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Continuous light increment perimetry compared to full threshold strategy in glaucoma

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PURPOSE. *Continuous light increment perimetry (CLIP) is an improved testing strategy for automated static perimetry designed to save test time and enhance patient compliance. CLIP uses a modified ramp stimulus where stimulus intensity is continuously increased according to patient reaction time, starting from a subthreshold intensity until recognition. The test is constantly modified according to patient performance. As CLIP showed good results in normal subjects in previous studies, the authors now compared CLIP to the standard 4/2-full threshold (4/2) strategy in glaucoma patients.*
METHODS. *Fifty-two patients with glaucomatous visual field defects (mean sensitivities 2.9 to 18.4 dB), all with perimetric experience, were tested with CLIP (three times) and 4/2 in a randomized fashion. Tests were performed at 55 test locations within the central 30° visual field (24-2 area) using the Twinfield perimeter.*
RESULTS. *Average mean sensitivity was significantly higher for CLIP than for 4/2 (t test, $p<0.0001$). Absolute scotomas and extension of scotomas were comparable for both strategies, whereas CLIP found less deep relative scotomas in some cases. Mean test time was significantly shorter for CLIP (5.6 min) compared to 4/2 (8.9 min) (Wilcoxon signed rank test, $p<0.0001$). Patient acceptance was better for CLIP than for 4/2.*
CONCLUSIONS. *CLIP showed comparable results to 4/2 with excellent patient acceptance. Mean sensitivities are 1.8 dB higher than for 4/2; similar results were found previously in normal subjects. CLIP was able to save a mean 38% of test time compared to full threshold strategy with good reproducibility. (Eur J Ophthalmol 2005; 15: 722-9)*

KEY WORDS. *Automated static perimetry, Glaucoma, Ramp stimulus*

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INTRODUCTION

Full threshold white-on-white perimetry has long been the gold standard for the diagnosis, grading, and detection of progression of glaucomatous visual field defects. However, this method is time-consuming and is subject to fatigue effects in patients (1-3). Another disadvantage is the fact that the test becomes more difficult at the end of the program as stimuli are presented near threshold.

Many new test algorithms have been investigated recently to save test time without losing reproducibility (4-12), but less impact has been put on patient performance and compliance.

The continuous light increment perimetry (CLIP) strategy was developed to save test time and increase patient compliance. Results of CLIP were promising in normal subjects (13, 14): reproducibility of CLIP was better than 4/2 and fast threshold strategy and as good as SITA standard and CLIP was able to save about 60% of test time. This study was conducted to confirm these results in glaucoma patients with regard to threshold, reproducibility, test time, and patient compliance.

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Fig. 1 - *Experimental design: twinfield-perimeter with test bowl, computer monitor, personal computer, and printer.*

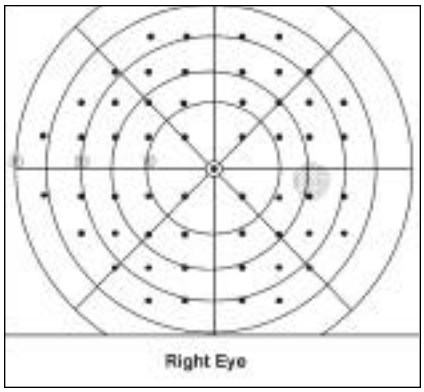

Fig. 2 - *24-2 test grid with 55 stimulus locations.*

SUBJECTS AND METHODS

Patients

Patients with known glaucoma defined as characteristic cupping of the disc and glaucomatous visual field defects in at least one eye were invited to participate, regardless of intraocular pressure level.

Fifty-two patients participated. Subjects were experienced visual field takers, having been tested on two or more occasions with automated static perimetry, and had a best-corrected visual acuity ≥0.3.

TABLE I - MEAN SENSITIVITY AND MEAN DEFECT (DB)

	Mean sensitivity				Mean defect			
	Mean	**SD**	**Min**	**Max**	**Mean**	**SD**	**Min**	**Max**
4/2	11.3	4.1	2.9	18.4	6.5	4.1	-0.7	16.0
CLIP 2	13.1	4.6	2.3	21.0	4.8	4.3	-3.1	16.6
CLIP 3	13.3	4.3	2.8	21.5	4.6	4.1	-3.7	16.1

CLIP = Continuous light increment perimetry

TABLE II - ABSOLUTE DIFFERENCES OF THRESHOLDS AT SINGLE TEST LOCATIONS (DB)

