Assessment of the Heidelberg Retina Tomograph in the detection of sight-threatening diabetic maculopathy

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Abstract

***Purpose*: To assess the potential role of the Heidelberg Retina Tomograph (HRT) in screening for sight-threatening macular oedema in diabetes.**

***Methods* One hundred and thirty-one eyes of 81 consecutive diabetic patients who fitted the inclusion criteria were included in the study. On HRT, the volume above the reference plane bound within a 2 mm diameter circle centred at the fovea was measured. The volumetric indices were compared with the mean measurement index in a group of 20 age-matched controls (mean score = 1, mean +2 SD score = 1.8). We also assessed the sensitivity of the subjective analysis of the intensity image and the addition of the three-dimensional map to the intensity image for detecting macular oedema and clinically significant macular oedema (CSMO).**

***Results* One hundred and twelve eyes of 71 patients had a corrected Snellen visual acuity of 6/9 or better. When considering eyes with 6/9 or better vision only, the system's sensitivity for detecting CSMO was 58.33% 'per eye' examined, and 81.82% 'per patient' examined using a cut-off volumetric index of 1.8. In our study eyes with 6/9 or better vision, we found a 21% prevalence of CSMO. The predictive values of a positive test were 38.89% and 45% (cut-off score 1.8, 'per eye' and 'per patient' respectively) for CSMO. The predictive values of a negative test were 86.84% and 90.48% (cut-off score 1.8, 'per eye' and 'per patient' respectively) for CSMO.**

***Conclusions* The volumetric assessment of diabetic maculopathy by HRT is a potentially useful method for screening eyes at risk. A larger group of patients with a greater number of eyes with minimal or no maculopathy is required to establish the specificity of this technique.**

Key words Diabetes, Heidelberg Retinal Tomograph, Macular oedema, screening

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Macular oedema is the leading cause of moderate visual loss in diabetic patients.[1,2] The overall incidence and prevalence increase with longer duration and greater severity level of diabetic retinopathy (DR).[3] Previous reports[4,5] have confirmed the beneficial effect of laser photocoagulation treatment of diabetic macular oedema. The ETDRS results showed that focal laser reduced the risk of visual loss by approximately 50% in eyes with clinically significant macular oedema (CSMO).[5] All eyes, irrespective of entry visual acuity, demonstrated this favourable effect, although this was greatest for those with initially poorer entry visual acuity (worse than 20/40).

As macular oedema is frequently asymptomatic in its early stages, before the centre of the macula is involved, it is important to detect early lesions when the vision is still good. Diabetic macular oedema is a well-defined microvascular complication of diabetes, the estimates of its prevalence and rate of progression have been identified, there is an effective treatment, and screening techniques are available, simple and safe as well as being cost-effective. This would therefore represent an excellent model for screening as it fulfils Wilson's criteria laid out in the principles for screening of human diseases.[6]

Numerous studies[7–15] have addressed the subject of screening for DR, but to our knowledge, none has specifically addressed screening for diabetic maculopathy against the gold standard, that is stereoscopic fundus biomicroscopy with a Goldmann contact lens by an ophthalmologist with an interest in diabetes.[16] Although one may argue that the 'gold standard' applied to screening for DR is seven-field stereo fundus photography or fluorescein angiography,[17] there is evidence that contact lens examination is probably more sensitive than the hand-held 90 or 78 dioptre (D) lens.[16] Furthermore, the paucity of their use is testimony of their disadvantages in terms of cost, time and (with fluorescein) occasional morbidity. In as far as the use of fluorescein

angiography is concerned in the context of detecting diabetic macular oedema, the decision to treat is based on the clinical examination and not on the fluorescein findings.[4,5] In addition, an increase in retinal thickness and associated loss in visual acuity may occur without any detectable fluorescein leakage, indicating that fluorescein leakage is a poor indicator of fluid accumulation.[18]

The importance of screening for sight-threatening DR (which includes maculopathy and in particular macular oedema) has been highlighted by the St Vincent Declaration.[19] The St Vincent task force recognised that there are a number of effective screening methods although the ideal method for screening remains a debatable issue.[8,20]

The detection of DR by scanning laser ophthalmoscopy (SLO) has been described in two preliminary studies.[21,22] Neither of these has looked specifically at the role of the SLO in identifying macular oedema. However, the assessment of macular retinal thickening using the Z-profile signal width analysis (reflectance intensity vs scan depth) has been described using custom software with the Heidelberg Retina Tomograph (HRT).[23] Other recently developed retinal imaging techniques for looking at the macula include retinal thickness analysis[18] and optical coherence tomography.[24]

The present study assesses the role of the HRT (Heidelberg GmbH, Germany) in identifying macular oedema in a series of 81 diabetic patients using software version 1.11 provided by Heidelberg. We have compared the volumetric assessment technique described in our previous publication[25] (measurement of the volume above reference plane), as well as the subjective evaluation of the HRT intensity image and topographic pseudo three-dimensional map of the macula, with the stereoscopic fundus examination of the macula with a Goldmann contact lens.

