

Scanning laser tomography Z profile signal width as an objective index of macular retinal thickening

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Abstract

Aims—(i) To evaluate the relation between retinal thickness and the Z profile signal width of a scanning laser tomographer in selected patients exhibiting clinically manifest and circumscribed macular retinal thickening; (ii) to compare the Z profile signal width values of a group of age similar normal subjects with those of the patients with macular retinal thickening; and (iii) to present the methodology underlying the Z profile signal width derivation.

Methods—Three patients with the following conditions were selected: widespread diabetic macular oedema; localised diabetic macular oedema; and macular hole. The patients were selected because they exhibited clinically manifest and circumscribed macular retinal thickening. Patients underwent fundus photography and a clinical examination which included fundus biomicroscopy. Fourteen age similar normal subjects were also assessed. The Heidelberg retina tomograph (HRT) was utilised to acquire seven topographic images of each macula. Z profile signal width data were analysed using custom software. Signal width was measured at 50% of the maximum intensity.

Results—For each patient with macular retinal thickening, Z profile signal width analysis (after normalisation to reduce the influence of variation in reflectance intensity between successive images) revealed a significant ($p < 0.0001$) localised increase of signal width which agreed with the HRT topographic analysis of retinal height, and also the clinical assessment of retinal thickness. The mean normalised Z profile signal width for the normal subjects (assessed over the whole image) ranged from 0.278 (SD 0.039) to 0.444 (0.063); these values compared with those obtained from patients in areas of macular retinal thickening of 0.761 (0.224) to 0.953 (0.194). Z profile signal width test-retest data for the patient with localised diabetic macular oedema were plus or minus 0.159 which compared with a mean signal width value of 0.761.

Conclusion—The evidence of this study, based upon three selected patients with macular retinal thickening and 14 normal subjects, would suggest that Z profile signal width analysis offers a non-invasive, objective, topographic, and reproducible index of macular retinal thickening. Studies employing larger

sample sizes are required to determine the true clinical worth of the technique.

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Scanning laser tomography (SLT) is a non-invasive technique which permits the objective, topographic measurement of the fundus.¹ SLT employs confocal optics to attain a high resolution not only perpendicular to (that is, x, y axis), but also along (that is, z axis), the optical axis. The influence of scattered light from outside the point focus of the laser source is suppressed by a pinhole positioned in front of a photodetector and conjugate to the focal plane. The point focus is deflected in two dimensions (that is, x, y) by computer controlled scanning mirrors so that an optical section is obtained through the object at the location of the focal plane. Reflectance intensity is determined as a function of scan depth for each picture element, or pixel, within the SLT image, such that:

$$I_{rel} = (I_i / I_{max}) \times 100$$

where I_{rel} is the relative intensity, I_i is the measured digitised intensity, and I_{max} is the maximum digitised intensity. The resulting plot of reflectance intensity versus scan depth is termed a Z profile or axial intensity distribution (Fig 1). The peak intensity of the Z profile is assumed to indicate the depth of the vitreous/internal limiting membrane (ILM) interface. The radius of the confocal pinhole and the intrinsic aberrations of the ocular refractive components limit the resolution of the depth measurement to approximately 300 μm .^{1,2} Comparison of reflectance intensity as a function of scan depth, however, results in a reproducibility of the depth measurement of less than 50 μm .³⁻⁵

SLT detection units register light from layers deep within the retina as well as from the ILM.^{6,7} Specular reflection occurs both at, or close to, the ILM and the retinal pigment epithelium (RPE), while diffuse reflection originates from the intraretinal layers. The Z profile represents the summation of specular reflections from the ILM and RPE, and diffuse reflection from the intraretinal layers. As a result, an increase in retinal thickness will result in a greater depth over which reflectance intensity can be measured (Fig 1). The normal human Z profile is narrow and symmetrically distributed at the fovea but is asymmetrically broadened in other macular locations where the retina is thicker.⁶ However, the effect of increased retinal thickness due to diabetic macular oedema on the width of the Z profile signal is unknown.

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Current clinical methods of assessing retinal thickness, which include contact lens and Volk lens fundus biomicroscopy and stereophotography, rely on the subjective judgment of retinal thickness at a given examination.^{8,9} Consequently, early retinal thickening can be difficult to distinguish from normal between subject variation in retinal thickness.¹⁰ Furthermore, the subjective evaluation of retinal thickness at a given examination confounds the interpretation of change in thickness over repeated examinations. The development of an objective measure to monitor change in retinal thickness is necessary both for the evaluation of therapeutic protocols and for the clinical management of retinal diseases such as diabetic macular oedema.^{11,12}

The aim of the study was to: (i) evaluate the relation between retinal thickness and Z profile signal width in a selected group of patients exhibiting clinically manifest and circumscribed macular retinal thickening; (ii) to compare the Z profile signal width values of a group of age similar normal subjects with those of the patients with macular retinal thickening; and (iii) to present the methodology underlying the

Z profile signal width derivation. The potential feasibility of the Z profile signal width technique as an objective index of macular retinal thickening was assessed using the Heidelberg retina tomograph, an instrument which may well become the "gold standard" retinal tomographer. This study reports the potential feasibility of the Z profile signal width technique in a selected group of patients with macular retinal thickening, and in a group of age similar normal subjects, and was undertaken before embarking upon a full clinical trial.

