Development of a New Fully Automated Kinetic Algorithm (Program K) for Detection of Glaucomatous Visual Field Loss

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Submitted: December 2, 2014
Accepted: February 28, 2015

Citation: Hashimoto S, Matsumoto C, Okuyama S, Takada S, Arimura-Koike E, Shimomura Y. Development of a new fully automated kinetic algorithm (Program K) for detection of glaucomatous visual field loss. *Invest Ophthalmol Vis Sci*. 2015;56:2092–2099. DOI:10.1167/iovs.14-16182

Purpose. In Program K, a new automated kinetic algorithm that we developed, the frequency distributions of the number of patients' response points were obtained for external angles to distinguish normal and abnormal isopters. We also assessed the agreement between the results of Program K and Goldmann manual kinetic perimetry (MKP).

Methods. Program K detected abnormalities in isopters by using the external angles of patients' response points. In experiment 1, a normal external angle range and endpoint for the algorithm were determined by using visual field (VF) results of 100 data sets. In experiment 2, the results of Program K and Goldmann MKP were compared in 63 virtual patients. Visual field loss was assessed by using stimuli of V/4e, III/4e, I/4e, I/3e, I/2e, and I/1e at a speed of 3 deg/s. The isopters by Program K and Goldmann MKP were overlapped and the area of intersection was expressed as a percentage of the union area. The intersection percentages and test durations were evaluated.

Results. A normal external angle range between 150° and 240° and phase 3 as the appropriate endpoint for the algorithm were determined. The intersection percentages for the six isopters were 84% (V/4e), 83% (III/4e), 78% (I/4e), 71% (I/3e), 60% (I/2e), and 50% (I/1e) (average, 71%). The average examination duration for Program K was 16.0 ± 3.2 minutes. The results of Program K and Goldmann MKP were comparable.

Conclusions. Program K is clinically efficient and useful for detection and evaluation of abnormalities in a kinetic VF.

Keywords: automated kinetic perimetry, Octopus 101, new kinetic algorithm, Program K, conventional Goldmann kinetic perimetry

In the field of perimetry, kinetic and static perimetry are the two methods for evaluating the visual field (VF). While kinetic perimetry uses a moving target with a fixed target size and luminance to determine an isopter, static perimetry uses a fixed target at a selected test point and the luminance is changed to assess the visibility at the test point.[1] Currently, static perimetry has gained more popularity than kinetic perimetry because it can be easily automated. Static perimetry is almost completely computer driven and therefore examiner-independent. On the other hand, kinetic perimetry remains an important method to evaluate the VF in patients with advanced glaucoma or other optic neuropathies. Its strategy of "edge detection of visual field" is very efficient particularly for advanced VF loss. From the revolutionary Perimetron[2,3] to the Octopus 101 kinetic program[4,5] and the Humphrey kinetic test,[6,7] various types of automated kinetic perimeters have been developed and several studies have evaluated kinetic perimetry by using a computer simulation program.[8–10] Methods to perform kinetic perimetry have been well described previously,[11] but insufficient accuracy due to variation in patients' responses and the limitations of isopter drawing remain unsolved issues in kinetic perimetry. Conventional Goldmann manual kinetic perimetry (Goldmann MKP) has many advantages over other automated kinetic perimetry techniques. It is the conventional manual kinetic perimetry on an original Goldmann cupola perimeter, which is no longer manufactured by Haag-Streit. Because it can measure the entire VF in a relatively short period of time, Goldmann MKP has been widely used in kinetic perimetry. However, its results can be considerably influenced by the examiner's skill and is therefore examiner-dependent.[11] The difficulties in ensuring consistent test results and the inconvenient manual operation have made it hard for Goldmann MKP to gain more popularity in clinical practice. Thus, there is a pressing need for an easy-to-use and efficient kinetic perimetric method with reliable and consistent accuracy.