Patients and methods

Eighty-one consecutive patients (131 eyes) who fitted the inclusion criteria were selected from the Diabetic Eye Service at the University Hospital of Nottingham. Informed consent was obtained for every patient including a detailed explanation of all the procedures involved as part of the study. The study protocol had ethics committee approval by the review board of the University Hospital of Nottingham.

The majority of patients (80%) were new referrals from the diabetic medical service or community opthalmic opticians for the assessment of retinopathy. A small proportion were referred for the assessment of unexplained visual loss in the absence of any significant visible DR (to the referring physician or ophthalmic optician). The others were under regular follow-up for monitoring of DR.

We excluded the very elderly (over 85 years of age) and patients who had a physical disability that prevented adequate clinical or HRT examination. Other exclusion criteria for the study included previous laser treatment, coexistent past or present ocular disease (other than DR), amblyopic visual loss and a distance refractive error greater than 7.00 D (average sphere). Patients with early cataract were not excluded unless this impaired the view of the posterior pole or was an indication for surgery.

We obtained an independent refraction and corrected Snellen visual acuity on all patients with 6/9 or worse visual acuity. All patients had a dilated examination by Goldmann contact lens biomicroscopy by one of two experienced ophthalmologists with a special interest in diabetes (H.J.Z. and S.A.V.) to determine the presence or absence of macular oedema and whether this met the ETDRS criteria for clinical significance.[4] However, in the presence of minimal (microaneurysms only, or haemorrhages located more than 2 disc diameters from the centre of the macula) or no maculopathy, the examination was limited to a stereoscopic fundus examination with a 78 D yellow-coated Volk lens.

An assessment of each patient's case notes was performed to determine the date of last follow-up, the number of laser sessions required to treat each eye with macular oedema, the corrected Snellen visual acuity and the presence or absence of macular oedema at last follow-up.

HRT examination and measurement of VARP

The HRT is a confocal SLO consisting of a scanning laser camera mounted on an ophthalmic stand with a head rest. The camera control panel is coupled to a computer system with a high-resolution monitor. The instrument uses a 670 nm diode laser source to illuminate the area of interest and scans the retina point by point by means of rotating prisms. A series of 32 confocal images are recorded in 1.6 s. The 32 cuts are parallel images taken in a plane perpendicular to the optical axis. The computer software aligns all 32 images to remove all eye movements.

HRT scans were taken at a subsequent visit within 1 week of the initial clinical examination. The patients were positioned in a chin rest position and were asked to fixate on an illuminated target with their companion eye to limit eye movements. If the HRT scanning unit was 'in the way', the scanning head was rotated just off-centre until the centre of the macula to be imaged was in the centre of the image on the HRT monitor screen. Three scans of each eye were taken after cycloplegia, all scans being centred on the fovea, and the best-quality scan is judged by the clarity and the detail seen on the monitor – that is a clear, well-illuminated scan centred on the fovea – was used for the analysis. The scan size was 20° by 20°.

A 2 mm diameter circle centred at the fovea was drawn using the circle draw facility. The height of any point on the circle is given by the contour line in green (HRT manual). The scale was set to 0.25 mm in order to magnify any variations in the height progression of the retinal surface along the contour line, and the reference plane, shown in red, was adjusted to the lower point of the contour line (Fig. 1). The volume above reference