Materials and methods

SAMPLE

Patients were selected on the basis that they exhibited clinically manifest and circumscribed macular retinal thickening (although the exact mechanism might differ between the different conditions). Three patients with the following conditions were selected: widespread diabetic macular oedema (age 52 years); localised diabetic macular oedema (age 66 years); and macular hole (age 76 years). These patients

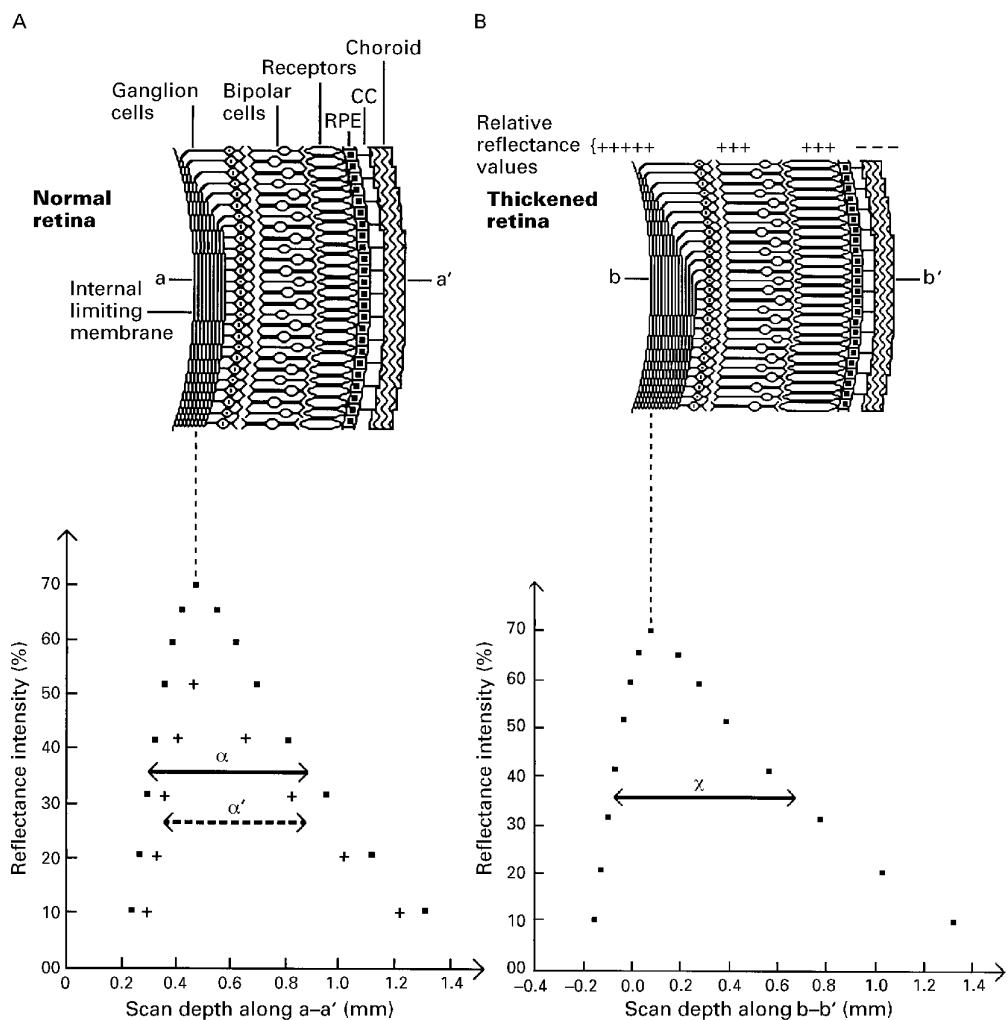


Figure 1 Schematic diagram to explain the relation between retinal thickness and the Z profile signal width of an SLT. (A) Retina of normal thickness (RPE = retinal pigment epithelium. CC = choriocapillaris). Reduced reflectance intensity—for example, because of laser misalignment, will result in an overall depression of the Z profile and an artefactual "compression" of the Z profile signal width (that is, a cf α). (B) Thickened retina. An increase in retinal thickness will produce an increase in the width of the Z profile assuming no change in the refractive index of the retina (that is, a cf γ).

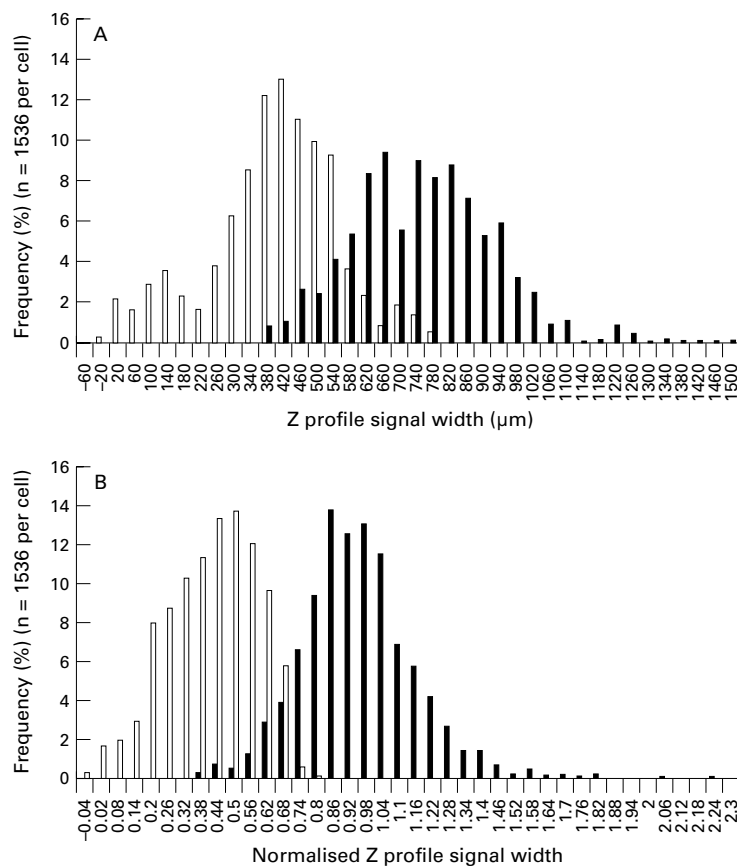


Figure 3 Frequency histogram (40 bins) illustrating the distribution of Z profile signal width values derived from six series images of the widespread diabetic macular oedema pathophysiological model for cells 1 (closed) and 2 (open). (A) Prenormalisation. (B) Normalised.

eye to be studied was dilated to a minimum diameter of 6 mm following refraction and the assessment of logMAR visual acuity. The clinical examination comprised Goldmann contact lens, Volk lens fundus biomicroscopy, or both.