The VF has a shape similar to the one portrayed by Traquair's visual island[12] and the shape can be determined by isopters, which are the lines connecting the points of equal visual field sensitivity.[13] A normal isopter usually appears in the form of an ellipse but any change in the VF will distort this shape. From this phenomenon, Program K was developed by using the external angles of patients' response points to depict the shape of an isopter that could reflect any abnormalities caused by VF changes. Using a simulation program we developed, we first tested Program K on 100 VFs that had

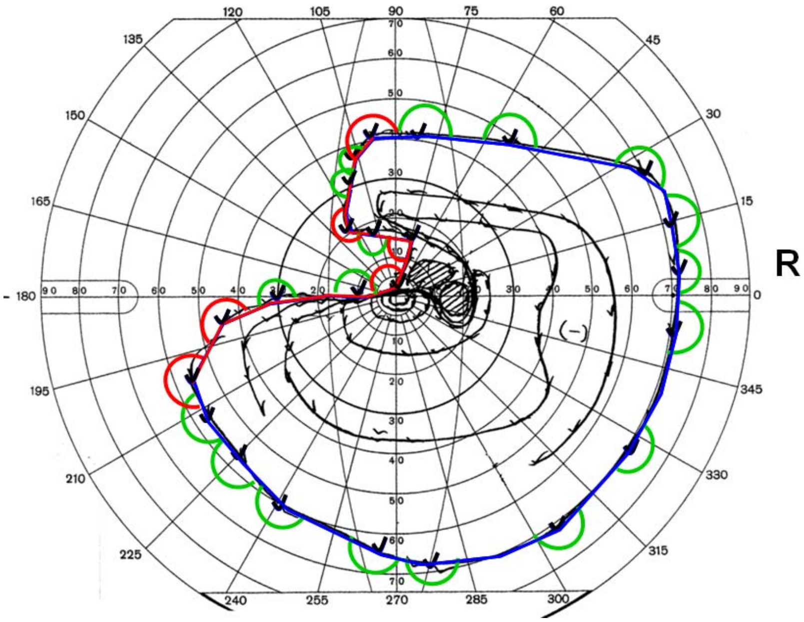

Figure 1. This shows examples of normal (*blue*) and abnormal (*red*) isopter lines as well as examples of normal (*green*) and abnormal (*red*) external angles. The external angle was defined as the angle on the outer side of the isopter that was formed by the two *straight lines* connecting the three generated response points.

been previously evaluated by Goldmann MKP to determine a normal range for the external angles and the most efficient endpoint for Program K. Subsequently, we performed Program K on 63 virtual patients and compared the results with those of Goldmann MKP. We superimposed the isopters obtained by Program K on those obtained by Goldmann MKP, and the areas of intersection were expressed as percentages of the union areas. The intersection percentages and test durations were evaluated.

In this study, we aimed to develop an easy-to-use kinetic method with sufficient and consistent accuracy and to assess its clinical usefulness for detecting abnormalities in the VF.

Methods

Experiment 1: Development of a New Automated Kinetic Algorithm, Program K

Basically, Program K was an algorithm that used the external angles of response points to determine any abnormalities in an isopter. When three response points were generated, the angle on the outer side of the isopter, which was formed by the two straight lines connecting the three response points, was defined as the external angle (Fig. 1). If a response point was found with an external angle outside the normal range, additional tests would be automatically added to the observed abnormal area of the isopter until a normal external angle was formed. As the process was repeated and more stimuli were added, subtler abnormalities would be detected and an accurate isopter could be finally depicted. Using a simulation program, we tested this algorithm on 100 eyes with glaucoma (average age, 63 ± 7.5 years; stage II: 30 eyes, stage III: 53 eyes, stage IV: 8 eyes, stage V: 5 eyes, and stage VI: 4 eyes by Aulhorn-Greve classification[14]) that had been previously tested by Goldmann MKP. From our assessment of the 100 data sets, we determined a normal range for the external angles and an efficient endpoint for Program K.