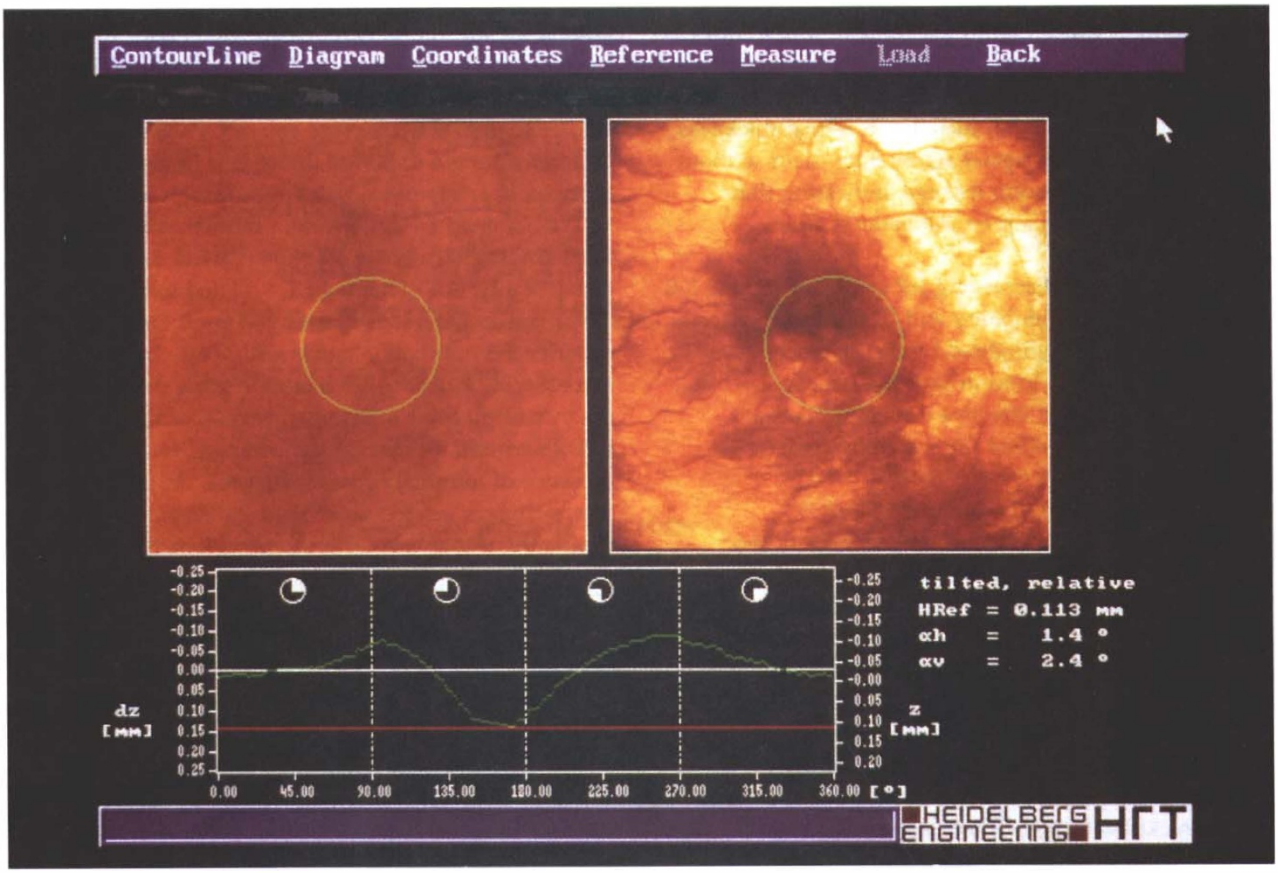

Fig. 1. *HRT scan of the left eye of a 54-year-old type 2 diabetic patient with extensive macular oedema (CSMO). The areas of oedema seen clinically were nasal, superior and inferior to the fovea. The intensity image is on the right, and the topography image on the left. The topography image represents a matrix of height measurements shown as a colour-coded map, whereas the intensity image is a colour image where each colour shows the amount of light reflected at each point. It is important to note that the colours shown are not true colours as would be seen from clinical examination. A 2 mm diameter circle is drawn with the fovea at its centre. The height variation of the contour line is shown in green in the lower half of the image. This demonstrates that the retinal surface is elevated in the areas corresponding to the zones of oedema identified clinically. The red line on the lower graph is the reference plane (for the purpose of this measurement technique, it is located at the lowest point of the height variation of the contour line), and the white line corresponds to the zero level of the scale axis (left-hand vertical axis, set at 0.25 mm).*

plane (VARP) was then calculated by the computer software. An independent resident ophthalmologist in training (T.K.H.B.) was trained to look at macular scans taken with the HRT, and measured the VARP for a 2 mm diameter circle by the method described above.[25] All measurements were performed in random order, without having previously seen or examined any of the patients involved in the study. The measurements were taken at the end of the study, in that none were known at the time of the clinical examination. In this study with screening in mind, only one measurement of the VARP was calculated for each eye.

Control subjects

A group of 20 age-matched controls were examined for comparison. One eye of each control subject was chosen randomly for examination. All had corrected visual acuities of 6/6 or better. Anterior segment examination and indirect fundus examination were normal. We calculated the mean of three VARP measurements of one good-quality HRT scan taken within the confines of a 2 mm diameter circle centred on the fovea by the same method described previously.

Assessment of the intensity image and of the pseudo three-dimensional map

One investigator (H.J.Z.) was shown all HRT scans (Fig. 1) in random order. These consisted of a topography image (left-hand image of Fig. 1) and an intensity image (right-hand image of Fig. 1). The topography image was not used as part of this assessment (as the details seen were far inferior to those obtained from the intensity image). The observer therefore concentrated on the intensity image only. The same observer was then shown the corresponding pseudo three-dimensional map (Fig. 2) for each intensity image seen without any knowledge of the identity of each scan. Based on observations from previous experience, the observer examined each intensity image and identified those with features indicating 'sight-threatening macular oedema' necessitating referral for further evaluation. These were the presence of hard exudates (increased reflectance) or haemorrhages (red dots) within 1 disc diameter of the fovea, or confluent red areas on the scan image within 1 disc diameter of the fovea indicating the presence of retinal thickening (Fig. 1). It is important to remember

