Short-wavelength sensitive visual field loss in patients with clinically significant diabetic macular oedema

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Summary The aim of the study was to compare the sensitivity of short-wavelength and conventional automated static threshold perimetry for the psychophysical detection of abnormality in patients with clinically significant diabetic macular oedema. The sample comprised 24 patients with clinically significant diabetic macular oedema (mean age 59.75 years, range 45–75 years). One eye of each patient was selected. Exclusion criteria included the presence of lenticular opacity. The sensitivity of the macular visual field of each patient was determined with programme 10–2 of the Humphrey Field Analyser on two occasions, using both short-wavelength and conventional stimulus parameters; the results of the second session were analysed to minimise learning effects. A pointwise horizontal hemifield asymmetry analysis was derived for short-wavelength perimetry (thereby negating the influence of pre-receptor absorption); the pointwise pattern deviation probability plot was analysed for conventional perimetry. Abnormality was defined as 3 or more contiguous stimulus locations with negative asymmetries (short-wavelength) or reduced sensitivity values (conventional)

that resulted in a statistical probability level of p less than 0.05. The fields of 8 patients were abnormal as assessed by conventional perimetry while all were classified as abnormal using short-wavelength perimetry. In the 8 patients who exhibited both abnormal conventional and abnormal short-wavelength perimetry results, the extent of field loss was generally greater using short-wavelength perimetry. The position of the localised field loss (i.e. as distinct from field loss that was generalised across the visual field) assessed by short-wavelength perimetry corresponded with the clinical mapping of the area of diabetic macular oedema but the extent of this loss was generally greater than that suggested by clinical assessment. Short-wavelength automated perimetry offers improved sensitivity for the psychophysical detection of clinically significant diabetic macular oedema. [Diabetologia (1998) 41: 918–928]

Keywords Perimetry, Visual Field, Short-Wavelength Sensitivity, Selective Loss, Diabetic Macular Oedema.

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Abbreviations: SWS, Short-wavelength sensitive; DMO, diabetic macular oedema; logMAR, log minimum angle of resolution; CNS, central nervous system; LOCS, Lens Opacities Classification System; NC, nuclear colour; NO, nuclear opalescence; C, cortical cataract; P, posterior sub-capsular cataract; HFA, Humphrey Field Analyser; SWAP, short-wavelength automated perimetry; dB, decibel; asb, apostilb

Perimetry comprises the assessment of visual sensitivity of retinal locations eccentric from the fovea. Short-wavelength automated perimetry employs a blue stimulus in order to preferentially stimulate the short-wavelength sensitive (SWS) pathway and a high luminance yellow background to saturate both the medium- and long-wavelength sensitive pathways and to simultaneously suppress rod activity [1]. Numerous studies have shown that short-wavelength perimetry detects glaucomatous visual field damage at an earlier stage in the disease process than conventional white-on-white perimetry [2–11].

A selective loss of SWS pathway sensitivity (i.e. in the absence of achromatic sensitivity loss) has been demonstrated in diabetic patients with minimal or no retinopathy using laboratory based paradigms and foveal stimuli [12–19]. SWS pathway sensitivity loss has been: (i) shown to be comparatively greater in diabetic patients than in glaucomatous patients (i.e. the reduction of achromatic sensitivity is minimal in diabetics) [16, 20] and; (ii) suggested to reflect the magnitude of diabetic macular oedema (DMO) [14, 18].

The psychophysical detection of early visual dysfunction in the diabetic eye may predict the development of sight-threatening retinopathy. However, few clinical studies have investigated the potential of short-wavelength perimetry for this purpose or for the assessment of the severity of diabetic retinopathy. Lutze and Bresnick [21] compared short-wavelength perimetry with conventional perimetry in a group of diabetic patients with varying degrees of retinopathy. The study failed to find a selective loss of short-wavelength sensitivity within the central 30° visual field but focal defects were found for both perimetry conditions that significantly correlated with the overall level of retinopathy. In addition, the absorption [22–23] and scatter [24] of short-wavelength light by the ocular media, and particularly the absorption of short-wavelength light by the macular pigment [25–26], has until now confounded the interpretation of short-wavelength perimetric thresholds within the macular region. The net effect of the pre-receptor “filters” is to produce a symmetrical reduction of SWS pathway sensitivity across the visual field. Consequently, analytical methodologies have been recommended that negate the attenuation of SWS pathway sensitivity by the ocular media [27] and by the macular pigment [26]. Furthermore, asymmetry analysis has been demonstrated to improve both the sensitivity and the specificity of short-wavelength automated perimetry in the detection of glaucomatous visual field loss when compared with analysis based upon absolute sensitivity [27].