Program K functioned in a sequence of phases. In phase 1, a total of 16 stimuli (four in each quadrant) were moved along previously selected meridians from the periphery to the fixation point. This is a commonly used approach in automated kinetic programs. A response point was determined when the subject pushed the response button. All 16 response points were recorded and connected. The external angles of the 16 response points were analyzed to locate any abnormal areas on the isopter. If no external angle was found outside the normal range, the test would be terminated at phase 1. Otherwise, phase 2 was initiated with additional stimuli automatically added to both sides of the response point with an abnormal external angle. This was done by moving two additional stimuli perpendicularly to the midpoints of the lines connecting the abnormal response point to its two neighboring response points. The same technique was used in Goldmann MKP.[11] Figure 2 shows a three-phase procedure of Program K in a case with abnormality observed in the upper nasal VF. In phase 1, four stimuli were presented to generate response points 1 to 4. The two external angles formed by the four response points were analyzed and point 3 was found with an external angle outside the normal range. In phase 2, two additional stimuli (points 5 and 6) were added and moved perpendicularly to the midpoints of the lines connecting point 3 to points 2 and 4. All the response points, including the newly added points 5 and 6, were connected. At the end of phase 2, points 2 and 5 were found with external angles outside the normal range and the algorithm further continued to phase 3. The depicted isopter at the end of phase 2 was more detailed than the one at the end of phase 1. In phase 3, the same procedure in phase 2 was repeated to the abnormal response points 2 and 5, and three more response points (7, 8, and 9) were generated. As a consequence, a much more accurate isopter reflecting subtler abnormalities was depicted at the end of phase 3 (Fig. 2).

Experiment 2: Evaluation of the Usefulness of Program K in Computer-Simulated Virtual Patients

To evaluate the usefulness of Program K, we compared its results with those of Goldmann MKP in computer-simulated virtual patients. Subjects in experiment 2 were 63 eyes of 63

