PERIMETRY UPDATE 1994/1995

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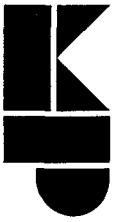
edited by Richard P. Mills and Michael Wall



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Preface

The XIth Annual Symposium of the International Perimetric Society was held in Washington, D C , USA on July 3–6, 1994 As always, there were thought-provoking and enlightening scientific sessions and the traditional lively social program The scientific sessions were divided into seven paper sessions and three poster sessions The many excellent presentations attest to the continued fine perimetry research on five continents Again, at this meeting one session and many posters were devoted to ophthalmic imaging; this field continues to thrive

From our 301 members, 108 abstracts were received Eighteen (17%) were rejected Of the 92 accepted, 45 were platform presentations and 45 were posters Sixty-one percent were from Europe, 15% from Japan and 20% from North America There was one from Argentina and one from Australia Overall, fourteen countries were represented Of these 92 presentations, 80 manuscripts were accepted for Perimetry Update 1994/95

The International Perimetric Society is indebted to the members of our Executive Committee for their peer review of the submitted manuscript President – Anders Heijl, Vice Presidents – Mario Zingirian and Eric Greve, Treasurer – Fritz Dannheim, Group Chairmen – John Wild, Bernard Schwartz, Jorg Weber, William Hart, Yoshiaki Kitazawa and Enrico Gandolfo, and Members at Large – Gordon Douglas, Christine Langerhorst, Toshifumi Otori and Mario Zulauf.

The Symposium was hosted by Richard Mills' team from Seattle, Washington The Society acknowledges the enormous effort of Suzanne Collum in organization of the meeting and this monograph

We are all looking forward to our next meeting, the XIIth International Visual Field Symposium in Würzburg, Germany, June 4–8, 1996.

Richard P Mills, MD
Michael Wall, MD
Editors

VISUAL FIELD CHANGE

Assessing progressive field loss in glaucoma using a self-organizing feature map

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Abstract

Purpose The large degree of variability in glaucomatous visual field defects makes it difficult to differentiate between non-significant random variations in the visual field and true progression The majority of research into the quantification of progression has concentrated on the use of global measures of defect depth, measures which take little or no account of spatial patterns within the data Artificial neural networks (ANNs) have potential to exploit spatial information and may assist the recognition of progressive change

Methods An ANN based on an unsupervised learning paradigm (Kohonen self-organizing feature map) has been trained with a population of glaucomatous defects (139 eyes) to cluster them on the basis of their pattern of loss

Results The output classes which can be derived from the ANN extend from the perfectly normal to absolute blindness and encompass all the phases of glaucoma described within the literature Examples will be presented showing how patients with progressive loss pass from one class to another and how this path through the derived classes varies from that of patients with noisy but stable defects

Conclusions Changes in the spatial characteristics of glaucomatous field loss as evidenced by the movement between classes derived from a Kohonen map are proposed as having potential in differentiating between progressive loss and random noise

Introduction

Artificial neural networks (ANNs) have been shown to be useful in differentiating visual field data[1–5] They possess a series of attributes that make them particularly useful to this task They utilize all the spatial information that exists within the field data. They have an ability to learn similarities among patterns directly from instances of them and without prior knowledge and they have an ability to generalize when used to process previously unseen data

These attributes are also of potential value in the harder task of detecting progressive loss. One way in which ANNs might assist in this task is by classifying glaucomatous patients on the basis of their pattern of loss and then establishing how patients with progressive loss pass from one class to another and whether this differs from patients with noisy but stable fields

A network particularly suited to this classification problem is the Kohonen self-organizing feature map[6] This network has an input layer, which in this case will receive the visual field data from a single examination, and a 2-dimensional output layer (map) of nodes The activa-

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tion of the output layer can be used to classify the input data. When the network has been trained, highly correlated input patterns (visual field defects) will activate the same output node while adjacent nodes will be activated by input patterns which, while being sufficiently different so as not to activate the same node, have a degree of similarity The output map shows a continuum of change as you pass from one node to its neighbor.

An important difference between the Kohonen map and the networks used in the papers cited above is that it employs an unsupervised learning paradigm It does not require the training examples to be classified using *a priori* information. Its final classification is based solely on the interrelationships between data included in the training set.

The anatomical separation of the superior and inferior field at the optic nerve head means that there is a degree of independence in the nature of the defects within the two hemi-fields. It also means that a spatially based classification of defects can result in a large number of classes which have either the same, or very similar, defects in one hemi-field but with varying types of loss in the other hemi-field. This problem can be overcome by classifying superior and inferior defects independently.

This paper demonstrates that a Kohonen self-organizing feature map can be trained with a number of glaucomatous visual fields to identify the common spatial characteristics of glaucomatous visual field loss The resulting 2-dimensional maps contain areas which respond to different conditions, ranging from an area responding to normal fields to an area responding to the most advanced defects. The intervening classes correspond to the clusters of defects present in the training set Typical glaucomatous defects (and different stages of their development) can be seen in the intervening classes. The chronological development of a defective field forms a locus across the map as the field moves from normal to advanced defect Different types of progressive loss will show different trace patterns and noisy, but essentially stable, series of fields would present further patterns which, hopefully, can be used to differentiate between progressing and stable defects.

Methods

Training data were selected from a database of Henson CFS2000 fields[7] Each record came from a threshold-related multiple stimulus supra-threshold test strategy which examined 132 locations within the central 25 degrees of the visual field The supra-threshold increment was 5 dB, missed stimuli being further quantified at 8 and 12 dB above the threshold estimate. 139 first visit fields from 139 patients with established glaucomatous visual field loss (one eye per patient) were selected to train the network. These fields were further classified according to whether they included a defect in the superior and/or inferior hemi-field 122 fields were identified as having a defect in the superior field while 103 were identified as having one in the inferior field.

In all training sets the depth information was eliminated by having only a binary distinction between a defective and normal test location Thus the network could learn features based only upon the spatial location and extent of a defect rather than upon the depth of the defect. In some experiments the fields were divided into the superior hemi-field (74 test locations) or inferior hemi-field (58 test locations) while other experiments used the entire field (132 test locations) Test locations falling within the blind spot (12 to 18 degrees temporal and 3 degrees superior to 6 degrees inferior) were removed and left eyes were reversed around the vertical meridian.

Kohonen networks (Neural Works Professional II[8]) with a 5 × 5 output layer were trained for the whole field, the superior field and the inferior field the number of iterations corresponding to 30 times the number of input vectors in the training set

As a means of graphically representing the characteristics of each output node within a given map, each network was tested with a database of 1376 eyes which included those used in the training set All the examples that activated a particular output node were combined to form a summary representing the location and frequency of missed points in that class An interpolation routine was then used to produce a grey scale representation of the summary.

The visual field data from 12 patients in whom there was a minimum of three records (maximum six) were classified by the networks to demonstrate how patients with progressive, stable and noisy field data trace patterns pass through the output maps

Results and discussion

Classification of defects

Figure 1 illustrates the results of a Kohonen network trained and tested on the whole field (central 25 degrees) Normal eyes are located within classes 18 and 23 while severe defects are in classes 1, 2 and 3 Isolated inferior arcuate defects can be found in classes 14 and 9 while isolated superior arcuate defects can be found in classes 12 and 11. Other classes represent isolated paracentral defects and hemi-field loss

The map trained on the whole field (Fig 1) shows some abrupt changes where a defect could not progress without making a large jump across the map. The occurrence of abrupt borders between classes is to be expected when the number of ways in which a pattern may change exceeds the number of neighbors within a 2-dimensional map. While this problem can never be totally overcome with a 2-dimensional map, it can be reduced by treating the superior and inferior hemi-field independently Such a division, which can be justified on the basis of the anatomical separation of the superior and inferior field at the optic nerve head, significantly reduces the potential number of ways in which a defect can progress and should, therefore, produce maps with less abrupt changes

Figures 2 and 3 give the output maps of networks trained on just the superior or inferior hemi-fields The gradual development of a defect is more notable in these maps For example, it is possible to see how a superior defect progressing from the blind spot would gradually move from class 14 to 18 to 17 to 16 and then depending upon whether it progressed more in the temporal or nasal field into class 15 or 12 Such fine classifications are not apparent in the whole field map Similar fine classifications are also seen in the inferior hemi-field map. The development of an inferior nasal defect would progress from class 19 to 14 to 9 to 4 while the development of a more central defect would pass from 19 to 23 to 22 to 21.

The grey scales in Figures 1 to 3 are only representations of each defect class rather than precise definitions. It is possible for examples to have missed points outside of the grey areas and for examples of a particular class to have a less extensive defect than the grey scales imply. For example, the rather patchy appearance representing class 7 in Figure 2 results from the superior hemi-field of the 9 field defects presented in Figure 4. Several of the defects have areas of loss which are not shown in the composite and none of them cover all the areas marked on the composite The defects do share some common traits such as the approximate number of missed points and the existence of misses on both sides of the vertical midline

Figure 4 demonstrates the diversity of defects placed within a particular class. It is difficult to imagine how a series of class boundaries could be drawn on a visual field chart which would selectively encompass these 9 defects This ability to generalize and to recognize patterns of loss which do not fit within tightly defined spatial boundaries may well be beneficial when differentiating between progressive loss and noise.

Figures 1–3 include, in the right hand corner of each grey scale, the number of examples of this class found within the whole data base. In some instances this number is low, *e g* , class 6 and 7 of Figure 3. When the numbers are low the grey scale representation fails to be a general representation of that class and additional care should be taken when making assumptions about the network's basis for classification

The data used for generating the maps of Figures 1–3 used a 5 dB cut-off for classifying a test location as either defective or normal. Raising this to either 8 or 12 dB did not meaningfully alter the feature maps.

The allocation of output nodes within the map is based upon the examples given within the training set. If this set contains a large number of similar defects, as may occur when multiple fields of the same patient are used, then the network may allocate a proportionately large

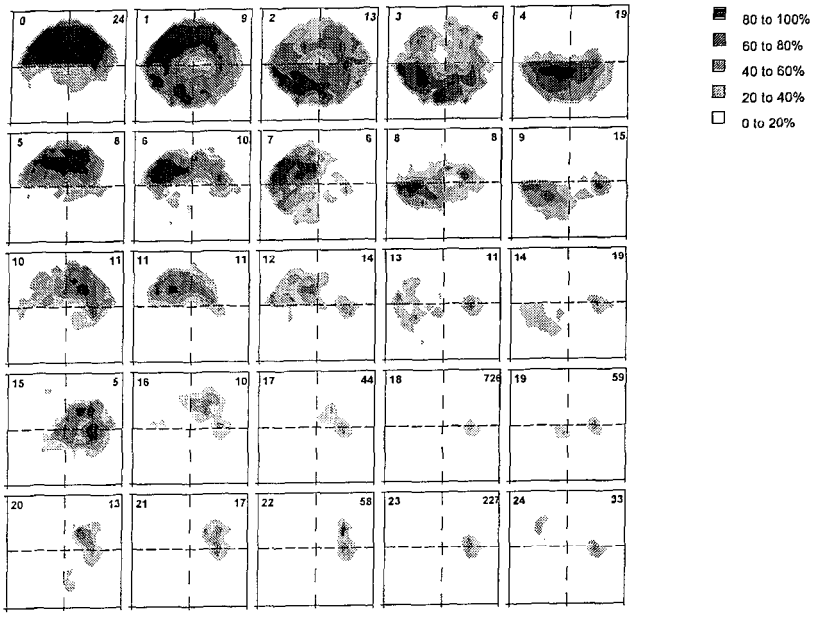

Fig 1 Output map of Kohonen network trained on 139 glaucomatous visual field defects. Training data came from 132 stimulus locations within the central 25 degrees of the visual field The number in the top left of each field pattern is the defect class while the number in the top right is the number of examples of that class within the data base.

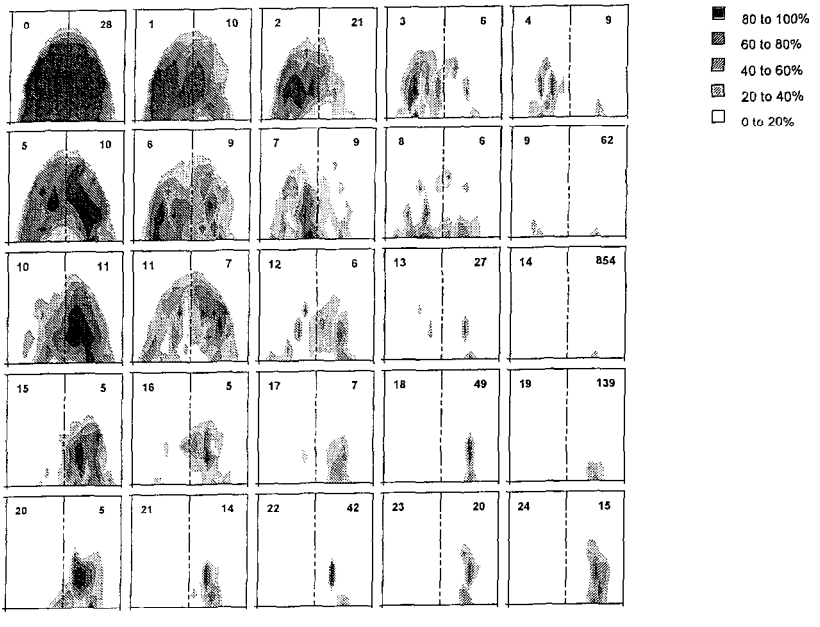

Fig 2. Output map of Kohonen network trained on 122 glaucomatous visual field defects. Training data came from 74 stimulus locations in the superior hemi-field of the central 25 degree of the visual field The number in the top left of each field pattern is the defect class while the number in the top right is the number of examples of that class within the data base

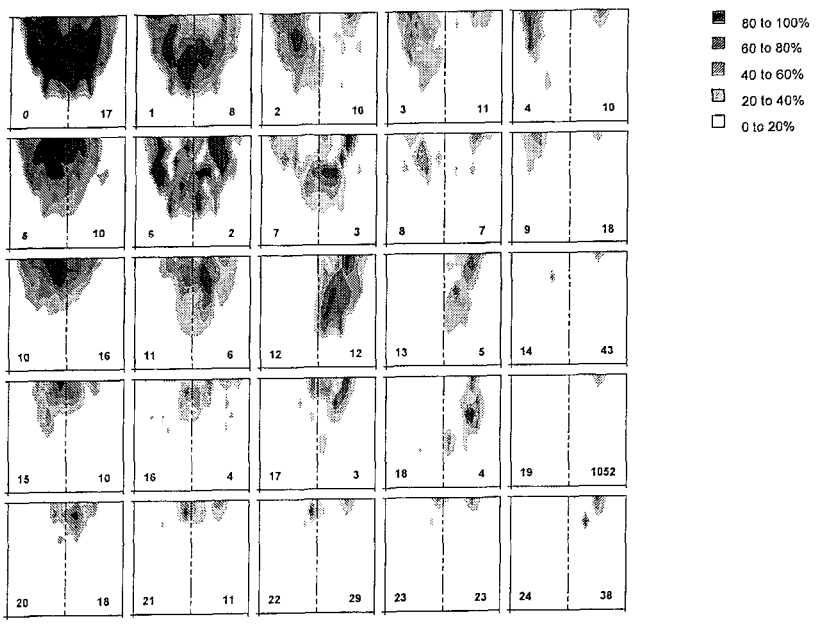

Fig 3 Output map of Kohonen network trained on 103 glaucomatous visual field defects Training data came from 58 stimulus locations in the inferior hemi-field of the central 25 degrees of the visual field. The number in the bottom left of each field pattern is the defect class while the number in the bottom right is the number of examples of that class within the data base

number of nodes to this type of loss. For these reasons the training set was composed of only the first visit results from one eye of each patient When establishing the data set, care was also taken to have a distribution of defects which range from the earliest to the most advanced loss If the data set has a preponderance of early defects then a proportionately large area of the map may be allocated to early loss. The Henson Visual Field Analysers are used primarily to detect glaucomatous loss and the data set used in this analysis may, therefore, have a larger proportion of early defects than exists within the overall glaucoma population. The collection of an unbiased population is not a trivial problem as most clinicians have preconceptions concerning the validity of certain measures.

The size of the Kohonen output map can be selected prior to training. Increasing its size results in a finer classification of defects while reducing its size forces the network to further generalizations. If the output map is made large then there is a danger that insignificant changes in the visual field will result in a change in the output class. If the network is reduced then there is a danger that significant changes will fall within the same output class. The selection of 25 output classes is a compromise based upon an empirical judgment of how many discrete patterns of loss are likely to be found in any one hemi-field. Further research is needed to establish whether an increase or decrease in output classes would be beneficial

Longitudinal data

Twelve patients in whom longitudinal data (three to six visits) were available have had each of their visual field charts classified by the maps given in Figures 2 and 3. The intention is to demonstrate how patients with progressive, stable and noisy data trace different patterns through the maps. Details of the patients are given in Table 1 and their patterns in Figures 5

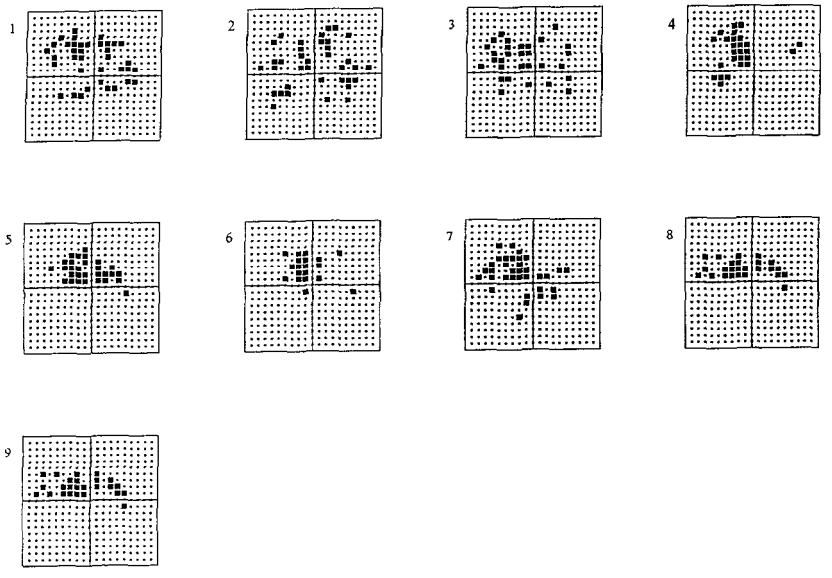

Fig 4 Eight visual field defects from class 7 of the Kohonen network trained on the superior hemi-field defects (Fig 2)

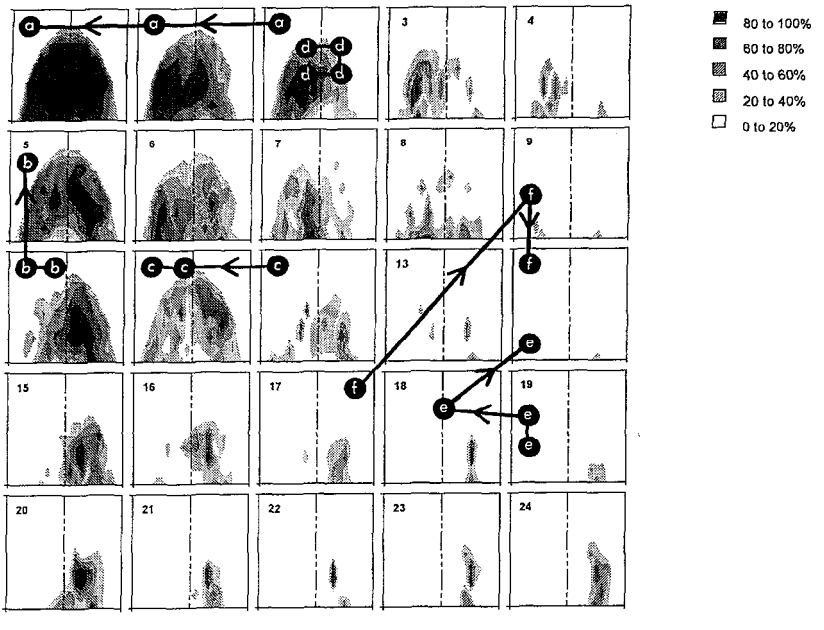

Fig 5. Examples of superior hemi-field trace patterns from patients with progressive changes (a), a mixture of progression and stability (b+c), stable fields (d) and noisy fields (e+f).

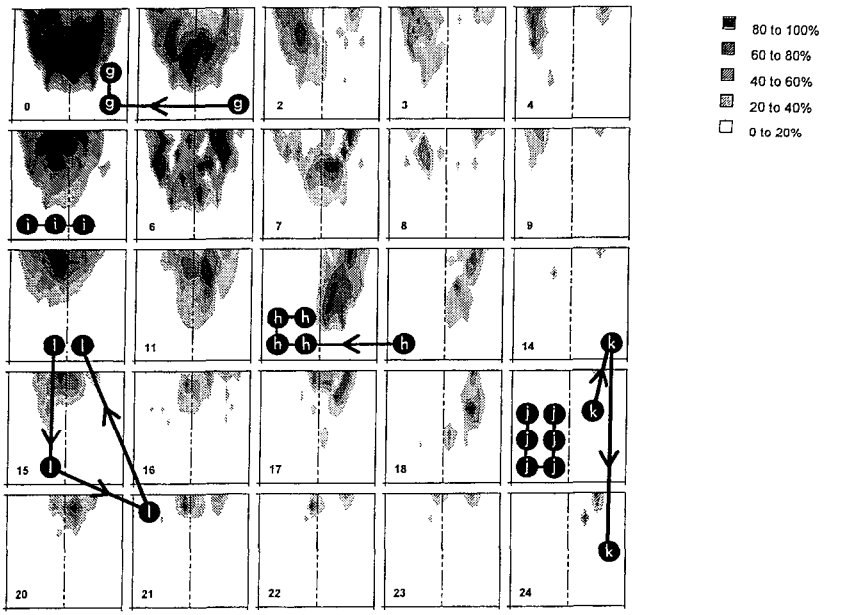

Fig 6 Examples of inferior hemi-field trace patterns from patients with progressive changes (g), a mixture of progression and stability (h), stable fields (i+j) and noisy fields (k+l).

Table 1 Dates of test for the longitudinal data shown in Figures 5 and 6

Superior hemi-field		*Test dates*					
Id	*Type*	*Field 1*	*Field 2*	*Field 3*	*Field 4*	*Field 5*	*Field 6*
a	progressing	12/87	3/88	10/88			
b	prog/stable	3/87	3/88	7/88			
c	prog/stable	3/87	7/87	7/88			
d	stable	12/86	9/87	3/88	5/88		
e	noisy	4/87	12/87	7/88	10/88		
f	noisy	4/87	9/87	2/88			

Inferior hemi-field		*Test dates*					
Id	*Type*	*Field 1*	*Field 2*	*Field 3*	*Field 4*	*Field 5*	*Field 6*
g	progressing	5/87	9/87	5/88			
h	prog/stable	10/86	12/86	6/87	2/88	7/88	
i	stable	10/87	5/88	10/88			
j	stable	1/87	3/87	5/87	7/87	12/87	3/88
k	noisy	12/87	3/88	10/88			
l	noisy	11/86	2/87	8/87	9/88		

and 6 The data used in this study was collected over a relatively short time period (approximately two years) and while there was clear evidence of progression in some of the patients its extent on the map was generally small.

Ideally, movement from one class to its neighbor should carry approximately the same level of significance for all regions of the map. Unfortunately, significance of change cannot be assessed from the data used in this study; it is, in fact, the absence of reliable estimates of change that has initiated this research. There is, however, a need for these and similar maps to be tested on longitudinal data in which there is an unequivocal decision as to whether the field is progressing, stable or noisy

Direction of movement within the map can convey important information about the nature of any change. In the maps shown in Figures 2 and 3 normals fall on the right hand edge and advanced defects in the top left hand corner. In this case, movement from the right hand edge to the top left signifies progression while movement in other directions may signify noise The direction and amplitude of movement may in the future lead to single numerical index of progression that could be used to aid clinical decisions

Conclusions

The Kohonen self-organizing map is useful for clustering glaucomatous visual field data into a number of different defect classes without any pre-existing classification or artificially imposed criteria for distinguishing defects

Data from the whole of the central field was, however, characterized by abrupt changes due to problems representing all modes of progression within a single two-dimensional map. Networks trained on either the superior or inferior hemi-fields overcome many of these problems with smooth paths of progression from normality to absolute loss. Within these maps typical glaucomatous defects can be identified including various stages of arcuate scotoma and extensions of the blind spot

Examples of longitudinal data have shown how these maps could be used to monitor changes in glaucomatous loss and to differentiate between progressive loss, stable loss and noisy data There is potential to use the output maps to provide indices of progression which are less sensitive to noise.

The use of a Kohonen self-organizing feature map to characterize spatial patterns of loss heralds a major departure from the current forms of analysis which are based almost exclusively upon measures of defect depth. Further research is ongoing which should establish the full potential of this form of analysis.

Acknowledgments

This work has been made possible by the kind contribution of visual field data from Dr R Harper (collected at Oxford Eye Hospital) and H Bryson (collected at Bristol Eye Hospital).

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Rate of change of visual fields over time in glaucoma – velocity versus acceleration

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Abstract

Trends of visual fields thresholds over time have usually been characterized by measurement of the slope of the linear regression or a curved linear fit Changes of visual field over time (dB/month) can be characterized as a velocity evaluation or a first derivative function From the velocity plot change of the slopes of visual fields over thresholds over time can be determined as an acceleration function in dB per month Examples of normal, ocular hypertensives treated and non-treated and open-angle glaucomas treated and non-treated eyes followed over time are shown to compare velocity versus acceleration functions In the acceleration plots, trends are present which are not apparent in the velocity plots The acceleration plots tend to be smoother curves with less scatter than the velocity plots Also acceleration plots may be multiphasic, indicating different rates of change of the visual field during the course of the disease Acceleration plots may be useful in further characterizing the course of open-angle glaucoma, particularly the effect of therapy at different stages of the disease

Introduction

In a chronic disease such as primary open-angle glaucoma, there is a need to determine the course of the disease over time Primary open-angle glaucoma can be characterized as a glaucomatous optic neuropathy in which pressure is a major risk factor The disease can be followed by changes in the visual field, optic disk and retinal nerve fiber layer. The trends of visual fields over time have been analyzed by linear regression analysis[1–7] Another analysis attempts to obtain the best fit curve of the visual field thresholds over time with polynomial and multiple regression techniques[8–10]

The change of visual fields over time as the slope of the linear regression line is analogous to a velocity measurement that is the measure of some parameter over time However, changes in the velocity or the rate of change of visual field thresholds over time can also be used to characterize the course of primary open-angle glaucoma Such changes in the velocity curve over time are analogous to the concept of acceleration.

The purpose of this study is to develop the concept of the use of acceleration curves of visual field thresholds over time and to illustrate their usefulness in following patients with primary open-angle glaucoma.

Methods

Measurements of visual field thresholds or sensitivities were done with an 2000R Octopus perimeter using either programs 31 or G1 The measurements of each visual field are then accumulated in a database[11]. Plots of threshold measurements for the total field and for nine different regions of the field are made over time[4] Mean values for the thresholds for the total

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field and for each region of the field over time can then be displayed and are analogous to a velocity plot. Linear regression techniques can be used to obtain the best fit of a line to all the threshold measurements over time as a slope and its standard deviation. Statistical analyses to obtain the trend of the data over time can utilize the Pearson parametric correlation coefficient and its significance as well as the non-parametric Spearman correlation coefficient and its significance[12]

To obtain an acceleration plot, that is the change of slope of visual field thresholds over time, the slope for the measurement of the first five fields are first determined using the linear regression technique Threshold measurements of each subsequent field is then added to the first five visual fields and a new slope is calculated. The acceleration plot is thus a continuous recalculation of the slope of visual field thresholds over time Similar to the velocity plot, a statistical analysis can be done to determine a Pearson or a Spearman correlation for significance

Samples for subjects representing various categories of open-angle glaucoma were then chosen to illustrate the comparison of the velocity versus the acceleration plots Categorization of the subjects included normals that is subjects with a normal ocular examination including examination by slit lamp gonioscopy with open angles, ophthalmoscopy and visual fields with the ocular pressures as measured by the Goldmann applanation tonometer consistently below 21 mmHg and no family history of glaucoma Ocular hypertensives included subjects who had ocular pressures greater or equal to 21 mmHg on two or more occasions with no evidence of visual field loss, open angles and a range of optic disk cupping and pallor High pressure open-angle glaucomas had ocular pressures consistently equal to or greater than 21 mm Hg, and open angles on slit lamp gonioscopy, abnormal visual fields demonstrating visual loss characteristic of open-angle glaucoma associated abnormalities of the optic disk with increased cupping and pallor Two ocular hypertensives and one open-angle glaucoma had greater than 2+ pigmentation of the trabeculum in all angles[13] and one open-angle glaucoma had evidence of exfoliation.

Results

Normal

Figures 1A and B are the velocity and acceleration plots respectively of the right eye of a normal subject (L B.). Figure 1A shows the plot of mean visual thresholds over time for the total field as the velocity plot while Figure 1B shows the plot of the slope for the mean thresholds over time vs time, that is the acceleration plot. The subject is a 60-year-old normal white female, who had a series of ten visual fields for approximately every three months for a period of 40 months or 3 3 years She had no known systemic disease and was on no medication Her visual acuity for the right eye was 20/20 during the performance of these visual fields. Analysis of the velocity plot shows a decreasing trend of the visual field thresholds with a borderline p value ($p = 0\ 08$) The acceleration plot (Fig. 1B) shows no trend

Ocular hypertension

Figures 2A and 2B show respectively the velocity and acceleration plots for the right eye of a 49-year-old white male untreated ocular hypertensive (J.F), who has pigmentary dispersion, with no known systemic disease. He is on no medication The patient was followed for about 15 years with 16 visual fields His visual acuity for the right eye during follow-up was 20/15. The velocity plot shows a borderline significant increase over time ($p = 0\ 097$). The acceleration plot is biphasic and shows a significant decrease in positive values for the slope. The acceleration plot indicates that during the first 95 months of follow-up, there was an increasing relative rate of visual field loss However, the slope was still positive as the visual field thresholds are showing less of an increase of values over time The velocity plot appears essentially flat, while the acceleration plot shows a definite trend.

Figures 3A and 3B are the velocity and acceleration plots respectively for the left eye of a

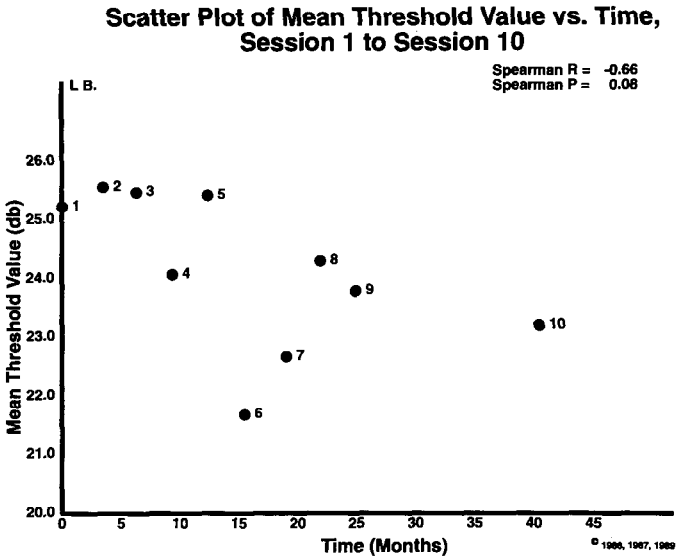

Fig 1A Normal subject – Threshold values (dB) plotted over time (months) for the total visual field (velocity plot). Figures in the plot indicate the sequence and number of the visual fields

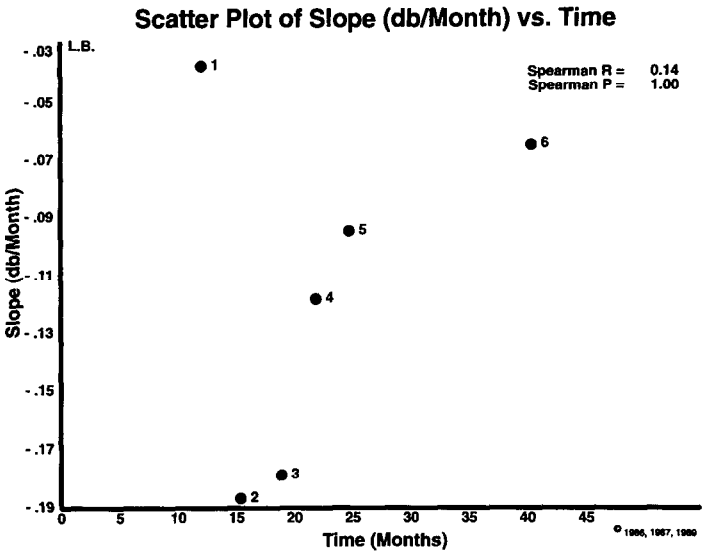

Fig 1B Normal subject – Plot of slope in dB/month plotted over time (months) (acceleration plot) Figures in the plot indicate the sequence and number of the visual fields used for analysis The first number is the slope of the first five visual fields from Figure 1A

77-year-old untreated ocular hypertensive white female (D.F.) followed for about ten years with 17 individual visual fields. The patient has hypothyroidism for which she is being treated with L-thyroxine. She has also vascular hypertension being treated with chlorthalidone. Her visual acuity for the left eye during follow-up was 20/25. The velocity plot for Figure 3A

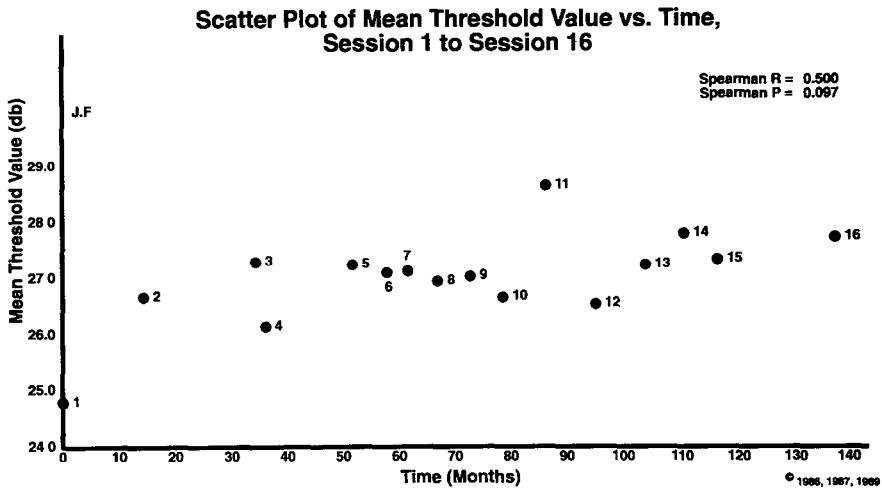

Fig 2A Untreated ocular hypertensive – Threshold values (dB) plotted over time (months) for the total visual field (velocity plot). Figures in the plot indicate the sequence and number of the visual fields.

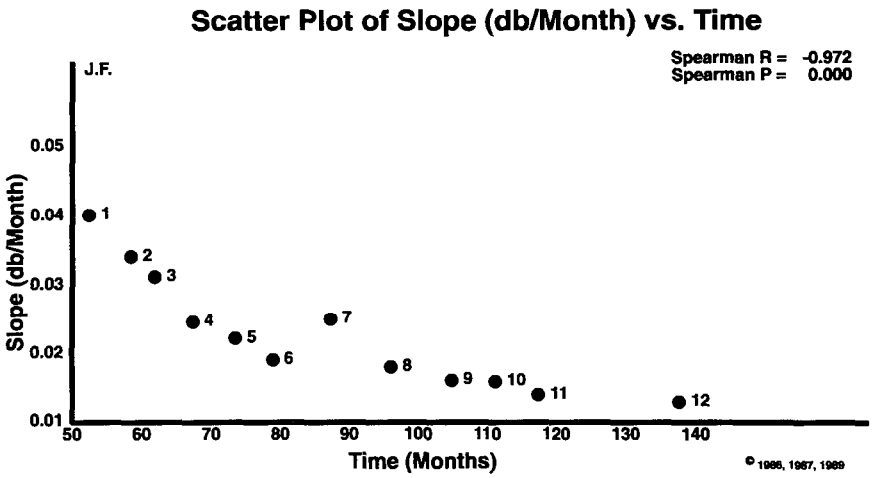

Fig 2B Untreated ocular hypertensive – Plot of slope in dB/month plotted over time (months) (acceleration plot). Figures in the plot indicate the sequence and number of the visual fields used for analysis. The first number is the slope of the first five visual fields from Figure 2A.

shows no significant trend even though the Spearman correlation is negative. However, the acceleration plot (Fig 3B) shows a significant increase in time in comparison to Figure 2B. Of particular note is that all the slopes for this patient are negative, that is she is losing visual field at varying rates. The patient's rate of losing field has decreased over time and has become relatively stable beginning about 60 months. Again similar to the untreated ocular hypertensive eye in Figures 2A and 2B, there is no indication in the velocity plot that there is a trend over time. However, the acceleration plot (Fig. 3B) for this eye appears to be relatively improved in showing a decreasing rate of visual field loss.

Figures 4A and 4B respectively show the velocity and acceleration plots for the left eye of a

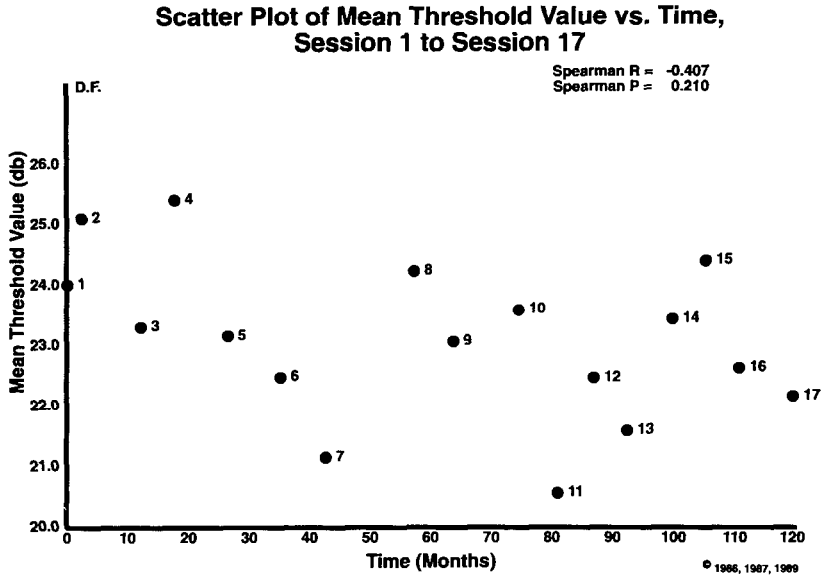

Fig 3A Untreated ocular hypertensive – Threshold value (dB) plotted over time (months) for the total visual field (velocity plot) Figures in the plot indicate the sequence and number of the visual fields.

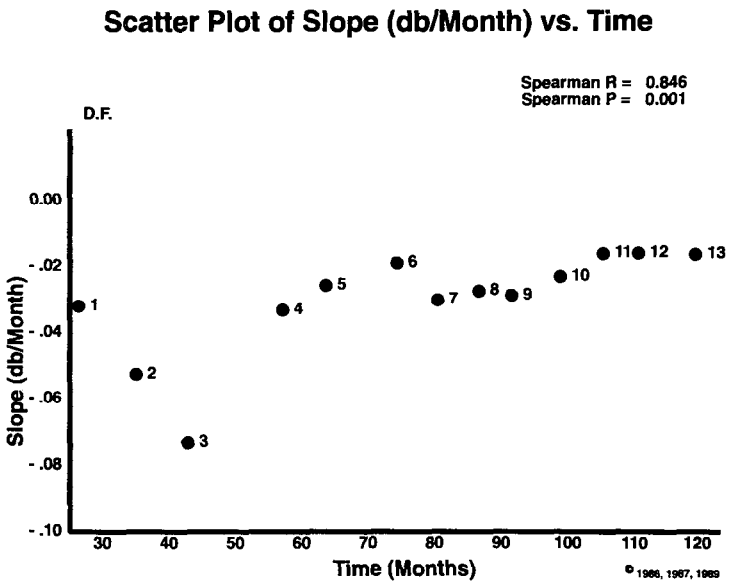

Fig. 3B Untreated ocular hypertensive – Plot of slope in dB/month plotted over time (months) (acceleration plot). Figures in the plot indicate the sequence and number of the visual fields used for analysis. The first number is the slope of the first five visual fields from Figure 3A.

72-year-old white treated ocular hypertensive male (B.D.) followed for about six years with 19 visual fields. The visual acuity for the left eye during follow-up was 20/20 This eye is being treated with 0.5% levobunolol b.i d. and 0 1% dipivalyl epinephrine b i.d The patient also has had diabetes mellitus for 20 years with no retinopathy and is being treated with insulin.

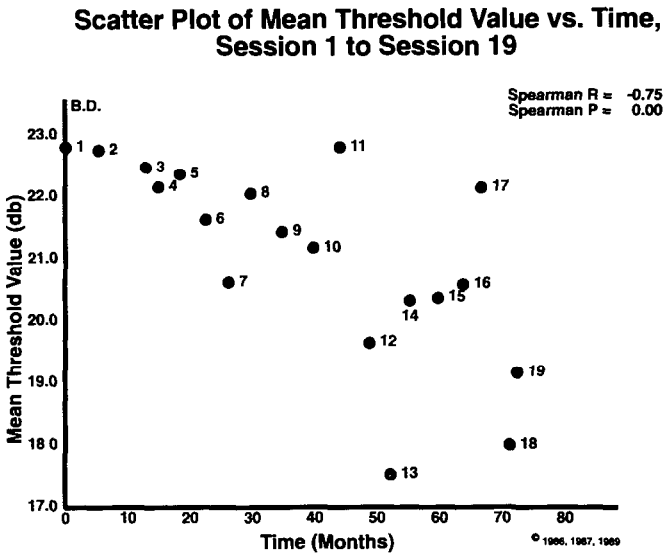

Fig. 4A Treated ocular hypertensive – Threshold values (dB) plotted over time (months) for the total visual field (velocity plot) Figures in the plot indicate the sequence and number of the visual fields

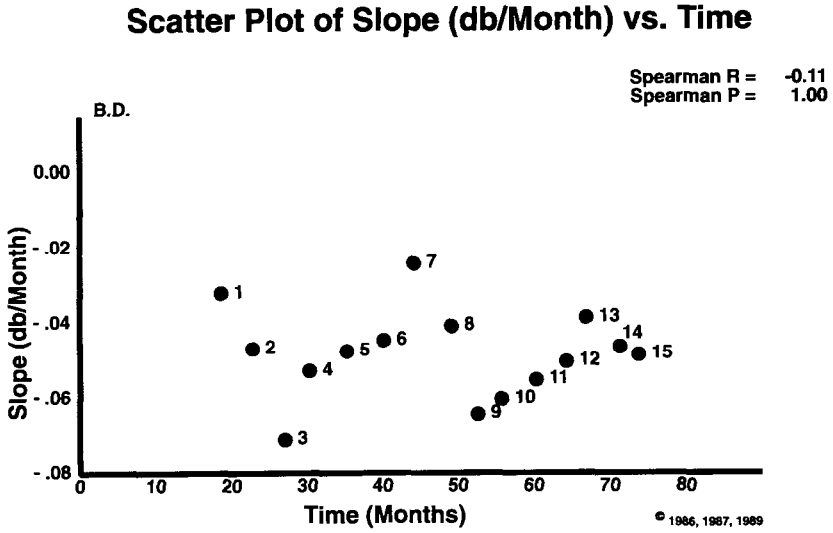

Fig 4B Treated ocular hypertensive – Plot of slope in dB/month plotted over time (months) (acceleration plot) Figures in the plot indicate the sequence and number of the visual fields used for analysis The first number is the slope of the first five visual fields from Figure 4A.

Figure 4A, the velocity plot, shows a significant trend over time with a decrease in the visual field thresholds. In Figure 4B, the acceleration plot, all the slopes are negative, indicating that the patient as shown on the velocity plot is losing field However, the acceleration plot is flat and shows no significant trend indicating the rate of visual field loss is at a constant rate

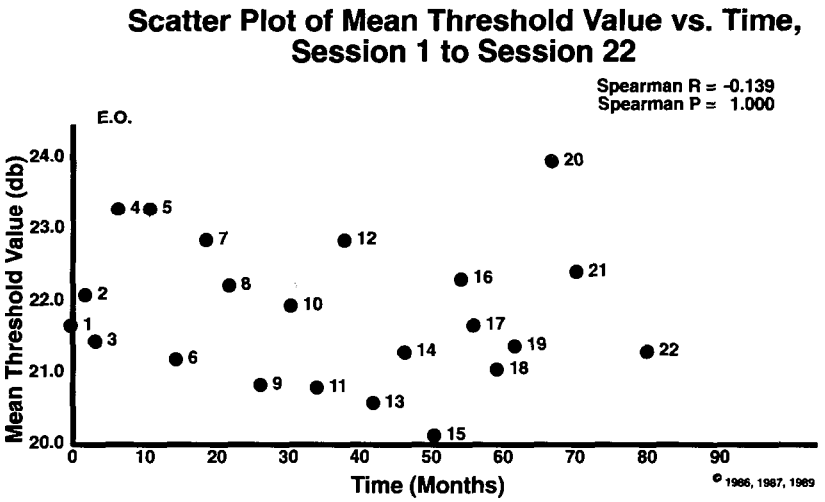

Fig 5A Treated open angle glaucoma – Threshold values (dB) plotted over time (months) for the total visual field (velocity plot) Figures in the plot indicate the sequence and number of the visual fields

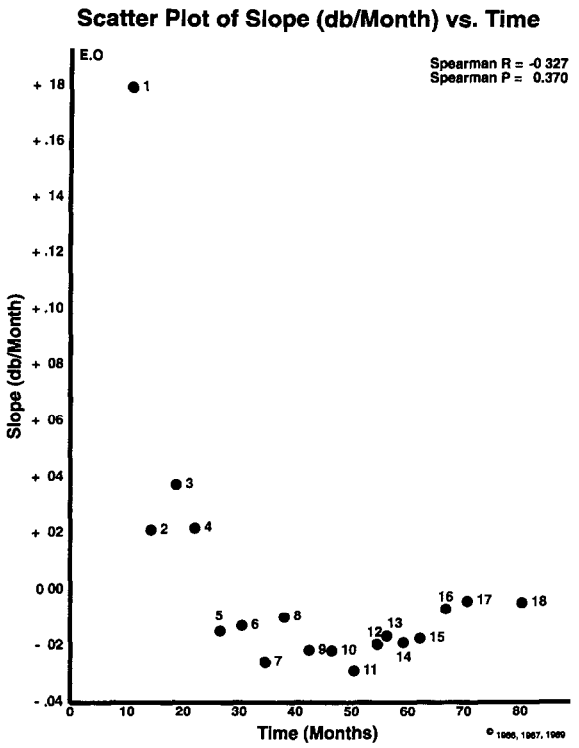

Fig. 5B Treated open angle glaucoma – Plot of slope in dB/month plotted over time (months) (acceleration plot) Figures in the plot indicate the sequence and number of the visual fields used for analysis The first number is the slope of the first five visual fields from Figure 5A

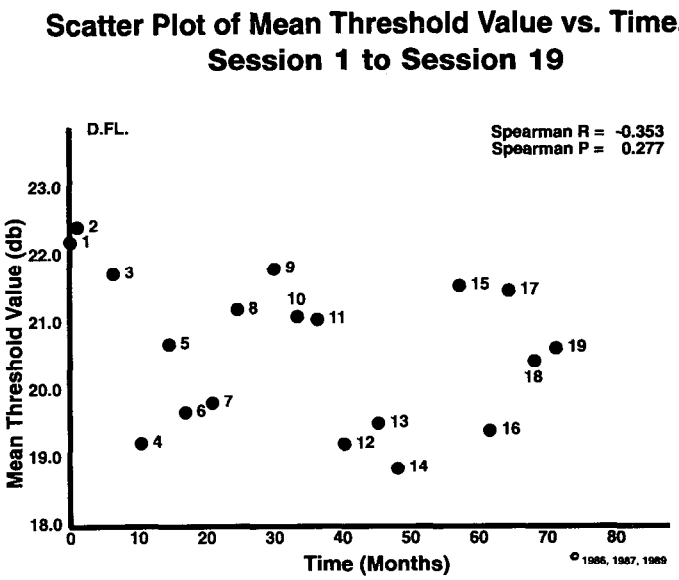

Fig 6A Treated open angle glaucoma – Threshold values (dB) plotted over time (months) for the total visual field (velocity plot) Figures in the plot indicate the sequence and number of the visual fields

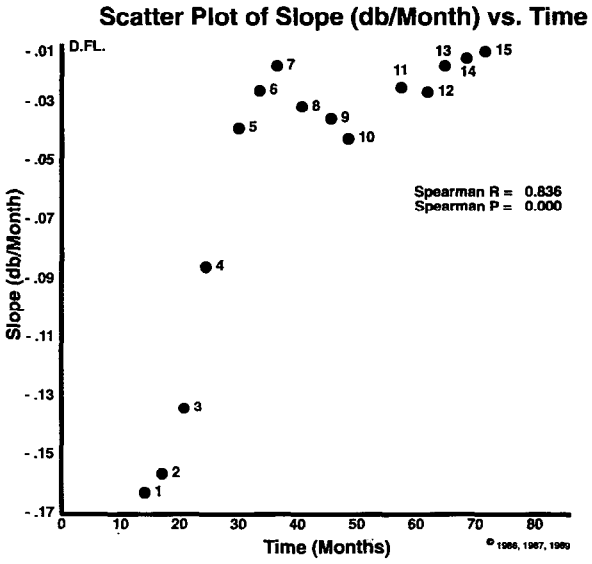

Fig 6B Treated open angle glaucoma – Plot of slope in dB/month plotted over time (months) (acceleration plot) Figures in the plot indicate the sequence and number of the visual fields used for analysis. The first number is the slope of the first five visual fields from Figure 6A

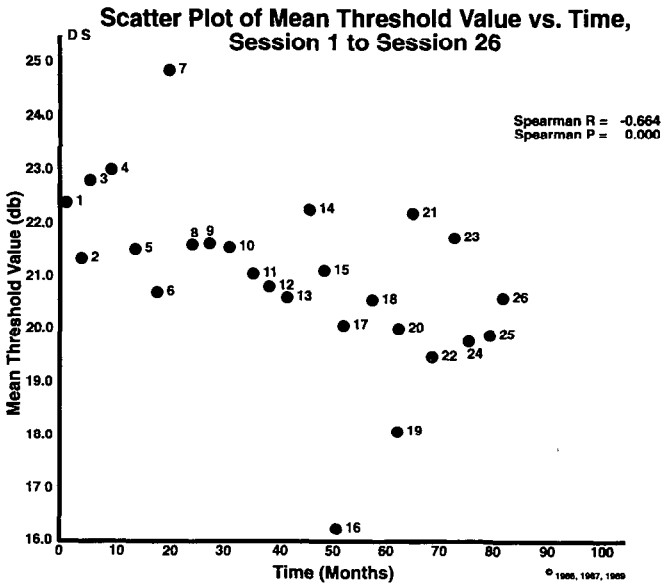

Fig 7A Treated open angle glaucoma – Threshold values (dB) plotted over time (months) for the total visual field (velocity plot). Figures in the plot indicate the sequence and number of the visual fields.

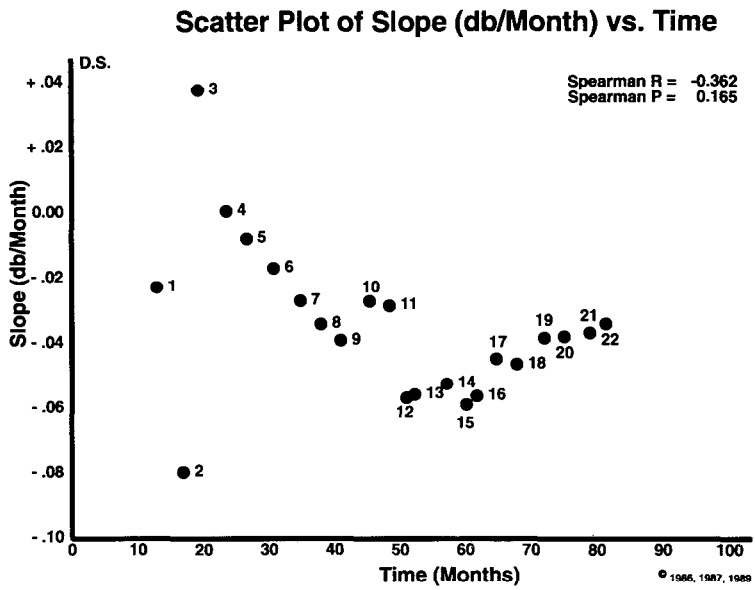

Fig 7B Treated open angle glaucoma – Plot of slope in dB/month plotted over time (months) (acceleration plot). Figures in the plot indicate the sequence and number of the visual fields used for analysis. The first number is the slope of the first five visual fields from Figure 7A

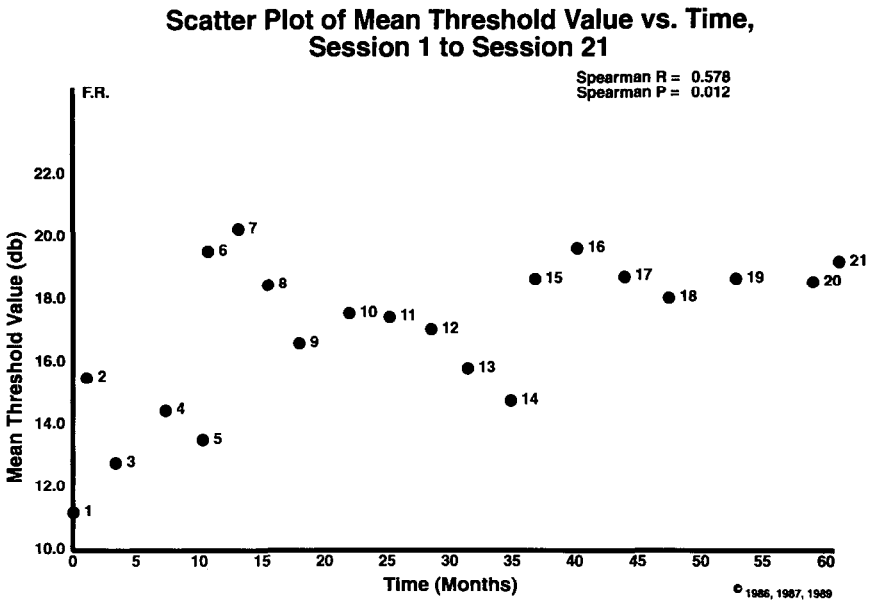

Fig 8A Treated open angle glaucoma – Threshold values (dB) plotted over time (months) for the total visual field (velocity plot) Figures in the plot indicate the sequence and number of the visual fields

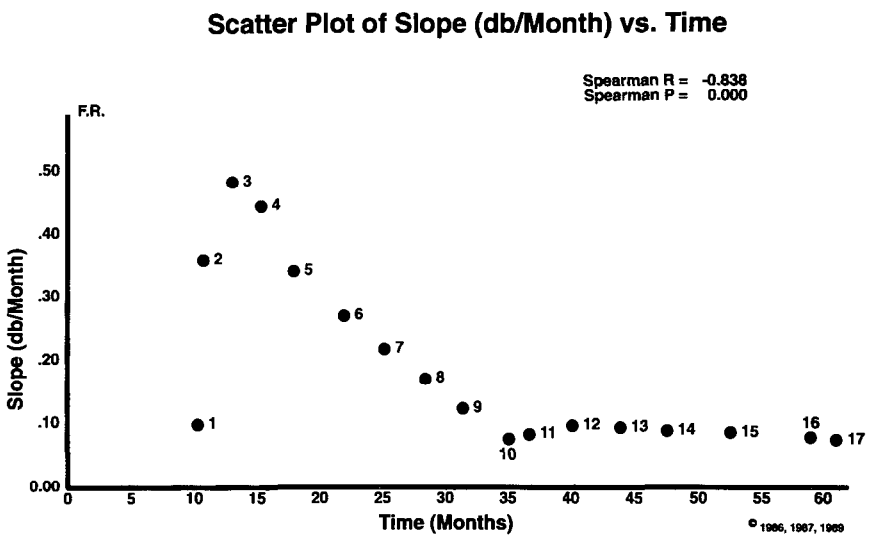

Fig 8B Treated open angle glaucoma – Plot of slope in dB/month plotted over time (months) (acceleration plot). Figures in the plot indicate the sequence and number of the visual fields used for analysis The first number is the slope of the first five visual fields from Figure 5A.

Open-angle glaucoma

Figures 5A and 5B show the velocity and acceleration plots respectively for the left eye of a 51-year-old white male (E.O.) who has been followed for about seven years with 22 visual fields The patient's visual acuity for the left eye during follow-up was 20/20. For his glaucoma he is using 0.5% timolol OU b i.d He has a history of ulcerative colitis and is being treated with sulfas and folic acid. He had one month of prednisone therapy 15 years before his first visual field. The velocity plot (Fig. 5A) shows no significant trend. The acceleration plot (Fig. 5B) is biphasic and appears relatively flat and beginning at about 26 months, the slopes which were previously positive have now become negative. The trend appears rather stable over time indicating that the patient is now losing field at a constant rate while previously he was increasing his rate of visual field gain.

Figures 6A and 6B show the velocity and acceleration plots respectively for the right eye of a 54-year-old white male (D Fl.) with treated open-angle glaucoma. This patient has been followed for about six years with 19 visual fields. The visual acuity for the right eye during follow-up was 20/15 He is being treated with 0.5% timolol OU b.i.d, 6% pilocarpine OU q i.d. and 0 1% dipivalyl epinephrine OU b.i d. He has had argon laser trabeculoplasty OU. He has no known systemic disease and is on no other medications. The velocity plot (Fig 6A) shows no significant trend and has a negative Spearman correlation The acceleration plot is biphasic (Fig. 6B) and the slopes show all negative values The acceleration plot shows a course quite different from the velocity plot. The negative values of the slopes have become less negative with time so that at about 40 months they level off and become relatively stable. The acceleration plot shows a decrease in the rate of loss of visual fields so that now field loss is occurring at a small constant rate

Figures 7A and 7B are respectively the velocity and acceleration plots for the left eye of a 78-year-old white female (D.S.) with treated open-angle glaucoma with exfoliation OS. She has been followed for about seven years with a total of 26 visual fields. The visual acuity for the left eye during follow-up was 20/20. She is being treated with 0.5% timolol OU b i.d , 6% pilocarpine OU q.i d and 0.1% dipivalyl epinephrine OU b.i.d. She has had argon laser trabeculoplasty OU. She is also being treated for vascular hypertension with hydrochlorothiazide and nifedipine. Figure 7A, the velocity plot, shows a significant negative trend and it appears that the patient is losing field at a constant rate although small in magnitude. The acceleration plot (Fig. 7B) is biphasic showing an increasing rate of losing visual field until about 50 months at which time the curve appears to have leveled off and recently has become less negative. The patient is still losing visual field now but at a smaller rate.

Figures 8A and 8B are the velocity and acceleration plots respectively for the left eye of a 65-year-old white male (F.R.) being treated for open-angle glaucoma. He has been followed for about 5 years with a series of 21 visual fields. His visual acuity for the left eye during follow-up was 20/20. He is being treated with 0 5% timolol OU b i.d., 4% pilocarpine OU q i d and 0.1% dipivalyl epinephrine OU b i d. He has had argon laser trabeculoplasty OU He has no known systemic diseases and is on no other medication. The velocity plot (Fig. 8A) shows a significant positive trend indicating that the patient has increased visual field threshold values over time but relatively flat since about 20 months. The acceleration plot (Fig. 8B) is biphasic and confirms this tendency. However, slopes are decreasingly positive up to about 35 months Thus the patient was relatively losing field at an increasing rate showing less positive slopes. After 35 months the curve is relatively flat, indicating that the patient has stabilized and is still gaining field but at a less constant rate

Discussion

These examples from a series of a normal subject, untreated ocular hypertensives, treated ocular hypertensives and treated open-angle glaucoma patients show some characteristics of acceleration plots that have distinctive advantages over simple trend analysis or a velocity plot of visual field thresholds over time. First the acceleration plots are relatively smooth, that is they show little scatter compared to the velocity plots Secondly, they show changes

occurring in the rate of visual field loss not apparent in the velocity plot. Thirdly, the rates of change of the visual field loss can be biphasic or even multiphasic which is not always evident in the velocity plots indicating differences in the course of the disease. These phases in the acceleration plots may be related to changes in treatment or perhaps reflect the natural course of the disease.

Of interest in the use of acceleration plots is the concept of the thinking of the course of glaucoma as a progressive disease occurring at different rates. Some of these examples show a definite decrease in the rate of loss of visual fields so that even though they were still losing visual field, it is at a fairly small constant rate which may be tolerable considering the age of the patient The relatively slow rate of change may suggest precluding surgical intervention.

Also the acceleration plots offer a substantial advantage in evaluating the effects of therapy of the disease for any patient. In the evaluation of therapeutic trials in glaucoma, not only velocity plots with trend analysis or change in the visual fields over time should be evaluated but also the rates of change of the visual field over time as in an acceleration plot should be obtained for the effect of the therapy during the course of the disease.

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Evaluation of a technique for determining glaucomatous visual field progression based on animation graphics

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Abstract

The authors wanted to determine the usefulness of a visual technique to help determine glaucomatous field progression The first two visual field examinations of 16 glaucoma suspects and 16 glaucoma patients followed for a median of 7 46 years with seven examinations were averaged Three-dimensional color-coded images of the field (hill of vision) were then generated After correcting for the expected test-retest variability and inserting one interpolated image per month of follow-up, the images were aligned and presented in rapid sequence to create an animation sequence After a short learning session five glaucoma specialists classified the visual field sequences as progressing or not progressing The inter-observer and intra-observer agreement rates were then estimated Perfect agreement (100% concordance) between the observers was obtained in 18 (56 3%) subjects while at least 80% concordance was obtained in 27 (84 4%) subjects (kappa = 0 572) Of the eight sequences that were repeated, four of the five observers had an intra-observer agreement of at least 87 5%

The full article will be published elsewhere

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Variability of normal visual fields in a prospective study

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Abstract

The authors present results from a prospective study of clinically normal subjects undergoing psychophysical tests including the 30-2 program of the Humphrey Field Analyzer, and the serial changes in inter-individual variability and intra-individual test-retest variability of the visual fields were examined A total of 144 subjects (mean age 50 24 years, range 30 to 84 years) were enrolled and are tested every six months Currently, 129 subjects have had a one-year follow-up (three examinations), 94 a two-year follow-up (five examinations) and nine a three-year follow-up (seven examinations) In all examinations, the inter-individual variability increased exponentially with eccentricity of test location At examination 1, the 95% confidence interval of threshold deviations of the fitted function was 18 dB for the most peripheral locations This value decreased to 13 dB for examinations 2 and 3 The corresponding values for the most central locations, however, remained constant at 6 dB for examinations 1–3 Test-retest variability was estimated in a manner described previously in glaucoma patients[1] Age effects on test-retest variability were not meaningful when subjects were divided into three age groups For locations with negative deviations, normal subjects had a larger regression-to-the mean effect compared to glaucoma patients The 90% confidence interval of test-retest variability was compared for deviations ranging –6 to 4 dB Even when matched for deviation level, glaucoma patients showed up to twice the test-retest variability compared to normal subjects

Introduction

Effective use of perimetry as a diagnostic tool depends on an understanding of the variability of results. Inter-individual variability in normals is important in comparing a particular test result to normal age-matched normals, while intra-individual variability between tests (test-retest variability) is important in determining whether a particular visual field has changed

Inter-individual variability characteristics in normals have been reported previously[2], however, it is not known how this variability changes over a series of tests. Additionally, while test-retest variability is known in glaucoma[1,3], studies are still lacking in normals.

The purpose of this study was to characterize these aspects of variability in a prospective study of normal subjects.

Materials and methods

Subjects

The sample contained 144 healthy subjects whose mean age was 50.24 years (range, 30 to 84 years). It was drawn from an ongoing study investigating the longitudinal changes in visual

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function in normal subjects measured with a small battery of psychophysical tests. Subjects are tested at six-monthly intervals

The inclusion criteria were. (i) best corrected visual acuity of 6/12 or better; (ii) normal ocular exam; and (iii) intraocular pressure less than 22 mmHg. The exclusion criteria were: (i) presence of any ocular disease; (ii) any systemic disease known to affect the visual field; (iii) any medication known to affect the visual field; (iv) family history of glaucoma; (v) distance refraction exceeding 5 00 D equivalent sphere and astigmatism exceeding 3.00 D: and (vi) aphakia or pseudophakia.

Testing method

One randomly selected eye was designated the study eye and is the only eye tested. The subjects were tested with program 30-2 of the Humphrey Field Analyzer (Humphrey Instruments Inc , San Leandro, CA)

Data analysis

We used only visual field results which were reliable defined according to a classification based on empirical data[4]. The data were analysed in terms of threshold deviations For the analysis of inter-individual variability we used the results of examinations 1, 2 and 3, while for the analysis of test-retest variability we used the results of examinations 2, 3, 4 and 5.

Results

Number of examinations

When the data were analysed, 129 subjects had a one-year follow-up (three examinations), 94 had a two-year follow-up (five examinations) and nine had a three-year follow-up (seven examinations)

Inter-individual variability

Inter-individual variability of threshold deviations in examinations 1, 2 and 3 is shown in Figure 1 In examination 1, the 95% confidence interval exceeded 25 dB at some locations, particularly in the superior field Inter-individual variability increased exponentially with eccentricity of test location (Fig. 2). In examinations 2 and 3, the slope of the fitted function shallowed with nearly a 30% reduction in inter-individual variability at the most peripheral locations In central locations, however, inter-individual variability remained constant

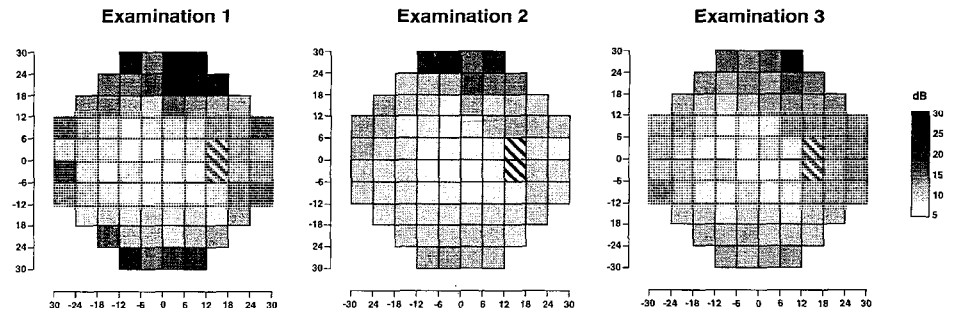

Fig 1 Grey-scale maps showing the pointwise inter-individual variability in 129 normal subjects over three examinations with program 30-2 of the Humphrey Field Analyzer

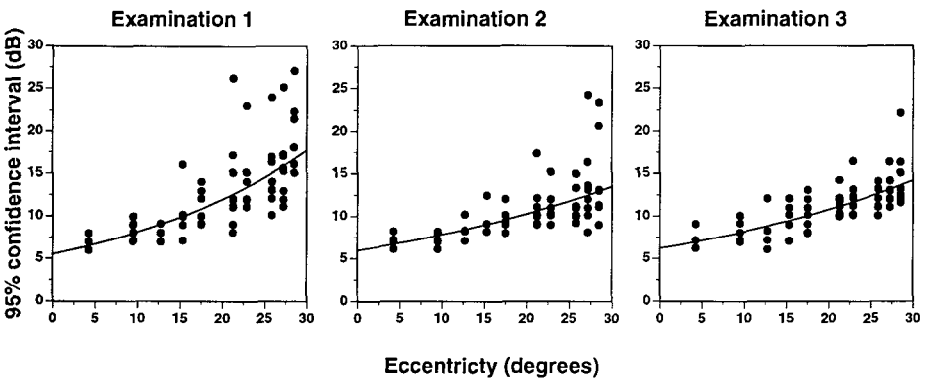

Fig 2 Inter-individual variability as a function of eccentricity in 129 normal subjects over three examination The solid lines show the best least-squares fit (exponential) through the data points

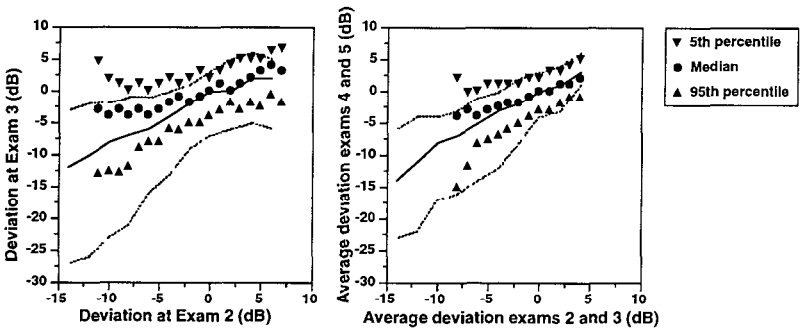

Fig 3 Intra-individual test-retest variability in 94 normal subjects for single exams (left) and averaged exams (right) Corresponding glaucoma data from Heijl and colleagues[1] are shown in solid lines

Test-retest variability

Inter-individual test-retest variability of threshold deviations for single and averaged tests is shown in Figure 3. Age effects were not meaningful when the sample was divided into three groups according to age (30–45 years, 46–60 years and > 60 years). Test-retest variability data in glaucoma patients were taken from a previous study published by Heijl and colleagues[1] For negative deviations, normals had more symmetric distributions of test-retest variability and a much larger regression-to-the-mean effect. Additionally, even when matched for deviation level, glaucoma patients showed up to twice the test-retest variability compared to normal subjects (Fig 3).

Discussion

Inter-individual variability is dependent on examination sequence. It is alarmingly high in peripheral locations in perimetrically naive subjects While some individuals have near normal threshold deviations in the periphery, others have profound increases raising the inter-individual variability After the first examination, there is a considerable decrease in inter-individual variability in these locations, but not in central ones These findings may be partially explained by a learning effect which is preferential in the periphery[5,6]. First examination re-

sults therefore should be avoided both for establishment of normal values and diagnostic purposes.

Matched for deviation level, normals have a larger regression-to-the-mean effect for negative deviations compared to glaucoma patients This means that "bad" points in normal subjects which were within around 5 dB of the expected threshold were much closer to normal values on retest compared to glaucoma patients Additionally when matched for deviation level, glaucoma patients exhibit as much as twice the test-retest variability This study, in conjunction to another[7], shows that both intra- and inter-test variability characteristics in normal subjects are different to glaucoma patients, even when matched for deviation level. These results suggest alterations in "normal" areas of glaucomatous fields.

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Determining progressive visual field loss

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Abstract

Serial Humphrey fields of 85 eyes were examined to detect progressive field loss over a mean follow-up period of 38 months We compared subjective clinical evaluation of serial grey scales with the following three commercially available computerized statistical algorithms for detecting progression: 1) Progressor Programme; 2) Linear Regression Analysis of Statpac (LRA [Statpac]); 3) Statpac 2 Glaucoma Change Probability (GCP) LRA [Statpac] identified progression in 13% of eyes, GCP identified progression in 26% of eyes and Progressor Programme identified progression in 31% of eyes In contrast to the other two algorithms, which detected progression in similar percentages of both eyes with ocular hypertension (OHT) and primary open angle glaucoma (POAG), Progressor Programme detected progression predominantly in eyes with POAG Clinical impression identified much less progression than any of the three algorithms, determining only eight eyes (9%) as showing deterioration Comparison against clinical impression suggested that none of these three algorithms, as used in this study, satisfied the criteria necessary to provide objective yet clinically signficant determination of field progression

Introduction

Automated perimetry (AP) provides objective visual field analysis[1] and has resulted in the earlier detection of glaucomatous field loss when compared to manual perimetry[2] Additionally AP has offered the hope of earlier and more objective determination of the progression of glaucomatous field loss[3]. However AP has also demonstrated the presence and importance of test-retest variability in visual field analysis[4] This long-term fluctuation, which is greater in glaucomatous compared with normal visual fields, remains a major obstacle to realizing the full potential of AP in the determination of the progression of glaucomatous field loss[5].

A variety of statistical algorithms, designed to make use of the numerical nature of the field data collected by AP, have been proposed to help differentiate true progression of field loss from long-term fluctuation[5–10]. At present however there is no agreement as to what constitutes clinically significant progression of the glaucomatous visual field over time using AP, nor any generally accepted technique for detecting it Subjective clinical impression based on simple visual inspection of a series of AP grey scales, in the context of associated clinical features, is probably still the most widely used means of determining progression.

The purpose of this study was to evaluate the three commercially available computerized algorithms for the Humphrey Visual Field Analyser (HVFA) and to compare them with subjective clinical impression in the determination of the progression of glaucomatous visual field loss. The three algorithms evaluated were: 1) Progressor Programme (Institute of Ophthalmology, London) which is the newest commercially available algorithm and uses linear regression analysis to derive a slope of change at each individual test location in the field in a

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pointwise fashion[10,11]; 2) linear regression analysis of Statpac (LRA [Statpac]) which derives a single slope of change for the entire field from the "global measure" of mean deviation (MD)[12]; 3) glaucoma change probability of Statpac 2 (GCP) which is another pointwise method of determining progression based on comparing change at each individual test location with an empirical database of the variability of stable glaucoma patients at these test locations to produce a probability map of change[9]

Patients and methods

Visual field data for this study was obtained by retrospective review of the hard disk of the HVFA in the glaucoma unit for the period 1988–93 All eyes met the following inclusion criteria: 1) Ocular hypertension (OHT) or primary open angle glaucoma (POAG) 2) At least five C24-2 or five C24-1 threshold tests with the HVFA 3) At least two years follow-up between first and last field 4) Previous automated perimetry experience prior to first field. 5) Good reliability indices throughout follow-up period. 6) Visual acuity 6/18 or better throughout the follow-up period Eyes with low tension glaucoma and artefactual or non-glaucomatous field loss were excluded.

One of us (PKW) made a subjective clinical assessment of the stability of each field series based on a visual inspection of the serial grey scales and global indices in conjunction with a review of the case records. This was done masked to the results of the analysis of the field series by each of the three algorithms. The three statistical algorithms were then applied to each field series and progression defined by the following criteria: Progressor Programme determining significant deterioration at a minimum of two non-edge points on analysis of the complete field series (default setting = 1 dB/year); LRA [Statpac] determining a negative slope greater than 0.5 dB/year ($p < 5\%$); GCP determining significant deterioration ($p < 5\%$) at a minimum of two adjacent non-edge points in last field compared with baseline pair For the ten HVFA programme C24-1 field series which could not be analysed by GCP we applied the following criteria as an alternative determinant of significant deterioration at a point: A point must have declined by 5 dB from the average of 3 baseline values, have declined at least 3 times the patient's short-term fluctuation and be outside all three baseline values. Point change identified by these criteria has previously been demonstrated to show a good correlation with point change identified by GCP[13] In similarity with our definition of deterioration by GCP a minimum two adjacent non-edge points had to meet these criteria.

Results

Field data from 85 eyes (48 patients) met the inclusion and exclusion criteria. The mean follow-up per eye was 38 months (minimum 24 months) and the mean of number of fields per eye was six (minimum five fields) Diagnosis at first field was OHT in 51 eyes and POAG in 34 eyes. This diagnosis was based on the following criteria for the presence field loss in the first field; pattern deviation probability plot showing at least three contiguous non-edge points depressed to the 5% probability level, with at least one non-edge point depressed to the 1% level[14]. The OHT eyes had a mean MD at first field of –1 65 dB and the POAG eyes had a wide spectrum of field defects with a range of MD from –0.24 to –23 35 dB and a mean MD of –7.55 dB Overall LRA [Statpac] detected progression in 11 of 85 eyes (13%), GCP detected progression in 22 of 85 (26%) eyes and Progressor Programme detected progression in 26 of 85 (31%) eyes. A total of 38 out of 85 eyes were identified as having deteriorated by at least one statistical algorithm All three algorithms reached agreement on progression in five of these 38 eyes Accounting for the 47 eyes in which all three algorithms reached agreement on stability, all three algorithms reached agreement (100% concordance) on stability or progression of field loss in 52 of 85 (61%) eyes Subjective clinical impression identified eight of 85 eyes (9%) as showing progression.