The aim of this study was to compare the sensitivity of short-wavelength with conventional automated static threshold perimetry in the detection of psychophysical abnormality in a cohort of patients with clinically significant DMO. The influence of the pre-receptor filters on short-wavelength perimetry was negated using a pointwise horizontal and vertical hemifield asymmetry analysis, i.e. the analysis was sensitive to variation in the shape of the “hill of vision” relative to that of a normal database rather than being dependent upon absolute sensitivity (as was also the case with conventional perimetry).

Subjects and methods

Sample. The sample comprised 24 patients (18 men and 6 women) with clinically significant DMO as defined by the Early Treatment Diabetic Retinopathy Study criteria [28] which study’s definition of clinically significant DMO includes any one, or a combination, of the following: (i) retinal thickening involving or within 500 µm of the centre of the macula; (ii) hard exudate(s) at or within 500 µm of the centre of the macula, if associated with thickening of the adjacent retina (but not residual hard exudates remaining after disappearance of retinal thickening); (iii) a zone or zones of retinal thickening one disc area or larger in size, any part of which is within 1 disc diameter of the centre of the macula. The mean age of the sample patients was 59.75 years (range 45–75 years). The mean time from diagnosis of diabetes was 8.5 years (range 2–18 years); 3 patients were insulin-dependent and 21 patients were non-insulin dependent and receiving oral hypoglycaemic medication. One eye was randomly assigned to the study if both eyes exhibited clinically significant DMO; 11 right eyes and 13 left eyes were assessed. The demographic details are shown in Table 1. A conservative standardised effect size of 1.0 was used for the sample size estimation (i.e. the standard deviation of sensitivity using short-wavelength perimetry was assumed to be equal to the expected effect size). Using a two-tailed alpha of 0.05 and a beta of 0.10 (i.e. power = 90%), then the minimum sample size for the diabetic patient group should be 21.

Two medical retina specialists independently confirmed the diagnosis of clinically significant DMO before inclusion of the patient in the study. Inclusion criteria for the diabetic patients included a visual acuity (i.e. log minimum angle of resolution, logMAR) of 0.25 or better using the 96% contrast Regan chart (i.e. Snellen equivalent visual acuity of 6/9 to 6/12). Exclusion criteria comprised: (i) a distance refractive error greater than ± 6.00 dioptres sphere or ± 1.50 dioptres cylinder or both; (ii) a family history of glaucoma in a first degree relative; (iii) an intra-ocular pressure 22 mmHg or more; (iv) any other eye disease or disorder (including lenticular opacity – see below); (v) any previous laser photocoagulation treatment; (vi) proliferative diabetic retinopathy and its sequelae, e.g. vitreous haemorrhage and retinal detachment; (vii) central nervous system (CNS) disorders or psychiatric illness and; (viii) systemic medication with known CNS effects, e.g. tranquillisers. Lenticular opacity was graded on the basis of slit lamp appearance and the Lens Opacities Classification System (LOCS) III [29]. Eyes with the following LOCS III grades were excluded from the study: (i) nuclear colour greater than NC2; (ii) nuclear opalescence greater than NO2; (iii) cortical cataract greater than C2 and; (iv) posterior sub-capsular cataract P1 or more.