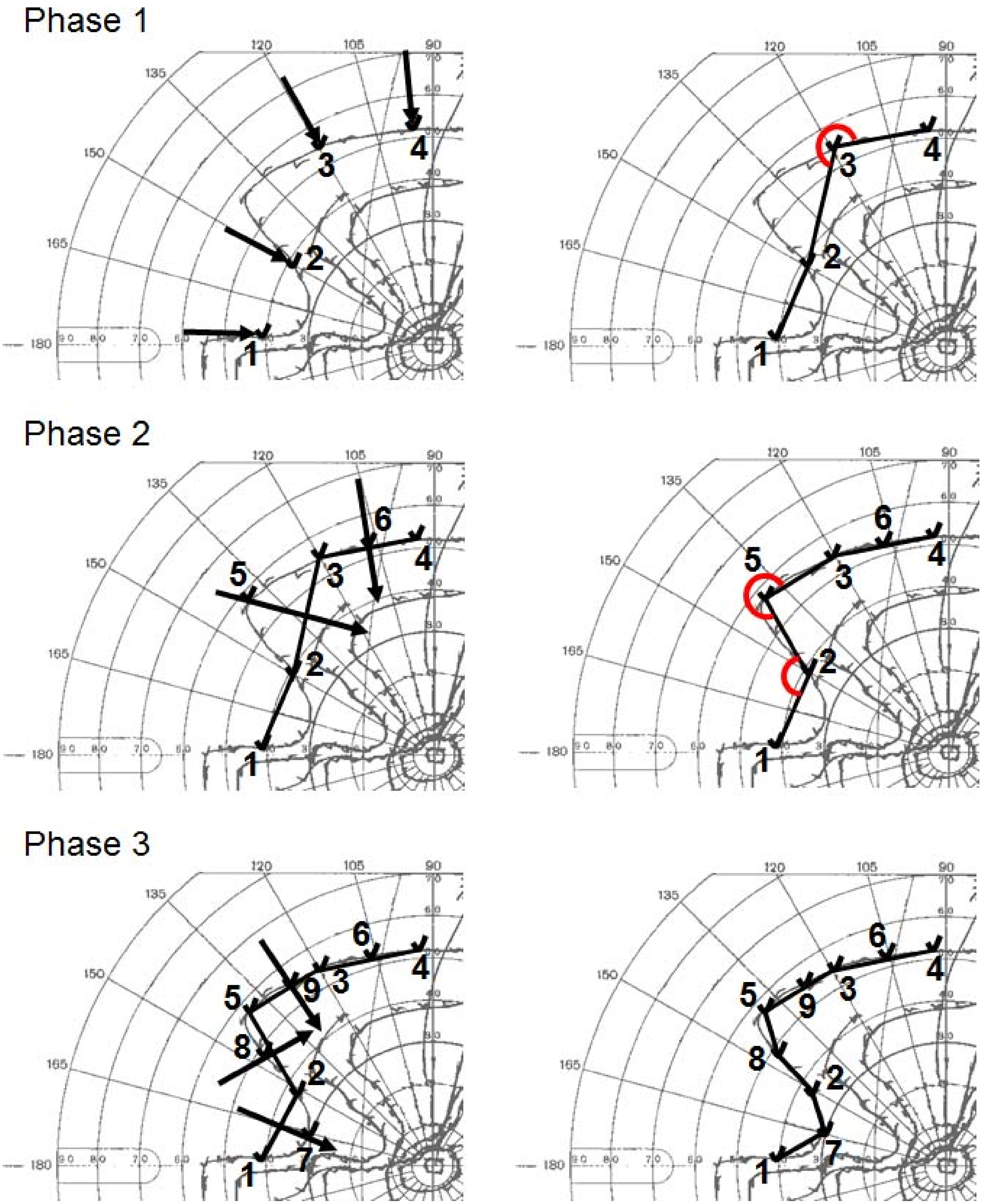

FIGURE 2. A simulated case demonstrating phases 1 to 3 of the new kinetic algorithm. As the phase advanced, a more detailed isopter with subtler abnormalities was depicted.

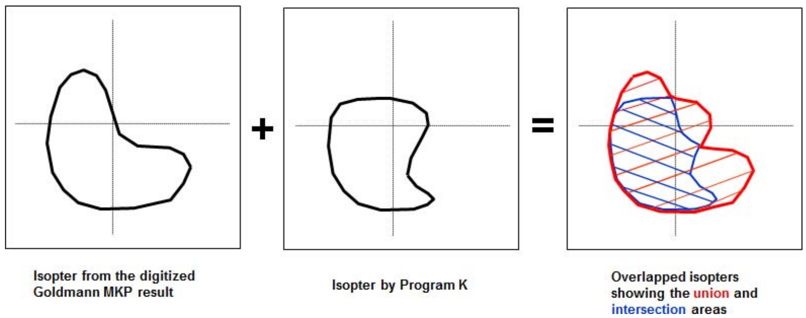

FIGURE 3. To compare the isopters depicted by Program K and Goldmann MKP, we overlapped both isopters and obtained the intersection percentage, which is the intersection (*blue*) area divided by the union (*red*) area.

patients with glaucoma (average age, 60.2 ± 15.4 years; stage I: 3 eyes, stage II: 16 eyes, stage III: 20 eyes, stage IV: 6 eyes, stage V: 15 eyes, and stage VI: 3 eyes by Aulhorn-Greve classification). They were tested by Goldmann MKP and the results were digitized by using a computer simulation program (K-Train) developed by Tuebingen University.[15] With the digitized data, K-Train created virtual patients for Program K.

The test conditions for Program K included six isopters with stimulus sizes and luminance of V/4e, III/4e, I/4e, I/3e, I/2e, and I/1e at a speed of 3 deg/s. Program K was performed in phase order and started with isopter V/4e. Because the test was almost completely automated, the examiner did not need to select a starting point or endpoint for the isopter. All the meridians of abnormal response points were tested at least twice to limit any variation in patients' responses. If a meridian had two response points with a difference more than 20°, the meridian was tested for a third time. Among the three response points, the average of the two closest response points was used as the final response point for that meridian. When the test ended, all the response points were connected and the isopter was automatically drawn. To compare the results of Program K with the digitized Goldmann MKP results, we superimposed the isopters by Program K on the digitized Goldmann MKP isopters to compare their shape and size. The intersection area could be expressed as a percentage of the union area (Fig. 3).[5,15] The intersection percentages for the six tested isopters and the test durations of Program K were evaluated.

Informed consent was obtained from all the subjects. All the experiments were performed in accordance with the Declaration of Helsinki for research involving human subjects.