SCANNING LASER TOMOGRAPHY

The Heidelberg retina tomograph (HRT) (Heidelberg Engineering, Heidelberg, Germany) was utilised to acquire topographic measurements of the fundus. The HRT comprises a scanning laser camera mounted on an ophthalmic stand, a headrest, an operation panel, and a personal computer.¹⁴ A diode laser operating at a wavelength of 670 nm provides a maximum retinal radiance of approximately 0.5 mW/cm. Single two dimensional section images, comprising 256×256 pixels (each with 8 bit intensity resolution), are recorded at a repetition rate of 20 Hz. Each section image therefore comprises 65 536 pixels. A $10^\circ \times 10^\circ$, $15^\circ \times 15^\circ$, or $20^\circ \times 20^\circ$ scan field can be selected. Consequently, there is a loss of resolution in the plane perpendicular to the optic axis with an increase in field size. Topographic fundus measurement is achieved by scanning 32 equally spaced section images (termed a series image) along the optical axis over a period of 1.6 seconds. The depth of the scan can be adjusted between 0.5 mm and 4.0 mm in 0.5 mm increments. As a result, the spacing between sections will vary between 16 µm and 130 µm depending on the selected scan

depth. The focal plane can be changed from -12 to $+12$ dioptres in steps of 0.25 dioptres to correct for refractive error.

The refractive error and corneal curvature of each volunteer was entered into the HRT database before image acquisition. The HRT does not have an internal fixation target; volunteers maintained steady distance fixation using a periscope device to see past the HRT with the fellow eye. The monitor aiming cross was employed to centre the image frame on the area of interest. For the patient group, the minimum field size was selected to attain complete coverage of the area of retinal abnormality and to include an apparently unaffected area of the retina. For the normal subject group, the $20^\circ \times 20^\circ$ scan field was selected to attain a wide range of normal Z profile signal width values. A minimum of seven series images were recorded, rather than three images recommended for clinical use,¹⁵ in order to gain a more realistic and reliable assessment of the inherent variability of the data.¹⁶ Scan depth and field were kept constant throughout repeated HRT image acquisition of a given eye.

DATA ANALYSIS

Topographic data analysis was carried out using the menu driven HRT operation software (version 1.11). Topography files were produced from individual series images (alignment to compensate for eye movements during image acquisition was undertaken at this stage). Mean topography (MT) files were generated comprising a minimum of seven topography images.

Z profile signal width data analysis was carried out using menu driven custom software provided by Heidelberg Engineering. Z profile signal width (ZP) files—that is, comprising the Z profile signal width values for each pixel within the SLT image, were generated from single series images immediately following determination of the corresponding aligned and topography images. The software applied separate gaussian functions to each side of the Z profile maximum intensity. The gaussian functions were of the form:

$$I_{(z)} = I_0 \exp - [(z - z_0)^2 / \sigma^2]$$

where I_0 is the maximum intensity, z_0 is the position of the peak reflectance intensity (I_0 and z_0 are common to both gaussian functions), and σ is the width of the gaussian function. The Z profile signal width at each pixel was defined as the combined width of the two gaussian functions at 50% of the maximum relative intensity. The ZP files were accessible as colour coded topographic maps illustrating the variation in Z profile signal width over the complete scan field. Numerical Z profile signal width data could be obtained using the "print screen" command. Mean Z profile signal width data were derived using a manual alignment technique. Transparent acetate film was fixed onto the monitor and the retinal vascular features of ZP1 were drawn onto the film. Two or three cells, each containing 16×16 pixels, were also drawn onto the film. The cells were selected for each pathophysiological model on