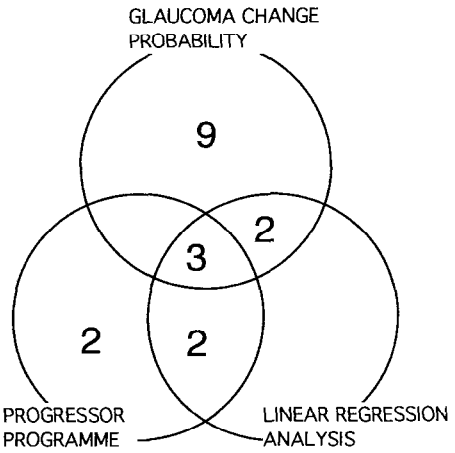

Fig 1. OHT eyes demonstrating progression by at least one statistical algorithm (n = 18 of 51 eyes).

OHT eyes

Considering the 51 OHT eyes in isolation, subjective clinical impression determined two eyes to have converted to POAG Analysis of progression by the three statistical algorithms determined 18 eyes to be significantly worse by at least one algorithm The concordance between the three algorithms in these 18 eyes is represented graphically by the The Venn diagram in Figure 1 All three statistical algorithms reached agreement on progression in only three OHT eyes including the two eyes deemed to be worse by clinical impression. Overall the three statistical algorithms gave very different results when applied to this same group of OHT eyes. By our criteria GCP detected twice as much progression as the other two algorithms in OHT eyes and seven times as much change as our clinical observer Additionally we applied the same criteria for the presence of a field defect[14] to the final field of each series in the OHT eyes, as already used for diagnosis at the first field By these criteria only two OHT eyes were determined to have a field defect in the final field and thus by implication to have converted to POAG These were the same two eyes as determined to have converted to POAG by subjective clinical impression

POAG eyes

Amongst the 34 POAG eyes subjective clinical impression determined six to have shown deterioration of the visual field. Of these six eyes all three statistical algorithms also reached agreement on progression in one eye, GCP and Progressor Programme agreed in a further four eyes and GCP alone detected progression in the remaining one eye. Overall 20 POAG eyes were determined to show progression of field loss by at least one statistical algorithm and the concordance between the results of the three algorithms in these eyes is shown in the The Venn diagram in Figure 2 Again there was a wide variation of results from analysis of the same group of eyes by the three different statistical algorithms. In the POAG eyes Progressor Programme was most likely to detect progression. It detected 2.4 times more progression than GCP, 4.75 times more progression than LRA [Statpac] and 3.2 times more progression than our clinical observer

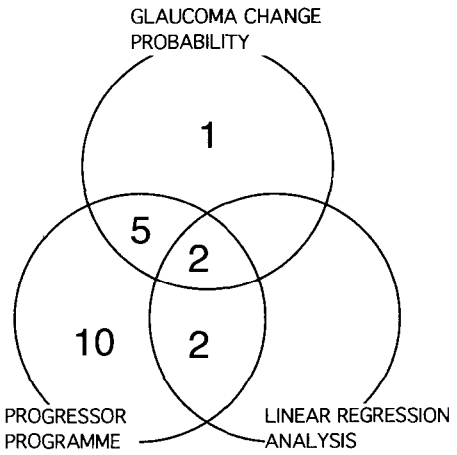

Fig 2 POAG eyes demonstrating progression by at least one statistical algorithm (n = 20 of 34 eyes)

Discussion

Early and objective determination of the progression of glaucomatous visual field loss is important because: Visual field progression is a commonly used criteria by which outcome is evaluated in glaucoma research[15]; in the clinical setting progression is also a major criteria by which disease control is measured and against which consequent decisions on medical or surgical therapy for an individual patient are made. Although AP provides objective field analysis[1] the presence of test-retest variability continues as a major obstacle to the early and objective determination of progression[5]. Subjective clinical impression almost certainly remains the most widely used means of determining progression in a series of AP fields in clinical practice. Unfortunately even experienced clinicians have been shown to demonstrate a high degree of disagreement when asked to determine progression in the same AP field series[15] Statistical algorithms have therefore been proposed, to make use of the numerical nature of the data collected by AP, to achieve both early and objective determination of true progression from long-term fluctuation At present there is no general agreement as to what constitutes clinically significant field progression in a series of AP fields, nor any generally accepted algorithm for detecting it. However, the three algorithms for the HVFA we evaluated are all commercially available and intended for use in the clinical setting.

We found a wide variation of results from analysis of the same field series with each the three algorithms LRA [Statpac] identified the least progression, detecting deterioration of the field in only 13% of eyes. GCP detected progression in 26% of eyes and Progressor Programme identified the most progression, detecting deterioration of the field in 31% of eyes. One possible explanation for LRA [Statpac] detecting the least progression of the three algorithms is that it is calculated from the "global measure" of MD and may therefore be insensitive to progression of early localized defects which have only a relatively small effect on the MD[5] LRA [Statpac] has also been criticized as being oversensitive to generalized depression such as may be caused by cataract[10]. Progressor Programme attempts to overcome these disadvantages of LRA [Statpac] by performing linear regression analysis on the threshold values at each individual test point in the visual field. There is however an estimation error for the analysis at each individual point which is then compounded when the field is considered as a whole[16] This could explain part or all of the greater tendency of Progressor Programme to detect progression in this study

LRA [Statpac] and GCP detected change in similar percentages of both OHT and POAG eyes. In contrast Progressor Programme detected change in a much higher percentage of

POAG eyes compared with OHT eyes It detected progression in 56% of POAG eyes compared with 14% of OHT eyes This may reflect either the capability of this algorithm to detect true progression in POAG eyes without the detection of equivalent amounts of fluctuation in OHT eyes, or simply a tendency to detect a high degree of spurious fluctuation, predominantly in eyes with existing defects

All three algorithms reached agreement, as to whether a field series demonstrated stability or progression in 52 of 85 (61%) of eyes. Comparisons with previous studies which have reported on the concordance between different statistical algorithms for determining progression[3,15] are difficult as they compared both a greater number of different algorithms and also included field improvement as a third possible outcome. Indeed a high degree of concordance between different algorithms is not to be expected unless all algorithms are almost equally effective What concordance between different algorithms does indicate is that some changing field series demonstrate a number of different characteristics which may individually be apparent to different algorithms

All three algorithms detected much more progression in the fields of OHT and POAG eyes than was evident by clinical impression As already discussed clinical impression has been demonstrated to be highly subjective[15] and therefore our determination of clinical impression cannot be used as a definitive "gold standard" against which to compare the algorithms However our clinical assessment was based on both review of serial fields and case notes Clinically we detected much less progression than all the three algorithms but in seven of eight eyes which were determined clinically to have deteriorated at least two or three algorithms also agreed on progression Additionally the two OHT eyes determined clinically to have converted to POAG were also the only eyes to show field defects in the last field by our defined criteria of field abnormality[14] We therefore suggest that our clinical determination of progression appears to have had at least a high specificity for true progression even if its sensitivity for true progression cannot be verified

Comparison of the three algorithms against clinical impression on this basis suggests that LRA [Statpac] was of little value, for while it was significant in the two OHT eyes that clinically appeared to convert to POAG, it was only significant in one of six POAG eyes deemed clinically to have deteriorated Previous authors have reached similar conclusions[5] and possible reasons for the failure of LRA [Statpac] to usefully determine progression have already been discussed. In contrast Progressor Programme identified progression in the two OHT eyes and five of the six POAG eyes deemed clinically to have deteriorated Additionally however it also detected significant change in a further 14 (45%) POAG eyes that appeared clinically stable Progressor Programme was the only algorithm to detect a much greater degree of progression in POAG eyes than OHT eyes Even treated POAG eyes might be expected to continue to loose field at a greater rate than OHT eyes convert to POAG. Our clinical impression also determined a greater degree of progression in POAG eyes than OHT eyes, if at a much lower overall level than determined by Progressor Programme Whether any or all of this high degree of progression detected in POAG eyes by Progressor Programme is genuine cannot be answered by this study GCP was significant in all eight OHT and POAG eyes determined clinically to have progressed Additionally it also detected the greatest amount of deterioration amongst the OHT eyes Clinically and by our definition of field defect in the final field only two OHT eyes converted to POAG making the clinical significance of deterioration at two adjacent non-edge points by GCP questionable. If we had defined significant change by GCP as deterioration at a minimum two adjacent non-edge points present, in not just the last, but in the last two fields as has been recommended[13] then GCP would have been significant in three OHT eyes but only one POAG eye and of possibly less clinical value

It appears from our evaluation that none of these three algorithms currently meets the criteria necessary to provide an objective determination of field progression by AP that is clinically significant Indeed some argue that this is not a realistic aim and that such algorithms will never be more than a limited aid to the continued determination of field progression by subjective clinical impression It is however interesting to note that of ten eyes in which GCP and Progressor Programme agreed on progression seven were also deemed clinically to have progressed. This is out of a total of only eight eyes deemed clinically to have progressed It may be that, while no current algorithm is able individually to accurately determine true pro-

gression, a combination of algorithms may come closer. Most recently a multivariate analysis[16] to determine field progression has been proposed with the aim of significant improvement over the univariate analyses evaluated in this study.

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Comparison of early visual field disturbances and their progression in POAG and NTG

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Abstract

The authors compared early central visual field disturbances and their progression in 152 eyes with primary open-angle glaucoma (POAG) and 151 eyes with normal-tension glaucoma (NTG) Central fields were examined with the Humphrey Field Analyzer program 24-2 and were classified using the box plot classification Using 52 examination points, excluding two examination points around the blind spot, the percentage of the eyes showing p values of less than 5%, 1% and 0 5% on pattern deviation at each examination point were calculated for each stage

In this study, we found some differences in early visual field changes, and also in the pattern of visual field progression to the middle stage, between eyes with POAG and NTG

Introduction

The visual field disturbances in primary open-angle glaucoma (POAG) and normal-tension glaucoma (NTG) have been reported by some to be different, and by others to be the same Thus, it is not yet clear whether or not differences in visual field changes actually exist between POAG and NTG

The Statpac program in the Humphrey Field Analyzer (HFA) calculates total deviation which is the difference between actual and age-related normal sensitivities, and pattern deviation which indicates localized sensitivity loss in the visual field[1].

In this study, visual field changes and their pattern of progression, were compared to the pattern deviation, in patients with POAG and NTG

Materials and methods

One-hundred and fifty-two eyes with POAG and 151 eyes with NTG were examined with the HFA program 30-2 or 24-2 and divided into four stages, *i e* , stage I to IV, according to the box plot classification[2] (Table 1) All eyes had visual acuities greater than 0 7, and reliability of the visual fields was satisfactory.

Using 52 examination points excluding two points around the blind spot (program 24-2), the ratio of abnormal points to total points for 5%, 1% and 0 5% probability levels on pattern deviation at each examination point were calculated for each stage

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Table 1. Number of eyes and average age in POAG and NTG. There was no statistical difference in average age at each stage between POAG and NTG (*t* test)

Box plot classification	*POAG*	*NTG*
Stage I	39 eyes 31 cases (59 3 ± 9 8 y/o)	22 eyes 20 cases (61.7 ± 8.2 y/o)
Stage II	37 eyes 24 cases (59 9 ± 14 3 y/o)	48 eyes 35 cases (59 8 ± 11 6 y/o)
Stage III	35 eyes 25 cases (59 1 ± 16 2 y/o)	43 eyes 31 cases (62 0 ± 10 6 y/o)
Stage IV	41 eyes 35 cases (61 9 ± 13 1 y/o)	38 eyes 24 cases (65 4 ± 12 4 y/o)
Total	152 eyes 115 cases (60.1 ± 13 2 y/o)	151 eyes 110 cases (62.1 ± 11 2 y/o)

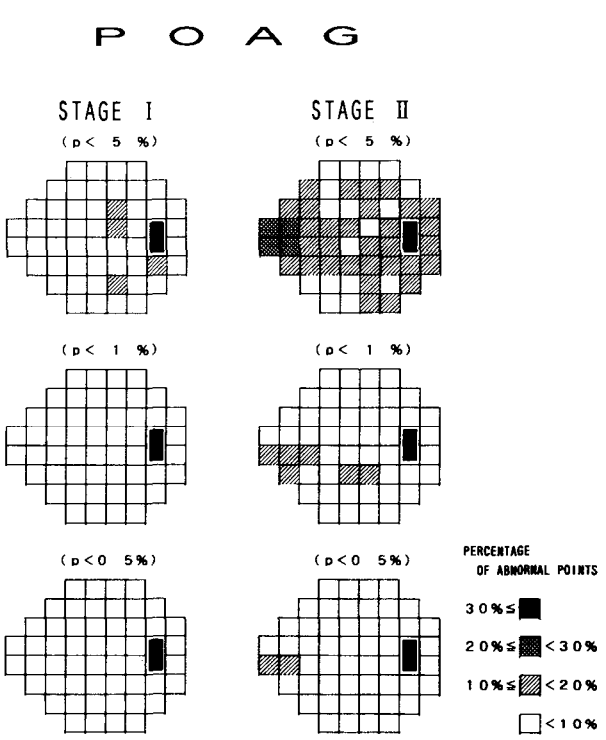

Fig 1 Percentage of abnormal points in the early stage (POAG) There was no significant difference in percentage for corresponding examination points in the upper and lower visual fields at each probability level

Results

Early visual field changes in POAG and in NTG

At the 5% probability level, points with a percentage of less than 20% lay scattered in both POAG and NTG in stage I, with no particular trend. In stage II, points with a percentage greater than 20% were found in only the upper and the lower nasal areas in POAG, and in the nasal and upper Bjerrum areas in NTG At the 1% probability level, there was no point with a percentage of more than 10% in stage I in both POAG and NTG In stage II, percentages of

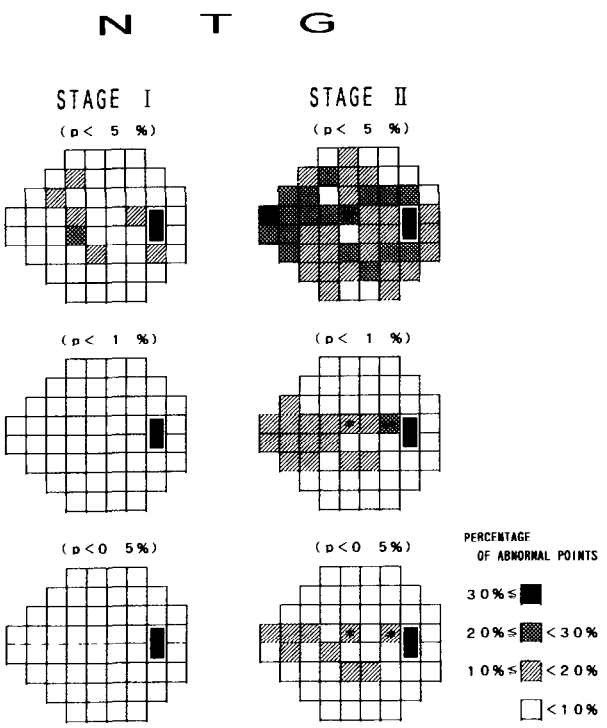

Fig 2 Percentage of abnormal points in the early stage (NTG). In a comparison of percentages for the corresponding points in the upper and the lower visual fields * represents a statistical probability level of less than 5% and ** represents that of less than 1% in the χ^2 test

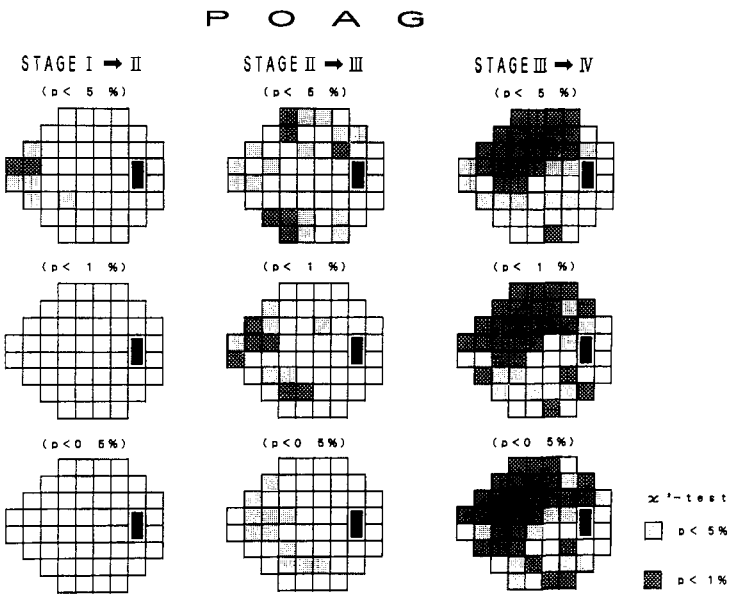

Fig 3 Pattern of visual field progression in POAG Percentage of abnormal points to total points at the various stages was compared using the χ^2 test

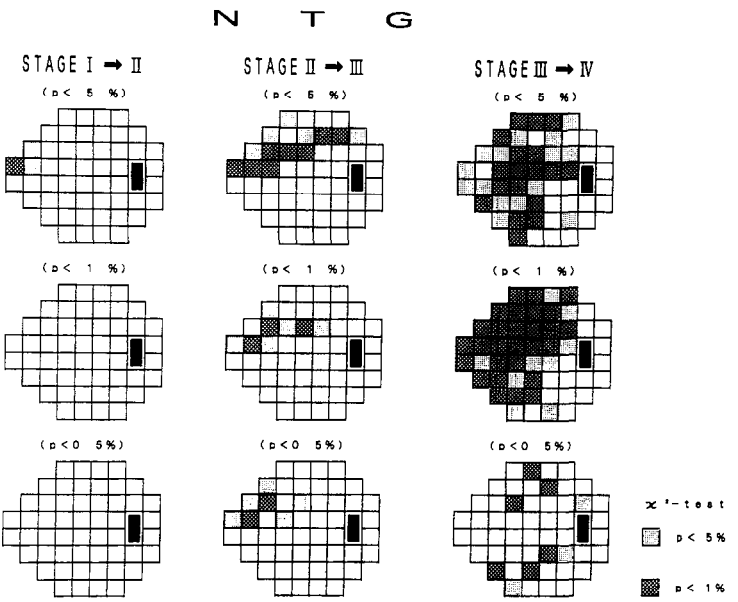

Fig 4 Pattern of visual field progression in NTG Percentage of abnormal points to total points at the various stages was compared using the χ^2 test.

more than 10% were found in the lower nasal and Bjerrum areas in POAG, and in the nasal, upper paracentral and lower Bjerrum areas in NTG. At the 0 5% probability level, there was no point with a percentage of more than 10% in stage I in both POAG and NTG. In stage II, percentages of greater than 10% were found in only the lower nasal area in POAG and in the nasal, upper paracentral and lower Bjerrum areas in NTG (Figs 1 and 2)

When the percentage of abnormal points to total points was compared in corresponding examination points in the upper and the lower visual fields, there was no significant difference at each probability level in stages I and II of POAG. In NTG, there was no significant difference in the percentages for corresponding points at each probability level in stage I. However, in the stage II, the paracentral point and the nasal point next to the blind spot in the upper visual field showed higher percentages at the 1% and 0.5% probability levels respectively, and the paracentral point in the upper visual field also showed a higher percentage at the 5% probability level (Figs 1 and 2).

These results indicate that POAG in the early stage had no significant difference in the percentage of abnormal points to total points between the upper and lower visual fields, although it had a tendency to present with defects of the nasal and Bjerrum areas in the lower visual field. On the other hand, NTG in the early stage had a tendency to present with defects of the upper nasal, paracentral and lower Bjerrum areas. In particular, the upper paracentral area in NTG had significantly higher percentages

Comparison of progression of visual field changes in POAG and in NTG

To investigate which locations were involved with progression of visual field defects, the percentage of abnormal points to total points was compared for the various stages in POAG and NTG.

In POAG, the nasal visual field was most involved as visual field defects progressed from stage I to stage II. The visual field damage then spread through the nasal area to the upper and lower fields with progression to stage III. By stage IV, however, visual field damage had spread to encompass the entire field with particular involvement of the upper rather than

lower field (Fig 3). In NTG, the nasal field was involved as visual field damage worsened from stage I to stage II, similar to POAG. However, unlike POAG, the visual field damage in NTG spread mainly to the upper field with progression to stage III. By stage IV, progression of visual field damage in NTG was again similar to that observed in POAG (Fig. 4)

Discussion

It has been reported that there are no differences in visual field changes between POAG and NTG[3–5]. On the other hand, it has also been reported that there are some changes characteristic of NTG including localized upper field defect, deep and steep defects near fixation, and absence of diffuse sensitivity loss[6–15]. Thus there is no clear concensus as to whether or not differences exist in visual field disturbances between POAG and NTG

In this study, we found that there was no significant difference between the upper and the lower visual fields in the early stage of POAG. However, the upper paracentral area in the early stage of NTG had a significantly higher percentage of abnormal points In addition, the visual field disturbances in POAG progressed in a parallel fashion in the upper and lower visual field until the middle stage (stage III), while those in NTG progressed mainly in the upper visual field only until the middle stage

These results suggest that the mechanism for optic nerve damage may be different in POAG as compared to NTG until the middle stages of disease.

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Correlation between IOP changes and deterioration of the visual field according to a nerve fiber bundle map

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Abstract

Purpose: To evaluate whether the rate of change in intraocular pressure influences the deterioration rate of the visual field in glaucomatous eyes

Method: To perform a retrospective study of 287 visual fields and the corresponding 287 diurnal intraocular pressure curves of 47 patients with chronic open-angle glaucoma (COAG) All patients had no additional corneal, retinal or optic nerve disease and were treated with a non-selective beta blocker for three and a half to ten years Eighteen (32%) patients had systemic hypertension, 29 (68%) patients had no further vascular disease A regression curve was calculated for every group of perimetric points in the visual fields (Octopus 201 program 31, worst eye approach) representing a nerve fiber bundle (according to the map of Weber and Ulrich) A correlation was calculated between the regression curve of the diurnal intraocular pressures and the regression curve of each nerve fiber bundle of every patient

Results: In the group of patients with systemic hypertension a statistically significant inverse correlation between IOP change and visual field deterioration was found in five nerve fiber bundles No such correlation was observed in the group without systemic hypertension

Discussion: We found that in patients with systemic hypertension the development of the visual field differs from those without systemic hypertension A reason for this might be found in their differing vascular properties

Introduction

Intraocular pressure (IOP) control and the rate of visual field deterioration are closely related parameters. Previous studies have analysed the progression of visual field loss depending on an average IOP reached by medical treatment or surgical therapy[1,2] As the IOP rarely remains stable in a patient during long-term observations, we applied a trend analysis to find a possible correlation between the rate of visual field loss and slowly progressive changes in IOP.

It has been reported that systemic hypertension correlates with the progression of visual field loss in glaucomatous patients[1] Additionally, to evaluate an influence of systemic hypertension on the visual field of patients with long-standing chronic open-angle glaucoma (COAG) treated with topical beta blockers, we correlated IOP changes and the visual field deterioration in individual nerve fiber bundles of patients with and without systemic hypertension

Materials and methods

The clinical charts of patients from our out-patient glaucoma department were evaluated retrospectively Patients are regularly checked for diurnal intraocular pressure and visual field at least once a year.

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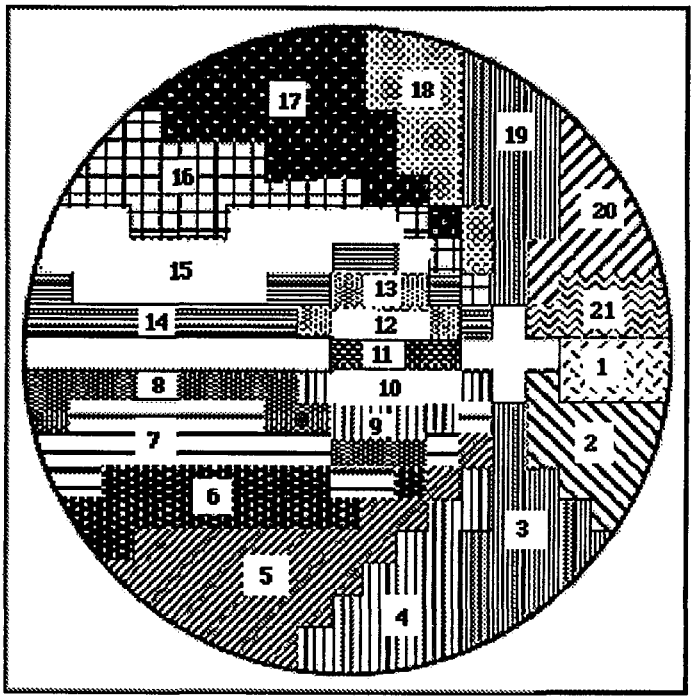

Fig 1. Nerve fiber bundle map according to Weber and Ulrich

Our inclusion criteria were:

1. chronic open-angle glaucoma treated with topical timolol 0.5% or carteolol 2% therapy for at least three and a half years without any additional therapeutic step necessary;
2. the maximum peak pressure of each diurnal IOP curve did not exceed 22 mmHg;
3. visual acuity better than 20/40,
4. no other retinal or optic nerve disease was observed;
5. at least four visual fields and their corresponding diurnal curves were available;
6 pupil diameter greater that two mm at each perimetric session;
7. previous perimetric experience;
8. no ocular surgery during the follow-up time.

Our exclusion criteria were:

1. poor reliability, defined as a false-positive error greater than 10% and false-negative error greater than 10%;
2. inexperience in perimetry

According to their vascular status two groups were created: (1) Eighteen patients with systemic arterial hypertension that was treated and stable. (2) Twenty-nine patients without known systemic arterial hypertension

The perimetry was performed using an Octopus 201 perimeter and program 31 Perimetric data were evaluated according to the perimetric nerve fiber bundle map of Weber and Ulrich[3] using the worse eye approach (Fig 1) A mean threshold value was calculated for every nerve fiber bundle of each visual field. Using these values a regression analysis of every nerve fiber bundle of each patient was performed

Table 1 Statistical comparison of age, mean IOP, follow-up time, gender, beta blocker and mean sensitivity at the beginning of the observation, between patients with systemic hypertension and without systemic hypertension

	Patients with hypertension *n = 18*	*Patients without* hypertension *n = 29*
Age (years)	65 11 ± 12 01	62 17 ± 13 25
Mean IOP (mmHg)	16.97 ± 1 38	16 98 ± 1 62
Follow-up time (years)	5 42 ± 1 87	5 41 ± 1.90
Sex (M/F)	6(33%)/12(67%)	10(34%)/19(66%)
Timolol/carteolol	12 (67%)/6(33%)	20(69%)/9(31%)
Mean sensitivity (dB)	20 8 ± 4.6	21 0 ± 4 2

The following parameters were evaluated

- Regression analysis of IOP during the observation period, calculated from the diurnal IOP curves.
- Regression analysis of the threshold sensitivity of every nerve fiber bundle during the observation period.
- Correlation between the above regression curves was performed for each nerve fiber bundle of systemically hypertensive and normotensive patients separately

Statistical analysis was carried out using the StatView 2 0 program, version 1.01 on an Apple Macintosh IIci computer

Results

The average age of the patients in group 1 and 2 was 65.11 ± 12.01 yr and 62.17 ± 13 25 yr respectively – not significantly different The mean follow-up time of the patients was 5 42 ± 1 87 yr and 5 41 ± 1 90 yr respectively There was no statistically significant difference in average IOP (16.97 ± 1 38 mmHg and 16 98 ± 1.62 mmHg respectively) or the regression coefficient of IOP (–0 01 ± 0 41 mmHg/yr and –0.10 ± 0.42 mmHg/yr respectively) during the observation period between the groups. There was no statistical difference between the two groups in sex distribution and the ratio of patients receiving timolol or carteolol medication

The mean sensitivity of the visual field for the two groups at the beginning of the observation period was not significantly different 20.8 ± 4 6 dB and 21 0 ± 4.2 dB for groups 1 and 2 respectively (Table 1).

There was no correlation between IOP change and visual field changes for non-hypertensive patients. In the systemic hypertensive group there was an inverse correlation for nerve fiber bundles 1, 4, 6, 13 and 19 ($p < 0\ 05$).

Discussion

In this study, patients with and without systemic arterial hypertension were compared for differences in their visual field development depending on progressive changes in IOP over a period of at least three and a half years In order to assess the changes, we used one of the few cluster maps that are defined from an empirical perimetric retinal map – the Weber and Ulrich nerve fiber bundle map[3]. To make a long-term observation of up to ten years possible and comparable we selected patients from our out-patient glaucoma department with COAG receiving only topical beta blocker treatment. Hypertensive and non-hypertensive patients were similar in mean age, follow-up time, IOP, IOP regression coefficient, treatment modality or sex distribution. We found that patients without systemic hypertension and IOP changes up to 22 mmHg showed no significant correlation between IOP and visual field deterioration

Patients with systemic hypertension on the other hand had a statistically significant negative correlation between visual field and IOP This correlation could be seen in five of 21 nerve fiber bundle areas Nerve fiber bundles in the temporal and especially temporal inferior retina and the inferior temporal disk region[4,5] are thought to be most vulnerable in COAG Corresponding observations are reported for visual field loss showing that the superior nasal visual field is most prone to deteriorate[1,6]. The nerve fiber bundles with the greatest correlation of IOP change and visual field deterioration in hypertensive patients could however not be placed in a specific region.

Leydhecker and Gramer found in a review of 126 eyes with COAG that 67 had a stable visual field for over five years if the IOP was below 21 mmHg at all visits[7] Similar results have been published by other authors[1,2] It is not fully understood which factors aside from ocular pressure are responsible for a favorable visual field development. Schulzer *et al* found subgroups of the glaucoma population depending on blood flow measurements, hematological and rheological variables[8] Our results show an influence of systemic hypertension on the course of glaucomatous visual field development. We suggest that glaucoma patients be divided into two subgroups, systemic normotensive and hypertensive, as these two populations differ in their vascular properties.

The vascular bed in hypertensive patients has decreased elasticity of the arterial wall. Administration of beta blockers has a different effect on blood vessels in normotensive and hypertensive patients The application of topical beta blockers in healthy volunteers showed a vasoconstrictive effect on human retinal arteries[9], while a long-term use of beta blockers in hypertensive patients ultimately leads to a fall in peripheral vascular resistance[10].

The systemic antihypertensive medication of the patients in our study showed a great diversity and varied over the period of observation It cannot be excluded, that the systemic antihypertensive medication is at least in part responsible for the observed effect on the visual field. Further evaluation of the effect of long-term systemic medical treatment of vascular hypertension on glaucoma is necessary.

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PERIMETRIC METHODOLOGY

Is there an accelerated loss at older age for normal sensitivity in the central visual field?

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Abstract

The aim of the present study was to verify whether or not an accelerated loss at older age is present for normal subjects in the central visual field 117 eyes of 117 subjects aged 9 to 86 years were tested with the Humphrey Field Analyzer 640, program 30-2, the Rodenstock Peristat 433 PRT, program GL1, the Octopus 1-2-3, program G1, our automated flicker perimeter[20,21] and the resolution perimeter of Frisén[22] Global indices were calculated as follows: mean light-difference sensitivity (MS) for the various light-sense perimeters, mean flicker fusion frequency (MF) for the flicker perimeter and mean ring score (MR) for the resolution perimeter For all procedures global sensitivity decreases with increasing age In order to verify whether or not a linear or bilinear model is appropriate for the description of the data, the statistical approach of Owsley *et al* [24] was used Both for the various light-sense perimeters and the resolution perimeter a statistically significant accelerated loss of sensitivity at older age is present This is not the case for flicker perimetry, however A possible explanation could be the stimulus configuration of flicker perimetry which is largely independent from preretinal factors

Introduction

Visual function decreases with increasing age due to
1. loss of transmission of the optical media[1–5],
2 neuronal loss in the retina[6,7], and
3 neuronal loss in the postretinal visual pathways[8,9]

The majority of studies investigating the age effect of lens transmission, absorption or autofluorescence suggests an accelerated increase of optical density at older age[1–5] There are only few authors claiming a continuous increase of lens density with increasing age[10,11]. The studies dealing with the influence of age on the cell populations of retinal and postretinal visual pathways are few and usually small in sample size[7–9] The age effects suggested by different authors are controversial, some authors suggest a monotonous decrease of cell number with increasing age[7–9], some authors even suggest a decelerated loss at older age[7]

The aim of the present study was to answer the following questions:
1. Is there an accelerated loss of normal visual function at an older age?
2. Is there an influence of the threshold criterion on the age effect?

When looking at the normal data published by various authors for automated perimetry the same controversy is present: some authors suggest a continuous loss of normal sensitivity in the visual field over the entire lifespan[12–15], others found an accelerated loss of sensitivity at older age[16–19] In order to clarify this controversy 117 eyes of 117 normal subjects were tested with five different automated perimeters

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Materials and methods

Normal population

117 normal subjects were recruited according to the following criteria: Subjects were excluded if they had corrected decimal visual acuity < 0.8 (20/25), refractive error > ± 5 dpt sph or 2 dpt cyl, intraocular pressure > 21 mmHg, media opacities (*e g*, nuclear sclerosis or subcapsular opacifications), abnormalities of the fundus (*e g*, pigmentary changes of the macula or sclerotic changes of the retinal vessels or the choroid), severe ocular trauma or any ocular surgeries, family history of glaucoma or any inheritable ocular diseases, history of poorly controlled hypertension, diabetes mellitus, multiple sclerosis, cerebrovascular accidents, epilepsy or ingestion of any psychotropic medication 24 hours prior to field testing. A complete ophthalmological examination was performed including refraction, tonometry, examination of the anterior segment with the slit lamp and examination of the fundus with indirect ophthalmoscopy in mydriasis If both eyes of a subject were eligible according to our exclusion criteria, one eye was chosen randomly for the study

The age distribution of our study population is as follows: mean 44 2 years, median 44.0 years, minimum 9 0 years, maximum 86.0 years, standard deviation 19.1 years

Instruments

Three light-sense perimeters were included in the present study: the Humphrey Field Analyzer 640 (HFA), the Rodenstock Peristat 433 (PRT) and the Octopus 1-2-3 (OCT) In addition, subjects were tested with the automated flicker perimeter (FLI) according to one of the authors[20,21] and with the resolution perimeter (FRI) developed by Frisén[22]. The light-sense perimeters are standard equipment used under clinical settings, details concerning the instrument parameters and testing conditions may be obtained from the manufacturers

The test grids of the five perimeters used for the present study are shown in Figure 1: for the HFA, program 30-2 was used, testing 77 points up to 30 degrees; for the PRT, program GL1 with 81 points up to 30 degrees was used; for the OCT, program G1 was used, testing 59 points up to 30 degrees; the program of the flicker perimeter (FLI) comprises 77 points up to 40 degrees; the standard program of the resolution perimeter (FRI) has 50 points up to 30 degrees. For each subject all tests were performed in random order. A short custom-made introductory learning test was used before the standard program for HFA, PRT, OCT and FLI and tests were run twice for FRI.

Statistical analysis

In order to study the age effect, global indices were calculated as follows: mean light difference sensitivity MS/HFA, MS/PRT and MS/OCT, mean flicker frequency MF, and mean ring score MR The MS/OCT values obtained in this study have to be increased by 1.3 dB in order to correct for a calibration error of the background luminance; the correction procedure is described elsewhere[23]. Left eyes were transformed onto a right eye grid. Statistical analysis was performed with the SPSS-software package.

Results

The scatterplots of the global indices MS/HFA, MS/PRT, MS/OCT, MF and MR as a function of age are shown in Figures 2a–e. Whereas MF shows a continuous loss over the entire life-span, there is an accelerated loss at older age for the other global indices. In order to verify whether or not a linear or bilinear fit is appropriate for our data distributions, the statistical approach of Owsley *et al*[24] was applied these authors have developed a maximum likelihood procedure for comparing linear vs bilinear fits. Two candidate models are calculated. The first model consists of a linear fit, *i e*, a single straight line. The second model defines two straight line segments which meet at a point. For each of the lines, the slope and the inter-

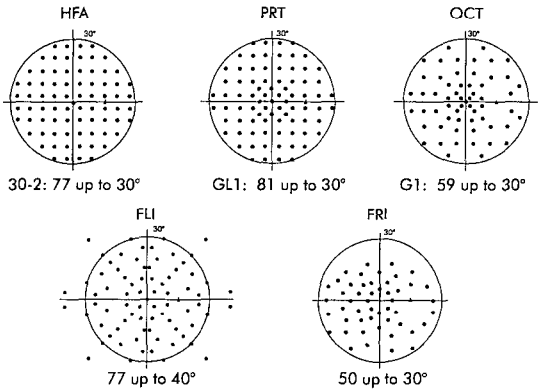


Fig 1 Test grids of the five automated perimeters used in the present study: Humphrey Field Analyzer 640, program 30-2 (top left), Rodenstock Peristat 433, program GL1 (top middle), Octopus 1-2-3, program G1 (top right), automated flicker perimeter according to Lachenmayr *et al* [20,21] (bottom left), and resolution perimeter according to Frisén[22] (bottom right)

Table 1 *P* values and age of intercept for the regression lines of the scatterplots of Fig 2a–e as calculated by the procedure of Owsley *et al* [24]

	p value	*Age of intercept (a)*
HFA	< 0 0001*	46 4
PRT	< 0 0001*	57 0
OCT	< 0 0001*	50 6
FLI	< 0 5649	—
FRI	< 0.0024*	57 0

*statistically significant

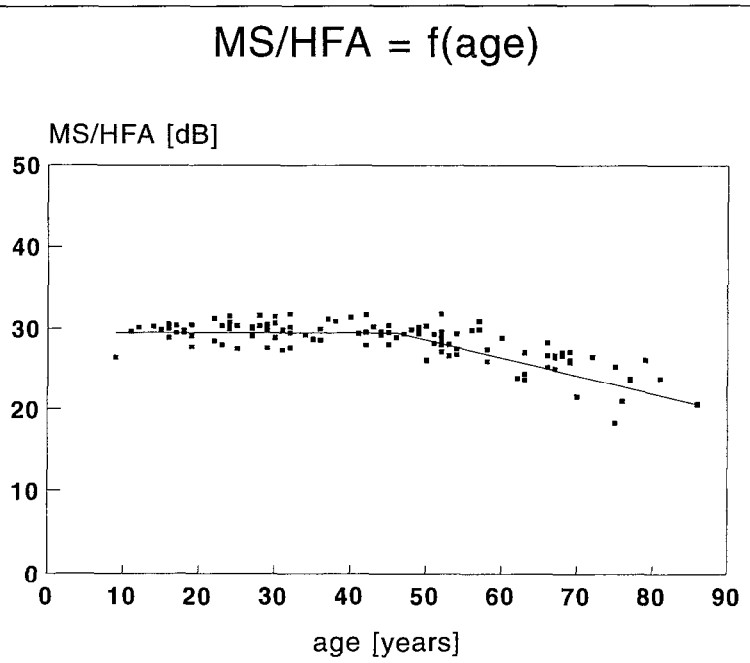
cept is calculated. In addition, the breakpoint, *i e*, the value of the abscissa where the two lines intercept, is given. For both models the multiple correlation coefficient is derived as the *r*-square value RSQ. A test is performed to decide whether the two-line model is necessary (Likelihood Ratio Test)

The model of Owsley *et al* [24] suggests a bilinear fit for HFA, PRT, OCT and FRI, whereas a bilinear fit is not appropriate for FLI (Table 1). The lines plotted into the diagrams of Figures 2a–e are the regression lines suggested by this statistical approach. Table 1 also gives the age of the intercept for HFA, PRT, OCT and FRI.

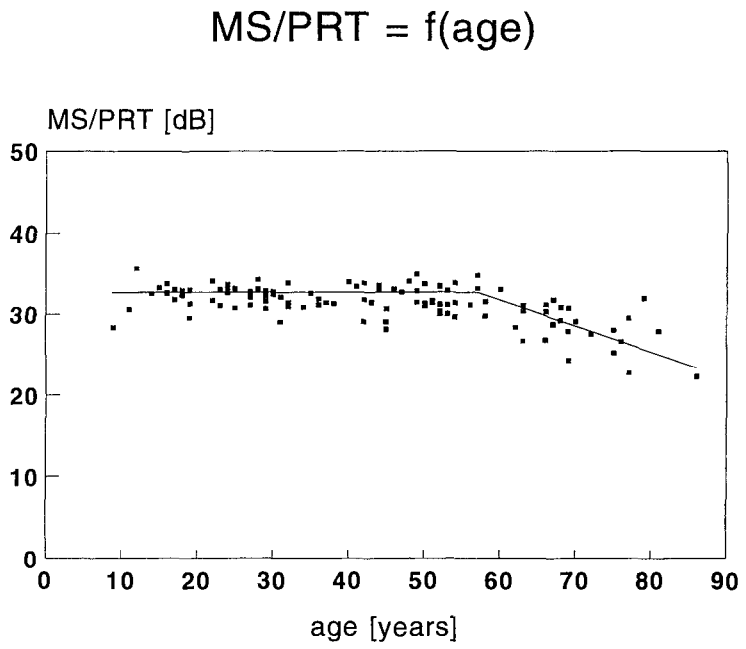
Discussion

Our data suggest that light-difference sensitivity and spatial resolution as assessed by the resolution perimeter show an accelerated loss of normal sensitivity for older subjects For flicker perimetry, in the same normal population, no such accelerated loss at older age is present. What is the explanation for this discrepancy?

The different threshold criteria of our test procedures are shown schematically in Figure 3 when testing light-difference sensitivity, an annular stimulus is projected onto a homogeneous surround; spatial resolution in the system of Frisén[22] is assessed by high-frequency filtered ring targets; flicker fusion frequency in our automated flicker perimeter[20,21] is measured with homogeneous flickering targets at the same average luminance level as the surrounding.

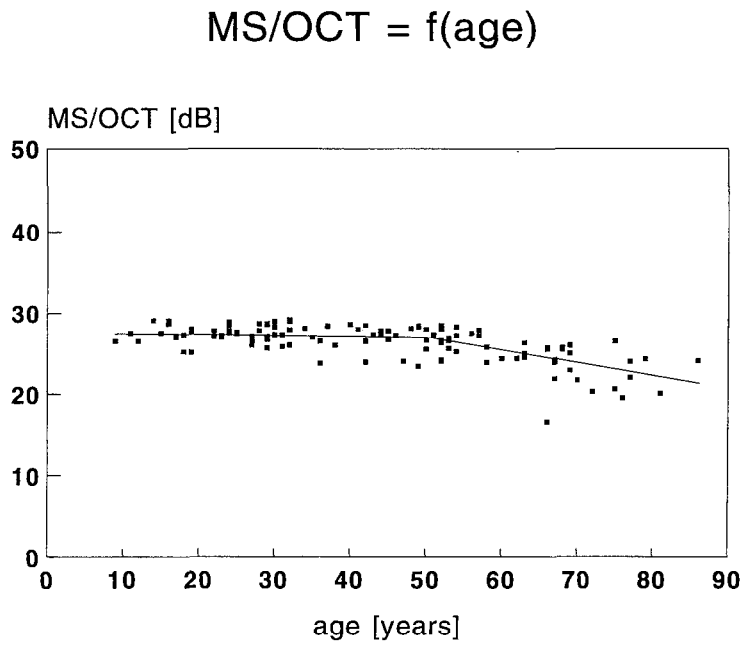


a

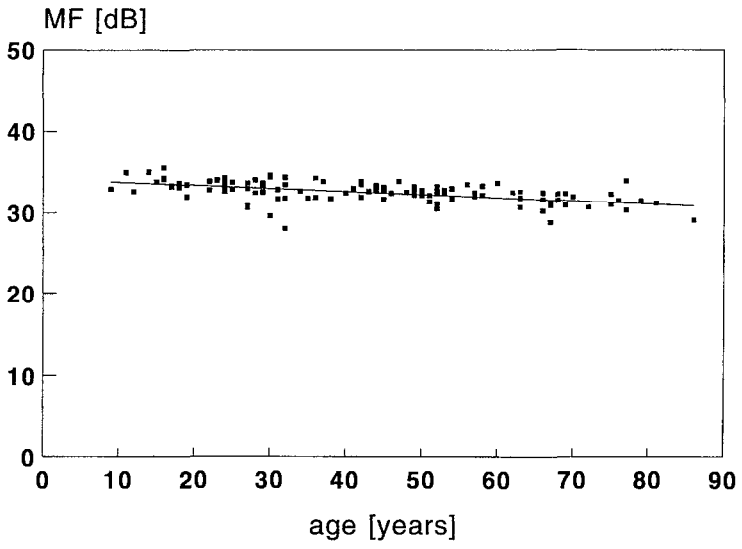


b

Fig 2 Mean light difference sensitivity MS/HFA (a), MS/PRT (b), MS/OCT (c), mean flicker fusion frequency MF (d), and mean ring score MR (e) as function of age (years). The regression lines plotted into the diagrams were calculated with the statistical model of Owsley *et al* [24]

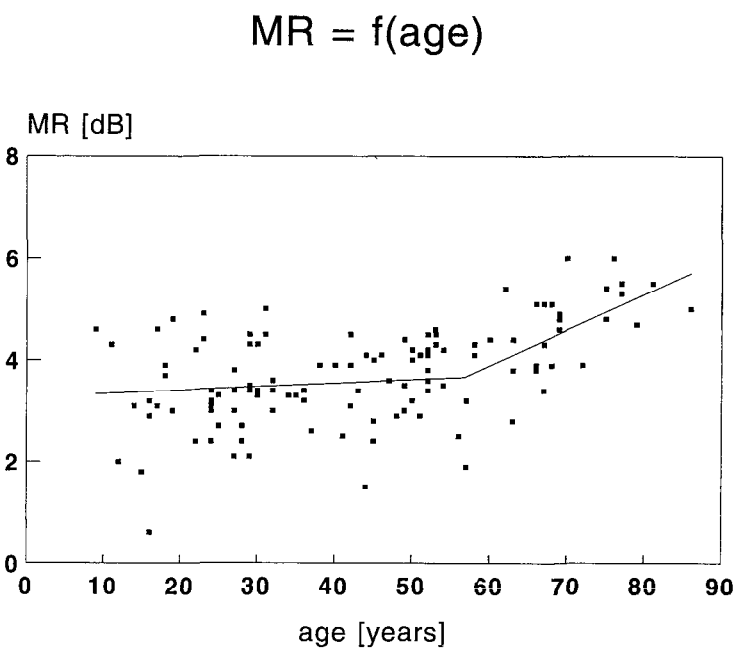

MS/OCT = f(age)
MS/OCT [dB]
50
40
30
20
10
0
0
10
20
30
40
50
60
70
80
90
age [years]

c


MF = f(age)
MF [dB]
50
40
30
20
10
0
0
10
20
30
40
50
60
70
80
90
age [years]

d

Fig 2c-d



e

Fig 2e

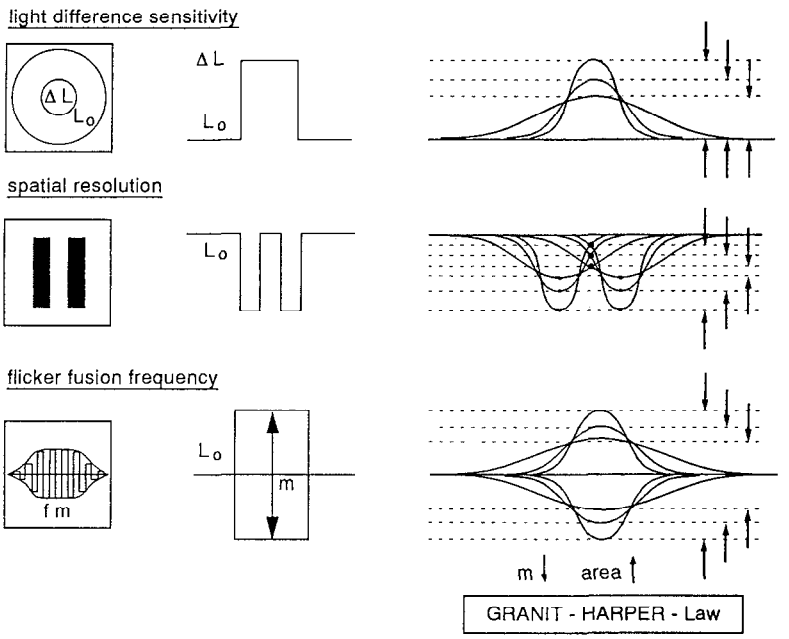


Fig 3 Schematic display of the threshold criteria used in the various automated perimeters of the present study: light-difference sensitivity (top), spatial resolution (middle), and flicker fusion frequency as measured with our system (bottom)

Figure 3 demonstrates that the threshold criteria of light sense and resolution perimetry depend on retinal image quality: when the retinal image is poor or impaired, sensitivity decreases and thresholds increase For flicker perimetry, however, blurring of the stimulus does not affect the threshold, even up to high amounts of blur Blurring the stimulus increases target area, thus compensating for the loss of contrast induced by blurring the stimulus. The increase of flicker fusion frequency with increasing stimulus area is described by the Granit-Harper law It is interesting to see that light-difference sensitivity and spatial resolution are strongly affected by refractive defocus[25–27], whereas flicker thresholds are independent from blur up to 9 dpt sph[25]

We suggest that the accelerated loss at an older age which we found for light-difference sensitivity and spatial resolution could be due to slight media opacities, present in older eyes even with normal visual acuity. Overall, light-difference sensitivity and spatial resolution in the central visual field show an accelerated loss in the older age group. However, flicker fusion frequency demonstrates a monotonous loss over the entire lifespan. The differences in behavior could be explained by the fact that flicker thresholds are largely independent from retinal image quality. Due to the lack of an accelerated loss at older age, flicker perimetry has a broader dynamic range and is less affected by artefacts from the optical media in older individuals

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Color-coded probability maps; separation of field defect types

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Introduction

The empirical Statpac probability maps have considerably facilitated visual field interpretation. Significant depressions are highlighted and many artifacts de-emphasized. The glaucoma hemifield test, GHT, was later developed based on those maps[1] The GHT is a knowledge-based expert system yielding a short written statement about a field's condition. Recently, important properties discriminating glaucomatous types of field depressions from other types caused by (*e.g*) artifacts, cataract or miosis have been explored in more detail[1–3].

It has thus been shown that· (1) physiologic threshold variability should be considered, as in *empirical probability maps*; (2) up-down comparisons, as in the *GHT*, are efficient in recognizing glaucomatous field loss[4]; (3) localized field depressions are more indicative of glaucoma if they follow the directions of the retinal nerve fiber layer as detected by *arcuate cluster analysis*[5]; and (4) diffuse visual field loss is *not* indicative of glaucoma[3].

The above four facts were all considered in the development of the color-coded probability map described here The aim was to separate: (1) glaucomatous types of field depression, (2) other localized types of field depression, (3) diffuse types of field depression, which affect the entire field, typically seen in the presence of *e.g*, cataract, and (4) apparent depressions *within* the range of physiological variability Color-coding was well suited for that purpose[6]

Test points, in Humphrey 30-2 full threshold fields, belonging to the various types of defects listed above are identified as follows:

1. *Points with glaucomatous types of depression* – all significant test points (in the pattern deviation probability map) belonging to
   (a) Glaucoma hemifield test (GHT) sectors abnormal enough to result in GHT classification "outside normal limits"[1] or
   (b) arcuate clusters (groups of significant test points adjacent along the directions of the retinal nerve fiber layer) with significant ($p < 0.01$) volume (sum of probability scores)[5].
2. *Points with other localized types of depression* – all significant test points (in the pattern deviation probability map) belonging to traditional clusters[5] with significant ($p < 0.01$) volume.
3. *Points affected by diffuse types of depression* – all test points in fields with significantly ($p < 0.005$) reduced general height (GH, *i.e.*, the 85th percentile of a subset of the total deviation values).[1]

The color-coded map is similar to the standard total deviation probability map. However, the symbols are plotted in *different colors* depending upon the results of the above-mentioned analyses Thus, all points with glaucomatous types of depression are plotted *red*; all, not yet

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colored, points with other localized types of depression are plotted *blue*; all, not yet colored, points affected by diffuse types of depression are plotted *cyan*; and all remaining test points are plotted *green*.

In fields from patients with well established glaucoma-typical glaucomatous field defects were highlighted in red color In normal visual fields the test points were plotted green. Cataract, in the absence of other ocular disorders, resulted in cyan-colored test points In fields from patients with glaucoma and cataract the glaucomatous defects stood out in red color while the remaining points were cyan Trial lens artifacts resulted only in significant traditional clusters and were thus plotted blue

Comments

Color-coding has been used before to show quantitative perimetric data. The map described here is an attempt to use color to describe *qualitative* perimetric data The analyses are based on modern knowledge of computer-assisted visual field interpretation. It is assumed that this color-coded map can aid the physician in discriminating between different defect entities. It may also be combined with text-based computer-assisted interpretation, *e g.* the GHT to clarify the text message. The need for two probability maps (total and pattern deviation) may be eliminated since discrimination between diffuse and localized defect entities are allowed within one single color-coded probability map

Similar to the GHT, the map is intended to be used in the diagnosis and follow-up of glaucoma. It is not yet applicable in neurological or retinal diseases. Further studies including visual field results from patients with such disorders may allow the construction of more general-purpose maps.

The full article will be published elsewhere

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Perimetric learning in glaucoma

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The influence of perimetric experience was prospectively studied in 37 glaucomatous eyes of 25 patients, who were all naive to any kind of perimetry Each patient underwent ten field examinations divided between five test sessions; inter-test intervals were approximately one week The 30-2 full threshold program of the Humphrey perimeter was used.

Improvement was obvious already in the greyscale representations in 57% of glaucomatous eyes. The number of normal points increased with learning and average mean deviation (MD) improved significantly ($p < 0\ 001$) between the first and second sessions, no significant differences were shown between tests two to five. Average improvement between first and fifth test sessions was 3.2 dB in right eyes and 2 7 dB in left eyes The difference in learning effect between right and left eyes was not significant Visual fields with moderate field loss showed larger improvements of sensitivity than fields with severe or mild loss

Pointwise analyses were performed to investigate learning effect *vs* eccentricity and test point status. A model was fitted which took into account the time course of learning The

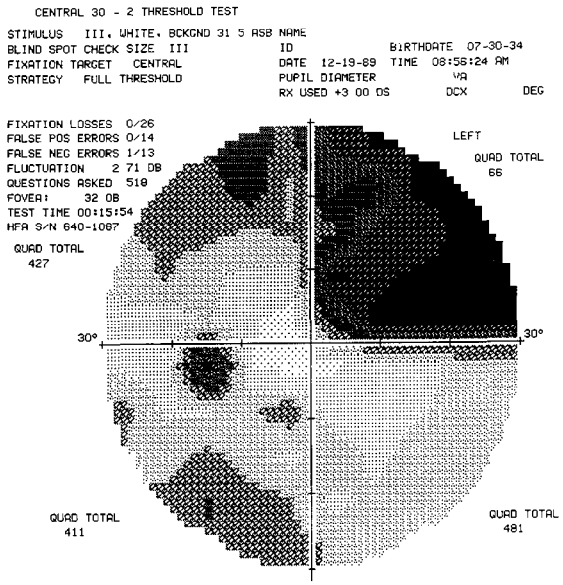

Fig 1a Series of five fields from one eye Large defect is apparent in the first field Learning effect is obvious between the first and second test session

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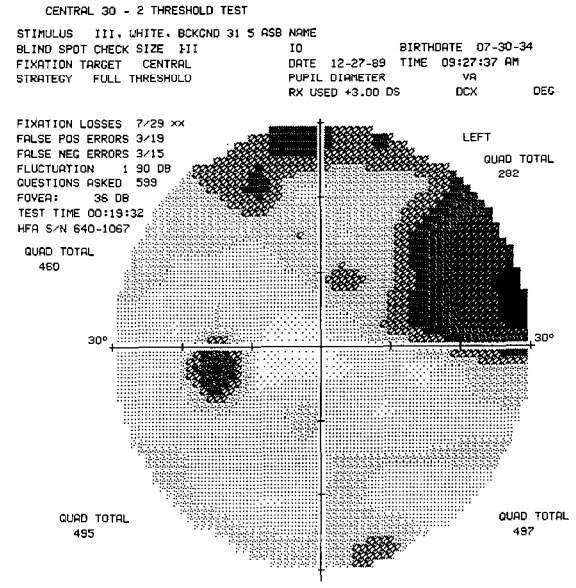

Fig 1b

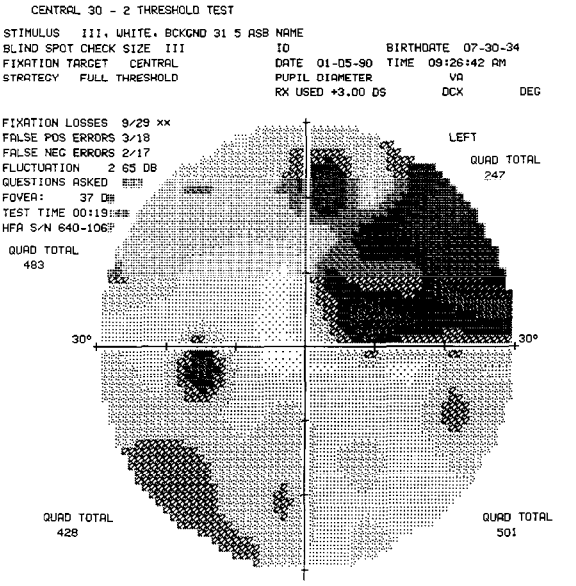

Fig 1c

learning effect and the "fully trained threshold value" were estimated for each point in each field The 30-2 test point pattern was divided into five concentric rings from the center to the mid-periphery A multiple regression analysis was then performed, using the five rings of eccentricity and the fully trained threshold value as independent variables The result showed that learning effects were more pronounced in the periphery than paracentrally Learning was also more pronounced at test point locations with better "fully trained threshold values", than at more abnormal locations

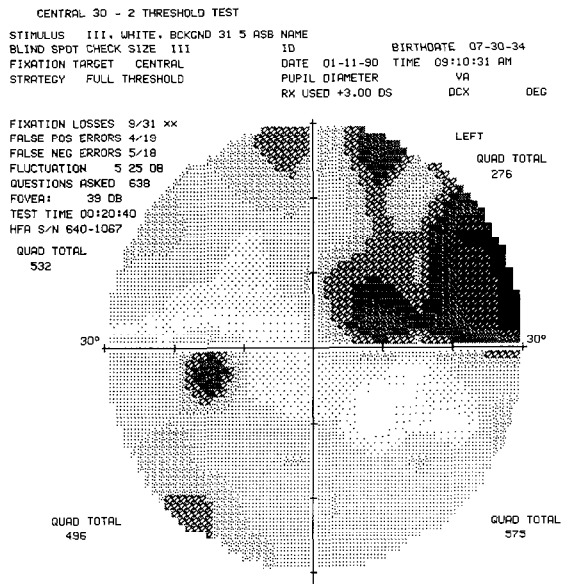

Fig 1d

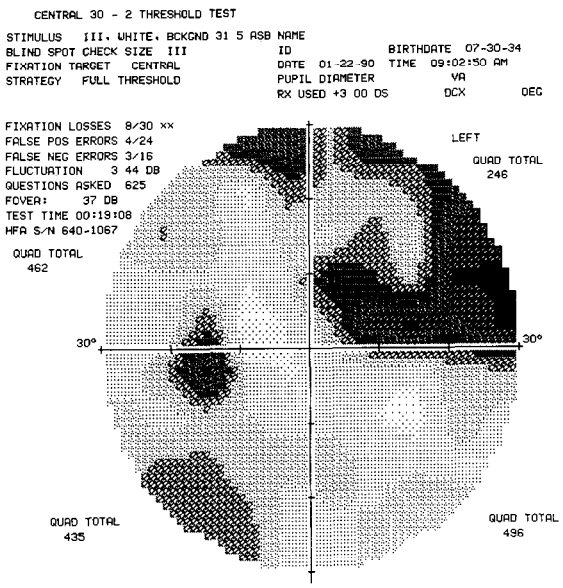

Fig 1e

The regular and large effects of perimetric learning in glaucomatous eye demonstrated by this study, clearly indicates that one initial field test is insufficient or at least not ideal as a baseline for future follow-up of glaucoma patients. Another important conclusion is that clinical studies of therapeutic measures in glaucoma require a randomized design with a control group to neutralize, as much as possible, the disturbing effects of perimetric learning

Spatial summation in glaucomatous visual fields

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Abstract

Spatial summation is the increase of sensitivity by increasing the spot size of a perimetric stimulus Despite Ricco's law and Piper's law, it is not a constant factor but dependent on sensitivity The authors investigated the amount of summation under different conditions

Study 1: Five normals and five glaucoma patients were examined with stimulus sizes I, II, III, IV and V (Goldmann notation) in random order using a Humphrey Field Analyzer in a custom program with 16 test points The resulting 80 summation curves of both groups showed great similarity The plot of sensitivity increase against initial sensitivity showed greatest summation for low sensitivity and very low summation for high sensitivity This relation was nearly linear and about the same for all stimulus sizes and both groups

Conclusion 1: Summation is mainly a function of basic sensitivity and not dependent on disease or basic stimulus size

Study 2: Forty glaucoma patients were examined with stimulus sizes III and V in random order using Humphrey program 24-2 The plot of sensitivity increase against initial sensitivity (IS) could be proved to be exactly linear It was +22 dB at IS=0 dB, +10 dB at IS=20 dB and 0 dB at IS=37 dB Eccentricity had no influence on this function The standard error of estimate of a linear regression analysis was only 2 47 dB

Conclusion 2: Summation is not dependent on eccentricity The sensitivity increase by changing from stimulus size III to V can be forecasted with very high precision The data should be used for conversion programs

The complete article will be published elsewhere.

The authors have no financial interest in the instruments used in the study

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Changes in spatial summation and SKD in the normal aging eye

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Abstract

Physiological statokinetic dissociation (SKD) and spatial summation (SS) effects are known to exist in normals, as well as in patients We have previously reported that increased SKD and SS are found in the same patients However, the relationship between these two variables needs to be assessed in the normal population as our first step in understanding how it is altered by pathology We used automated static and kinetic perimetry to investigate SS and SKD in a group of 46 normals ranging from 20 to 80 years of age We found that both SKD and SS increase with age and the two variables are directly related in all age groups. Furthermore, the slope of the function relating the amount of SKD and SS increases substantially with age These findings suggest (1) a role for changes in the number and interaction of functional detectors across the visual field with aging and (2) that caution is needed in the comparison of static and kinetic fields in older individuals.

Introduction

Statokinetic dissociation (SKD) refers to the difference between sensitivity to identical kinetic and static perimetric targets. This difference was first reported by Riddoch in 1917[1] when he noted a greater impairment for the detection of stationary targets than for the detection of moving targets in a small group of patients with post-chiasmal lesions. Since that time, this phenomenon has been described in a number of clinical populations including patients with pre-chiasmal lesions and optic neuropathies[2–6]. Physiological SKD has also been reported in normal subjects, although it is not clear how age affects this phenomenon[5–7].

In addition to reporting increased amounts of SKD in one group of optic neuritis patients, Casson *et al.* (1991) reported evidence for pathological spatial summation in another, similar group of patients[6] Spatial summation (SS) refers to increases in sensitivity associated with increases in the size of the perimetric target presented in a specific location in the visual field. There have been numerous recent studies of SS in both normals[8–10] and in clinical populations[8,11–14]. Again, the impact of age on the characteristics of SS as measured with perimetric targets has had only limited study[10].

As mentioned previously, Casson and coworkers have suggested a relationship between pathological SKD and SS, as have previous authors[5–6,15]. In this study we investigated the nature of SKD and SS in the normal, aging population and the relationship between these two variables in their physiological, rather than pathological, form.

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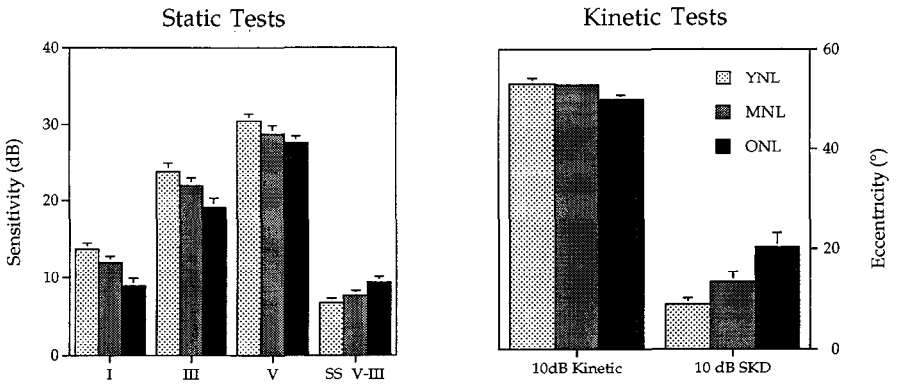

Fig 1 Average sensitivity values for static and kinetic testing for the three age groups Left panel shows the results for static testing along with the average values for the SS index Right panel shows the results for kinetic testing and the average values for SKD Error bars indicate one standard error.

Methods

We tested 46 normals (one eye only) using customized static and kinetic testing procedures on a Humphrey Field Analyzer (HFA, 10 cd/m^2 background). Static testing consisted of obtaining two threshold estimates (sensitivity in decibels [dB]) at eight equally spaced test locations between 7° and 60° along the four, 45° meridians in the visual field. Three target sizes were used in the static testing: 0 11° (Goldmann size I), 0 41° (size III) and 1.44° (size V). Five estimates of threshold to a moving target (in terms of isopters in degrees) were obtained along the same meridians in each individual, using the Humphrey kinetic testing program. A 0 11°, 10 dB target (Goldmann I4E) moving at 4°/sec was used to obtain these estimates of kinetic threshold. Static testing was done prior to kinetic testing, and the order of testing for target size and location was randomized.

The subjects ranged in age from 20 to 80 years. For the purposes of some graphs, the results were grouped according to age (12 YNL (20–35 yr), 21 MNL (35–55 yr), 13 ONL (55–80 yr)). Each of these subjects had a visual acuity of at least 20/40 and no evidence of ocular pathology or systemic disease likely to affect visual fields.

Twenty-five of the subjects were also tested on the same eye with the low contrast Regan Letter Acuity Chart (25%) with and without the brightness acuity tester (BAT) set to medium intensity[16] These subjects ranged in age from 19 to 75

The SS index was estimated by taking the average difference in sensitivity to the size V and III targets along each meridian

Estimates of SKD were obtained by comparing the average eccentricity at which the kinetic target was first seen to a value derived by interpolating from the static size I results. These were used to determine the greatest eccentricity at which a size I, 10 dB static target would be detectable. The difference between these values was obtained for each meridian tested.

The difference in performance on the 25% Regan Acuity Chart with and without the BAT (25 eyes) was used to estimate the potential impact of forward light scatter on the sensitivity to the different targets

Results

The overall estimates of sensitivity to static (left panel) and kinetic targets (right panel) are presented in Figure 1 along with the average values for the indices of SS and SKD. These data represent averages based on mean values for each individual where individuals have been separated into three different age groups as mentioned above. Sensitivity to all targets de-

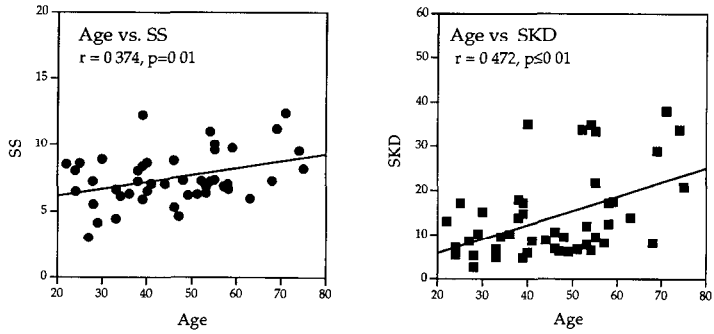

Fig 2 Scatterplots of individual mean SS values (left) and SKD values (right) against the age of the subject Regression lines are indicated Correlation values and probabilities are indicated in the upper left of each panel.

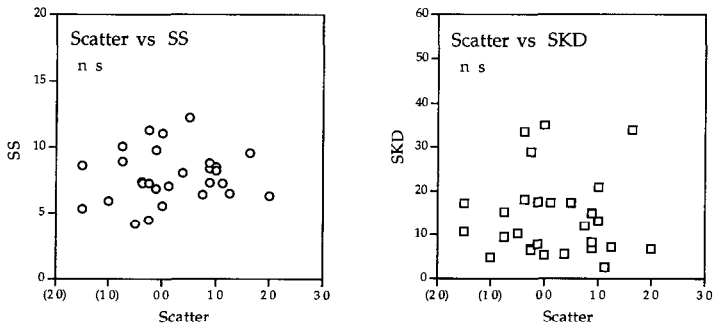

Fig 3. Scatterplots of individual mean SS values (left) and SKD values (right) against the estimates of the effect of scatter for each individual tested Probabilities are indicated as non-significant in upper left of each panel, thus no regression line is given

creases with age, but it decreases more for smaller, static targets. The SS index and the SKD index increase significantly with age ($p < 0\ 01$ and 0.02 respectively)

Figure 2 shows the mean SS and SKD values for each individual plotted as a continuous function of age. Note that both SS and SKD are positively related to age ($p \leq 0\ 01$). To determine if this increase could be due to increased light scatter in the aging lens and vitreous, we obtained estimates of scatter from 25 of our subjects The scattergrams plotting these values against SS and SKD are shown in Figure 3 In both cases the correlations are non-significant.

Figure 4 demonstrates the relationship between SS and SKD and compares the results for the YNL and ONL groups. Values for all four meridians tested are shown for each individual. All data have been normalized using the quadrant means and SDs for the YNL group to remove variability due to quadrant differences. There is a significant positive relationship (r = 0.421 and 0.579, $p < 0.01$) between SS and SKD, such that greater amounts of spatial summation in a given portion of the visual field correspond with larger estimates of statokinetic dissociation. In each case the regression line accounts for a significant amount of the variance However, the slope of the function relating SS to SKD appears to be greater in the older group; that is, the same level of SS in an older person is associated with larger amounts of SKD.

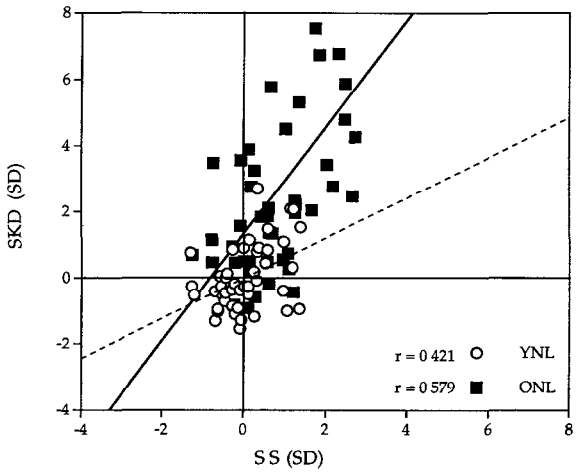

Fig 4 Scatterplot of quadrant means for SS vs SKD for younger (YNL) and older (ONL) subjects Regression lines (YNL dashed; ONL solid) and significant ($p < 0\ 01$) correlations are given.

Discussion

Our results indicate that both SKD and SS, as we have measured them, increase significantly and continuously with age These results differ from those reported by Hudson *et al.* (1991)[7] who found no significant increases in SKD with age. However, they used a different method to calculate SKD which may not be as sensitive as that used in this study.

These age-related changes cannot be due to increases in light scatter that also occur with age, since there is no significant correlation between measures of SKD or SS and estimates of scatter obtained from a cross-section of our subjects.

We have also demonstrated that there is a significant positive relationship between SKD and SS in subjects in both the older and younger age groups. This suggests, as we have previously postulated, that SKD or the greater sensitivity to moving *vs* stationary size I targets, is at least in part due to the nature of spatial summation across local areas of the visual field A moving target is summed across space and thus can act like a larger static target. Increases in SS, due to age or individual differences, indicate a relative preservation of sensitivity to large *vs* small targets. On this view, SKD, or the sensitivity to a small moving target relative to a stationary target of the same size, will increase as SS increases

If SKD is the result of the characteristics of spatial summation, any explanation of the age-related SS increases will also serve as an explanation for the age-related increases in SKD.

The characteristics of spatial summation at each visual field location and the resultant SS index are the result of two factors: classic spatial summation and probability summation. Classic SS, which occurs for smaller targets, refers to the integration of the retinal responses across an area. Probability summation, which predominates when the target is larger than the receptive fields at a given visual field location and has a much shallower slope than classical SS, is the result of probabilistically summing the responses of independent detectors within a specific retinal area. Reductions of the numbers of detectors will have a significant impact for classic SS and sensitivity to smaller targets, where sensitivity is directly related to the number of detectors. There will be less impact on probability summation and the sensitivity to larger targets, since increases or decreases in sensitivity depend on something closer to the square root of the number of detectors[17]

Curcio and Drucker (1993)[18] have reported age-related losses in ganglion cell density across the retina This would account for the reduced sensitivity to smaller static targets in the older group. Due to probability summation between detectors, sensitivity to larger targets

would be more resistant to this loss This would result in greater values for the SS index in the older group. Given a relationship between SS and SKD, this also helps to explain the increase in SKD with age.

Conclusions

Age-related changes in SKD and SS do occur and both may reflect age-related neural losses, such as those reported by Curcio and Drucker[18]. Measurements of SS and SKD may be a useful tool in characterizing age-related and pathologic changes in the visual system These results also suggest that the relationship between static and kinetic perimetry and between static perimetry with different target sizes is complex and can change with age and possibly pathology

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High resolution central visual field to detect progressive glaucomatous damage

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Introduction

Since automated perimetry was introduced in the mid-1970s, the 30° field has emerged as the most commonly tested field size when evaluating glaucoma patients One feature of the computerized perimeter is the ability to vary the tested field size and spacing, allowing high resolution testing of any portion of the field. Although most patients with early glaucomatous visual field loss have well preserved 10° fields, there are occasional patients who demonstrate reproducible paracentral defects with otherwise intact 30° fields In contrast, many patients with advanced glaucomatous damage have small remaining central islands of vision. It is this spectrum of glaucoma involving the central 8° of the visual field which has traditionally been followed by ophthalmologists with central visual field testing

Purpose

The purpose of the study was to compare a widely used standardized program, G1, with a central high resolution program, C08, each performed longitudinally with the Octopus 201 perimeter on a patient population with glaucomatous scotomata involving the central visual field. Both the ability to detect glaucomatous progression and inter-observer concordance were assessed with the two field types

Methods

Octopus G1 was performed in a standard fashion. C08 is a customized central 8° field centered on fixation with linear 2° spacing. Fifty-seven locations were tested with a single 4-2-1 dB staircase strategy Typically, 350 questions were asked during a single C08 session The overall study design was to review the charts of glaucoma patients with a minimum of four pairs of same-day G1 and C08 tests spanning a minimum of one year Typically, the G1 was performed first on a given day. Patients with confounding macular pathology were excluded so all field loss was deemed glaucomatous. Eighty patients were thus identified with a mean of 5 7 visual field pairs over a mean of 53 months The visual fields were photocopied, the G1s were separated from the C08s and chronologically arranged The patients' name and age were masked, but the reliability indices, mean defect, and variance data were available to the reviewers. Three experienced reviewers were then asked to independently review all of the fields with the G1s separated from the C08s. The reviewers were asked to make a binary as-

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Table 1 Number of patients progressing by reviewer and field type

Reviewer	*1*	*2*	*3*	*Overall*
G1 worse	22	19	22	18
C08 worse	37	36	28	34
Patient worse*	38	42	37	39
"Sensitivity" G1	58%	45%	60%	46%
"Sensitivity" C08	97%	87%	76%	87%

$p < 0\ 0001\ \chi^2$
*Patient worse = either field worse

Table 2 Inter-observer concordance (kappa index)

Reviewer	*1–2*	*1–3*	*2–3*	*Average*
G1	0 394	0 640	0.436	0 490
C08	0 654	0 536	0.616	0.602
Patient	0 501	0 577	0 573	0 550

signment for each patient and visual field type as to whether the glaucoma was stable or worse. Criteria for progression were specifically non-standardized. All three reviewers were well familiar with prior published criteria for statistical field progression. Reviewers were asked to consider long-term fluctuation and reliability indices on a case-by-case basis when determining progression. For overall results, two out of three reviewer agreement defined progression. In order to determine sensitivity of a given test, patients were considered to have progressed if either visual field type was determined to have worsened.