The respective perimetry results from the patients were compared with databases of normal fields. Normative data was modelled for each stimulus location to reflect the influence of age on sensitivity (and on the range of sensitivity values) across a group of normal subjects. The pointwise perimetric sensitivity of the patient was then directly compared to normative data of the appropriate age. For conventional perimetry, the established Statpac II normal database [30] of Humphrey Field Analyser (HFA, Humphrey Instruments Inc., San Leandro, Calif., USA) programme 10–2 was used. For short-wavelength automated perimetry (SWAP), normal HFA programme 10–2 sensitivity values were derived from the results of 400 normal subjects between the ages of 18 and 84 years (mean age 48 years, SD 17 years) who had undergone short-wavelength automated perimetry (SWAP) using programme 30–2 i.e. the HFA Statpac for SWAP database. Of the subjects 230 were aged 18–50 years, 90 were aged 51–65 years and 80 were aged 66–84 years. Normal subjects were recruited at vari-

Table 1. Demographic details for the diabetic patients (Px, patient number; Dur., duration of diabetes; Haem., haemoglobin; VA, log MAR visual acuity at 100 cdm⁻²; SW, short-wavelength automated perimetry; RE, right eye; LE, left eye)

Px	Age (yrs)	Dur. (yrs)	Diabetes Type	Haem. A1c (at Visit 2) (%)	Glucose (mmol/l)	Eye	VA	SW order (at Visit 2)
1	59	6	I	6.6	7.7	LE	0.1	2nd
2	63	5	II	8.2	17.4	RE	0.2	1st
3	58	18	II	7.6	12.3	RE	0.2	1st
4	59	2	II	8.6	5.6	LE	0.0	2nd
5	61	10	II	10.5	16.5	LE	0.25	1st
6	61	8	II	7.3	8.4	LE	0.25	1st
7	66	3	II	7.6	10.2	LE	0.1	1st
8	58	10	II	7.7	11.0	RE	0.2	1st
9	71	5	II	5.4	8.4	RE	0.0	2nd
10	52	7	II	12.2	19.3	RE	0.0	1st
11	47	11	I	N/A	19.9	RE	0.0	1st
12	70	16	II	9.1	12.3	LE	0.2	1st
13	55	3	II	9.6	11.3	RE	0.25	1st
14	61	7	II	9.3	8.0	LE	0.1	2nd
15	59	3	II	9.2	9.5	LE	0.1	2nd
16	66	17	II	12.9	17.8	RE	0.0	2nd
17	75	15	II	7.7	11.9	LE	0.0	1st
18	58	12	I	7.9	20.5	LE	0.0	1st
19	64	7	II	7.2	4.0	LE	0.0	1st
20	60	15	II	5.5	6.9	RE	0.2	1st
21	45	10	II	6.3	3.9	RE	0.0	2nd
22	50	7	II	7.3	13.5	RE	0.1	1st
23	45	3	II	8.7	12.3	LE	0.25	2nd
24	71	5	II	8.4	19.7	LE	0.0	2nd

ous international centres for the HFA Statpac II and the Statpac for SWAP databases using equivalent inclusion and exclusion criteria to those used for the diabetic patients in this study.

Procedures. Perimetry was undertaken using the HFA 640, an automated static threshold projection perimeter. Static stimuli were presented for a duration of 200 ms onto a cupola of 33 cm radius. The standard, full threshold strategy was used throughout the study; the thresholding strategy used a double staircase algorithm in which threshold was initially crossed using a 4 decibel (dB) step size and was then crossed in the opposite direction using a 2 dB step size. The last seen stimulus was taken as threshold at each location. The initial stimulus was presented at an intensity slightly brighter than the patient's expected age-matched threshold [31].

For conventional perimetry, the HFA 640 used a bowl illumination of 10 cdm⁻² and a Goldmann equivalent size III (angular subtense 0.431°) default static stimulus. The bowl illumination and stimulus were produced using polychromatic light sources. The sensitivity scale was referenced to a maximum stimulus luminance of 10,000 apostilbs (asb). For short-wavelength perimetry, the HFA used a yellow (Schott OG530 filter) bowl illumination of 100 cdm⁻² and a 440 nm narrow-band (27 nm half power bandwidth) blue stimulus [32]. The default static stimulus for short-wavelength perimetry was a Goldmann equivalent size V (angular subtense 1.724°). The sensitivity scale was referenced to a maximum stimulus luminance of 64.56 asb. These parameters have been shown to provide approximately 1 log unit of SWS pathway isolation [32]; the relatively narrow-band characteristics of the 440 nm stimulus filter ensured that chromatic aberration did not result in stimulation of the medium-wavelength sensitive pathway.