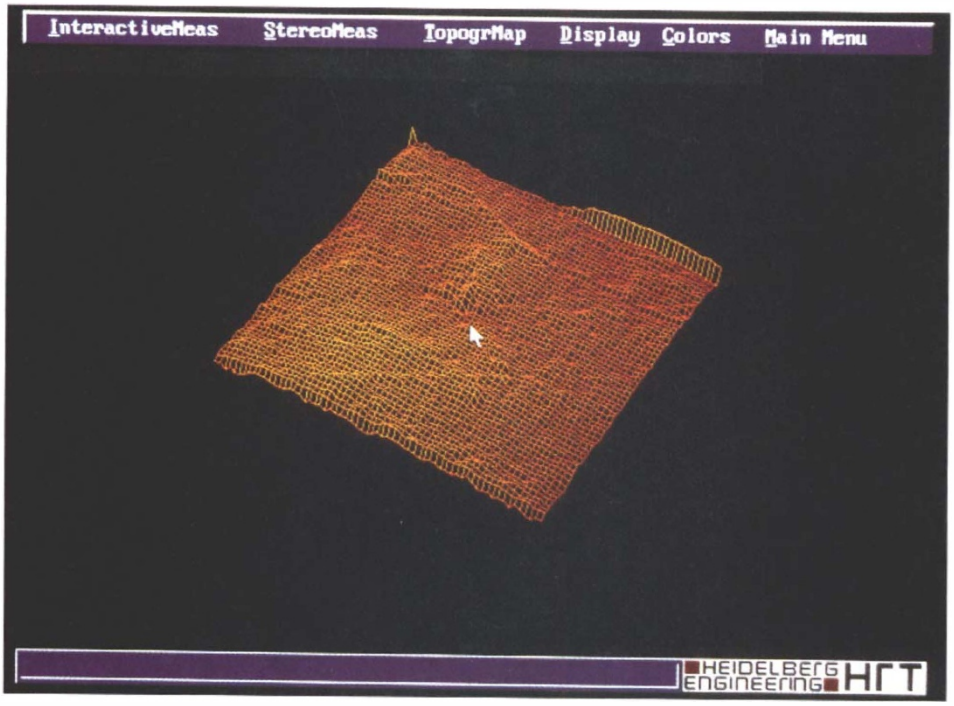

Fig. 2. *Pseudo three-dimensional map of the macula corresponding to Fig. 1. The fovea can be identified as a 'dip', and areas of retinal thickening as zones of retinal surface irregularity and elevation, in particular above and below and nasal (in this view to the left of the fovea) to the fovea (white arrow).*

that this assessment of the intensity image is purely subjective, and does not include a circle and height variation of the contour line.

A similar subjective scoring system was applied to the addition of the pseudo three-dimensional map to the intensity image. The features indicative of retinal thickening on the map were focal or diffuse irregularities of the map surface that could not be attributed to radial elevations due to blood vessels (Fig. 2).

Statistical analysis

Given the setting of the study – a diabetic eye clinic – and the high number of eyes with maculopathy, we can only give reliable estimates of the sensitivity of the method used for screening – that is a measure of the false negatives. The sensitivities and predictive values (and the 95% confidence intervals) for the VARP measurements were calculated for eyes with 6/9 or better corrected vision only (112 eyes). The same calculations were performed 'per patient' when both eyes fitted the entry criteria and had 6/9 or better vision (41 patients); a positive result was recorded if either eye of each patient had a positive test, and a negative result was recorded if both eyes were test negatives.

All calculations of VARP were converted into a 'VARP index', where the mean volumetric index for the control eyes was 1. We compared the measured volumetric indices in all eyes examined with the following three cut-off volumetric indices: 1.8 (score for the mean + 2 SD of control eyes), 2.2 (score for the mean + 3 SD of control eyes), 2.6 (score for the mean + 4 SD of control eyes). The sensitivity calculations for the intensity images and for the addition of the pseudo three-dimensional map to the intensity image examination are also given.

Using all eyes (131 eyes), the reproducibility of repeat examinations (for the subjective assessment of the intensity images and the addition of the pseudo three-dimensional map to the intensity image) by the same observer, before any feedback was obtained, was assessed by measuring the Cohen kappa coefficients.

We also calculated the degree of association between the VARP index at entry into the study and the presence of macular oedema or CSMO by chi-squared analysis for the three cut-off indices (1.8, 2.2 and 2.6) using all 131 eyes.

Using all 131 eyes, the predictive value of the VARP index at entry for identifying eyes that will develop macular oedema or CSMO is calculated by a Fisher's exact test. The eyes included in this part of the analysis were those that did not have any oedema at entry and had a complete follow-up examination, that is 63 eyes (76 minus the 13 that had no follow-up).

Results

Patient characteristics

There were 112 eyes (71 patients) with 6/9 or better vision. Thirty-seven patients were male and 34 female. The patients' mean age was 58.51 years (SD 13.06 years, range 27–81 years), and mean duration of diabetes was 13.85 years (SD 7.94 years, range 1–35 years). Thirteen patients (18%) had type 1 diabetes, 46 patients (65%) had type 2 diabetes and 12 patients (16%) were insulin-treated maturity-onset diabetics. Thirty-one patients (43%) were hypertensives on treatment. The mean