Results

Table 1 displays progression rates for individual and overall reviewers for each visual field type. Table 2 displays inter-observer concordance with kappa indices for each visual field type and overall patient progression. Unanimous agreement by all three reviewers that glaucoma was stable on both field types was found for 27 patients Five patients were evaluated by all three reviewers as having G1 fields that were stable, while the C08 worsened. No patients were felt to unanimously worsen on G1 while remaining stable on C08. Nine patients unanimously worsened on both field types.

Conclusion

Central visual field testing is more sensitive than standard perimetry in detecting subtle progression in this patient population with glaucomatous central visual field loss The specificity of the high resolution test remains unclear. Central visual field testing may have a higher inter-observer concordance regarding glaucoma progression compared with standard sized testing. Long-term fluctuation remains a major factor in determining progression in glaucoma patients Overall, independent reviewer concordance is only moderate when evaluating series of visual fields for glaucomatous progression.

Spatially enhanced modelling of sensitivity decay in low-tension glaucoma

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Abstract

Statistical modelling and image processing techniques are used to describe sensitivity decay over time in normal (low)-tension glaucoma (NTG). Twelve initially normal fellow eyes of confirmed LTG were used as the initial test-bed for these methods All subjects had at least 16 Humphrey visual fields (mean follow-up 5 7 years) Competing statistical models of sensitivity loss were investigated using pointwise y (sensitivity; dB) and x (time; years) data with curve fitting software The goodness of fit and predictive performance were examined Fields were then filtered using a spatial process which extracts and quantifies the inherent variability in field data The effect of this image processing technique on the modelling of sensitivity loss was assessed It was found in this group that complex polynomial expressions provided the best fit to pointwise sensitivity loss. However, a linear model of glaucomatous field decay provided the best prediction of future field status This predictive power was enhanced by an image processing technique

Introduction

The detection of true visual field deterioration is critically important to the management of glaucoma[12]. However, a clear, early diagnosis of glaucomatous field decay is difficult Firstly the rate of progression is often slow. Moreover this progression is frequently masked by the contaminating effects of variability and noise between field tests. Progression of glaucomatous field loss has been previously evaluated by monitoring a summary measure of the field over time Such global analyses are generally regarded as less sensitive than some form of pointwise assessment of field loss Change-point probability analysis[3], pointwise regression analysis[4–6] and modelling using field order in conjunction with polynomial surface fitting[7] have all recently been advocated.

In this study linear and other higher order regression models are applied to pointwise longitudinal field data. The long-term objective is to identify an appropriate pointwise model that may provide useful predictions of future field status. This could reduce the time elapsed and therefore the number of field tests needed before true deterioration can be diagnosed. The test-bed for this initial investigation is a sample of untreated eyes at high risk of developing normal (low)-tension glaucoma (NTG) with individual locations which were deteriorating Using time of field test (x) and sensitivity (y) data from each of these locations an array of candidate curvilinear and linear models are firstly assessed on the extent to which they adequately fit

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sensitivity loss over time (*curve-fitting analysis*) Secondly, they are assessed on the potential to forecast future sensitivity values when projected over time (*prediction analysis*).

Additionally this paper illustrates how the predictive performance of the optimum point-wise model can be improved This method uses an image processing technique which exploits the spatial dependence that exists between the sensitivities of neighboring locations[8]. This method has the joint effect of reducing the variability between tests and adding spatial information into the modelling procedure which in turn can improve forecasting precision.

Methods

Subjects and data

Twelve patients with confirmed normal (low)-tension glaucoma (NTG) were selected. All had visual field defects in one eye but initially normal fields in the other eye. Humphrey field (30-2 program) series were chosen from these latter eyes which, as fellow eyes of confirmed NTG, were considered at high risk of developing field defects. A normal initial field status was defined as no clusters of more than three locations with symbols representing a probability of abnormality ($p < 2\%$) on the Humphrey Statpac pattern deviation plot in either field two or three[9] (The first field of all eyes was excluded to reduce learning effect) Additionally, none of the eyes had significant MD (mean: (0 4, SD: 1 0 dB) or CPSD (mean: 1.3; SD: 1.0 dB) in either fields two or three

All patients had in excess of 16 fields available with mean follow-up of 5 7 years (SD: 0 4 years) Any additional fields in excess of 15 (after learning field exclusion) were omitted. This equalized the number of fields for each patient and balanced, as far as possible, the follow-up period and time elapsed between tests (mean: 0 4 and SD 0.1 years) The peripheral locations of the 30-2 grid (x or y coordinates of +/– 27) and locations above and below the blind spot were excluded from further analysis

Locations for the curve fitting and prediction analysis were selected from this cohort if they demonstrated unequivocal loss at the final two fields of the series of 15 fields. The criterion for this loss was the development of a threshold which was depressed by more than 10 dB below the age-matched Humphrey normal database value and was reproducible in both the final two fields Five of the initially normal 12 eyes had at least one location which fulfilled this inclusion criteria resulting in 51 locations in total This sample was reduced to 47 locations by further exclusion of locations with final thresholds of zero dB This value may represent a luminance sensitivity outside the dynamic range of the perimeter

Curve fitting analysis

Data from each of the 47 locations expressed as x (time in years) and y (luminance sensitivity dB) was analyzed separately using automated curve-fitting software (Tablecurve, Jandel Scientific Corporation). This program automatically applies 221 different curve models to the data Models which provided a statistically significant fit ($p < 0\ 01$) were then ranked according to the level of *goodness of fit* in descending order of R^2 (least squares). The model which provided the best fit (highest R^2) was recorded. Additionally R^2 values of four other candidate models, namely linear ($y = a + bx$), quadratic ($y = a + bx^2$), cubic ($y = a + bx^3$) and exponential ($y = a + be^x$) were recorded

Prediction analysis

The potential of the candidate models to predict future sensitivity at each location was investigated by firstly repeating the curve fitting analysis using only the first five fields The best fitting model (normally a high-order polynomial) and the four other candidate models were then extrapolated to the date of the final (15th) field The projected or predicted threshold at this point was then compared with the actual measured threshold for each location and for each candidate model.

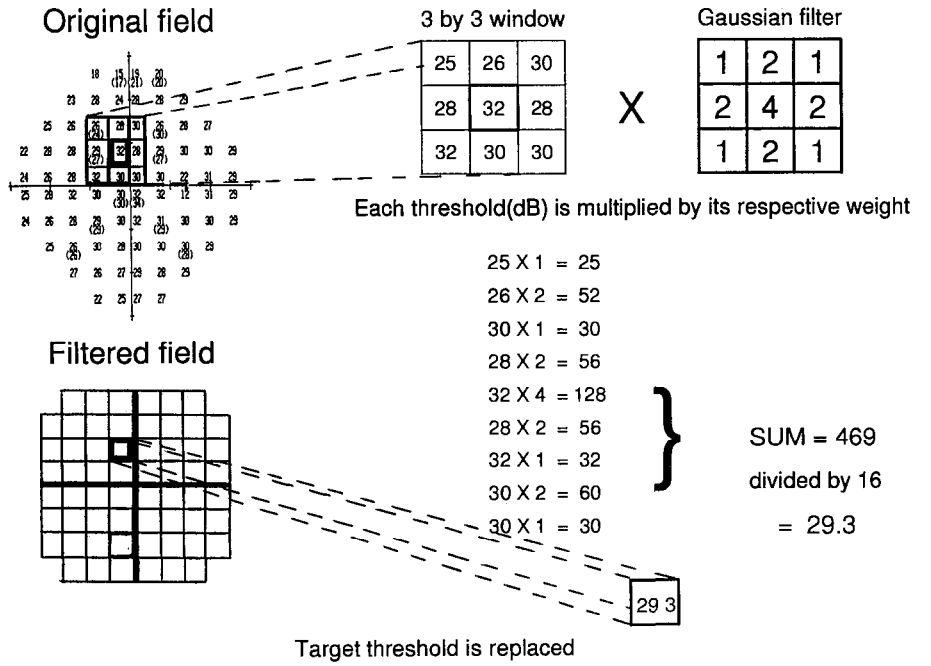

Fig 1 Gaussian filter process

Table 1 Summary of R^2 values for candidate models

Curve model	*Median R^2*	*Range*	*No of locations fitted*
Best fit curve (complex polynomial)	0 93	0 48 to 0 99	47
Exponential curve $y = a + be^2$	0 61	0 26 to 0 95	35
Cubic curve $y = a + bx^3$	0 55	0 29 to 0 90	38
Quadratic curve $y = a + bx^2$	0 55	0 28 to 0 92	38
Linear curve $y = a + bx$	0 53	0 26 to 0 85	36

Image processing and predictive performance

Spatial filtering is a widely used image processing technique Here the visual field is considered as a digital image composed of a matrix of luminance threshold values. A filter, which can be thought of as a small 3 × 3 window, is passed over each location in turn across the original field. In this application a Gaussian filter is used (Fig 1) Each central value in the 3 × 3 window or neighborhood is replaced by a weighted average of the adjacent values. Partial neighborhoods are used at field edges and corners.

For this analysis all the locations from the five eyes that had at least one location that fulfilled the progression criteria were used. The model that provided the optimum prediction performance from above was fitted to the first five fields and projected forward to give a forecast of sensitivity at the final (15th) field for all locations The predicted value, from these raw

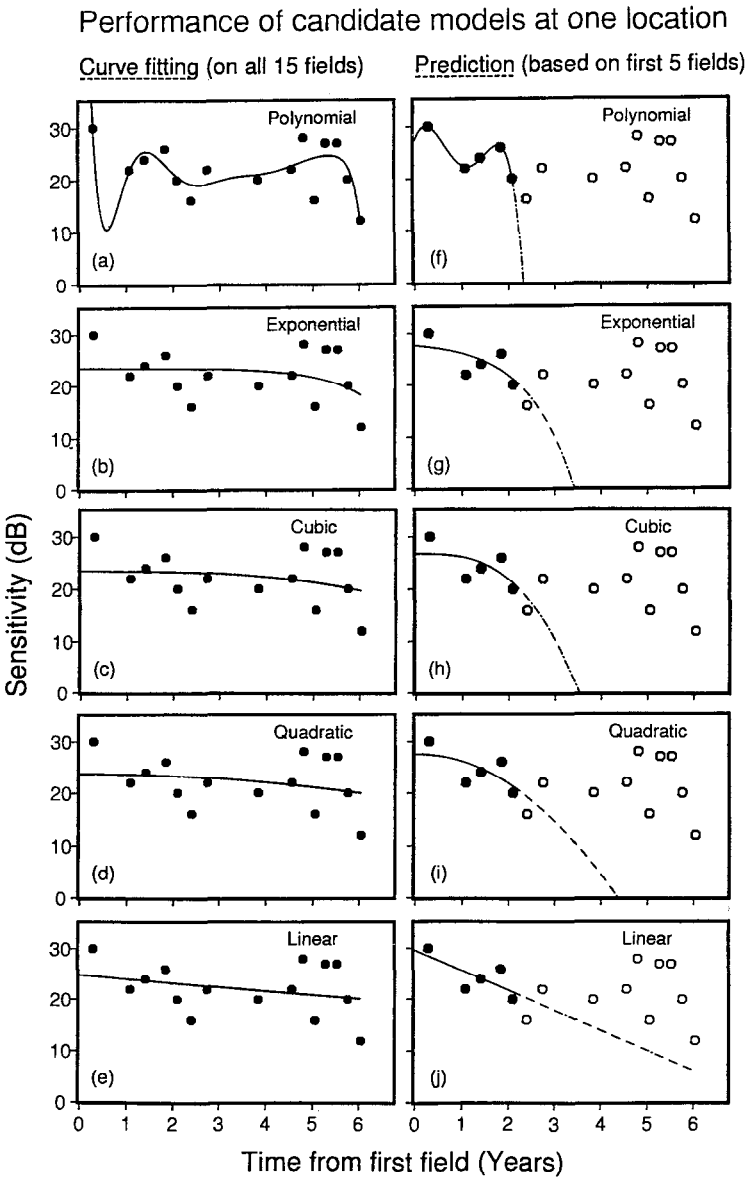

Fig 2 Example location from one of the studied eyes (a) to (e) show fit of candidate models to all 15 fields in time. Dashed lines on (f) to (j) represent predicted projections. Only the linear prediction lies inside the illustrated range

data, was compared to the actual measured value. This operation was repeated using the processed fields (1 to 5) generated by the Gaussian filter. The extrapolated value at the final (15th) field, from these processed data, was then compared to the actual measured value to ascertain any improvement in predictive performance due to the spatial filtering

Table 2 Summary of predictive performance of candidate models

Curve model	*Median absolute prediction error*	*Range*
Best fit curve (complex polynomial)	1116 dB	0 to 7589 dB
Exponential $y = a + be^x$	374 dB	107 to 1117 dB
Cubic $y = a + bx^3$	209 dB	37 to 1157 dB
Quadratic $y = a + bx^2$	44 dB	0 to 219 dB
Linear $y = a + bx$	11 dB	0 to 44 dB

Results

Curve fitting analysis

The results of the curve fitting analysis on the 47 locations are summarized in Table 1 Large numbers of actual significant fits and high R^2 are indicators for best fitting models. Clearly the models which demonstrated the best fit using these criteria were all complex high-order polynominal expressions The median R^2 of the best (polynomial) models for each location was 0.93 (range 0 48–0.99). The less complex curvilinear and linear candidate model demonstrated a statistically significant fit at fewer locations and exhibited lower median R^2 for those locations that were fitted There was a statistically significant difference between the median R^2 of the best (complex polynomial) models and all four of the simpler models (Kruskal-Wallis test $p < 0\ 001$). Figure 2a–e shows an example location fitted with all the candidate curve models

Prediction analysis

The candidate models were fitted to the first five fields and extrapolated to generate a prediction of the sensitivity of the location at the final (15th) field An illustration of this and the behavior of the candidate models is shown for an example location in Figure 2f–j. The dashed line represents the path of the model projected to the final (15th) field The actual prediction error for each model at each of the 47 locations was calculated as the absolute difference between the predicted and actual threshold measurements. Summary results for the candidate models are shown in Table 2. These clearly indicate that the magnitude and spread of the prediction errors are largest with the complex polynomial models and smallest (most accurate) with the linear model, with others intermediate

Image processing and predictive performance

All the locations from the five eyes that fulfilled the progression criteria were used (290 locations). Figure 3 illustrates results from one of these eyes Each individual plot represents its particular location with sensitivity (dB; y) and time (years; x) The linear model (best predictive accuracy from above) was fitted to the first five fields (filled symbols) and extrapolated (dashed line) to the date of the final (15th) field. The *error* shown for each location is the absolute difference (dB) between the predicted and measured value at the final (15th) field. Figure 4 shows a similar representation of the same eye with a linear model fitted to the first five fields which, in this case, have all been separately processed by the Gaussian filter. Note the linear projections now have slopes that are more consistent in direction and gradient. Bold axes and an asterix symbol indicate that the prediction error at that location has decreased as a

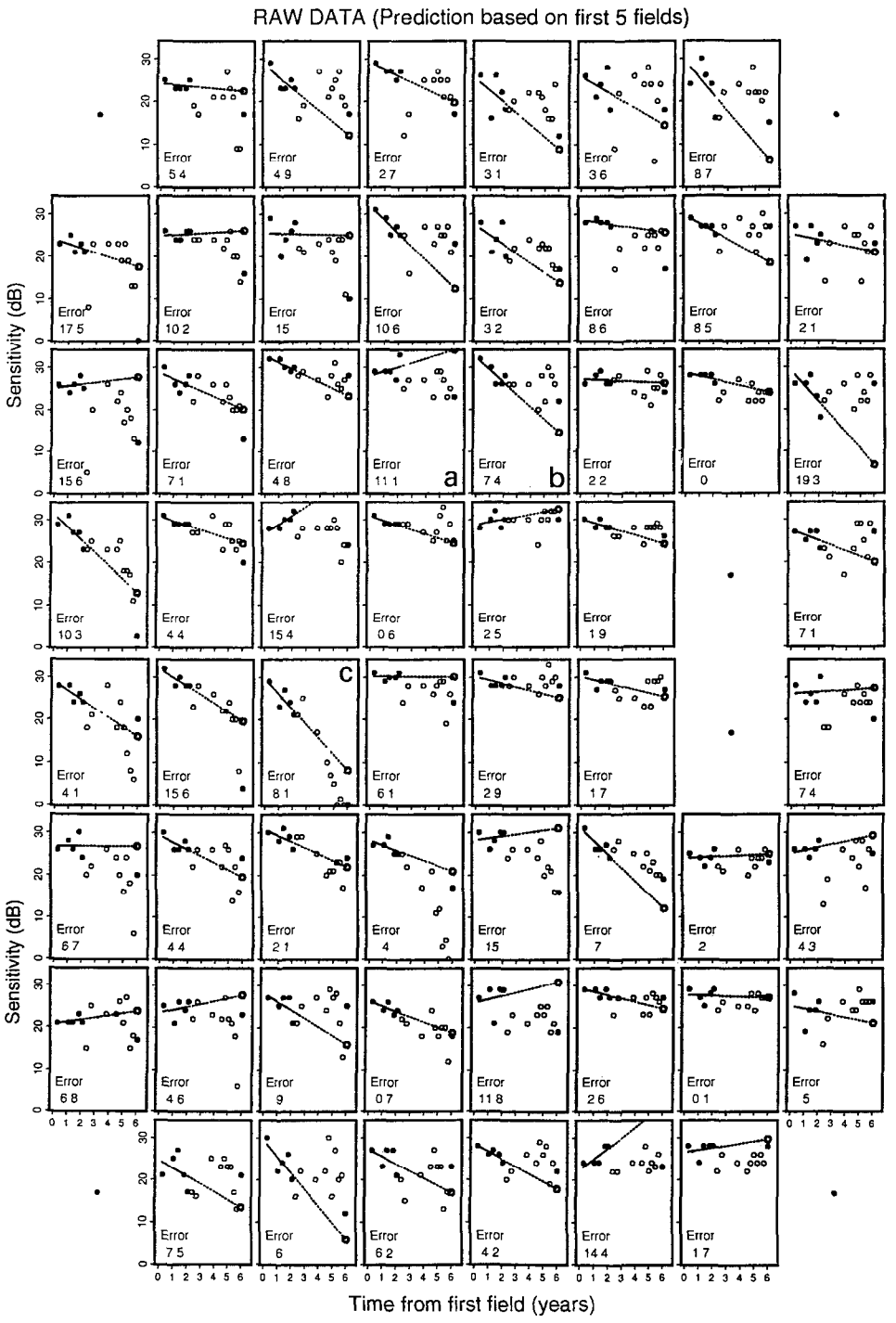

Fig 3 Locations modelled for an example eye (raw data)

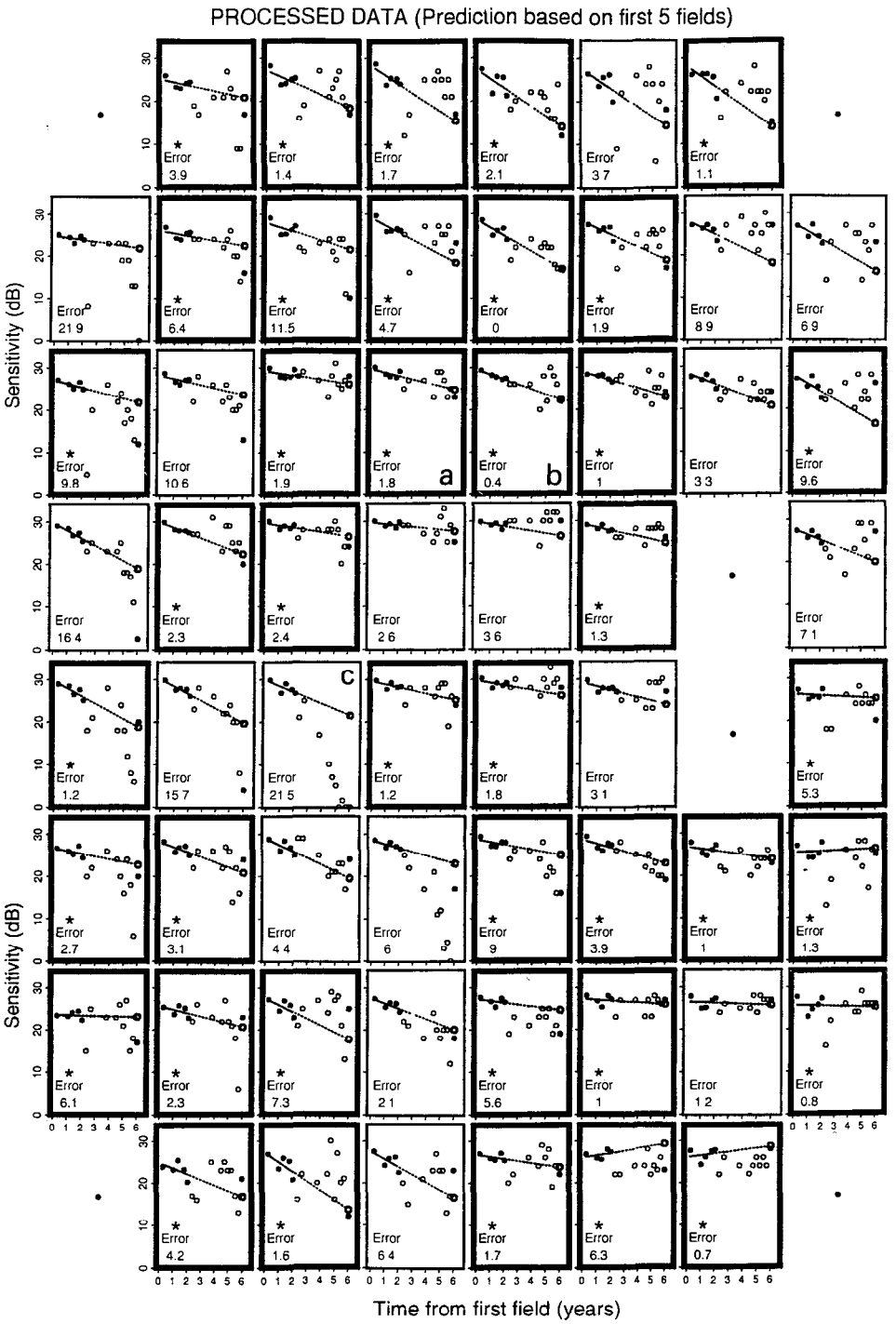

Fig 4 As Figure 3 but with predictions based on modelling the processed data Bold axes and asterix indicate a location with improved prediction error as a result of processing

result of the image processing technique. In this case 40 locations (69%) exhibited an improved prediction error. In fact for the whole sample (five eyes) 74% of the 290 locations had an improved prediction error as a result of modelling the processed data. Moreover, the overall median forecast error was reduced from 9.6 dB (range 0 to 44.4 dB) to 7 3 dB (range 0 to 29.4 dB) as a result of modelling the processed data. This represents a statistically significant improvement in the predictive performance (Wilcoxon ranked paired test; $p < 0.01$).

The reduction of between test variability and spatial processing has improved the specificity of identifying progression with the pointwise linear model Illustrative examples are the locations labeled (a) and (b) in Figures 3 and 4. However, this particular filter process causes the pointwise linear model to be relatively insensitive to localized loss. (For example, the location labeled (c) in Figures 3 and 4)

Discussion

The results of the curve-fitting analysis on 47 Humphrey locations from five initially normal fellow eyes of NTG show that complex polynomial models give the best R^2 values to pointwise longitudinal data. Simpler expressions fitted fewer locations significantly and demonstrated lower R^2 values However, when the potential to predict future visual field status was assessed, the best predictive power was demonstrated by the linear model in spite of lowest R^2 values. This seemingly apparent contradiction can be explained with some insight of statistical modelling Increasingly complex models provide a better fit but at the expense of modelling more of the variation inherent in the data R^2 alone is a poor indicator of the suitability of a given model to describe a trend, particularly if the data are subject to variability or noise. Moreover, R^2 simply increases às a function of the number of parameters within a model. Generally the most appropriate model is a simple expression which both fits the data and gives the lowest prediction error. The results reported here suggest that pointwise glaucomatous sensitivity decay in this group of NTG eyes is adequately described by a linear model. Adopting such a model violates statistical assumptions such as the non-independence of the longitudinal data in both time and space. Other issues include the dangers of extrapolation and the use of the significance of fit. Nevertheless the seemingly monotonic underlying trend, or rate of loss, in glaucomatous progression is amenable to pointwise linear modelling techniques.

Image processing techniques can improve the repeatability of visual field testing as well as extract and quantify the variability within the data[10,11]. Importantly, image processing techniques can provide a framework within which reduction of between test variability and important spatial information can be built into the modelling of visual field loss. An example has been reported here demonstrating how the predictive performance of the linear model was improved by pre-processing the modelled fields using a simple Gaussian filter. However this particular process is insensitive to highly localized loss. One solution to this problem may be to develop an algorithm which *switches* between modelling the raw and processed data points. Moreover, other image processing operations are currently under investigation, including those customized specifically to the pathological configuration of the field, that reduce *noise* and detect important *signal* changes. Used in tandem with pointwise linear modelling these methods may provide an important advance in the detection of true glaucomatous field progression.

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Acceptable false response rates for reliable perimetric outcomes

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Abstract

A 33% false-positive (FP) or false-negative (FN) rate is commonly used to flag an unreliable test This criterion has been determined by considering the response profiles of normal observers rather than the effect that such errors have on perimetric outcomes In this study, we evaluate the effect that different false-positive and false-negative rates have on perimetric results

Artificial FP and FN rates (0%, 33% and 50%) were generated in a random manner, while a subject underwent full thresholding of 100 points within the central 30° Four repeat tests were performed in the same one-hour test session Mean threshold, field variance and the number of abnormal points were calculated and compared for the three FP and FN rates; field variance is the mean of the point-wise variance (in dB^2) of the field over the four tests

Mean threshold was significantly increased by a 33% FP rate and significantly decreased by a 33% FN rate Field variance increased significantly for the 33% FP or FN rate The number of abnormally supersensitive points was significantly increased by a 33% FP rate and the number of abnormally depressed points was significantly increased by a 33% FN rate These findings lead us to conclude that a 33% reliability criterion is too generous for accurate clinical perimetry with significant changes in field parameters occurring by this level Accepting a 33% false response rate may hinder the detection of field loss or progression

Introduction

Automated perimetry is a psychophysical task and as such is subject to all the trappings of behavioral experimentation performed on human subjects. Several factors limit the capacity of such measurements, namely fluctuations and false responses Fluctuation is sometimes called stimulus-related noise. It arises from an inherent variability in the stimulus or the visual system's response to such stimulation[1]. On the other hand, false responses are subject dependent and can be termed extraneous noise[1]. They manifest in otherwise reliable observers[2] but usually not at a very high rate. It has been suggested that such false responses are more numerous in the early stages of a perimetric test when a significant learning effect is present[3] although others have failed to show any association between false responses and learning[4].

False responses can be of two types; false positive or false negative A false positive occurs whenever the subject responds in the absence of a stimulus[5]. This suggests a certain level of "trigger happiness" and that the subject's response may be driven by factors other than the presentation of a stimulus. These driving factors may be sounds, entopic phenomena, a lack of

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understanding of the test procedure (including slow responses) or a desire to perform well at the test. A false negative occurs when the subject fails to respond to a stimulus due to inattention or for other reasons In automated perimetry, false negatives are measured by determining the miss rate for a suprathreshold stimulus[5].

The effect that such false responses have on perimetric outcome varies False positives act to elevate the lower limit of the psychometric function whereas false negatives act to lower the upper limit of this function. In perimetry most staircase procedures use a limited number of responses to estimate threshold and assume a reliable observer. Therefore the presence of false positives or false negatives will act to reduce or elevate the resultant threshold respectively. The clinical interpretation of false negatives is less clear than for false positives. The presence of a moving scotoma can increase the false negative rate even in reliable subjects[6]. Furthermore, high FN rates have been reported in glaucoma patients suggesting that this may be a sign or consequence of glaucomatous change rather than an index of reliability[7,8].

The purpose of this study was to investigate the consequence of elevated false response rates on the perimetric outcomes obtained in an otherwise reliable observer

Materials and methods

The Medmont M600® perimeter was used in this study. This is an LED perimeter that has been described in detail elsewhere[9,10] In short, the perimeter has a 3.2 cd/m^2 (10 asb) background intensity and a maximum stimulus brightness of 318 cd/m^2 (1000 asb). LEDs (0.43° diameter at 33 cm viewing distance, λ_{max} = 565 nm) are arranged in concentric rings at various eccentricities. For this study a full threshold logic was used in the central visual field (< 30°). The thresholding algorithm in this perimeter uses a 6/3 dB staircase procedure. During thresholding, approximately 6% of all stimuli are FP or FN catch trials. FP catch trials consist of a 1.2-second pause in stimulus presentation, any patient response in this period is counted as a FP response FN catch trials only commence once threshold has been estimated at some locations No response to a stimulus that is 9 dB brighter than the previous threshold estimate is registered as a FN response

Special software was written for this experiment to artificially generate false responses internally (positive or negative but not both in the same test) in a random manner at any rate between 1 and 99%. For example, when set to the 10% FP rate there was a 10% probability that any "not seen" response would return a "seen" status to the staircase algorithm Similarly for FN rates, the selected proportion of "seen" responses would be registered as "not seen". This logic did not apply to the fixation monitor so that reliable information regarding fixation was always available

Two rates of artificial false responses were examined, 33% and 50% These were used for both FPs and FNs with a 0% condition being used as the control It should be noted that under the control (0%) condition the observer's internal false response rate was present A total of five test sessions, each lasting about one hour, were required to gather the data over a two-day period The order of the sessions was randomized prior to commencement of the study. Four repeat thresholds were obtained at each level of false response studied. The data presented in this study were obtained from a 25-year-old well trained observer who has no systemic or ocular disorder.

Three factors were used to assess the effect that these false responses have on visual field outcomes, *viz* , the mean threshold, the field variance and the number of abnormal points Each of these measures were considered important for the clinical interpretation of perimetric data. Mean threshold was calculated as the mean of the four repeat tests over all points. Field variance was calculated as the average pointwise variance of the four repeat tests. The number of points with abnormal thresholds were assessed by performing a pointwise comparison between the mean threshold at each location and the threshold expected from age-matched norms used by the manufacturer. A point was considered abnormal if it was removed from the normal value at the $p < 0.05$ level. The significance of the number of abnormal points was as-

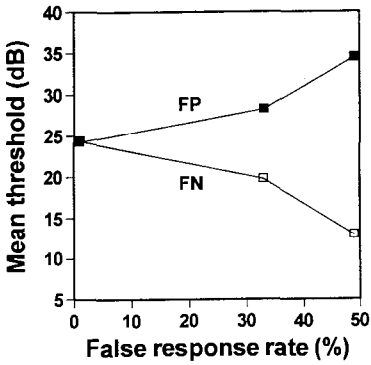

Fig 1 Mean threshold (dB) versus percentage false response rate Standard error of the mean is smaller than the symbol

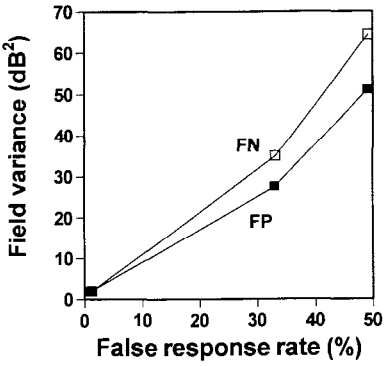

Fig 2 Field variance (dB^2) versus percentage false response rate Standard error of the mean is smaller than the symbol

sessed using a χ^2 analysis, other comparisons were made to the control condition (0%) using a paired *t* test

Finally, we considered how well the internal catch trials actually detected the false responses being generated. This was done by comparing the specified false response rate to that reported by the perimeter. This issue is important because it reflects the clinician's capacity to identify unreliable tests

Results

The mean thresholds for the five false response states is shown in Figure 1 There is a significant increase for the 33% and 50% FP rates ($p < 0.0000$) False negatives have the opposite effect and there is a significant reduction for the 33% and 50% FN rates ($p < 0.0000$).

Field variance (FV) for the five false response states is shown in Figure 2. It can be seen that the FV is significantly increased by 33% and 50% FP and FN rate ($p < 0.0000$)

The number of abnormal points in the field is shown in Figure 3a These data show that there is an increase in the number of abnormal points by a 33% FP rate. By a 33% FN rate the number of abnormal points is also increased However, Figure 3a indicates that even at the 0% false response rate our observer generates a substantial number of abnormal points with high sensitivity This is because our highly trained observer is more sensitive than is the average control. If correction is made for this higher than expected sensitivity (Fig 3b) then the data for the 0% false response rate generate no abnormal points Figure 3b shows that even after such sensitivity normalization there is a significant number of abnormal points when 33% false positives ($p < 0.005$) or 33% false negatives ($p < 0.005$) are occurring.

The number of false positives and false negatives detected by the usual catch trials are shown in Figure 4. The filled symbols indicate those false responses that are under study whereas the unfilled symbols indicate the fellow false response category It can be seen that the average number of false responses detected by catch trials is close to the true number occurring. However, a substantial spread is found about these values (small symbols Fig. 4) When 33% of responses were generated as false, the percentage detected by the catch trials ranged from 7% to 57%. For the 50% false response rate the percentage detected by catch trials ranged from 36% to 64%

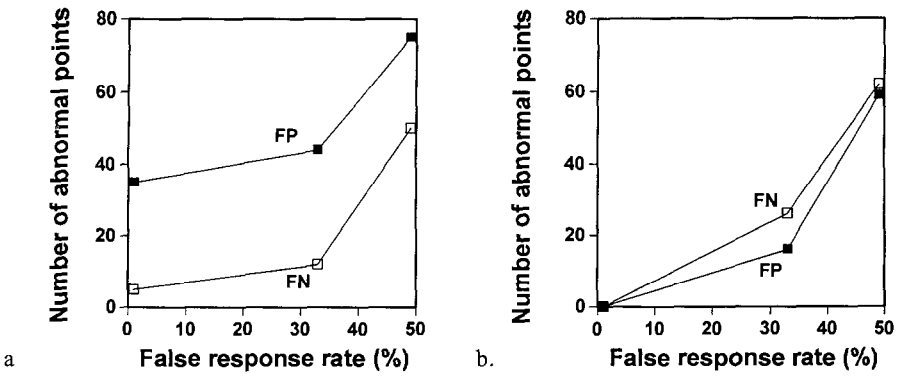

Fig 3 Number of points with abnormal sensitivity as a function of false response rate, a) shows uncorrected data (LHS) and b) shows data normalized for the subject's sensitivity (RHS)

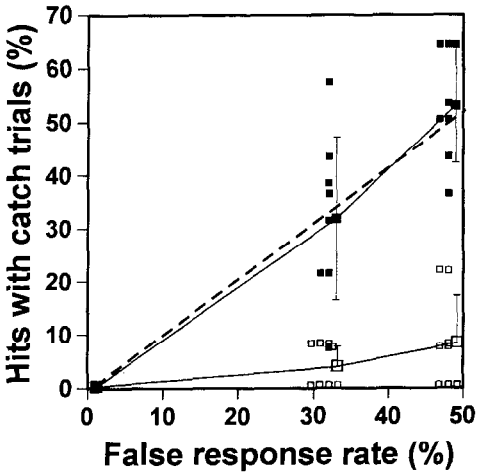

Fig 4 Average hit rate (+ SD; large symbols) as a function of the actual false response rate Individual data are shown as small symbols, these have been displaced along the x axis for clarity

Discussion

False responses act to artifactually elevate sensitivity if they are false positives or lower sensitivity if they are false negatives (Fig. 1). This has been reported previously by Katz and Sommer who note a mean depression of 9 dB in glaucoma patients and 7 dB in normals when the FN rate was greater than 33%[11] This report compares well with our data where a 33–50% FN rate depressed sensitivity by about 5–11 dB (Fig 1).

An increase in variability is also seen when false response rates are elevated Johnson *et al* found that the occurrence of a single mistake (a false response) during a threshold estimation led to a loss of accuracy[12]. Since full threshold algorithms in most perimeters require at least 4–5 responses per location to determine an end-point, and since only one of these responses need be erroneous to lead to a reduction of accuracy, then it is apparent that a 20–25% false response rate will cause an increase in variability Our finding of a significant increase in variability by a 33% false response rate is consistent with this proposal.

Step size was shown to be an important factor in determining the effect of fluctuation and false responses[12] This is likely to be a function of the number of trials needed to find a threshold and whether a method of limits or staircase logic is being used. Although the perimeter used in this trial adopts a 6/3 dB staircase, we believe that similar trends would be found for most of the step sizes used by modern perimeters and that a method of limits would be particularly affected by such errors

It is interesting to consider the number of false positives and false negatives that were actually detected by the catch trials during the thresholding procedure (Fig. 4). This is an important factor as it is the only flag that indicates to the clinician that the test is unreliable. When 33% false responses were occurring the detection rates varied between 7% and 57% Out of the eight tests performed with a 33% false response rate, four (50%) yielded a catch trial rate of less than 33% and would not have been flagged as unreliable. When a 50% false response rate was occurring, all tests had a reported catch trial rate of higher than 33% and thus all would have been flagged as unreliable. The fact that the observed false response rate is low (< 1%) in the control condition (Fig 4) confirms that our observer was reliable and that internal variability could not have accounted for this spread in the data. Instead it must have been associated with the limited sampling capacity of the false response monitor. The increased false response rate for the fellow category (unfilled symbols Fig. 4) is to be expected and has been reported in the presence of a high FP rate. These false positives give rise to an artifactual increase in the FN reports[5]

The major use of automated perimetry is for the detection and monitoring of progression of field loss. False responses cause field parameters to depart from their "true" values Mean threshold, field variance and the number of abnormal points are all altered significantly at the currently accepted criterion for test reliability (33%) False responses will complicate the clinical interpretation of data because they may cause an abnormal field to appear normal, a normal field to appear abnormal, a worsening field to appear stable and a stable field to improve or deteriorate What is even more important is that the catch trial monitor can provide inaccurate information regarding the true false response rate Our data would suggest that any reported high values (> 33%) would most likely be unreliable, any low values (<10%) are most likely reliable whereas intermediate values need to be viewed cautiously. Clinical judgment should be deferred in the absence of reliable information Further work to elucidate the practical significance of this problem is presently being undertaken in our laboratory.

Conclusion

This study shows that the accepted criterion for reliable outcomes in automated perimetry (33%) allows significant changes in visual field parameters. Our data suggest that reported false response rates of less than 10% are likely to be reliable. Relaxation of reliability criteria would only serve to obscure subtle field loss and hinder monitoring of visual field progression. Given that half of the tests with a 33% false response rate are not flagged to the clinician caution needs to be exercised when interpreting outcomes in the presence of moderate levels of false responses (11–33%)

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NEW METHODS OF PERIMETRY

Short-wavelength automated perimetry (SWAP) in optic neuritis

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Abstract

Short-wavelength automated perimetry (SWAP) was compared to standard automated perimetry in 26 eyes of 13 patients with recovered optic neuritis and/or multiple sclerosis Fifteen out of 26 eyes showed greater amounts of visual field loss for SWAP testing than for standard automated perimetry, eight out of 26 eyes showed either equivalent loss or normal visual fields for both procedures, and three out of 26 eyes showed a greater number of abnormal visual field locations for standard automated perimetry than for SWAP testing. On the average, SWAP testing showed a 50% greater number of abnormal visual field locations than for standard automated perimetry Our preliminary findings suggest that SWAP may be useful for detecting subtle visual field abnormalities in multiple sclerosis, optic neuritis, and other optic neuropathies

Introduction

Short-wavelength automated perimetry (SWAP) is a visual field test procedure that uses a high luminance yellow background and a large (size V) short-wavelength target to isolate and measure the sensitivity of short-wavelength mechanisms throughout the central visual field Previous longitudinal investigations[1–12] of ocular hypertensive and glaucoma patients have established the following results: (1) short-wavelength deficits have been found in about 15–20% of ocular hypertensives with normal visual fields for standard automated perimetry, (2) short-wavelength deficits are more prevalent in high-risk glaucoma suspects and ocular hypertensives than in those with low or moderate risk, (3) short-wavelength deficits in ocular hypertensives are predictive of the onset and location of impending visual field loss for standard automated perimetry, (4) short-wavelength deficits are larger in size than for standard automated perimetry losses in patients with early glaucomatous visual field abnormalities, (5) the rate of progression of SWAP deficits is approximately twice as great as for standard automated perimetry losses in glaucoma, and (6) SWAP deficits in glaucoma patients are predictive of the onset and location of progression of visual field loss for standard automated perimetry. These findings indicate that SWAP is a useful clinical procedure for detecting early visual field loss and subtle visual field changes in patients with glaucoma and ocular hypertension

The purpose of the present study was to determine whether SWAP testing was capable of detecting early or subtle abnormalities in other optic neuropathies that were not revealed by standard automated perimetry In particular, we evaluated a group of patients with recovered

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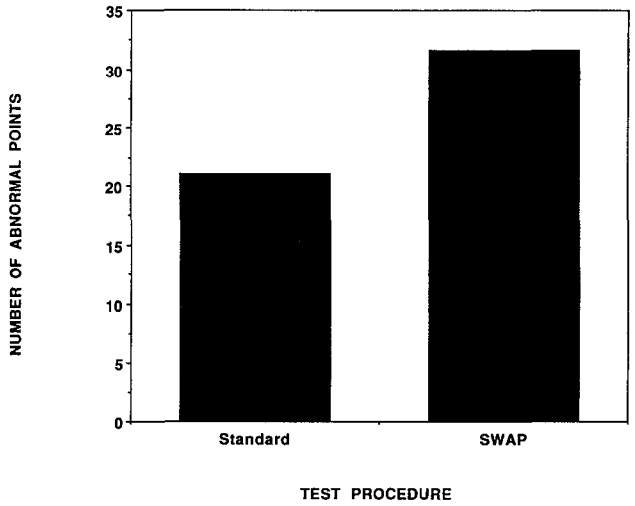

Fig 1 Average number of abnormal visual field locations (beyond the normal 5% probability level) for standard automated perimetry and SWAP in 26 eyes of 13 patients with recovered optic neuritis and/or multiple sclerosis

optic neuritis and/or multiple sclerosis to compare SWAP and standard automated perimetry results. Our motivation for this study was based in part on an unexpected finding of a reproducible homonymous hemianopsia for SWAP testing and normal visual fields for standard automated perimetry in a patient with a probable diagnosis of multiple sclerosis and disseminated plaques in her MRI scan, particularly in the occipito-parietal region.

Methods

Detailed descriptions of our short-wavelength automated perimetry (SWAP) test procedure have been published previously[7,8,13]. Both standard automated perimetry and SWAP testing were performed using a modified Humphrey Field Analyzer. Standard automated perimetry was conducted using a size III white target superimposed on a 31 5 asb white background. SWAP testing was performed with a size V blue stimulus (OCLI 500 nm cutoff filter) superimposed on a 635 asb yellow (Schott OG 530 filter) background. These test conditions provide approximately 15 dB (1.5 log units) of isolation of short-wavelength mechanisms throughout the central 30 degree visual field. For both procedures, the program 30-2 target presentation pattern was used, a full threshold strategy was employed, and appropriate lens correction was placed before the eye to be tested, and an eye patch was used to occlude the non-tested eye Both test procedures took approximately 15 minutes per eye to perform. For this study, standard Humphrey visual fields were performed first, and SWAP visual fields were performed second following a rest period of at least 20 minutes Periodic rests were provided throughout testing as needed by individual patients.

To correct SWAP results for short-wavelength transmission losses produced by the ocular media, we measured the wavelength-dependent absorption properties of the lens using a non-invasive video-based procedure we developed, known as the lens absorption monitor (LAM)[14] This procedure has been previously described in detail Basically, the procedure involves measuring the intensity of the Purkinje image IV in comparison to a reference standard for eight different wavelengths (410, 420, 430, 450, 470, 500, 530, and 550 nm). Measurements of scattered light above and below Purkinje image IV are also obtained Sixteen measures of Purkinje image IV and scattered light are obtained for the eight wavelengths in less

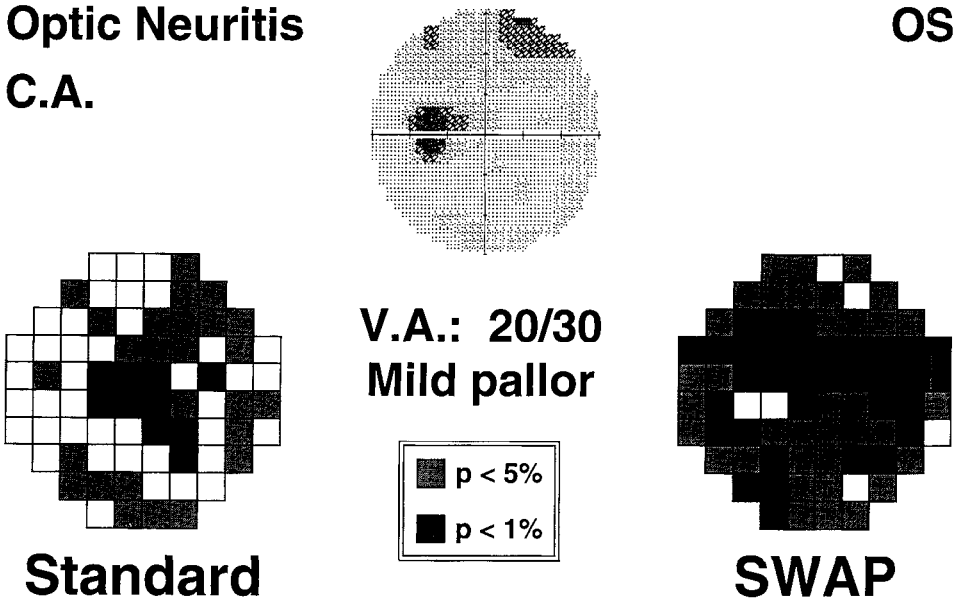

Fig 2 An example of standard automated perimetry and SWAP testing in the left eye of a 28-year-old male patient with a history of optic neuritis and multiple sclerosis, mild optic disk pallor and 20/30 visual acuity. The top figure shows the gray-scale representation for standard automated perimetry. Visual field locations with sensitivity below the normal 5% (stippled squares) and 1% (dark squares) probability levels are presented in the lower left figure for standard automated perimetry and in the lower right for SWAP testing

than two seconds. Spurious results produced by small eye movements are removed by a software artifact rejection procedure, and transmission properties of the lens for the eight wavelengths are then calculated The LAM measures are then used to correct SWAP results for individual differences in lenticular absorption of short-wavelength light

Both eyes of 13 patients with recovered optic neuritis and/or multiple sclerosis were examined. Comparison of standard automated perimetry and SWAP results were conducted by comparing the results of each to age-matched normative values for the two test procedures Visual field locations with sensitivities below the 5% and 1% normal limits were determined for each test. Descriptions of the normal population and the visual field characteristics for standard automated perimetry and SWAP testing from this population have been previously published[13,15]

Results

Figure 1 presents the average number of visual field locations (beyond the normal age-matched 5% probability level) for standard automated perimetry and SWAP testing in the 26 eyes of 13 patients with optic neuritis and/or multiple sclerosis. It can be readily observed that there was an approximately 50% increase in the number of abnormal SWAP sensitivity values as compared to abnormal sensitivity values for standard automated perimetric testing. In general, the location of visual field abnormalities was similar for the two tests, with SWAP deficits demonstrating a larger size for the area of abnormality. In 15 of the 26 eyes tested, there were a larger number of abnormal visual field locations for SWAP testing as compared to standard automated perimetry. Eight eyes demonstrated either equivalent numbers of abnormal visual field locations for standard and SWAP visual field testing, or the visual fields for

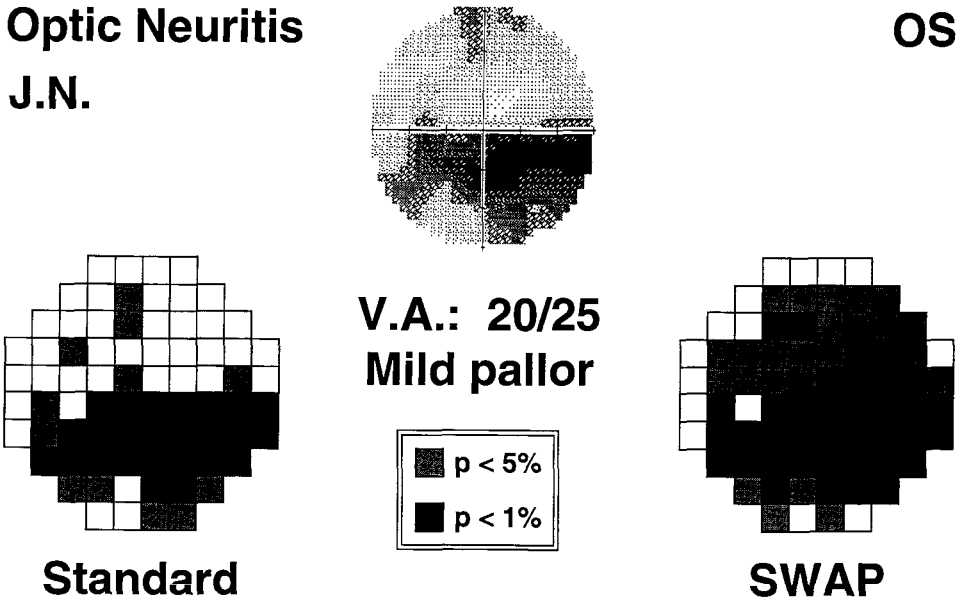

Fig 3. An example of standard automated perimetry and SWAP testing in the left eye of a 50-year-old female patient with recovered optic neuritis, mild optic disk pallor, 20/25 visual acuity and an inferior visual field defect. The top figure shows the gray-scale representation for standard automated perimetry Visual field locations with sensitivity below the normal 5% (stippled squares) and 1% (dark squares) probability levels are presented in the lower left figure for standard automated perimetry and in the lower right for SWAP testing

both procedures were within normal limits. Only three of the 26 eyes showed a greater number of abnormal locations for standard automated perimetry than for SWAP.

Figure 2 presents an example of standard and SWAP testing in the left eye of a 28-year-old male patient with a history of optic neuritis and multiple sclerosis, mild optic disk pallor, and 20/30 visual acuity. The top center figure shows the gray scale representation for standard visual field testing, and the lower figures show the points beyond the 5% and 1% probability levels for standard automated perimetry on the left and SWAP testing on the right. The SWAP results show a more extensive and severe amount of visual field loss in comparison to standard automated perimetry

A second example is shown in Figure 3, which presents standard automated perimetry and SWAP results for the left eye of a 50-year-old female patient with recovered optic neuritis, mild optic disk pallor, 20/25 visual acuity, and an inferior arcuate visual field defect. The gray scale representation for standard automated perimetry is shown in the top center figure, with the visual field locations with sensitivity below the 5% and 1% normal probability levels shown in the lower left for standard automated perimetry and in the lower right for SWAP testing. Both procedures reveal the inferior arcuate deficit, but the SWAP abnormalities extend into the superior visual field as well

A more subtle example is shown in Figure 4, which presents the right eye of a 37-year-old female patient with a history of optic neuritis and multiple sclerosis, no optic disk pallor and 20/20 visual acuity. The top center figure shows the gray-scale representation for standard automated perimetry. Visual field locations beyond the normal 5% and 1% probability levels are shown for standard automated perimetry on the lower left and for SWAP testing on the lower right. Standard automated perimetry results show a few abnormal visual field sensitivities in the superior visual field, primarily clustered about the superior temporal midline. A more extensive amount of abnormality is observed for SWAP results in the superior visual field.

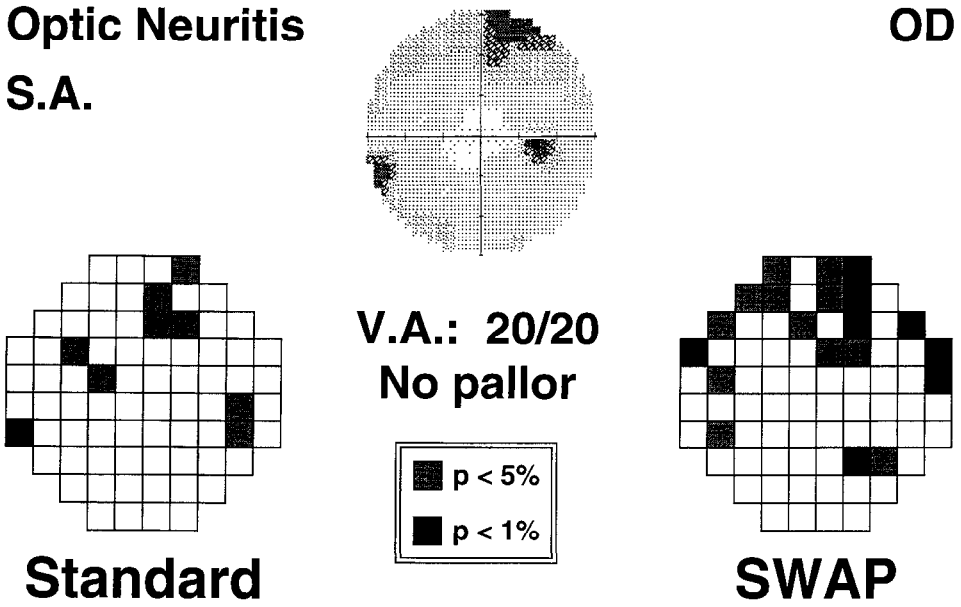

Fig 4 An example of standard automated perimetry and SWAP testing in the right eye of a 37-year-old female patient with a history of optic neuritis and multiple sclerosis, no optic disk pallor and 20/20 visual acuity The top figure shows the gray-scale representation for standard automated perimetry. Visual field locations with sensitivity below the normal 5% (stippled squares) and 1% (dark squares) probability levels are presented in the lower left figure for standard automated perimetry and in the lower right for SWAP testing

Discussion

Our preliminary findings for SWAP testing in optic neuritis and/or multiple sclerosis patients indicate that in most cases, SWAP testing reveals more extensive visual field loss than standard automated perimetry using a white target on a white background. These findings suggest that SWAP testing may be useful in detecting subtle visual field deficits in optic neuritis and/or multiple sclerosis Further investigations will be needed to determine whether these SWAP abnormalities are due to a selective loss of optic nerve fibers conveying short-wavelength information or whether subtle abnormalities are more readily detected with SWAP due to the reduced redundancy or undersampling of the short wavelength sensitive mechanisms[16]

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Automated perimetry for a blue test light on an intense white background in glaucoma

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Abstract

In this study, the authors applied the procedures for a blue test light on an intense white background with automated perimetry for early diagnosis of glaucoma. We set the test stimuli as a blue light using Kodak wratten filter No 47B and altered the background intensity from 31 4 asb (10 cd/m^2) to 314 asb (100 cd/m^2) to detect the S cone responses on each eccentricity of the retina Thirty patients with ocular hypertension or early glaucoma were studied We found that the distribution in sensitivity for blue-on-white perimetry differed from that of both normals and Humphrey in early glaucoma patients The differences are remarkable in a 10–20 degree area of the total and/or specific quadrant of visual field

As a result, it was suggested that this method might be useful for early diagnosis of glaucoma as much as the blue-on-yellow perimetry and easy to apply clinically

Introduction

The vulnerability of the short wavelength sensitive cone (S cone) system in glaucoma has been pointed out[1] as well as in retinal and optic nerve diseases Therefore, several attempts have been made to detect the S-cone system in ocular hypertension and glaucoma patients

Recently, the usefulness of so called blue-on-yellow perimetry for detecting early visual field changes in glaucoma has been reported[2–4] On the other hand, spectral sensitivity measurements on an intense white background have been applied in order to investigate the characteristics of opponent channel damage in patients with glaucoma[5–7].

In this study, we applied the procedures that were used in the spectral sensitivity measurement on an intense white background with automated perimetry for early diagnosis of glaucoma. Then we investigated the differences between the results from blue-on-white and white-on-white using the Humphrey Field Analyzer.

Methods

Preliminary experiments

Previously, we investigated the necessary intensity of the white background for detecting the S-cone pathway sensitivity by measuring the extra-foveal spectral sensitivities on various intensities of white backgrounds Consequently, it was suggested that the necessary intensity of white background to detect the S-cone pathway would be more than 2 log photopic trolands (Tp)[8]

To confirm this result, the increment threshold versus intensity (t v i.) curve was measured

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with a blue test light on a white background at various eccentricities on the retina. A two-channel Maxwellian view optical system with a 150-watt xenon arc as a light source was used. A one degree diameter circular test field was superimposed in the center of an eight degree circular background field. The test light was exposed for 200 msec every 1 5 seconds. The Kodak wratten filter No 47B was used for the test light. The observer's fixation was controlled by a small red light from an accessory system. The biting board was adjusted at each eccentric position in order to allow the test flash and the background light to pass directly through the center of the pupil.

Blue-on-an intense white perimetry

For the blue-on-white perimetry, an automated perimeter made by Topcon company (Tokyo, Japan) was used and the necessary intensity of the white background for detecting the S-cone pathway was obtained using a power supply Kodak wratten filter No. 47B. was installed for the test light

The perimetry examinations were performed for ten normal subjects, 30 ocular hypertension or early glaucoma patients, and each patient was examined with both Humphrey Field Analyzer and blue-on-white perimetry The distribution of age of normal subjects was between 28 and 45 (mean 36) The age of the patients had the same distribution as the normal group, in order to compare both results without any aging factors

Measuring strategy employed static threshold field testing using the 30-2 threshold program and STD 340 program of Topcon perimetry which tests the same locations as the 30-2 threshold program of the Humphrey Field Analyzer

The mean sensitivities obtained from both perimeter were normalized using the mean values within two degrees from the fovea of each perimeter for comparison

Results

Preliminary experiments

The t.v.i. curves measured for a blue test light on a white background at the extra fovea consist of at least two branches Figure 1 represents the t v i. curve at ten degrees temporal retina. The lower branch represents the response of the rod function and the upper one the response of the S cones The absolute values for S cones were determined by measuring the dark adaptation curve for the blue test light. The results indicate that the necessary intensity of a white background is at least 2 log Tp

Based on this and our previous results, it was suggested that enough intensity of white background to distinguish the S cone system from others required approximately 100 cd/m^2 for normal pupil in automated perimetry

Automated perimetry examinations

The results of the Humphrey Field Analyzer (on the top) and the blue-on-white perimetry (on the bottom) for a representative case of ocular hypertension are shown in Figure 2. In this case, Humphrey results show an almost normal distribution of sensitivity and there are no unusual features in either the total or pattern deviation of Statpac On the other hand, in blue-on-white perimetry we can find the attenuation of sensitivity connecting to the Mariott scotoma These results suggests the blue-on-white perimetry might be useful to detect minor changes of glaucomatous visual field.

We compared these two perimetry methods by dividing the whole field into 12 areas, that is, zero to ten degrees, ten to 20 degrees and 20 to 30 degrees of each quadrant.

Figure 3 represents the results of the Humphrey Field Analyzer (on the top) and the blue-on-white perimetry (on the bottom) of the average of ten normal subjects The horizontal axis indicates the eccentricity and vertical axis indicates the normalized sensitivity. Both results show the gradual decrease in sensitivity with an increase in eccentricity for all quadrants.

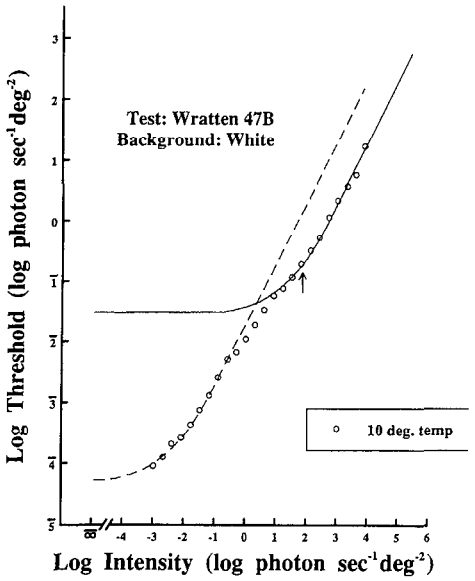

Fig 1 The increment threshold versus intensity curve at ten degrees temporal retina for normal observer

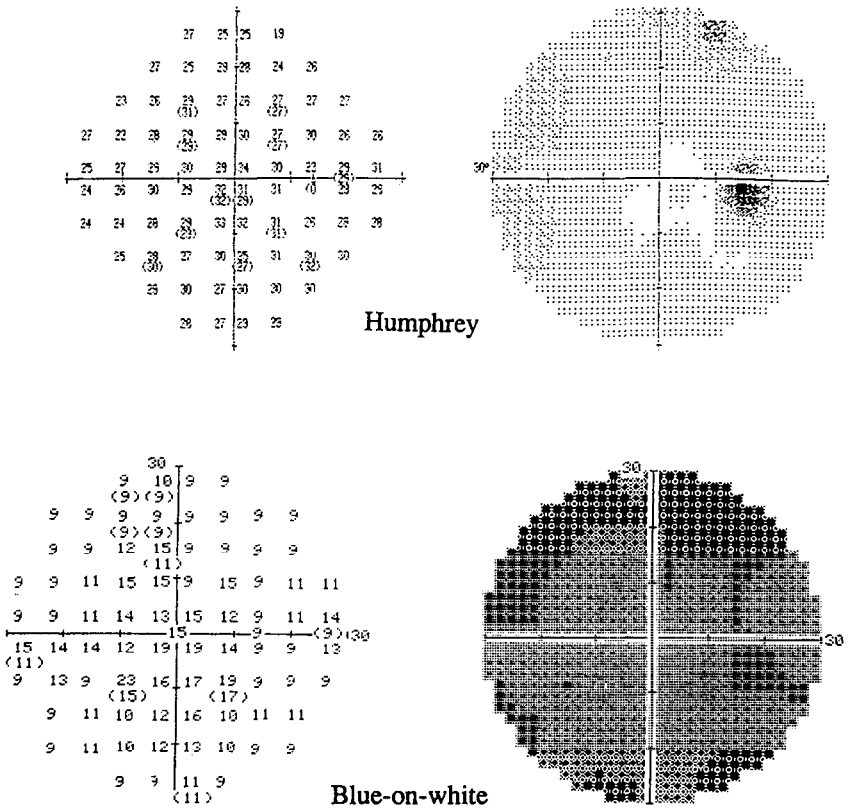

Fig 2 The results of the Humphrey Field Analyzer (on the top) and the blue-on-white perimetry (on the bottom) for a representative case of ocular hypertension

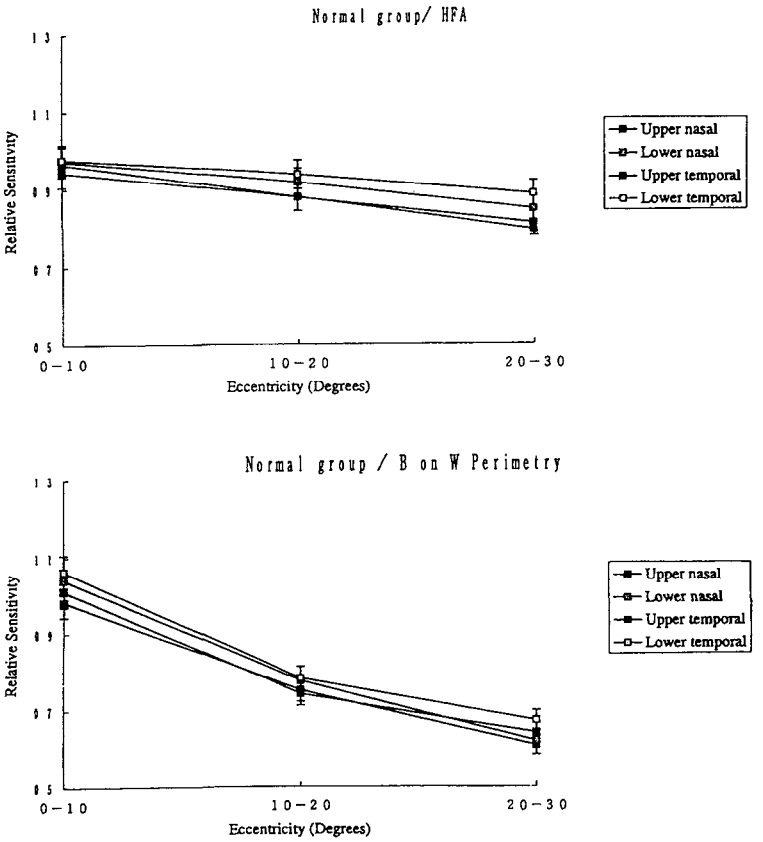

Fig 3 The results of the Humphrey Field Analyzer (top figure) and the blue-on-white perimetry (bottom) of average of ten normal subjects The distribution of their age was between 28 and 45, and average age was 36 The horizontal axis indicates the eccentricity and vertical axis indicates the normalized sensitivity The result of blue-on-white perimetry and HFA for a slightly advanced glaucoma patient

Figure 4a–d represents the results of four glaucoma suspects. These patients have a normal distribution of sensitivity in Humphrey perimetry and were diagnosed as normal. All figures show the Humphrey results on the top and blue-on-white perimetric results on the bottom For blue-on-white perimetry, the distribution in sensitivity of four quadrants differs from the normal pattern for all of the four patients. There are different sensitivity characteristics in each quadrant and a significant sensitivity loss in particular visual areas The most noticeable differences in both perimetric results is sensitivity loss in the 10–20° area in blue-on-white perimetry

Discussion

The short wavelength sensitivity responses have been thoroughly investigated in various ophthalmic diseases because of the vulnerability of the S-cone systems. One of the techniques for detecting S-cone responses is the spectral sensitivity measurements for a low temporal frequency test flash on an intense white background. In normal subjects, the spectral sensitivity curve shows three peaks which are about 440 nm, 530 nm and 610 nm. The peak near 440 nm can be accounted for by the action of S cones, while the narrowed two peaks have been attributed to linear subtractive interaction between the M and L cones. Previously, we investigated

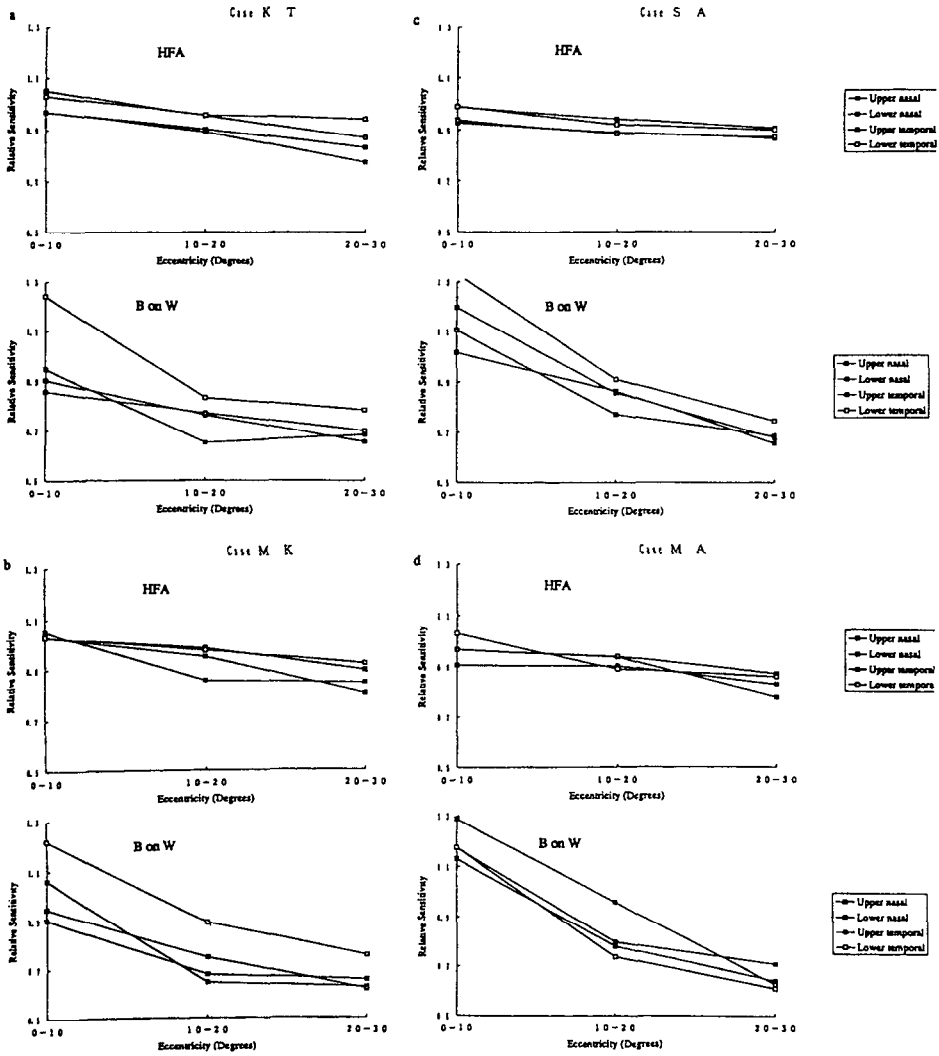

Fig 4 The results of four glaucoma suspects These patients have a normal distribution of sensitivity in Humphrey perimetry and were diagnosed as normal All figures show the Humphrey results on the top and blue-on-white perimetric results on the bottom

the extra foveal spectral sensitivity on an intense white background and found that the peak at about 440 nm remained prominent even at 15 degrees from the fovea[9]

In this study, we applied the technique of spectral sensitivity measurement directly to the perimetric strategy We set the test stimuli as a blue light using Kodak wratten filter No. 47B and altered the background intensity from 31.4 asb (10 cd/m^2) to 314 asb (100 cd/m^2) to detect the S-cone responses on each eccentricity of the retina. We found that the distribution in sensitivity for blue-on-white perimetry differed from that of both normals and Humphrey in early glaucoma patients The differences are remarkable in a 10–20 degree area of the total and/or specific quadrant of visual field.

As a result, it was suggested that this method might be useful for early diagnosis of glaucoma as much as the blue-on-yellow perimetry and easy to apply clinically. However, please

note that the relatively young age of the subjects in this study may mean that the results achieved may not necessarily apply to the diagnosis of glaucoma if the patients are elderly and cataractous changes are present

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Displacement threshold perimetry in glaucoma using a Macintosh computer system and a 21-inch monitor

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Abstract

Displacement threshold perimetry is a technique that measures motion displacement thresholds for 60 locations within the central 30 degree visual field, using a 21-inch high resolution monitor and a Macintosh IIfx computer system Preliminary comparisons of displacement threshold perimetry and conventional automated perimetry (Humphrey 30-2 threshold procedure) were conducted in 38 ocular hypertensive or glaucomatous eyes Results for both tests in patients were compared to age-matched normal values obtained in a group of control subjects between the ages of 21 and 83 In eyes with glaucomatous visual field loss, there was good correspondence in the location of visual field deficits between the two test procedures However, many of the glaucomatous eyes showed more extensive losses for displacement threshold perimetry than for standard automated perimetry Several ocular hypertensive eyes showed nerve fiber bundle-like deficits for displacement threshold perimetry in the presence of a normal visual field for standard automated perimetry These preliminary results suggest that displacement threshold perimetry may be a useful procedure for identifying early glaucomatous damage

Introduction

Recently, several investigators have utilized various motion stimuli to evaluate ocular hypertensives, patients at risk of developing glaucoma, and patients with early glaucomatous damage[1–5]. These studies have found that motion or displacement sensitivity losses are sometimes present in patients with normal visual field sensitivity, and suggest that motion sensitivity deficits may represent earlier glaucomatous damage than that revealed by conventional perimetry One of the limitations of previous motion and displacement sensitivity investigations is that the procedures either stimulated rather large areas of the visual field or were only able to examine a small number of localized visual field regions In this view, we have recently developed a procedure for measuring movement displacement thresholds for a number of localized regions of the central visual field.

The purpose of the present study was to conduct a preliminary evaluation of displacement threshold perimetry, a new technique that measures motion displacement sensitivity at 60 locations throughout the central 30 degree visual field using a 21-inch high resolution monitor and a Macintosh IIfx computer system Our preliminary investigation consisted of measure-

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ments of displacement threshold perimetry and standard automated perimetry (Humphrey Field Analyzer) in 38 patients with ocular hypertension or early-to-moderate glaucomatous visual field loss For both tests, patient results were compared to age-matched normal population values derived from 60 individuals between the ages of 21 and 83 years.

Methods

Peripheral displacement thresholds were obtained for 60 visual field locations within the central 30 degrees The 60 locations are in a grid pattern bracketing the horizontal and vertical meridians, with a six degree spacing between points. Basically, the target presentation pattern for displacement threshold perimetry is identical to that of Humphrey 30-2 pattern with the four outermost points in the superior, inferior, nasal and temporal visual field removed

Displacement thresholds were determined by means of a staircase procedure similar to that employed for standard automated perimetry. Staircases began with a step size of 24 minutes or arc. Each staircase reversal resulted in a halving of the step size down to the minimum of three minutes of arc. The staircase was terminated by two staircase reversals at the minimum step size, and the mean of the two reversals was taken as the threshold displacement value The lower displacement limit was three minutes of arc and the upper limit was five degrees. Each displacement threshold perimetry session consisted of approximately 400 stimulus trials to obtain 60 threshold determinations, and lasted approximately 12 to 15 minutes.

Stimuli were displayed on a 21-inch Raster-Ops Model 2168 high resolution monitor controlled by a Macintosh IIfx computer system with a 24-bit color video controller Background luminance of the high resolution monitor was adjusted to 31.5 asb (10 cd/m^2) and the luminance of targets was 158 asb (50 cd/m^2) Each stimulus was a small white square (ten by ten pixels) that subtended approximately 0.6 degrees of visual angle at the 30 cm viewing distance. During testing, the entire grid of 60 test points were presented concurrently. For each trial, one of the test locations was selected and was randomly displaced to the right or the left for a period of 50 msec and then returned to its original position. Subjects were instructed to depress a mouse button each time they noticed the movement of one of the elements in the grid.

Preliminary studies indicated that presentation of a single target that was then displaced led many subjects to confuse target onset and target motion, thereby generating a large number of false-positive responses For this reason, all elements of the grid pattern were presented concurrently After every eight to ten stimulus trials, the entire grid was faded out for a period of one second, remained extinguished for two seconds, and then faded back in over a one-second period Additional trials were initiated 1.5 seconds after the grid had been completely faded back in. The intermittent fade-out and fade-in of the target grid pattern was done to minimize the influence of Troxler fading in the periphery and the build-up of afterimages of the grid pattern. Subjects with good fixation would often experience Troxler fading and disappearance of portions of the grid pattern after 30–40 seconds of continuous presentation. With prolonged viewing of the grid, subjects with poorer fixation would experience distractions from the negative afterimage "shadow" grid pattern which would move with their fixational instability. The fade-out and fade-in of the grid pattern following every eight to ten trials avoided both of these problems

Displacement thresholds were determined by means of a staircase procedure similar to that employed for standard automated perimetry. Staircases were terminated by two staircase reversals at the minimum step size, and the mean of the two reversals was taken as the threshold displacement value. Each displacement threshold perimetry session consisted of approximately 400 stimulus trials to obtain 60 threshold determinations, and lasted approximately 12 to 15 minutes

Standard automated perimetry was performed on a Humphrey Field Analyzer, using the 30-2 target presentation program, a full threshold test strategy and the standard stimulus conditions (size III target, 31.5 asb background) For both test procedures, an appropriate near lens correction was placed before the eye to be tested and an eye patch was used to occlude the non-tested eye.