Programme 10–2 of the HFA 640 was used and comprised 69 stimulus locations within 10° eccentricity of the fovea (including foveal threshold). The distance refractive correction of the study eye, together with the appropriate near addition

for the patient's age, was used to correct for a viewing distance of 33 cm. The refraction was checked prior to each perimetry session to compensate for any transient refractive changes associated with diabetes [33]. Perimetry was undertaken on two separate occasions using conventional and short-wavelength perimetry parameters; the mean interval between the two visits was 12 days (range 1 to 31 days). Mandatory rest periods were given at least every 5 min during each perimetry session to minimise the influence of fatigue [34]. The order of stimulus condition (i.e. conventional or short-wavelength) at visit 1 was varied between patients and was then systematically varied between visits (i.e. short-wavelength was undertaken first at visit 1 and second at visit 2). For visit 2, 15 diabetic patients underwent short-wavelength perimetry first and 9 patients underwent conventional perimetry first. The results of the second perimetry session were analysed to minimise the influence of learning [35]. The group mean times to complete each stimulus condition as a function of order for visit 2 were: conventional first ($n = 9$), 12 min 30 s (SD 45 s); conventional second ($n = 15$), 12 min (SD 45 s); short-wavelength first, 15 min (SD 1 min 47 s); and short-wavelength second, 15 min 47 s (SD 2 min 13 s).

The two medical retina specialists mapped the extent of DMO onto a clear acetate sheet which detailed the retinal vascular pattern of each eye as derived from a 20° × 20° scanning laser tomography image. The extent of DMO was assessed using contact, or Volk, lens fundus biomicroscopy Volk, Ohio, USA. This image (acquired at visit 1) and the mapping of the extent of DMO (visit 2) were both undertaken following perimetry. Each medical retina specialist was blind to the perimetry results and to each other's assessment of the extent of DMO. The level of agreement of the mapping of the extent of DMO between the medical retina specialists (i.e. any two from GST, HCC, or LBY) was high (in terms of the allocation of retinal thickening on a quadrant-wise basis). The medical retina specialists disagreed on the extent of DMO in only 2 pa-

Fig. 1. Stimulus locations of HFA programme 10-2. The filled squares (i.e. ■ and ▨) show the stimulus locations of HFA programme 30-2 that were used to interpolate normal short-wavelength sensitivity values for programme 10-2 (■ represent 30-2 stimulus locations which do not coincide with 10-2 locations, while ▨ represent coincident stimulus locations). Stimulus location x,y and the four surrounding HFA 30-2 stimulus locations are indicated by the arrows

tients (i.e. no. 4, no. 9); in each of these patients, agreement was reached for 1 or 2 quadrants but disagreement occurred on the presence of DMO in another quadrant. In these 2 patients, the extent of DMO was allocated to every indicated quadrant whether, or not, agreement was reached between the two medical retina specialists.

Analysis. Fields that resulted in a false-positive or false-negative response rate greater than 33 %, and those that exhibited fixation losses greater than 20 % (i.e. Heijl-Krakau technique [36]), were excluded from the analysis.

For conventional perimetry, the pattern deviation plot of the HFA Statpac II database was used to illustrate the pointwise deviation of the shape of the visual field from the age-matched normal field [37]. This was achieved by correcting for generalised shifts in the overall sensitivity which consequently emphasised localised sensitivity loss (i.e. as distinct from field loss that was generalised across the visual field). Those points that had the highest measured sensitivities were assumed to be unaffected by localised visual field loss. The general sensitivity level for the pattern deviation plot was calculated from the stimulus location with the seventh highest sensitivity [38]. For this study, abnormality was defined as three or more contiguous stimulus locations of the pattern deviation plot with statistical probability levels of p less than 0.05. The total deviation probability plots are also presented in the figures.