	Median	**Mean**	**75% quartile**	**95% quartile**
Difference 4/2 - CLIP 2	3	3.92	6	13
Difference 4/2 - CLIP 3	3	4.06	6	13
Difference CLIP 2 - CLIP 3	3	3.84	5	13

CLIP = Continuous light increment perimetry

TABLE III - DIFFERENCES OF THRESHOLDS DEPENDING ON DEFECT CLASSIFICATION (COMPARISON 4/2 – CLIP 2); ALL VALUES IN DB

Defect classification			**Mean**	**Standard deviation**	**Absolute differences 75% quartile**	**90% quartile**
1	0dB	Absolute	60% abs. scotoma for CLIP		7	12
2	1–10dB	Deep relative	-2.84	6.71	9	11
3	11–18 dB	Relative	-1.34	4.78	5	8
4	>18 dB	Mild/normal	0.18	3.40	3	5

CLIP = Continuous light increment perimetry

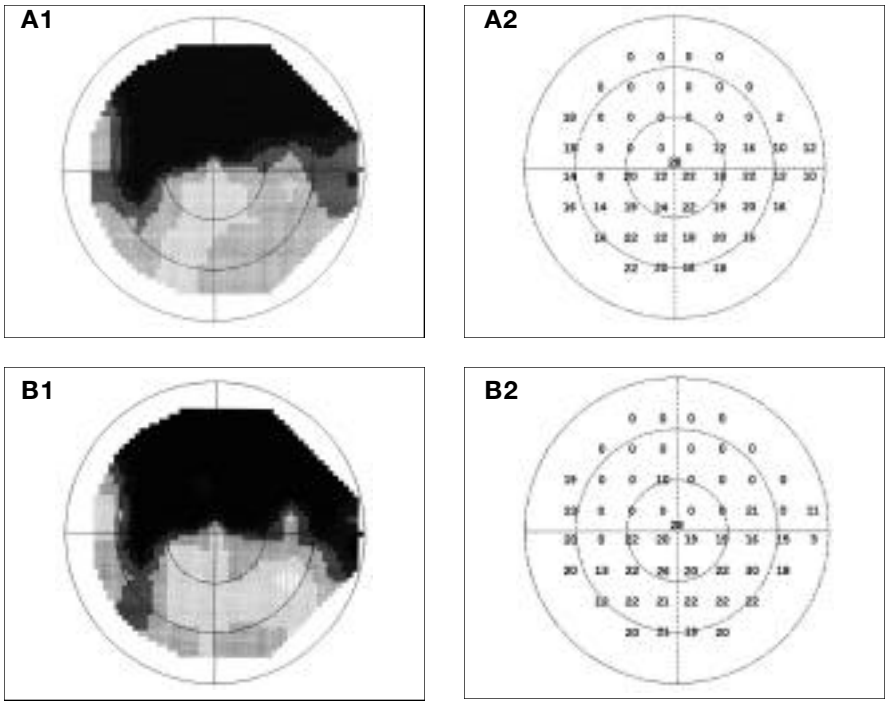

Fig. 3 - *Patient 41, Bjerrum scotoma with good correlation.* (**A**) *4/2 strategy.* (**B**) *Continuous light increment perimetry strategy with thresholds and gray scales.*

If both eyes had glaucoma and met the inclusion criteria, the eye to be tested was selected by the investigator before initiation of the study.

An attempt was made to perform testing on eyes with a wide range of visual field defects.

Eleven of the patients had to be excluded from further evaluation after visual field testing because they were not able to meet the inclusion criteria of less than 30% fixation errors (10 patients) and less than 30% false positive answers (1 patient).

Informed consent was obtained from all patients according to the tenets of the Declaration of Helsinki.

Twinfield perimeter

All visual field testing was performed on a Twinfield perimeter (Oculus Inc., Wetzlar, Germany). The experimental design is shown in Figure 1: stimuli are presented in a semi-transparent test bowl (radius 30 cm) using back-projection.

An integrated infrared camera monitors eye movements and pupil size, with results being presented on a computer monitor and processed by a personal computer. Head position can be corrected by clicking on the middle of a patient's pupil on the monitor.

Four red fixation marks are located at 1° of eccentricity. Maximum luminance is 318 cd/m^2, background luminance is 10 cd/m^2.

The Twinfield perimeter can perform static and kinetic perimetry (manual or automatic) using stimuli Goldmann size III or I. Static perimetry test strategies include CLIP, 4/2, fast threshold (using information of neighboring test points), and suprathreshold tests. Test grids can either be chosen from a list or self-generated.