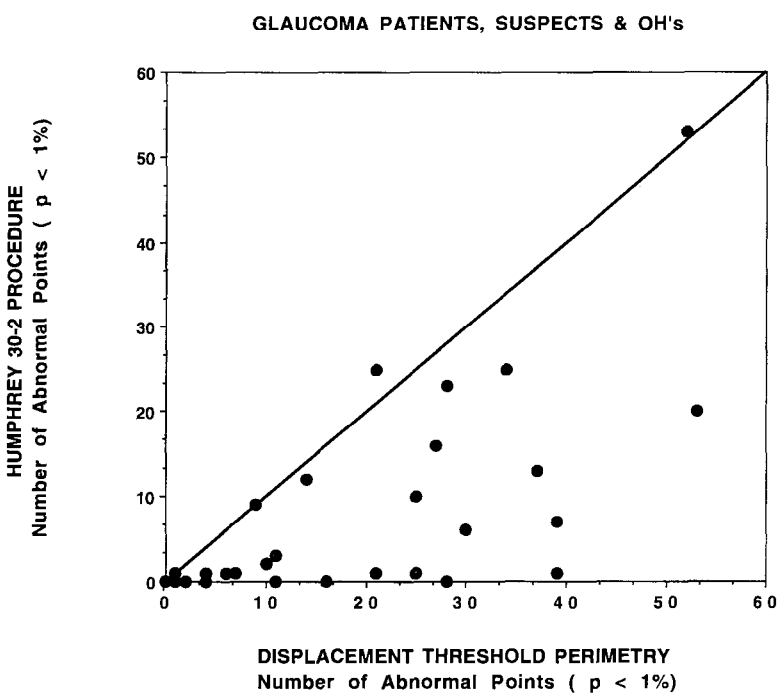

Fig 1 Number of abnormal points at the $p < 1\%$ level for standard automated perimetry using the Humphrey 30-2 threshold program, plotted as a function of the number of abnormal points at the $p < 1\%$ level for displacement threshold perimetry Only the 60 locations of the 30-2 procedure that corresponded to the displacement threshold perimetry target presentation pattern were included in the analysis Results for 38 glaucomatous and ocular hypertensive eyes are presented Note that some data points at and near the lower left corner overlap for individual patients

A normative database for displacement threshold perimetry was established by testing the right eye of 60 normal volunteers (38 females, 22 males) between the ages of 21 and 83 The normal subjects were divided into three age groups (20–39, 40–59, 60–83 years old), each containing 20 individuals. Normal subjects were included if they had a normal eye exam, at least 20/30 best-corrected visual acuity OU, refractive errors of less than 5 diopters sphere and 2 diopters cylinder, intraocular pressures less than 20 mmHg OU, normal visual fields (Humphrey 30-2), a negative history of ocular or neurologic disease or surgery, a negative history of diabetes or other systemic disorders, and were not taking any medications known to affect visual field sensitivity.

Ocular hypertensive and glaucoma patients had to meet the same criteria as outlined above for normal subjects, except for the following differences: (1) IOP was greater than 21 mmHg (off medication) for ocular hypertensive and primary open-angle glaucoma patients; (2) glaucoma patients had early to moderate visual field deficits in one or both eyes for standard automated perimetry

Results

Figure 1 presents the number of visual field locations with sensitivity below the 1% limit of the normal population for standard automated perimetry (Humphrey 30-2) and displacement threshold perimetry in 38 eyes of glaucoma patients, glaucoma suspects and ocular

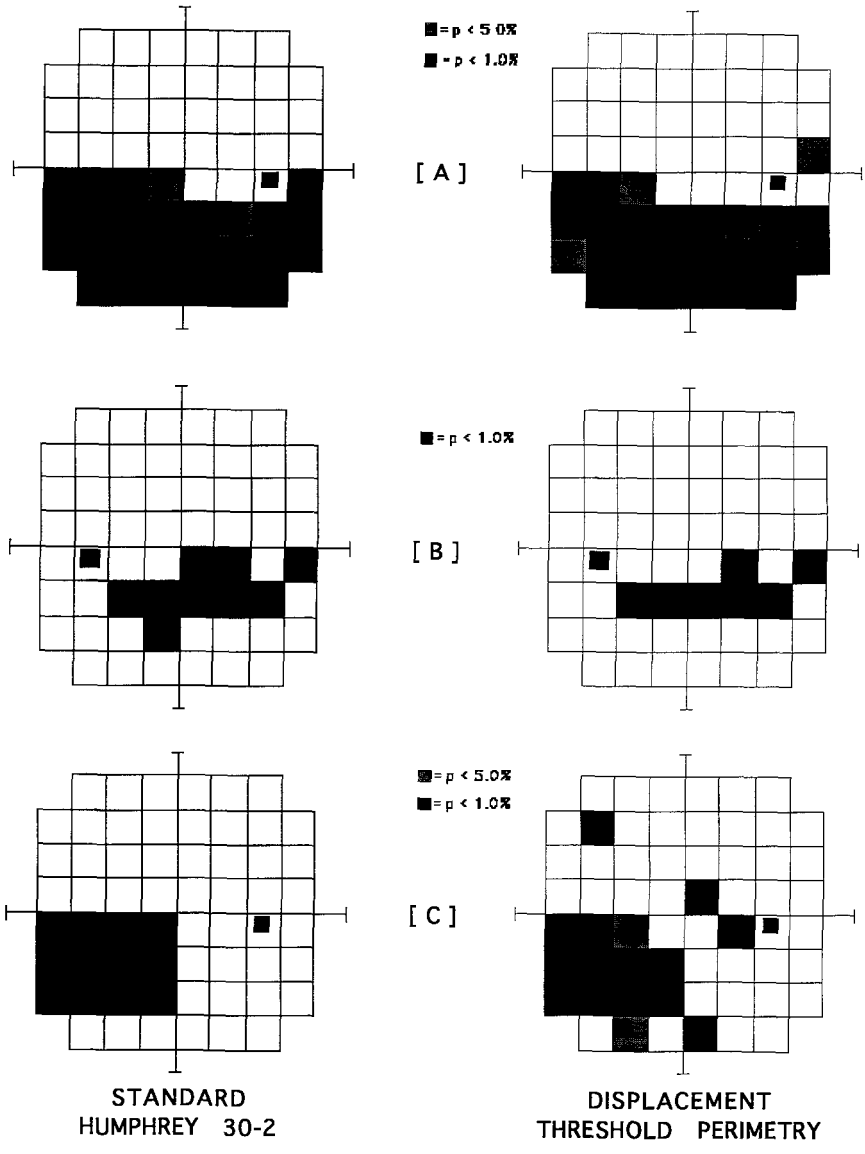

Fig 2 Three examples of good correspondence between standard automated perimetry results and displacement threshold perimetry findings in eyes with glaucomatous visual field loss The examples show locations exceeding the normal 5% and 1% limits for standard automated perimetry (left figures) and displacement threshold perimetry (right figures) [A] Results for the right eye of a 65-year-old male glaucoma patient [B] Results for the left eye of a 52-year-old female glaucoma patient [C] Results for the right eye of a 68-year-old male glaucoma patient

hypertensives that were tested with both procedures Only the 60 visual field locations that were common to both test procedures were evaluated Thus the outermost (27 degree) four points in the superior, inferior, nasal and temporal quadrants of the Humphrey 30-2 program were not considered in the analysis.

The diagonal line in Figure 1 represents equal numbers of abnormal test locations for the standard Humphrey 30-2 procedure and displacement threshold perimetry It can be readily

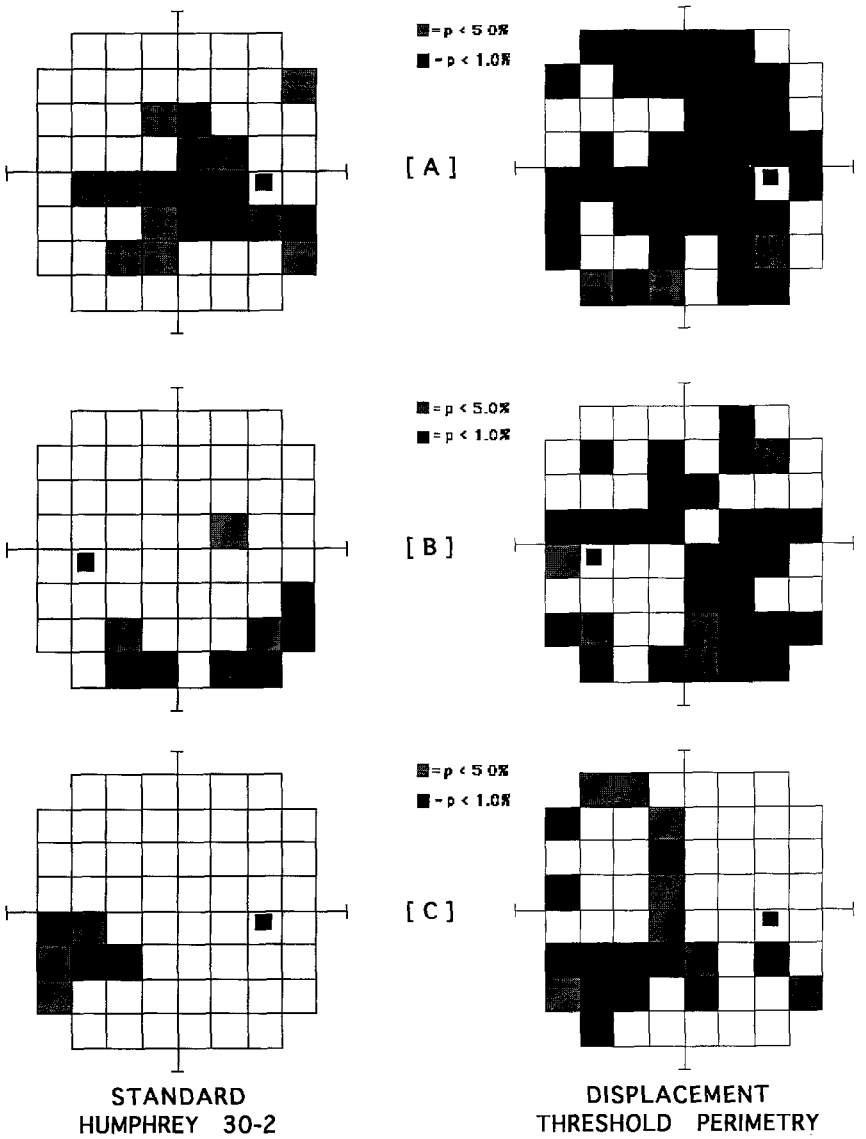

Fig 3 Three examples of eyes with glaucomatous visual field loss in which the displacement threshold perimetry results indicate more extensive loss than that shown by standard automated perimetry findings. The examples show locations exceeding the normal 5% and 1% limits for standard automated perimetry (left figures) and displacement threshold perimetry (right figures) [A] Results for the right eye of a 76-year-old male glaucoma patient [B] Results for the left eye of another 76-year-old male glaucoma patient [C] Results for the right eye of a 69-year-old male patient with glaucoma.

observed that for all eyes, the number of visual field locations with displacement threshold abnormalities is equal to or greater than those found for the Humphrey Field Analyzer Note that some of the data points overlap for different patients at and near the lower left corner of the figure.

Figure 2 presents three examples of good correspondence between displacement threshold perimetry results and standard automated perimetry. Visual field locations with sensitivity be-

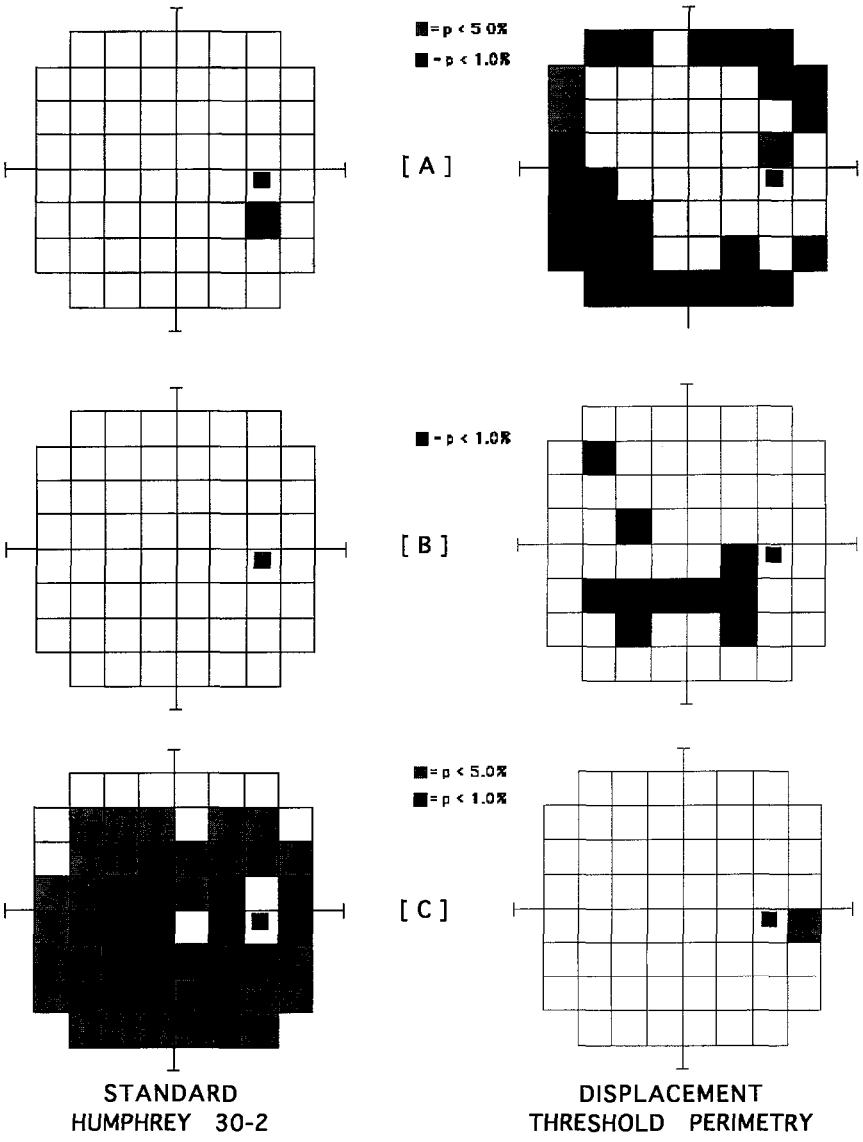

Fig 4. The top two examples show two ocular hypertensive eyes with essentially normal visual fields for standard automated perimetry (left figures) and nerve fiber bundle-like deficits for displacement threshold perimetry (right figures). [A] Results for the right eye of a 50-year-old female ocular hypertensive patient [B] Results for the right eye of a 53-year-old male ocular hypertensive patient. The bottom example [C] shows the results for standard automated perimetry (left) and displacement threshold perimetry (right) in the right eye of a 52-year-old male with 20/60 visual acuity due to cataract

low the 5% and 1% limits are presented at the 60 corresponding visual field locations for each procedure. Standard automated perimetry results are presented on the left and displacement threshold perimetry findings are presented on the right. Figure 2[A] displays the right eye of a glaucoma patient with an inferior arcuate defect, Figure 2[B] shows the left eye of a glaucoma patient with an inferior nerve fiber bundle defect, and Figure 2[C] displays the results for the

right eye of a glaucoma patient with an inferior nasal step In each case, there is good agreement in the size and location of visual field deficits for both perimetric techniques

Figure 3 presents three examples of glaucomatous eyes which have greater deficits for displacement threshold perimetry than for standard automated perimetry Figure 3[A] shows the results for the right eye of a glaucoma patient with an inferior nerve fiber bundle defect and a paracentral scotoma. The displacement threshold perimetry results reveal more extensive losses superiorly and inferiorly Figure 3[B] displays the left eye of a patient with glaucoma exhibiting an inferior nerve fiber bundle defect. Displacement threshold perimetry results show more extensive losses inferiorly as well as deficits in the superior visual field Figure 3[C] shows the results for the right eye of a glaucoma patient with an inferior nasal step, with the displacement threshold perimetry results showing more extensive loss

The top two examples in Figure 4[A] and 4[B] present the results for the right eyes of two high-risk ocular hypertensive patients with essentially normal visual fields for standard automated perimetry and deficits for displacement threshold perimetry with nerve fiber bundle-type patterns of loss The bottom example, Figure 4[C] displays the results for the right eye of a patient with 20/60 visual acuity due to cataract Standard automated perimetry results show generalized central depression, whereas the displacement threshold perimetry findings are essentially normal This suggests that displacement threshold perimetry is more resistant to image degradation than standard automated perimetry

Discussion

Our preliminary findings indicate that in patients with early to moderate visual field loss, displacement threshold perimetry deficits are equal to or larger than those obtained for standard automated perimetry. In addition, several ocular hypertensives with normal visual fields on standard automated perimetry were found to have nerve fiber bundle-like deficits for displacement threshold perimetry Future longitudinal investigations will be necessary to determine whether these deficits are predictive of impending glaucomatous visual field loss as revealed by standard automated perimetry.

In conjunction with the findings of previous studies[1–5], these preliminary results suggest that motion sensitivity deficits in localized regions of the visual field may reflect early glaucomatous damage that precedes visual field losses with conventional automated perimetry Another potential advantage for displacement threshold perimetry as a clinical test procedure for glaucoma is its resistance to image degradation produced by cataract and other optical factors As indicated in the example shown in Figure 4[C], displacement thresholds are less affected by cataract than increment thresholds (standard automated perimetry) This is consistent with previous reports, which have shown that displacement thresholds are minimally affected by refractive error, pupil size and media opacities[2,6] Although additional investigations will be needed to establish the clinical efficacy of this procedure, findings to date suggest that displacement threshold perimetry may be a useful procedure for identifying early glaucomatous deficits

Acknowledgments

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Motion perimetry in optic neuropathies

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Abstract

Motion perimetry is a method that measures a subject's ability to detect a coherent shift in position of dots in a circular area against a background of non-moving dots We define motion size threshold as the smallest detectable circular area in which the subject can detect motion Subjects respond by touching a computer screen with a light-pen where they detect motion stimuli Their reaction times and localization errors (number of pixels from target center) are then calculated

Motion thresholds to 44 points were tested within the central 21° (6° spaced grid) and Humphrey 24-2 testing was done on one eye of 80 patients with optic neuropathies (20 each with idiopathic intracranial hypertension, optic neuritis, glaucoma, ocular hypertension) We also tested 15 normal subjects per decade for comparison data. We found that patients with optic neuropathies often have abnormal motion perception Motion perimetry deficits correlate well with conventional perimetry findings and occur in areas with normal conventional perimetry results

Introduction

Perimetry is our most comprehensive and diagnostically important method of visual assessment. In spite of the integration of new technology, considerable histologic optic nerve damage can be present with a normal manual or automated visual field examination[1,2]. It is common, especially in patients with ocular hypertension, to visualize damage of the optic nerve head while conventional automated perimetry remains normal[3]. Visual loss, hidden to conventional automated perimetry, also occurs commonly in patients with optic neuritis For example, in patients followed in a treatment trial protocol (Optic Neuritis Treatment Trial), 80% had the return of conventional automated perimetry to normal after six months, but only 45% had recovery of normal pupil responses (H S Thompson, personal communication)

Because of these problems, many new types of perimetry have been developed in the past ten years. Computer graphics perimeters have been found to have many advantages as they allow: 1) a wide variety of stimuli and test parameters, 2) improved patient ergonomics, 3) feedback of results for the patient[4–6] To develop a more sensitive method of perimetry, we have designed a computer graphics perimeter that measures a subject's motion perception size threshold and its associated reaction time and localization error. Hence, we report our experience in 80 patients with optic neuropathies and 75 controls.

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Methods

Twenty patients each with idiopathic intracranial hypertension, optic neuritis, ocular hypertension and glaucoma and 15 normal subjects per decade (20–70 years) gave informed consent to participate in the study. Most of the normals were paid volunteers who were employees of the hospital or were friends or family members of eye clinic patients The protocol was approved by the University of Iowa Investigational Review Board. All subjects underwent neuro-ophthalmologic examination. Normals were included if they had no history of eye disease except refractive error of less than 5 diopters, a normal examination and normal automated perimetry results (Humphrey Visual Field Analyzer, program 24-2) All patients underwent Humphrey perimetry with program 24-2 or 30-2 and motion perimetry of one eye on the same day

The patients with idiopathic intracranial hypertension met the modified Dandy criteria[7]. The optic neuritis patients were between 18 and 46 years with a history of acute unilateral visual loss They had a relative afferent pupillary defect and they worsened over one to three weeks and improved over one to two months; the subjects were tested at least six months from their initial symptom The ocular hypertension patients had a cup to disk ratio of less than 0.6, an intraocular pressure of greater than 23 and no optic cup or retinal nerve fiber layer damage. In addition, they had normal conventional automated perimetry. The glaucoma patients had elevated intraocular pressure sufficient to produce optic nerve damage with characteristic visual field loss on conventional automated perimetry Most of the patients were experienced in conventional automated perimetry; most of the normals were not. None of the patients or normals were experienced with motion perimetry.

Conventional automated perimetry was performed with the Humphrey Visual Field Analyzer using the manufacturer's recommendations. The patients' appropriate near correction was used. Subjects were tested with a program using a 6° spaced grid of the central 21° or 27° Rest breaks were given as often as requested.

Motion perimetry

Motion perimetry was performed in a darkened room using an IBM compatible 486 computer with software we have developed The patients' appropriate near correction was again used. Care was taken to prevent lens rim artifact by asking if the subject could see each corner of the video display while looking at the fixation target

The test background for motion perimetry is composed of 5000 randomly positioned white dots – 2 2% of pixels are illuminated The dots are one pixel (0 28 mm) in size and 580 asb (2.25 log units above background) The dots are randomly displayed on a gray background (luminance = 31 5 asb) using a VGA video display – 640 × 480 pixels (Fig 1) The motion targets are circular random dot cinematograms within which 50% of the dots move in one of four directions relative to fixation (up, down, left or right) and 50% move in random directions. The circular target itself is stationary (dots move within the target). Each trial is composed of eight cinematogram frames, each displayed for 16 msec. Each dot moves five pixels – about ½° per frame – giving a velocity of about 30°/sec Dots moving out of the circular window are wrapped back to the point 180° from the dot exit position The stimulus presentation time is 128 msec (shorter than the 200 ± 30 msec latency time of a saccadic eye movement) The targets are of 20 sizes with a step factor is $10^{.1} = 1.26$ The angle subtended by the targets ranges from 0.25° to 21°. The size of the stimulus window varies from trial to trial, and a 2/1 staircase procedure is used to bracket the threshold The test, therefore, continues until the smallest target size seen (size threshold) at each test point is bracketed by the staircase procedure Stimulus presentation is randomized among the preselected test loci. Fixation is monitored by the visual field technician. We tested 44 locations; these match the 24-2 Humphrey perimetry test points except for absence of the top and bottom rows (y = 21° and –21°) and the two points along the nasal horizontal (x = –27°)

Valid responses are defined by 1) having a reaction time greater than 110 msec and less than one second and 2) having a localization error of no more than 10° from the center of where the target is presented The testing distance from the screen is fixed at 22 cm by a lens holder attached to the monitor. The monitor is on an adjustable-height table and is set so that

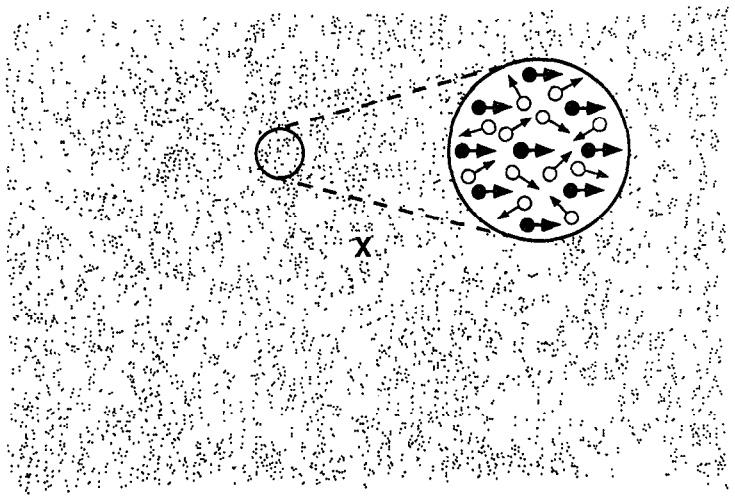

Fig 1 Diagram of the motion perimetry video display The small circle represents a motion perimetry target The enlargement of the target shows 50% of the dots moving at random and 50% moving in one direction (bold figures) The "X" represents the fixation target

a test subject is comfortably seated looking slightly down The 17 inch diagonal monitor gives a 21° test field (42° by 42° total)

The subject fixes on a central cross while a target is displayed for 128 msec (Fig. 1) as he holds a light-pen less than one cm from the monitor. The subject then touches the pen to the center of the bottom of the screen to indicate the target is seen We used the FTG Data Systems high resolution light-pen model FT-1000 It has a response time of less than 250 nsec The maximum diameter of a detected circle with the pen touching the screen is 0 14 cm at normal viewing intensities. The reaction time is calculated using a high resolution timer function with one to ten microsecond accuracy[8] The subject then touches the monitor a second time at the position on the screen where they perceive the center of the test target This two-step response becomes automatic for nearly all subjects after 15–25 practice trials (performed prior to the test) The localization error is calculated using the distance from the target center x and y pixel coordinates (corrected for distortion from monitor screen parallax) to the x and y pixel coordinates of where the patient points with the light-pen The calculation is done using the method of least square distance. The subject receives feedback of the localization error at the end of each trial To help maintain attention, if the subject comes within three pixels of the target center, reinforcement is given as a computer-simulated fireworks display

Statistical analysis

For the size threshold data the target areas were used So that the criteria for parametric statistics could be met, we normalized the distribution for the size threshold data by transforming it with its base ten logarithm The primary outcome variables (motion size threshold, reaction time and localization error) were all normally distributed Results were considered significant if $p < 0\ 05$

Point-wise probability plots similar to those used for the Humphrey Visual Field Analyzer were generated by tabulating whether the tested point in the patients fell outside the upper 95 or 99% confidence bound of the normal subjects[9] To be considered abnormal, three contiguous test points had to be abnormal at a $p < 0.05$ level or two contiguous points abnormal, one at the $p < 0\ 01$ level in a clinically suspicious area For example, in the Bjerrum area three abnormal points would be sufficient for an abnormal classification, but three abnormal points at the superior periphery would not The two types of perimetry were compared using these plots for the 44 test loci common to both tests

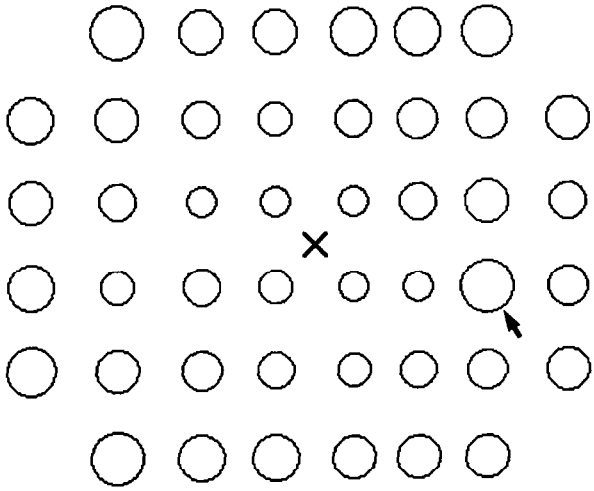

Fig 2 Mean circle size for the 44 test points of the age-matched normal subjects for motion perimetry The increased threshold at the blind spot is shown with the arrowhead

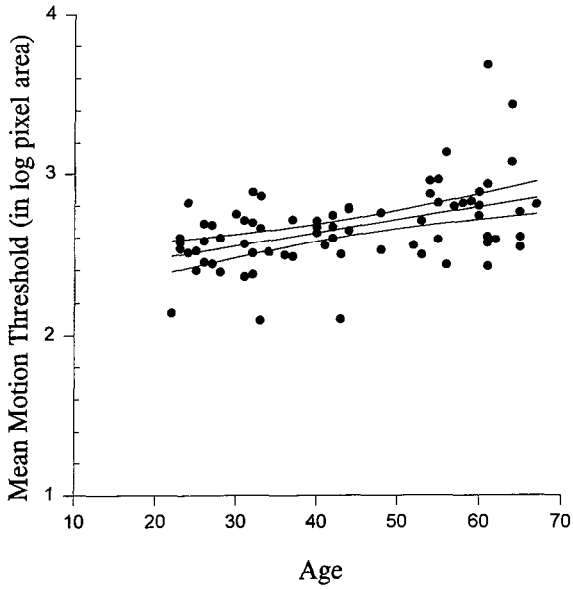

Fig 3 Regression of mean motion perimetry size threshold against age Note the gradual increase of threshold with age

Results

The mean motion perimetry size thresholds of the 75 normal subjects aged 20–70 at the 44 test locations is shown in Figure 2 The location of the blind spot (arrowhead) also has a higher threshold. Notice the slight increase in threshold with eccentricity. There is also an increase in size threshold with age in the normal subjects (Fig. 3). The motion size thresholds for the optic neuritis, idiopathic intracranial hypertension, and glaucoma patients were signifi-

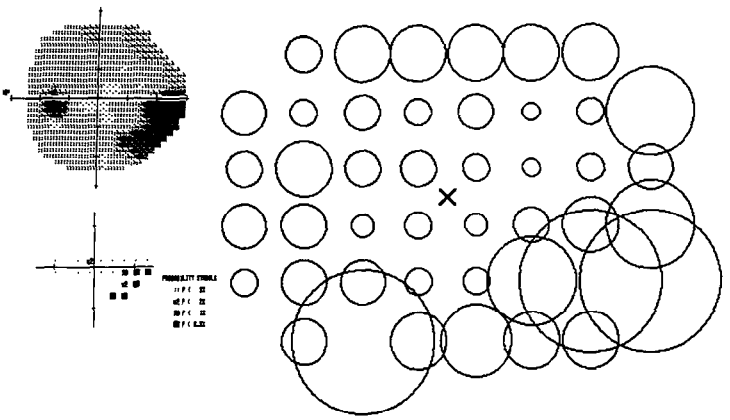

Fig 4 A glaucoma patient with an inferior nasal step to conventional automated perimetry has a full inferior arcuate defect to motion perimetry

cantly different than sets of age-matched normals ($p < 0.0001$) There was no difference for the ocular hypertension patients

Regarding the probability plot comparisons – the deficits present usually paralleled the conventional automated perimetry results However, we did find nerve fiber bundle defects in 32% of cases in areas that tested normally to conventional automated perimetry (four of 20 each of the ocular hypertension and optic neuritis patients and nine of 20 each of the idiopathic intracranial hypertension and glaucoma patients). The data on reaction times and localization errors will be reported in future publications.

Motion perimetry can show defects in areas that test normally to conventional automated perimetry For example, in Figure 4 a glaucoma patient with near normal conventional perimetry has a large inferior arcuate defect and a smaller superior arcuate defect with motion perimetry However, the defects we found usually were similar with the two tests, as in a glaucoma patient with an inferior nasal step defect to conventional automated perimetry (Fig 5) With motion perimetry, a full inferior arcuate defect is present.

Discussion

Patients with optic neuropathies have elevated motion thresholds in the central 21° of the visual field. The deficits, in general, closely resemble the conventional perimetry defects as in Figure 5 · Comparing results of tests having different measures (differential light sensitivity versus motion perception) is very difficult. We believe comparison of probability plots gives the most unbiased comparison since these plots represent the statistical likelihood that a test point is normal. Using these plots, motion perimetry identified localized defects in 32% patients in areas of the visual field where conventional perimetry results were normal. This suggests that motion perimetry may be a more sensitive test for optic neuropathies We believe the defects found using this method of analysis are real because they conform to anatomic (nerve fiber bundle) patterns. If these defects are due to artifact, the confounding process is not apparent.

The detection of motion perception defects in areas testing normal with conventional automated perimetry might be explained by the architecture of the sensory visual system. There are at least two parallel streams of visual information processing in non-human primates[10–12]. The small fiber, slower conducting P system originates in small retinal ganglion cells and travels via small axons to synapse in the parvocellular layers of the lateral geniculate nucleus Fibers then course through the optic radiations to synapse in the 4cβ layer of V1 Fibers then

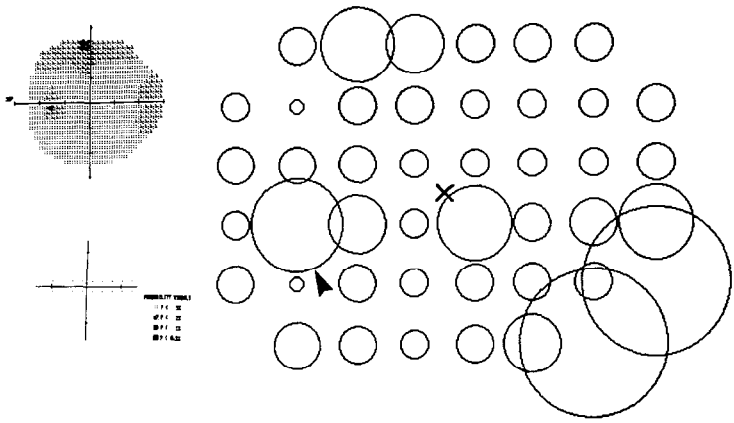

Fig 5 Glaucoma patient with near normal conventional perimetry has a large inferior arcuate defect and a smaller superior arcuate defect with motion perimetry

pass ventromedially to occipito-temporal cortex The large fiber, faster conducting M system synapses in the magnocellular lateral geniculate nucleus Fibers then course through the optic radiations to synapse in the 4cα layer of occipital cortex The pathway then flows dorsolaterally in the temporal lobe to area MT (V5). Lateral geniculate lesions of the P layers in rhesus monkeys affect perception of fine spatial resolution, color, size discrimination and fine stereopsis[10]. M or magnocellular pathway lesions affect perception of motion, and high temporal frequency flicker[10].

Early damage to large diameter optic nerve fibers in idiopathic intracranial hypertension[13] or glaucoma[14], could explain why some nerve fiber bundle defects, present to motion stimuli, are not found with conventional perimetry. An alternative explanation is that the light detection system and the motion system are damaged simultaneously; visual field defects may be seen only in the motion processing system if there is less redundancy[15] We favor the latter explanation.

In summary, about 1/3 of patients with optic neuropathies had nerve fiber bundle defects to motion stimuli in areas testing normal with normal conventional perimetry The deficits though were usually similar between the two tests Motion perimetry appears to be a sensitive test for visual loss in patients with optic neuropathies

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Pupil perimetry: methods of threshold determination and comparison with visual responses

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Abstract

Purpose: To determine an optimal method of pupil threshold determination, enabling pupil and visual threshold to be compared at different locations within the visual field

Method: Two different methods were compared for determining pupil threshold; one method used cumulative probability functions and the other used stimulus-response functions of the pupil A computerized infrared pupillometer was linked to a Humphrey Field Analyzer to record pupil contractions to stimuli over a range of intensities at ten different locations in the visual field of normal subjects

Results: There was a highly linear correlation between pupil threshold determined by probability function compared to that determined from stimulus-response curves ($R^2 > 0\ 9$) Using these methods, the "hill of pupil threshold" was steeper compared to visual threshold under mesopic conditions

Conclusions: When the variability of pupil responses at a given stimulus intensity followed a normal Gaussian distribution, the two methods of threshold determination compared favorably This implied that the stimulus-response curve at a given perimetric location can be used to derive threshold

Introduction

Classically, visual field defects due to retinal or optic nerve disease have been measured as a function of visual threshold. While this system has great clinical usefulness, it still depends upon the subjective responses of the patient to light stimuli Recently, a method of using the pupil as a means of mapping the visual field (pupil perimetry) has been developed using a computerized infrared pupillometer linked to an automated perimeter[1–4]

It has been shown, using monochromatic light sources, that the pupillomotor and visual sensitivity in the center of the retina and the periphery are parallel under dark adapted conditions, with the pupil being about 1.5 log units less sensitive[5,6]. A number of studies comparing pupillomotor and visual threshold at different perimetric locations have shown that the two differ as a function of eccentricity However, the results vary in each study depending on the state of retinal adaptation (background illumination), size of stimulus light, wavelength of stimulus, duration of stimulus, and methods used to determine threshold for the visual and pupillomotor systems[7–11].

One important question is whether the pupillary and visual thresholds parallel each other in normal and damaged areas of the visual field under mesopic conditions. Before addressing this question it is necessary to determine how to best measure pupillary threshold and whether it can be derived from suprathreshold pupil responses How does criterion level affect pupillary threshold? We set out to answer these questions by comparing two methods of pupil threshold determination along the horizontal meridian in normal subjects. The normal "hill" of pupillary response was also compared with visual threshold in the same eyes

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Methods

Each eye of eight normal subjects was tested for visual threshold at two different background intensities (31.5 abs and 3.15 abs), three stimulus sizes (0.431, 0.9, and 1.7 degrees = Goldmann size III, IV, and V), and at ten locations along the horizontal meridian. Visual threshold at each location was recorded as the mean of three determinations using the Humphrey Visual Field Analyzer staircase method. The methods of performing pupil perimetry and analyzing pupillary responses have been described in detail previously. Pupil contractions were recorded using a computerized infrared pupillometer linked to a Humphrey Field Analyzer. With random stimuli, a total of ten pupil responses were recorded for each stimulus intensity at each of the ten locations. A total of eight intensities were used over a 35 dB range in five dB steps (from 35 to 0 dB attenuation; 0 dB atten = 10,000 apostilbs on the Humphrey Field Analyzer)

Pupil threshold was determined using two different methods: a "frequency of seeing" method and a stimulus response curve method In the frequency of seeing method, a cumulative probability distribution yielded the stimulus intensity where a 50% response rate occurred. The probability distributions were constructed using five different criterian levels (> 0, 0.05, 0 1, 0 2, and 0.3 mm contraction amplitude) for what was arbitrarily considered a pupil response to see what effect criterion would have on the shape of the function and the threshold. In the stimulus-response curve method, a Naka-Rushton non-linear curve was fit to the log intensity vs pupil contraction data at each location The intensity on the curve where each of the five criteria were met was taken as threshold and compared with the probability method.

Results

The pupil contraction amplitude as a function of stimulus intensity fit the Naka-Rushton function well at all locations. In most subjects, the foveal location had a much different function compared to peripheral locations The foveal stimulus-response function showed a shallower slope (decrease in n parameter) and a larger maximum.

The variability of pupil contractions as a function of stimulus intensity is shown for a single location in Figure 1 These data were transformed into cumulative probability functions by

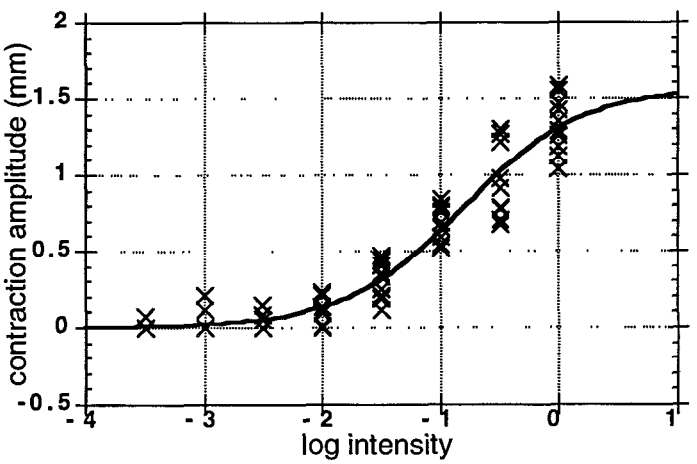

Fig 1 Stimuls-response curve for location 15 3

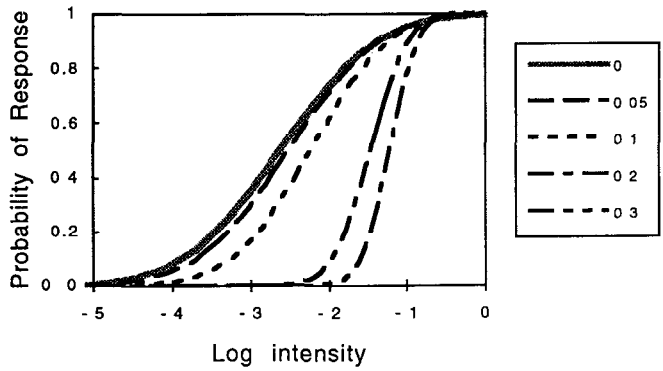

Fig 2 Probability of response vs intensity using five criteria

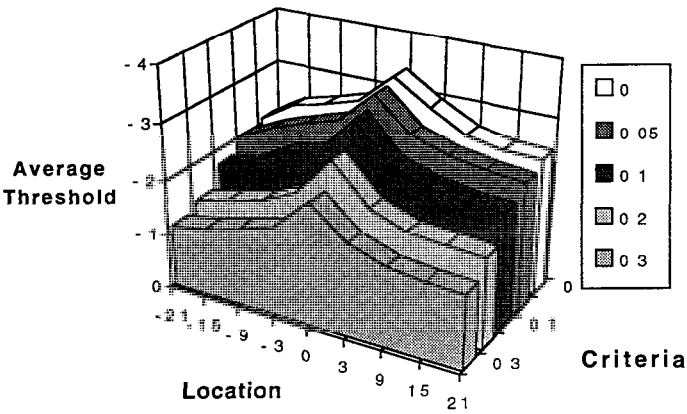

Fig 3 Average threshold for all subjects vs location

using different criteria. At each intensity, single pupil contractions were counted as a "yes" response if they met or exceeded the criterion or were counted as a "no" response if the criterion was not met. An example of the resulting cumulative probability curves for differing criteria is shown in Figure 2. Typically, at higher criterion, the curves shifted to the right, with higher thresholds, as expected. A consistent finding was a steepening (decrease in standard deviation of the normal distribution) in the cumulative probability curve at higher criteria levels.

The shape of the average pupil threshold "hill" of vision is shown along the horizontal meridian for differing criteria levels in Figure 3. The hill consistently peaked at the fovea and sloped down in the periphery. At higher criteria levels, the hill flattened more. This is in contrast to the hill of visual threshold for the same locations, which was flat (Fig 4), except near the blind spot (the points were all located three degrees above the horizontal meridian) Smaller sized stimuli or brighter bowl background raised the visual threshold, but did not appreciably change its flat shape.

Pupil threshold determinations from the Naka-Rushton stimulus response curves for each criteria showed a significant linear correlation (Fig 5) with the probability method of pupil threshold determination (R^2 = 0 90 for 0.3 mm criteria, R^2 = 0 92 for 0 2 mm criteria, R^2 = 0.79 for 0.1 mm criteria).

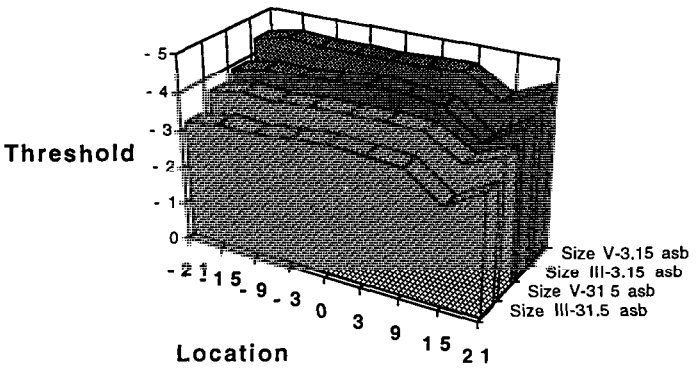

Fig 4 Visual threshold vs location – all subjects

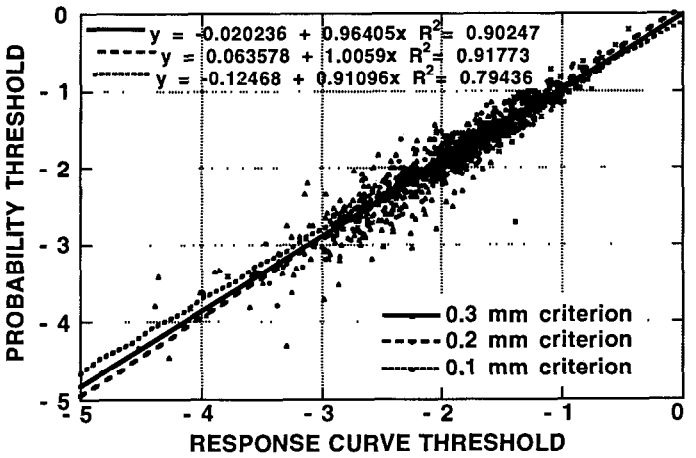

Fig 5 Probability threshold vs threshold derived from Naka-Rushton response curves

Discussion

The difference in the normal island shape between pupil and visual threshold under mesopic conditions highlights the fact that the two systems show some fundamental differences. Although the two systems share the same photoreceptors, the receptive field organization at the ganglion cell level is probably very dissimilar The pupillomotor system has fewer ganglion cells and summates area of stimulus very efficiently. The results shown here were obtained under mesopic conditions and using a 1 7 degree stimulus size. It is likely that both adaptive state and stimulus size affect the shape of the hill of pupil response. The broad shallow slope of the foveal response function also may imply that the pupillomotor input channels are organized differently in this location

We found a very high correlation between the two different methods of pupil threshold determination. Provided the pupil contractions are distributed normally at each intensity, it is not surprising that the Naka-Rushton curve fit intersects the criterion level (contraction amplitude) at the same intensity as the 50% level on the probability function. For normally distributed data, the 50% level should equal the mean and if the Naka-Rushton fit is reasonably good, it too should intersect the mean (and median) of each level of contraction amplitude. It

was only at the lowest criteria (0 and 0.05 contraction amplitude) that the correlation between the two methods diminished We believe this is because the data become less normally distributed at the lower intensities where more and more of the response hit bottom (no contraction) (See Fig. 1) The good correlation between the two methods implies that pupil threshold may be derived from suprathreshold responses by using the Naka-Rushton fit from the higher intensity responses These suprathreshold responses are more reliably measured and since every stimulus light elicits a response within this range, threshold determination would become more time efficient

Another interesting finding was the increased slope of the probability functions at higher criteria A higher slope would be more advantageous for threshold determination because theoretically the variability would be less. One explanation for this finding would be the increasing slope of the stimulus-response functions at contraction amplitudes approaching the highest criteria levels that were used. Although the higher criteria would be expected to elevate threshold, there may be substantial improvement in the repeatability of the threshold determination in the higher slope area of the curve

We are presently investigating the effect of optic nerve disease on the stimulus-response functions derived from pupil perimetry. The shape of the response function appears to provide new information with regard to the probability of seeing curve and may help to explain how disease affects threshold measurement.

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Pupil perimetry with the Octopus 1-2-3: first experience

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Abstract

Purpose: To determine parameters appropriate for pupil perimetry with an Octopus 1-2-3 To evaluate quantification of the pupillary light reflex (PLR) using cross-correlations and line-fitting techniques

Materials and methods: In 60 healthy volunteers (mean age ± S D = 39 3 ± 2.6 years), parameters A [Goldmann stimulus size (ss) 5 at 410 apostilbs (asb) intensity, dark background] were compared with three experimental conditions: B [ss3 at 1632 asb], C [ss3 at 4100 asb], both dark background, and D [ss5 at 410 asb, 31 4 asb background] The inter-individual coefficient of variability (ICV) of the latency time of the PLR, and the response amplitude was calculated for each experimental condition at 20°/20° eccentricity

Results: The variability for latency of PLR onset ($ICV_{latency}$ = 8 1%) was considerably smaller than for amplitude ($ICV_{amplitude}$ = 48.1%) Experimental condition B and C were equivalent Condition D compared unfavorably with A ($ICV_{amplitude}$ = 52 % versus 86 2%; valid responses 76% versus 52%)

Conclusions: Our own software using line-fitting techniques was preferred to cross-correlations, because the results are not given on a nominal scale ("seen" and "not-seen") and, instead, quantifications on an interval scale were obtained. Condition D [ss5 at 410 asb intensity, 31 4 asb background] with its higher inter-individual variability and fewer valid responses appears to be less suitable for pupil perimetry

Introduction

Automated perimetry is currently a standard, universally available test of visual function for early diagnosis and follow-up of a variety of diseases. However, standard perimetry requires reliable patient cooperation, which is often limited[1–4]. Pupil perimetry[5–13] is an objective type of perimetry originally proposed by Harms[14] which has received some attention in the 1970s[15–20]. It requires less cooperation and can be considered useful for legal documentation of impaired visual function. Incongruities between standard perimetry and pupil perimetry can substantiate the diagnosis of functional visual loss. In standard perimetry, pupillary light reactions could be considered in addition to catch-trials when evaluating the patient's reliability, because catch-trials are considered to be poor measures of patient reliability[21].

The study's aim was to optimize the two examination parameters background luminance and stimulus size as well as to evaluate the software provided by the manufacturer of the Octopus 1-2-3 to quantify the pupillary light reflex (PLR) during pupil perimetry Subsequently, an improved software to quantify the pupillary light reflex was developed.

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The authors have no proprietary interest in the hardware or software mentioned

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Materials and methods

Informed consent was obtained from each subject to meet the regulations of the local authorities. Medical history was obtained to exclude any systemic diseases An ophthalmic history was taken, and a complete ocular examination was performed to exclude all eyes with ocular disease or trauma. Eyes with a visual acuity ≤ 20/25 or with intraocular pressures of ≥ 21 mmHg were excluded. Following these criteria, one subject was excluded, because low-tension glaucoma was diagnosed. The evaluated data set consists of 60 eyes of 60 subjects, average age 39 3 ± 2.6 years, pupillary diameter in the dark 6 1 ± 0 9 mm, 35 were females, 25 were males.

A slightly modified Octopus 1-2-3[22] was remotely controlled by a 486/40 mHz personal computer. The Octopus 1-2-3 measures the pupil size at a rate of 50 Hz and transmits the measurements to the PC. An illustration of a typical PLR is given by Turtschi *et al* 1994[13]

The subjects completed a customized program with 29 test locations, *i.e* , a selection of program G1[23]. Each test location was tested four times. In addition, five reference test locations which were tested twice had an eccentricity of –5/–5, +5/+5, –10/–10, and +10/+10 degrees Stimulus duration was always set to 200 milliseconds, the stimulus interval to approximately three seconds, and a dim single fixation point was chosen ("7" on the Octopus 1-2-3 scale) No acoustic or visual cue preceded the stimulus, otherwise introduced to minimize blinking artifacts Each subject completed two tests, once with test condition A (no background illumination, Goldmann stimulus size (ss) 5 or 1 7°), and once with one of the following three experimental conditions; B (ss5 at 1632 asb intensity), C (ss3 at 4100 asb intensity), both with no background illumination, or D (ss5 at 410 asb on a 31.4 asb background).

The raw data were processed with the analysis package provided by the manufacturer Essentially, it is a batch of commands which let the mathematical software package, Matlab[24] perform cross-correlations to evaluate the PLRs as produced by the Octopus 1-2-3. This mathematical procedure compares each PLR with an average of the ten reference PLRs If the correlation coefficient of the two curves exceeds $r = 0.7$, the two curves are considered similar, thus the stimulus has been "seen".

Our self-designed software consists of a code written in the programming language C++. The beginning of the pupillary constriction was defined as the intersection of two optimally fitted lines within the first 25 pixels (500 ms) after the beginning of the stimulus presentation. "Latency" is the time interval between the beginning of the stimulus presentation and the beginning of the PLR No filtering was applied when fitting these two lines. The slope of the first line reflects the contraction velocity before the PLR begins. The slope of the second line reflects the velocity of the PLR In case of a late onset of the PLR, the time frame of pixel 10–35 (200–700 ms) was chosen. After filtering by a moving average of five pixels, a fifth-order polynomial was fitted beginning 20 pixels (400 ms) after the beginning of the stimulus presentation and continuing up to a maximum of 60 pixels (1200 ms) after the onset of the stimulus presentation or until the fit got worse The first minimum of this polynomial defined the maximal contraction of the pupil. "Amplitude" is the difference in pupil diameter between the onset of the PLR and the maximal contraction. The redilation velocity was defined as the slope of a line fitted into the time frame of 5–20 pixels (100–400 ms) after the maximal pupillary contraction

A PLR was rejected if (except for the velocity of the redilation) one of the above-mentioned lines and curves could not be fitted. The average of the four PLRs for each test location of each examined eye was calculated However, this study reports only on the test location at an eccentricity of +20/+20 degrees. The inter-individual coefficient of variability (ICV) of these averages per test location was chosen as measure of scatter This parameter is dimensionless and is often called "relative error". However, the latency can never reach 0. Therefore, $ICV_{latency}$ is similar to the variance depending on the size of the variable and may falsely suggest a high measurement reproducibility.

Table 1 The results refer to the test location at an eccentricity of 20/20 degrees, the test condition A = stimulus size 5, 410 asb intensity, no background illumination; test condition B = stimulus size 3, 1642 asb intensity, no background; test condition C = stimulus size 3, 4100 asb intensity, no background; test condition D = stimulus size 5, 410 asb intensity, 31 4 asb background

	Mean	*Minimum*	*Maximum*	*ICV*	*Valid responses*
Test condition A versus B					
Latency A	322	265	377	8 3%	76%
Latency B	348	295	403	8 9%	80%
Amplitude A	2 2	1 1	3 1	44 9%	76%
Amplitude B	1 8	1 0	2 8	52 4%	80%
Test condition A versus C					
Latency A	332	261	408	9 6%	76%
Latency C	338	270	378	8 3%	76%
Amplitude A	1 9	0 8	2 7	44 9%	76%
Amplitude C	1 7	0 9	2 4	51 7%	76%
Test condition A versus D					
Latency A	334	286	394	8.5%	76%
Latency C	334	258	412	9 0%	52%
Amplitude A	1 9	0 9	3 0	52 8%	76%
Amplitude C	1 2	0 6	2 0	86 2%	52%

Latencies are given in ms, amplitudes in mm ICV = inter-individual coefficient of variability = relative error

Results

The quantification by the Matlab batch of commands performing cross-correlations took approximately 12 minutes for 126 pupillary light reflexes For experimental condition A, including 29 test locations of 60 persons, *i.e* , 1740 test locations, 44 or 2.53% were classified as "not seen" or no pupillary light reflex was detected by the algorithm

The quantification using our own software on the same system was performed within approximately 20 seconds Table 1 summarizes the number of valid quantifications and the inter-individual coefficient of variability or relative error for each set of stimulus parameters Test condition D, *i.e.*, with a background illuminance of 31 4 asb, was considered less apt, as the number of valid quantifications was considerably lower and $ICV_{latency}$ comparatively higher.

Discussion

The concept of cross-correlations to quantify the PLR

In the test condition with Goldmann stimulus size 5, at 410 apostilbs intensity and dark background, 2.53% of the stimulus presentations were presumably wrongly classified as "not seen", or no pupillary light reflex was detected using cross-correlations Individual inspection of these 44 wrongly classified PLRs revealed vulnerability of the algorithm (at least in its current version) to blinking artifacts, fixation losses and pupils smaller than 3 mm. Cross-correlations were performed with a Matlab routine which interpreted a set of commands. On our system this took approximately 12 minutes or 126 stimuli Furthermore, cross-correlations give only the nominal quantification of "seen" or "non-seen".

The concept line-fitting to quantify the PLR

The onset of the PLR was defined as the intersection of two fitted lines. The maximal contraction was defined as the minimum of a fifth-order polynomial fitted to the pupil sizes within an appropriate time frame The velocity of redilation was defined as the slope of a best-fitted line after the maximal pupil contraction. This is a very robust technique to quantify even PLRs with considerable noise[1] superimposed Current investigation will reveal if our way of quantification is, indeed, a better method than that proposed by Kardon *et al* [11] in which the onset and the end of the PLR is defined as first and second derivatives of the pupil size.

Stimulus parameters for clinical pupil perimetry

The search of optimal stimulus parameters had to remain within the technical limits given by the Octopus 1-2-3 perimeter, *i.e* , the stimulus size had to be less than approximately two degrees, and the background luminance could not be less than three asb. However, the latter could be turned off. The current investigation revealed very disturbing hippus (*i e* , steady-state pupillary dynamics without stimulus) with 31.4 asb background luminance. As no background is a poorly defined physiologic state, we are currently investigating a background luminance of three asb.

The results were similar with either stimulus size Stimulus size three at an intensity of 4100 asb corresponds to the maximal stimulus brightness of the Octopus 1-2-3 Entoptic stray light might be a major problem at such stimulus intensities Therefore, the larger stimulus at an intensity of 410 asb is preferred.

Further research is required to investigate whether lower stimulus intensities yield reliable PLRs. Less intense stimuli would permit less recovery time after the stimulus presentation, and, therefore might allow shorter stimulus intervals

Acknowledgments

The authors appreciate the helpful advice of Prof H Bebie in designing our own software for the quantification of the pupillary light reflex

[1] This "noise" of 10–20 Herz occurs infrequently but is still of unknown origin

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Correlation between large field sinusoidal flicker and automated perimetry indices in glaucoma patients

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Abstract

Purpose: To compare quantitative indices of large field sinusoidal flicker testing to automated light threshold perimetry in glaucoma patients

Method: Forty-one chronic open-angle glaucoma patients (age 40–60) with intraocular pressure normalized below 21 mmHg were tested by a) the flicker system, b) the Humphrey Visual Field Analyzer program 30-2 Quantitative indices, LFSF, MD, and CPSD were generated by these systems

Results: There was a statistically significant correlation between LFSF and MD ($r = -0\ 51$, $p < 1\%$) The relationship of LFSF and CPSD was not statistically significant

Conclusion: Large field sinusoidal flicker tests might be useful in screening and follow-up of glaucoma patients, especially when diffuse damage appears to be an active component

Introduction

Light threshold automated perimetry has become the standard in the diagnosis and follow-up of glaucoma. However, it is a long test, accessible only to those patients capable of performing it and in any case not necessarily well adapted to screening. There is, therefore, a real need for an easier and faster test Among tests to consider, we have selected the temporal-contrast test, specifically the large field sinusoidal flicker test[3,4,6,8,11–13]. After initially demonstrating[2] that this test qualitatively differentiates mean curves of glaucoma patients from normal controls, we described[1] a quantitative index for large field sinusoidal flicker (LFSF). In this report, LFSF is compared to quantitative indices of the Humphrey Visual Field Analyzer, specifically mean defect (MD) and corrected pattern standard deviation (CPSD), in an homogeneous glaucoma population.

Methods

Our stimulating device uses a yellow color (585 nm) light-emitting diode (Hewlett Packard, HLMP/4719) with maximum illumination located photo-optically at 21 candelas/m^2 The flickering target is projected onto a black background at a distance of 25 mm and observed under a 30 degree angle through an optical viewer providing a Maxwellian-like view Using a custom program, temporal modulation can be studied from 1–70 Hz. In this study, seven mean and high flickering frequencies (15,20,25,30,35,40,45 Hz) were studied. In addition, the stimulus luminosity was modulated sinusoidally (Delta system), from 0.1%, 0.2%, 0.4%, 0.8%, 1%, 1 5%, 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, 15%, 20%, 40%, 50%, 80%, 100%

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During the examination for each frequency presented in a randomized simulation sequence, contrast threshold of flicker fusion (or perception) is determined using a bracketing technique which ultimately leads to identifying the infra- and supra-liminal thresholds. The infra-liminal threshold is downloaded and represents the "fusion threshold". Sensitivity curves for a wide field sinusoidal flicker function are expressed as a function of a frequency logarithm (along the x axis) and a logarithm of an inverted modulation rate (along the y axis), which is known as a temporal modulation transport function (TMTF) curve, also referred to as a De Lange curve

For each glaucoma patient, we calculated the mean contrast (LFSF) obtained from the total number of recorded frequencies (15,20,25,30,35,40,45 Hz) defined by the formula

$$\text{LFSF} = \frac{1}{7} \sum_{i=1}^{7} \text{Cr}[f(i)]$$

The light threshold perimetry test was carried out using the Humphrey Field Analyzer with optimum optical correction. Indices, MD and CPSD, were generated by Statpac

Definition of patients groups

Our 41 glaucoma patients were aged between 40 and 60 years (mean age 51.9) and included 21 males and 20 females. Visual acuity was > 8/10 (20/25) for distance and > J1 for near. In all cases, the left eye was arbitrarily chosen except when only the right eye met the visual acuity criteria. The glaucomatous visual field was defined as having a mean defect > 3 dB on the Humphrey Field Analyzer, program 30-2 or local defect > 3 dB as definited by the CPSD. Disk cupping was defined as > 0.6. In 29 patients with chronic open-angle glaucoma, intraocular pressure was greater than 21 mmHg confirmed by several measurements. However, LFSF, MD, and CPSD were performed after normalization of intraocular pressure by either medical, laser and/or surgical, treatment[9,10,14,15]. Eyes with other ocular or optic nerve lesions were excluded.

Results

We have noted a statistically significant correlation between MD and LFSF ($r = -0.51$, $p < 1\%$) The regression curve slope is negative (–0.026, with confidence interval of –0.04 to –0 01) (Fig. 1). There is no statistically significant correlation, however, between CPSD and LFSF ($r = 0.18$, confidence interval –0.14, –0.47) (Fig 2)

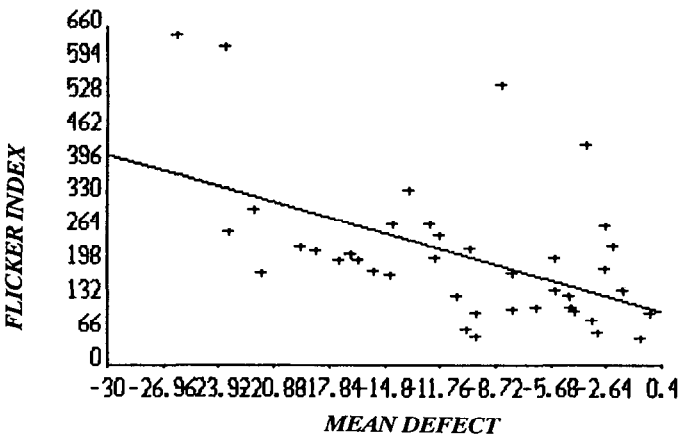

Fig 1

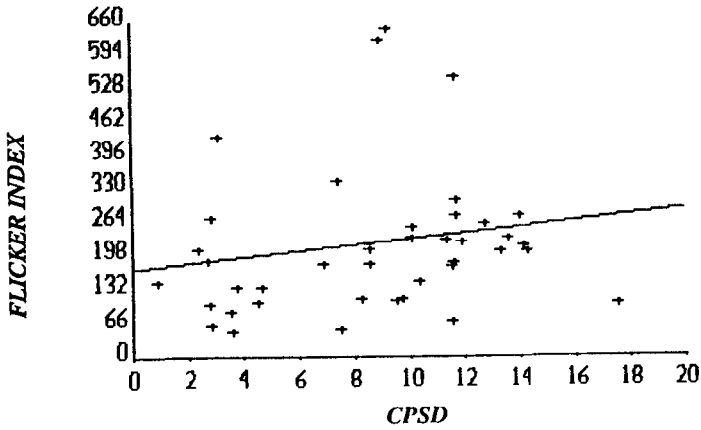

Fig 2

Discussion

The clinician screening for glaucoma must be able to perform a rapid psychophysical test to identify visual function disturbances. Many tests could be considered for this role, but large field sinusoidal flicker sensitivity is most promising[11] After a quick demonstration, the test takes but two to three minutes and is quite easy for patients

Its inter- and intra-individual reproducibility is good[5] and since the test is not sensitive to retinal image degradation therefore may be used in the face of a poor refraction[7] or a cataract

The fairly good correlation shown between LFSF and MD suggests this to be a good test for population screening although small localized defects, with little effect on MD, would be missed. Combining this test with fundus examination or red free disk photos would render the screening effort most comprehensive.

Conclusion

Large field sinusoidal flicker tests might be useful in screening and follow-up of glaucoma patients, especially when diffuse damage appears to be an active component.

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Forced choice flicker perimetry in glaucoma and ocular hypertension

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Abstract

The authors have used a prototype flicker perimeter of their own design to investigate temporal contrast sensitivity in patients with glaucoma, high-risk ocular hypertension (OHT) and normal controls Three novel thresholding strategies were used based on critical flicker fusion frequency, stimulus modulation and differential light sensitivity (luminance threshold) respectively

The results for each strategy correlated closely both with each other and with the mean sensitivities for corresponding visual field locations as measured by the Humphrey Visual Field Analyzer using program 24-2 All strategies identified similar field defects in the glaucomatous subjects For the ocular hypertensive subjects (normal fields with 24-2) the mean flicker perimetry threshold values did not differ significantly from those of the normal controls There were significant differences however between the standard deviations of the two groups of subjects when thresholding by the critical flicker fusion (CFF) strategy (p = 0 005) These results confirm the use of forced choice strategies for flicker perimetry in glaucoma and provide further evidence for flicker field defects in ocular hypertensives

Introduction

Eyes with glaucoma suffer a preferential loss of magnocellular retinal ganglion cells early in the disease process[1,2] These cells are responsive to stimuli of low spatial but high temporal contrast[3] and consequently much interest has arisen in the development of psychophysical methods to demonstrate abnormalities of sensitivity to flicker[4–12]. Despite the promising results of these and other similar studies, flicker perimetry has yet to become widely used in clinical practice

We have previously described a prototype flicker perimetry, the main feature of which is an array of red light emitting diodes (LEDs) which are not equiluminant with the (white) background[13]. In order to investigate the use of threshold strategies based on the different components of a flickering stimulus and in an attempt to make our instrument "patient-friendly" we have devised new test routines based on forced choice; *i e* the identification of the presence of a flickering stimulus amongst a group of other non-flickering stimuli. The aim of this study was to confirm the use of the test routines to detect visual field defects in glaucoma patients and to compare the various strategies.

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Subjects

The following groups of subjects were identified from the glaucoma clinic (see below): patients with primary open-angle glaucoma (n = 12, mean age 57 6 years, range 45–71 years), high-risk ocular hypertension (n = 10, mean age 64.1 years, range 46–77 years) and normal controls (n = 12, mean age 65 years, range 43–78 years). There were no significant differences between the ages of the groups (p = 0.27, ANOVA) All subjects had clear ocular media and a best corrected visual acuity of 6/12 or better. All subjects had previous experience of perimetry using both the Humphrey Visual Field Analyzer (HVFA) and the prototype flicker perimeter. Potential subjects were excluded if there was a history of ocular or neurological disease or surgery, diabetes, or the systemic administration of any medication known to have ocular side effects.

Glaucoma group: All had an established diagnosis of primary open-angle glaucoma with intraocular pressure (IOP) greater than 21 mmHg, characteristic cupping of the optic disk and a reproducible visual field defect using HVFA (program 24-2) A visual field was considered abnormal if the HVFA pattern deviation plot contained three contiguous locations with defects of greater than or equal to 5 dB.

High-risk ocular hypertension group: All had normal visual fields when tested by HVFA (program 24-2). The subjects satisfied the criteria of Yablonski *et al* [14] by having a history of IOP greater than or equal to 28 mmHg and a cup:disk ratio of greater than or equal to 0 6.

Normal controls: These had a normal ocular examination, including a normal optic disk appearance, an intraocular pressure of less than 21 mmHg and normal visual fields (by HVFA).

Methods

Threshold values were obtained at 16 test locations of 1° situated within the central 50° of the visual field (Fig 1). Stimuli were provided by 5 mm diameter red "superbright" light-emitting diodes The background illumination was 10 cd/m^2. Sine wave flicker was used throughout Three threshold strategies were employed (Table 1):

Flicker luminance threshold test: This test strategy is similar to that of many other automated perimeters and is comprised of presentations of flickering stimuli at single locations. The subject was instructed to respond to perception of the stimulus and not to its flickering nature per se. Mean luminance varied according to a threshold algorithm using a 4-2 dB staircase. The modulation of the stimulus, *i e* , the ratio of the peak–trough amplitude of the sine wave to its mean luminance, was kept constant. Flicker frequency was also constant at 15 Hz.

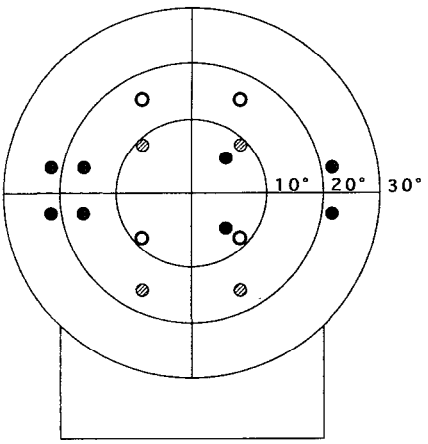

Fig 1 Stimulus locations (as for right eye), groups for forced choice tests identified by different shading

Table 1. Stimulus parameters for the luminance, modulation and critical flicker fusion threshold tests

	Threshold strategy		
Parameters	*Luminance*	*Modulation*	*CFF*
Luminance (dB)	4–2 staircase	30	30
Modulation (dB)	54% of mean luminance	4–2 staircase	8
Flicker frequency (Hz)	15	15	8–2 staircase
Duration (ms)	200	600	600

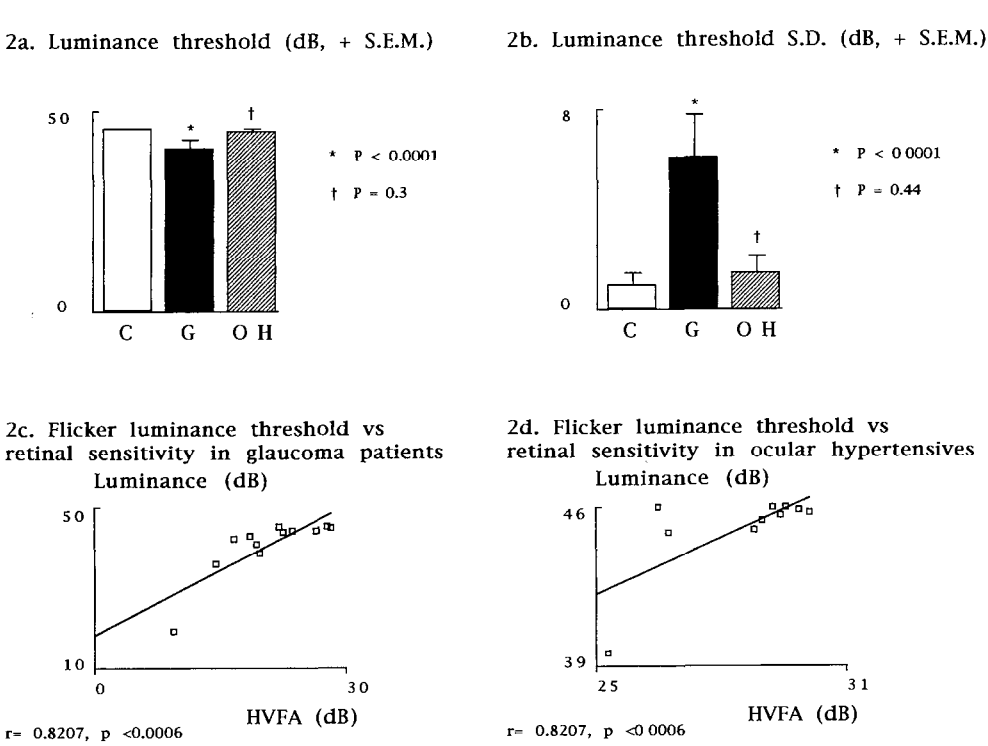

Fig 2. Histograms and scattergrams for the luminance threshold test

CFF and modulation threshold (forced choice strategies): These tests require the subject to respond to the perception of the flicker of the stimulus Groups of four LEDs were illuminated in a pseudo-random sequence. Only one of the four was made to flicker during any one stimulus presentation. The mean luminance of all four LEDs in the group was kept constant during stimulus presentation. Critical flicker fusion threshold values were obtained using an 8-2 Hz staircase, modulation being constant Similarly modulation values were obtained by varying the amplitude of the stimulus according to a 4-2 dB staircase, frequently being constant

As the forced choice tests represented a departure from the traditional thresholding methods with which the subjects were familiar a double checking of the first crossing of the threshold from "seen" to "unseen" was employed Thus the direction on the staircase and step size were not changed until the subject had failed to respond to a stimulus twice

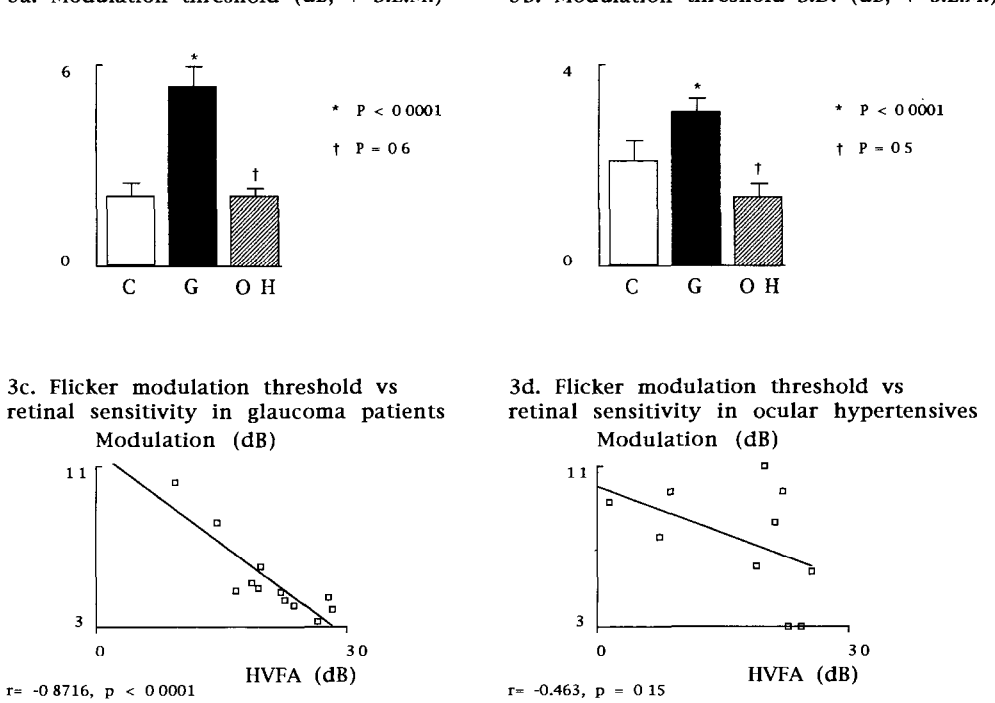

Fig 3 Histograms and scattergrams for the modulation threshold test

Fixation was monitored throughout the test via a telescope behind the fixation target Pupil diameter was measured prior to testing in all subjects, no pupil had a diameter of less than 2 5 mm and in no case was pupillary dilation required.

In addition all subjects had visual fields performed using the Humphrey Visual Field Analyzer, using program 24-2 for the glaucoma and ocular hypertensive patients and either 24-2 or the Armaly full field screening program (with quantify defects strategy) for the controls.

Results

The histograms show the mean threshold values (+ SEM, Figs 2a, 3a, 4a) and the standard deviation of the threshold values (+ SEM, Figs 2b, 3b, 4b) for each of the groups for each of the flicker tests The glaucoma group result is significantly different from the controls in each case (Mann-Whitney U test). The high-risk ocular hypertensives behaved, as a group, in a very similar way to the controls The ocular hypertension group's standard deviations for the CFF threshold test were significantly different however (p = 0.005, Mann-Whitney U test).

The scattergrams show the glaucoma patients' (Figs. 2c, 3c, 4c) and ocular hypertensives' (Figs. 2d, 3d, 4d) mean threshold values for each of the flicker tests plotted against the mean sensitivity for the equivalent locations in the visual field as measured by the HVFA. Simple regression analysis reveals a significant correlation for the glaucoma patients for all three tests, and for the ocular hypertensives for the flicker luminance threshold test. There was no significant correlation however between the mean threshold values for HVFA and the flicker modulation and CFF thresholds for the ocular hypertensives

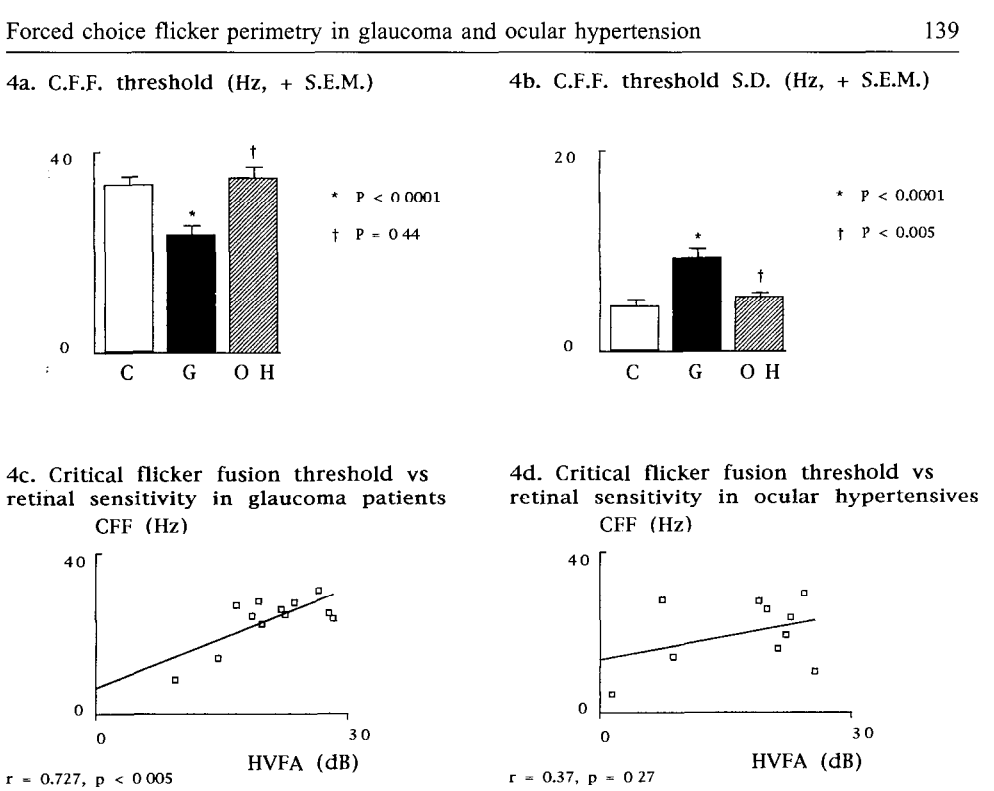

Fig 4. Histograms and scattergrams for the critical flicker fusion frequency (CFF) threshold test

Discussion

The results of the present study confirm the presence of flicker visual field defects in glaucoma and the ability of the prototype flicker perimeter to detect them. With the exception of the CFF threshold test for one patient (who had very early glaucoma) all the test strategies revealed abnormal threshold values at some locations in the visual fields of all the glaucoma patients.