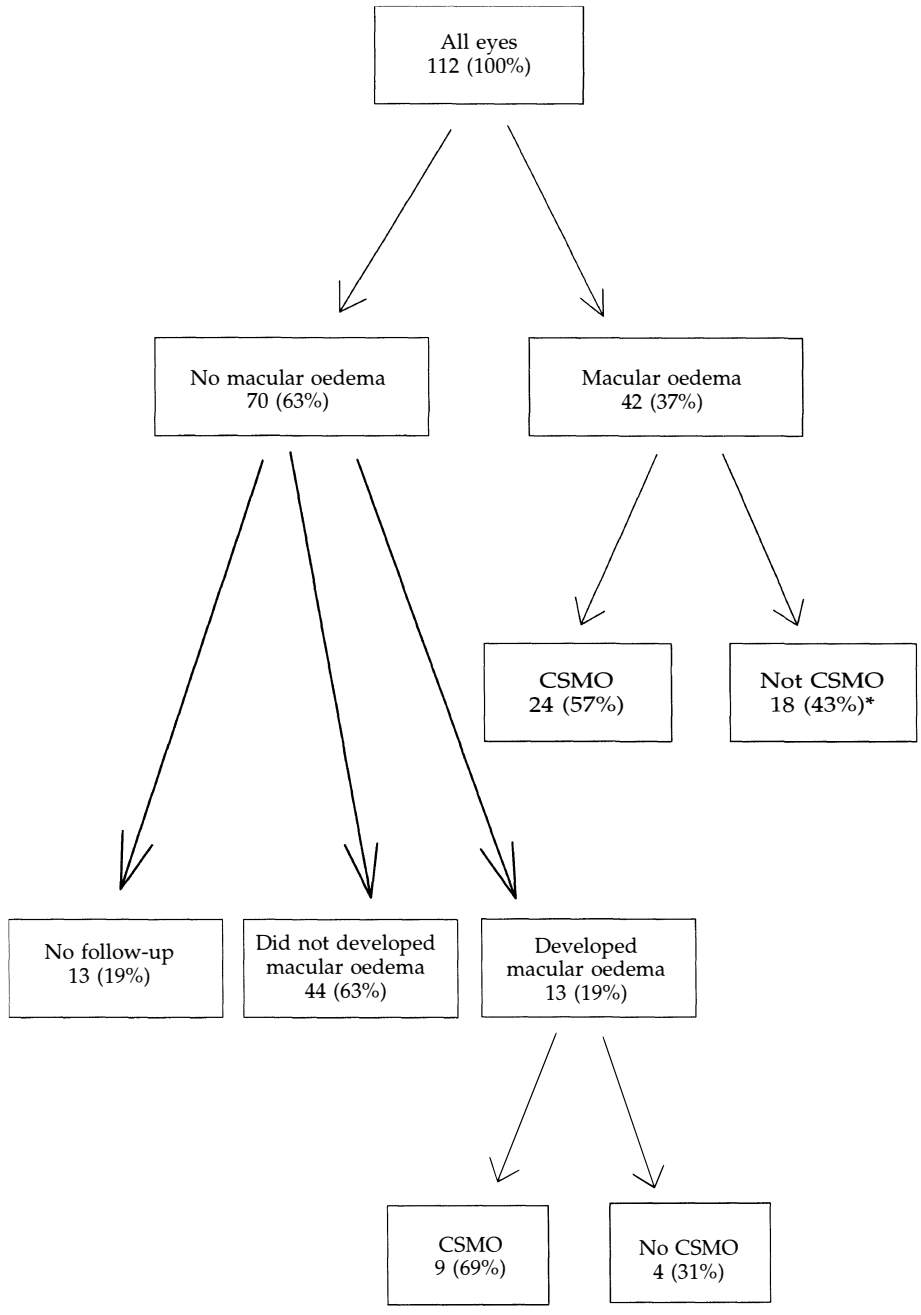

Fig. 3. *Chart summary of macular oedema and CSMO for 112 eyes of 71 patients. *Four eyes of 18 developed CSMO during their follow-up but were not included in the 'developed oedema' group because they had some oedema at entry into the study.*

refractive error was 0.18 D (SD 1.68 D, range −6.125 to 3.75 D), and the maximum cylinder was 1.5 D. Follow-up was available in 99 eyes. The mean follow-up was 15.43 months (SD 4.02 months, range 4–22 months).

Macular oedema

Seventy eyes (63%) had no macular oedema at their initial clinical examination, and 42 eyes (37%) had macular oedema. Twenty-four eyes out of 42 (57%) had CSMO, and 18 (43%) did not. Of 70 eyes with no oedema at entry into the study, 13 (19%) developed macular oedema, 44 (63%) did not and 13 (19%) had no follow-up. Of the 13 eyes that developed oedema, 9 had CSMO (69%) and 4 (31%) did not. A summary of the above results is given in Fig. 3.

Control eyes characteristics

The mean age of the control subjects was 60.25 years (SD 8.66 years, range 46–76 years). The mean VARP was 0.105 mm^3 (to which a score of 1 was assigned) and the SD was 0.042 mm^3.

Argon laser photocoagulation treatments

Thirty eyes (27%) had one laser session for macular oedema, 17 eyes (15%) had two laser sessions, 5 eyes (4%) had three laser sessions, 1 eye (1%) had four laser sessions, and 46 eyes (41%) did not require any laser treatment. There were no follow-up data on the number of laser sessions in 13 eyes (12%).