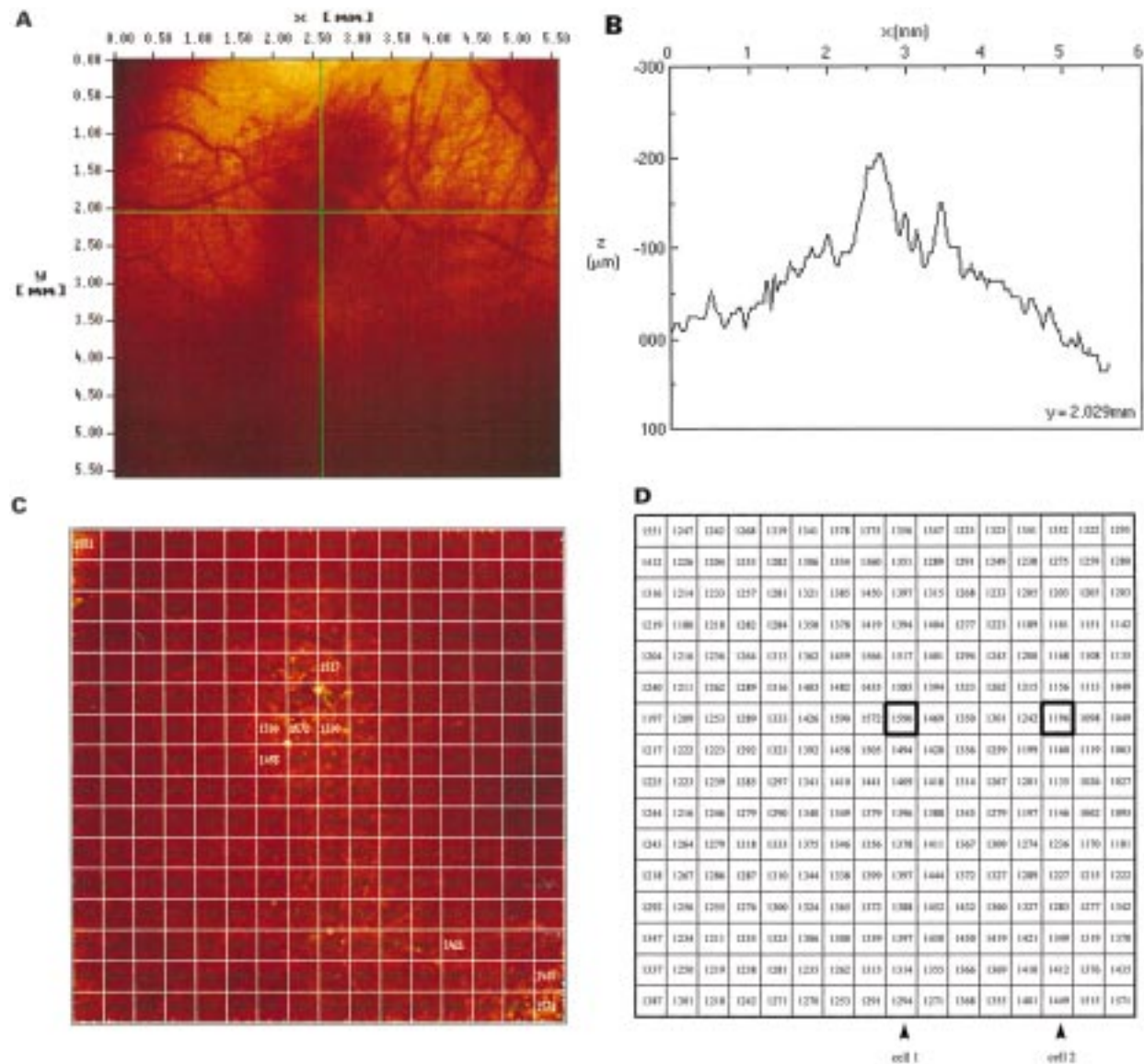


Figure 4 Localised diabetic macular oedema (left eye). (A) Intensity image. (B) Horizontal retinal profile. (C) Z profile signal width topographic map (lighter shades represent increased signal width). (D) Numerical grid showing mean (of 16×16 pixels) Z profile signal width values (prenormalisation) and the position of cells 1 and 2 (bold squares).

the basis that one cell should be located within a pronounced area of localised retinal thickening, while the other cell(s) should be distant from the area of retinal thickening. Also, cells were free from the influence of any prominent retinal capillaries. The film was realigned for subsequent ZP files (that is, ZP2, ZP3, etc) and the 16×16 pixels of each cell were defined using the markings on the acetate film. The selection of cells was expected to strongly influence the results (and thereby validate the Z profile signal width methodology). For the normal subjects, mean Z profile signal width values for the whole $20^\circ \times 20^\circ$ image were calculated (the Z profile signal width images of normal subjects exhibited no obvious localised increase of signal width).

The derivation of Z profile signal width is dependent upon reflectance intensity since the measurement is taken at a fixed percentage (that is, 50%) of the maximum relative intensity. However, reflectance intensity is

influenced by numerous factors including eye and head movement, laser alignment and distance, photodetector sensitivity, transmission characteristics of the ocular media, and tear film and pupil size^{17 18}; this results in a variation of reflectance intensity between successive images. Reduced reflectance intensity—for example, because of laser misalignment, will result in an overall depression of the Z profile and, consequently, an artefactual “compression” of the Z profile signal width (Fig 1(A, B)). This artefactual “compression” of the Z profile signal width was reduced by calculating signal width at 50% of the maximum relative intensity. It was further minimised, however, by expressing the signal width as a function of the minimum and maximum signal width values within a given image, that is, normalisation. The influence of these confounding factors was reduced using a normalising function of the form:

$$\text{normalised SW}_i = (\text{SW}_i - \text{SW}_{\min}) / (\text{SW}_{\max} - \text{SW}_{\min})$$

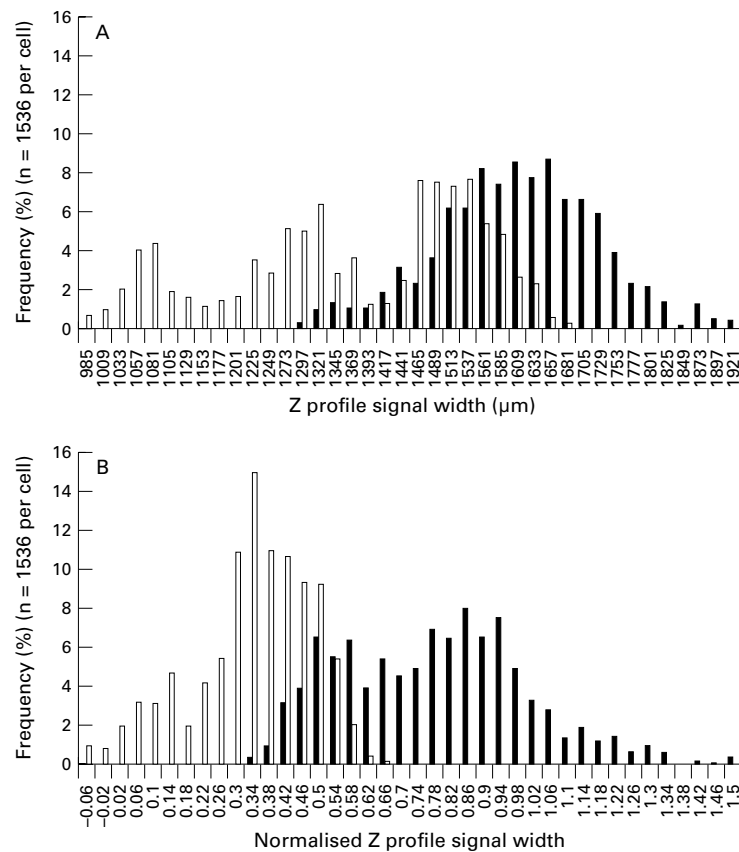


Figure 5 Frequency histogram (40 bins) illustrating the distribution of Z profile values derived from six series images of the localised diabetic macular oedema pathophysiological model for cells 1 (closed) and 2 (open). (A) Prenomormalisation. (B) Normalised.

where SW_{\min} and SW_{\max} are the minimum and maximum mean Z profile signal width values of all cells containing 16×16 pixels within the complete scan field. As a result of the normalisation of the data, the determination of retinal thickness is a relative measurement and the units of normalised Z profile signal width are arbitrary. The outer cell values were ignored since alignment to compensate for eye movements can result in erroneous Z profile signal width values at the edge of the image.