RESULTS

Experiment 1

From the theory that a normal isopter usually appears in the form of an ellipse and any change in the VF will deform this shape, normality and abnormality of isopters were judged visually. For example, in Figure 1, the isopter lines in blue were determined to be normal and the isopter lines in red with a distorted curve were abnormal. The external angles of both normal and abnormal isopters were calculated, and Figure 4 shows the distributions of the normal and abnormal external angles from the 100 data sets for the three commonly used stimuli V/4e, I/4e, and I/3e. The external angles of the normal isopters ranged from 150° to 240° in these three histograms. Furthermore, with the six isopters, the respective numbers of response points required in phase 1 to 4 were 123.4 ± 16.2, 169 ± 21.4, 186 ± 25.1, and 193 ± 25.1 points. The required test durations were 15.5 ± 2.7, 15.7 ± 2.6, 16.7 ± 2.7, and 17.7 ± 2.7 minutes, respectively. It was possible to obtain isopters with even better precision if the tests were continued to more advanced phases. However, this would considerably extend the test duration. The results of the 100 data sets indicated that a three-phase algorithm was sufficient to produce results that were comparable to those of Goldmann MKP. Considering the required number of response points, test duration, and accuracy of the final isopters, we concluded that Program K with a three-phase algorithm would perform with the best efficiency.

Experiment 2

Our results indicated that the isopters by Program K were comparable to those by Goldmann MKP. Figures 5 and 6 show the comparison between the results by the two methods in two cases. The case in Figure 5 indicated defects in the nasal VF caused by glaucoma. The isopters by Goldmann MKP and Program K had an intersection percentage of 74% and the test duration for Program K was 12 minutes and 44 seconds. The case in Figure 6 showed concentric contraction due to glaucoma. The intersection percentage was 72% and the test duration for Program K was 5 minutes and 54 seconds. In the 63 patients, the intersection percentages for the six isopters were 84% (V/4e), 83% (III/4e), 78% (I/4e), 71% (I/3e), 60% (I/2e), and 50% (I/1e) with an average of 71%. The intersection percentages with respect to the glaucoma stage were 77% (stage I), 76% (stage II), 73% (stage III), 64% (stage IV), 62% (stage V), and 45% (stage VI). The average test duration for Program K was 16.0 ± 3.2 minutes.

DISCUSSION

Our results showed that Program K could automatically depict isopters with subtle abnormalities and the results were comparable to those by Goldmann MKP. Moreover, this could be achieved free from the influence of the examiner and within a tolerable test duration. This suggests that Program K can be a useful and efficient kinetic perimetric method for clinical practice.

In kinetic perimetry, Goldmann MKP has been used widely but it has several disadvantages such as lack of standardization and intra-examiner differences in stimulus velocity selection.[5] Because of the manual aspect of Goldmann MKP, examiner bias is a serious drawback of this method. A previous study has shown that the test–retest variabilities of Goldmann MKP for the V/4e and III/4e targets at 95% coefficient of repeatability are 32.8% and 23.7%, respectively.[16] That study also suggests that by using a single experienced examiner, the test–retest variability can be limited to <20%. Automated kinetic perimetry can help eliminate the problem of examiner bias. Comparison between Goldmann MKP and other semiauto-