For short-wavelength perimetry, a pointwise hemifield asymmetry analysis was established. Using this analytical approach, the influence of pre-receptor absorption [22, 23, 25, 26] and light scatter [24] was negated since the overall effect of these factors results in a symmetrical attenuation of the “hill of vision”. In addition, this analysis can be expected to avoid the artifactual assigning of abnormality in patients with high ocular media absorption and the problems associated with the limited measurement range of short-wavelength perimetry; this is of particular relevance in diabetic patients who are known to exhibit exaggerated ocular media absorption values [39]. A weighted linear interpolation procedure, based

upon the angular distance between the 10-2 stimulus location to be derived and the four surrounding 30-2 locations, was used (Fig. 1). Consider stimulus location x,y of programme 10-2; the nearest supero-temporal stimulus location (right eye) of programme 30-2 is 4.5° , the nearest supero-nasal location is 5.6° , the nearest infero-nasal location is 4.5° and the nearest infero-temporal location is 2.8° . For each decade, the interpolated sensitivity (dB) of stimulus location x,y of programme 10-2 is given by:

$$dB_{x,y} = [(dB_{ST} \times 17.5/4.5) + (dB_{SN} \times 17.5/5.6) + (dB_{IN} \times 17.5/4.5) + (dB_{IT} \times 17.5/2.8)] / 17.15$$

where dB_{ST} , dB_{SN} , dB_{IN} and dB_{IT} represent age-matched normal data of the nearest supero-temporal, supero-nasal, infero-nasal and infero-temporal programme 30-2 stimulus locations respectively.

The pointwise difference of programme 10-2 short-wavelength interpolated sensitivity between corresponding stimulus locations in the opposite horizontal hemifield was calculated; the group mean of differences and the standard deviation of the differences were used to establish confidence limits for the asymmetry of pointwise horizontal hemifield sensitivity values. For this study, abnormality was defined as three or more contiguous stimulus locations of the pointwise horizontal hemifield asymmetry plot with statistical probability levels of p less than 0.05. A pointwise vertical hemifield asymmetry analysis was also undertaken in order to show the full extent of any localised field loss, i.e. if the localised field loss was evenly distributed across the horizontal midline and located in one hemifield, the full extent of the defect may be underestimated (assuming an equal magnitude of sensitivity loss on either side of the midline) using solely the horizontal hemifield asymmetry analysis.

The extent of any localised sensitivity loss was approximated for both perimetry conditions by determining whether or not field loss had occurred within each of the four quadrants. For a given quadrant to be assigned as containing a localised field loss, three contiguous stimulus locations with statistical probability levels of p less than 0.05 had to lie within the quadrant. For conventional perimetry, the pointwise pattern deviation plot was used to determine the extent of the localised sensitivity loss while for short-wavelength perimetry the pointwise horizontal and the vertical hemifield asymmetry plots were both evaluated.

Results

A detailed summary of the results is given in Table 2. One patient was excluded from the analysis owing to a false-positive response rate greater than 33 %. Examples of representative conventional and short-wavelength perimetry pointwise probability plots are given in Figures 2 to 6.

No diabetic patient exhibited normal results for both perimetry conditions. The fields of 8 patients were abnormal as assessed by conventional perimetry, whilst all 23 fields were classified as abnormal using short-wavelength perimetry (Table 2). In the 8 diabetic patients exhibiting both abnormal conventional and abnormal short-wavelength perimetry results, the position of the localised field loss corresponded using the two perimetry conditions (Table 2). Howev-

Table 2. Results summary table showing the position (by quadrant) of retinal thickening and the position of localised sensitivity loss for conventional and short-wavelength, automated perimetry (A, abnormal; N, normal; ¹, foveal involvement; SN, supero-nasal; ST, supero-temporal; IT, infero-temporal; IN, infero-nasal). For a given quadrant to be assigned

as containing a localised field loss (i.e. X), three contiguous stimulus locations with statistical probability levels of $p < 0.05$ had to lie within the quadrant. Note: localised oedema in the inferior temporal quadrant of the retina will result in a superior nasal visual field defect after projection through the nodal point of the eye