A repeated measures analysis of variance (ANOVA) was undertaken on the normalised Z profile signal width values of each patient. Z profile signal width test-retest data were obtained with an interval of 7 days between the two visits for the localised diabetic macular oedema model. Seven series images were acquired at each visit and the repeatability of the technique was assessed for a single cell containing 16×16 pixels.

Results

WIDESPREAD DIABETIC MACULAR OEDEMA

LogMAR visual acuity of the eye with widespread diabetic macular oedema was 0.90 log units. Clinical examination revealed a relatively symmetrical “bull’s eye” oedema centred on the foveola.

SLT was undertaken using a 20° scan field and a scan depth of 2.0 mm. The SLT intensity image of the widespread diabetic macular oedema is shown in Figure 2 (MT image comprising seven series images; mean (SD) $33.91 \mu\text{m}$). Topographic data analysis revealed an

elevation of the parafoveal retina of approximately $400\text{--}450 \mu\text{m}$ relative to the foveola (Fig 2). The magnitude of retinal elevation decreased steeply with increase in eccentricity from the foveola such that at $2.5\text{--}3.0 \text{ mm}$ eccentricity the retina was approximately $100 \mu\text{m}$ anterior to the foveola.

The Z profile signal width topographic map of the widespread diabetic macular oedema derived from a single series image is shown in Figure 2. Qualitative data evaluation revealed an increase of Z profile signal width in the area of retina immediately surrounding the foveola and extending into the superior temporal retina (a repeat clinical examination confirmed the extension of oedema into the superior temporal retina). In order to quantify the variation in Z profile signal width across the widespread diabetic macular oedema and surrounding retina, the mean normalised ZP data of six series images (one image was not of sufficient clarity to permit accurate alignment of the acetate film) was determined for two cells each containing 16×16 pixels: cell 1 was located at the temporal rim of elevated retina adjacent to the foveola and cell 2 was located approximately 10° inferotemporally from the foveola (Fig 2, numerically). The mean normalised Z profile signal width (SD) for cell 1 and cell 2 was 0.953 (0.194) and 0.366 (0.162) respectively. A frequency histogram illustrating the distribution of normalised Z profile signal width values for the two cells, and the effect of the normalising function on the data, is shown in Figure 3. A repeated measures ANOVA revealed the normalised Z profile signal width values of cell 1 to be significantly greater than those of cell 2 ($p < 0.0001$).

LOCALISED DIABETIC MACULAR OEDEMA

LogMAR visual acuity of the eye with localised diabetic macular oedema was 0.10 log units. Clinical examination revealed an area of localised diabetic macular oedema and associated hard exudates above the fovea.

SLT was undertaken using a scan field of 20° and scan depth of 2.0 mm. The SLT intensity image of the localised diabetic macular oedema is shown in Figure 4 (MT image comprising seven series images; mean (SD) $37.82 \mu\text{m}$). Topographic data analysis revealed a localised area of retinal elevation approximately 5° superior to the fovea; the area was vertically oval with a horizontal dimension of approximately 1.5 mm and a vertical dimension of 2.0 mm. The maximum magnitude of retinal elevation within the localised area of diabetic macular oedema was approximately $120 \mu\text{m}$ relative to the adjacent retina (Fig 4).

The Z profile signal width topographic map of the localised diabetic macular oedema derived from a single series image is shown in Figure 4. Qualitative data evaluation revealed an increase of Z profile signal width, which exhibited a stippled pattern (rather than the homogeneous pattern exhibited by the eye with widespread diabetic macular oedema), within a circumscribed area approximately 5° superior to the fovea. In order to quantify the variation