CLIP

In this study we used an improved threshold strategy called CLIP (13, 14). CLIP uses a modified ramp stimulus, where stimulus intensity is continuously raised beginning from a subthreshold starting position until recognition. The central threshold is initially tested with a staircase strategy.

Then a luminance class is chosen according to the central threshold.

Reaction times are estimated at eight test locations, two locations per visual field quadrant, using stimuli 5 dB brighter than the presumed threshold.

Mean reaction time is calculated from these eight reaction times. If a stimulus is not detected initially, the same location is retested with maximum luminance to check for an absolute scotoma. In this case, this reaction time is not included.

The start position at the other test locations is 5 dB dimmer than the presumed threshold (5 dB subthreshold), taking into account age and central threshold. The light intensi-

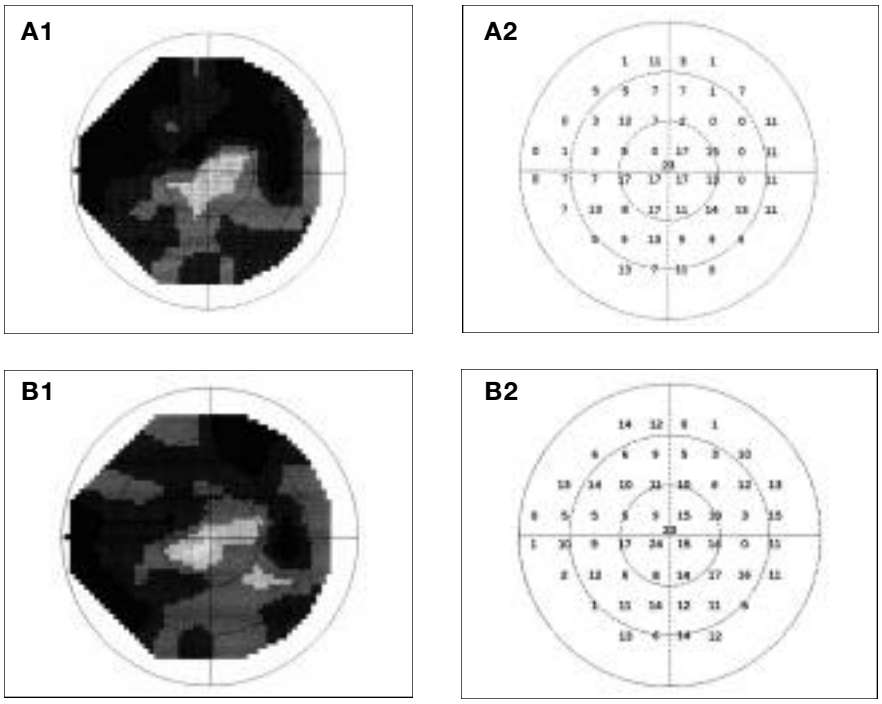

Fig. 4 - *Patient 50: advanced glaucomatous visual field defect with moderate correlation. (**A**) 4/2 strategy (**B**) CLIP strategy with thresholds and gray scales.*

ty is continuously enhanced by 1 dB per reaction time. If the patient did not press the answer button after eight reaction times (8 dB luminance increments), the stimulus intensity is then directly enhanced by 2 dB per reaction time for three steps. If a patient did not recognize the stimulus even then (in total 14 dB brighter than start position, 9 dB brighter than the presumed threshold), the stimulus intensity is enhanced by 4dB per reaction time until recognition.

Therefore stimulus luminance is increasing faster in deeper scotomas.The last level of stimulus intensity before recognition is assumed to be the threshold (therefore correcting the effect of reaction time).

Absolute scotomas which were detected during reaction time testing are not retested. The test is constantly modified according to patient performance.

If the stimulus is for example seen within less than three reaction times from the initial luminance, it is retested starting from a 5 dB dimmer level. If a threshold differs by more than 10 dB from the quadrant mean threshold, it is automatically retested at the end of the examination.

Study design

All subjects performed 4/2-full threshold program and three times the CLIP strategy in randomized order. Tests were performed using a 24-2 test grid (55 test locations within the central 30° of visual field) (Fig. 2). Stimulus size was Goldmann III (0.43°) in all tests, background luminance was 10 cd/m^2. All tests per subject were completed within 1 day with rest breaks as requested. At the end of the examination all patients were invited to choose their favorite strategy and to give their comments about both tests.