Table 1. *Sensitivity (and 95% confidence interval) calculations (%) for screening for diabetic macular oedema and CSMO 'per eye' (112 eyes) and 'per patient' with two eyes in the study (41 patients) all of whom had 6/9 or better vision*

	To detect oedema		To detect CSMO	
VARP cut-off score	Per eye (112 eyes)	Per patient (41 patients)	Per eye (112 eyes)	Per patient (41 patients)
1.8	42.86 (27.89 to 57.83)	57.89 (35.69 to 80.09)	58.33 (38.60 to 78.05)	81.82 (59.03 to 100)
2.2	28.57 (14.91 to 42.23)	36.84 (15.15 to 58.53)	37.50 (18.13 to 56.87)	45.45 (16.02 to 74.88)
2.6	14.28 (3.70 to 24.86)	5.26 (0 to 15.30)	12.50 (0 to 25.73	9.09 (0 to 26.08)

Sensitivity calculations for detecting macular oedema

The sensitivity of the VARP for detecting macular oedema against three cut-off VARP indices are summarised in Table 1. These were better for identifying CSMO than for identifying macular oedema and measured 58.33% 'per eye' and 81.82% 'per patient'.

Using data from all 131 eyes, we found a statistically significant association between the VARP indices and the presence of macular oedema or CSMO at all three cut-off points chosen. These results are summarised in Table 2. However, we found that the VARP did not predict which eyes with no oedema at entry into the study developed macular oedema during their follow up ($0.28 < p < 1$).

The intensity image sensitivity and the results of the addition of the pseudo three-dimensional map to the intensity image at detecting macular oedema and CSMO are summarised in Table 3. Both these subjective imaging modalities proved highly sensitive at identifying 'eyes' and 'patients' at risk of visual loss.

Reproducibility

We found good agreement on repeat scoring of the intensity images by the same observer and for the addition of the pseudo three-dimensional images. The Cohen kappa coefficients were 0.80 and 0.75 respectively, indicating good agreement between the two scoring rounds.

Predictive value calculations

Tables 4 to 6 summarise the calculations of the predictive values for 112 eyes and 41 patients analysed.

Discussion

For the purpose of this study we selected patients who had either just been referred for the assessment of retinopathy or who were currently under observation with some retinopathy in order to assess the HRT in the detection of macular oedema. The detailed analysis of the subgroup of patients with good vision is particularly important because patients with poor vision would be referred to a specialist even without a fundus examination (although not with the same degree of urgency). With this in mind, we asked the question whether the HRT could give the ophthalmic specialist any additional information about the presence or absence of macular oedema to supplement the clinical impression of the overall state of retinopathy from the referring physician or optometrist. As laser treatment induces only limited visual gain but reduces the risk of visual loss,[4,5] we must identify patients in need of treatment early and before visual loss has occurred. This process starts with screening and is followed by the assessment of patients in a specialist ophthalmic clinic.

In the United Kingdom (and probably other countries) there is little doubt that a consultant ophthalmologist with a special interest in diabetes using contact lens biomicroscopy is the gold standard for identifying macular oedema. However, this group of specialists would be too expensive and too few in number, as well as having other duties to fulfil, and therefore cannot act as screeners at present. The same would apply in other developed countries as well as in less developed areas where an ophthalmologist's time is probably best spent dealing with other common blinding conditions.

Overall, the performance of diabetic physicians is disappointing (detection rate of less than half the cases of serious retinopathy) and significantly variable between consultant staff and juniors in training.[26] The detection rates quoted by Taylor *et al.*[14] indicate a poor performance for all grades of hospital doctors in detecting maculopathy (sensitivity 57%) and appear consistent with another study[26] based at a university centre in the United States that quoted an error rate of 60%. However, Harding *et al.*[7] found a sensitivity of 64% for detecting sight-threatening maculopathy by an experienced registrar in ophthalmology using dilated direct ophthalmoscopy, and an excellent specificity of 100%. Another study[15] has shown a particularly high detection rate by a hospital doctor using dilated direct ophthalmoscopy, exceeding other reports by far (sensitivity of 94% and a specificity of 95% for detecting maculopathy).

Table 2. *Degree of association between the VARP index at entry and the presence of macular oedema or CSMO at entry for all three cut-off indices chosen*

	'Per eye'		'Per eye'		'Per eye'		'Per patient'	
VARP index cut-off	Chi-squared	p value	Chi-squared	p value	Chi-squared	p value	Chi-squared	p value
1.8	8.515	0.004	5.620	0.018	18.885	<0.00001	9.194	0.002
2.2	11.041	0.001	6.696	0.01	19.680	<0.00001	8.511	0.004
2.6	15.591	<0.00001	7.663	0.006	18.217	<0.00001	9.693	0.002

Table 3. *Sensitivity (and 95% confidence intervals) calculations (%) for identifying macular oedema or CSMO 'per eye' (112 eyes) and 'per patient' (41 patients with two eyes in the study) all of whom had 6/9 or better vision*

	To detect oedema	To detect CSMO
Intensity image[a]	90.48 (81.60 to 99.36)	100 (100 to 100)
Intensity image and three-dimensional map[a]	95.24 (88.70 to 100)	100 (100 to 100)
Intensity image and three-dimensional map[b]	94 74 (84.70 to 100)	100 (100 to 100)

[a]Sensitivity calculations per eye (112 eyes).
[b]Sensitivity calculations for 41 patients (that is only those for whom both eyes fitted the entry criteria in the study).