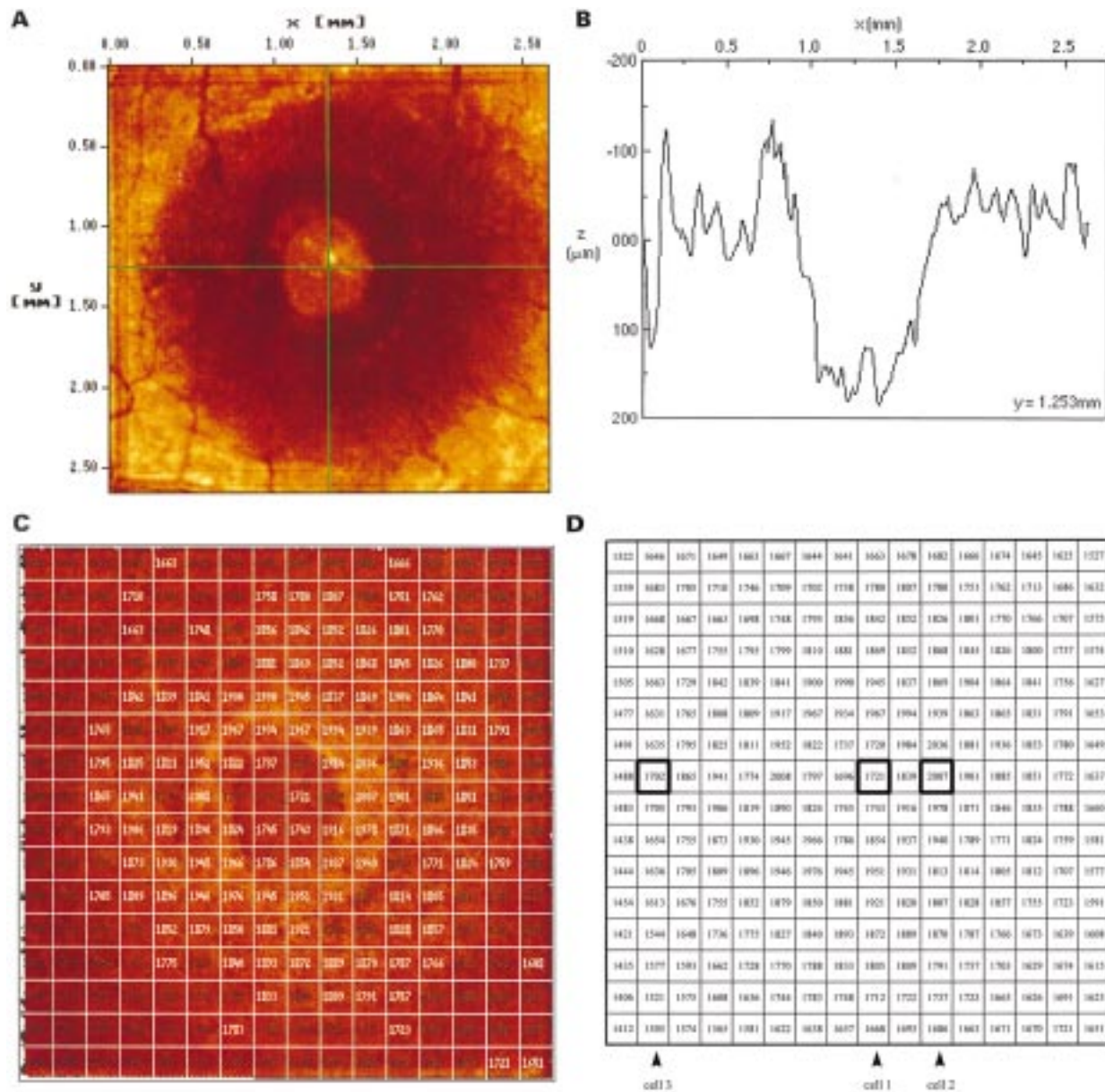


Figure 6 Macular hole (right eye). (A) Intensity image. (B) Horizontal retinal profile. (C) Z profile signal width topographic map (lighter shades represent increased signal width). (D) Numerical grid showing mean (of 16×16 pixels) Z profile signal width values (prenormalisation) and the position of cells 1, 2, and 3 (bold squares).

in Z profile signal width across the localised diabetic macular oedema and surrounding retina, the mean normalised ZP data of six series images (one image was not of sufficient clarity to permit accurate alignment of the acetate film) was determined for two cells each containing 16×16 pixels: cell 1 was located within the area of elevated retina and cell 2 was located approximately 10° inferotemporally from the fovea (Fig 4, numerical grid). The mean normalised Z profile signal width (SD) for cell 1 and cell 2 was 0.761 (0.224) and 0.323 (0.142) respectively. A frequency histogram illustrating the distribution of normalised Z profile signal width values for the two cells, and the effect of the normalising function on the data, is shown in Figure 5. A repeated measures ANOVA revealed the normalised Z profile signal width values of cell 1 to be

significantly greater than those of cell 2 ($p < 0.0001$).

MACULAR HOLE

LogMAR visual acuity of the eye with the macular hole was 0.90 log units. Clinical examination revealed a long standing stage 4 idiopathic macular hole with a surrounding rim of thickened and elevated neurosensory retina.

SLT was undertaken using a 10° scan field and a scan depth of 2.5 mm. The SLT intensity image of the macular hole is shown in Figure 6 (MT image comprising seven series images; mean (SD) 25.00 μm). Topographic data analysis revealed a depression in the centre of the macula of approximately 200 μm depth and 0.75 mm diameter (Fig 6).

The Z profile signal width topographic map of the macular hole derived from a single series

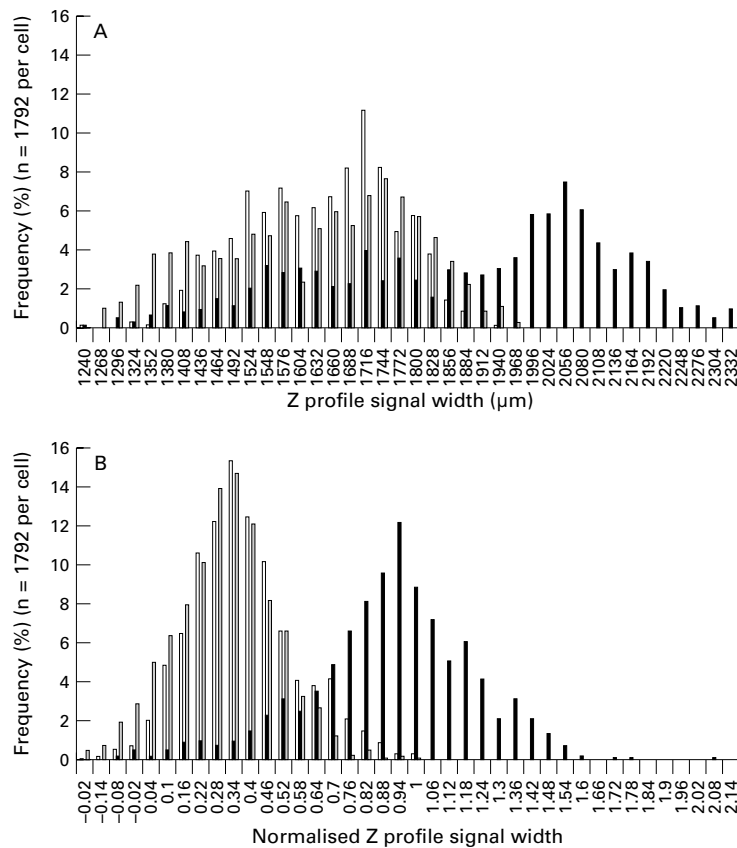


Figure 7 Frequency histogram (40 bins) illustrating the distribution of Z profile values derived from seven series images of the macular hole pathophysiological model for cells 1 (open), 2 (closed), and 3 (shaded). (A) Prenormalisation. (B) Normalised.