They could give their free answers as we wanted to know their subjective feelings about advantages and disadvantages of both strategies without giving a predefined choice of answers. So no statistic evaluation can be performed on these data.

Fixation was assessed by monitoring eye movements on the infrared monitor and by presenting central stimuli 8 dB brighter than central threshold.

Testing for false-positive answers was performed by presenting only the acoustic signal without following stimulus presentation.

Results of the first CLIP examinations were not further evaluated. Three test locations were excluded from further assessment in all tests: two at the area of the blind spot (11.31°/15.3° and 348.61°/15.3°) and the central thresholds, as these were tested in all cases by a staircase strategy.

Results of left eyes were mirrored in right eye results for better comparison.

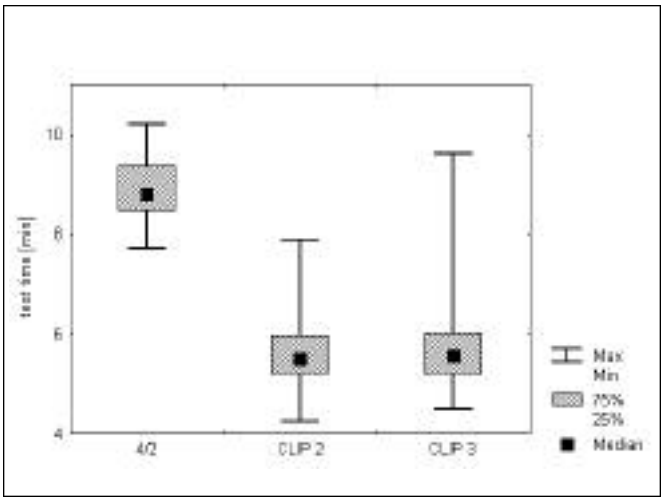

Fig. 5 - *Mean test time in minutes for 4/2 and CLIP 2 and 3.*

RESULTS

Patients

Forty-one glaucomatous eyes of 41 patients met the inclusion criteria. The mean age (±SD) of the subjects was 61.3 (±11.5) years (range 37–82 years). Of the 41 patients 17 were male and 24 female. Twenty-six patients had primary open angle glaucoma, 10 had normal tension glaucoma, and 5 had other forms of glaucoma as pseudoexfoliative glaucoma or secondary glaucoma with chronic uveitis. Visual acuity ranged from 0.3 to 1.2, refraction ranged from –6.25 to +4 D spheric and from 0 to 4 D cyl. Intraocular pressure on the day of examination was between 8 and 24 mmHg. The right eye was tested in 20 cases, the left in 21 cases.

Quality controls

A mean of 3% of all stimulus presentations were used to test for false-positive answers, 5–6% to test for fixation controls. Due to the different test strategy, the absolute number of stimulus presentations for CLIP was therefore less than one third of the 4/2 strategy.

For all three tests the frequency of false-positive answers was 3% in mean. One patient had to be excluded from further evaluation because he could not meet the inclusion criterion of 33% or less of false-positive answers (see Materials and Methods).

The mean number of fixation errors was 11% for the 4/2 strategy, and 12%-14% for the second and third CLIP testing. No significant age correlation could be found for either test. Ten patients had to be excluded because of fixation instability.

Comparison of mean sensitivity and mean defect

Results of mean sensitivity and mean defects are presented in Table I. Average mean sensitivity was significantly higher for CLIP than for 4/2 (t test, $p<0.0001$). Mean defect was worse in the 4/2 fields compared to those in the CLIP fields (t test, $p<0.0001$ for both comparisons). There were no significant differences between both CLIP testings.

Topographic analysis

Evaluation of pairs of visual fields seemed to demonstrate good qualitative and pattern similarities in defects between both tests. Two examples are shown in Figures 3 and 4. Patient 41 (Fig. 3) is an example of good correlation between strategies. Patient 50 (Fig. 4) is the patient with the worst correlation in this study: the deep relative scotoma in the upper part of the visual field is less pronounced in CLIP compared to 4/2. This tendency for shallower relative defects for specific localized scotomas with CLIP could be observed in several patients.

Point by point analysis

Absolute differences at single test locations are shown in Table II. Large differences were mostly located at the borders of absolute scotomas, where the test location was within the absolute scotoma with one strategy and within a normal area with the other strategy. This was also true for the comparison of absolute differences between both CLIP sessions.