Previous reports of flicker perimetry in glaucoma have used various test strategies for determining temporal contrast sensitivity. Lachenmayr *et al*[5,7] have developed a system based on thresholding the CFF frequency, and have shown evidence of good correlation between the results of flicker perimetry and other techniques. Johnson and Casson[11,12] using a technique measuring modulation sensitivity, have demonstrated defects in flicker perimetry which predate changes detectable by conventional perimetry. Both of these techniques utilize stimuli which are equiluminant with the surround. Feghali *et al*[6] report visual field defects in glaucoma and ocular hypertension using flickering stimuli with a luminance threshold based strategy, the greatest deficit being demonstrated at mid frequency This finding was supported by our earlier report[15]. In the present study we have also found a close correlation between the threshold values obtained for the various flicker tests and the HVFA program 24-2 for the group of glaucoma patients. This was not the case however for the high-risk ocular hypertensive subjects and may reflect early field changes not detectable by conventional methods. It is also of interest that our normal controls exhibited a relatively larger range of values for the modulation and CFF tests than for the flicker luminance threshold test. Casson and Johnson have described both a greater age-related decrease, and ocular hypertension-related increase of modulation sensitivity at 16 Hz compared with lower frequencies[12]. Our results would tend to confirm these findings, although alternative explanations include a greater range of retinal

sensitivity for these functions for our apparatus, the presence of as yet unrecognized disease or simply the early part of a learning effect.

In conclusion, forced choice strategies may provide an effective alternative in flicker perimetry for the detection of visual field defects in glaucoma The test strategy and stimulus parameters which best separate glaucoma sufferers from normals remain to be fully elucidated and are under further investigation

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Automated flicker perimetry in glaucoma

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Abstract

Using the Octopus 1-2-3 and its remote software package, we studied flicker fields of 150 eyes of 82 early glaucoma patients Static fields of these patients were also tested using the program No 32 of the Octopus 201 In this study we tested the same test points using both our own flicker perimeter and the Octopus 201 In addition, using red free fundus photographs and a scanning laser ophthalmoscope, we studied the correlation between the values of differential light sensitivity and the critical fusion frequency in the area where nerve fiber layer defects were observed. When the values of differential light sensitivity of the test points decreased from 30 dB to 20 dB, the cff of these points decreased remarkably from 40 Hz to 5 Hz It was found that 47% of the test points showed a sensitivity loss of more than 30 Hz by flicker perimetry It was confirmed that automated static flicker perimetry was more sensitive in detecting early glaucomatous visual field defects than Octopus perimetry

Introduction

Glaucomatous damage causes both morphological changes of the nerve fiber layers and functional loss of the corresponding area. It is known that optic nerve fiber damage in early glaucoma often remains undetected by traditional perimetric techniques[1]. It is therefore very important to establish more sensitive perimetric methods to detect early glaucomatous visual field loss. Previous investigators have reported that flicker perimetry is more sensitive than traditional light threshold perimetry for detecting early glaucomatous visual field defects[2–6] Using the Octopus 1-2-3 (Interzeag) and its remote software package, we developed a strategy for automated flicker perimetry to measure the critical fusion frequency (cff) in the central field[7]. The aim of the present study was to compare flicker perimetry with light threshold perimetry in the detection of glaucomatous field defects. Using red free fundus photographs and a scanning laser ophthalmoscope (SLO, Rodenstock), we studied the correlation between the values of differential light sensitivity and the cff of the same test points in the area where nerve fiber layer defects (NFLD) were observed.

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Subjects and method

Patients

Measurement was carried out in a total of 150 eyes of 82 subjects; 121 eyes of 67 patients with primary open-angle glaucoma, 25 eyes of 13 patients with normal-tension glaucoma, and four eyes of two patients with secondary glaucoma The stages of their visual fields were as follows 64 eyes with stage 0–1, 56 eyes with stage 1, and 30 eyes with stage 2 according to Aulhorn's classification modified by Greve[8] The mean age of the study population was 52.7 ± 11.1 years (minimum, 27 years, maximum, 75 years). The inclusion criteria were as follows pupil diameter of ≥ 3.0 mm; corrected visual acuity of ≥ 20/20; refractive errors of ≤ 6.5 D (spherical) and ≤ 3 D (cylindrical) and clear optical media

Visual field tests

For the assessment of glaucomatous visual field damage, we performed both conventional differential light threshold perimetry and flicker perimetry Differential light threshold perimetry was performed using the Octopus 201 (Interzeag) For this investigation, we used the program 32 which tests 76 points in the central 30 degree visual field. Differential light threshold perimetry was performed with a stimulus size 3 under the background luminance of 10 cd/m^2 The duration of each target stimulus was 100 msec. The Peridata (Interzeag) was used for each individual field analysis.

Flicker perimetry was performed using our original program for the Octopus 1-2-3 and its remote software package[7] The arrangement of test points was the same as that of test points of the Octopus standard program No 38. Flicker perimetry was performed with a stimulus size 3 under the background luminance of 31.5 asb The duration of each target stimulus was one second. Age-related normal values from 100 normal eyes of 100 individuals were used for flicker field analysis. Differential light threshold perimetry and flicker perimetry were performed within a period of two months

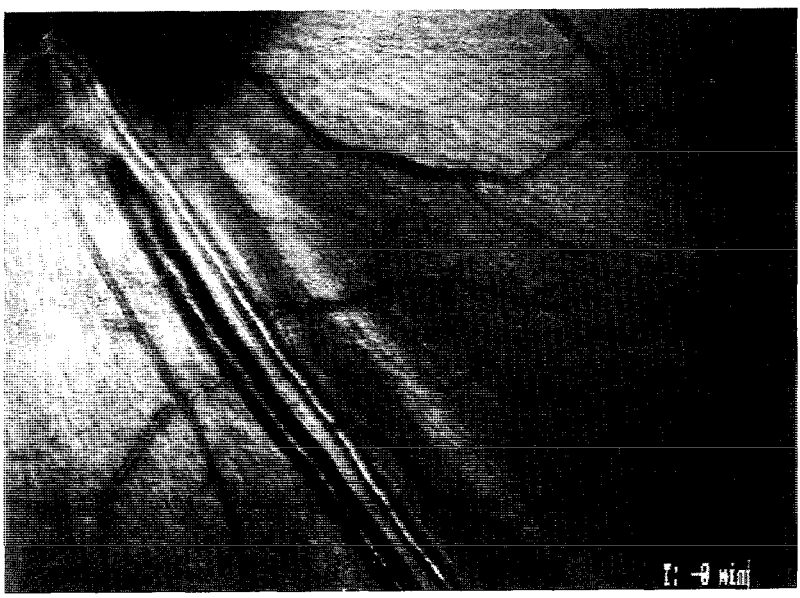

Fig 1 SLO images of typical wedge-shaped NFLD

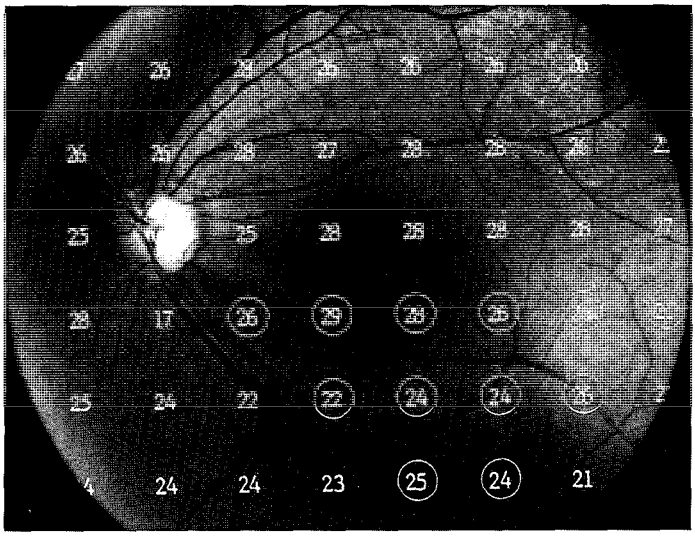

Fig 2 A composed image of a red free fundus photograph and a visual field Circled test points were located in the area of NFLD

Fundus examination

Red free fundus photographs and a SLO were used for the detection of NFLD. Red free fundus photographs were taken through a dilated pupil with a CF-60U (Canon) 60 degree fundus camera, using Kodak 2414 Technical Pan film and a Kodak Wratten filter No 44A. A SLO was also used for the detection of NFLD with an argon blue laser beam and a C1 aperture.

In this study we chose patients who had wedge-shaped NFLD on red free fundus photograph and/or SLO images (Fig 1). Using composed images of red free fundus photographs and visual fields, we compared the difference between the cff and the value of differential light sensitivity in the area where wedge-shaped NFLD was observed (Fig. 2)

Results

A study of red free fundus photographs and SLO images revealed that wedge-shaped NFLD was detected in 75 eyes out of 150 eyes tested. Figure 3 shows the relationship between the cff and the value of differential light sensitivity of 792 test points in the area of NFLD. Sizes of the rings are proportional to the number of the test points which are plotted at the same point. When the values of differential light sensitivity of the test points decreased from 30 dB to 20 dB, the cff of these points decreased remarkably from 40 Hz to 5 Hz Many test points where the values of differential light sensitivity were less than 15 dB were shown to be 0 Hz by flicker perimetry.

Figure 4 shows a histogram of the difference from the age-related normal values of differential light sensitivity in the area of NFLD. In a total of 792 test points with NFLD, 523 test points were judged as abnormal by differential light threshold perimetry. Figure 5 shows a histogram of the difference from the age-related normal values of the cff in the area of NFLD In a total of 792 test points with NFLD, 595 test points were judged as abnormal by flicker perimetry. It was found that 47% of the test points showed a sensitivity loss of more than 30 Hz by flicker perimetry

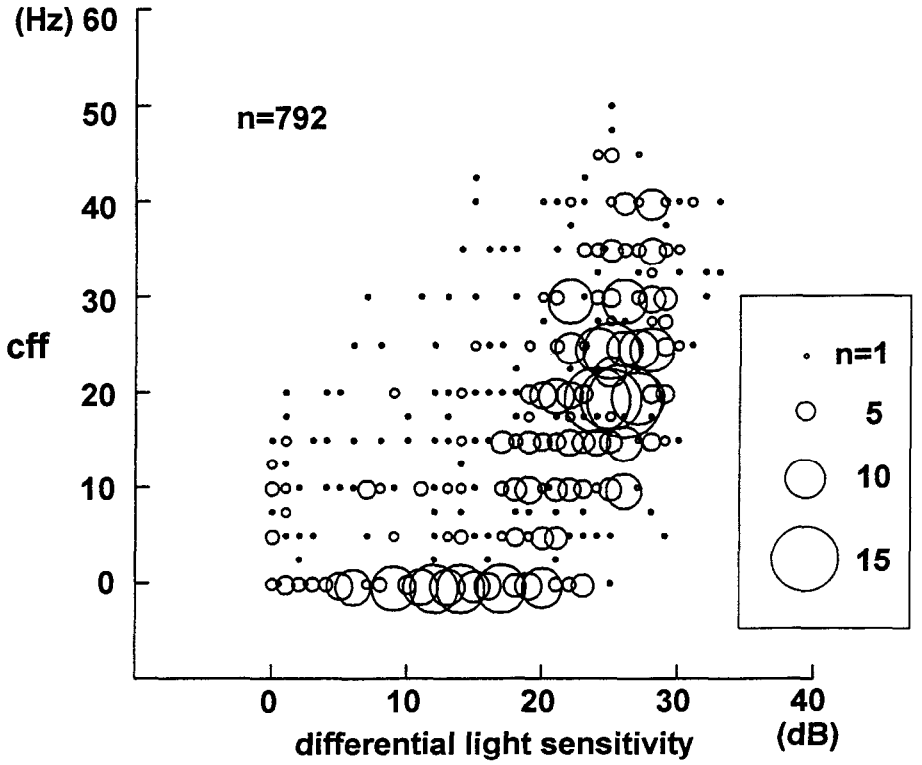

Fig 3 The relationship between the cff and the values of differential light sensitivity of 792 test points in the area of NFLD Sizes of the rings are proportional to the number of test points which are plotted at the same point

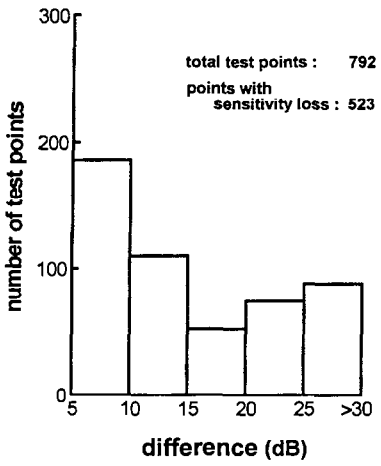

Fig 4 A histogram of the differences from the age-related normal values of differential light sensitivity in the area of NFLD

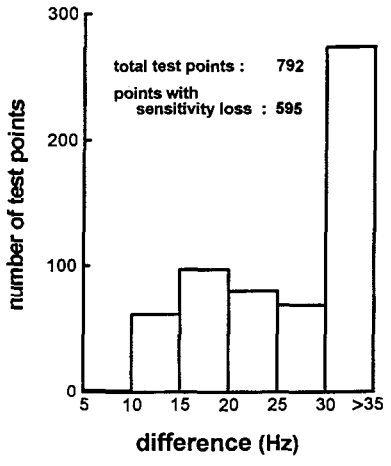

Fig 5 A histogram of the differences from the age-related normal values of the cff in the area of NFLD

Discussion

NFLD is one of the most important signs of glaucomatous optic nerve damage Several authors have reported on various methods for classification of NFLD in glaucoma[9–11] The purpose of our present study was to compare the cff with the values of differential light sensitivity in the area where obvious glaucomatous damage was observed. A study of red free fundus photographs and SLO images revealed that there was a well-demarcated NFLD margin on the blind spot side, but that the peripheral side was obscure Therefore, in this study, we chose cases of typical wedge-shaped NFLD as cases of glaucomatous field defects

In our study, in a total of 792 test points of wedge-shaped NFLD, 269 test points were judged as normal by differential light threshold perimetry and 197 test points were judged as normal by flicker perimetry. Okubo and Mizokami reported that in cases of wedge-shaped NFLD, either the area of no depression or the area of very shallow depression could be detected near the blind spot by kinetic fundus perimetry and Octopus perimetry, while the area of deeper depression was detected farther away from the blind spot[12]. Most of the points of normal sensitivity were located near the blind spot in our study. The area of NFLD contained several grades of damaged nerve fibers and most of these damaged fibers were found to come from the retinal ganglion cells located in the more peripheral nasal retina. Therefore, sensitivity gradients could probably be detected in the area of NFLD

In our study, we compared the cff with the values of differential light sensitivity in the area of wedge-shaped NFLD at each individual examination point Our results indicated that the cff showed a larger decrease from the normal values than those of differential light sensitivity in the area of wedge-shaped NFLD Lachenmayr *et al* reported that flicker perimetry showed the better correlation with NFLD as compared with differential light threshold perimetry and resolution perimetry which used global indices and NFLD score[13] These results suggest that exposure of a flickering target is one of the most sensitive stimuli to detect early glaucomatous visual field defects

Quigley *et al.* reported that large optic nerve fibers were selectively damaged in early glaucoma[14]. It is well known that a magnocellar pathway which has large optic nerve fibers is more sensitive to the target stimulus of high contrast and high temporal resolution Our findings that flicker perimetry is more sensitive than differential light threshold perimetry seem to support the idea that the magnocellar pathway is mainly damaged in early glaucoma.

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Glaucomatous visual field loss detected by threshold light offset stimuli

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The visual system has differential sensitivity to both light onsets and light offsets It is possible that testing with light offset (dark-on-bright) stimuli may facilitate the diagnosis of visual field loss in glaucoma. Twenty-one primary open-angle glaucoma (POAG) patients (mean age 63 yr; range 37–76 yr), 21 ocular hypertensive (OHT) patients (mean age 61 yr; range: 39–75 yr) and 13 normal individuals (mean age 60 yr; range 40–84 yr) were tested with the full threshold test program 24-2 of the Humphrey Visual Field Analyser, using conventional light onset stimuli. The same eyes were also tested with offset stimuli created on a video-display unit (VDU), using an ascending staircase single crossing threshold combined with a computerized moving fixation method. The test grid for light offsets was identical to that of the 24-2 program and consisted of 54 test locations. Both onset and offset stimuli were of 16 mm^2 (size IV) and presented for 0 2 seconds on 10 cd/m^2 background. The threshold 95% confidence interval (CI) levels were calculated at each test location for both types of stimuli in the control group Test locations with decreased sensitivity outside the 95% CI were determined in the POAG and OHT groups and global field indices of "mean defect" (MD) and "loss variance" (LV) were calculated for each eye. The offset stimuli had 95% (20/21) sensitivity in the POAG group and 100% specificity in the control group In the OHT group, offset stimuli indicated field abnormality in 59% (12/21) of the eyes which tended to be the ones with higher risk of developing glaucomatous visual field loss according to the regression formula devised by Hart and coworkers. The topographical distribution of the field defects to light offset stimuli in the POAG and OHT groups was found to be nerve fiber layer type, involving superior and inferior Bjerrum areas with respect to horizontal meridian as similar to that revealed by light onset stimuli in the POAG group The results suggest that light offset stimuli provide a satisfactory indication of glaucomatous visual damage and may also reveal visual loss undetected by conventional onset stimuli in high risk ocular hypertensive eyes. Full results will be published elsewhere.

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Ramp stimulation perimetry in testing the X-system

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Introduction

Visual function can be described by the characteristics of the receptive field of the optic nerve. We measured thresholds in various stimulation sizes, drew the diameter-threshold curves, and examined the shapes, areas and densities of the receptive fields using computer simulations[1–5] We studied the receptive fields using both pulse and ramp stimuli, and found that the Y-system was excited by pulse stimulation and the X-system by ramp stimulation[3] The experiments were carried out using a fundus perimeter with a Maxwellian view system The procedure was too complicated to apply to clinical cases because of the machine size, the necessity of precise machine settings and the long period of time needed for the examination At the last IPS meeting in Japan we demonstrated diameter-threshold curves in normal and pathologic subjects using an automated perimeter[4]. The resulting pulse stimuli were similar to those obtained using a fundus perimeter. In this paper we will discuss receptive fields for ramp stimulation using an automatic perimeter.

Method

Two minor modifications were made to a Topcon Computerized Perimeter SBP-2020. First, a wedge filter was inserted The target intensity was smoothly increased in a logarithmically linear pattern through the use of a stepping motor The slope, height and initial luminance of the stimulus were left to our own discretion. The second modification was the addition of a smaller stimulus, 1 6 min in diameter.

Five retinal points were tested: 0, 5, 10, 15 and 20° from the fovea on the upper nasal meridian Six stimulus sizes 1.6, 3 2, 6 5, 13, 26, and 52 min in diameter were used The background luminance was set 31.5 asb. Threshold was determined using ramp and/or pulse stimuli.

During the ramp stimulation sequences the stimulus intensity was initially set about 15 dB lower than the normal threshold and was gradually increased The subject was asked to press a button the instant he or she saw the stimulus. The stimulus was turned off when the button was pressed, and the intensity was registered as the threshold.

During the pulse stimulation sequences, the stimulus duration was 200 msec. One dB threshold steps were decided on by using a standard threshold bracketing strategy[4].

Experiment 1

The height of the ramp increment was set at 30 dB Stimulus size was 3.2 min in diameter A normal subject was examined, and the increment period was changed to 3, 5, 8, 10, 15 and 20 sec respectively. The examination at each increment was done five times

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Experiment 2

Fifteen eyes of 15 normal subjects were examined using ramp stimuli. The subjects consisted of six males and nine females, whose ages ranged from 24 to 41, with a mean of 30.0 years. The increment period was 15 sec Some clinical cases were also examined.

Results and discussion

Experiment 1

Figure 1 shows the threshold and the period of ramp increments at 0 and 15° of eccentricity, respectively. When the period was longer than 15 sec, the threshold was almost constant.

Okamoto *et al* [3] examined receptive fields using ramp stimuli and concluded that his results could correspond to the X-system of the optic nerve. Ramp stimulation in his experiments during the increment period was 3 sec with a constant increment height. He measured the threshold using the up-and-down method This procedure took too much time for practical clinical use.

In our experiments the threshold was determined as the brightness when the subject pressed the button The reaction time affects the results The reaction time is normally 300 to 600 msec with an average distribution of ± 150 msec per individual[6]. In the 15-sec increment period, 600 msec corresponded to 0 3 dB. So the error caused by reaction time and the distribution was 0 4 to 1 5 dB. In ordinary static perimetry, we wait less than one second for the response and determine the threshold in 2 dB steps The error caused by reaction delay might be acceptable for clinical testing

It was not easy for the subject to maintain attention to the stimulus for more than 15 sec. Subjects preferred a 15-sec increment period. We decided that 15 sec would be suitable for clinical examinations Thus we used the 15-sec increment period for further experiments.

Experiment 2

In Figure 2 the foveal threshold (log ΔI) was plotted against the stimulus diameter in 15 normal subjects. Average diameter-threshold curves with standard deviations examined at 0, 10 and 20° of eccentricity are shown in Figure 3

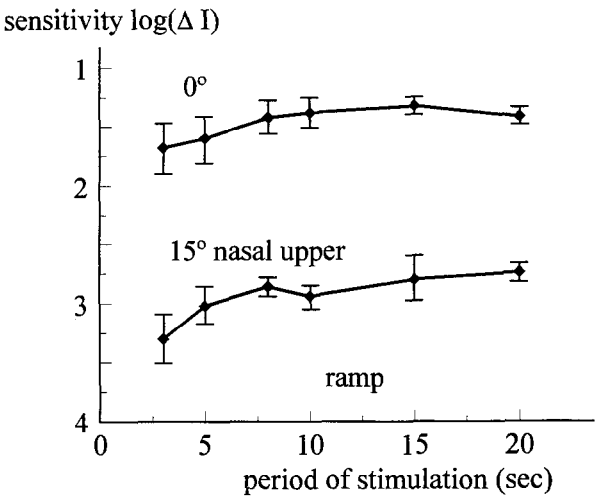

Fig 1 Sensitivity and period of ramp stimulation Abscissa indicates full period of ramp stimulation. Height of ramp was set at 30 dB. Stimulus diameter was 3.2 min Upper trace at the center, and lower trace 15° from the center.

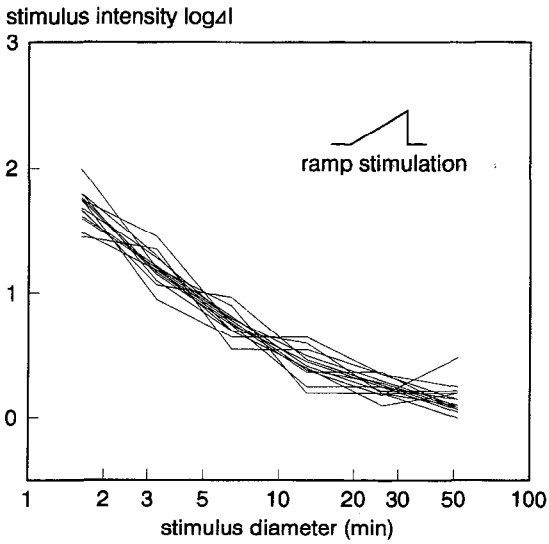

Fig. 2 Diameter-threshold curves testing using ramp stimulation at the center of the visual field Abscissa indicates the stimulus diameter, and ordinate relative threshold. Each curve represents 15 normal eyes.

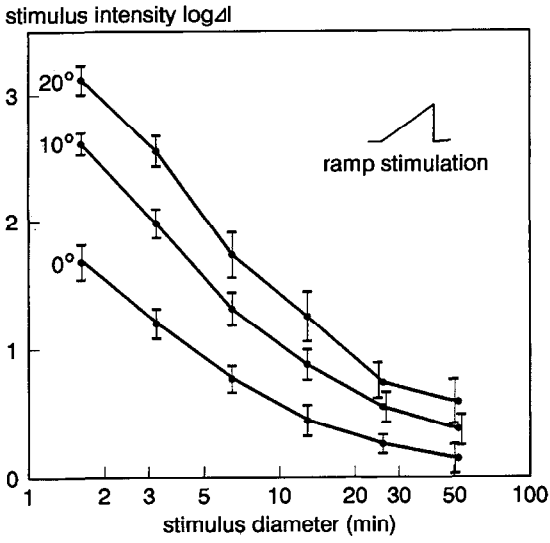

Fig 3. Diameter-threshold curves of 15 normal subjects. Average and standard deviation at 0, 10 and 20° from the center on upper nasal meridian

In Figure 4 the threshold energy was calculated as log(I+ΔI)S, with "I" being background intensity, "ΔI" being increment intensity and "S" being the stimulus area. The diameter-threshold curves are parallel to the abscissa where the stimuli are smaller than 6.5 min in diameter at 20° of eccentricity. This shows complete summation Where the stimuli are larger than 26 min in diameter, the slopes of the curves approach 45° at every tested point, showing non-summation. For stimuli between 6.5 and 26 min in diameter, incomplete summation was found.

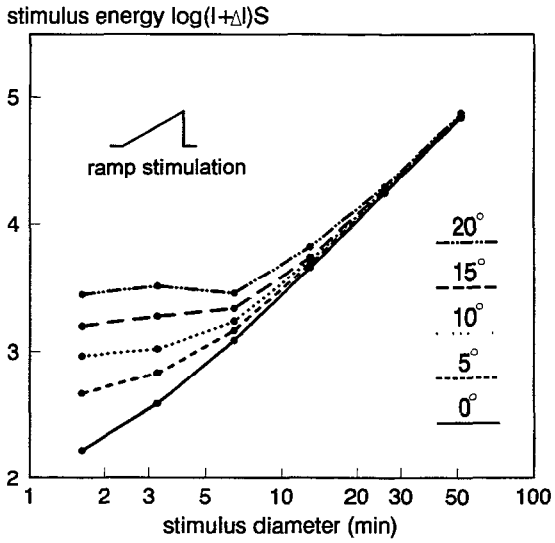

Fig 4 Average diameter-threshold curves at each point are plotted against the ordinate in stimulus energy, log(I+ΔI)S, "I" being background intensity, "ΔI" being increment intensity and "S" being the stimulus area

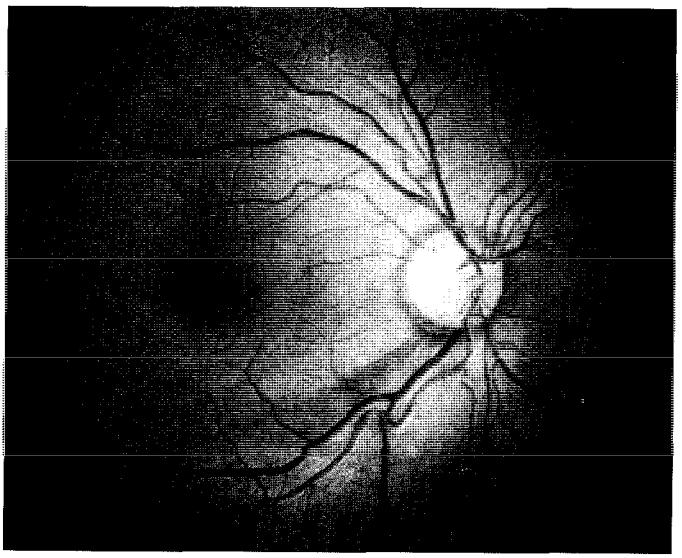

Fig 5 The right fundus of Case 1 A disk with a large cupping and nerve fiber bundle defects are seen

Clinical cases

Case 1 H.Y. This 41-year-old female was referred to our department for a diabetic retinopathy examination. Her fundi indicated no diabetic retinopathy, but a disk with a large cup was found in each eye and nerve fiber bundle defects were found in her right eye (Fig. 5).

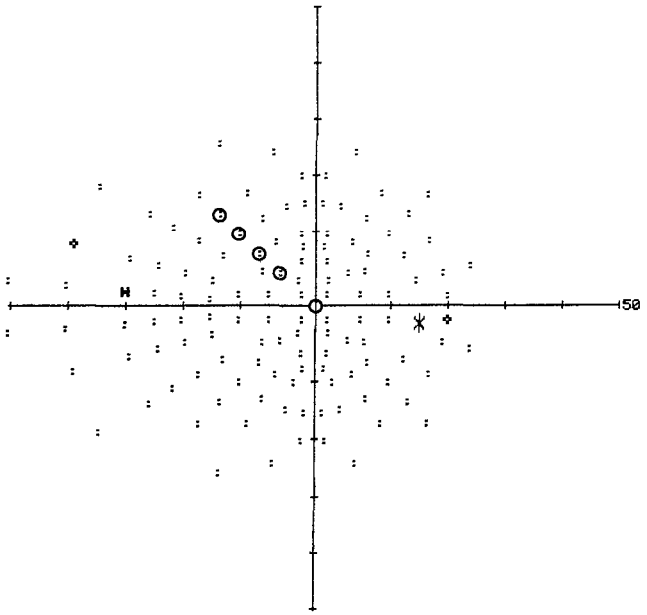

Fig 6 Visual field of the right eye in Case 1 Circles indicate tested points

Neither eye demonstrated elevated intraocular pressure. Her best corrected visual acuity was R.E : 1 5 and L E : 1.5 A very small scotoma was found in the nasal periphery of the right eye (Fig. 6). Her thresholds were examined using both pulse and ramp stimulations. The diameter-threshold curves are shown in Figure 7 Threshold elevation was found at the 10° nasal upper, by using pulse stimulation These results correspond with previous findings stating that Y cells are thick and have large receptive fields, and that they may be more easily damaged by pressure than X cells.

Case 2. O K This 28-yr-old female had noticed a visual disturbance in her left eye since her seventh month of pregnancy. By using suprathreshold perimetry several scattered points in her left temporal visual field were shown to demonstrate a slightly elevated threshold, while there were only a few points in her right temporal visual field that demonstrated this condition, indicating a slight bitemporal hemianopia (Fig. 8) The ramp and pulse measurements were taken at the points on the nasal lower and the temporal lower meridian where there was no sensitivity loss. The diameter-threshold curves are irregular at every point (Fig. 9) Abnormalities under pulse stimulation are clearer than those under ramp stimulation This may indicate more damage to Y cells than to X cells.

In Figure 10, the diameter-threshold curves obtained using ramp stimuli in 15 normal subjects are compared to those obtained using pulse stimuli The energy necessary for ramp stimulation is lower than that necessary for pulse stimulation at 0° and 5° The nearer the position of the test point to the center, the clearer this tendency becomes.

These curves are similar to those obtained by precise psychophysical examinations using a fundus perimeter[1,3] In our experiment, diameter-threshold curves at 10, 15 and 20° showed no difference between ramp and pulse stimulations. These results cannot be compared to Okamoto's results because he examined retinal points that were 10° or less from the fovea[3] However, in clinical cases different curves were obtained even at 10, 15 and 20° (Figs. 7 and 9). It is not clear whether we could measure the difference between X- and Y-systems, but there is some possibility that we were measuring different visual processes

The diameter-threshold curves obtained using ramp and pulse stimuli were obviously different at 0° (Fig. 11). As the stimulus size increases the curve for ramp stimulus eventually

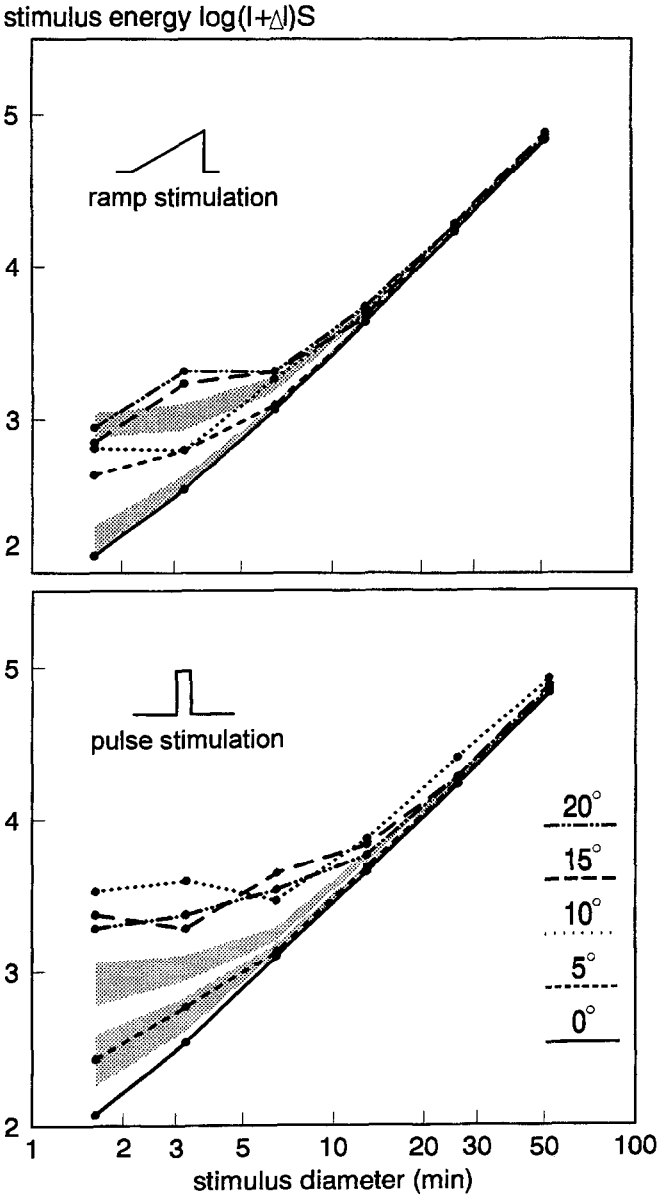

Fig 7 Diameter-threshold curves in Case 1 that were measured at the points (Fig 6) using ramp (upper) and pulse (lower) stimulation The shadows show standard deviation for the 15 normal subjects at 0 and 10° eccentricity

Fig 9 Diameter-threshold curves in Case 2 The two upper figures were under ramp stimulation and the lower two were under pulse, the right two were the results on the temporal lower meridian and the left two, on nasal lower meridian (Fig 8). The shadows show standard deviation of 15 normal subjects at 0 and 10° eccentricity.

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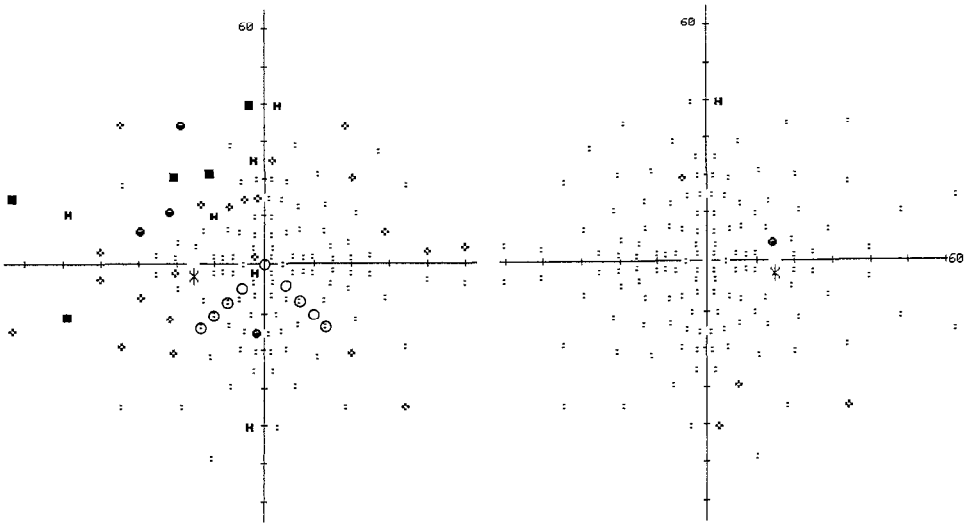
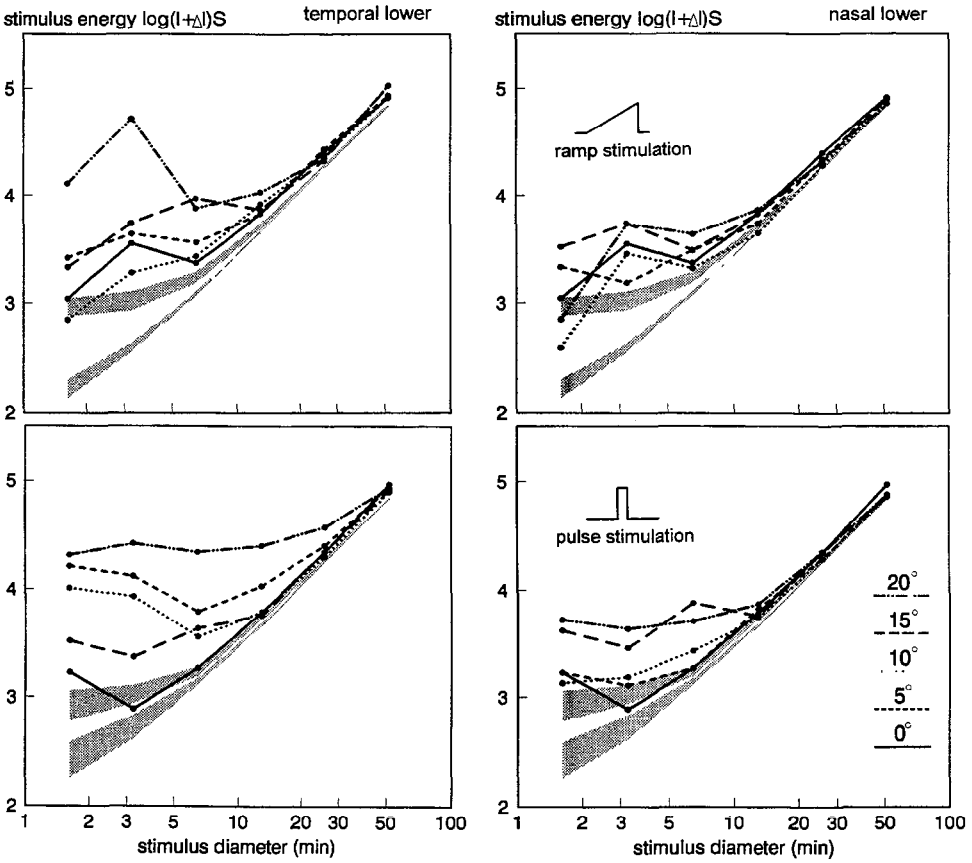


Fig 8 Visual field of Case 2 Circles indicate tested points



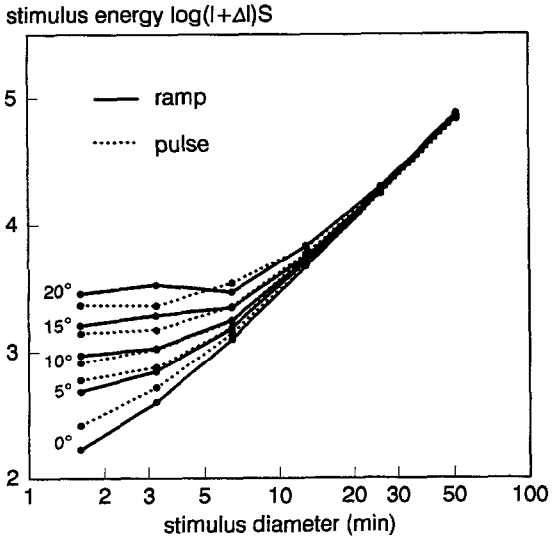


Fig 10 Diameter-threshold curves in normal subjects. Solid lines show ramp stimulation and dotted lines show pulse stimulation

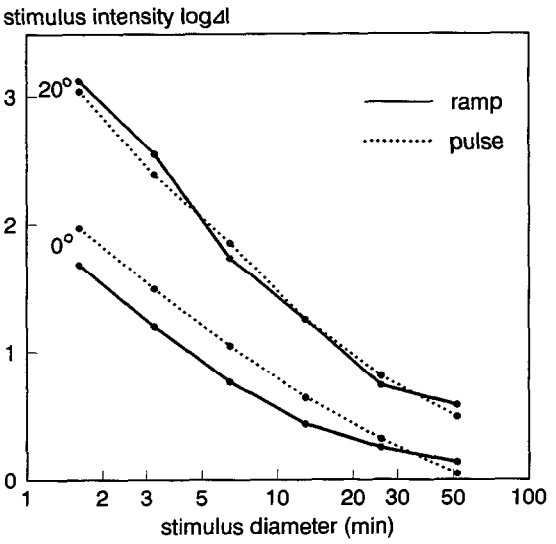


Fig 11. Average diameter-threshold curves tested at 0 to 20° eccentricity in normal eyes. The solid line shows the results under ramp stimulation and dotted line shows pulse stimulation.

becomes a horizontal line, which suggests that lateral inhibition in the receptive field reacting to ramp stimulation is larger or stronger than that to pulse stimuli

Our purpose was to easily measure the characteristics of the human retinal receptive field Okamoto's experiments using the fundus perimeter suggests that ramp stimulation reveals the characteristics of the X cells. We used a computerized perimeter to measure the threshold and got similar results. We could not use smaller targets because of optical and technical limitations. The complete summation area could not be measured using ramp stimuli. However, if

smaller stimuli had been used, the receptive fields at fovea and near fovea could have been measured. We will continue our experiments, attempting to apply our findings to clinical cases

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Multi-dimensional color, flicker and increment perimetry

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Abstract

Isolating color or flicker mechanisms may help identify early visual loss The authors consider whether a multi-dimensional stimulus (simultaneously containing a luminance increment, color and flicker attributes) can be used to isolate such mechanisms For this study we used a commercial LED perimeter that presents green LEDs flickered at frequencies between 0 and 36 Hz Thresholds were obtained with a 6/3 dB staircase with subjects responding to different detection criteria (increment, flicker or color) We tested three experienced observers (aged 24–32) at 0–22° along a single meridian (45°); two extensively and one with a reduced protocol The means and SDs of multiple threshold estimates were analysed

Color, flicker and increment sensitivity vary at different rates as a function of eccentricity and can be modeled using power functions Flicker and increment detection power functions coincide for flicker frequencies < 9 Hz We propose that two detection mechanisms can be isolated using multi-dimensional stimuli and criterion priming One is sensitive to fast flicker and the other is sensitive to low frequency (static) increments: both have color and achromatic components Differentiation between these temporal filters is achieved by using a 9–18 Hz flicker rate We suggest a protocol for clinical application that taps the fast flicker mechanism and show how such testing can provide additional information for patient management

Introduction

Anatomical segregation occurs within the primate visual system and produces a corresponding functional segregation involving the color and temporal properties of a stimulus[1] Lateral geniculate (LGN) neurons that have their cell bodies in the magnocellular layers have higher temporal resolution than those neurons with their cell bodies in the parvocellular layers of the LGN[2]. Although some overlap in processing exists, losses of magnocellular neurons primarily produce defects for fast flicker thresholds[1] whereas losses of parvocellular neurons lead to color defects[1,3].

Anatomical studies of glaucomatous optic nerves show that there might be a tendency for larger caliber axons to be selectively lost[4–6] It is not possible to tell from these studies, whether the effected axons were magno- or parvocellular, moreover, a recent reanalysis of this work questions the validity of the conclusion that large cells are selectively damaged[7]. However, since the magnocellular ganglion cells mediate the detection of fast flicker[2], some investigators have suggested the use of fast flicker rates for the disclosure of early glaucomatous damage[8–12] Likewise, the larger parvocellular ganglion cells are thought to be of the blue-yellow opponent type[13]. For this reason blue sensitivity has been investigated as a tool for the early detection of glaucoma[11,14,15]. Both modalities have been found to precede losses of standard increment

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threshold by up to 3–5 years[11] although the widespread involvement found with such losses[16,17] is not consistent with a model of selective anatomical damage.

Apart from being able to favor the responses of sub-populations of ganglion cells, varying the flicker rate of a stimulus has other benefits that may prove useful for the detection of early disease One of these is the capacity to isolate channels that are operating at different adaptational states (*i e* , linear versus Weber)[18]. This capacity may be useful for the detection of dysfunction because the adaptational state of visual mechanisms has been shown to be affected differentially by ocular disease[15,19,20]

The problem with testing flicker and color sensitivity using a detection paradigm is that the stimulus needs to contain only the attribute under study. Such stimuli require complex methods for their generation However, we propose an alternative approach to test such mechanisms. The fact that the visual system processes information in separate channels can be used to advantage by asking the observer to selectively attend to one or other of these channels Such selective attention is possible because visual processing occurs along labeled lines specific for a given sensorial attribute[21]. Such techniques have been successfully applied to study color, temporal and achromatic processing using a detection criterion[22,23] or in discrimination experiments[24–26]. However, the use of these methods has the potential to lead to ambiguous results due to altered higher-level processes such as attentional shifts; strategies have been proposed to deal with such problems[27].

In this study we investigate the ability of normal observers to discriminate "flicker" and "color" from a luminance increment using multi-dimensional stimuli that have concurrent flicker, color and luminance information This capacity is tested in the fovea and periphery at different flicker rates. We show that normals have a good capacity to perform these tasks, that they are reliable over repeated measures and that such methods are successful when applied to a limited sample of clinical subjects

Materials and methods

The Medmont M600® perimeter was used in this study. This is an LED perimeter that has been described in detail elsewhere[28,29]. In short, this perimeter has a 3.2 cd/m^2 (10 asb) background intensity and a maximum stimulus brightness of 318 cd/m^2 (1000 asb). LEDs (0.43° diameter at 33 cm viewing distance, λ_{max} = 565 nm, half bandwidth = 28 nm) are arranged in concentric rings at various eccentricities (1°–50°). To obtain foveal thresholds, subjects fixated eccentrically at a fixation mark placed adjacent to an LED The flicker has a duty cycle of 50% and was shown in a 500 msec temporal square-wave window.

Three normal subjects (aged 25–33) were tested for their capacity to isolate color, luminance and flicker; two extensively and one with a reduced protocol. The extensive protocol required 6–10 repeat threshold measurements for each response criterion at six eccentricities (fovea, 3°, 6°, 10°, 15° & 22°) on the 45° meridian. Each threshold was obtained for six temporal frequencies (0, 3, 9, 18, 24 & 36 Hz) For the reduced protocol, five repeat threshold measurements were made for each response criterion at three flicker rates (0, 3 and 18 Hz) and eccentricities (3°, 10° & 15°) on the same meridian. A single response criterion was tested during any session including; (a) the detection of a spot (static perimetry), (b) the presence of flicker and, (c) the presence of color

Central 30° thresholds were also obtained on three patients (aged 23, 33 & 26) with static and flickering targets using different response criteria (detection and flicker). One patient was a normal control (23), one had optic nerve hypoplasia (33) and the other had suffered from a previous episode of the occult form of migraine (26)

Results

Figure 1 shows the average thresholds (± SEM) of the three normal observers. The three curves show the thresholds obtained using different criteria; detection, flicker perception and color perception. Figure 1a gives the thresholds obtained at 3° and Figure 1b the data for 10°. In

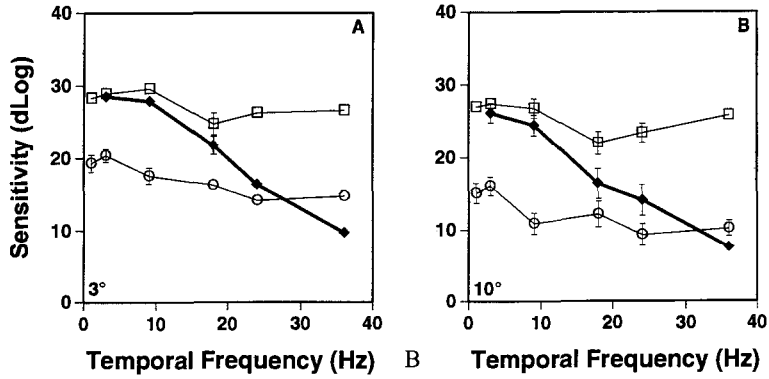

Fig 1 The average sensitivity (± SEM) of three normal observers for a flickering spot using three different criteria for response: detection (unfilled squares, thin line), perception of color (unfilled circles, thin line) and perception of flicker (filled diamond, thick line). For clarity, error bars smaller than the symbol have not been shown *A* Results for 3° eccentricity *B*. Results for 10° eccentricity

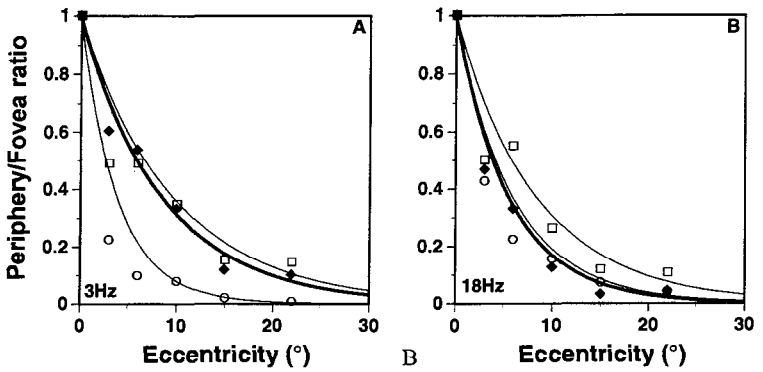

Fig 2 Eccentricity-related changes in sensitivity normalized to foveal thresholds (periphery/fovea). The labeling is as per Figure 1 and the curves show the power functions fitted through the points *A* Data for 3 Hz *B* Data for 18 Hz

Figure 1 the thresholds obtained with flickering targets have been adjusted for the time-averaged luminance change associated with the duty cycle. A two-way ANOVA with post-hoc analysis (Student-Newman-Keuls) found a significant difference ($p < 0.001$) between color and detection thresholds at all flicker rates. The difference between detection and flicker thresholds was not significant at ≤ 9 Hz but was significant ($p < 0.01$) at > 9 Hz over all eccentricities This suggests that fast flicker perception is being mediated by a different mechanism to slow flicker or static increments The error bars indicate that the thresholds were highly repeatable over observers and test sessions.

Figure 2 shows the eccentricity-related change in sensitivity for the two extensively tested observers using the criteria of Figure 1. The data have been normalized for each observer by dividing the peripheral data by foveal sensitivity (P/F). Figure 2a was obtained with a 3 Hz stimulus and Figure 2b shows the equivalent data for an 18 Hz stimulus. Data sets were fitted by a power function using the equation Threshold = Eccentricity^k and the resultant curves are shown on the Figure with the thick line indicating the flicker relationship. Table 1 lists the power functions obtained by fitting the entire set of data over all temporal frequencies. A two-way

Table 1 Exponents of power functions for the six flicker rates

Criterion	*Flicker rate (Hz)*					
	Static	*3*	*9*	*18*	*24*	*36*
Detection	–0 090	–0 102	–0 136	–0 118	–0 135	–0 092
Color	–0 232	–0 252	–0 234	–0 164	–0 196	–0 268
Flicker	NA	–0 116	–0 165	–0 177	–0 257	–0 199

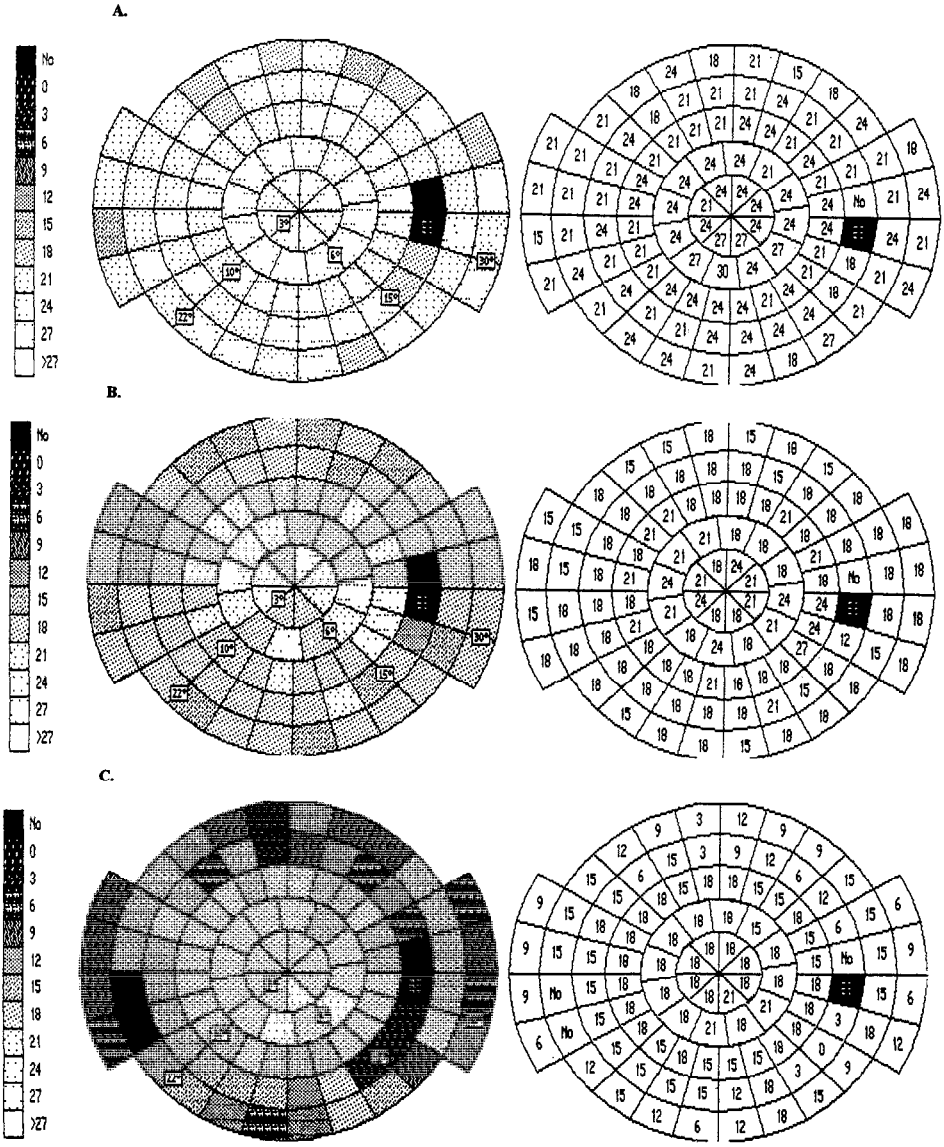

Fig 3 The perimetric results obtained for a normal control (age 23) *A* Static perimetry *B*. 18 Hz flicker perimetry using a detection criterion *C* 18 Hz flicker perimetry responding to the perception of flicker

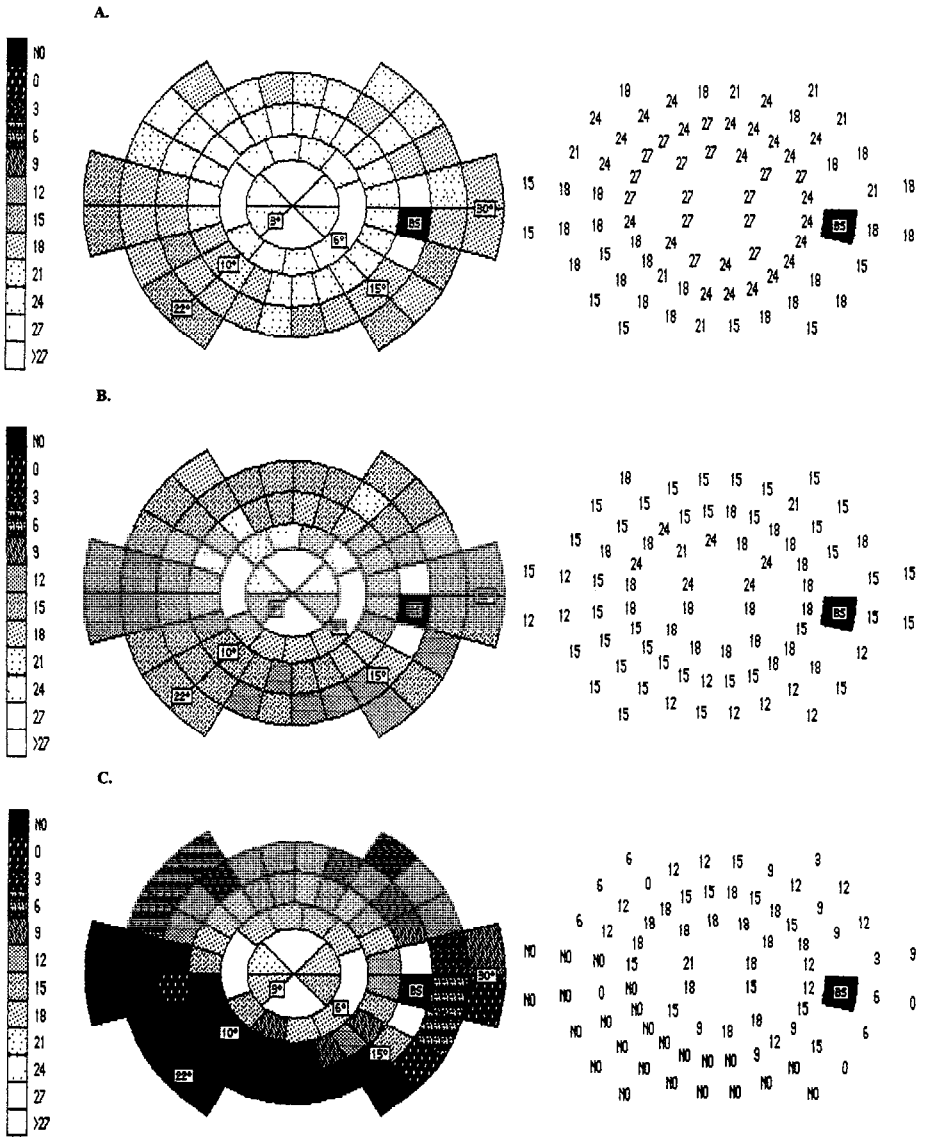

Fig 4 The perimetric results obtained for a patient with optic nerve hypoplasia (age 33) *A* Static perimetry *B* 18 Hz flicker perimetry using a detection criterion *C* 18 Hz flicker perimetry responding to the perception of flicker

ANOVA with post-hoc (Student-Newman-Keuls) analyses found a significant difference between the average color (–0 224) and detection (–0.112) power functions ($p < 0.01$) and between the average flicker (–0 181) and detection power functions ($p < 0.04$) over all flicker rates This shows that both color and flicker have a much steeper eccentricity related fall-off in their sensitivity than does static perimetry It is also apparent that the flicker slope is not significantly removed from the detection slope at 3 Hz ($p = 0.23$) but is significantly different at higher frequencies (Fig. 2, Table 1)

Figures 3–5 show the thresholds obtained with the Medmont perimeter when applied clinically to three subjects The fields were obtained using similar criteria to those given previously,

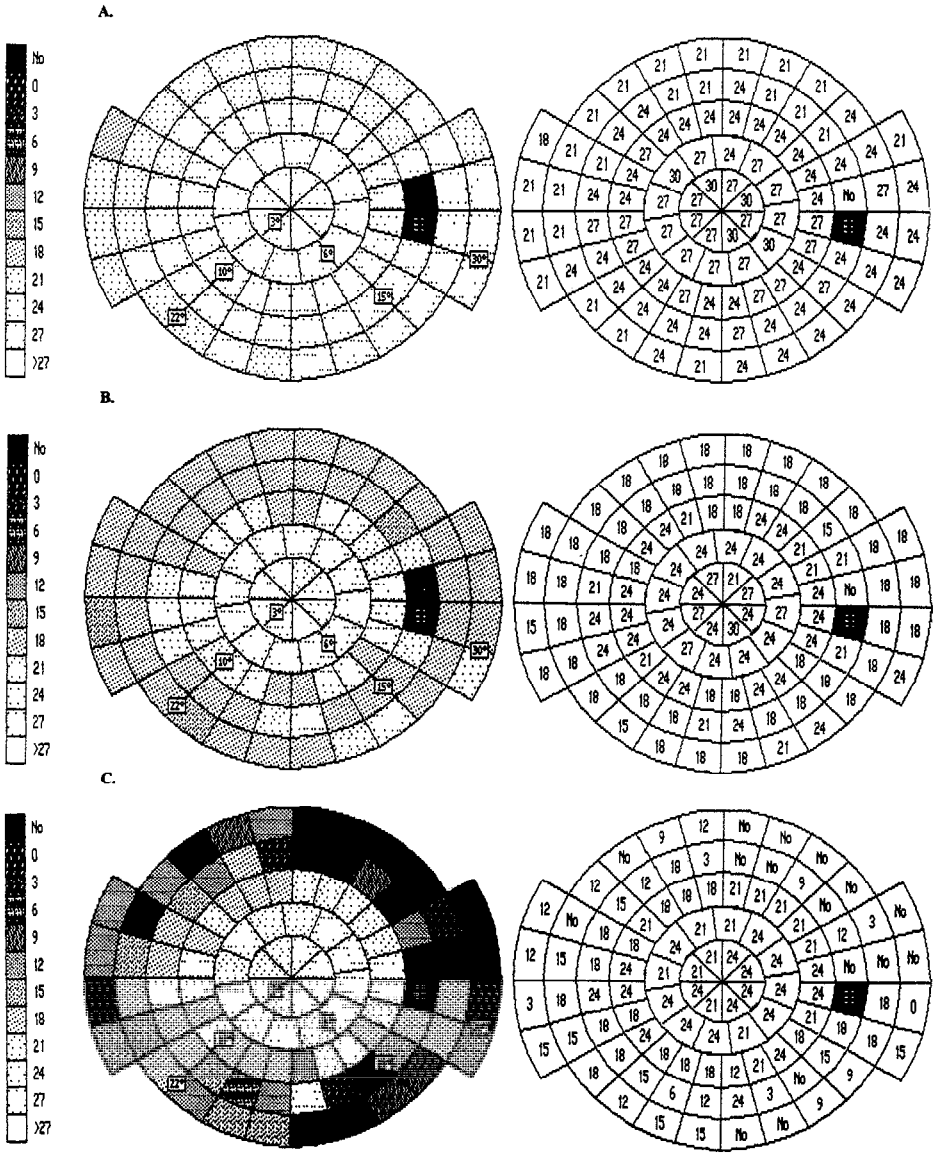

Fig 5 The perimetric results obtained for a migraineur (age 26) *A* Static perimetry *B* 18 Hz flicker perimetry using a detection criterion *C* 18 Hz flicker perimetry responding to the perception of flicker

namely, (a) detection of a static stimulus, (b) detection of an 18 Hz stimulus and, (c) perception of flicker for an 18 Hz stimulus. The data give the decibel (right) and grey scale (left) representations for each field. The vertical strip on the far left is the legend for the grey scale. Figure 3 shows results for a normal observer which confirm trends for a rapid eccentricity-related loss of sensitivity noted in Figure 2.

Figures 4 and 5 show that static perimetry fails to find any defect in these patients as does using an 18 Hz target with a detection criterion. Both subjects show defects however, when tested with the 18 Hz target when responding to the perception of flicker. The migraineur had last suf-

fered a migraine attack some 30 months prior to the most recent measurements. During the acute phase of this attack (Dec 1991) he showed a slight defect on a Humphrey 30-2 threshold (12–18 dB loss) in the superior temporal quadrant. This loss of static sensitivity had resolved by the next day but a flicker loss remained to the time of the most recent test (June, 1994; Fig 4).

Discussion

It can be seen from Figure 1 that the curve representing flicker perception has the characteristic shape reported by DeLange for the detection of temporal modulation[30] The location of the peak of the curve and fall-off in sensitivity with increasing temporal frequency suggest that the flicker mechanism is being isolated by using a multi-dimensional stimulus and criterion priming The projected CFFs agree with those demonstrated at similar eccentricities for a like sized stimulus[31]

In Figure 1, there is an interval between stimulus detection and the perception of color. This suggests that the stimulus increment is being detected by an achromatic and possibly non-opponent channel whereas after the stimulus intensity has increased substantially it activates the color-opponent channel resulting in a color percept Harwerth *et al.*[32] show that opponent and non-opponent mechanisms are responsible for detection thresholds measured using the Humphrey perimeter. The existence of labeled lines in the visual system would support the possibility for extraction of a particular stimulus attribute in the presence of distracters[21] This would suggest that complex stimuli can isolate different channels when subjects are asked to respond to different stimulus attributes Our data are consistent with this possibility and the small error bars indicate that the measurements are highly repeatable. Moreover, we show that this method allows isolation of a flicker mechanism in a clinical context (Figs. 3–5).

The fact that the eccentricity-related changes for 3 Hz flicker and increment detection are similar (Fig. 2 & Table 1) suggest that these processes may be subserved by the same neurological substrate On the other hand, the color process has markedly different attributes and shows a steep fall-off with eccentricity A similar steeper fall-off is also seen for fast flicker rates (> 9 Hz) where the function aligns more closely to the color than the detection profile Our findings are consistent with similar and more extensive data reported by Metha *et al* [26].

Such observations would imply that at least two different temporal filters act during the perimetry of a small spot: one is responsible for slow flicker (< 9 Hz) and has the characteristics of the luminance increment process whereas the other is sensitive to fast flicker (> 9 Hz) and shows a significant eccentricity-related loss. This rapid loss of sensitivity means that testing with 18 Hz flicker rates will be limited to the central 10–15° because of the reduced operating range provided by this stimulus, although lower frequencies can be used to test peripheral regions.

Nevertheless, isolating this fast flicker mechanism provides useful clinical data regarding the vision of patients who otherwise have normal static perimetry results (Figs 4 & 5). Two examples are given where significant losses of sensitivity are found in the absence of any static loss. A similar outcome has been reported elsewhere for a patient with retinal pigment epithelial detachment[33] Such losses are only present if the subject responds to the perception of flicker which shows the importance of ensuring that the appropriate response is being given by the patient. We suggest that a static false-positive monitor be included whenever performing this type of testing to allow the clinician to ascertain that the patient is responding correctly.

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Pericecal sensitivity studied by means of scanning laser ophthalmoscope

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Abstract

The scanning laser ophthalmoscope (SLO) allows a precise point-to-point correspondence between the fundus image and the perimetric results and is useful for following functional variations of pericecal sensitivity

The variations of pericecal sensitivity were studied in 20 glaucomatous subjects (12 males, eight females) age range 40–55 years, with initial visual field defects detected using program threshold centra 24/2 of the Humphrey Field Analyzer, and in 20 normal subjects (11 males, nine females) of equivalent age range with no visual field defect

Fundus perimetry was performed with SLO in the pericecal area which was divided into four sectors: superior, inferior, temporal and nasal Five points were examined for each sector

The superior sectors of the pericecal region exhibited statistically significantly higher values of sensitivity compared to the lower sectors

Introduction

Microperimetry with the scanning laser ophthalmoscope (SLO) allows us to see the stimuli presented on the retina in real time

This permits accurate monitoring of the patient and easy localization of the scotomatous areas. With the SLO it is possible to correlate anatomical or pathological features directly with retinal function, by passing elaborate photofield mapping techniques

Glaucoma pathogenesis is due to the alteration of the feeding vessels of the optic nerve, especially in the prelaminar layer where choroidal vessels have the characteristics of autoregulation. This autoregulation is remarkably decreased in glaucomatous patients[1].

Parapapillary chorioretinal atrophy has been reported to be more common and larger in glaucomatous eyes than in normal eyes or eyes with ocular hypertension[2–5]; and was studied by Jonas *et al* [6] using kinetic Goldmann perimetry

In this study we examined the variations of pericecal sensitivity by means of the SLO in two groups of subjects without parapapillary atrophy A. normal subjects with no visual field defects; B. glaucomatous patients with early visual field defects

Materials and methods

We studied 20 eyes of 20 normal subjects (12 males, eight females, age range 40–55 years, mean = 48.7) (group A), and 20 eyes of 20 patients (11 males, nine females) with open-angle glaucoma in the same age range (mean = 46 9) (group B) and well controlled with beta blockers.

Inclusion criteria:

– corrected visual acuity: 20/20

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- refractive error no more than ± 3 diopters
- good cooperation
- intraocular pressure (IOP) < 21 mmHg
- absence of parapapillary atrophy
- group A: normal threshold visual fields with program 24/2 of Humphrey Field Analyzer (HFA)
- group B: superior nasal step, or initial superior arcuate scotoma with the above-mentioned program

In group A, the C/D ratio calculated on the fundus photograph was 0.32 horizontally and 0.40 vertically. In group B, the C/D ratio was 0.48 horizontally and 0 52 vertically. All patients performed fundus controlled perimetry with the SLO in the pericecal area. Each subject performed two tests per eye, but only the second, performed three days after the first, was considered

The *parameters* used were:

- background illumination: 1 cd/m^2
- stimulus size and shape: a Goldmann III spot
- stimulus color: red (633 nm)
- fixation target: central

A transparent sheet of paper was divided into four equal 90° sectors (superior, inferior, nasal, temporal) for each patient. This sheet of paper was applied to the monitor screen for each examination in order to test five points around the peripapillary scleral ring for each sector (20 points in total). On the sheet of paper, for each patient, we established the points to be tested, avoiding the angioscotomas.

A threshold staircase procedure with 2 dB–1 dB steps was used for testing the points.

Our strategy was to begin with "the not seen stimulus" and to arrive at "the seen stimulus". When the stimulus was not seen, we presented a 2 dB higher intensity stimulus until the patient responded

If the stimulus was seen we presented a 1 dB lower intensity stimulus.

Threshold was defined as the last stimulus seen.

The values in dB for each point of each sector were written on the transparent sheet of paper for every patient.

We studied:

1. The average of the values of sensitivity in dB of all 20 points in each patient. The averages of group A were compared with those of group B using Student's t test.
2. The averages of the values in dB of the five points of each sector for all subjects of group A were compared with those of the subjects of group B using Student's t test.
3. In each patient the average values of the superior sectors were compared with the average values of the inferior sectors (both sectors had similar sensitivity), using the paired t test, in group A and in group B.

Results

1. The average values of sensitivity in dB of all 20 points in group A compared with those of group B were not statistically significant ($t = 0.9$, p = n.s.) (Table 1).
2. The averages of the values in dB of the five points of each sector for all subjects of group A compared with those of the subjects of group B were not statistically significant in the superior sectors ($t = 0.227$), in the nasal sectors ($t = 0.308$), and in the temporal sectors ($t = 0.491$), but were significantly different in the inferior sectors ($t = 2.915$, $p < 0.01$) (Table 2).
3. In each patient average values of the superior sectors compared with the average values of the inferior sectors showed: no significant difference in group A ($t = 0.08$, p = n.s.) but a significant difference in group B ($t = 5.67$, $p < 0.01$) (Table 3).

Table 1 Average values in dB of all 20 points of group A and group B and comparison with Student's *t* test

Group A	*Group B*	*Group A vs B*
14.8 ± 2.5	14 4 ± 2 6	$t = 0\ 9, p =$ n s.

Table 2 Average values in dB of each sector Group A compared with group B with Student's *t* test

Sector	*Group A*	*Group B*	*Group A vs B*
Temporal	13 3 ± 2 7	13 6 ± 2 4	$t = 0\ 491, p =$ n s
Nasal	16 2 ± 2 1	16.4 ± 2 0	$t = 0.308, p =$ n s
Superior	14 8 ± 2 2	15 0 ± 2 0	$t = 0\ 227, p =$ n s
Inferior	14 9 ± 2 1	12 7 ± 2 5	$t = 2\ 915, p < 0.01$

Table 3 Average values of superior sectors compared with average values of inferior sectors in group A and group B with the paired *t* test

Group A	*Group B*
$t = 0.08, p =$ n s	$t = 5\ 67, p < 0\ 01$

Conclusions

Recently, several studies have shown the importance of a decreased differential light sensitivity around the optic disk in about 40% of patients with early glaucoma[7, 8]

In fact, a depression of differential light sensitivity around the blind spot was demonstrated with a standard program of HFA[8].

Similar results were obtained by Jonas *et al*[6] who found significant correlations between the blind spot size and the total area of the optic disk, the peripapillary scleral ring, and parapapillary chorioretinal atrophy.

Jonas divided the parapapillary chorioretinal atrophy into two zones, in zone beta (located close to the peripapillary scleral ring) in which there were absolute scotomas, and in zone alpha (a peripheral zone situated beyond zone beta and characterized by irregular hypopigmentation and hyperpigmentation) in which there were relative scotomas[6]

We wanted to analyze the damage of the photoreceptors in the pericecal area due to the initial choroidal atrophy. The optic disks we studied did not have parapapillary chorioretinal atrophy detectable at ophthalmoscopic observation. We studied the area around the optic disk using fundus perimetry. This technique allows an exact point-to-point correspondence and an observation of detail in real time. Angioscotomas were avoided since we were able to look at the area we were testing on the screen[9]

In the case of the first comparison we did not find a statistically significant difference between group A and group B In the second comparison a statistically significant difference was found in the inferior sectors. In the last comparison we found a statistically significant difference, with lower values in the inferior sectors, only in group B. There was a sector correspondence with fascicular defects in the computerized visual field (HFA) In fact all our patients had defects in the superior sectors.

The study of the pericecal area is useful in the monitoring of glaucomatous patients, especially with respect to superior and inferior sectors, before anatomical damage becomes detectable at ophthalmoscopic examination

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Static automated perimetry and scanning laser ophthalmoscope microperimetry in the assessment of functional damage in operating microscope light retinopathy

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Abstract

Computerized automated perimetry (CAP) was used to test 15 patients with retinal damage resulting from the illumination of the operating microscope during cataract surgery Fluorescein angiography was performed in all cases and the extension of the area involved was measured with the Ophthalmic Imaging System. Differential light sensitivity was studied with the Humphrey 30-2 program and a 2-degree-grid custom test, centered on the retinal lesion Eight patients underwent scanning laser ophthalmoscope microperimetry (SLOM), using a fine grid of points and a manual static strategy

With CAP one or more depressed points were found in 12 of the 15 eyes The defect was always relative and a trend towards improvement was sometimes observed in the follow-up

With SLOM a statistically significant difference between the involved area and the surrounding points was found in all cases

SLOM seems to be superior to CAP in small retinal lesion testing Setting up new fully automatic strategies should improve the efficiency and ease of SLOM, reducing the test time

Introduction

The damaging effects of the microscope light on the retina have been known since McDonald and Irvine in 1983 reported the first case of such a lesion after an uncomplicated extracapsular cataract extraction. In the last ten years about 80 cases of microscope light retinopathy have been reported, but very few of them were studied either with manual or automated perimetry[1–3]

In this study we used computerized automated perimetry (CAP) and scanning laser ophthalmoscope microperimetry (SLOM) to test patients with cataract surgery retinal burns

Materials and methods

Three hundred consecutive patients, who underwent cataract extraction with various techniques (ECCE, 222 cases; phacoemulsification, 78 cases) in the Department of Ophthalmology at the Hospital of San Donà di Piave in eight months, were studied. Surgery was performed by different surgeons, with a Zeiss OPMI-6 microscope with halogen fiberoptic illumination, and a 175 mm objective lens. In all cases an IOL was inserted during the operation. All the patients underwent a dilated fundus examination, using a 90-D Volk lens, carefully searching the posterior pole for any retinal lesion likely to be related to a phototrauma.