image is shown in Figure 6. Qualitative data evaluation revealed an increase of Z profile signal width in the area of retina immediately surrounding the macular hole (Fig 6). In order to quantify the variation in Z profile signal width across the macular hole and surrounding retina, the mean normalised ZP data of seven series images were determined for three cells each containing 16×16 pixels: cell 1 was located within the macular hole, cell 2 was located at the nasal edge of retina immediately adjacent to the hole and cell 3 was located approximately 4° temporally from the centre of

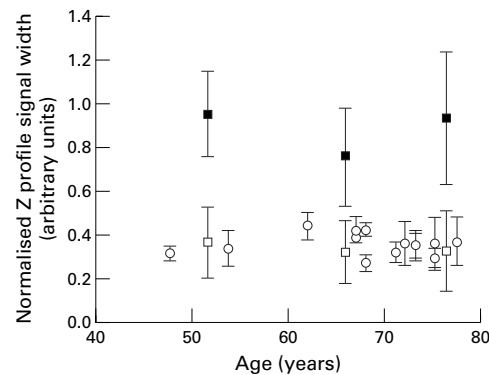


Figure 8 Normalised Z profile signal width as a function of age (open circles = normal subject data for whole scan field. Closed squares = patient data for 16×16 pixel cell within the area of macular retinal thickening. Open squares = patient data for 16×16 pixel cell distant from the area of macular retinal thickening). The error bars represent plus or minus 1 standard deviation of the mean.

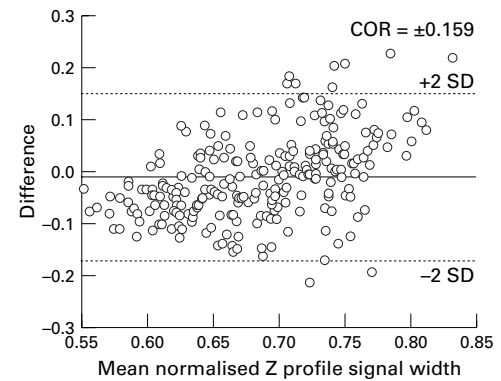


Figure 9 The difference in normalised Z profile signal width between test and retest values (interval 7 days, mean of six series images per test) as a function of the mean value for each of 256 pixels of the localised diabetic macular oedema pathophysiological model (assessed for cell 1 of Figure 4). Mean and 2 standard deviations (SD) of the differences are shown for reference.

the hole (Fig 6, numerical grid). The mean normalised Z profile signal width (SD) for cells 1, 2, and 3 was 0.403 (0.192), 0.940 (0.301), and 0.333 (0.184) respectively. A frequency histogram illustrating the distribution of Z profile signal width values for the three cells, and the effect of the normalising function on the data, is shown in Figure 7. A repeated measures ANOVA revealed the differences in normalised Z profile signal width between the three cells to be statistically significant ($p < 0.0001$). The normalised Z profile signal width of cell 2 was significantly greater ($p < 0.0001$) than that of cell 1 or cell 3 (least squares means analysis). In addition, the normalised Z profile signal width of cell 1 was significantly greater ($p < 0.001$) than that of cell 3.

NORMAL DATA

The mean normalised Z profile signal width (that is, the mean of the means of the constituent images) for the normal subjects, assessed over the whole $20^\circ \times 20^\circ$ image, ranged from 0.278 (0.039) to 0.444 (0.063). The normal Z profile signal width data are shown in Figure 8, along with the Z profile signal width values from the patients with macular retinal thickening.

REPEATABILITY

The normalised Z profile signal width test-retest data of the localised diabetic macular oedema model (cell 1), expressed in terms of the difference in mean (of six ZP images) normalised Z profile signal width between the two visits as a function of the mean value of the two visits, is shown in Figure 9. Cell 1 of the localised diabetic macular oedema model was chosen since it exhibited a wide range of Z profile signal width values (see Fig 5). Consequently, test-retest data were determined for 256 data points ($\times 6$ images = 1536 data points per visit). The coefficient of repeatability (COR—that is, the 95% confidence limits for the repeatability of the measurement procedure) of the normalised Z profile signal width measure was plus or minus 0.159 for the localised diabetic macular oedema model.

Discussion

Macular oedema, manifested by an increase in retinal thickness, is the leading cause of visual impairment and legal blindness in diabetics.^{19, 20} The subjective evaluation of retinal thickness at a given examination¹⁰ confounds the interpretation of change in thickness over repeated examinations. There is an obvious need to develop an objective measure of retinal thickness both for the clinical management of retinal disease and the evaluation of therapeutic protocols.^{11, 12} In this study, Z profile signal width analysis agreed both with the SLT topographic analysis of retinal height and the clinical assessment of retinal thickness based on fundus biomicroscopy and fundus photography. It should be noted that although the Z profile signal width technique is objective, the sampling was performed by an experienced operator.