Differences of sensitivity depending on defect classification

Depending on the results for the 4/2 strategy, test locations were classified in four defect classes:
0 dB (absolute scotoma) 399 single test locations;
1–10 dB (deep relative scotoma) 487 single test locations;
11–18 dB (relative scotoma) 846 single test locations;
>18 dB (mild scotoma and normal values) 400 single test locations.

A detailed comparison of threshold differences between 4/2 and CLIP 2 grouped by defect classes is presented in

Table III. CLIP found less deep scotomas compared to the 4/2 strategy, which accounts for the overall higher mean sensitivity, whereas differences were lower in areas of normal sensitivity or shallow scotomas.

Test time

Results of test times are presented in Figure 6. Test times were significantly shorter for CLIP 2 (median 5.48 min, mean 5.64 min, SD 0.78) and 3 (median 5.57, mean 5.72 min, SD 0.92) as compared with 4/2 (median 8.80, mean 8.92, SD 0.64) (Wilcoxon signed rank test, $p<0.0001$). CLIP saved a mean of 36% of test time. All subjects had shorter test times with CLIP (2 and 3) than with 4/2.

Mean reaction times for CLIP were 461 ms, SD 61 ms (second testing) and 465 ms, SD 73 ms (third testing) and ranged from 352 to 651 ms and 312 to 686 ms, respectively. No correlation between total test time of CLIP and reaction time was found.

Test time for 4/2 strategy was correlated with mean defect (Pearson coefficient $R=-0.61$, $p<0.0001$) and with mean sensitivity (Pearson coefficient $R=0.58$, $p<0.0001$), implicating that 4/2 strategy gets faster for advanced visual field loss with many absolute scotomas. Concerning CLIP, there was a tendency to an opposite result, although this was not significant.

Patient evaluation

Most subjects preferred CLIP compared to 4/2: they believed that 4/2 put too much pressure on them and was too fast. A lot of people mentioned that they needed to concentrate more with 4/2, especially at the end of the examination, and that they often were not sure if there really was a stimulus. The minority of people who found CLIP more tiring than 4/2 (despite a shorter test time) all had very large scotomas. Most persons preferred CLIP over 4/2 because it seemed to be more at their pace. They found it positive that stimuli were clearly seen at a certain luminance, even at the end of the examination. A few people told the examiner that if they were not sure if there really was a stimulus, they just waited for the stimulus to become a little brighter to be sure.

All subjects preferred CLIP because of the shorter test time.

DISCUSSION

Studies concerning the so called ramp stimulus, comparable to CLIP, were basically undertaken before 1970 (15-19), when the staircase strategies appeared in automated perimetry (6). However, findings of Capris et al (20) suggested that continuous luminance changes can be a good alternative to staircase procedures.

In this study, CLIP showed similar scotoma detection compared to standard full threshold strategy (4/2) in a significantly shorter test time. Absolute scotomas and extension of scotomas were comparable for both strategies, whereas CLIP found less deep relative scotomas in some cases. Large differences at single test points were found mostly at the borders of absolute scotomas. Mean sensitivities were 1.8 dB higher than with 4/2 strategy, absolute differences at single test locations (and therefore reproducibility) were comparable between 4/2 and CLIP and between separate CLIP tests. Most patients preferred CLIP over 4/2, possibly due to the shorter testing time, but also because the strategy seems easier to perform and less tiring in itself than standard full strategy.

The results of this study confirm our findings in normal subjects and preliminary findings in glaucoma patients (13, 14): mean sensitivity in normal subjects was about 2 dB higher than 4/2, reproducibility of CLIP was significantly better compared to 4/2 and fast threshold strategy and as good as SITA standard. In normal subjects CLIP was able to save a mean 58% (53–60%) of test time and was the shortest strategy in all subjects (out of 4/2, fast threshold and SITA standard). All normal subjects preferred the CLIP strategy. In glaucoma patients thresholds were about 1.5 dB higher than in 4/2, test time was significantly shorter than for 4/2.

Analyzing the CLIP strategy, local adaptation (Troxler in 1804 in (6), Cibis and Monjé in 1954 in (21)) and summation phenomena (6) could both affect the results. As mean sensitivities are higher in CLIP, it can be presumed that this could be more an effect of temporal summation.