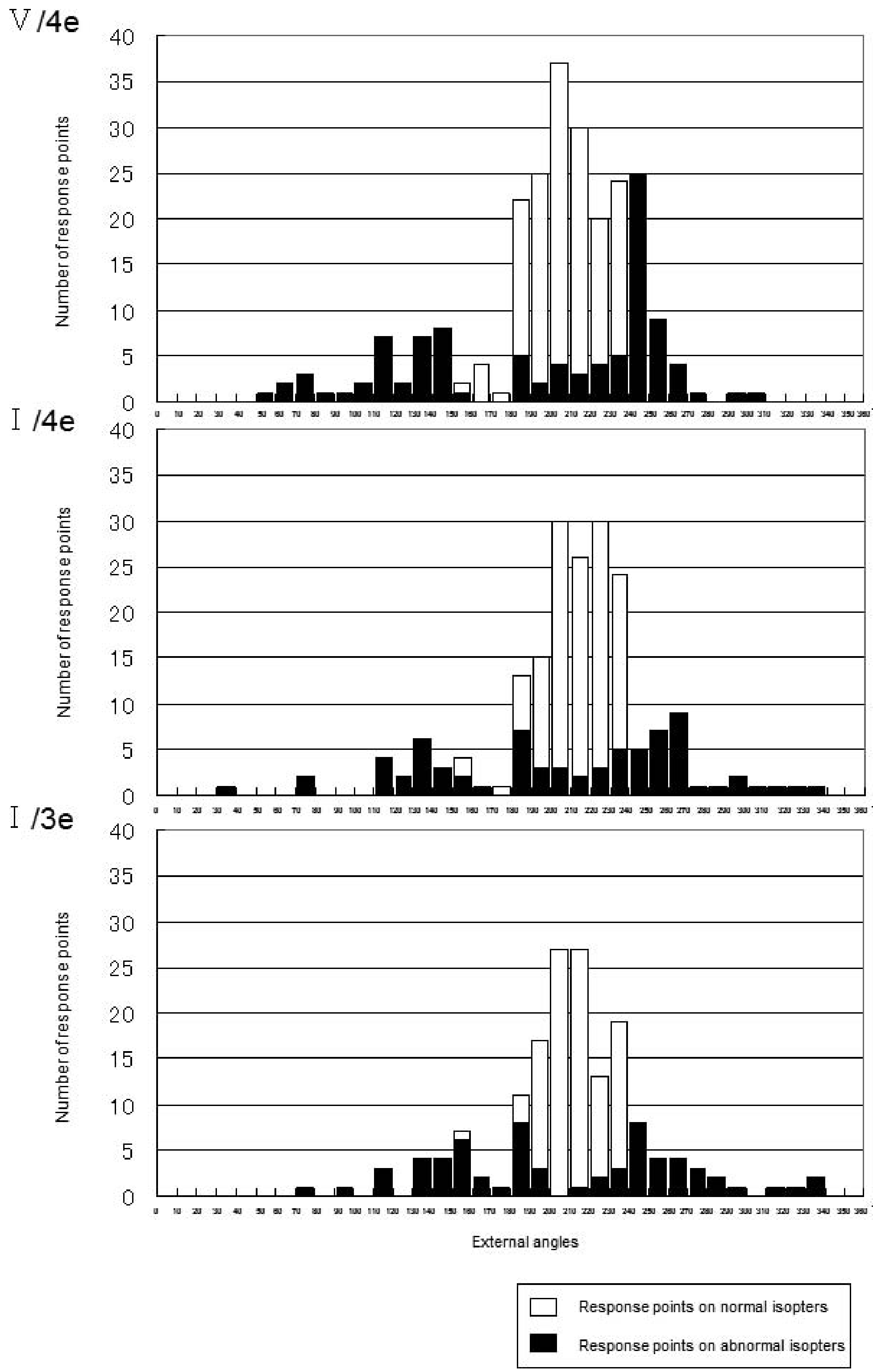

FIGURE 4. Distributions of the number of response points over external angles (0°–360°) for normal and abnormal isopters of V/4e, I/4e, and I/3e. The normal isopters in these three histograms distribute over a range of 150° to 240°, which was determined to be the normal range for the external angles.

mated and automated kinetic perimetry methods has been done previously. In 2005, Nowomiejska and colleagues[5] compared semiautomated kinetic perimetry and Goldmann MKP for advanced visual field loss. They report that visual fields derived by automated testing are slightly larger than those measured manually. They also have verified that examiner bias and technical problem can be diminished with the automated methods. Automated kinetic perimetry, however, also faces several challenges. Because the initial and additional vectors are individually defined by the examiner