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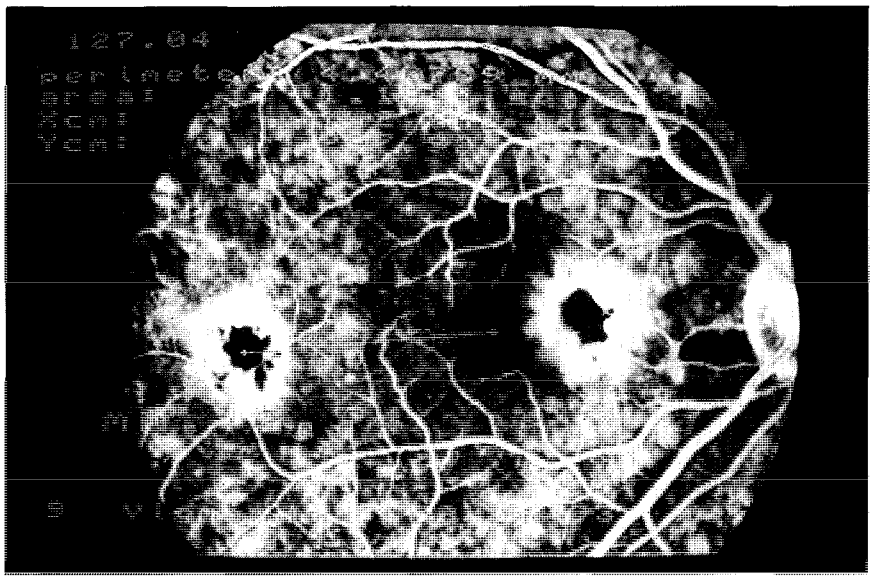

Fig 1 Two light-induced retinal lesions in a 59-year-old patient, who underwent a 45-minute uncomplicated phacoemulsification (fluorescein angiography processed with Ophthalmic Imaging System)

All suspected cases underwent fluorescein angiography to confirm the diagnosis. All but one of the patients were then tested with CAP, using the Humphrey 30-2 threshold test, one to six months after surgery Moreover, a 2-degree-grid threshold custom test was centered on the retinal lesion on the basis of the angiographic results. Stimulus III was employed We calculated the area of burned retina and the distance from the fovea with the Ophthalmic Imaging System Eight patients underwent a SLOM in the University Eye Department of Padua, ten to 16 months after surgery, to quantify retinal sensitivity in the damaged area A background illumination of ten candelas/m^2, Goldmann III stimulus and central fixation were used. Manual threshold microperimetry was used, and a fine grid, with an interstimulus distance chosen individually, was superimposed directly on the retinal lesion

Moreover, six patients were tested a second time with CAP eight to 11 months after the first examination, using the same custom grid.

For interpretation of the automated perimetry results we used the Statpac pattern deviation probability maps, taking as abnormal depressed points with a $p < 2\%$. With custom grids we considered as abnormal the points with a sensitivity depression > 4 dB with respect to sensitivity of neighboring points

With SLOM, we measured the sensitivity in the burned area and compared it with the sensitivity of surrounding normal areas.

Results

Sixteen of the 300 patients (5.3%) showed evidence of light retinopathy. Their age ranged from 48 to 83 years (mean 71 years).

Mean corrected visual acuity in these patients was 7/10, ranging from 2/10 to 10/10. Mean operating time was 45 1 ± 9 minutes, ranging from 25 to 63 minutes. This value is significantly higher than mean time registered in patients without retinal lesions (38.9 ± 12.3, $p <$ 0 05). In four cases a phacoemulsification had been performed. The other 12 had had an extracapsular cataract extraction with IOL implant, in the posterior chamber in ten cases and in the anterior chamber, due to a posterior capsule break, in two eyes

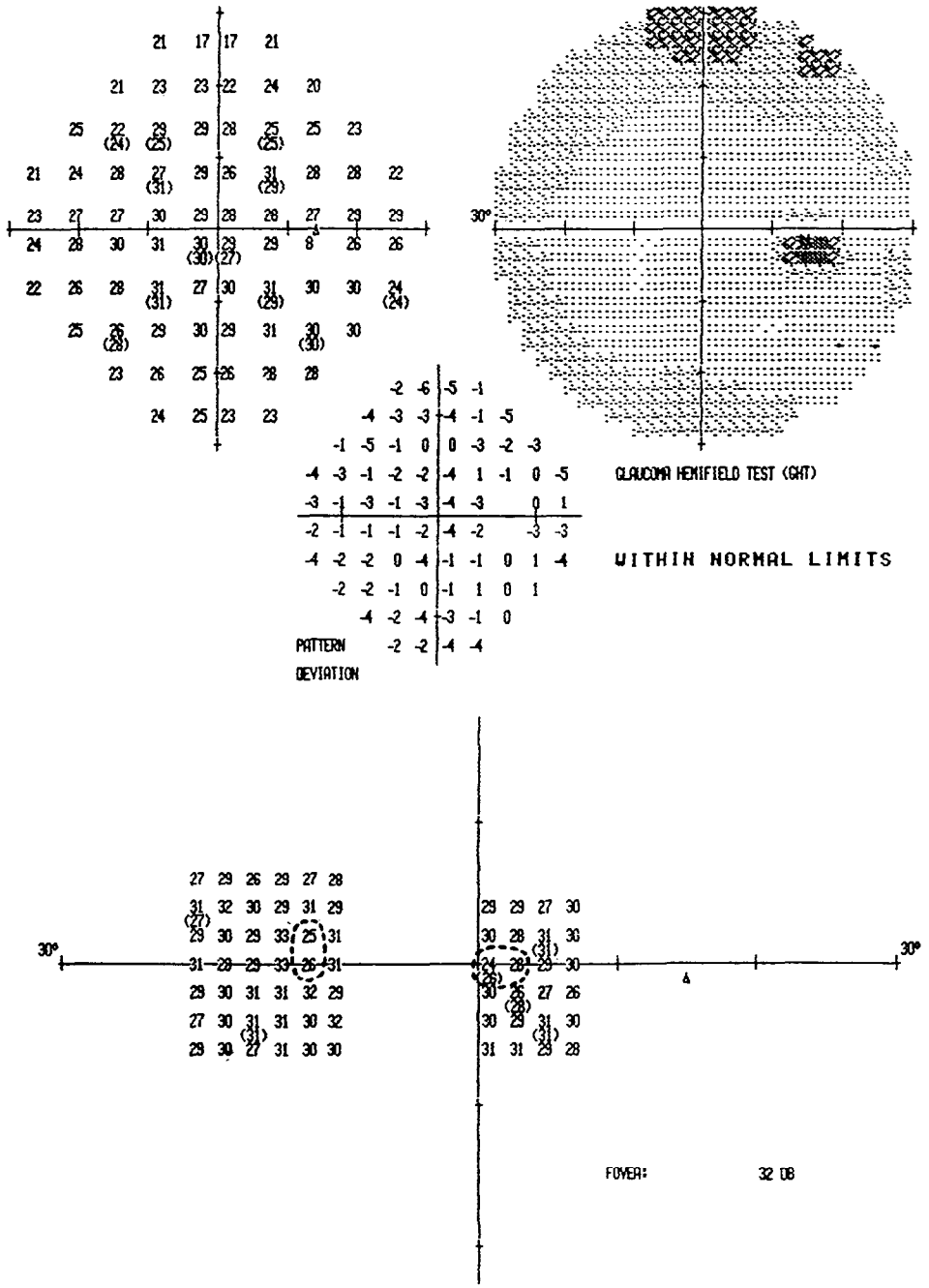

Fig 2 The Humphrey 30-2 threshold test is normal Some slight depressed points (broken lines) are shown with the 2-degree-grid custom test.

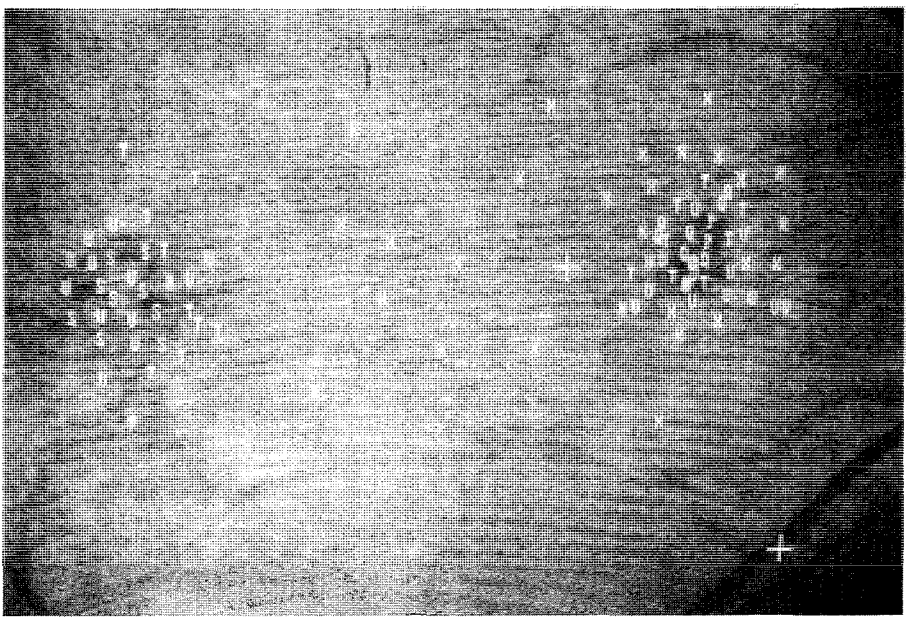

Fig 3 Scanning laser ophthalmoscope microperimetry shows depressed sensitivity in the retinal lesions

The mean area of retinal burns was 2.02 mm^2 (range: 0 52–3 2) The mean distance from the fovea was 2 07 mm (range: 0 1–2 96). The lesion was inferior to the macula in 11 cases, temporal in two, and centered on the fovea in another one In two cases there were two distinct retinal burns, located respectively in the interpapillo-macular and temporal area, and in the interpapillo-macular and superior area.

Automated standard perimetry (program 30-2), performed in 15 eyes, showed some abnormal points in the corresponding area in ten eyes. A significant depression in foveal sensitivity ($p < 2\%$) was found in nine cases. Using grid custom test, a significant depression in one or more points was found in 12 eyes. The defect was always relative, ranging from a depth of 6 dB to 18 dB. In the six patients tested twice, the second custom test showed a smaller defect in three eyes, and was stationary in two. The defect worsened in one case only With SLOM the mean sensitivity in the burned areas was 15 9 ± 2.2 dB, whereas surrounding normal areas had a sensitivity of 22 6 ± 2.1 dB The difference was statistically significant ($p < 0.0001$)

Discussion

A cause-and-effect relationship between retinal lesions and exposure to light from the operating microscope has already been demonstrated both clinically and experimentally[4–10]. These lesions are typically located either inferior or superior to the fovea, because modern operating microscopes are not perfectly coaxial, and so the beam is not directed on the fovea A retinal edema may be observed within 24–48 hours after the exposure, together with mild pigmentary alterations. Fluorescein angiography at this stage shows a discrete hyperfluorescence with late staining (Fig. 1). Various types of alterations in pigmentation may be observed after a few days, but lesions tend to became smaller after the first month.

Visual field examination shows an usually slight depression of sensitivity, corresponding to retinal lesion (Fig 2). The use of high-resolution grids of points provides a more precise and accurate definition of edges and depth of defects Our results suggest that there is a trend towards an improvement of the functional damage after some months. This observation is con-

sistent with previous reports[3,11], which demonstrated a marked recovery from retinal phototoxicity.

SLOM is a new way of analysing the sensitivity of selected retinal areas, particularly if they are localized at the posterior pole. Age-related macular degeneration, and macular holes/pseudoholes have been investigated with this technique[12–15]. With respect to conventional automated perimetry, SLOM allows for a precise localization of stimulus on the retina, and an accurate check of fixation. In this study we have shown that, even on a long-term basis, retinal sensitivity is significantly depressed in areas which have undergone a photic damage (Fig. 3). There is also a close relationship between the morphological aspect of retinal lesions and sensitivity – with a more central depressed area and a halo with average sensitivity In testing this kind of lesion, SLOM seems to be superior to CAP, which sometimes fails to demonstrate any damage at all. There are different possible explanations for these results 1) SLOM precisely tests the retinal lesion, while the CAP grid is centered on the basis of retinography and/or fluorangiography results; in some cases the grid could not to be superimposed on the lesion and this may explain why CAP can give normal results when SLOM shows a sensitivity depression; 2) the 2-degree-resolution used with the custom tests may not be sufficiently dense to find a very small defect. With SLOM, the interstimulus distance is chosen according to the case and can theoretically reach 100 μm; 3) SLOM, for reasons still not clear, may, in fact, be more sensitive than CAP.

The main disadvantage of SLOM is the relatively time-consuming manual determination of thresholds: 15 to 20 minutes However, new fully automatic programs are on the horizon.

In conclusion, operating microscope light retinopathy is not a rare occurrence. Fortunately, the visual involvement is modest and often recovery may be observed With a good testing program, CAP will show a slight sensitivity depression in most cases. SLOM would seem to be an interesting and exciting technique for the particularly small defects, which are often missed with CAP.

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HIGH-PASS RESOLUTION PERIMETRY

High-pass resolution perimetry: central-field neuroretinal correlates

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Abstract

Minimum angles of resolution (MAR) were measured at 0–10° horizontal eccentricity in three normal subjects, using high-pass spatial frequency filtered ring targets, at four different contrast levels Results were correlated with recent data on human cone and ganglion cell separations in corresponding retinal locations

MARs and cone separations showed a close proportionality through the origin for all contrast levels

Ganglion cell correlates were more difficult to elucidate as the cell bodies are displaced from their receptive field centers However, taking a functional estimate of the displacement into account, the number of ganglion cells appears to be large enough to uphold the same proportional relationship to MAR that previously has been described outside 10° of eccentricity Analysis of the nature of age effects provides support for this model

The full report will appear in Vision Research

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Resolution perimetry in glaucoma follow-up

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Introduction

A major use of perimetry for glaucoma is diagnosis and follow-up Regarding follow-up the results from differential light sense (DLS) perimetry have been inconclusive. Recent DLS studies on treated glaucoma patients report improvement rates of 5–57% (mean 23%) and deterioration rates of 20–51% (mean 28%)[1–6]

The aim of the present study was to find out to what extent high-pass resolution perimetry (HRP) could detect any changes in patients with newly diagnosed glaucoma during a treatment follow-up period of two to three years. An untreated group of patients with ocular hypertension (OH), examined in a similar way, served as control

Subjects and methods

Fifty-six consecutive patients with newly diagnosed glaucoma and 15 with untreated ocular hypertension were examined at the time of diagnosis and once a year thereafter for two to three years The treatments were 0 5% betaxolol twice a day (16 patients), 0 5% timolol twice a day (19 patients), 4% pilocarpine three times a day (seven patients), or a combination of these drugs (14 patients). Two patients in the combination group were also treated with argon laser trabeculoplasty

Results

Fifty-nine of the 71 examined patients showed lower resolution thresholds, *i e*, increased sensitivity, after two years, compared to initial values. The threshold decrease was significantly larger in the treated glaucoma patients (median 1.22 dB) than in the untreated ocular hypertensive patients (0.48 dB) (Fig 1).

Mean intraocular pressure was significantly reduced in the treated glaucoma group ($p < 0.01$, Student's t test). There was a significant correlation between intraocular pressure level during the follow-up period and resolution threshold improvement ($r = -0.28$, $p < 0.05$)

Discussion

The threshold decrease in the untreated ocular hypertensive group corresponds to a previously described learning effect In 35 of the 56 treated glaucoma patients the thresholds im-

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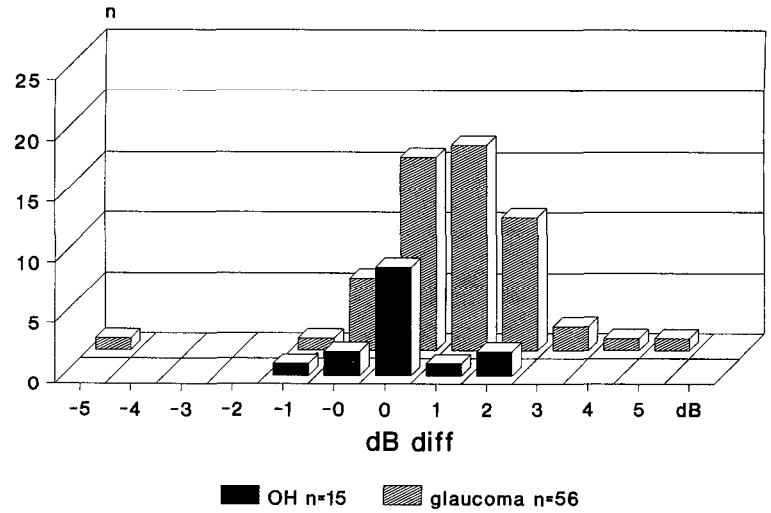

Fig 1 Resolution threshold changes in dB after two years of treatment Minus (–) indicates deterioration

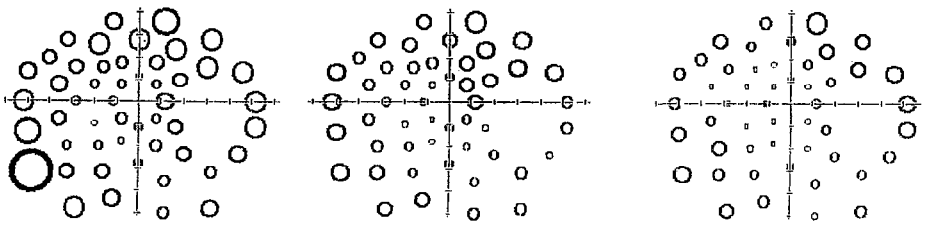

Fig 2a Improved visual fields from a glaucoma patient (male, age 72) Resolution threshold at examination one = 6 02 dB, two = 5 0 dB, and three = 3 94 dB Note progressively smaller rings in all tested locations

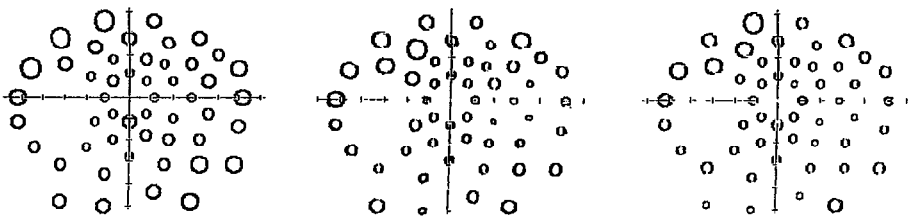

Fig 2b Unchanged visual fields from a glaucoma patient (male, age 67) Resolution threshold at examination one = 4 67 dB, two = 4 6 dB, and three = 4 4 dB Note similar ring sizes in most tested locations

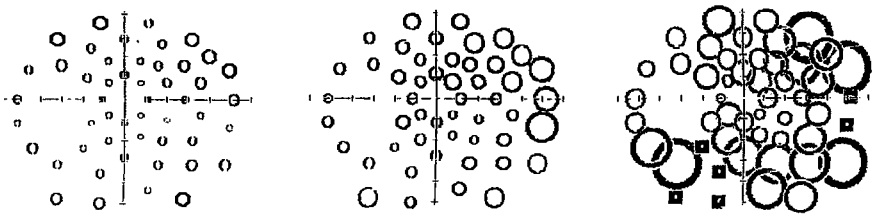

Fig 2c Deteriorated visual fields from a glaucoma patient (female, age 68) Resolution threshold at examination one = 3 9 dB, two = 5 96 dB, and three = 8 91 dB Note progressively larger rings in all tested locations

proved more than 0.84 dB, the upper confidence limit in the untreated group, which may indicate a beneficial effect of antiglaucoma therapy in these patients

Examples of visual fields are shown in Figure 2a–c

The threshold change was unrelated to initial resolution thresholds and can not be explained by a "sorting" effect

Conclusion

High-pass resolution perimetry has been reported to be a sensitive means for detecting early glaucomatous damage[7] and was found to be useful in glaucoma management[8] The findings in the current study imply that the method gives valuable information also in glaucoma follow-up

The full article will be published elsewhere.

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Computerized automated perimetry and high-pass resolution perimetry in diabetic patients

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Abstract

Eighty-one patients suffering from diabetes mellitus underwent a visual field examination with either computerized automated perimetry (Humphrey 30-2 program) and high-pass resolution perimetry Thirty-nine had a minimal to mild background retinopathy, and 42 showed no clinically detectable retinal lesions Similar results were obtained with both methods in patients with no retinopathy, while HRP indicated defects in a significantly higher percentage of cases with diabetic retinopathy (64 1% against 38 4% with CAP) HRP, quicker and less tiring for patients, is a sensitive and useful technique in the functional testing of diabetic patients

Introduction

The involvement of the visual system in diabetic patients is a common finding when retinopathy is clinically detectable. In these patients visual field damage may be found either with manual or computerized automated perimetry (CAP) On the other hand, as already shown in glaucoma, also in diabetic patients with minimal or no retinopathy, defects in the retinal nerve fiber layer can often be seen[1] Since automated static perimetry may not demonstrate any alteration in glaucomatous eyes even with a 20% nerve fiber loss[2], it would be useful to have a testing method more sensitive than traditional CAP to show very early functional damage in diabetic patients, too.

High-pass resolution perimetry (HRP) has proved to be at least as sensitive as CAP in detecting early glaucomatous and neurological visual field defects[3–7]. In multiple sclerosis patients, HRP seems to be a very useful and powerful technique, even better than CAP in showing a subclinical optic nerve damage[8]

In this study we used CAP and HRP to test a group of diabetic patients with and without background retinopathy. The purpose of this research was to see if HRP could also be a useful technique for these patients.

Material and methods

Eighty-one patients with diabetes mellitus, who met the inclusion criteria reported below, were taken into consideration. Ten were insulin-dependent and 71 were non-insulin-dependent Their age varied between 29 and 81 years (mean 62.5 ± 81 4 years) All cases were previously examined with fluorescein angiography. Thirty-nine had a minimal to mild background diabetic retinopathy, while 42 had no signs of retinopathy (fewer than five microaneurysms

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with no evidence of fluorescein leakage with angiography) No patient had previous experience with automated perimetry.

Only patients with a visual acuity better than 20/25, with a refractive defect less then 4 diopters, and with an IOP < 20 mmHg were included in this study. Patients with other associated ocular or general diseases and eyes previously treated with laser photocoagulation were excluded. No eye had history of trauma, surgical intervention, or congenital anomaly of the optic disk Only one eye per patient was considered, usually the one with either the best visual acuity, with the lower refractive defect, with the best reliability indices, or without any other associated ocular diseases When both eyes were similar, the eye to be considered was randomly chosen.

CAP was performed with a Humphrey Field Analyzer model 640 (Zeiss-Allergan, San Leandro, CA), using the 30-2 threshold test. A two-minute demo test was usually performed before starting patient examination. When visual field alterations were inconsistent with the patient ocular state, the test was repeated after a few days Patients with poor cooperation or visual fields with obvious artifacts were excluded from the study.

HRP was performed with the Ophthimus Frisén Ring perimeter (Nikon-HighTech Vision, Malmö, Sweden), already described elsewhere[9,10]. Also with this instrument, a short learning program preceded the test.

For the interpretation of CAP results, some Statpac global field indices (MD, PSD, and CPSD), and pattern standard deviation probability maps were considered The following criteria were adopted to classify a visual field as abnormal 1) presence of one or more statistically abnormal global indices ($p < 2\%$) and 2) visual fields with normal field indices, but with either two or more neighboring statistically abnormal points with a $p < 1\%$ or three or more abnormal points with a $p < 2\%$ on the pattern standard deviation probability map.

With HRP the following criteria for abnormality were taken: 1) abnormally high thresholds as stated in the descriptive report and 2) statistically abnormal ($p < 1\%$) global deviation, and/or local deviation, and/or form index. The neural capacity index was also taken into account. Statistical analysis of results was performed using Student's t test and χ^2 test

Results

Results obtained in diabetic patients without retinopathy are shown in Table 1.

A purely diffuse loss was found in four eyes with CAP and in three with HRP. A local defect was found in five eyes with both techniques A mixed defect was present in four eyes

Table 1 Visual field results in diabetic patients with no retinopathy 42 cases)

	CAP *No of eyes (%)*	*HRP* *No of eyes (%)*
Normal	29 (69.0%)	28 (66 7%)
Abnormal	13 (31 0%)	14 (33 3%)

The differences between CAP and HRP are not statistically significant

Table 2 Results obtained in 39 diabetic patients with background retinopathy

	CAP *No of eyes (%)*	*HRP* *No of eyes (%)*
Normal	24 (61 5%)	14 (35 9%)
Abnormal	15 (38 5%)	25 (64.1%)

The differences between CAP and HRP are statistically significant ($p < 0$ 05)

with CAP and six with HRP. The local defects were usually located in the mean periphery, between 20° and 30°, and in the upper quadrants

In this group the mean neural capacity was 86 4% ± 15.1, ranging from 54% to 108%

Table 2 shows the results obtained in the group of patients with background retinopathy. CAP indicated a diffuse loss in four cases, a local defect in three, and a mixed defect in another eight cases. With HRP the same alterations were found in nine, eight and eight cases, respectively. The local defects were equally distributed in the upper and in lower quadrants. The neural capacity ranged from 43% to 115%, with a mean of 78 0% ± 20.4. This value is significantly lower ($p < 0.05$) than that found in the group of patients with no retinopathy

Discussion

The assessment of visual function, together with the fluorescein angiography, which of course remains the fundamental test, is important in the management of diabetic patients. When a clinically detectable retinopathy has developed, a visual field defect, either diffuse or localized, is a common finding, as reported by several authors[11–18]. With CAP, more than one third of our cases showed some statistically significant visual field damage. HRP, on the other hand, was statistically abnormal in 64% of cases This result suggests that HRP can distinguish a visual dysfunction in these patients earlier than CAP Looking at individual results, however, some discrepancies may be found. Twelve of the 24 eyes normal with CAP were classified as abnormal with HRP. On the other hand, among 14 eyes normal with HRP, three were abnormal using CAP.

As partly expected, different results were obtained by examining patients without a clinically detectable diabetic retinopathy The percentage of eyes with visual field damage was lower with both methods, in agreement with Roth's report, but higher than that reported by other authors[12,19]. These discrepancies may be explained by the different testing methods used and the abnormality criteria adopted It is interesting to note that, in our study, the difference with respect to the other group of patients is very small using CAP, while with HRP, on the contrary, the number of abnormal results in patients with retinopathy was almost twice as high when compared with the cases with no retinopathy. The real meaning of this behavior is not clear but may be attributed to the different targets used Resolution thresholds are directly proportional to retinal ganglion cell separations, unlike conventional different light sense perimetry thresholds. Since the neural involvement in diabetes seems to precede the vascular lesions, with an early and selective damage of retinal ganglion cells, this can perhaps explain the higher sensitivity of HRP in patients with minimal retinopathy. The reason why HRP is no more sensitive than CAP in patients with no signs of retinopathy has to be clarified However, it is likely that the difference in the frequency with which visual field defects can be detected with the two methods increases in parallel with the development of diabetic retinopathy. Even in patients with no retinopathy the two techniques showed some discrepancies. Eight eyes among 29 normal with CAP were classified as abnormal with HRP. Vice versa, six of 28 eyes, normal with HRP, were considered as abnormal using CAP Of course, these data have to be interpreted with caution, because the dividing line between normal and abnormal is heavily dependent on criteria chosen arbitrarily Small variations in these criteria can lead to very different results In this study we adopted fairly strict criteria for abnormality, as similar as possible for both the testing methods. Even with these limits, there is no doubt that HRP is more sensitive than CAP in patient with early background diabetic retinopathy.

According to some authors[20], CAP, together with macular recovery and chromatic sense tests, would be able to identify those patients who risk developing diabetic retinopathy Even if it might seem possible that HRP could be a predictive test for diabetic retinopathy development, no data are at present available to support such a hypothesis, which would have to be demonstrated by long-term prospective studies. However, the data from our study suggest that this technique, which is specific and fast, could be easily and usefully used as a screening test for these patients.

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We would like to thank Mrs Annalisa Caselli and Mrs Donatella Schiavo for their valuable help in examining the patients

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A comparative study between differential light sensitivity perimetry and high-pass resolution perimetry in congenital glaucoma

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Abstract

The population of congenital glaucoma patients presented at the 1990 IPS Meeting was further studied by performing visual field examinations with Octopus 1-2-3 and high-pass resolution perimetry and confocal tomography with the Heidelberg Retina Tomograph, with which optic disk parameters were assessed

The population was divided into three groups: G1: congenital glaucomas operated once before two years of age; G2: congenital glaucomas operated once or more times; and G3: late congenital glaucoma, goniodysgenesis, Rieger's syndrome and juvenile open-angle glaucoma

These new examinations were performed after a follow-up ranging between 10 and 28 years Group 2 presented worse damage of visual field and optic disk

Introduction

Comparisons between differential light sensitivity (DLS) perimetry and high-pass resolution perimetry (HRP) in adults have been conducted by several researchers[1–4] but their relationship was not studied in children with congenital glaucoma (CG).

We have previously reported at the IPS Meeting in Malmo, 1990, that diffuse damage was the only defect observed in children operated for congenital glaucoma.

Subjects and methods

The authors have studied three different populations which had pediatric glaucomas during childhood.

The first group (19 eyes) consisted of persons operated on as infants for congenital glaucoma, some of them before the first year of age, and others, before the second In most of them the intraocular pressure (IOP) was regulated with one surgery and the axial length of the eye stopped its enlargement after one surgery.

The second group (12 eyes) consisted of persons with re-operated congenital glaucomas in which the IOP was regulated and the axial length of the eye stopped its enlargement after two to six re-operations.

The third group (29 eyes) consisted of persons with late congenital glaucomas, goniodysgenesis, Rieger's syndrome, and juvenile open-angle glaucoma, etc., but as these diseases became manifest later, generally between four and six years of age, the axial length did not grow despite the ocular hypertension. The IOP was regulated with medical therapy or surgery

Groups 1 and 2 consisted of primary congenital glaucomas with an onset during the first 24 months of age.

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Table 1 Patient material

		No	*Age (yrs)*	*Male*	*Female*
Group 1	Primary congenital glaucomas operated once	19	12–28	13	6
Group 2	Re-operated primary congenital glaucomas	12	7–22	10	2
Group 3	Goniodysgenesis	29	11–23	15	14
Total		60	7–24	38	22

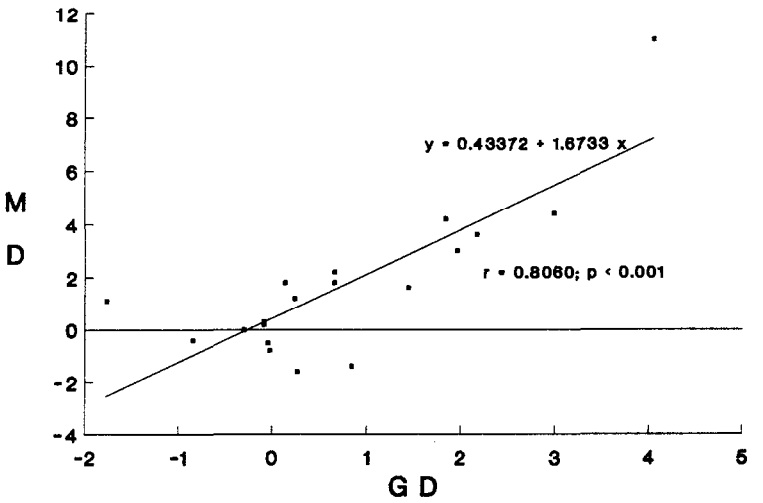

Fig 1 Relationship between MD and GD in group 1

Between 10 and 28 years after surgery the results were assessed by analysis of axial length (echometry), IOP, myopia and visual field. Visual field examinations were performed with Octopus 1-2-3 (Interzeag, program G1, 59 locations within 30 degrees of the visual field) and Ophthimus high-pass resolution perimetry (HighTech Vision, Malmo, version 2.0) (50 locations are measured within the central 30 degrees of the visual field).

In this study, Pearson's correlation coefficient was calculated between MD (mean defect) and NC (neural capacity), MD and GD (global deviation), and CLV (corrected loss variance) and LD (local deviation) in three groups NC is an index estimating total number of functioning retinal ganglion cells.

The axial length was different in the three groups. After surgery, group 1 remained at the values reached before surgery, in group 2 (re-operated cases), the axial length was bigger, and in group 3 it fell within the normal range because the sclera does not enlarge after five years of age.

The myopia was also different in the three groups Group 2 was highly myopic, group 1, mildly and the third group was almost emmetropic

The best visual acuity was found in group 3, the worst in group 2 and in group 1 it was intermediate

Regarding visual fields we have previously reported (IPS Meeting, Malmo, 1990)[5] that it is remarkable that diffuse damage is the only defect observed in children We think that diffuse

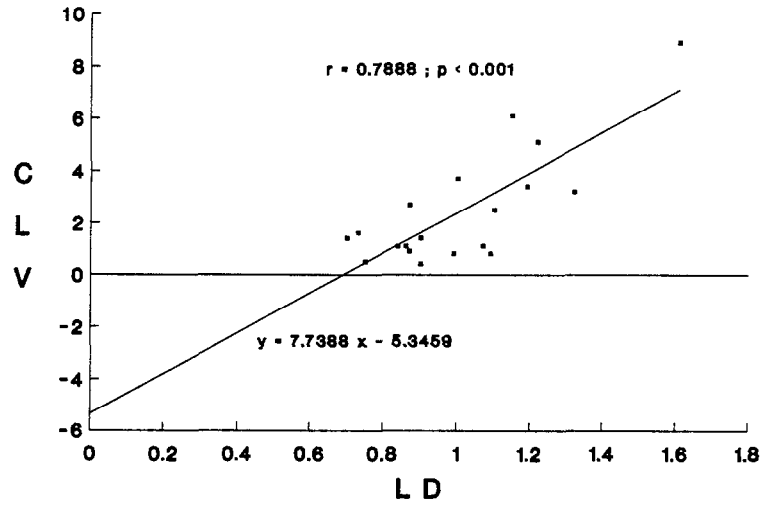

Fig 2 Relationship between CLV and LD in group 1

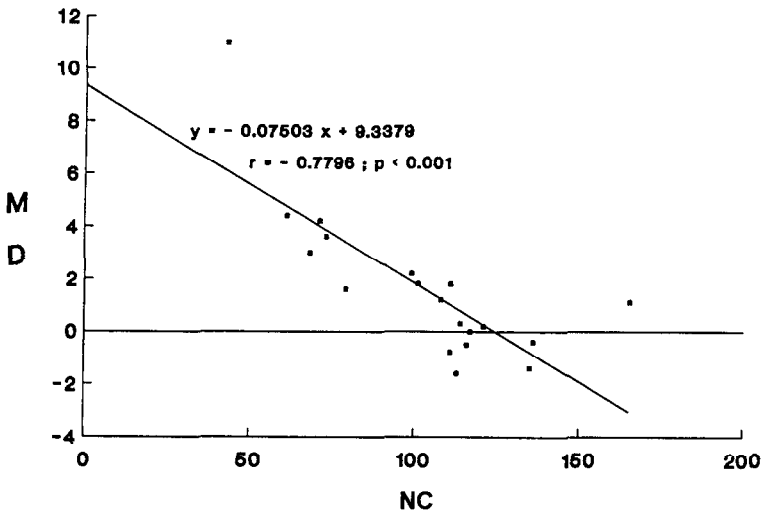

Fig 3. Relationship between MD and NC in group 1

depression is due to the fact that children have a healthy vascular system; hemorrhages and microinfarctions that can lead to scotomatous defects are not possible Macular scotomas were only found in children with amblyopia, generally in eyes with an axial length of 30 mm or more

In cases of group 1, which are cured after the first surgery, the visual field is generally normal or has a mild diffuse depression. In group 2 (re-operated cases), the diffuse depression is bigger

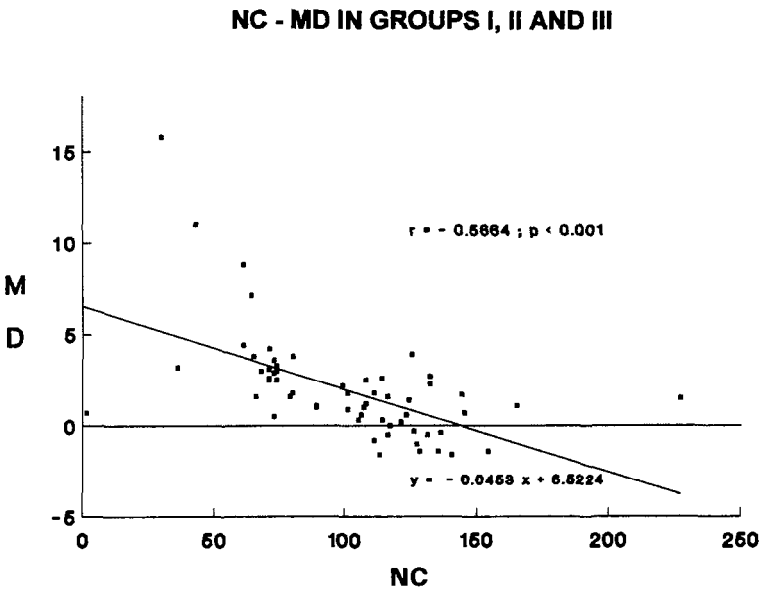

Fig 4 Two groups of cases can be found: one located far from the zero line and the other, surrounding it The correlation is not represented by a straight line but rather by a curve. This means that in many cases the MD is normal but the NC is pathological

Results

We have studied 60 eyes of 30 patients belonging to the three groups with and without optic disk glaucomatous damage who were followed up in the Glaucoma Clinic of the Department of Ophthalmology of the University of Buenos Aires, Argentina

Relationship between mean defect (MD) and global deviation (GD)

In group 1 MD and GD correlated significantly: $r = 0.80$, $p < 0.0001$ (Fig. 1).
In groups 2 and 3 the correlation was not significant.

Relationship between corrected loss variance (CLV) and local deviation (LD)

In group 1, CLV and LD correlated significantly: $r = 0.78$, $p < 0\ 0001$ (Fig. 2).
Group 2 was not significant.
Group 3 had a fairly significant correlation: $r = 0.45$, $p < 0\ 01$

Relationship between MD and neural capacity (NC)

The first group correlated significantly: $r = 0.78$, $p < 0.0001$ (Fig. 3).
Group 2 was not significant
Group 3 was fairly significant, $r = 0.42$, $p < 0\ 02$

However, when we tried to correlate the three groups together we found two groups of cases; one located far from the zero line and the other, surrounding it. The correlation is not represented by a straight line but rather by a curve This means that in many cases the MD is normal but the NC is pathological. The correlation between these two indices is far from perfect (Fig. 4).

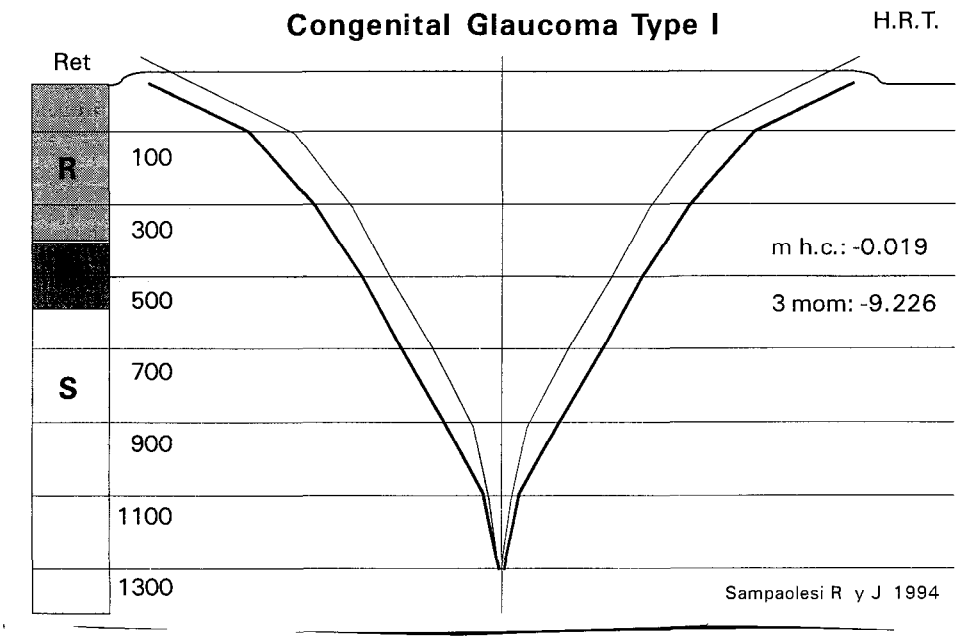

Fig 5a. Thin line: normal optic disk profile; thick line: optic disk profile of type I congenital glaucoma R: retina; C: choroid; S: sclera; m h c : mean height of contour line; 3 mom: third moment in contour line.

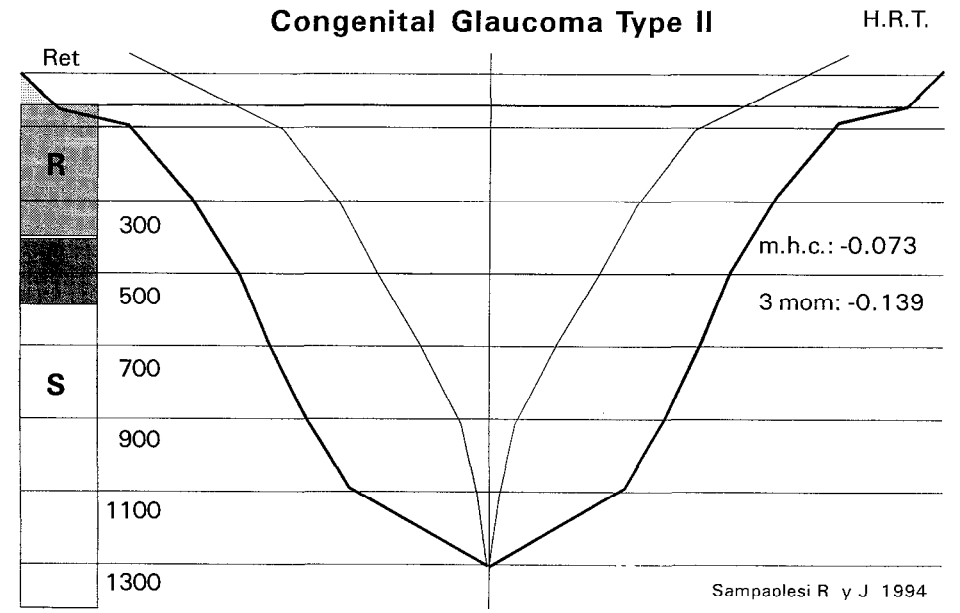

Fig 5b. Thin line: normal optic disk profile; thick line: optic disk profile of type III congenital glaucoma. R: retina; C: choroid; S: sclera; m h c.: mean height of contour line; 3 mom: third moment in contour line

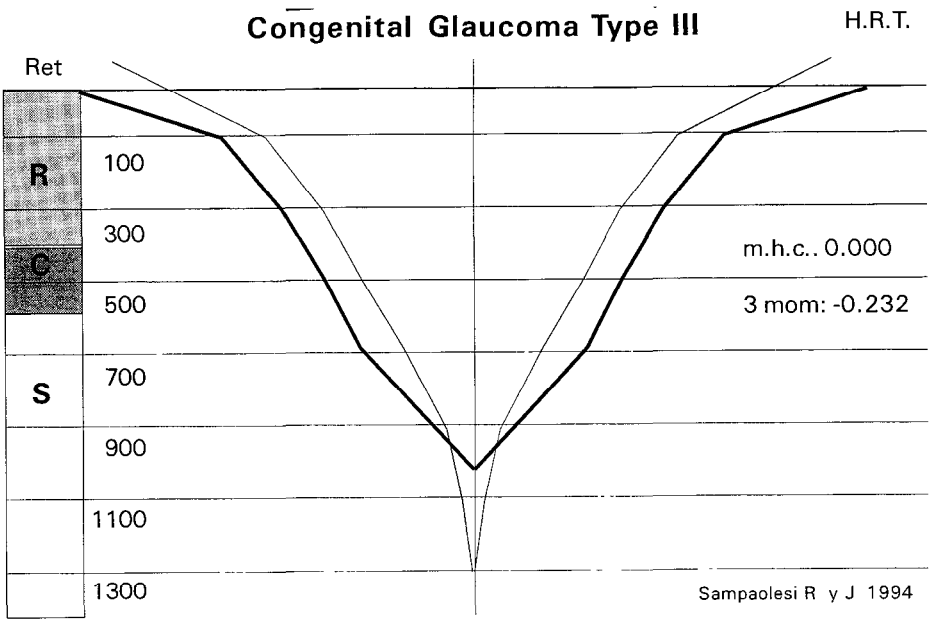

Fig 6 Thin line: normal optic disk profile; thick line: optic disk profile of type II congenital glaucoma R: retina; C: choroid; S: sclera; m h c : mean height of contour line; 3 mom: third moment in contour line

In our opinion, these different methods of psychophysical tests measure different aspects of the visual field system.

Both at the 1990 IPS Meeting held in Malmo, and now, we think we have been the first ones to study the visual field in children with differential light sensitivity perimetry (Octopus 2000 and 1-2-3 perimeters) and with high-pass resolution perimetry With both perimeters it is possible to obtain reliable results in children between five and ten years of age In order to be sure of the accuracy of our results, we have used a reliability factor not higher than ten. Both perimetric methods have shown that there are no scotomas in the visual fields of children The only visual field damage that can be found in children is diffuse sensitivity depression, *i e* , pathological MD values.

In the same population we studied the optic disk in the three groups with the Heidelberg Retina Tomograph (HRT)

We measured the different parameters of the optic nerve head and with the data obtained with the HRT (software 1.09), we built the mean profile of the optic nerve head in each group In order to compare them to the mean profile of a normal disk, we studied a normal group of 100 young persons between nine and 25 years of age.

The profiles of groups 1 and 3 can be observed in Figures 5a and b Both groups show a slight difference with the normal group. This reveals the presence of a mild deterioration of the optic nerve (dotted line: normal profile, full line: groups 1 and 3).

In Figure 6, representing the profile of group 2, *re-operated cases*, there is a great difference with the normal profile, indicating severe deterioration of the optic nerve.

In addition to the study of the profiles, we also studied the parameters of the optic disk according to the HRT: effective area, area below reference, volume below surface, volume below reference, mean height of contour line, effective mean depth, third moment in contour and neuroretinal rim

Almost all these parameters showed a significant deviation towards the pathological side, specially in group 2 of re-operated cases. Regarding the neuroretinal rim we studied only the

surface, which showed no significant difference among the three groups because as the eye enlarges, the pupil surface also enlarges

As regards the values of all these parameters, they can be found in the paper "Optic disk damage in congenital glaucoma" (in press), presented at the Glaucoma Society Meeting, Quebec City, June 22–24, 1994

Discussion

In children from five to eight years of age, it is possible to examine the visual field both with differential light sensitivity perimetry and with high-pass resolution perimetry (HRP)

Before starting with the examination we conduct a special program for them to get acquainted with its functioning. We only accept results with a reliability factor of ten or lower.

According to our experience, the HRP is very useful in children. They accept the examination better because it is easier and it takes only six minutes per eye

With both perimetric methods the only defect found is diffuse sensitivity loss. In cases with normal MD values, with HRP we also find a pathological neural capacity. This fact reveals that the indices of both methods reflect different aspects of the condition of the visual field system

In 85% of the cases, optic nerve defects begin ten years earlier than visual field damage (Goldmann, Leydhecker, Caprioli, Schwartz).

In order to help congenital glaucoma children, from the clinical point of view, it can be said that congenital glaucomas must be subject to surgery as soon as diagnosed and if the axial length continues to grow despite surgery because the IOP failed to be regulated, there is still time before visual field damage occurs, so as many re-operations as necessary must be performed. Congenital glaucomas are glaucomas of good prognosis The goal is to prevent the optic nerve head from further deterioration.

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High-pass resolution perimetry in suspected glaucoma and ibopamine test positive patients

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Abstract

Ibopamine is a new drug with mydriatic, not cycloplegic, properties Topically administered it induces IOP increase in a high percentage of patients with open-angle glaucoma, but not in normal subjects. Subjects with increased IOP could be ibopamine test positive or negative

High-pass resolution perimetry was performed in 15 ibopamine positive and in 15 negative test subjects with increased IOP Neural capacity, mean score, global deviation, local deviation and form index were analyzed. The mean value of all these parameters was worse in the ibopamine positive test group, although the differences were not statistically significant using Student's *t* test

It is possible that the ibopamine positive test subjects are more susceptible to glaucomatous damage than ibopamine negative test subjects Therefore, the ibopamine test could be a predictive test for developing glaucoma, and be particularly useful for diagnosis of those conditions with increased IOP

Introduction

Ibopamine, the 3,4-diisobutiryl ester of N-methyldopamine, is an orally active dopamine analog with positive inotropic activity and vasodilating effect.

Studies *in vivo* and *in vitro* show that ibopamine stimulates dopaminergic receptors, beta-adrenergic receptors and, at higher concentrations, alpha-adrenergic receptors. Studies in humans show that drops of ibopamine solution in the conjunctival sac determines mydriasis without cycloplegia. This kind of administration is well tolerated locally and systemically.

2% or 4% ibopamine solution in normal subjects does not increase intraocular pressure On the contrary, in patients with open-angle glaucoma it induces a transient increase of intraocular pressure 30 to 60 minutes after administration Increase of intraocular pressure is also observed in certain subjects with ocular hypertension It is possible that it occurs in subjects in danger of developing glaucoma, so that ibopamine could be useful as a provocative test for glaucoma

High-pass resolution perimetry (HRP), a new technique that determinates resolution threshold in the visual field has been shown to be a sensitive test for glaucomatous damage. Our aim was to investigate whether there is a difference between ibopamine test positive and negative patients with HRP

Subjects and methods

The sample included 30 patients with ocular hypertension (IOP > 21 mmHg in more than two measurements), normal visual field (Humphrey 30-2 or Octopus G1 programs), normal

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optic disk and visual acuity 20/25 or better All subjects were free of ocular or neurological diseases. They had no systemic diseases with known ophthalmic complications The iridocorneal angle in all subjects was open

The first group included 15 patients (mean age, 63 4 ± 11.5) who had shown an increase of intraocular pressure of 4 mmHg or more, 45 minutes after the administration of a 2% ibopamine solution (ibopamine test positive subjects); the second group included 15 patients (mean age, 58 2 ± 10 6) who had shown no modification of intraocular pressure or an increase of less than 4 mmHg (ibopamine test negative subjects) after the same time period

All subjects underwent a HRP test using the Ophthimus ring perimeter (HighTech Vision, Malmö, Sweden). One eye per patient was chosen randomly or according to reliability of patient response, tests with poor reliability were rejected.

Neural capacity, mean score, global deviation, local deviation, and form index were compared with Student's *t* test, for statistical analysis

Results

The ibopamine negative group showed a mean neural capacity of 101 ± 15.2%, a mean mean score of 4.1 ± 1.0, a mean global deviation of –0.13 ± 1 0 dB, a mean local deviation of 0 78 ± 0 16 dB, a mean form index of 0.72 ± 0 11.

The ibopamine positive group showed a mean neural capacity of 92 5 ± 18.7%, a mean mean score of 4 45 ± 1.1, a mean global deviation of –0.6 ± 1 0 dB, a mean local deviation of 0 84 ± 0 16 dB, a mean form index of 0 78 ± 0.07

The statistical analysis did not show significant differences between the two groups.

Discussion

Even though there are no statistically significant differences between the two groups, the mean value of the HRP parameters considered, are consistently worse in the ibopamine positive test group

Previous studies suggest that HRP is a very sensitive technique in suspected or early glaucoma. The typical finding in early glaucoma is a uniform increase of the mean resolution threshold.

With these results, we suggest that the ibopamine positive test subjects are more susceptible to glaucomatous damage.

Of course, further studies* will be necessary to verify this theory. Our aim is to carry out the ibopamine test and HRP on a greater number of subjects with increased intraocular pressure to increase our statistical power Furthermore, we will be following these subjects in the following years using conventional automatic perimetry to detect the onset of visual field loss

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Reliability indices in glaucoma. A comparison between conventional and high-pass resolution perimetry

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Abstract

Reliability of high-pass resolution perimetry (HRP) was studied in 134 visual fields from subjects with glaucoma or ocular hypertension In badly damaged fields, false-negative responses were common The results of this study suggest that a large false-negative response rate is not a sign of poor cooperation, but a sign of large variability, common in visual fields of glaucoma patients In a second study, reliability of HRP and Humphrey Field Analyzer (HFA) was compared Fixation losses were more common in HRP than in HFA, especially in visual fields damaged from glaucoma Whether this discrepancy reflects a true difference in subject's fixation behavior or a difference in detecting fixation instability between the two instruments remains unknown

Introduction

The reliability of differential light sense perimetry has been studied by several authors[1–4] Common to most studies is a large percentage of unreliable visual field tests. It is also common for patients with glaucoma to exhibit less reliable results than normal subjects. For example, Katz and Sommer[1] found that 45% of field tests in patients with glaucoma were rejected by one or more of the three criteria used by the Humphrey Field Analyzer (HFA) (Allergan-Humphrey, San Leandro, CA): fixation losses, false-positive and false-negative rates. In normal subjects, 30% of the fields were judged unreliable. A major discrepancy between the two groups was a higher percentage of false-negative answers in the glaucoma group. Similar findings have been reported by Johnson *et al* [5]

Reliability indices for high-pass resolution perimetry (HRP) were studied by Chauhan *et al.*[6]. HRP is a new perimetric technique[7] determining spatial resolution thresholds instead of luminance increment thresholds. In normal subjects, reliability of HRP did not differ significantly from HFA. About 10% of visual fields from normal subjects were rejected using the established HFA criteria (9 6% in HFA, 11 6% in HRP). The difference was due to a somewhat larger percentage of fixation losses in HRP and was attributed to the larger dimension of its blind-spot stimulus For HFA, there was a notable difference in rejection rate compared to the study of Katz and Sommer[1], the reason for this was not obvious.

Reliability indices common to HFA and HRP are fixation losses, false-negative and false-positive rates. In addition, HRP determines mean test-retest change and its standard deviation. These five indices are summarized in an overall judgement of reliability in three grades: good, dubious, or poor. The reliability criteria for HRP are summarized in Table 1 The number of presentations of fixation, blank, and catch targets is typically about 10. These criteria differ from those of HFA that are < 20% fixation losses and < 33% false-negative and false-positive rates.

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Table 1. Reliability criteria for Ophthimus

Reliability	*Fix loss*	*FP*	*FN*	*Retest*	*Retest SD*
Good	≤ 2	≤ 2	≤ 2	< Mean + 2 SD	< Mean + 2 SD
Dubious	≤ 5	≤ 5	≤ 5	< Mean + 2 5 SD	< Mean + 2 5 SD
Poor	> 5	> 5	> 5	≥ Mean + 2 5 SD	≥ Mean + 2.5 SD

FP = false-positive response, FN = false-negative response, Retest = test-retest change, Retest SD = standard deviation of test-retest change

A unique measure in HRP is the calculation of functional neural channels ("functional channels" or "neural capacity" depending on software version). HRP measures peripheral resolution and resolution is proportional to ganglion cell separation[8] The threshold in each test position can therefore be used to estimate the number of functional ganglion cells in the corresponding part of the retina. These figures are compared to age-corrected means and the results are summed over the measured visual field to give an overall ratio Unlike global indices offered by other perimetric techniques, neural capacity has a sound anatomical and physiological basis and is therefore used in the following as an index of the state of the visual system Like other global perimetric indices it is affected by factors other than neuronal loss, *e g*, media opacities

The present study presents HRP reliability results in patients with ocular hypertension or glaucoma with various degrees of visual field damage. It also compares reliability indices for HRP and HFA in another group of patients with glaucoma or ocular hypertension tested by both methods

Subjects and methods

Records from the glaucoma files at the Department of Ophthalmology, University of Göteborg, were studied in retrospect Of all patients with ocular hypertension or glaucoma subjected to repeated HRP testing, results from one eye were randomly chosen (Study 1). The first test was discarded and the second was used for the reliability analyses. HRP was performed using the Ophthimus Ring Perimeter version 1 or 2 (HighTech Vision, Göteborg, Sweden) according to the manufacturer's instructions

For a comparison study between HRP and HFA, all subjects with ocular hypertension or stable glaucoma that had undergone HRP and HFA field tests within an interval of one month were selected (Study 2). HFA was performed using the programs 24-2 or 30-2 and the results were analyzed with Statpac software version 1 (Allergan-Humphrey, San Leandro, CA). The results from one eye were randomly chosen for the analyses

All visual field tests were performed by trained technicians. Patients with cataract or visual disorders other than ocular hypertension or glaucoma were excluded from analysis.

Statistical analyses were performed using Systat statistical software (Systat version 5, Evanston, IL) Statistical significance was set to $p < 0\ 05$

Results

Study 1 Reliability indices in HRP

Visual fields from 134 eyes (134 patients) with ocular hypertension or glaucoma were analyzed. The mean age of the subjects was 67 years (range 15–86). The distribution is shown in Figure 1. The HRP statistical evaluation interpreted 84 (63%) of the fields as abnormal, 30 (22%) as suspicious, and 20 (15%) as normal The mean neural capacity was 70% (range 2–150). Using the HRP criteria, 81 examinations (60%) were found to have good, 30 (22%)

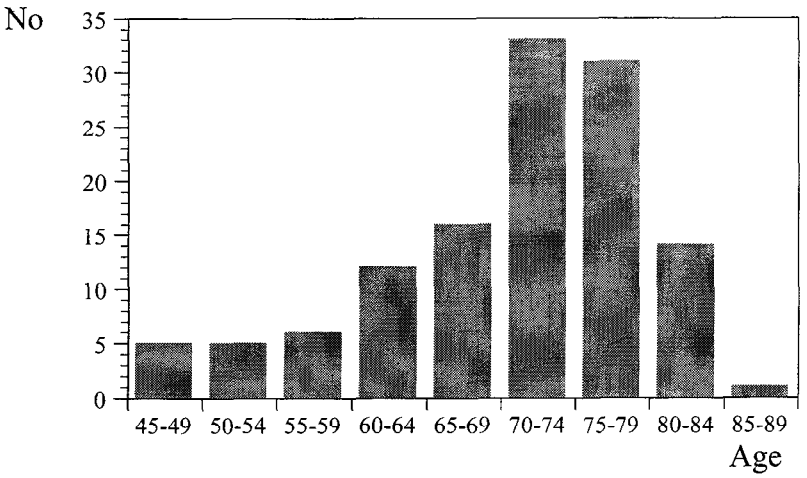

Fig 1 Age distribution in study 1 group

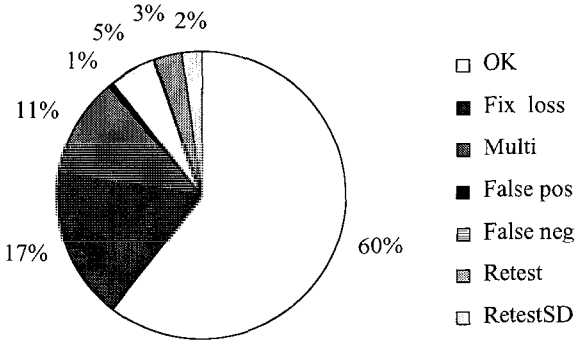

Fig 2 Reasons for abnormal reliability results in high-pass resolution perimetry "Multi" refers to cases in which more than one reliability index was outside the normal range Study 1

dubious, and 23 (17%) poor reliability. In the following, the two latter categories will be grouped together as "abnormal" Reliability results are shown in Figure 2 ANOVA tests failed to show any significant influence of age, neural capacity, or visual acuity on reliability. If instead, standard reliability criteria for HFA were applied to the HRP results, 85 (63%) were found reliable and 49 (37%) unreliable.

A large percentage of fixation losses was the single most common cause for dubious or poor reliability. Thirty-four (25%) of the fields had fixation losses exceeding the Ophthimus criteria (more than two seen blind spot presentations). In 23 cases (17%) a large number of fixation losses was the only sign of defective reliability, the other indices being within normal limits (Fig. 2). Using HFA criteria (less than 20% fixation losses), 43 of the fields (32%) were unreliable due to poor fixation. In Figures 3 and 4, reliability results are plotted against age and neural capacity, respectively. Multiple regression analysis showed a significant correlation between fixation losses and neural capacity ($p = 0.036$) (Fig 3) while age failed to show such correlation when neural capacity was accounted for (Fig. 4) Thus, fixation errors were more common in fields with higher neural capacity score.

False-positive answers (when a patient responds to a blank presentation) accounted for only a few unreliable fields. Seven fields (5%) had more than two false-positive answers (the cut-

off criterium for HRP) (Fig. 2). In one case it was the only sign of poor reliability. Using HFA standard criteria (less then 33% false-positive answers) only one field was judged unreliable on these grounds

False-negative answers accounted for a larger number of unreliable fields. Using the Ophthimus criterion (more than two missed supraliminal targets), 14 fields (10%) were judged unreliable In seven fields (5%) this was the only sign of defective reliability (Fig. 2) With thc HFA criterion (less than 33% false-negative answers), thc number of unreliable fields was eight (6%) Multiple regression analysis showed a significant inverse correlation between false-negative responses and neural capacity (p = 0 009) (Fig. 3) whereas age failed to show a correlation when neural capacity was accounted for (Fig 4) Thus, false-negative responses were more common in severely damaged visual fields, regardless of the subject's age

Test-retest changes accounted for a small number of unreliable fields A large mean retest change was found in ten fields (7%); in four (3%) it was the only reliability index that was outside the normal range (Fig 2). The standard deviation of mean retest change was abnormally large in nine fields (7%), in three it was the only reason that the result was judged to be unreliable The fields with a large test-retest change and a large test-retest standard deviation were different except for one case

Fifteen fields (11%) were judged unreliable because two or more of the reliability indices were abnormally high. In 11 of these, fixation losses were outside the normal range.

Study 2 Comparison between reliability indices in HFA and HRP

HRP and HFA visual fields from 44 patients with ocular hypertension or glaucoma were studied. Mean age was 61 years (range 13 to 83) The age distribution was very similar to Figure 1 except that it was shifted about five years towards lower ages. HRP software classified 24 (55%) of the visual fields as abnormal, ten (23%) as suspicious, and ten (23%) as normal. Mean neural capacity was 79% (range 31 to 133).

Using the machine-specific criteria, the reliability of 30 (68%) HRP fields was classified as good, eight (18%) as dubious, and six (14%) as poor. Of the dubious or poor fields, seven failed because of fixation errors, five because of false-negative and two because of false-positive errors If instead HFA criteria were applied to the HRP fields, only nine (20%) were judged as unreliable; six because of fixation errors, two because of false-negative errors, and one of a combination of both factors.

Thirty-nine (89%) of the HFA fields were found to be reliable using the HFA criteria. Four failed because of fixation errors, and one because of false-negative errors

Mean test time for HRP was five min 57 sec (range four min 32 sec to 11 min 29 sec) while for HFA it was 13 min three sec (range eight min 38 sec to 20 min 47 sec)

Discussion

Study 1 Reliability indices in HRP

Reliability in perimetry, as measured with reliability indices, varies among studies. Common to most is the finding that reliability is better in normal subjects than in patients with glaucoma. An explanation for this is that visual field damage has negative effects on perimetric reliability. Another explanation is that glaucoma patients generally are elderly and that advancing age is detrimental to perimetric reliability.

The present study failed to show any statistically significant difference in overall reliability due to age, neural capacity, or visual acuity in a group of patients with ocular hypertension or glaucoma However, the reason for poor reliability differed depending on the degree of visual field damage Fixation losses were more common in undamaged fields, while false-negative errors were more common in more damaged fields (Fig 3) Age had no significant impact on these indices when neural capacity was accounted for. Thus, among the ten most damaged fields in this study, one was judged to be unreliable because of fixation losses and three be-

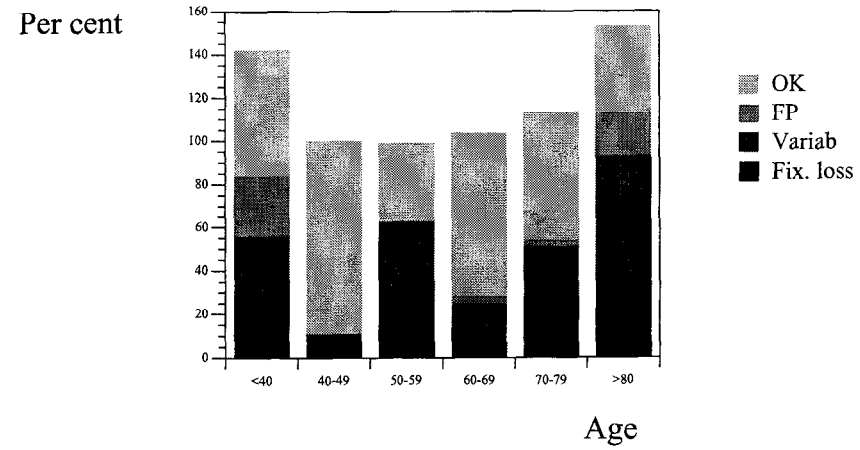

Fig 3 Reliability results plotted against age. "Variab" refers to cases in which one or more of the following reliability indices were abnormal: false-negative responses, retest change, and standard deviation of retest change FP = false-positive response Because each field could show abnormal results in more than one of the categories the total figure exceeds 100%. Study 1

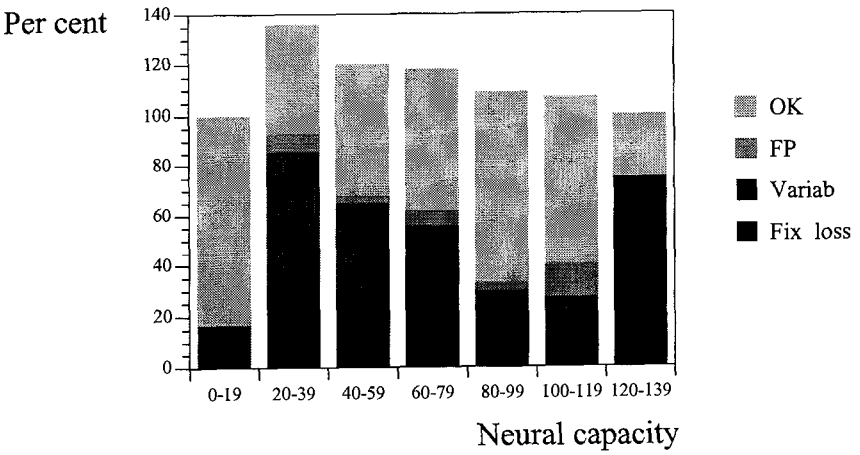

Fig 4. Reliability results plotted against neural capacity "Variab" refers to cases in which one or more of the following reliability indices were abnormal: false-negative responses, retest change, and standard deviation of retest change, FP = false-positive response Because each field could show abnormal results in more than one of the categories the total figure exceeds 100% Study 1

cause of false-negative errors. Among the ten fields with the largest neural capacity scores, six failed because of fixation losses and none because of false-negative errors. A plausible explanation for these findings is that fixation losses falsely improve the visual field result and that such fields are more common in the group of normal or super-normal fields.

There is no doubt that fixation errors reflect poor patient cooperation (provided that the initial blind spot monitoring was adequately performed and that the contralateral eye was thoroughly occluded). However, head tilts occurring after initial blind spot mapping is another cause of "fixation losses". False-negative errors, on the other hand, may reflect poor cooperation but could also reflect increased threshold variability. Variability has been shown to be

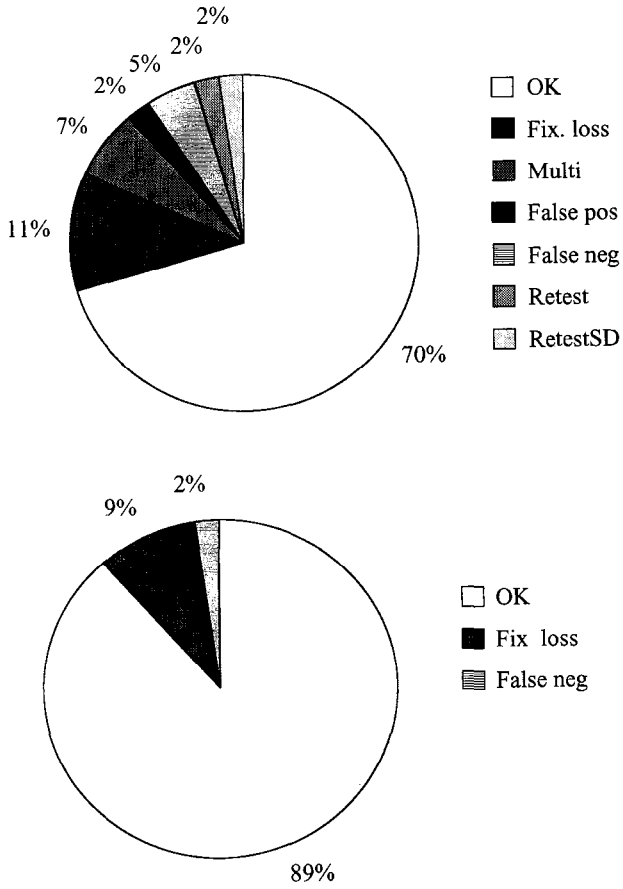

Fig 5. Reliability results in high-pass resolution perimetry (top) and conventional automated perimetry (bottom) Study 2.

larger in glaucomatous eyes[9]. Since glaucoma patients with advanced field defects do not show any other sign of defective reliability, the author proposes that the large number of false-negative errors in this group are due to increased variability due to the disease process. Thus, at least in this group of patients, a large number of false-negative errors should not disqualify the field results as unreliable. A large false-negative response index is instead a sign of glaucomatous damage

Study 2· Comparison between HFA and HRP

As previously shown[6], fixation losses are more common in HRP than in HFA. The explanation may be that the blind spot target in HRP is larger (1 degree diameter) than in HFA (0.43 degree diameter). Another possible source of error is incomplete occlusion of the untested eye. Because of the large dimension of the correction lens in the HRP system, prismatic effects could render the blind spot target visible through even a very small nasal opening in the eye cover. Another possibility is lack of a chin rest which allows more head tilting after initial blind spot mapping.

It was also found that false-negative errors were more common in HRP than in HFA. This can partly be explained by different cut-off criteria: the 33% normal limit in HFA is large

enough to allow almost every field to pass. However, when similar criteria were applied to the two tests, false-negative errors seemed more common in HRP The explanation may be the different test strategies of the two instruments: Humphrey presents catch targets with a 9 dB luminance increment to previously measured thresholds, while catch targets in Ophthimus are presented with a 2 dB increase in size. However, scaling is not exactly comparable between the two instruments.

In the study of Chauhan *et al* [6], 12.2% of HRP fields from normal subjects were judged unreliable using standard HFA criteria. This contrasts to 37% in the present study in patients with ocular hypertension or glaucoma in study group 1 and 20% in study group 2 The reason for the difference between the two groups may be that group 2 was biased towards younger subjects with less damaged fields On the other hand, only 11% of HFA fields in study group 2 were judged unreliable, a figure very close to that for normal subjects (9 4%)[6]. Reliability in HFA thus seemed similar in a normal group and a group with ocular hypertension or glaucoma, while reliability in HRP was worse in the latter group. This discrepancy remained also if false-positive and false-negative errors were excluded and the comparison was restricted to fixation errors. Thus, it appears that fixation is less prone to deteriorate with increasing age or field damage in HFA than in HRP. The reason for this is not clear. One factor could be the fixation monitoring video camera in HFA, which allows the examiner to discover unsteady fixation also between blind spot presentations and to encourage the patient to better fixation.

General conclusions

To summarize, HRP reliability criteria are more strict than HFA In part this has to do with two indices in HRP lacking a counterpart in HFA; retest change and its standard deviation. If HFA criteria are applied also to HRP fields, reliability interpretation becomes more comparable between the two tests. However, a large fixation error score is more common in HRP, especially in eyes with glaucoma damage. Whether this reflects a true difference in fixation behavior between the two instruments or just different sensitivity for detecting fixation deviations is not known Nor is it known which is the optimum sensitivity for such detection, or indeed what impact deficient fixation has on the perimetric result. In HRP it was common for glaucoma fields to be rejected because of large false-negative answer rate. This was especially true for eyes with advanced field defects. It is probable that a large false-negative rate is not a sign of poor cooperation but rather of advanced disease

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Relationship between quadrants of neuroretinal rim area of glaucomatous optic disk and both "neural capacity" of high-pass resolution perimetry and mean deviation of HFA: A comparative study

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Purpose

"Neural capacity" (NC) index of high-pass resolution perimetry (HRP) is correlated with neuroretinal rim area of the optic disk To clarify whether HRP or conventional differential light sensitivity (DLS) perimetry relates better to glaucomatous optic disk abnormalities, the authors investigated the relationship between the rim area and both NC and mean deviation (MD)

Subjects and Methods

Forty-seven eyes of 33 normal-tension glaucoma (NTG) patients were enrolled in this study. High-pass resolution perimetry was performed with the Ophthimus system version 2.50. DLS perimetry was performed with program central 30-2, using Humphrey Field Analyzer 630 (HFA) According to Aulhorn-Greve's classification, 21 eyes were classified into "early stage" eyes (stages I and II) and 26 eyes into "advanced stage" eyes (stages III, IV and V) The total rim area and the area of its temporal, superior, nasal and inferior quadrants were obtained using laser scanning tomograph (Heidelberg Retina Tomograph) Local mean NC (LMNC) was calculated using the resolution thresholds corresponding to the quadrant. Local MD (LMD) was calculated using total deviations of HFA.

Results

In a total of 47 eyes, NC showed a significant correlation with the total rim area ($r = 0\ 394$, $p < 0.01$), but MD failed to. Furthermore, NC showed a significant correlation with the total rim area in eyes with early visual field changes ($r = 0\ 495$, $p < 0.05$), but not in eyes with advanced changes. The superior and inferior rim areas showed significant correlations with both LMNC and LMD (superior, $r = 0\ 503$, $p < 0.01$ for LMNC; $r = 0\ 309$, $p < 0.05$ for LMD inferior, $r = 0.456$, $p < 0.01$ for LMNC; $r = 0.403$, $p < 0\ 01$ for LMD). However, no correlation was found between the rim areas and both LMNC and LMD in either temporal or nasal quadrant

Conclusion

The results indicate that NC may relate to glaucomatous optic disk changes better than MD in NTG, especially in the early stage

The results of the study will be published in detail elsewhere

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Optic disk features and "neural capacity" of high-pass resolution perimetry

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Abstract

The correlation between disk changes, measured by using computerized Topcon Image-net videostereography, and visual field defects observed with high-pass resolution perimetry (HRP), which provides quantified results as a percentage of "neural capacity", could give useful hints on the level of nerve suffering in early glaucoma In glaucomatous eyes, the rim/disk ratio showed a direct correlation with the neural capacity (NC) ($r = 0\ 335$; $p = 0\ 045$; $n = 36$) and an indirect correlation with the global defect (GD) ($r = -0\ 342$; $p = 0\ 041$; $n = 36$)

Our results suggest that HRP correlates well with some disk changes in glaucoma and shows potential advantages for the assessment of nerve damage in glaucoma

Introduction

There is evidence in ophthalmic literature that a series of psycho-functional parameters are widely affected before standard conventional visual field thresholds in early glaucoma[1,2].

There is also evidence that, due to the redundancy of ganglion cells, a large number of nerve fibers has to be damaged before a reliable visual field change is recognized as such in conventional differential light sensitivity testing[3].

High-pass resolution perimetry (HRP) represents a unique system for evaluating visual function in glaucoma. In particular, it has been claimed that this method can give information on the relationship which exists between resolution thresholds and ganglion cell density, based on the assumption that over the retina minimal angle of resolution and ganglion cell spacing are proportional[4].

Glaucomatous damage seems to act primarily on the ganglion cell population If this is confirmed, the possibility of relying on a system able to monitor ganglion cell function could be of the utmost importance Furthermore optic disk changes in early glaucoma are supposed to precede functional damage[5–8]

The aim of this paper is to describe the correlations existing between some typical glaucomatous optic disk changes and the results of HRP in ocular hypertension and early glaucomas.

Materials and methods

Thirty-six ocular hypertensive ($n = 15$) or glaucomatous eyes ($n = 21$) were selected at random among patients being treated at the Glaucoma Service of the Department of Ophthalmology of the University of Genoa.

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Criteria for selection were:
- intraocular pressure between 22 and 25 mmHg (APL) without medication in at least three consecutive measurements;
- possibility of pupil dilation over 7 mm of diameter;
- patient's consent to participate in the study;
- moderate optic disk changes: stage I, II and III (stage I: rim area = 1.60 ± 0.36 mm^2, the neuroretinal rim was even in width in all locations of the optic disk; stage II: rim area = 1 23 ± 0.35 mm^2 characterized by rim notches; stage III· rim area = 0.91 ± 030 mm^2, the rim loss is present mainly in the temporal horizontal disk region where the rim is now thinner than in the other disk sectors)[9];
- visual field: MD > –24; CPSD < 10;
- no media opacities able to disturb vision or reduce contrast sensitivity;
- best corrected visual acuity equal or higher than 7/10 (20/30);
- no sytemic disease able to affect visual field and psycho-functional testing;
- ametropia between +3.00 and –8.00 dpt with astigmatic error lower than 1.50 dpt.