Hammond *et al.*[12] found that optometrists identified 'any maculopathy' with a sensitivity of 65% and 'moderate to severe maculopathy' with a sensitivity of 77%, indicating relatively good concordance with an ophthalmic clinical assistant. The rate of retinopathy requiring laser treatment amongst patients found by their optometrist to have sight-threatening retinopathy was 37% in the Burns-Cox study.[13] However, the outcome of identifying maculopathy was not evaluated separately and no attempt was made to identify macular oedema by contact lens biomicroscopy.[13] It is interesting that the added effect of measuring visual acuity does not improve the detection rate of sight-threatening retinopathy by optometrists as shown in the Liverpool study.[7] This did, however, detect a larger number of incidental cataracts, and although it increased the sensitivity by 2%, it reduced the specificity by 10%.[7]

When considering general practitioners (GPs) as screeners, several studies[8,20] have confirmed their inability to perform reliably, even after a period of formalised training.[27] A high rate of false positive referrals has been identified, with almost 50% of referrals having no retinopathy.[28] Such a high false positive rate would make any screening programme unacceptable.

Furthermore, the rate of unusable photographs using undilated Polaroid photography varies from 6% to 22%,[9,11] but this improves significantly with pupillary dilatation.[11] This experience, however, is not universal, as one study showed between 57% and 84% of photographs to be fair or excellent[8] and Taylor *et al.*[14] found only 10% of poor-quality photographs using undilated Polaroid films. However, it may well be that better-quality photographs can be obtained by well-motivated research-oriented workers than by a busy medical photographer.[15]

The Liverpool Study[7] found less than 2% ungradable photographs using pupillary dilatation and a Canon CR4NM camera with 35 mm transparencies; however, a further 9% were ungradable due to media opacity. Taylor's study[14] reported a 74% sensitivity for detecting maculopathy using undilated Polaroid photography. The specificity[14] was low at 55%, indicating a high number of false positives. However, the reference standard in Taylor's study[14] did not specifically look for macular oedema or CSMO. Although this study concluded that undilated Polaroid photography is at least as good as ophthalmoscopy with mydriasis,[14] another large British study[8] found that direct ophthalmoscopy and undilated Polaroid photography had equally poor efficacy as both failed to refer 33% of serious retinopathy. On the other hand, the sensitivity of the Canon CR4NM camera using dilated 35 mm transparencies has a sensitivity of 61% for detecting sight-threatening maculopathy, and a specificity of 99%.[8] The superiority of 35 mm colour transparencies compared with Polaroid photography was also demonstrated by Jones *et al.*[11] Digital photography, although currently expensive, will no doubt replace most photographic techniques presently used, and will enable easy access to fundus photographs with facilities for image contrast enhancement and magnification of suspicious areas. Furthermore, it appears that the use of combined dilated retinal photography and ophthalmoscopy by specialist optometrists provides better results for detecting sight-threatening retinopathy, although the authors did not analyse their results in terms of identifying maculopathy.[10]

The sensitivity of the HRT VARP assessment (cut-off index 1.8) analysed 'per patient' for identifying CSMO was 81.82%, with a predictive value of 45% for a positive test and a predictive value of 90.48% for a negative test. The sensitivity figures for the higher cut-offs were too low to be of any use clinically (Table 1). From a screening point of view, we feel it is important to consider the sensitivity results analysed per patient because DR is almost always a bilateral condition. It would therefore be sufficient to identify one eye of one patient for ophthalmic referral to take place. In such circumstances, the fellow eye would be identified on subsequent clinical examination if it had macular oedema, even if it had a normal VARP on HRT.

It is particularly encouraging to find that the intensity map identifies almost every true positive and that the addition of the three-dimensional map identifies 100% of

Table 4. *Predictive value (and 95% confidence intervals) calculations (%) for 112 eyes (6/9 or better vision) for detecting macular oedema and CSMO by volumetric analysis (PV +ve and PV −ve are the respective predictive values of a positive and of a negative test)*

	To detect oedema		To detect CSMO	
VARP cut-off score	PV +ve test	PV −ve test	PV +ve test	PV −ve test
1.8	50 (33.67 to 66.33)	68.42 (57.97 to 78.88)	38.89 (22.96 to 54.81)	86.84 (79.24 to 94.44)
2.2	54.54 (33.73 to 75.35)	66.67 (56.93 to 76.41)	40.90 (20.35 to 61.44)	83.33 (75.63 to 91.03)
2.6	66.67 (35.87 to 97.47)	65.05 (55.84 to 74.26)	33.33 (2.53 to 64.13)	79.61 (71.83 to 87.39)