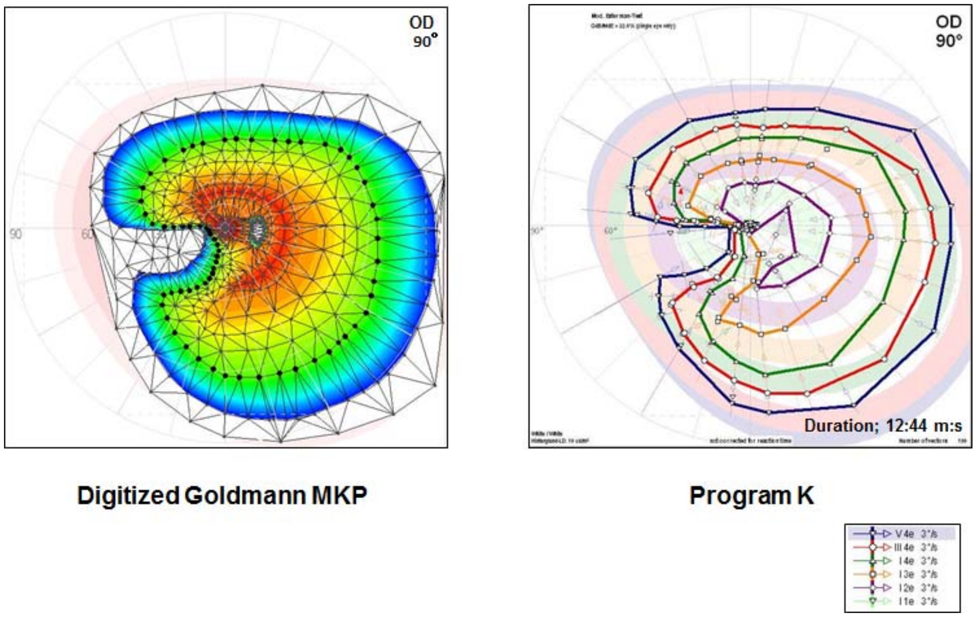

Figure 5. Isopters depicted by both methods for a 59-year-old female patient with primary open angle glaucoma in the right eye. Program K detected a defect in the lower nasal area of the VF.

and the isopter is basically drawn by the examiner, the result can be considerably influenced by the examiner's skill. As the kinetic stimuli are automatically moved along selected meridians at a fixed speed, variations in patient's responses can result in spikes in the depicted isopter pattern. In 1990, Lynn et al.[6] examined automated kinetic perimetry with the Humphrey Field Analyzer. They have pointed out several problems in automated kinetic perimetry such as the incidence of spurious spikes and isopter lines and other operational problems during testing. With Program K, many of these difficulties can be overcome.

In Program K, the VF was analyzed as a single closed figure. Determined by the external angles of response points, any deformation to this closed figure was regarded as a reflection of changes in the VF. Using the external angles as an index of normality, a computer program in Program K took all the measurements automatically and thus, simplified the task for the examiner. Theoretically, if a normal range can be found for the external angles, any area on the isopter with an external angle outside this normal range can be considered as an area with abnormality. Therefore, determination of an appropriate normal range for the external angles is important in developing this new kinetic method. If the angle range is too narrow, more response points will have to be generated to determine normality, thereby extending the test duration. On the contrary, if the angle range is too wide, the probability of

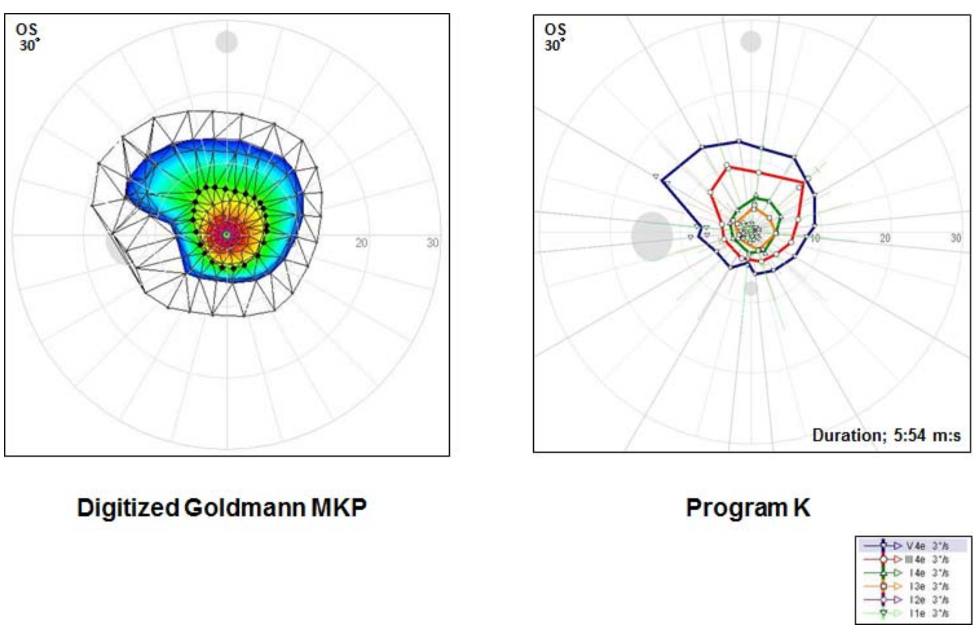

Figure 6. Isopters depicted by both methods for a 63-year-old male patient with primary open angle glaucoma in the left eye. Program K detected concentric contraction in the VF.