All patients were under medical therapy including beta-blocking, sympaticomimetic, carbonic anhydrase inhibitor agents which lowered intraocular pressure to a presumed safe level. No patient was on miotics

Each patient underwent computerized Humphrey VFA 640 (central 30-2) perimetry, Ophthimus 2 4 HRP (NiKon) and computerized morphometric analysis of simultaneous stereoscopic videographs of the optic nerve by means of the "new retinal nerve fiber layer" (New RNFL) program of the Topcon Image-net X System (IS-X) optic disk analyser

All the examinations were performed on the same day, if possible, or within a week.

Thresholds of spatial resolution perimetry were measured using the automated ring perimeter "Ophthimus" (High Tech Vision, Malmo). The stimulus is a ring target, introduced by Frisén, having a bright core and dark borders The space-averaged luminance of the target is equal to the background. Thresholds are determined by varying the size of the stimulus. The threshold is the smallest target seen by the subject at each test point. We used the standard program which measures the spatial thresholds at 50 locations in the central visual field[10].

Global deviation (GD), local deviation (LD), neural capacity (NC) and retest standard deviation (RSD) were the HRP indices considered for this study.

Optic disk morphology was observed by means of the Topcon Image-net X System (IS X) (rev-3 51b), which is examining simultaneous stereovideographs, and gives quantitative evaluation of optic disk features.

The IS X is a system of image digitalization able to capture, store and analyze simultaneous stereoscopic images of the optic disk. It is composed of hardware, including a stereo retinograph (Topcon TRC-SS2), interfaced to 2 video cameras, a 386 personal computer with mathematical processor, an optical disk drive and a printer Software with especially designed multiple programs allowing the storage, enhancement, digitization and analysis of the stereo-images is implemented in the computer. The results of this process can be printed in numbers or graphs[11]

The instrument projects a grid on each optic disk stereo-image (to be photographed) in order to increase the possibility of having corresponding reference points on the two images and more reliable measurements[12].

Juxtapapillary nerve fiber layer height was measured by means of the "New RNFL" program. In this program the operator has to use four points to identify the outer edge of the optic disk in just one image of the stereopair. Then he has to mark two points on corresponding locations of the two stereo-images Finally the computer warps the right image to obtain the best possible correspondence with the points of the left one The quality of such correspondence is calculated and expressed as percent of "bad points" indicating the number of points lacking correspondence. The percentage of bad point constitutes an indicator of the quality of the images collected and then forecasts the possibility of accuracy of the subsequent analysis.

In our study all the images having a "bad points" percentage higher than five were discarded and repeated[13].

The disk parameters taken into consideration were two the rim/disk area ratio (R/D) and the juxtapapillary retinal nerve fiber layer height (RNFLH)

Table 1 Results

Eye	*R/D*	*RNFLH*	*GD*	*LD*	*RSD*	*NC*
1	0.61	–0 090	4 08	1 05	0 71	18
2	0 405	–0 073	4 82	1 31	0.89	21
3	0 722	0 242	1 03	0 92	1.30	71
4	0 658	0 117	0 61	0 81	0 75	75
5	0 88	0 381	–0 49	0 69	0	99
6	0 72	0 13	–0 26	0 7	0	46
7	0.46	0 178	1 61	0 85	1 72	63
8	0.69	0 104	1 16	1.04	1 32	72
9	0.90	0 288	2 24	0 65	0 98	56
10	0.79	0 079	1.98	0 91	0 71	59
11	0.54	0 2	1.23	0 92	0 92	66
12	0 71	0 189	1 28	1 11	1 12	62
13	0 50	–0.124	0 71	0 88	1 10	79
14	0 61	0.242	1 29	0 98	0 45	68
15	0 70	–0 058	1 39	0 80	0 96	67
16	0 74	0.215	0 59	0 78	0 45	81
17	0 527	0 005	0 90	0 84	1 27	71
18	0 513	0 551	1 30	0 86	0 67	67
19	0 66	–0.356	–0 7	0 85	0 84	105
20	0 39	0 424	5 02	1 38	0	13
21	0 52	0 014	–0.90	0 65	0 75	116
22	0.60	0.111	2 22	0 76	1 26	56
23	0 70	0 451	0 73	0 71	1 04	75
24	0 90	–0.004	0.91	1 71	0 71	92
25	0 94	0.134	–0 83	0 59	0 82	90
26	0 55	–0 069	–0 37	0 62	0 71	97
27	0 56	–0 042	1.86	0 90	1 26	61
28	0 94	0 030	0 15	0 77	1 21	86
29	0 96	0.099	–0 16	0 78	1 12	91
30	0 77	0.414	3 03	2 06	1 21	47
31	1	0 834	3 77	1 88	1 05	39
32	0 94	0 701	0 88	0 73	1 11	80
33	0 77	0.254	0.43	0 46	0 82	85
34	0 85	–0 127	–0 55	0 61	0 98	108
35	0.73	–0 034	0 41	0 97	0 64	87
36	0 78	0 145	–0 76	0 82	0	112

Table 2 Correlations between optic disk morphometric parameters and HRP indices in ocular hypertension and glaucoma

R/D vs NC	$r = 0\ 335$	$p = 0\ 0458$
R/D vs GD	$r = -0\ 342$	$p = 0\ 0409$
R/D vs LD	$r = 0\ 016$	$p = 0\ 9264$
R/D vs RSD	$r = 0.001$	$p = 0\ 9953$
RNFL vs NC	$r = -0\ 288$	$p = 0\ 0876$
RNFL vs GD	$r = 0\ 286$	$p = 0\ 0905$
RNFL vs LD	$r = 0\ 280$	$p = 0\ 0977$
RNFL vs RSD	$r = 0\ 034$	$p = 0\ 8472$

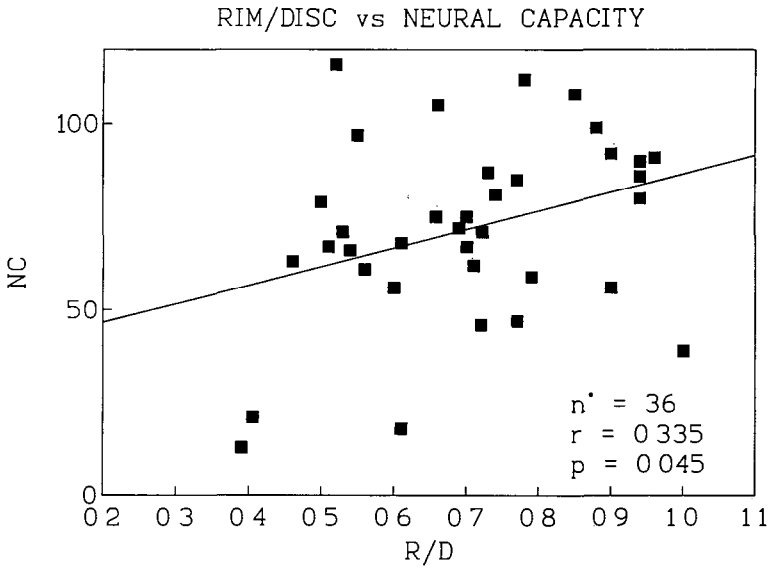

Fig 1 Results Correlation between rim/disk area (R/D) and neural capacity (NC) at HRP in ocular hypertensive and glaucomatous eyes.

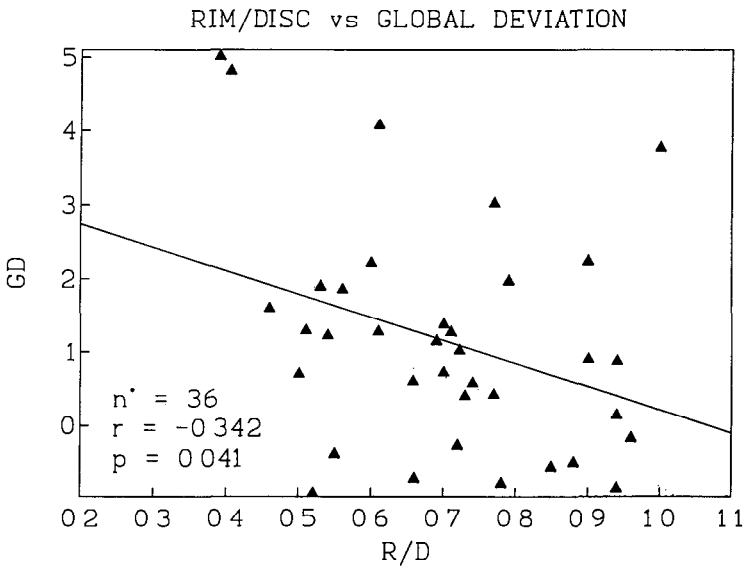

Fig 2 Results Correlation between rim/disk area (R/D) and global deviation (GD) at HRP in ocular hypertensive and glaucomatous eyes

The results of HRP and optic disk morphometric analysis were correlated by means of linear regression analysis

Results

The details of the results are displayed in Table 1

A statistically significant ($p < 0\ 05$) correlation was present between R/D and NC (Fig. 1),

R/D and GD (Fig. 2) No significant correlation was present between R/D and LD and RSD, and RNFLH and HRP results (Table 2)

Discussion

The definition of damage induced by glaucomatous disease is difficult especially in early phases when it is very difficult to diskriminate between glaucoma suspect (ocular hypertensive) and glaucoma It has been reported that in 85% of patients typical optic disk damage is present before the appearance of typical visual field localized scotomas[8], on the other hand a number of glaucoma suspects, when followed with time, will show localized visual field defects in the absence of optic disk changes recognizable as typical for glaucoma[14] This clearly indicates that both morphometry of the optic disk and psycho-functional evaluation, by themselves, are not sufficient to accurately provide diskriminative diagnostic elements. In this respect the search for correlation between morphometric and psycho-functional data can be the clue for the improvement of our diagnostic capabilities in early glaucoma.

HRP was designed to establish a proportional relationship between the resolution threshold and the underlying ganglion cell density[1]. If that is true, HRP will give direct information about ganglion cell survival in glaucoma With HRP Lachenmayr *et al* found a borderline significant relationship between neuroretinal rim area and mean sensitivity[15].

HRP evaluation gave controversial results in eyes with glaucoma and ocular hypertension. Sample and colleagues show that there is a change in HRP with age and that age matching improves the sensibility of the system; but the authors could not show any superiority of HRP versus static light threshold sensitivity perimetry in detecting glaucomatous neuropathy[2]

Wanger and Persson found abnormal HRP results in a high percentage of eyes with suspected or early glaucoma when compared to results in normal eyes[16]. Dannheim and coworkers compared automated sensitivity perimetry with HRP in glaucoma and found good agreement in the number of eyes detected as abnormal for each method[17]. Lachenmayr *et al.*, on the other hand, showed HRP to be less sensitive than differential light sensitivity or flicker perimetry[18]

Our results show good correlation between R/D and NC and R/D and GD showing a nice correspondence between morphometrical parameters and this resolution test. Nevertheless it was not possible to find a correlation between juxtapapillary retinal nerve fiber layer height and HRP indices This could be due to the restricted reproducibility of the measurements of nerve layer height as performed by our instrument or to the fact that HRP stimuli are thought to be collected by the smaller ganglion cells which are not the type of fibers most often damage in early glaucoma

HRP is a very quick system for analyzing psycho-functional performances in glaucoma and it is very well accepted by patients. Nevertheless its superiority in sensitivity as diagnostic system for glaucoma has not been shown

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TEST STRATEGIES

Improving estimation of false-positive and false-negative responses in computerized perimetry

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Abstract

The authors have developed new methods for estimating the false-positive and false-negative responses during visual field testing without the use of catch trials Frequencies are estimated with maximum likelihood techniques using full staircase data assuming a model; (1) that false responses occur randomly (with fixed intensity), (2) that the threshold value at each test point location is a random variable with Gaussian distribution.

Twenty-one glaucoma patients underwent computerized testing of the central 30° field two times each FP and FN frequencies were evaluated with our new method and the standard catch trial method FP and FN variability decreased with the new method Thus the square root of the average test-retest FP variance decreased from 7 6% to 1 6% for FP, and from 4 7% to 4 2% for FN These new methods can thus simultaneously improve FP/FN accuracy and decrease test time

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The effect of audio and visual cueing on visual field testing

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Abstract

A Humphrey perimeter was modified to give audio or visual cues before each test stimulus to see if subject test performance could be improved.

Thirty-seven patients and 42 normals were each given a custom visual field test in one eye, once with audio cueing (frequency = 1000 Hz, duration = 100 msec, 300 msec before stimulus), once with visual cueing (red light at fixation point 300 msec before stimulus) and once with no cueing

There was a trend for normal subjects and possibly patients to have a better visual threshold and a smaller short-term fluctuation with cueing than without cueing. However, normal subjects were seen to have a significantly higher percentage of fixation losses with audio cueing than with no cueing

We concluded that the improved visual threshold and decrease in short-term fluctuation associated with cueing represent a modest improvement in subject performance, but at a cost of increased fixation losses

Introduction

A patient must maintain a high state of visual alertness to perform an automated threshold visual field examination. In one-third or more of such tests patients fail the manufacturer's reliability standards[1], with over 33% false-positive or false-negative responses on catch trials, or over 20% fixation losses when tested by periodic stimulus appearance within the physiologic blind spot. Even if fixation losses do not exceed the cut-off level of 20%, a lower rate may cast some uncertainty on the test results

Moreover, because threshold testing may take up to 15 to 25 minutes for each eye, the patient may become fatigued. As time goes on, patients can forget to fixate, or even fall asleep Even healthy, alert young subjects cannot be assumed to have stable fixation. In one study, 20% of this population had fixation losses exceeding 20%[2]

Previous work with the Dicon TKS4000 perimeter has shown an improvement in visual threshold with no increase in short-term fluctuation when utilizing a central fixation target that moves to a new position before each test stimulus[3]. One hypothesis for these findings was that the heightened alertness resulting from the moving fixation target cued the patient to the appearance of the next stimulus. In that study, however, reliability parameters were not measured.

The objective of this study was to find out if a simple audio or visual cue prior to stimulus appearance during the visual field test would help patients improve their performance without

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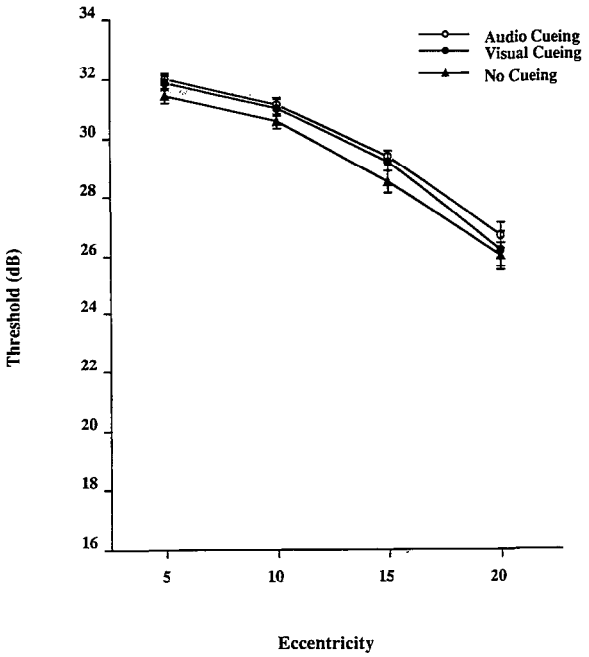

Fig 1. Mean thresholds at four eccentricities from fixation in 37 normal subjects using no cueing (triangles), audio cueing (closed circles), and visual cueing (open circles).

sacrificing test reliability in terms of false-positive and -negative catch trials, or fixation losses.

Materials and methods

A Humphrey Visual Field Analyzer was modified to provide audio cueing (frequency = 1000 Hz, duration = 100 msec, 300 msec before stimulus) and visual cueing (red light at fixation point beginning 300 msec before stimulus) as a menu option One randomly selected eye of 42 normal subjects ages 18–90 were recruited from a population of normal individuals. Thirty-seven (18–90 years), including those undergoing routine visual field testing for glaucoma, glaucoma suspects, and those with retinal, or neuro-ophthalmic indications, were also included All subjects had best corrected vision of at least 20/40 and a pupil at least 2.5 mm. The subjects also must have had some previous experience with threshold perimetry. In several cases when a normal subject lacked experience, he or she was allowed to participate only after taking at least two standard threshold tests.

Our custom threshold program tested 16 points along the four diagonal meridians at five degree intervals and then retested the same points, allowing calculation of short-term fluctuation The program was run in random sequence three times; once with no cueing, once with visual cueing, and once with audio cueing

Before the start of the tests, the type of cue being used was explained fully to the subject. Subjects were allowed to take breaks as needed. In all three tests in the cueing study, patients were monitored by the technician and were repeatedly encouraged to fixate on the fixation target.

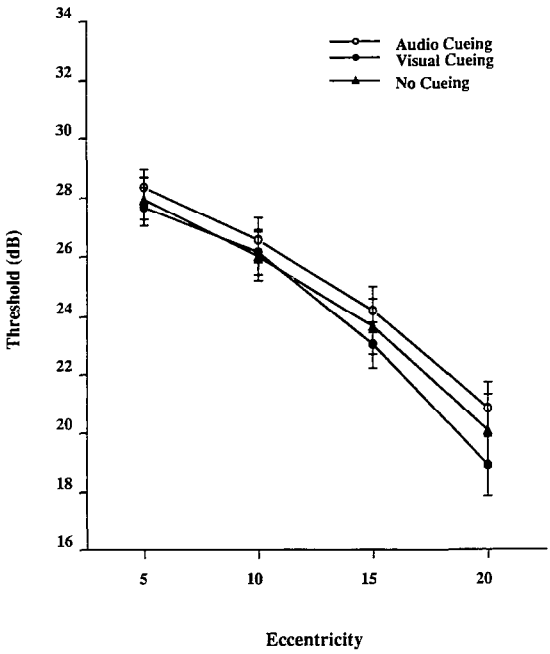

Fig 2 Mean thresholds at four eccentricities from fixation in 42 patients using no cueing (triangles), audio cueing (closed circles), and visual cueing (open circles)

Results

All subjects were able to perceive the audio and visual cues without any difficulty In both the normal group and the patient group, there was a trend, although not significant, for the threshold for the points with audio cueing to be better than that for no cueing. In only the normal group, the visual cueing also seemed to show a trend towards better threshold values compared to no cueing at all (Figs. 1 and 2).

In the normal group, there seems to be a trend for audio cueing to have the lowest short-term fluctuation of the three tests, although the trend is not significant. There is also a non-significant trend for short-term fluctuation of visual cueing to be lower than that for no cueing at all However, in the patient group, these trends are not apparent (Figs. 3 and 4).

In the normal group, there was a significantly higher percentage of fixation losses for audio cueing compared to that of no cueing ($p < 0\ 01$, Fig. 5). There also seemed to be more fixation losses for visual cueing compared to no cueing, but this was not significant The number of false-positives and false-negatives did not seem to differ between audio cueing, visual cueing, and no cueing.

In the patient group, there seemed to be a higher rate of fixation losses for audio cueing and, to a lesser extent, for visual cueing, compared to that for no cueing, but this was not significant. The number of false-positives and false-negatives were similar in all cueing situations (Fig. 6).

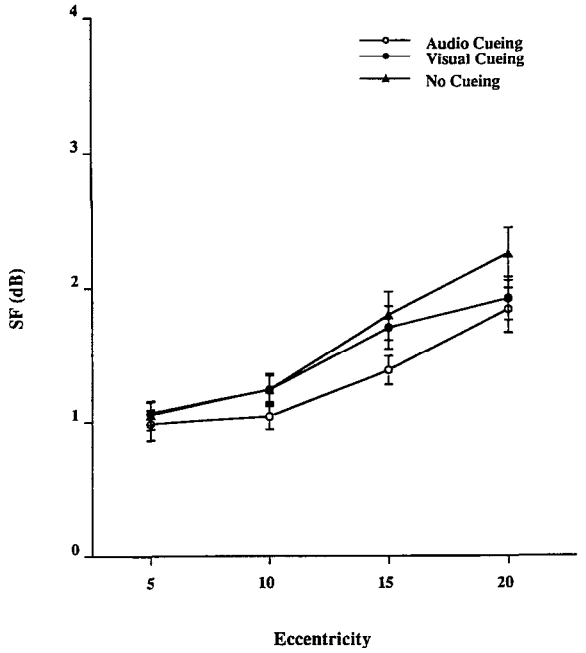

Fig 3 Mean short-term fluctuations at four eccentricities from fixation in 37 normal subjects using no cueing (triangles), audio cueing (closed circles), and visual cueing (open circles).

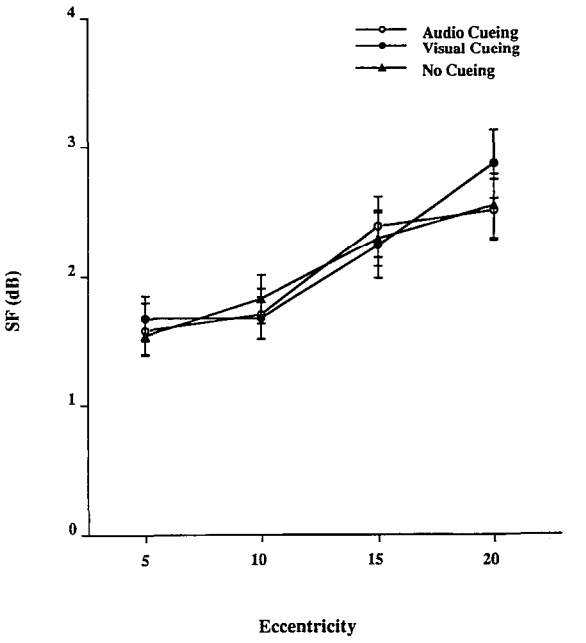

Fig 4 Mean short-term fluctuations at four eccentricities from fixation in 42 patients using no cueing (triangles), audio cueing (closed circles), and visual cueing (open circles).

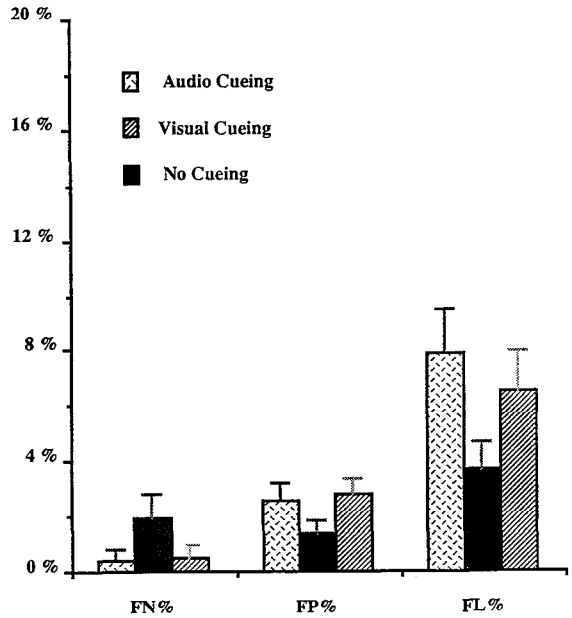

Fig 5. Mean reliability parameters of 37 normal subjects during testing with no cueing (black fill), audio cueing (gray fill) and visual cueing (diagonal cross-hatching) FN%=number of false-negative responses/total number of false-negative catch trials FP%=number of false-positive responses/total number of false positive catch trials. FL%=number of fixation losses/total number of stimulus presentations within the physiologic blind spot.

Discussion

Even though the trends towards lower thresholds during testing with audio and, to a lesser extent, video cueing are not significant, there is a fairly consistent trend It is our feeling that this slight improvement in average threshold indicates a modestly better patient performance One might speculate that, in both normal and patient populations, cueing would cause apparent improvements in threshold because subjects would respond only because of the cue, and not because they see a stimulus. However, we see that, in both populations, there is no significant difference among the false-positive rates for both types of cueing and for no cueing.

For patients, the thresholds for visual cueing also were not significantly different compared to that of no cueing. There even seems to be a slight trend for thresholds for visual cueing to be poorer. For some patients, we feel that this may indicate that the visual cue may actually be a nuisance, as is discussed below.

We found that, for normal subjects, there was a decrease in short-term fluctuation when cueing was added. We feel that this shows that cueing may boost subject performance by making each result more reliable. However, any sort of trend seems to be missing among the patient population when looking at short-term fluctuation Actually, it seems as if most trends seen among normals are less pronounced or missing in the patient group. This may be related to the fact that patients would generally have more experience with perimeters than normal healthy subjects.

When the projector moves around to project the next stimulus, its motor makes an audible sound A certain time interval after the projector stops moving, the stimulus appears. Patients with experience can, consciously, or unconsciously, know approximately when the stimulus will appear. For patients who have found this out, a cue would be redundant and would not

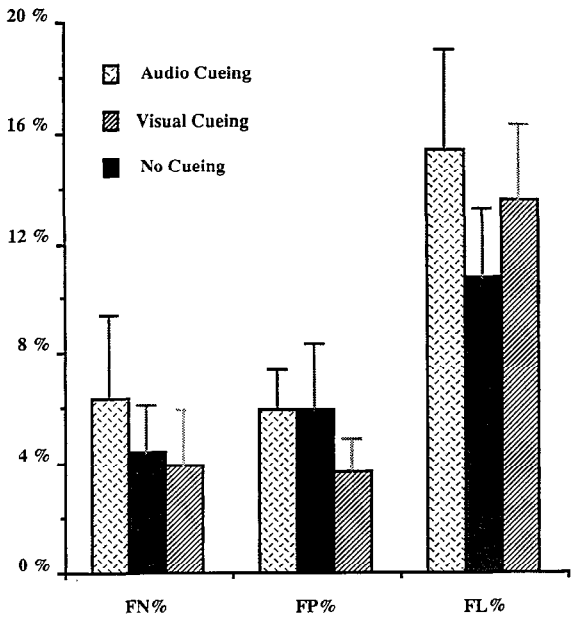

Fig 6 Mean reliability parameters of 42 patients during testing with no cueing (black fill), audio cueing (gray fill), and visual cueing (diagonal cross-hatching). FN%=number of false-negative responses/total number of false-negative catch trials FP%=number of false-positive responses/total number of false-positive catch trials FL%=number of fixation losses/total number of stimulus presentations within the physiologic blind spot

make much of a difference. In the design of the study, we made sure that all subjects had at least some experience with the perimeter For some normal subjects, this may have consisted of only a few tests previous to the cueing test This may not have been enough for the subject to recognize such a subtle cue

The improvement in threshold and decrease in SF was not as prominent as that we noted in an earlier study using the Dicon TKS4000 perimeter[3]. The cue in that device is provided by movement of the fixation target to a new location prior to each stimulus. The cue is thus more varied and compelling than the ones we used in this study. In that study, we could not measure changes in reliability parameters to determine if an increased fixation loss rate resulted from the moving fixation cue

In this study, the significant increase in fixation losses among the normal subjects when undergoing audio cueing is bothersome. We also see a non-significant increase in fixation losses among the patient subjects. Even though the Humphrey uses the intermittent "Heijl-Krakau" method of periodic blind spot checks, we believe that this increase in fixation loss rates probably represents a real increase in fixation losses, induced by the challenge of the cue to search for the stimulus. These fixation losses are also likely to be greater than five degrees of eye movement, since periodic blind spot checks are insensitive to smaller movements[4]. Fixation losses among normal patients merely lead to increased variation, but in glaucoma patients they can lead to "smoothing" over of real defects[5].

Of course, there is the likely possibility that the difference in performance we were hoping to find would appear only with a larger test group. Admittedly, there would have to be a large difference in average threshold to be significant among only 37 normal subjects or 42 patient subjects. However, we are hesitant to combine the results from both populations because of their many differences By the very fact that they are patients, we would expect a poorer mean

threshold compared to that of normal subjects We would also expect patients to have a greater short-term fluctuation.

Through most of the results, we see that the effect of cueing on short-term fluctuation, threshold, and false-positive rates seem more pronounced with audio cueing than with visual cueing This may well be related to the design of the visual cue. The stimulus turns from green to red 300 msec before the cue, and then turns back to green after the patient presses the trigger, or after one second if the trigger is not pressed Because of the rapid pace at which the test is run, the fixation point often seems to be just flashing red and green. Unless there is a conscious effort on the part of the patient to watch for the time at which the red light appears, the cue may be of little help Some subjects even stated that they preferred to ignore it. Indeed, in the patient group, the thresholds with visual cueing actually seem a bit lower than without cueing, although this difference is not significant.

Even though cueing may decrease short-term fluctuation and may improve threshold slightly for normal subjects, it is questionable whether audio or visual cueing as presented in this study would be helpful in a clinical setting. Not only were the trends not significant, but they were even less evident in the patient population After all, it is mostly patients that threshold testing is designed to test, not normal subjects

The most disturbing result is the significant increase in the fixation loss rate in normals and slightly in patients. The increase in fixation loss rate will cause more cued fields to be regarded as unreliable or questionable

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Perimetric fatigue and its reduction using strategies to improve vigilance

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Abstract

Purpose: Quantification of the perimetric fatigue effect and its reduction using strategies designed to improve vigilance

Methods: Twenty-one normal subjects (mean age 57 yr) performed routine automated perimetry using program 30-2 of the HFA 630. Seven sessions were undertaken including a training session and a baseline test The other five sessions represented different strategies intended to improve vigilance and included visual and auditory cues, enforced rests and encouragement The study employed a simple randomized cross-over design with the order of eye examination randomly assigned and maintained for each session A repeated measures ANCOVA was performed with eye sequence, stage and strategy as separate within-subject factors

Results: There was a significant effect for eye sequence and stage for all strategies but *no* effect for strategy itself

Conclusions: The fatigue effect dominated all attempted strategies to maintain a singular level of performance throughout the examination period in a trained, normal, elderly population

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Fastpac error is within the long-term fluctuation of standard Humphrey threshold visual field testing

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Abstract

The Fastpac strategy of visual field assessment using the Humphrey Field Analyzer was compared to a series of field examinations using the standard 4-2 dB threshold strategy Sixty-one eyes of 37 patients with ocular hypertension or stable glaucoma were examined. The Fastpac results are very likely to fall within the long-term fluctuation of the standard 4-2 dB algorithm Fastpac underestimates the mean deviation and the corrected pattern standard deviation but overestimates the short-term fluctuation We postulate that these differences may be within clinically acceptable limits and that Fastpac is a valid alternative to the standard 4-2 dB strategy in all but a few specific clinical situations

Introduction

Automated perimetry was introduced to provide accurate objective visual field assessment by standardizing stimulus conditions and test procedures

Standard visual field analysis using the Humphrey Field Analyzer (HFA) is commonly performed utilizing the standard 4-2 dB strategy. The Fastpack strategy is a recently introduced method of analysis designed to decrease the time taken for the field examination by utilizing a single 3 dB crossing of threshold[1].

Previous studies comparing Fastpac to the standard 4-2 dB strategy have shown the advantage of Fastpac in decreasing the examination time but have shown conflicting results regarding Fastpac's ability to correctly estimate the mean deviation (MD), corrected pattern standard deviation (CPSD) and the intratest variation (short-term fluctuation SF) Some of these studies[2,4,7] were performed by repeating the strategies on the same day or within a few days of each other and compared a single examination using the standard strategy with a single examination using the Fastpac strategy. However, it was felt that in assessing the accuracy of Fastpac, comparison with a single 4-2 dB examination may not provide a valid conclusion as inter-test variation (long-term fluctuation) may contaminate any difference between the two strategies

Long-term fluctuation is defined as the variation in threshold measurements over a period of time after the variation due to repeated measurements at a given time has been removed[2]. Alternatively it can be defined as the reversible variation in threshold measurements over two or more examinations exclusive of reproducible deterioration or improvement and exclusive of identifiable artefacts[5]. The results of automated perimetry are contaminated by the presence of the long-term fluctuation which confounds the accurate quantitative comparison of serial visual fields and makes the identification of genuine field change difficult

The aim of this study was to assess the accuracy of Fastpac in comparison to a series of fields performed over a period of years with the standard 4-2 dB strategy and to estimate the

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likelihood of a Fastpac result falling within the long-term fluctuation of a particular Statpac series

Patients and methods

The study group consisted of 61 eyes of 37 patients (22 males and 15 females) with an average age of 60 years. Thirty-seven eyes were diagnosed as having ocular hypertension (raised intraocular pressure, normal visual fields and normal optic disks) and 24 eyes were considered to have stable glaucoma with non-progressive field loss and were on treatment for raised intraocular pressure. All patients were attending the glaucoma clinic and had undergone at least three successive 4-2 dB threshold examinations using program 24-2 over a period of three to five years. Each patient then underwent a Fastpac examination followed after a period of months by a further examination with the standard strategy

In all, 323 visual fields were assessed with particular reference to the mean deviation, corrected pattern standard deviation and short-term fluctuation

The stable glaucoma group was further subdivided according to the severity of visual field loss into those with more severe field loss *i e* , an MD of greater than 4.30 dB or a CPSD of greater than 4.00 dB and those with less severe field loss *i.e* , an MD less than 4.30 dB or a CPSD less than 4.00 dB

Statistical analysis

A paired t test was performed on the results obtained from the examinations.

The Fastpac results were scored depending on whether the result fell above the maximum standard strategy result (score +1), between the maximum and minimum standard strategy result (score 0) or below the minimum standard strategy result (score −1). This would enable an estimation of the likelihood of the Fastpac result falling within the long-term fluctuation of the standard strategy series.

The extent of agreement between the two strategies was measured to enable an estimation of the likelihood that Fastpac could replace the standard strategy in visual field assessment[6]. The results of field analysis using these two strategies are unlikely to agree exactly but the measure of agreement enables a decision about the clinical acceptability of Fastpac.

Results

The results of the comparison of the study parameters in both Statpac and Fastpac are shown graphically in Figures 1–4, and tabulated in Tables 1–4

Fastpac underestimated the MD and CPSD of the standard strategy in all groups except that with more severe visual field loss. This difference was statistically significant in all cases ($p < 0.005$) except for the MD of the less severe field loss group

SF was greater with Fastpac in all groups, being statistically significant in all but the less severe field loss group

Examination time was decreased in all groups with a 33% decrease in the more severe visual field loss category, a 35% decrease in the stable glaucoma group overall, a 38% in the less severe field loss group and a 42% decrease in the ocular hypertensive group.

The likelihood of the Fastpac result falling within the long-term fluctuation of the standard strategy is shown in Table 5. In all cases the Fastpac result is very likely to fall within the long-term fluctuation with the greatest likelihood of 84%, in the MD group of the stable glaucoma group.

Table 6 shows the assessment of the limits of agreement of the Fastpac result compared to the standard strategy result The figures show by how much the Fastpac indices results vary around the indices for the standard strategy.

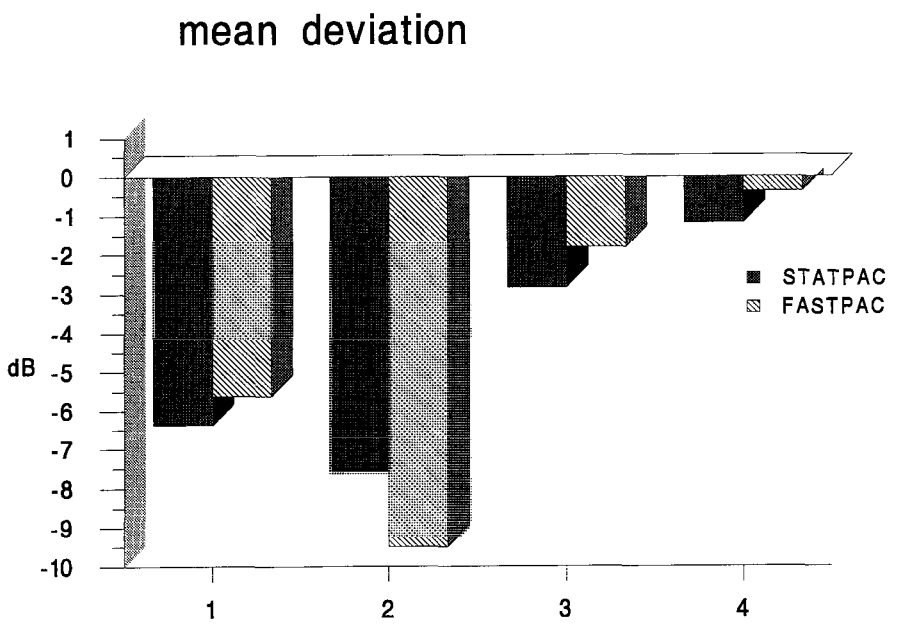

Fig. 1 Standard strategy (Statpac) and Fastpac mean deviation. 1 stable glaucoma; 2. more severe field loss; 3. less severe field loss; 4 OHT

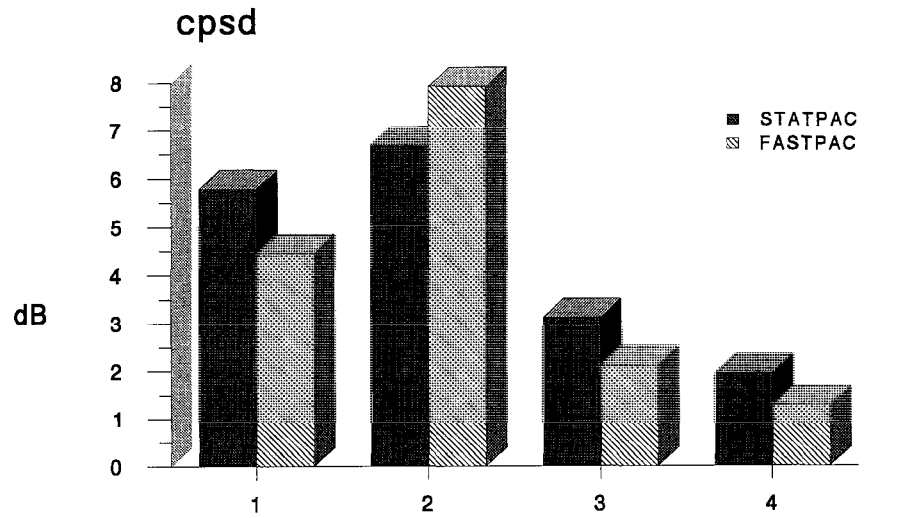

Fig 2. Standard strategy (Statpac) and Fastpac corrected pattern standard deviation 1. stable glaucoma; 2. more severe field loss; 3 less severe field loss; 4. OHT

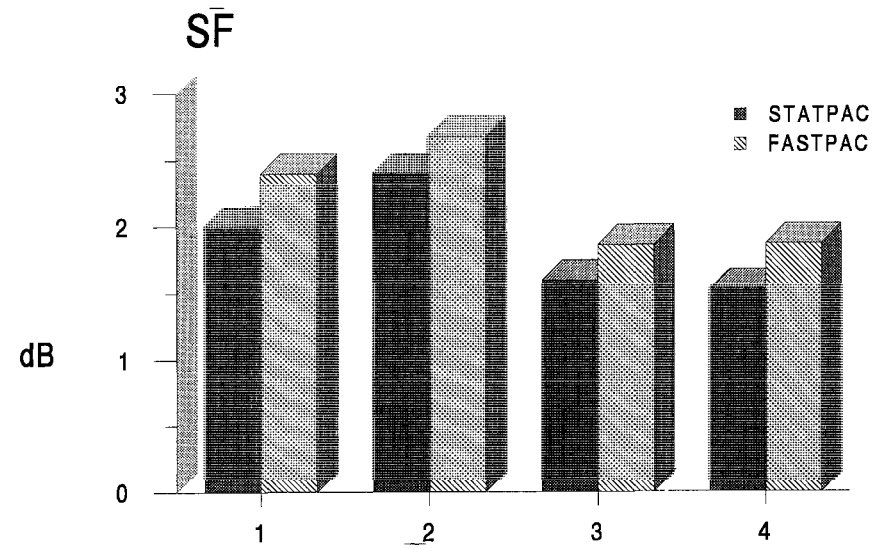

Fig. 3 Standard strategy (Statpac) and Fastpac short-term fluctuation 1 stable glaucoma; 2. more severe field loss; 3 less severe field loss; 4. OHT.

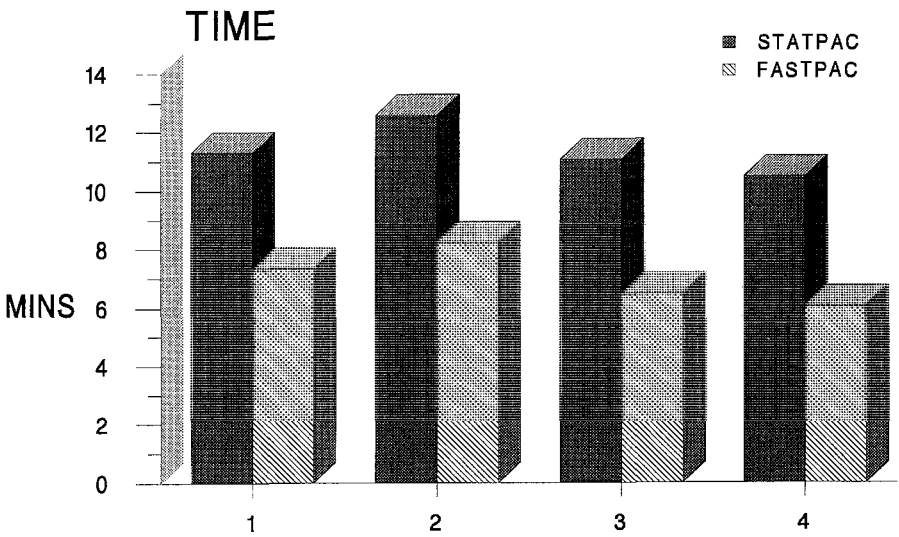

Fig 4 Standard strategy (Statpac) and Fastpac: examination time 1 stable glaucoma; 2. more severe field loss; 3 less severe field loss; 4 OHT

Discussion

The Fastpac strategy presents the stimuli in 3 dB steps and uses a single threshold crossing. Thus the overall examination time decreases, which by reducing the effect of patient fatigue offers the advantage of a quicker visual field assessment However this altered examination technique has been shown to lead to differences in the results obtained for MD and SF when compared to the standard examination technique.

Previous studies comparing the two algorithms performed the two tests either on the same day or within a short period of time of each other and did not consider the effect of inter-test

Table 1 Stable glaucoma Standard (Std) algorithm and Fastpac (FP) visual field indices and examination time (mean values from 24 eyes in dB)

	Std	*(SD)*	*FP*	*(SD)*
MD	–6 37	(4 91)	–5 63	(4 96)
CPSD	5 78	(2 94)	4 45	(3 53)
SF	2 00	(2 17)	2 40	(1 00)
Time (min)	11 31	(6 50)	7 34	(1 42)

MD: mean deviation; CPSD: corrected pattern standard deviation; SF: short-term fluctuation; SD: standard deviation

Table 2 More severe field defect. Standard (Std) algorithm and Fastpac (FP) visual field indices and examination time for the more severe field loss category (mean values from 18 eyes in dB)

	Std	*(SD)*	*FP*	*(SD)*
MD	–7 59	(5.25)	–9 5	(5 59)
CPSD	6 68	(2 95)	7 93	(3 98)
SF	2 40	(0 48)	2 68	(1 24)
Time (min)	12 59	(1.37)	8 25	(1 42)

MD: mean deviation; CPSD: corrected pattern standard deviation; SF: short-term fluctuation; SD: standard deviation

Table 3 Less severe field defect. Standard (Std) algorithm and Fastpac (FP) visual field indices and examination time for the less severe field defect category (mean values from 6 eyes in dB)

	Std	*(SD)*	*FP*	*(SD)*
MD	–2 84	(1.42)	–1 82	(1 41)
CPSD	3 12	(0 84)	2 12	(0.77)
SF	1 60	(0 29)	1 86	(0 35)
Time (min)	11 06	(1.28)	6 48	(1 03)

MD: mean deviation; CPSD: corrected pattern standard deviation; SF: short-term fluctuation; SD: standard deviation

variation on the results obtained. Flanagan *et al.*[3] described results similar to ours showing that Fastpac underestimates the MD and CPSD but overestimates the SF. O'Brien *et al* [4] again found the MD and CPSD to be underestimated but found no statistically significant difference in the SF. Iwase *et al.*[7], however, found Fastpac to overestimate MD and SF, CPSD did not differ significantly between the two strategies. All these studies were in agreement in that the overall examination time was decreased by approximately 35%. Our study is unique in that the two strategies were compared after taking into account the long-term fluctuation of the standard strategy.

Long-term fluctuation occurs because the physiological state of the visual system is not static and undergoes a continuous variation from one day to the next The long-term fluctuation has two components, a homogeneous component in which there is a uniform change in threshold at all locations and a heterogeneous component when the amount of threshold change varies between locations[8]. Long-term fluctuation has been shown to be greater in glaucoma patients and glaucoma suspects as compared to the normal population[9].

We assumed that in our two groups any change in threshold over the time period of the test was due to long-term fluctuation in view of the diagnoses of the study groups. The effect of a learning curve could also be excluded as all the patients had previous experience of field analysis.

Table 4 OHT Standard (Std) algorithm and Fastpac (FP) visual field indices for the ocular hypertensive group (mean values from 37 eyes in dB)

	Std	*(SD)*	*FP*	*(SD)*
MD	−1 17	(0 88)	−0.37	(0.89)
CPSD	1 94	(0 95)	1 28	(1 35)
SF	1 53	(2.32)	1 87	(0.55)
Time (min)	10 48	(0 92)	6 08	(0.93)

MD: mean deviation; CPSD: corrected pattern standard deviation; SF: short-term fluctuation; SD: standard deviation

Table 5. Percentage likelihood of Fastpac falling within long-term fluctuation of the standard strategy

Stable glaucoma		*OHT*	
MD	84%	MD	46%
CPSD	63%	CPSD	65%
SF	66%	SF	51%

MD: mean deviation; CPSD: corrected pattern standard deviation; SF: short-term fluctuation

Table 6 Assessment of the extent of agreement between Fastpac and the standard strategy showing the variation of Fastpac around the standard strategy

Stable glaucoma		*OHT*	
MD	2 38 <Std> 3 98	MD	2.38 <Std> 3.98
CPSD	2.1 <Std> 3.35	CPSD	2.06 <Std> 4 50
SF	1 96 <Std> 2 65	SF	2 8 <Std> 2.35

MD: mean deviation; CPSD: corrected pattern standard deviation; SF: short-term fluctuation

We have shown that the results of the Fastpac analysis when compared to a series of standard examinations give similar differences to those of Flanagan *et al* [3] and O'Brien *et al* [4]. However, when considering the long-term fluctuation in a series of standard strategy fields these differences between the two strategies fall within the variation of the indices due to long-term fluctuation. Thus we feel that it is incorrect for other studies[3,4] to suggest that Fastpac is a less accurate method of visual field analysis, as the differences these studies show may also have occurred due to long-term fluctuation. We feel that in most clinical situations of visual field testing the 40% time saving in performing Fastpac is a considerable advantage. Patient acceptability is high with Fastpac and a greater number of tests may be performed with the Humphrey Field Analyser. If absolute data are required such as in the precise quantification of early field loss or if the visual field results are part of an ongoing trial, then the standard strategy would be preferred as it is the accepted standard and therefore comparable with other studies.

Further studies using Fastpac may determine if the lessening of the patient fatigue with the shorter test time leads to a more accurate test in patients who would be fatigued using the standard strategy.

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Evaluation of the repeatability of Fastpac in glaucoma

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Abstract

Purpose: To evaluate the repeatability of Fastpac in a glaucomatous population

Method: Sixty glaucoma patients (mean age 66 9 yr) with repeatable glaucomatous visual field abnormality and previous experience in automated perimetry were examined on three separate occasions, two weeks apart, with both standard full threshold and Fastpac strategies using program 30-2 of the HFA 630 Examination strategy was randomized across the sample and maintained at each session

Results: Concordant with previous studies there was a small decrease in MD, PSD and CPSD, but an increase in the SF when Fastpac was used There was a small increase in the FN and FP catch trials along with the expected reduction in examination time and number of questions asked However, there was a remarkable similarity between the repeatability of the two strategies When considering the 95% confidence limits for change the resulting limits were identical

Conclusions: In spite of the increased intra-test variance Fastpac was as repeatable as the standard strategy for threshold estimation in an elderly, glaucomatous population This was considered mainly due to a reduction in fatigue

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The influence of the stimulus duration on perimetric thresholds in the central 30° visual field

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Abstract

The authors studied the influence of stimulus duration on perimetric thresholds in the central 30° visual field in normal subjects and early glaucoma patients using the Octopus 1-2-3 and its remote software package We developed programs on an IBM personal computer in order to measure differential light sensitivity using various stimulus durations First, as preliminary experiments, we measured the differential light sensitivity of the upper nasal profile along the 135° meridian in two normal subjects using stimulus durations of 5, 10, 20, 50, 100, 200, 500, 1000, 2000 and 3000 msec and target sizes of –2, –1, 0, 1, 2, 3, 4 and 5. Studies were then made of temporal and spatial summation by analyzing the threshold-duration curves and the threshold-area curves Secondly, the same test points of the Octopus program No 38 were measured using stimulus durations of 10, 50, 100 and 500 msec and target size 3 in 39 eyes of 39 normal subjects and 37 eyes of 27 glaucoma patients The normal critical time of temporal summation was almost the same (approximately 100 msec) across the central 30° visual field, while the normal critical area of spatial summation became larger toward the periphery The use of stimulus durations of 10, 50, 100 and 500 msec in normal subjects caused little changes in short-term fluctuation, interindividual variance of sensitivity and the slope of the profile of the visual field It was suggested that the use of stimulus durations shorter than the critical time was a sensitive and useful method for detecting early glaucomatous visual field defects

Introduction

The stimulus duration which is related to temporal summation[1] is one of the most important conditions of static perimetry In automated static perimeters that are currently available, the stimulus durations have been set to be equal to or slightly longer than the normal critical time of temporal summation It is the purpose of this paper to reappraise the influence of very short and long stimulus durations on static perimetric thresholds in the central 30° visual field.

Subjects and methods

Perimeter

Using the Octopus 1-2-3 and its remote software package, we developed new programs on an IBM personal computer in order to measure differential light sensitivity using stimulus durations of 5, 10, 20, 50, 100, 200, 500, 1000, 2000 and 3000 msec. In addition, we modified

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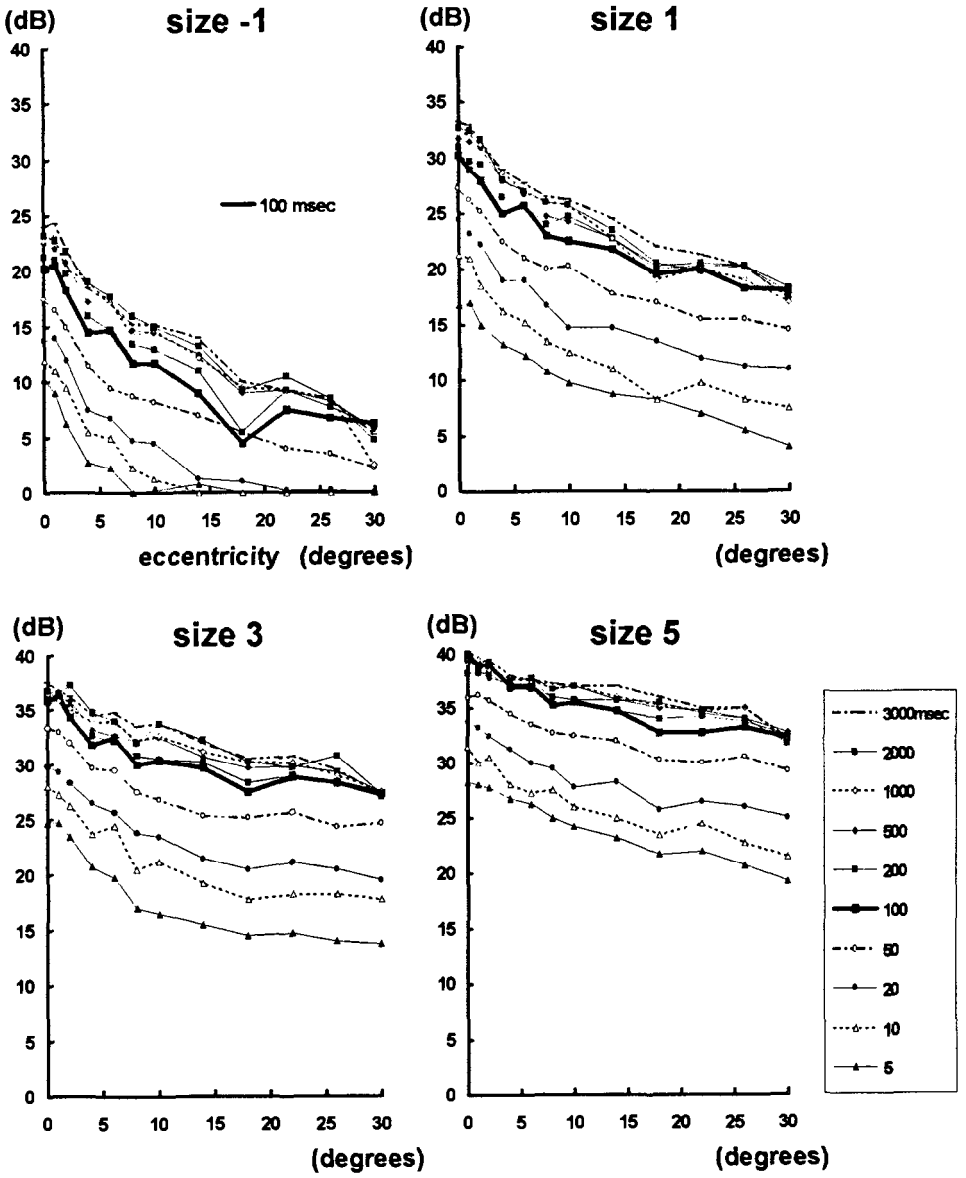

Fig 1 Profiles in a 29-year-old normal male of the central 30° visual field along the 135° meridian for ten stimulus durations and four stimulus sizes

the Octopus 1-2-3 in our laboratory using custom filters to produce target sizes of –2, –1, 0, 1, 2, 3, 4 and 5.

Preliminary experiments

We measured the values of differential light sensitivity of the upper nasal profile along the 135° meridian of the right eye in two normal subjects. Eccentricities of the test points were 0, 1, 2, 4, 6, 8, 10, 14, 18, 22, 26 and 30°. Using the above-mentioned ten stimulus durations and

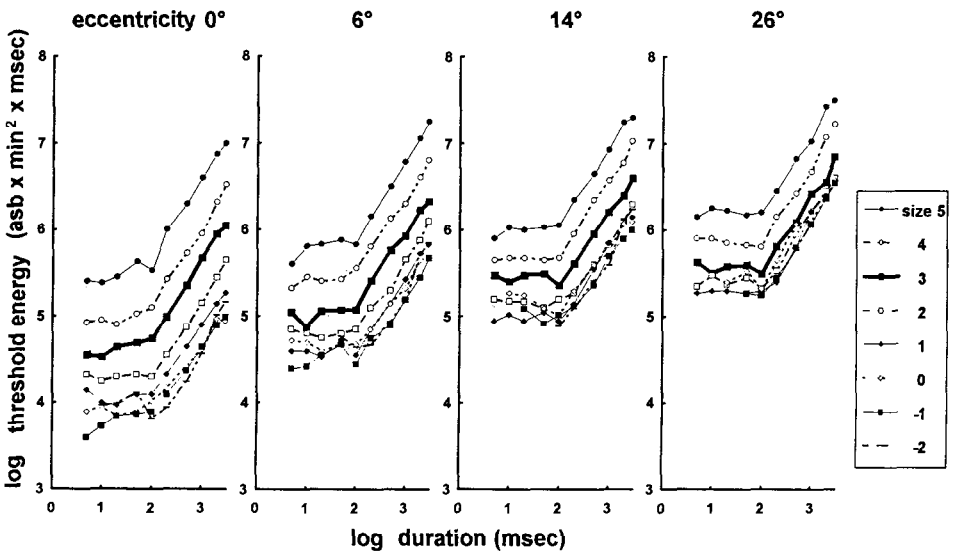

Fig 2. Threshold-duration curves for eccentricities of 0, 6, 14 and 26° for each target size of the same subject as Figure 1.

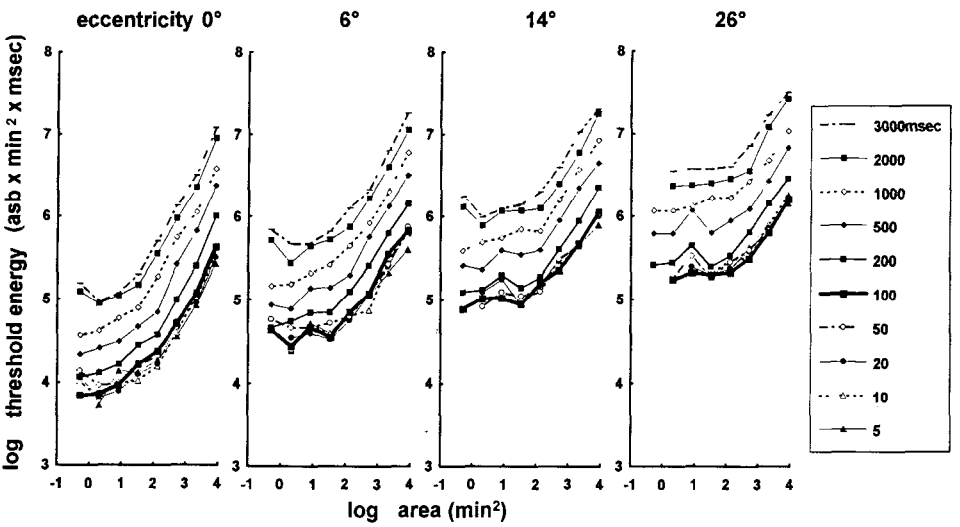

Fig 3. Threshold-area curves for eccentricities of 0, 6, 14 and 26° for each stimulus duration of the same subject as Figure 1

eight target sizes, we determined perimetric thresholds of the 12 test points randomly in steps of 1 dB using a bracketing strategy. We calculated the arithmetic mean of the thresholds obtained from four thresholds for each test point in each subject. Temporal summation and spatial summation were then studied by analyzing the threshold-duration curves and the threshold-area curves

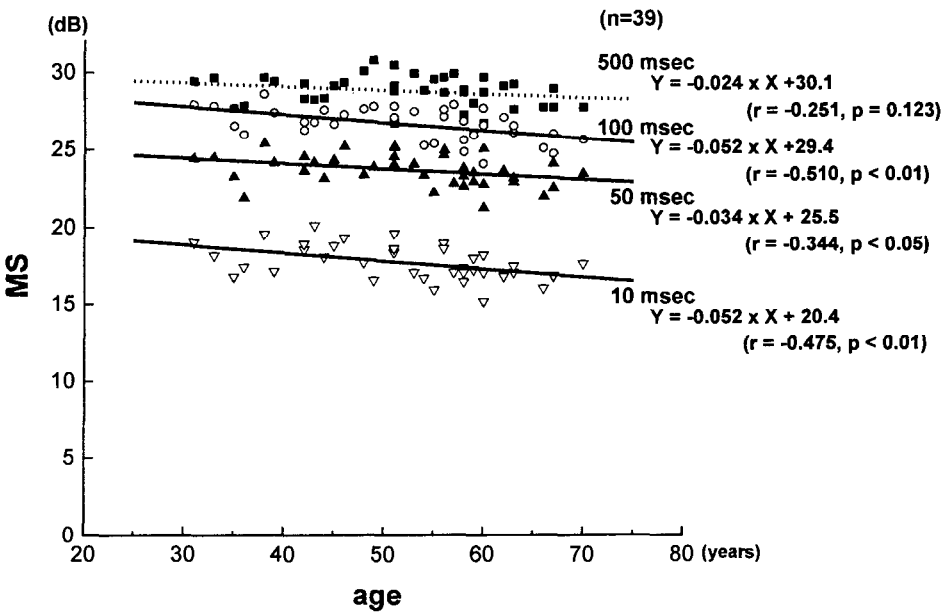

Fig 4. The relationship between the age and mean sensitivity (MS) for stimulus durations of 10, 50, 100 and 500 msec in normal subjects

Clinical experiments using stimulus durations of 10, 50, 100 and 500 msec

Using stimulus durations of 10, 50, 100 and 500 msec and target size 3, we measured the differential light sensitivity at 77 test points in the central 30° visual field of 39 eyes of 39 Japanese normal subjects (31–70 years of age). The arrangement of these test points was almost the same as that of the Octopus program No. 38. Differential thresholds of test points on both the 45°–225° and 135°–315° meridians were measured twice randomly in order to calculate the short-term fluctuation. All normal subjects in this study had corrected vision of 20/20 or better. The refractive error was within 3 0 D of spherical error and within 2.0 D of cylindrical error. The intraocular pressures were lower than 21 mmHg. The optical media and fundi were normal The subjects were free of systemic diseases which were likely to affect their visual functions and had no family history of glaucoma. The pupil size was greater than 3 mm. In addition, the experiment was undertaken on 37 eyes of 27 early glaucoma patients. To analyze the threshold values, two test points corresponding to the right or left blind spot were excluded.

Results

Preliminary experiments

Figure 1 shows the profiles of the central 30° visual field in a 29-year-old normal male for the ten stimulus durations and target sizes of –1, 1, 3 and 5. The thickest solid line in each graph indicates the profile for 100 msec. The profiles for each stimulus duration were nearly parallel to each other. In addition, when the duration was shorter than 100 msec, the dynamic range became smaller as the stimulus durations decreased. The profiles for the smaller target sizes were steeper for all of the stimulus durations we used. The dynamic range became smaller as target size decreased

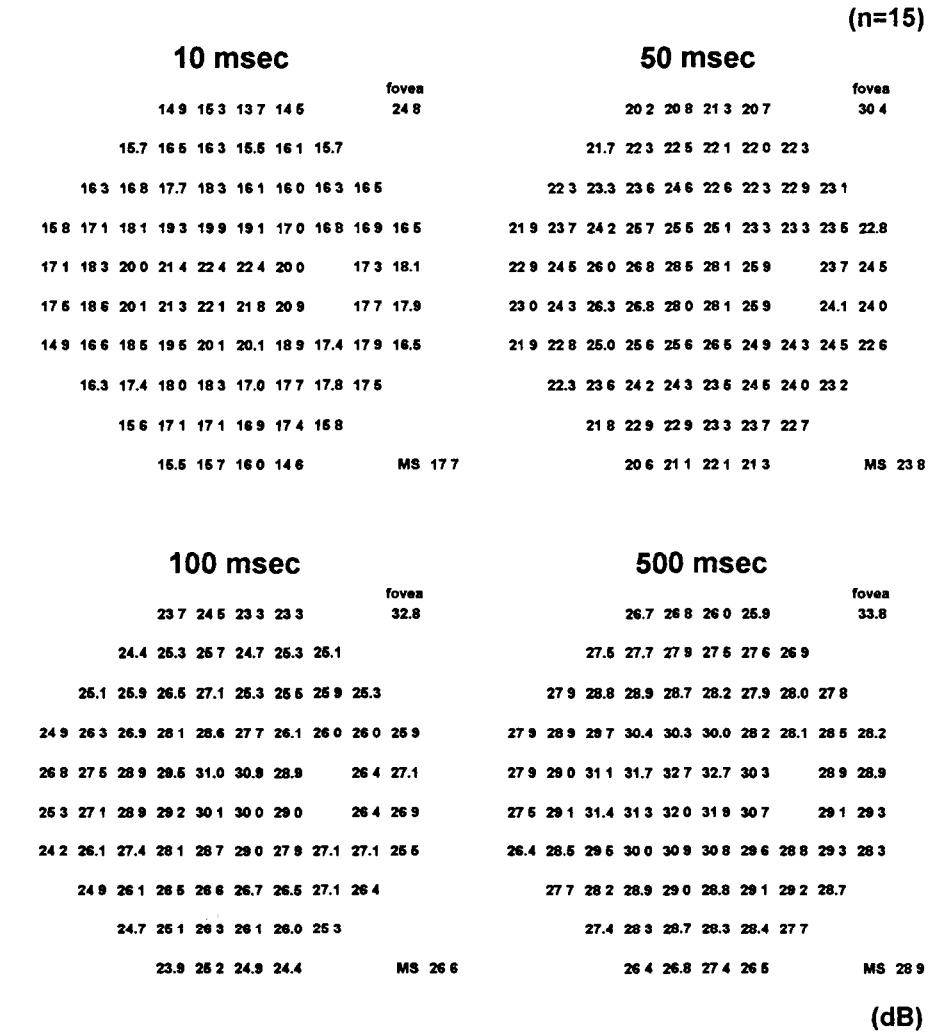

Fig. 5 Mean values of sensitivity of normal subjects in their 50s at each test point for stimulus durations of 10, 50, 100 and 500 msec

Figure 2 shows the relationship between the threshold energy and the stimulus duration at different eccentricities for each target size. Here, the threshold energy is the product of target luminance, target area and stimulus duration At shorter stimulus durations, the threshold energy remained unchanged, indicating that temporal summation was complete. The critical time of temporal summation was almost the same, that is, approximately 100 msec for each eccentricity. The relationship between threshold energy and target area indicated that the critical area of spatial summation became larger toward the periphery (Fig. 3).

Measurement of the central 30° visual field with stimulus durations of 10, 50, 100 and 500 msec in normal subjects

False-negative responses and false-positive responses in all examinations of all normal subjects were less than 15% In addition, the short-term fluctuation of all examinations was less than 2.0 dB.

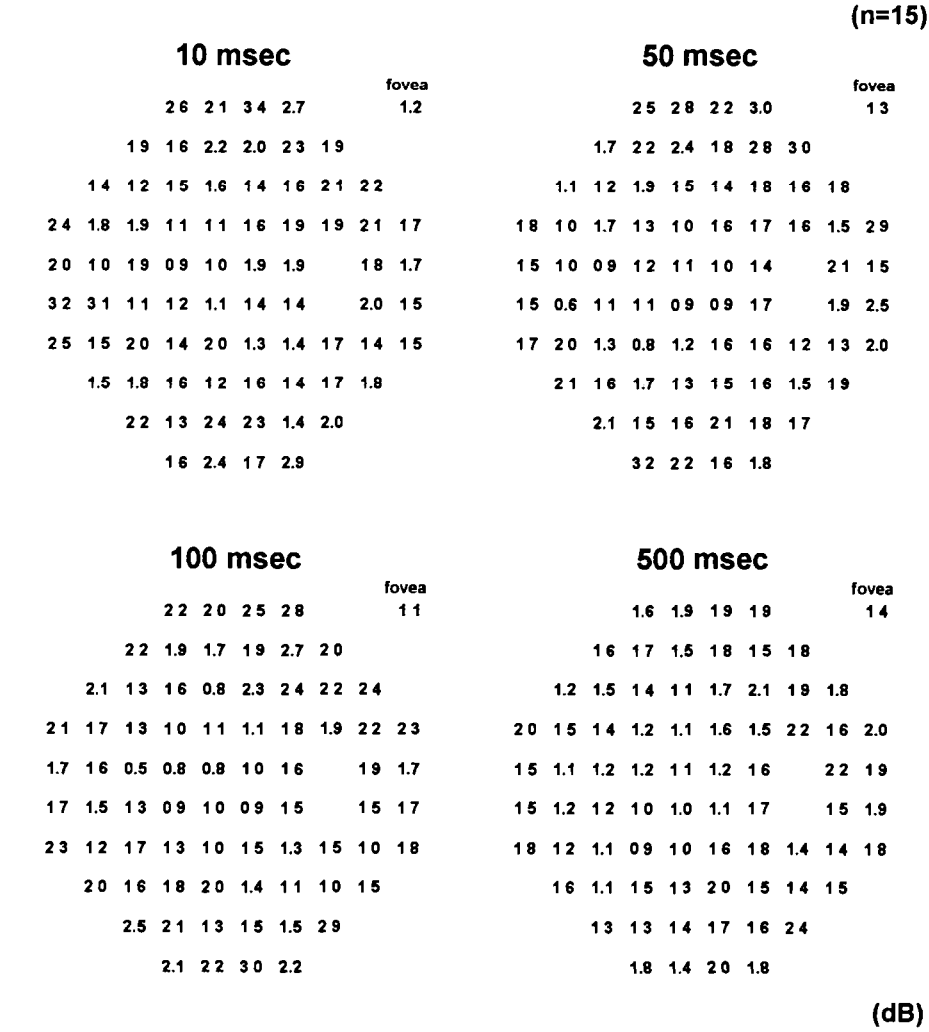

Fig 6. Standard deviation of differential light sensitivity of normal subjects in their 50s for each test point for stimulus durations of 10, 50, 100 and 500 msec

Figure 4 shows the relationship between the age and the mean sensitivity (MS) of individual eyes for each stimulus duration. MS for 500 msec did not decrease with age significantly. The slopes of the regression lines for 100 msec and 10 msec were almost the same.

We then calculated the arithmetic mean and standard deviation of the sensitivity for each test point in each age group. Figure 5 shows the mean values of sensitivity for each stimulus duration in 15 normal subjects in their 50s. We also calculated the difference between the mean values of sensitivity for 100 msec and those for the other stimulus durations for each test point. These differences of the values of sensitivity were almost the same throughout the central 30° visual field Therefore, we could confirm that the profiles for each stimulus duration were nearly parallel to each other along all meridians Figure 6 shows the standard deviation of the values of differential light sensitivity at each test point for each stimulus duration in the above-mentioned 15 normal subjects in their 50s. The use of these stimulus durations caused little change in the standard deviation of the thresholds.

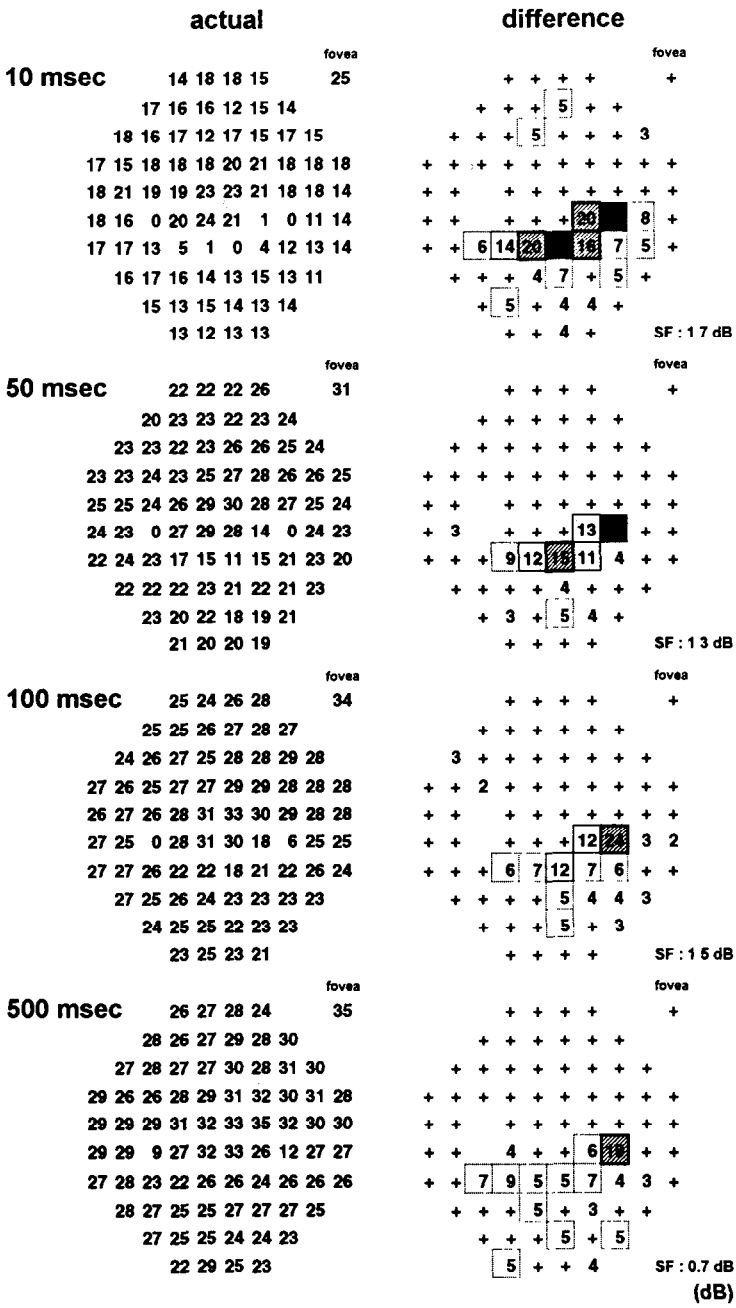

Fig 7 Actual value tables and difference tables for stimulus durations of 10, 50, 100 and 500 msec in the left eye of an early glaucoma patient.

A clinical case of early glaucoma

The case was a 44-year-old female with primary open-angle glaucoma. Figure 7 shows actual value tables and difference tables of her left eye for stimulus durations of 10, 50, 100 and 500 msec. If an actual value was lower than the mean value of sensitivity minus two times the standard deviation of the normal value, the difference value was shown in the difference table. If a difference value was more than 15 dB, it was shown as a stripe-hatched square If an actual value was 0 dB, it was shown as a black square. The patient had three stripe-hatched squares and two black squares in the lower field in the difference table for 10 msec. On the other hand, there was only one stripe-hatched square in the difference tables for 100 and 500 msec.

Discussion

In our preliminary experiments, we were able to confirm several previously reported characteristics of temporal summation in normal subjects. The critical time of temporal summation was almost the same (approximately 100 msec) throughout the central 30° visual field, while the critical area of spatial summation became larger toward the periphery.

Previous studies have suggested that the examination of temporal summation is less useful for detecting disturbances of visual function than static perimetry[2,3]. In addition the static perimetric thresholds in glaucomatous relative scotoma are likely to fluctuate more than those in unaffected area[4]. Therefore, in clinical experiments, we did not attempt to study temporal summation itself as performed in the preliminary experiments

We used four stimulus durations including shorter durations and an obviously longer duration than the normal critical time of temporal summation. It may be possible that the rate of false responses or fluctuation of perimetric thresholds or tiredness of the examinee will increase if we use very short stimulus durations. However, the use of stimulus durations of 10, 50, 100 and 500 msec in normal subjects caused little change in the rate of false responses, short-term fluctuation, and interindividual variance of sensitivity. Therefore, it is suggested that the stimulus durations used in this study may be clinically valid if used with care

Studies of pathological cases suggest that the careful use of stimulus durations shorter than the critical time is a sensitive and useful method for detecting early glaucomatous visual field defects, even though the dynamic range of the threshold is narrow However, a stimulus duration shorter than 10 msec presented with the Octopus 1-2-3 leads to a reduction in the dynamic range which may be too narrow to detect pathological visual field defects.

Acknowledgment

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Fixation accuracy of patients with glaucoma during full threshold perimetry

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Abstract

Purpose: A significant problem in perimetry is the enhanced variability of visual field in patients with and suspected of having glaucoma One possible source of this problem is poor fixation The purpose of this study was to determine the accuracy of fixation in a population of glaucoma patients during a full threshold visual field examination

Methods: Results were collected from 16 clinically stable glaucoma patients all of whom exhibited a definitive nerve fiber bundle defect Eye position was monitored with a video-based system which captured a magnified image of the eye during each stimulus presentation The locations of the first and forth Purkinje images of a collimated infrared source were used to give a measure of eye position which was accurate to within 10 min of arc in both the horizontal and vertical meridians.

Results: Fixation accuracy was generally very good although there were significant differences from one patient to another Comparisons with the Heijl-Krakau index indicate that patients with very poor fixation may be inadvertently classed as good fixators with this index and that patients with good fixation may have significant number of reported errors The results found no relationship between the extent of visual field loss and fixation accuracy and there was little evidence to show a change in accuracy of fixation with course of the examination

Introduction

In automatic static perimetry the differential light sensitivity is normally measured with a bracketing strategy. While repeat measures of this threshold show a small amount of variability in normal patients, in patients with glaucoma the variability is greatly enhanced[1,2] The extent of this increase in variability, which is particularly noticeable at the edge of defects[3,4] is really quite staggering. Heijl *et al* [5] have reported that patients with an 8–18 dB loss will show variability (95% confidence limits) which exceeds the measurement range of the Humphrey Visual Field Analyzer (0–40 dB) This increase in variability makes it difficult to differentiate between non-significant random variations in the visual field and true progression It often requires several visual field results, taken over a long period of time, before a significant trend can be detected and appropriate changes in treatment made[5,6]

The causes of this increased variability are as yet unknown although various researchers have suggested that it is the result of reduced number of nerve fibers, increased susceptibility to fatigue and poor fixation control[7,8,9].