Temporal summation was found to have no strong influence for stimulus durations above 320 ms relatively independent of eccentricity (22, 23) or above 500 ms with a stronger influence 5° temporal than centrally (24). In one study larger and deeper scotoma were found for stimulus durations of 250 ms compared to 500 ms (25). Between 65 and 500 ms, sensitivity increased with increasing stimulus duration, but there was no influence on fluctuation (26). Another study confirms these results, showing that summation is only strong for stimulus durations up to 100 ms and that the influence on stimuli longer than 200 ms especially longer than 500 ms is small. There was no effect of disease on the critical duration (27).

Newer studies indicate that the ramp stimulus tests other cell populations than pulse stimulation. A study of Okamoto et al (28) suggests that the y-system is excited by pulse stimuli, the x-system by ramp stimuli. Kani et al (29) found smaller diameter of receptive fields for ramp stimuli compared to pulse stimulation; responses were also different from those obtained by pulse stimulation. The density of receptive fields was similar to that of x-cells, for pulse stimuli parameters were similar to the y-cells.

Takashima et al (30) found similar results in normal subjects with higher sensitivities for ramp stimuli than pulse stimuli, especially in central areas of the visual field. In the few examined patients these differences were present in all areas. Their hypothesis was that it could be differences between the x- and y-system.

In this study, CLIP uses a ramp stimulus with one step per reaction time of a mean of 461 ms, so stimuli are longer than in 4/2 (200 ms) and even a small effect of temporal summation could contribute to the difference of mean 1.8 dB. Mean sensitivities were even higher despite the fact that some subjects reported that they just waited until the stimulus was a little brighter, if they were not sure. Relative scotomas are found to be less deep with CLIP, whereas differences are smallest at relatively normal test locations.

Fixation instability seems no probable explanation, as in fact all evaluated patients in this study had stable fixation proven by fixation tests and by continuous observation on the monitor. CLIP even found less deep scotomas in larger areas of relative scotomas, where some degree of fixation error would not immediately result in stimulus detection by a more sensitive fundus location. Therefore, differences could possibly be explained by effects of temporal summation and by different affection of the x- and y-system in scotomas.

All new test strategies are, as CLIP, able to save test time compared to 4/2 strategy. Test time is shortened by 30% up to 80% (4, 7-9, 31-36) depending on the strategy and the subjects included: test time is generally shorter and savings are larger in normal subjects, as found with CLIP. For increasing visual field loss, test time generally increases. This is also known for SITA and FASTPAC (35, 36).

Evaluation of mean sensitivity in studies concerning other new strategies like FASTPAC, SITA, and TOP was inconsistent. In some studies there were also higher mean sensitivities compared to standard full threshold as we found with CLIP (8, 9, 32, 34, 35), whereas other studies did not find differences (7, 31, 33). It was presumed that higher sensitivities could be due to a shorter test time and therefore less fatigue effect (3, 34). As this was also true for CLIP compared to 4/2, this could also contribute to the higher mean sensitivity in CLIP.

Patient acceptance was not generally evaluated in studies about new strategies. Perhaps it was presumed that a shorter test time would be sufficient. However, not only test time should be kept in mind, but also patient compliance.

In this study we found that subjects with minimal to moderate affected visual fields liked CLIP. Subjects with strongly affected visual fields generally found CLIP and 4/2 hard to perform. This is easy to explain as one of the advantages of CLIP is the fact that the stimulus luminance increases until the patient can see it and is getting performance feedback. Except in absolute scotomas and the blind spot area all the stimuli are expected to be seen at a certain luminance level. In comparison with 4/2 a larger proportion of stimuli is finally seen. Patients with absolute scotomas cannot detect a stimulus in this area and consequently have to wait longer until they can see the next one.

In the future CLIP could be modified in two ways: if an absolute scotoma is found in one area, CLIP could start with a brighter stimulus in surrounding test locations. If the patient is retested, the initial result could be taken into account. This will help to make CLIP even more acceptable in these sorts of visual fields and shorten the test time (although even now CLIP was significantly shorter than 4/2 even in advanced glaucomatous field defects). Another proposition would be the implementation of tests for false-negative answers.

Further studies will show if CLIP performs as well in other diseases, e.g., ocular hypertension, as in glaucoma patients. The fact that CLIP is easy to perform could also be used to examine patients with less experience, although fixation problems could be more relevant in these patients.

In conclusion, CLIP is a new strategy in automated visual field testing designed to save test time and enhance patient compliance. In glaucoma patients CLIP showed comparable results to 4/2 with excellent patient acceptance. CLIP was able to save a mean of 38% of test time compared to full threshold strategy with good reproducibility.

The authors do not have proprietary interest in the Twinfield-perimeter or the CLIP-strategy.

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