Analysis of the Z profile data of the widespread diabetic macular oedema model revealed a significantly greater signal width arising from the temporal area of elevated retina adjacent to the foveola compared with that arising distant from the foveola. These findings are in agreement both with the results of SLT topographic analysis and the clinical observation of an annulus of oedema centred on the foveola. Interestingly, evaluation of the Z profile signal width topographic map revealed extension of the oedema into the superior temporal retina which was not initially apparent on clinical examination. Similarly, Z profile analysis of the localised diabetic macular oedema model revealed a significantly greater signal width arising within the area of elevated retina compared with that arising distant from the area of elevated retina; these findings are also in agreement with both SLT topographic analysis and clinical observation.

Analysis of the Z profile data of the macular hole model revealed a significantly greater signal width arising from the nasal edge of retina immediately adjacent to the hole compared with that arising from either within, or distant from, the hole. This was in agreement with both the results of SLT topographic analysis and the clinical observation of a rim of raised retina surrounding the macular hole. Conversely, Z profile analysis also revealed a significantly greater signal width arising from within the hole compared with that arising distant from the hole. This finding is contrary to the results of both SLT topographic analysis and clinical observation. The macular hole model was included, however, partly to examine the influence of a localised variation in the reflectance properties of the macula; the exposed RPE within the macular hole is likely to have considerably different reflectance properties from those of the intact ILM around the hole. The Z profile software determines signal width at 50% of the maximum relative intensity; this type of reduction in the intensity of reflected light will particularly reduce the maximum relative intensity and will also increase the Z profile signal width. The normalising function will minimise variation in the Z profile signal width owing to change in

reflectance intensity between successive images but will not negate the influence of a major variation in the reflectance properties of the first reflecting surface of the retina. Figures 3, 5, and 7 illustrate the effect of the normalisation function on the Z profile signal width data—that is, the normalised data show better separation of the samples and are more normally distributed than the raw data. Nevertheless, Z profile signal width analysis was able to distinguish the increase in retinal thickness surrounding the macular hole. Indeed, differences in the retinal reflectance properties between individuals may result in a wide range of interindividual Z profile signal width values.

The mean normalised Z profile signal width for the normal subjects (assessed over the whole image) ranged from 0.278 (SD 0.039) to 0.444 (0.063). These values compared with those obtained from patients in areas of macular retinal thickening of 0.761 (0.224) to 0.953 (0.194), and in areas distant from retinal thickening (excluding cell 1 of the macular hole model) of 0.323 (0.142) to 0.366 (0.162). Considerable separation of normalised Z profile signal width values exists between the normal subjects and the patients in areas of macular retinal thickening (Fig 8).

Using the localised diabetic macular oedema model (which exhibited a wide range of signal width values), the Z profile signal width test-retest value, expressed in terms of the COR, was plus or minus 0.159. This compares to a mean signal width value of 0.761—that is, the repeatability of the technique was found to be approximately 20% of the mean measured value. The repeatability of the technique will be improved by the employment of an automated image alignment system; this would also facilitate the analysis of the entire image. Given the wide range of Z profile signal width values within cell 1 of the localised diabetic macular oedema model, and the fact that a manual alignment system was employed, this estimate of the repeatability of the Z profile signal width technique probably represents the “worst case scenario”. Repeatability determines in part the sensitivity of the technique to detect change in retinal thickness. Further study is required to determine the sensitivity and specificity of the Z profile signal width measurement and to compare the results with existing clinical protocols in a larger patient population. In addition, the determination of the repeatability of the Z profile signal width measure in a larger sample of normal subjects, and in patients with diabetic macular oedema, is in progress.

The increase in Z profile signal width in retinal oedema can be attributed to two underlying mechanisms. An increase in retinal thickness will result in a greater depth over which reflectance intensity can be measured. In addition, a reduction in the refractive index of the ILM and retina will reduce the maximum reflectance intensity resulting in an increase of Z profile signal width in the absence of any change in retinal thickness. Both the thickness and refractive index mechanisms probably

contribute to the increase in Z profile signal width in retinal oedema. Consequently, the technique cannot be assumed to be a pure measure of thickness when evaluating retinal oedema. The combined effects of the thickness and refractive index mechanisms, however, will result in a greater increase of Z profile signal width than either mechanism operating alone and may also increase the sensitivity of the technique to detect retinal oedema.

Change over time in the relative contributions of specular reflection from the ILM and RPE to the resultant Z profile will influence the signal width in the absence of any change in retinal thickness. Typically, the magnitude of such an effect will be of the order of plus or minus 10% of the mean Z profile signal width; in the most extreme situation (when a weak specular reflection is attained from the ILM) a 50% reduction of signal width will result. Consequently, the technique is inappropriate for the detection of any condition that results in a reduction of retinal thickness. However, in this study the increase in retinal thickness exhibited by both diabetic macular oedema models resulted in a greater than twofold increase of Z profile signal width (when compared with a non-oedematous area of retina)—that is, the signal to noise ratio can be predicted to be more favourable when the technique is used for the detection of diabetic macular oedema compared with that for the detection of nerve fibre layer atrophy.²¹

Alternative techniques of assessing retinal thickness include the retinal thickness analyser (RTA)²² (based upon parallax imaging) and optical coherence tomography (OCT).^{23, 24} While both of these methods claim to offer improved sensitivity when compared to clinical evaluation neither are truly topographic. The RTA sequentially scans a discrete slit of laser light across the retina to produce approximately nine vertical retinal cross sections within a 6.6° square area (acquisition time 0.25 seconds), while OCT only provides single cross sections of the retina. In addition, the resolution of the RTA is directly limited by the intrinsic aberrations of the human eye, while OCT permits a depth resolution of 10 µm (thus providing detail of the internal retinal structures).²⁴ However, OCT image acquisition time is 2.5 seconds and therefore eye movements are likely to impair resolution.

This study demonstrates how Z profile signal width analysis can provide an objective measure of macular retinal thickening based upon the results attained from three selected patients and 14 normal subjects. In addition, Z profile signal width analysis is non-invasive and

provides a reproducible and topographic evaluation of retinal thickening. Studies employing larger sample sizes are required to determine the clinical feasibility of the technique.

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