the peripheral visual field that are likely of greatest importance to real-world performance (e.g. inferior and temporal visual field) rather than over the entire 360° circumference of the visual field. Finally, application of the OPI will make it possible to adapt stimulus speed more interactively to the response latencies of the patient and to the location of the stimulus (faster in the periphery, and slower in the centre of the visual field).

Our study demonstrated that precise estimates of peripheral isopters can be obtained from a fully automated kinetic approach when repeated presentations are offered. Further work is now being performed in our and other laboratories to improve the efficiency of this approach, to investigate how it can best be used to complement information obtained with static perimetry, and to answer the question of how perimetry of the entire visual field can help to improve clinical decision-making in patients with glaucoma.[29, 57-60]

Acknowlegments

This work is supported by unrestricted Project Grant from the Merck Investigator Studies Programme (DPC, VM), by research support from Haag-Streit International (Köniz, Switzerland; loan of the Octopus perimeter, and by a grant from Fight for Sight (UK) to PHA. The inspiration for the title of this paper was a keynote lecture by Lars Frisen (Goteborg) at the Imaging and Perimetry Society (IPS) meeting in Barcelona, 2001.

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