Table 5. *Predictive value (and 95% confidence intervals) calculations (%) for 41 patients (6/9 or better vision and with both eyes in the study) for detecting macular oedema and CSMO by volumetric analysis (PV +ve and PV −ve are the respective predictive values of a positive and of a negative test*

	To detect oedema		To detect CSMO	
VARP cut-off score	PV +ve test	PV −ve test	PV +ve test	PV −ve test
1.8	55 (33.19 to 76.80)	61.90 (41.13 to 82.67)	45 (23206 to 66.80)	90.48 (77.93 to 100)
2.2	58.33 (30.43 to 86.22)	58.62 (40.69 to 76.55)	41.67 (13.77 to 69.56)	79.31 (64.57 to 94.05)
2.6	50 (0 to 100)	53.85 (38.20 to 69.50)	50 (0 to 100)	74.36 (60.66 to 88.06)

all true positives (Table 3). The predictive values of a negative test for identifying macular oedema or CSMO are particularly good (>90%), but the predictive values of a positive test for identifying macular oedema are low at 50–60% and for identifying CSMO are 30–36% (Table 6), indicating a significant number of false positives. In addition, the three-dimensional map does not appear to add to the information gained from the intensity image analysis.

The authors feel that the best 'combination' for identifying sight-threatening macular oedema with the HRT would be the subjective analysis of the intensity image and the volumetric analysis against a cut-off index of 1.8. We would recommend that if one eye of one patient clearly demonstrates a positive result on both assessment measures, the patient should definitely be referred for an urgent opinion. Similarly, if both eyes demonstrate negative results on both tests, the patient need not be referred for the assessment of maculopathy (although they may need to be seen for another reason). For those in whom the objective volumetric analysis does not agree with the subjective analysis, we would recommend being guided by the volumetric analysis measurement because of its better predictive value for a positive test of 39–45% for CSMO (Tables 4, 5) in this setting. The predictive value for a negative test for the VARP index cut-off of 1.8 would also be good at 87–90% for CSMO.

The volumetric technique described in this paper has certain limitations. In particular, the VARP is likely to be artificially low when a macula with diffuse oedema is scanned. However, areas of oedema seen on the HRT scans (for instance as an elevation of the height variation of the contour line) correlate well with areas of oedema seen on clinical examination.[25] The measurements obtained are likely to be variable when poor-quality scans are taken. Furthermore, the circle drawn must be very accurately centred at the fovea, and the reference plane carefully positioned by magnifying any variations of the height variation of the contour line by setting the scale at 0.25 mm.[29]

This study measures the sensitivity of the volumetric analysis technique (VARP index) and of the subjective assessment of the intensity image and the three-dimensional map using the HRT. However, to determine the specificity of this technique (currently under investigation in our unit) the same study needs to be performed in a group of patients with minimal or no maculopathy (for instance in patients currently attending a diabetic medical clinic but not necessarily requiring ophthalmic referral). In the present study there is a large proportion of eyes with maculopathy (almost all) but not necessarily macular oedema (thus ideal for measuring sensitivity), which probably contributes significantly to the high false positive rate observed.

In summary, the high predictive values of a negative test of the intensity image (90% for identifying CSMO per patient) would avoid the need to see about 25% of patients referred for the assessment of maculopathy. If the VARP assessment is also normal (index <1.8) for both eyes, then the patient almost definitely does not require a further clinical assessment of the macula. The intensity image analysis alone can therefore be used to screen those who need a volumetric assessment from those who do not. The assessment of the VARP index would allow prioritising patients in order of severity of their maculopathy, assuming that they are not referred because of proliferative DR. Patients who have a VARP index greater than 1.8 would therefore need an urgent assessment with a view to treatment. The case for using yearly HRT assessments to supplement ophthalmoscopy in general diabetic clinics appears quite good. This study has demonstrated that the HRT may be useful in reducing the number of unnecessary diabetic referrals, and in identifying patients requiring an urgent macular assessment by an ophthalmologist.

Table 6. *Predictive value (and 95% confidence intervals) calculations (%) for 112 eyes (6/9 or better vision) and for 41 patients[a] (6/9 or better vision in both eyes and with both eyes in the study) for detecting macular oedema and CSMO by the subjective evaluation of the intensity image and the addition of the three-dimensional map to the intensity image (PV +ve and PV −ve are the respective predictive values of a positive and of a negative test)*

	To detect oedema		To detect CSMO	
	PV +ve test	PV −ve test	PV +ve test	PV −ve test
Intensity image	51.35 (39.96 to 62.74)	89.47 (79.71 to 99.23)	32.43 (21.76 to 43.10)	100 (100 to 100)
Intensity image and pseudo three-dimensional map	49.38 (38.49 to 60.27)	93.55 (84.90 to 100)	29.63 (19.70 to 39.57)	100 (100 to 100)
Intensity image and pseudo three-dimensional map[a]	60 (42.47 to 77.53)	90.90 (73.90 to 100)	36.67 (19.42 to 53.91)	100 (100 to 100)

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