Px	Clinical assessment of DMO				Conventional perimetry				Short-wavelength perimetry					
	Location of thickening:				A/N	Position of localised field loss:				A/N	Position of localised field loss:			
	Quadrant:					Quadrant:								
	SN	ST	IT	IN		IT	IN	SN	ST		IT	IN	SN	ST
1	X ¹				A	X				A	X		X	
2		X	X		N					A		X	X	X
3		X	X		A		X	X		A		X	X	X
4		X	X		A		X	X		A		X	X	X
5	X			X	N					A		X	X	X
6	X	X	X		A				X	A		X	X	X
7		X			N					A	X	X		X
8			X ¹	X ¹	A				X	A			X	X
9	X		X	X	N					A	X	X		X
10		X			N					A		X		
11		X ¹			A		X			A		X	X	
12			X ¹	X ¹	A			X	X	A			X	X
13			X ¹	X ¹	N					A	X	X	X	X
14	X				–					–				
15			X		A			X		A		X	X	X
16	X ¹			X ¹	N					A		X	X	X
17		X	X		N					A	X		X	X
18	X ¹	X ¹	X ¹	X ¹	N					A	X		X	
19	X	X	X		N					A			X	
20	X	X			N					A	X		X	
21	X	X		X	N					A	X			
22	X	X			N					A	X	X		
23		X			N					A		X		
24	X	X	X		N					A		X	X	X

er, the extent of the localised field loss was generally greater (i.e. in 7 of the 8 patients) using short-wavelength perimetry (Figs. 5, 6). In the 15 patients who only exhibited abnormality using short-wavelength perimetry, the results of conventional perimetry were “teetering” in four cases i.e. two contiguous stimulus locations showed abnormality (or a number of non-contiguous stimulus locations showed abnormality) in the same quadrant(s) as the short-wavelength localised field loss (Fig. 4).

The position of the localised field loss assessed both by conventional and short-wavelength perimetry generally corresponded to the clinical mapping of the extent of DMO (Table 2). The extent of the localised sensitivity loss, however, was greater for short-wavelength perimetry than that suggested by clinical assessment in 11 of the 23 diabetic patients; the area was approximately of equal extent in 9 patients and was less than that suggested by clinical assessment in the 3 remaining patients. As expected, analysis of both the pointwise horizontal and the pointwise vertical hemifield asymmetry plots resulted in a greater extent of localised SWS pathway sensitivity loss for 18 of the diabetic patients than if only the pointwise horizontal hemifield asymmetry plot had been analysed.

Discussion

DMO is the largest single cause of visual impairment and legal blindness in diabetic patients [40–41]. Prompt laser photocoagulation of clinically significant (i.e. sight-threatening) DMO will stabilise vision in approximately 60 % of eyes [42–45]. However, the clinical assessment of macular oedema, using contact lens or Volk lens fundus biomicroscopy, relies upon the subjective recognition of retinal thickening [46–47]. The differentiation of thickened retina from normal between-subject variation is difficult [48] and the detection of change in retinal thickening over time is problematic. Alternative means of detecting and monitoring DMO are necessary to improve the clinical management of this sight threatening complication of diabetes and for the evaluation of therapeutic protocols [49].

The pointwise hemifield asymmetry analysis of short-wavelength perimetry could represent a useful clinical tool for the psychophysical detection of DMO; it was conceived to negate the pre-receptoral attenuation of the blue stimulus by the ocular media and macular pigment and to avoid the problems associated with the limited measurement range of short-