missing an abnormality in the VF will be much higher. It would be ideal to obtain a normal range for the external angles by using age-corrected isopters derived by semiautomated kinetic perimetry in a normal population. However, this will be extremely time- and labor-consuming and it will be difficult to determine a cutoff value for both normal VF and glaucomatous VF with subtle abnormality, using data from a normal population. Our results of the 100 data sets showed that with the five isopters tested in this study, the external angles of the isopters judged as normal distributed over the range of 150° to 240° (Fig. 4). We therefore used this range as the normal range for external angles in the algorithm.

Our result also showed that a three-phase algorithm was sufficient to produce an accurate isopter pattern. As the phase advanced, abnormal external angles that reflected subtler VF changes were selected and analyzed. A final isopter without the subjective influence of the examiner could be accurately depicted. To efficiently control the test duration, measurements of normal areas were kept to a minimum and extra meridians were added only to areas indicating abnormalities. Furthermore, to minimize variations in patients' responses and prevent the occurrence of false spikes, meridians of abnormal response points were tested two or three times. With the six isopters, the respective numbers of response points required in phase 2 to 4 were 169 $\pm$ 21.4, 186 $\pm$ 25.1, and 193 $\pm$ 25.1 points, and the required test durations were 15.7 $\pm$ 2.6, 16.7 $\pm$ 2.7, and 17.7 $\pm$ 2.7 minutes. From phase 2 to 4, the test duration was extended for approximately 1 minute for each phase while the response points increased for approximately 17 points (phases 2–3) and 7 points (phases 3–4). Considering patient's tolerance for test duration, it is clear that phase 3 was the endpoint with the best efficiency. Especially in phases 2 and 3, it is important to monitor the subject's fixation to ensure that it does not drift toward the region where stimuli are being presented.

It is also important to correct the isopter extent according to individual reaction time in kinetic perimetry.[17] Both Program K and K-Train have a correction mode to compensate for reaction time difference, although we did not need to use this function in this study.

Within a tolerable test duration, Program K detected subtler or progressing VF changes in the area from the periphery to the central 30°, which is a difficult area for conventional automated kinetic perimetry. In experiment 2, Program K was performed on 63 virtual subjects with glaucoma ranging from stage I to VI, using isopters V/4e, III/4e, I/4e, I/3e, I/2e, and I/1e, and a close correspondence was seen between the results of Goldmann MKP and Program K (Figs. 5, 6). Although a closer correlation between the results of Program K and Goldmann MKP was observed as the Program K phase advanced, the intersection percentage became lower as the glaucoma stage advanced. Furthermore, the intersection percentage also decreased with decreasing isopter size and luminance. It has been reported that in kinetic perimetry, the VF is affected by test conditions such as stimulus speed, size, and luminance particularly within the central 30°.[18–21] This suggests that Program K may not be suitable for patients with complicated VF defects. Although Program K had demonstrated a high degree of accuracy and efficiency, it could be further improved. Currently, the average test duration for six isopters is approximately 16 minutes for one eye and this could be further shortened. Moreover, Program K cannot be applied to patients with advanced glaucoma because separated abnormal isopters often occur in such cases. In the future, we are also interested in applying Program K to patients with other VF defects such as scotoma.

In conclusion, we have demonstrated that Program K is an easy-to-use and efficient search algorithm with a high potential for clinical application. With better test accuracy and greater time efficiency, Program K can further promote kinetic perimetry. Together with automated static methods, kinetic perimetry can diagnostically and therapeutically benefit patients with various VF changes.[22,23]

Acknowledgments

The authors thank Reiyo Tahara for editorial help.

The authors alone are responsible for the content and writing of the paper.

Disclosure: **S. Hashimoto**, None; **C. Matsumoto**, None; **S. Okuyama**, None; **S. Takada**, None; **E. Arimura-Koike**, None; **Y. Shimomura**, None

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