Fig. 2. Automated perimetry pointwise probability plots for diabetic patient no. 19 (Left eye, visit 2, short-wavelength perimetry undertaken after conventional perimetry). Top left; Total deviation plot of conventional perimetry. Top right; Pattern deviation plot of conventional perimetry. Bottom left; Horizontal hemifield asymmetry plot of short-wavelength perimetry. Bottom right; Vertical hemifield asymmetry plot of short-wavelength perimetry

wavelength perimetry. Alternative methods have been proposed for the analysis of short-wavelength perimetry in the glaucomatous eye [10]. Experience has shown, though, that total deviation and pattern deviation analyses frequently lack sufficient measurement range especially in patients who exhibit high ocular media absorption values. There is, however, a need to assess the specificity of the pointwise hemifield asymmetry analysis of short-wavelength perimetry, both in normal subjects and in diabetic patients with no DMO, prior to its use in a clinical setting. In addition, it has been suggested that some oral hypoglycaemics affect colour vision [50]; however, the precise nature of the suggested colour vision loss and the methodology used to show this acquired

defect are vague. It is not unreasonable to assume, however, that any acquired colour vision loss resulting from oral hypoglycaemics would result in a diffuse loss of colour perception. The analysis used in this study for short-wavelength automated perimetry identified localised short-wavelength visual field defects rather than a symmetrical reduction of short-wavelength visual sensitivity. Conversely, Lutze and Bresnick [21] failed to find a selective loss of sensitivity using short-wavelength perimetry, in conjunction with HFA programme 30-2 (6° square grid inter-stimulus spacing), in a group of diabetic patients with varying degrees of retinopathy (i.e. ranging from no retinopathy to proliferative retinopathy). The results reported in this paper were attained, however, from a cohort of patients with clinically significant DMO who had undergone HFA programme 10-2 (2° square grid inter-stimulus spacing).

Although different forms of analysis have been used in this study to define abnormality for conventional and short-wavelength perimetry both were referenced to that of an age-matched normal database and were designed to elucidate deviation of the shape of the visual field from that of the normal eye. It is therefore argued that the analyses were equivalent

Fig. 3. Automated perimetry pointwise probability plots for diabetic patient no. 2 (Right eye, visit 2, short-wavelength perimetry undertaken before conventional perimetry). Top left; Total deviation plot of conventional perimetry. Top right; Pattern deviation plot of conventional perimetry. Bottom left; Horizontal hemifield asymmetry plot of short-wavelength perimetry. Bottom right; Vertical hemifield asymmetry plot of short-wavelength perimetry

although the precise methodology (i.e. pattern deviation compared with pointwise hemifield asymmetry analysis) differed. The necessity to use different analyses for conventional and for short-wavelength perimetry was dictated by the preferential attenuation of the blue stimulus by the ocular media and macular pigment. A pointwise hemifield asymmetry analysis could also have been used for conventional perimetry but this would have entailed discarding the “gold standard” methodology of the pattern deviation probability plot. In addition, the pattern deviation probability plot used for the analysis of conventional perimetry assumed that those points with the highest sensitivities are unaffected by localised visual field loss; examination of the total deviation probability

plots confirmed the validity of this assumption since no patient exhibited a generalised depression of visual field sensitivity.

The use of three or more contiguous stimulus locations with statistical probability levels of p less than 0.05 to define abnormality is similar to criteria used previously [38]. More importantly, the same criteria (i.e. three or more contiguous stimulus locations with statistical probability levels of p less than 0.05) were used for the analysis of conventional and of short-wavelength perimetry; however, abnormality as thus defined can occur in normal subjects (i.e. a false-positive assignment of abnormality) [51]. The fact that some of the diabetic patients exhibited abnormal short-wavelength fields and “teetering” conventional fields suggests that SWS pathway sensitivity loss precedes achromatic sensitivity loss (i.e. loss assessed using conventional perimetry).

The analysis of the extent of localised sensitivity loss was not equivalent between the two perimetry conditions. The pointwise pattern deviation plot was analysed for conventional perimetry while for short-wavelength perimetry both the pointwise horizontal and the pointwise vertical hemifield asymmetry plots were evaluated. Analysis of only the hori-

Fig. 4. Automated perimetry pointwise probability plots for diabetic patient no. 24 (Left eye, visit 2, short-wavelength perimetry undertaken before conventional perimetry). Top left; Total deviation plot of conventional perimetry. Top right; Pattern deviation plot of conventional perimetry. Bottom left; Horizontal hemifield asymmetry plot of short-wavelength perimetry. Bottom right; Vertical hemifield asymmetry plot of short-wavelength perimetry

zonal hemifield asymmetry plot could result in underestimation of the extent of localised SWS pathway sensitivity loss if the field defect was evenly distributed (and of an equal magnitude of sensitivity loss) across the horizontal midline and located in one hemifield. Indeed, analysis of both the pointwise horizontal and the pointwise vertical hemifield asymmetry plots frequently resulted in a greater extent of localised SWS pathway sensitivity loss than when compared with that of the pointwise horizontal hemifield asymmetry plot alone. Conversely, the extent of localised field loss using short-wavelength perimetry was found to be greater than that suggested by the clinical assessment of DMO in 11 of the 23 patients (Table 2); however, this may be explained

by the false-positive flagging of abnormality since the same sensitivity values have been analysed twice to determine the extent of short-wavelength sensitivity loss (i.e. both for the pointwise horizontal and the pointwise vertical hemifield asymmetry plots).

Interpolation procedures for the estimation of perimetric sensitivity have been demonstrated to be as accurate as direct measurements (given the inherent variability) for an inter-stimulus separation of 6° or less [52]. The accuracy of the interpolation procedure used in this study can be predicted to be high since the interpolation was limited to within 10° eccentricity of the fovea where the visual field exhibits the greatest symmetry and the within-test measurement variability (i.e. short-term fluctuation) is minimal [53–54]. It is conceivable that a diffuse, or widespread, distribution of DMO may produce a symmetrical loss of short-wavelength sensitivity and consequently may be missed using the pointwise horizontal hemifield asymmetry analysis. However, a diffuse distribution of DMO may not necessarily result in a symmetrical reduction of short-wavelength sensitivity and such gross retinal changes would be obvious on clinical examination.

Fig. 5. Automated perimetry pointwise probability plots for diabetic patient no. 15 (Left eye, visit 2, short-wavelength perimetry undertaken after conventional perimetry). Top left; Total deviation plot of conventional perimetry. Top right; Pattern deviation plot of conventional perimetry. Bottom left; Horizontal hemifield asymmetry plot of short-wavelength perimetry. Bottom right; Vertical hemifield asymmetry plot of short-wavelength perimetry

The reason for the improved sensitivity in the psychophysical detection of clinically significant DMO offered by short-wavelength perimetry is intriguing. Recent studies have shown that diabetic patients with minimal retinopathy can exhibit selective variations of short-wavelength sensitivity as a result of short and severe manipulation of blood glucose levels [55–56]; this variation of short-wavelength sensitivity is generalised (i.e. rather than localised) and is reversible. The reversible change of short-wavelength sensitivity exhibited by diabetic patients with minimal retinopathy and the SWS pathway localised visual field loss exhibited by patients with DMO may share a common patho-physiological mechanism.

Now, the potential value offered by the pointwise hemifield asymmetry analysis of short-wavelength perimetry (assuming a satisfactory level of specificity) is as a clinical tool for the psychophysical detection of DMO. The technique could be used as a screening procedure for “at risk” diabetic patients and may also be of value for the monitoring of visual function in controlled trials of new treatment regimens. The decision to treat patients with laser photocoagulation, however, will still be based upon morphological criteria until the localised loss of short-wavelength sensitivity can be directly attributed to DMO. A complete understanding of the extraneous factors which impact upon the SWS pathway sensitivity is required before short-wavelength automated perimetry can be used as a reliable indicator of treatment in patients with clinically significant DMO.

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Fig. 6. Automated perimetry pointwise probability plots for diabetic patient no. 8 (Right eye, visit 2, short-wavelength perimetry undertaken before conventional perimetry). Top left; Total deviation plot of conventional perimetry. Top right; Pattern deviation plot of conventional perimetry. Bottom left; Horizontal hemifield asymmetry plot of short-wavelength perimetry. Bottom right; Vertical hemifield asymmetry plot of short-wavelength perimetry

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