The isolated scotomas found in the visual fields of patients with glaucoma often have steep sensitivity profiles and even small inaccuracies of fixation can result in a stimulus falling into or climbing out of one of these defects. Inaccuracies of fixation can, therefore, in the presence

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of steep sensitivity gradients result in an increase in test/retest variability. A relationship between the number of edges in the visual field and test/retest variability has already been demonstrated[9] and the effects of instability in normal experienced observers quantified[8].

Previous research into the accuracy of fixation during perimetry has either used relatively insensitive, and often indirect, techniques of measuring fixation accuracy[10,11] or has used experienced observers rather than glaucoma patients[8,12,13] and continuously recorded fixation position rather than sampling it during the presentation time of the perimetric stimulus[8,12].

This study reports upon the fixation accuracy of a population of glaucoma patients during routine full threshold perimetry The eye movement recorded is accurate (10 min arc), non-invasive and linked to the perimeter in such a way that fixation accuracy can be measured during the presentation time of the perimetric stimuli.

Materials and methods

Patients

Results were collected from nine right and seven left eyes of 16 clinically stable glaucoma patients, ten male, six female, whose average age was 74.94 years (61–88) All exhibited a definitive nerve fiber bundle visual field defect, as detected by previous Octopus perimetry. This visual field loss ranged from small isolated paracentral scotoma, through single and multiple arcuate defects onto quadrantopic loss and altitudinal loss and finally one patient with only a small residual island of vision extending into the temporal hemi-field. The inclusion criteria were, an acuity of better than 6/18 (62.5% of eyes had an acuity better than or equal to 6/9), the absence of any other known ocular, neurologic, or systemic disease likely to affect the visual field and relatively clear media with an intact crystalline lens.

Eye position recorder

Eye position was monitored with a video-based system which captured a highly magnified image of the eye during each stimulus presentation. The location of the first and forth Purkinje images of a collimated infrared source extracted from each image and stored in a computer file. The relative positions of these two images was used to give a measure of eye position which was accurate to within 10 min of arc in both the horizontal and vertical meridians over a measuring range of ± 8 degrees. This technique of recording eye position was selected on the basis of it being non-invasive, accurate and relatively insensitive to translational eye movements[14].

A large dichromatic mirror placed in front of the patient's eye allowed the recorder's imaging path and the patient's viewing path to be separated. The patient having an uninterupted view of the visual field screen out to an eccentricity of 25 degrees in all meridians

Method

At the onset of each examination the patient performed a series of calibration movements to 4 LED targets placed 1 degree from the fixation target along the 0, 90, 180 and 270 degree meridians. The fixation target for perimetric testing was the same as that used in a standard Henson CFA3000, *i e* , a 2 mm white spot[15]

The patient underwent a full threshold visual field test[16,17] covering the central 24 degrees of the visual field on a 6 degree matrix decentered 3 degrees from the vertical and horizontal midlines Double determinations of the threshold were made at every test location (52 in all).

This examination included

- the standard Heijl-Krakau blind spot checking procedure for estimating fixation accuracy[11,12]
- measures of false positive and false negative rates.
- computation of the indices, mean defect, loss variance, fluctuation and corrected loss variance as described by Flammer *et al.*[18].

The status of the visual field test and the video signals were continuously monitored by the perimetrist who, depending upon the status of the patient, included rest periods as per a standard visual field examination

Results and discussion

Each visual field examination contained, on average, 528 stimulus presentations (range 300–596) and took, on average, 21.50 min to complete (range 11 41–26 20). Fixation position was measured every fourth presentation which resulted in an average of 136 measures (range 75–163) for each eye.

An example of the results from the first 50 samples of a typical subject are given in Figure 1 As can be seen from this figure the patient typically maintained fixation within 2 degrees of the target with occasional errors in excess of this, most of these larger errors being down and to the right

The results from all the patients, grouped according to the size of errors, are given in Figure 2 While most patients were able to maintain accurate fixation throughout the visual field examination, rarely being more than 1 degree away from the fixation point, others (GM, JA and AJ) are more than 1 degree away on over 50% of the presentations and, not infrequently, have errors in excess of 3 degrees The fixation accuracy of AJ was notably worse than the others and could not, seemingly, be improved despite continued requests by the perimetrist/researcher to maintain fixation and to keep the eye still

The relationship between the Heijl-Krakau (H-K) index of fixation accuracy and fixation errors is also given in Figure 2. This index generally reported very few fixation losses with eight patients having 0% and no patients exceeding the 20% cut-off criteria, frequently used in clinical ophthalmology, between reliable and unreliable patients.

Some patients with very good fixation had a H-K index greater than 0% This result can be explained on the basis of the accuracy of the blind spot location routine used at the onset of the examination. The spatial resolution of the perimeter is 3 degrees (the LEDs are located on a 3 degree square matrix) and it is highly likely that the established blind spot location did not always coincide with the center of the blind spot. In these cases a small fixation error in one direction could trigger a fixation loss while a similar error in the other direction would not The problems associated with locating the center of the blind spot have been highlighted by Sanabria *et al* [19] who used the term "pseudo-loss" to describe situations in which there is a high frequency of fixation losses in a patient who by all other measures seems to be very reliable.

Given that the average size of the blind spot is in the order of 5.5 × 7 5 degrees and that its location has been determined with reasonable accuracy, it is unlikely that small fixation errors (< 2 degrees) would result in positive responses to the H-K test The results of patients DA, LAW and RH who show perfect fixation accuracy on the H-K index but who have a fairly high number of small fixation errors (< 2 degrees) can be explained on this basis Similar conclusions were reached by Demirel and Vingrys[12] who reported a less than 20% chance of 2 degree errors being detected by the H-K sampling procedure.

Most studies of reliability indices[19–22] have reported much higher percentages of fixation losses than found in this study Two factors which might account for this disparity are 1) the patient selection procedures and 2) the nature of the examination.

While no conscious effort was made to select reliable patients for this study the inclusion criteria of good VA, lack of other pathology and mobility may have inadvertently selected the more able patients with potentially better fixation.

The nature of this study necessitated special examination procedures in which a highly trained and motivated clinician was responsible for all the data collection. This clinician was in attendance during the whole of the examination and was continually monitoring the data to see if there were any signs of fatigue and whether the patient needed a break There have been several reports of how the attentive presence of the perimetrist improves the quality of the perimetric data and the reduced number of fixation errors, as measured by the H-K index, may simply be a reflection of this

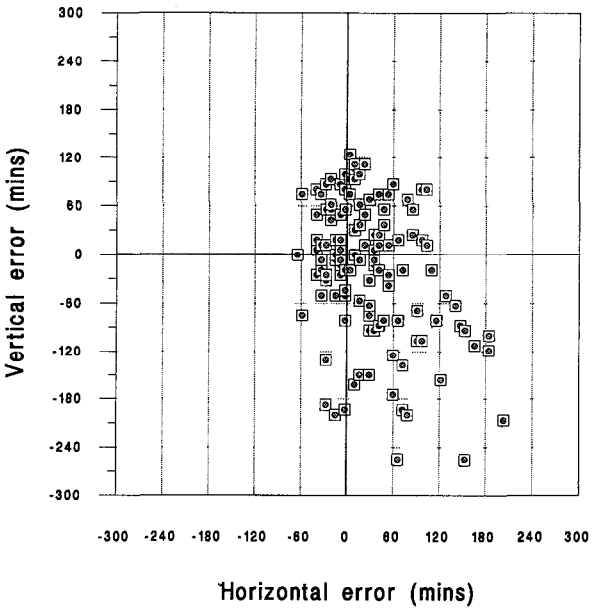

Fig 1 Results from a typical patient (LA) Each point represents the direction and extent of the fixation error during a single stimulus presentation.

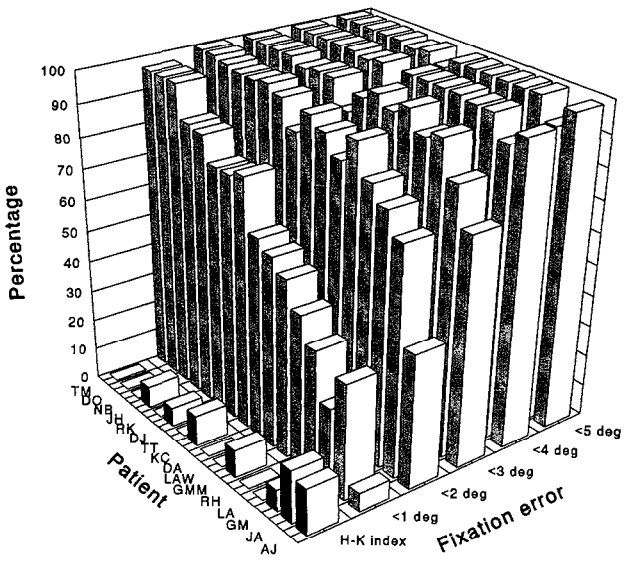

Fig 2. Frequency of fixation errors, grouped according to size, for each patient Also shown is the Heijl-Krakau index of fixation accuracy for each patient

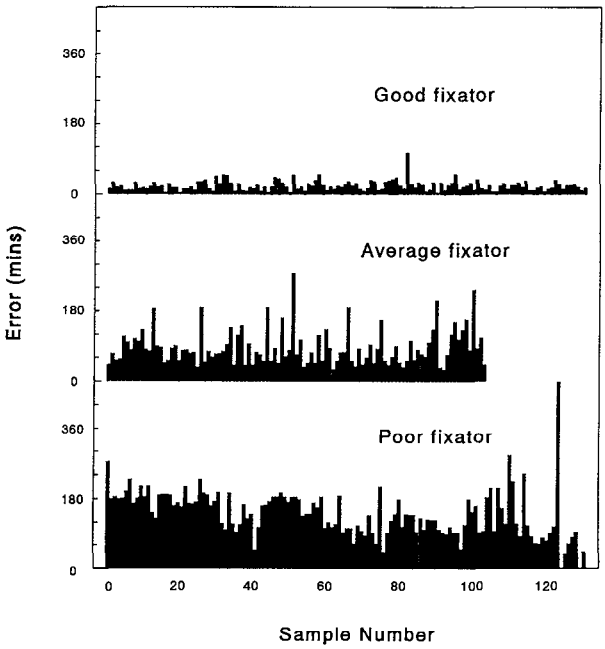

Fig 3 The amplitude of the fixation error at each sample time throughout the examination. The results from 3 patients, one good fixator, one average fixator and one poor fixator.

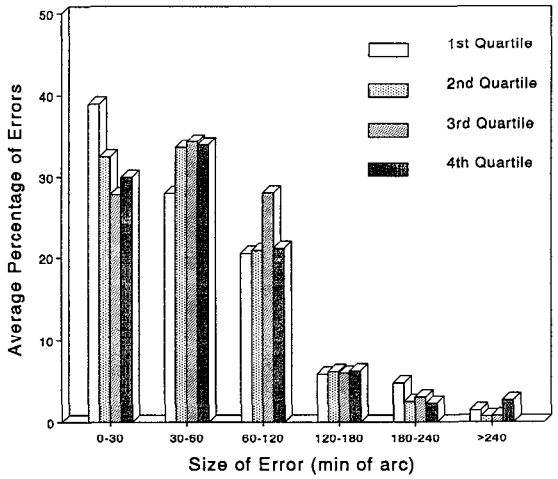

Fig 4 Distribution of fixation errors during each quartile of the examination. Averaged results from all 16 patients.

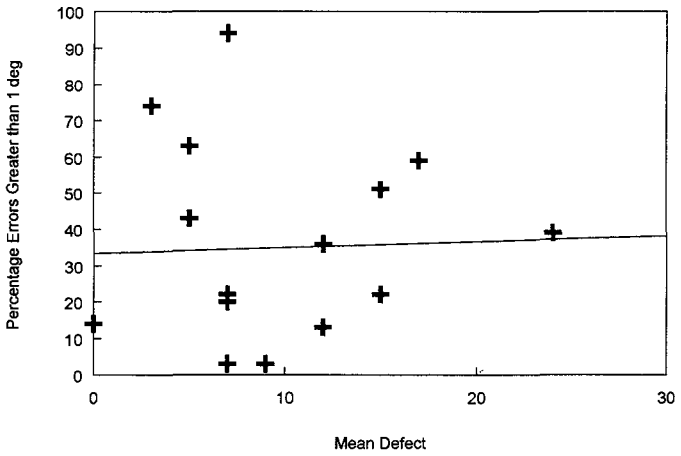

Fig 5 The relationship between the extent of field loss (mean defect) and fixation accuracy (percentage of fixation errors greater than 1 degree) The line through the data is the best fitting (least squares) regression line

Patient AJ whose fixation can only be described as very poor obtained an H-K index within the clinically accepted high reliability range. This patient was frequently more than 3 degrees away from the fixation target and more often than not more than 2 degrees away. Such a result indicates that the cut-off routinely used by clinicians (20%) is unlikely to detect all patients with poor fixation and should not be considered hypersensitive as suggested by Bickler-Bluth *et al* [21]

The amplitude of the fixation error vs time for three patients, one good fixator, one average fixator and one poor fixator, are given in Figure 3 This figure again highlights the differences between patients and also demonstrates that there was little evidence of an increase in the amplitude of errors with time. Fixation accuracy was sampled at every fourth stimulus presentation which, depending upon the selected rate of presentation, would be at intervals of between nine and 12 seconds

Any effect of fatigue upon fixation accuracy is further highlighted in Figure 4 where the average fixation error of all patients is calculated for each quartile. This figure reveals little, if any, increase in the amplitude of fixation errors throughout the period of the examination. Although there may be some evidence to indicate a small shift from the accurate fixation (< 30 min) to small errors (30–60 min) after the first quartile. When looking at these data it should be recalled that the duration of each examination varied significantly from one patient to another as did the number of presentations. It should also be recalled that rest periods were included when deemed necessary by the perimetrist.

The chosen sample included patients with both early and advanced visual field loss An analysis of the fixation accuracy vs the extent of loss, as quantified by the index mean defect (see Fig 5) revealed no significant relationship. The regression line (least squares) drawn on this figure has a small positive gradient and a correlation coefficient of only +0 03. There is, therefore, no evidence to support the hypothesis that patients with advanced peripheral field loss develop diffferent fixation patterns when undergoing visual field examination. Some support for such a hypothesis was given by the work of Katz *et al.*[22] who found that hypertensive and glaucomatous patients had worse reliability indices, and in particular more fixation losses, than normal patients.

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The control of blinking during pupil perimetry

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Abstract

Pupil perimetry requires that tested subjects refrain from blinking during presentation of the light stimulus and the ensuing pupillary contraction For this purpose, a sound can be generated before the appearance of each light stimulus, as a signal to the subject to blink immediately and then to keep his eyes open for a few seconds When performed with an illuminated background, however, the reopening of the eyes results in a transient pupillary contraction.

This study was undertaken to determine, under 3 asb background conditions, the minimal time lag required between the sound and the light stimuli to prevent superimposition of the pupillary contraction following reopening of the eyes on the contraction induced by the light stimulus

Seventeen normal subjects were tested, using an Octopus 1-2-3 automated perimeter, fitted with a pupillographic recording device Background intensity was 3 asb A 150-msec tone was presented at ten-second intervals Tested subjects were required to blink immediately on hearing the tone Pupillary recordings were averaged with respect to the time of tone presentation

The act of blinking following the tone resulted in a transient pupil contraction and redilation Changes in pupil diameter ranged from 0 01 to 0 33 mm (mean 0 12 mm), with a peak-time ranging from 1 04 to 1 99 sec (mean 1 54 sec) following the presentation of the tone The following redilation was completed from 1.02 to 2.96 sec (mean 2 18 sec) following the presentation of the tone

When performing pupil perimetry using the procedure described above, at least three seconds should elapse between the presentation of the tone and the light stimulus

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Test time and efficiency of the dynamic strategy in glaucoma perimetry

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The dynamic strategy is a perimetric measurement procedure using variable ("dynamic") luminance steps instead of constant steps[1]. These steps were derived from physiological data showing small threshold zones in visual field locations with high sensitivity and wide threshold zones in locations with low sensitivity[2] Based on a computer simulation, the optimal step size varies between 2 dB in the high sensitivity range and 10 dB in the low sensitivity range.

We examined 40 glaucoma patients with both the traditional (double reversal) and the dynamic strategy (single reversal) using a modified Octopus 1-2-3 Sixteen visual field locations were examined alternately with both strategies, three times each The order of the initial strategy was randomized.

The variance of the three measurements was calculated as a measure of reproducibility. The number of presented stimuli was recorded as a measure of test time. After eliminating starting points, absolute scotomata and fields showing progression, 255 measured locations were available for evalution

To compare both methods, we calculated the benefit/cost-ratio

Benefit	= reproducibility	= 1/variance
Cost	= time	= number of presentations
Benefit/cost	= 1/(variance * number of presentations)	

The variance of the three measurements depended on sensitivity It is shown in Table 1. In the normal sensitivity range, the dynamic strategy had a markedly lower variance For relative defects, the variance was higher using the dynamic method For low sensitivities, the dynamic strategy showed a lower sensitivity.

Reproducibility shown in Table 2 by definition indicated that the dynamic strategy was more reproducible in the high and low ranges and less reproducible in the medium ranges

The number of stimulus presentations per point is given in Table 3. It ranged from 2.09 to 2 50 using the dynamic strategy and was almost independent of sensitivity Using the traditional strategy, the number of stimulus presentations decreased with increasing sensitivity from 6.12 down to 4.20. More than half of the test time was saved using the dynamic strategy

Regarding Table 4 the benefit/cost ratio (reproducibility/number of presentations) of the dynamic strategy was higher in all sensitivity classes

The dynamic strategy shows comparable reproducibility, but markedly reduced test time after a single reversal. This finding is also valid for the range of slightly abnormal sensitivities which is important for the decision of normality of borderline fields This finding is in accordance with a former study[3].

The dynamic strategy is superior in normal and borderline fields In lower sensitivities, the dynamic strategy is less reproducible, but this disadvantage is balanced by immense savings in test time. However, regarding clearly damaged fields, the long-term fluctuation is more im-

*J Weber holds international patents on the dynamic strategy

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Table 1 Variances of the three measurements at the same test point

DLS (dB)	*Points*	*Variance Dynamic (dB^2)*	*Variance Traditional (dB^2)*	*Ratio of variances*
1–10	25	17.75	29 54	0 60
11–20	84	20 73	13 29	1 56
21–25	81	6 18	4 37	1 41
26–30	65	2 08	3 60	0 58

DLS = differential light sensitivity

Table 2 Reproducibilities of the three measurements at the same test point

DLS (dB)	*Points*	*Reproducibility Dynamic ($1/dB^2$)*	*Reproducibility Traditional ($1/dB^2$)*	*Ratio of reproducibility*
1–10	25	0.056	0 034	1.67
11–20	84	0 048	0.075	0.64
21–25	81	0 162	0.229	0 71
26–30	65	0 481	0 278	1 72

Table 3 Number of stimulus presentations (mean of three examinations) at particular test points

DLS (dB)	*Points*	*No presentations Dynamic*	*No presentations Traditional*	*Ratio of No presentations*
1–10	25	2.09	6 12	0 34
11–20	84	2 45	5 80	0.42
21–25	81	2 50	5 08	0 49
26–30	65	2 39	4.20	0 57

Table 4 Benefit/cost ratio of the measurement procedure for both strategies

DLS (dB)	*Points*	*Benefit/cost Dynamic*	*Benefit/cost Traditional*	*Ratio of benefit/cost*
1–10	25	0 02696	0 00553	4 87
11–20	84	0 01969	0 01297	1 52
21–25	81	0.06472	0.04505	1 44
26–30	65	0 20116	0 06614	3.04

portant than the reproducibility Whether the shorter test time provokes less fatigue than long-term fluctuation is yet unknown Preliminary results from another center indicate such a correlation

The dynamic strategy is a time-saving alternative in damaged fields. The effects of long-term follow-up are under investigation.

A complete article will be published elsewhere.

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Efficiency of the standard Octopus bracketing procedure compared to that of the "dynamic strategy" of Weber

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Abstract

Introduction: There is ample reason to strive for a shorter test without losing solid and reproducible information on the function of the eye Intuitively, a long test should render a more precise and reproducible result, but in clinical reality fatigue etc may yield just the opposite[1–3] There are two main ways to shorten visual field tests: An optimal distribution of test locations[4,5], and an optimal test strategy may be chosen Fastpac[6–8] and the "dynamic strategy" of Weber[9–12] are recent attempts to optimize strategies in perimetry

Purpose: To compare the standard Octopus strategy with the "dynamic strategy" of Weber in terms of reproducibility of the results, *i e* , short-term as well as long-term fluctuations in glaucoma

Materials and methods: On a Octopus 1-2-3 automated perimeter, 23 experienced, glaucomatous patients with predominantly local loss completed three test sessions, each consisting of a short training test followed by six visual fields, first "stage" (16 test locations) of program G1x, beginning at random with one strategy, then alternating the strategies

Results: The mean defect (MD) obtained with the dynamic strategy was (mean ± S D) 4 67 ± 7 3 dB; that obtained with the standard strategy, 5 2 ± 7 5 dB (p <0 01) Short-term fluctuation (SF) averaged 3 2 ± 4 1 dB for the former and 2.9 ± 3 8 dB for the latter strategy The total long-term fluctuation (LF) averaged 7 8 ± 19 2 dB and 6 4 ± 16 5 dB, respectively whereas the LF of MD averaged 1 3 ± 1 7 dB and 1 8 ± 2 7 dB, respectively The number of stimuli applied were 5 6 ± 1 4 and 3 0 ± 1 0, respectively In test locations with a normal sensitivity (defect < ± 4 0 dB), MD averaged 1 1 ± 1 2 and 0 8 ± 1 5 dB, SF 1 4 ± 1 7 and 1 5 ± 1 7 dB, the total LF 1 0 ± 1.1 and 1 2 ± 1.7 dB, and the number or stimuli averaged 2 6 ± 0 7 and 5 1 ± 0 7, respectively

Conclusions: For Weber's dynamic strategy, SF and LF in individual test locations increase (15% and 21%, respectively) as test time decreases (43%) Remarkable is the lower LF of MD (27%) The advantage of the dynamic strategy with regard to efficiency was greatest in normal areas

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New thresholding algorithms for automated static perimetry

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Abstract

A new type of algorithm for threshold determination in automated static perimetry is presented The new test algorithms employ advanced models of normal and glaucomatous visual fields to calculate a posterior distribution of thresholds which is used for threshold estimation and for estimating measurement errors in real time Algorithms can optimize stimulus presentation, and interrupt testing at prespecified levels of accuracy This may reduce measurement errors and/or the number of questions

We evaluated the new algorithms in simulations:

1 Measurement errors were reduced by approximately 15% when using the new method for threshold estimation, without changing the standard staircase strategy

2 The new data acquisition methods were tested in 50 normal fields, and 50 glaucomatous fields As compared with the standard Humphrey full threshold algorithm the mean squared threshold error decreased from 3 0 to 2.5 dB^2 in normal and from 4 6 to 4 5 dB^2 in glaucomatous fields The number of questions decreased from 462 to 322 in normal and from 496 to 385 in glaucoma fields The reduction in the number of questions without increased measurement error shows the usefulness of the visual field models and the ability to keep control of accuracy

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EARLY DIAGNOSIS OF GLAUCOMA

The significance of the peripheral visual field in detecting early visual field changes in glaucoma

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Abstract

In some glaucoma suspects we find a normal central visual field tested with the Octopus program G1 and defects in the peripheral visual field which is measured only semiquantitatively We therefore were interested whether the quantitative testing of the peripheral visual field could give us additional information about the visual field in glaucoma suspects

Patients: Seventy-seven patients with either early glaucoma or ocular hypertension were tested with the program G1 and a special Sargon program for the quantitative testing of the peripheral visual field

Results: We found that 12% of the patients tested had an abnormal peripheral visual field but a normal central visual field Defects are statistically significantly increased in the upper, upper nasal and nasal peripheral visual field compared to the rest of the visual field

Conclusions: We believe that it is necessary to test the peripheral visual field in patients having ocular hypertension and a normal central visual field

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Early perimetric diagnosis of glaucoma by stato-kinetic dissociation assessment

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Abstract

A recent investigation[11] demonstrated that glaucomatous eyes with mild perimetric defects had a significant decrease of stato-kinetic dissociation (SKD), particularly in the central and paracentral visual field (VF). The aim of the present study was to verify if this alteration was also present in eyes of ocular hypertensives, as a sign of initial optic nerve damage

Material and methods: Fifty ocular hypertensive subjects with normal VF (Humphrey 30-2) underwent a perimetric custom test designed for the assessment of SKD The results were compared with those of two control groups (50 normal and 50 glaucomatous subjects), by means of the analysis of variance (ANOVA).

Results: In comparison with the normal group, SKD was, on average, significantly decreased both in glaucomatous ($p < 0\ 001$) and in ocular hypertensive ($p < 0\ 001$) patients The difference between the glaucoma and ocular hypertensive groups was also significant ($p < 0\ 01$)

Discussion – conclusions: A statistical limit was calculated to separate abnormal responses inside the group of ocular hypertensive subjects In our sample, 16 out 50 ocular hypertensive subjects showed a pathological SKD, that could represent the first sign of optic nerve damage, even if further investigations and an extended follow-up are needed to confirm our hypothesis

Introduction

Stato-kinetic dissociation (SKD) is a well-known perimetric phenomenon The first report dates back to the first decades of the century (1917), when Riddoch gave a description of SKD in subjects suffering from occipital cortex lesions[1]

In recent years, SKD was the subject of many investigations, and its presence was demonstrated in patients with optic nerve[2], optic tract[2] and chiasmal[3] abnormalities, and in normals too[4–9].

Hudson and Wild[10] carried out an in-depth study, that allowed them to quantify importance of SKD in normals, using the Humphrey Field Analyzer, model 640 They demonstrated that SKD is a physiological phenomenon, independent from the stimulus size and only partly influenced by the rate of movement of kinetic targets[10].

In a recent investigation[11], the following SKD characteristics were pointed out·

- SKD is a constant physiological phenomenon;
- SKD is influenced by eccentricity· it is increased in the peripheral visual field (VF);
- SKD is influenced by age: it is increased in elderly subjects, especially in the periphery of VF;

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- SKD is partly influenced by sex (in the centro-paracentral VF it is more evident in males) and by the specific VF area explored (it is greater in the upper VF)

The SKD assessment in subjects with perimetric defects due to different diseases allowed us to observe the following[11]:
- in subjects with cataract, SKD increased only in the peripheral VF;
- in subjects with retinopathies, SKD increased in all VF areas, but especially in the periphery;
- in subjects with optic nerve or chiasmal lesions, SKD was not modified;
- in subjects with occipital cortex damage, SKD increased, especially in VF periphery;
- in glaucomatous subjects, SKD decreased in centro-paracentral VF areas.

Only statistically significant differences (analysis of variance, ANOVA) were taken in account.

Such results, and above all the peculiar SKD decrease in VF areas with early glaucomatous damage, suggested that we verify if this behavior was also present in subjects with ocular hypertension, as an initial sign of optic nerve damage, in absence of typical perimetric defects.

Materials and methods

Fifty subjects with definite ocular hypertension and normal visual field (Humphrey 30-2) were tested by an automatic perimetric program especially designed for SKD assessment. The results obtained were compared with those of two control groups (normal subjects and glaucomatous patients), each consisting of 50 individuals, homogeneous for age and other characteristics:

First control group (50 normal subjects)
- Age: 62.78 ± 11.58 years (min 41; max.: 83);
- Sex 29 females and 21 males;
- Pupillary diameter: normal (between 2 5 and 5 mm);
- Refractive error: less than 3 D of global ametropia, with less than 1 D of astigmatism;
- No ocular or general diseases;
- Visual acuity: more than 0.7;
- Previous experience of automated perimetry (static and kinetic);

Second control group (50 glaucomatous subjects)
- Age: 60 52 ± 13 01 years (min.: 21; max.: 79);
- Sex: 27 females and 23 males;
- Pupillary diameter. normal (between 2.5 and 5 mm);
- Refractive error: less than 3 D of global ametropia, with less than 1 D of astigmatism;
- No ocular or general diseases (except for a confirmed bilateral open-angle glaucoma, well controlled by beta-blockers, with initial typical VF defects, stable in several perimetric examinations);
- Visual acuity: more than 0 7;
- Previous experience of automated perimetry (static and kinetic);

Third group (50 ocular hypertensive subjects)
- Age: 61.64 ± 8.93 years (min : 41; max.: 80);
- Sex: 24 females and 26 males;
- Pupillary diameter: normal (between 2.5 and 5 mm);
- Refractive error less than 3 D of global ametropia, with less than 1 D of astigmatism;
- No ocular or general diseases (except for a confirmed ocular hypertension, with bilateral IOP more than 22 mmHg, detected during at least three controls and with normal VF in several perimetric tests carried out with the program 30-2 of the Humphrey VFA);

Table 1 Comparison among the ages of the three enrolled groups

Compared groups (ANOVA)	*Mean ages ± SD*	*p*
Normals vs glaucomas	62 78 ± 11 58 / 60.52 ± 13.01	0 36*
Normals vs hypertensives	62 78 ± 11.58 / 61 64 ± 8 93	0 58*
Hypertensives vs glaucomas	61 64 ± 8 93 / 60 52 ± 13 01	0 62*

*no significant difference among the considered samples

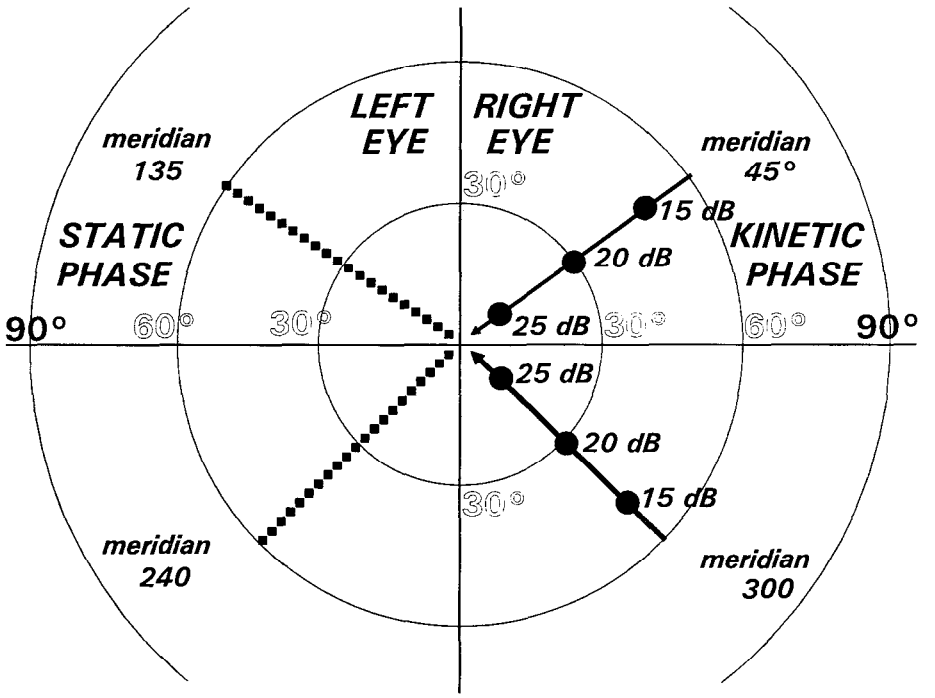

Fig 1 Custom program "STAT-CIN" designed for the assessment of "stato-kinetic dissociation" by automatic perimetry.

- Visual acuity: more than 0.7;
- Previous experience of automated perimetry (static and kinetic);

The three groups were evaluated by the analysis of variance (ANOVA), in order to verify if the mean ages were comparable. The results obtained (Table 1) confirmed the lack of significant differences among the mean ages of all enrolled groups.

For the SKD quantification, we used a custom perimetric program, named "STAT-CIN" with the Perikon PCL 90[12] perimeter. This program performs a kinetic test along two meridians placed in the superior and inferior temporal VF sectors, by means of three stimuli with area 1/4 mm^2 (target I, of the Goldmann set) and decreasing luminances (15, 20, 25 dB). The standard rate of movement of the above-mentioned test strategy was 5° per sec in the VF periphery and 3° per sec inside the central 30° The meridians were chosen in such a way as to avoid the cecal and pericecal areas – regions in normal subjects where considerable threshold variations are present (meridians 45 and 300 for the right eye, meridians 135 and 240 for the left eye).

After the kinetic phase, the program proceeded with a static threshold test along the same meridians, by means of randomized presentations at the following eccentricities: 3-6-9-12-15-18-21-24-27-30-33-36-39-42-45-48-51-54-57-60° (Fig. 1).

Table 2 Static thresholds corresponding to the kinetic stimuli (15, 20 and 25 dB) perception eccentricities in the three considered groups

Kinetic stimulus	*Corresponding static threshold (Mean ± SD)*
Normal subjects	
15 dB	13 25 ± 2 38 dB
20 dB	17 37 ± 1 89 dB
25 dB	21 49 ± 1 71 dB
Glaucomatous subjects	
15 dB	13 47 ± 2 33 dB
20 dB	17 47 ± 2 16 dB
25 dB	23 65 ± 2 64 dB
Hypertensive subjects	
15 dB	13 01 ± 2.29 dB
20 dB	17 61 ± 2 69 dB
25 dB	22 69 ± 3 29 dB

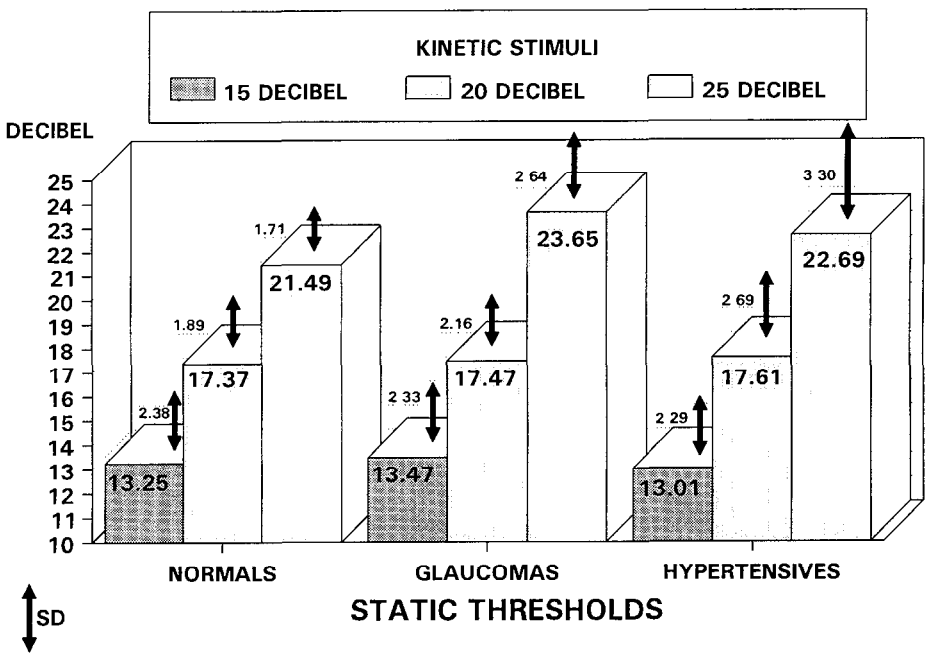

Fig 2 Static thresholds in the three studied groups, at the perception eccentricities of the used kinetic stimuli (15, 20 and 25 dB)

Therefore, the "STAT-CIN" program allowed us to establish the eccentricities at which the three kinetic stimuli were perceived and the static threshold of the target with the same area at those eccentricites was determined.

When the kinetic threshold did not exactly coincide with one of the statically tested eccentricites, a theoretical static threshold value was calculated interpolating the immediate peripheral and central thresholds

Table 3 Statistical comparison among the static thresholds of the three groups

Compared groups (ANOVA)	*Mean static threshold ± SD*	*p*
Peripheral visual field		
Normals vs glaucomas	13 25 ± 2 58 / 13 47 ± 2 33	0 51*
Normals vs hypertensives	13 25 ± 2 58 / 13 01 ± 2 24	0 16*
Hypertensive vs glaucomas	13 01 ± 2 24 / 13 47 ± 2 33	0 15*
Intermediate visual field		
Normals vs glaucomas	17 37 ± 1 89 / 17 47 ± 2 16	0 73*
Normals vs hypertensives	17 37 ± 1 89 / 17 61 ± 2 69	0 47*
Hypertensives vs glaucomas	17 61 ± 2 69 / 17 47 ± 2 16	0 69*
Central and paracentral visual field		
Normals vs glaucomas	21 49 ± 1 71 / 23 65 ± 2 64	< 0 001
Normals vs hypertensives	21 49 ± 1 71 / 22 69 ± 3 29	< 0 001
Hypertensives vs glaucomas	22 69 ± 3 29 / 23 65 ± 2 64	< 0 01

* no statistically significant differences

Table 4. Individual results analysis (50 hypertensive subjects)

Threshold limit value considered = 21 49 + 3 42 = 24 91 dB
Number of hypertensive subjects showing static threshold more than 24 91 dB at least in one location = 16 (32%)

Statistical analysis

ANOVA was used to compare the static thresholds detected at the kinetic stimuli perception eccentricities in the enrolled groups, for the three VF zones

For the individual results analysis, we established the normal limit value as double the SD detected in the normal subjects. We considered as abnormal those ocular hypertensive patients in whom SKD was less than this limit

Results

The static thresholds detected at the eccentricities of perception of the three kinetic stimuli (15, 20 and 25 dB) are shown in Table 2 and Figure 2.

The statistical comparison (ANOVA) between kinetic and static thresholds showed in all cases a highly significant difference ($p < 0\ 0001$). The statistical comparison (ANOVA) among the static thresholds of the three groups showed no significant differences with respect to the peripheral and intermediate VF areas.

Ón the contrary, with respect to the central and paracentral VF, the differences among the means were statistically significant, both in the comparison between normal and glaucomatous or hypertensive subjects and between glaucomatous and hypertensive patients (Table 3)

For the analysis of individual results in ocular hypertensive patients (Table 4), we considered eyes with a sure SKD alteration, those with one or more static thresholds, in the central or paracentral VF, more than the mean normal value (21.49 dB) plus double the SD (1.71 × 2 = 3.42).

Conclusions

The present investigation demonstrates in more than 30% of ocular hypertensive patients that there is a significant reduction of the physiological SKD, similar to that typical of glaucomatous subjects with true VF damage.

Such results agree with recent investigations that showed alteration of movement detection in the VF of glaucomatous subjects[13]. We conclude, that a significant SKD reduction may represent, in absence of true perimetric defects, an early sign of glaucomatous damage of the visual system. It may be suitable for separating patients with initial damage caused by ocular hypertension, who need drug administration or more frequent and in-depth control. Certainly, further studies and an extended follow-up are necessary to confirm this hypothesis.

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Central visual dysfunction in early-stage glaucoma

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Abstract

The authors statistically evaluated the central visual function of glaucoma patients for analysis of early central visual dysfunction-type glaucoma. 167 eyes of 124 patients with primary open-angle glaucoma showing early to moderately advanced visual field changes were examined Contrast sensitivity function and visual acuity after correction were examined in all subjects

Presence of nerve fiber layer defect in the papillo-macular bundle was also determined The mean values of age, corrected refraction (D), and stage of visual field damage were compared between the central visual dysfunction and normal central function glaucoma group

Contrast sensitivity dysfunction and poor visual acuity were observed frequently in patients in the younger and myopic group Myopia with refraction of –4D to –8D was observed only in the low visual acuity group Corrected refraction was more frequently between 0D and –6D in patients with positive nerve fiber layer defect (NFLD) than in those with no NFLD

Younger patients with moderate myopia may be at risk to have an early central visual dysfunction-type glaucoma.

Introduction

Recently, visual function in glaucoma has been studied by tests of contrast sensitivity (CS)[1], color vision[2], and pattern ERG[3], and central visual dysfunctions have been shown to develop already at an early stage of glaucoma.

Also, some patients lose visual acuity already at a stage when the peripheral visual field remains relatively intact[4,5], a phenomenon at variance from the accepted pattern of progression of glaucomatous visual impairment.

In this study, we statistically evaluated the central visual function of glaucoma patients for analysis of this early central visual dysfunction-type glaucoma.

Subjects and methods

167 eyes of 124 patients of primary open-angle glaucoma with high ocular pressure (over 21 mmHg) aged 12 to 75 years (mean 51.5 years) were examined.

Forty eyes showed no visual field change but had an abnormal visual field in the opposite eye; 127 eyes showed early to moderately advanced visual field changes (up to stage III-b by Kosaki's staging[6], I–a: normal field by kinetic Goldmann perimetry, I–b: abnormal field detected only when more precise method is used, II–a: normal for isopter I–4, but abnormal for isopters I–3, I–2 and I–1, II–b: abnormal for isopter I–4, III–a: field loss not exceeding a quarter of the V–4 isopter, III–b: defects not exceeding half of the V–4 isopter). All patients had no other disorders in the anterior structures of the eye, optic media, or the fundus. No patient had a history of intraocular surgery.

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Evaluation of central visual functions

Visual acuity after correction and CS were examined in all subjects. CS was evaluated by measuring the thresholds using an CS meter controlled with a microcomputer[7]. Under conditions of an eye-screen distance of 1 m, a mean screen brightness of 20 cd/m, and an image size of 4 × 5 degrees, the threshold was measured three times each at six levels of spatial frequency of 0 7, 1.4, 2 5, 3 5, 7.0, and 15.0 cpd, and the mean of the three measurements was calculated. The subjects were divided into those aged less than 40 years, those in their 40's, those in their 50's, and those aged 60 years or above, and the mean and the standard deviation were calculated for each level of spatial frequency in each group The threshold was considered to be reduced when the value was lower than the mean minus the standard deviation at two or more levels of spatial frequency (CS dysfunction).

The mean values of the age, corrected refraction (D), and stage of visual field damage (Kosaki's staging) were compared between the CS dysfunction and normal central function group (Student's t test)

Visual field changes staged as I–a, I–b, II–a, II–b, III–a, and III–b by Kosaki were scored 1, 2, 3, 4, 5, and 6, respectively. The differences in the mean value of the score were examined

Nerve fiber layer defect (NFLD) in the papillo-macular bundle

NFLD in the papillo-macular bundle was determined according to the method described in a previous report[7] by red-free fundus photography (Canon CF60Z, Kodak Wratten filter No 58) in 105 eyes of 74 patients The mean values of various parameters were compared between the eyes with no NFLD (none and slit type combined) and those with positive NFLD (band type and diffuse type combined) (Student's t test).

Results

Relationship between central visual functions and various factors

Stage III–a visual field changes were observed more frequently in the CS dysfunction group, but the mean score of visual field changes was 4.27 ± 1 29 and 3 20 ± 1 68 in the CS dysfunction group and normal central function group, respectively. The difference was not significant (NS) (Table 1)

CS dysfunctions were observed more frequently in patients in their 10's and 20's, but the mean age of that group was 46 1 ± 13 5 years while that of the normal function group was 52.9 ± 12 8 years (NS) (Table 2)

Myopia with refraction between –2D and –6D tended to be more frequent in the CS dysfunction group than in the normal group, and the mean refraction was –2.47D ± 2.86 and –1.40D ± 2.73, respectively, with a significant difference ($p < 0$ 05) (Table 3).

Low visual acuity (less than 1.0) was observed frequently in patients in their 10's and 20's, and the mean age of the low visual acuity group was 34.7 ± 14.2 years while that of the normal group was 52 2 ± 12.7 years (Table 4).

Low visual acuity was observed only in the myopic group with refraction of –4D to –8D, and the mean refraction was –5 86D ± 1 54 in the low visual acuity group but –1.46D ± 2.69 in the normal group (significant at $p < 0.01$) (Table 5)

Relationship between NFLD in the papillo-macular bundle and various factors

The mean values of various parameters in patients with no NFLD were compared with those with positive NFLD.

The mean age was 49.8 ± 10 4 years and 47.8 ± 14 5 years (NS): the mean score of visual field changes was 3 02 ± 1 71 and 4.11 ± 1.55, respectively (NS). However, corrected refraction was more frequently between 0D and –6D in patients with positive NFLD than in those with no NFLD. The mean refraction was –2 61D ± 2.59 and –0 88D ± 2.36, respectively, with a significant difference ($p < 0.01$) (Table 6)

Table 1 Contrast sensitivity and visual field damage

Visual field		*Contrast sensitivity*	
Count	*Kosaki*	*Normal*	*Dysfunction*
1	I–a	37	3
2	I–b	9	3
3	II–a	21	4
4	II–b	21	4
5	III–a	36	19
6	III–b	8	2
Total (167 eyes)		132	35
	Mean	3 20	4 27
	SD	1 68	1 29*

*NS

Table 2 Contrast sensitivity and age

Age	*Contrast sensitivity*	
(yr)	*Normal*	*Dysfunction*
10–19	3	3
20–29	6	5
30–39	12	5
40–49	27	5
50–59	33	11
60–69	45	6
70–75	6	0
Total (167 eyes)	132	35
Mean	52 90	46 10 yr
SD	12 80	13 50*

*NS

Table 3 Contrast sensitivity and refractive error

Refractive	*Contrast sensitivity*	
error (D)	*Normal*	*Dysfunction*
–6– –8	5	2
–4– –6	15	9
–2– –4	11	7
0– –2	32	5
0– +2	62	10
+2– +4	8	1
Total (167 eyes)	132	35
Mean	–1 4	–2 47 D
SD	2 73	2 86 *

* Significant, $p = 0\ 05$ Student's t

Table 4 Visual acuity and age

Age (yr)	*Visual acuity*	
	> 1 0	*< 1 0*
10–19	4	2
20–29	8	3
30–39	17	
40–49	32	
50–59	44	
60–69	50	1
70–75	6	
Total (167 eyes)	161	6
Mean	52 2	34 7 yr
SD	12 7	14 2 *

* Significant, $p = 0\ 01$ Student's t

Table 5 Visual acuity and refractive error

Refractive error (D)	*Visual acuity*	
	> 1 0	*< 1 0*
–6– –8	10	2
–4– –6	24	4
–2– –4	21	
0– –2	25	
0– + 2	72	
+2– +4	9	
Total (167 eyes)	161	6
Mean	–1 46	–5 86 D
SD	2 69	1 54 *

* Significant, $p = 0\ 01$ Student's t

Table 6 Macula nerve fiber layer defect (NFLD) and refractive error

Refractive error (D)	*Macula NFLD*	
	–	+
–6– –8	2	2
–4– –6	5	9
–2– –4	8	9
0– –2	24	13
0– + 2	30	11
+2– +4	2	0
Total (105 eyes)	61	44
Mean	–0 88	–2 61 D
SD	2.36	2 59 *

* Significant, $p = 0\ 01$ Student's t

Discussion

As we reported previously[8], the severity of central visual dysfunctions associated with glaucoma varies widely. Central visual dysfunctions other than a reduction in the central visual acuity associated with a degree of impairment of the papillo-macular fibers are observed in some patients even at a stage when the visual acuity is intact and visual field changes are still unremarkable.

In this study, we evaluated central visual function in glaucoma patients using contrast sensitivity and visual acuity after correction Myopia tended to be more advanced, and younger patients with moderate myopia were encountered more frequently in the central visual dysfunction group Significant differences were observed between the central visual dysfunction group and the normal central function group in the mean value of the corrected refraction and the age (Tables 3, 4, 5). Of the six patients classified in the low visual acuity group, many were in their 10's or 20's and had moderate myopia (Figs 4, 5). In this study there may be too few glaucoma patients in the group with low visual acuity to make a significant statement other than that the visual acuity loss is serious and represents the final stage of central visual dysfunction

The diagnosis of these patients is considered to be an early central visual dysfunction-type glaucoma, which is not consistent with the expected pattern of progression of glaucomatous visual dysfunction NFLD in the papillo-macular bundles was evaluated as an objective index of central visual dysfunction. A significant difference was observed in the mean corrected refraction between a group with positive NFLD and a group with no NFLD, and the positive NFLD group included more patients with myopia between 0D and -6D (Table 6)

However, no significant difference was observed in factors such as the age and the stage of visual field changes between the two groups.

These results suggest that myopia is a risk factor of central visual dysfunctions in glaucoma Progression of visual dysfunctions is known to be quicker when glaucoma is complicated by myopia[9], and this may be explained by increased vulnerability of axons to changes in the intraocular pressure due to abnormal morphology and circulatory disorders of the optic disk in myopic eyes.

Central visual dysfunctions tend to occur at relatively young ages Dysfunctions in the peripheries of the retina are considered to be more likely to occur in older individuals, in whom the number of axons is reduced due to aging. Thus, peripheral visual dysfunctions may become apparent in older people before the development of central visual dysfunctions due to myopia[10]. This may also indicate a difference in the resistance of peripheral visual functions to changes in the intraocular pressure between younger and older individuals.

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Updating the role of diffuse field loss in glaucoma diagnosis

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Abstract

The aim of this study was to investigate whether a global reduction of light sensitivity can be considered as the earliest perimetric sign of glaucoma, by using other clinical tests, in addition to automated perimetry We defined a significant difference in mean deviation (MD) to be more than 1 5 dB Sixty-five glaucoma suspects with a normal visual field, but with this MD asymmetry underwent threshold perimetry (Humphrey, 30-2), high-pass resolution perimetry, optic nerve head computerized analysis ("retinal nerve fiber layer height" program) and pattern electroretinography When the results of at least two of these additional tests were significantly abnormal, the subjects were arbitrarily classified as glaucoma patients Our results showed 31 (88 57%) of the 35 subjects whose difference in MD value between the two eyes was less than 1 8 dB had normal responses to the other tests Among the 30 subjects who showed a difference of more than 1 8 dB, 14 (46 6%) had a glaucoma diagnosis confirmed by the other tests

Introduction

The hypothesis that a diffuse reduction of differential light sensitivity could be considered as the earliest perimetric sign of glaucoma[1–3] is controversial[4–11] We studied whether this hypothesis could be confirmed using other clinical tests: high-pass resolution perimetry (HRP), estimates of retinal nerve fiber layer height (RNFLH) and pattern electroretinography (PERG).

Materials and methods

We selected 65 glaucoma suspects, evaluated during the last three years Their ages were between 26 and 58 years (average age: 44 26 ± 10.29) They were already tested with Humphrey 640 VFA, program 30-2, with normal perimetric findings, but with asymmetry in MD value, more than 1 5 dB[12–14]. The subjects had a family history of glaucoma and/or an intraocular pressure of 22 mmHg or more. Exclusion criterion were. (1) subjects taking medications, such as tranquilizers, that might influence their responses during the visual field (VF) examinations; (2) those with poor reliability indices altered; (3) subjects with any ocular or systemic disease that might interfere with the VF results; (4) those whose best corrected visual acuity was 0.7 or worse; (5) subjects who required more than ± 5.0 diopters of spherical refractive correction; (6) those with asymmetry of refractive error of more than 1.5 diopters of spherical or cylindrical correction; (7) those whose pupils smaller than 2 5 mm; (8) subjects

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Table 1 Comparison (ANOVA) between the means of age and refractive errors of the two groups (normals and glaucoma suspects)

No	*Normal subjects 25 (50 eyes)*	*Glaucoma subjects 65 (130 eyes)*	*p*
Age	45 64±9 35	44 26 ± 10 29	0 41
Refractive error	+ 0 09 ± 1 65	+ 0 19 ± 1 87	0 74

no statistically significant differences

with no more than one isolated point with a p value < 2% and no more than two adjacent points with a p value < 5% in both their "total deviation" and "pattern deviation" maps. As a control group, we selected 25 normal subjecs, whose average age and refractive data were similar to those of glaucoma suspects (Table 1), but with normal IOP and MD asymmetry less than 1 dB. In order to compare the average values of age and of refractive data in the two groups and to test the uniformity of the samples, ANOVA method was utilized

All subjects underwent: (1) standard perimetry; (2) high-pass resolution perimetry (High-Tech Vision, Sweden), evaluating both the mean score (MS) and the "functional channel fraction" (FCF) indices[15–18]; (3) optic nerve head computerized analysis (Image-net IS 100 system, Topcon, Japan), program "retinal nerve fiber layer height" (RNFLH); with regard to that program, we took into consideration the relationship between the height of the nerve fibers lying on the vertical meridian and those lying on the horizontal one (V/H ratio: average normal value = 4/1))[19–22]; (4) pattern electroretinography was performed[23–26], by using the Amplaid SD 15 and by utilizing the following standards:

- recording electrode: at the inferior conjunctival fornix
- ground electrode: at vertex (Fpz 10–20 International System)
- reference: linked mastoids
- video monitor subtending 20° of visual angle
- video monitor luminance 100 cd/m^2
- bandpass. 0 5–50 Hz
- sampling time· 150 msec
- stimulus: vertical sinusoidal bars
- contrast: 75%
- spatial frequency: 1°
- temporal frequency 7 Hz
- number of stimuli 500

Our normative values can be found in a previous study[27].

We took into consideration the peak to peak amplitude, which is related to the density of the ganglion cells.

The results obtained in all clinical tests were compared by means of linear regression, in order to verify the significance of the correlations In order to analyze the individual results, we considered the subjects who had at least two abnormal additional tests as glaucomatous patients, following the criteria indicated below.

The values we considered as normal reference limits, with regard to the additional clinical tests, derived from literature data (RNFLH and PERG)[20–27] or from the data from the control group (MS and FCF indices of the ring perimetry).

HRP

The normal subjects showed the following average differences between the two eyes: MS = 0 4 ± 0 26; FCF = 8.76 ± 5.99 We considered as abnormal the subjects whose difference between the two eyes was more than the normal mean value plus twice the standard deviation

Table 2 Calculation of the normal limits concerning "MS" and "FCF" on the basis of the normal group results (25 people, 50 eyes)

Mean difference between the two eyes + 2 SD ("MS")	*Mean difference between the two eyes + 2 SD ("FCF")*
0 40 + 2 × 0 26 = 0 40 + 0 52	8 76 + 2 × 5 99 = 8 76 + 11 98
Normal limit ("MS") = 0.92	Normal limit ("FCF") = 20 74

Table 3 Correlation between the tests (linear regression)

Correlation	*T*	*df*	*p*
MD vs MS	9 59	178	< 0 0001
MD vs FCF	13 90	178	< 0 0001
MD vs PERG	10 45	178	< 0 0001
MD vs RNFLH	3 19	178	< 0 01
MS vs FCF	7.12	178	< 0 0001
MS vs PERG	9 32	178	< 0 0001
MS vs RNFLH	3 22	178	< 0 01
PERG vs FCF	7.40	178	< 0 0001
RNFLH vs FCF	3 38	178	< 0 001
PERG vs RNFLH	2 49	178	< 0 1

MD = mean deviation (Humphrey 30-2); MS = mean score (HRP); FCF = functional channels fraction (HRP); PERG = pattern electroretinogram (Amplaid SD 15); RNFLH = retinal nerve fiber layer height (Image-net)

(SD) value in one or both these indices (MS = 0 4 + 0 26 × 2 = 0 4 + 0.52 = 0.92; FCF = 8.76 + 5 99 × 2 = 8.76 + 11.98 = 20.74) (Table 2).

RNFLH

Previous experiences[20–22] suggested to us to consider as abnormal a difference between the two eyes of more than 1.5, as far as the V/H ratio is concerned

PERG

A difference of the peak to peak amplitude of more than 1.04 μV, between the two eyes, was considered as abnormal, on the basis of our previous experiences[27]

Results

Thirty-one (88.57%) of the 35 subjects whose difference in MD value between the two eyes was less than 1.8 dB showed normal responses to the other tests; only two subjects showed mild alterations of HRP. Two other subjects had an alteration of nerve fiber height, while only one subject had a significant alteration of PERG All these alterations were present in different patients and not associated.

Among the 30 subjects who showed a difference of MD more than 1 8 dB, 14 (46.6%) had a "glaucoma diagnosis" confirmed by the other tests: nine subjects had both HRP and PERG alterations; the other five subjects had both HRP and RNFLH alterations In all these cases, the "worst" eye was the one with a higher MD value. Statistical analysis (linear regression) showed significant correlations between the results obtained with the various tests performed, although with different significance levels (Table 3).

Discussion

We observed a good correlation between the MD value and the results of the additional tests that we performed. The results of this study do not allow us, of course, to affirm that a global mean sensitivity depression is the earliest perimetric sign of glaucomatous damage. We think, however, that this condition may occur, at least in some cases. In particular, we would like to emphasize the importance of the asymmetry of MD values between the two eyes, as a sign that suggests early optic nerve damage. We believe the presence of an MD asymmetry in a glaucoma suspect is evidence of abnormal optic nerve function: look at this asymmetry between the two eyes!

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Location of early field deterioration in glaucoma suspects

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Abstract

Purpose: To investigate the frequency and spatial distribution of visual field locations showing the earliest evidence of deterioration in two groups: ocular hypertensives and initially normal fellow eyes of unilateral normal-tension glaucoma patients

Method: All initial visual fields were normal in both ocular hypertensives (OHT) and fellow eyes of unilateral normal-tension glaucoma subjects (NTG) Visual fields were analysed using pointwise regression analysis. Eyes which demonstrated at least one location with a statistically significant ($p < 0\ 05$) negative regression slope and rate of loss faster than 1 dB/year were defined as progressing In each of those eyes defined as progressing the site(s) and number of the first regression slope(s) which met the progression criteria were recorded

Results: In OHT, 12 eyes of 12 patients from a group of 380 were identified as showing visual field progression In NTG, 17 fellow eyes from a group of 51 subjects demonstrated visual field progression There was a statistically significant difference between the number of locations showing the earliest evidence of progression in OHT and NTG (Mann Whitney Rank Sum $p < 0\ 01$): OHT demonstrated the earliest appearance of regression slopes satisfying the definition of deterioration at more locations simultaneously than those eyes with NTG. There were differences in the spatial distribution of the earliest deteriorating locations between both groups.

Conclusion: The earliest evidence of visual field progression in OHT involve more field locations than normal fellow eyes in NTG The sites involved were closer to fixation in the NTG eyes This may suggest differences in the mode of onset of visual field loss in high-tension glaucoma and normal-tension glaucoma

Introduction

There may be differences between the distribution of field defects in patients with glaucoma associated with a high intraocular pressure (IOP) and those patients with normal levels of IOP. Drance and coworkers[1] have described more diffuse loss in high-tension and more focal losses in NTG which has been supported by other studies[2–7].

This study describes use of pointwise linear regression analysis[8–10] to identify those locations within an initially normal visual field which show the earliest evidence of deterioration over time. The analysis method allows identification of the number of locations which begin to deteriorate simultaneously as well as the site(s) within the field which are affected The analysis method has been applied to visual field data from two groups of glaucoma suspects· ocular hypertensives and initially normal fellow-eyes of normal-tension glaucoma patients (NTG). Eyes from both groups which demonstrated deterioration at at least one Humphrey field location have been compared. Differences in the mode of onset of the earliest defects in OHT and NTG are described.

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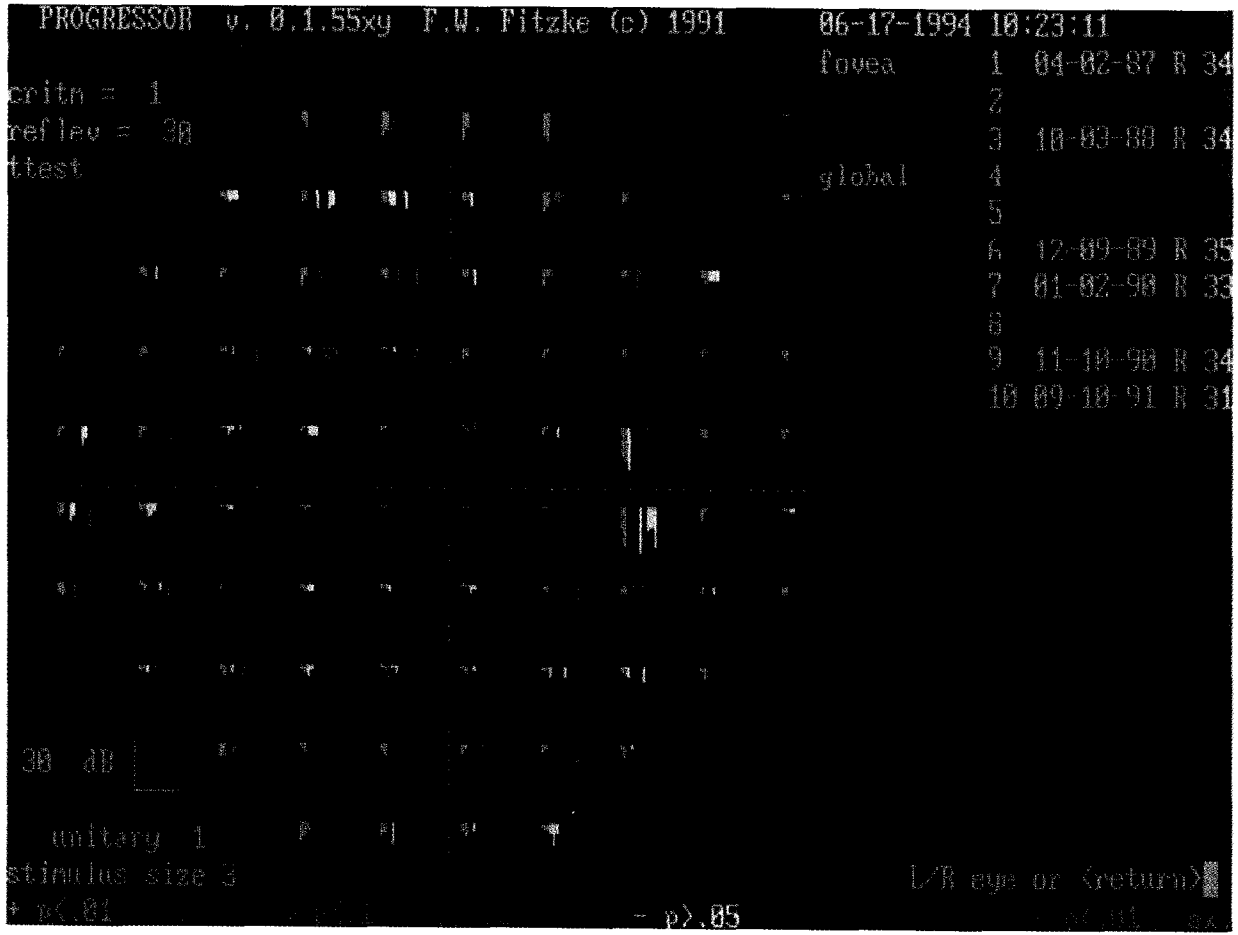


Fig. 1a. Example of an ocular hypertensive patient developing visual field progression faster than 1 dB/year on the linear regression analysis at several locations simultaneously.

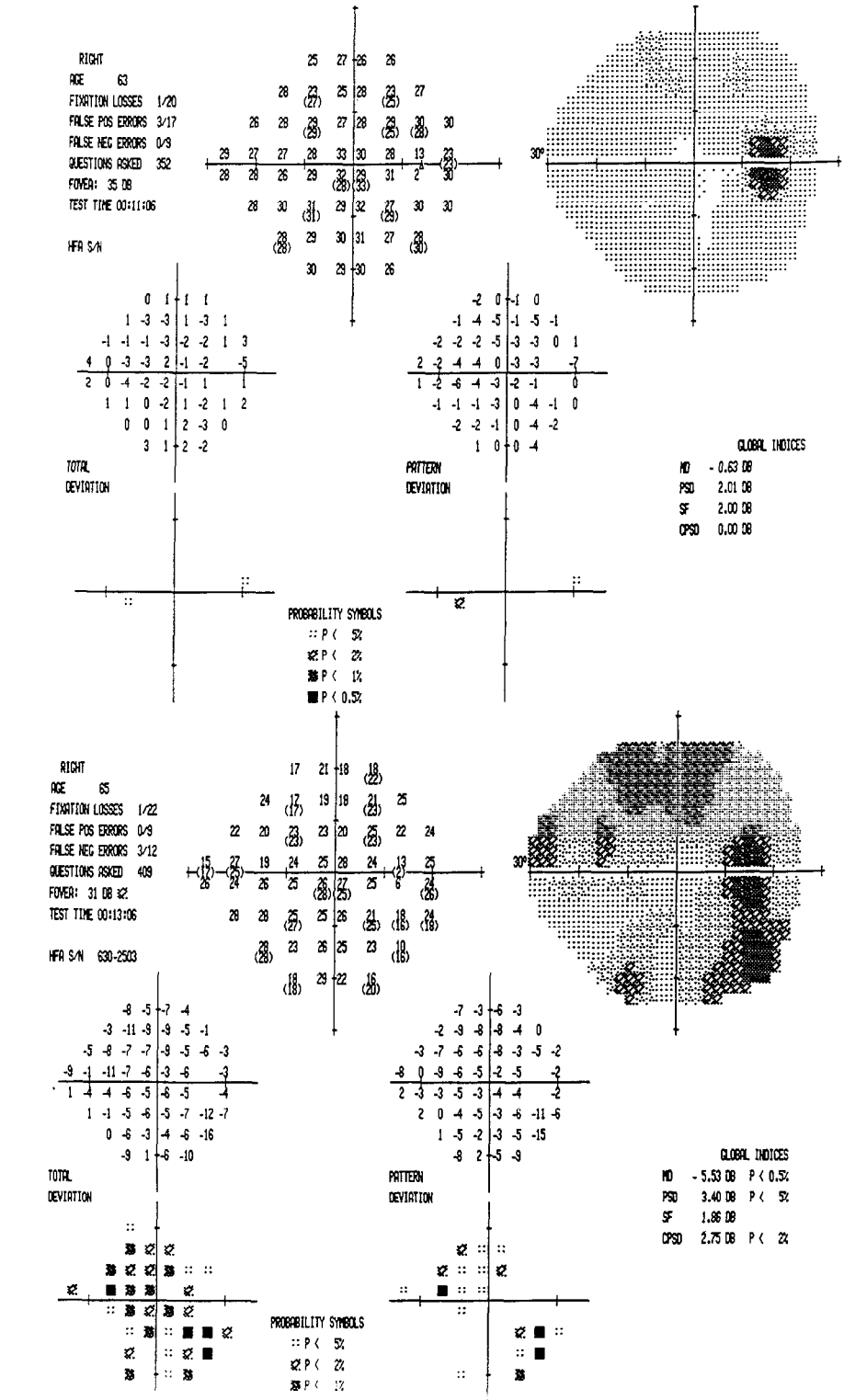


Fig 1b Early and late Humphrey visual field from the same field series showing the development of relatively diffuse loss

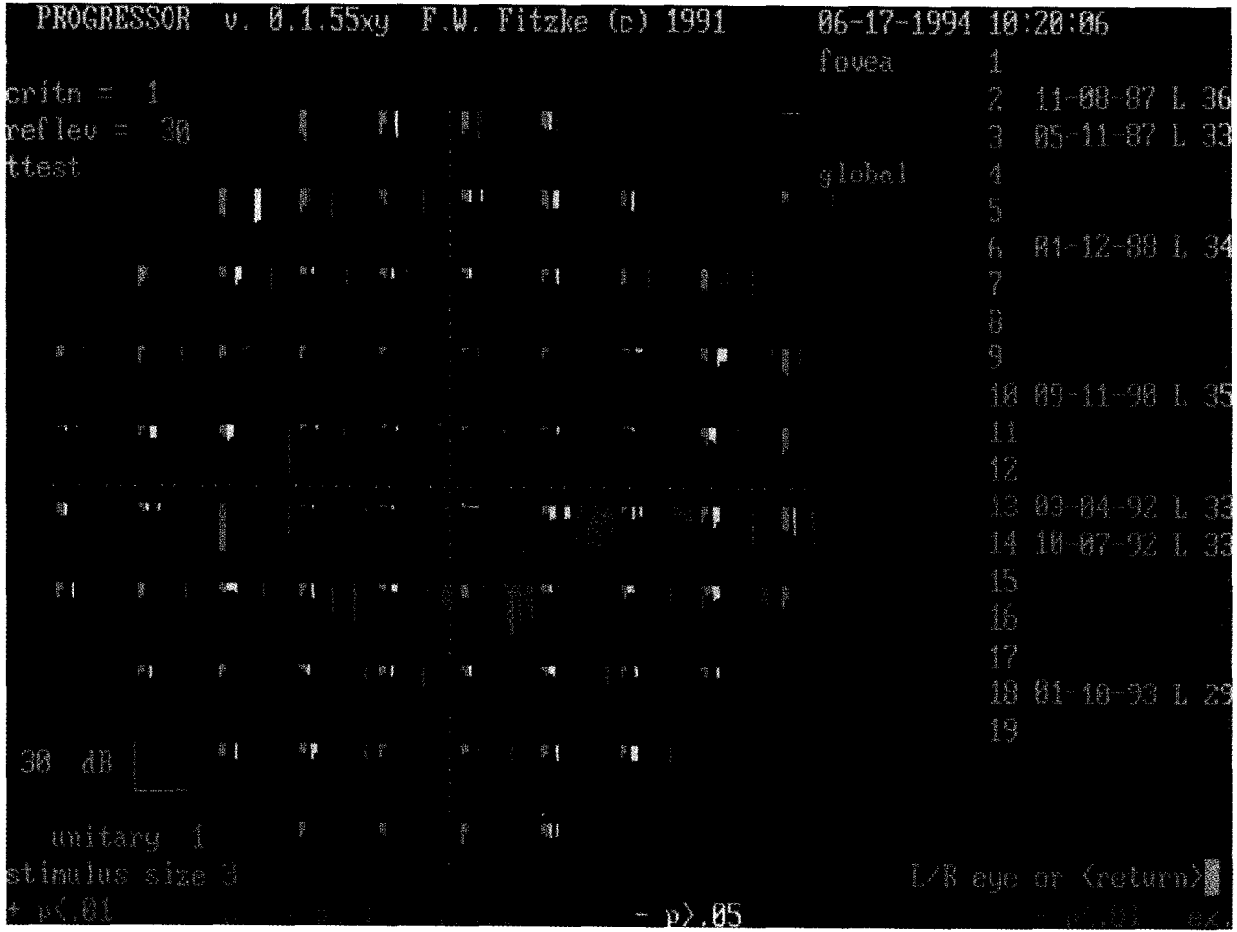
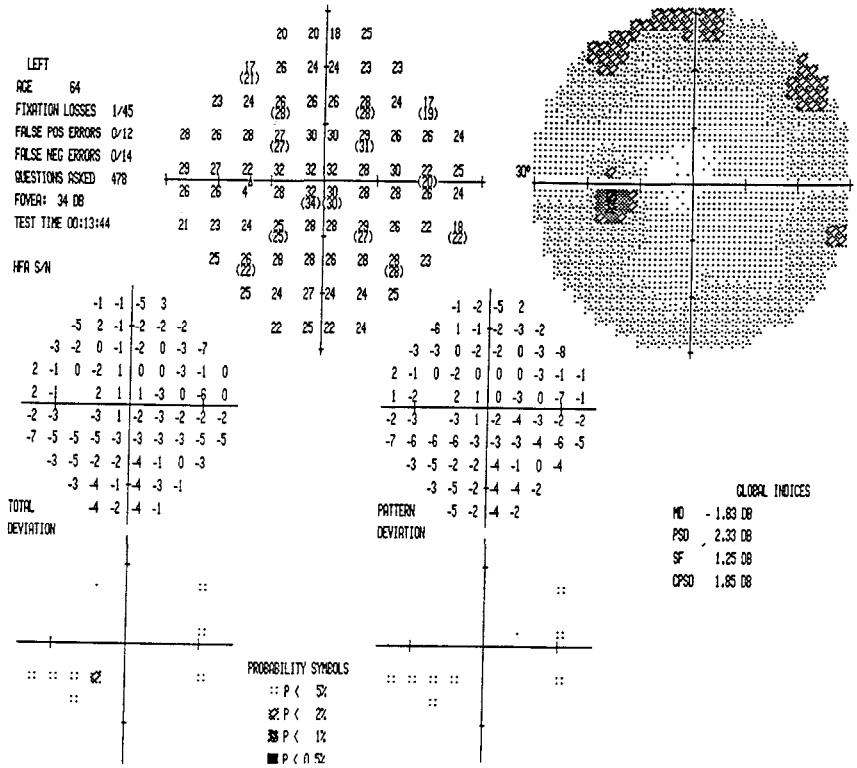


Fig. 2a. Example of a normotensive eye developing visual field progression at fewer locations and showing a more focal distribution within ten degrees of fixation.



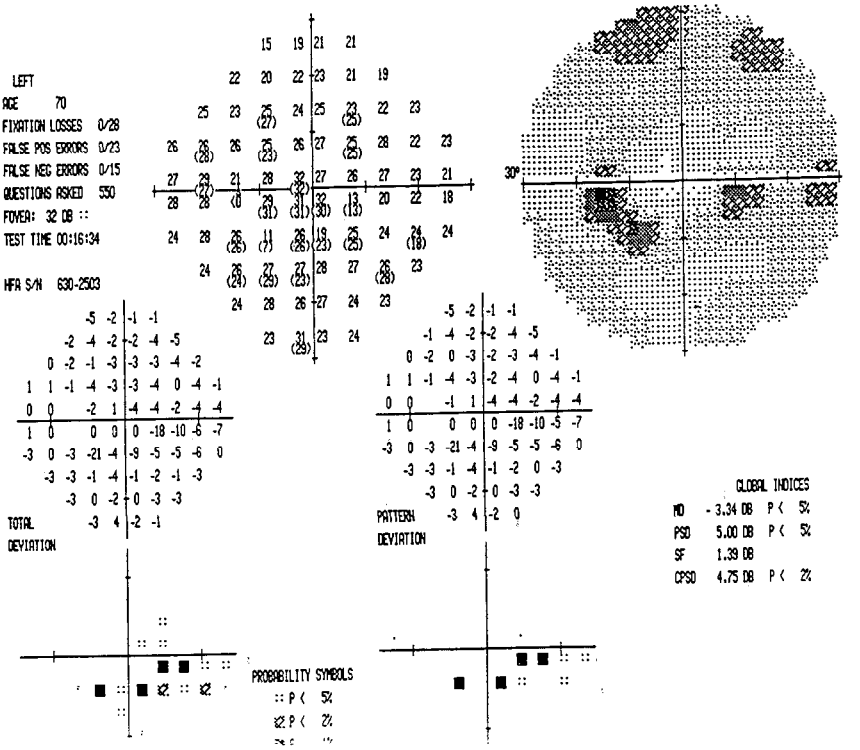


Fig 2b Early and late field from the same eye

Patients and methods

Visual field data from patients with a diagnosis of normal tension glaucoma (IOP < 21 mm Hg) or ocular hypertension (presenting IOP > 21 mmHg) was reviewed using a computerized visual field database. Of 220 patients with normal-tension glaucoma, 51 were found to have had an initially normal Humphrey visual field in one eye at presentation (the diagnosis of NTG having been established in the fellow eye).

An initially normal Humphrey field was defined as no clusters of > three neighboring locations showing loss in excess of 5 dB below the age-matched Humphrey normal database in field two or three[11]. Additionally, neither field two or three demonstrated significant (p < 0 05) deviations of either MD or CPSD

The onset of visual field deterioration was defined as a statistically significant negative regression slope (p < 0 05) at any location with a rate of loss faster than 1 dB/year[12]. Eyes fulfilling this definition were selected

In the OHT group, the initial visual fields were defined as normal using the same definition as above. The definition of deterioration was applied to a database of 380 OHT subjects and eyes fulfilling the definition were selected

Additionally, all selected eyes had corrected central visual acuity better than 6/9 and did not lose more than one line of Snellen acuity during follow-up

Visual field analysis. Pointwise linear regression analysis

The software automatically performs pointwise linear regression analysis on all available visual fields from an eye. The result is displayed as a color-coded representation which indicates those locations showing a statistically significant rate of threshold decay. The adoption of a linear model for glaucomatous threshold decay has followed curve-fitting experiments in NTG subjects with long historical field series[11]. The definition of deterioration of a significant negative regression slope showing a rate of loss faster than 1 dB/year has been found to closely correlate with the Humphrey Statpac2 "glaucoma change probability" software.

Results

Of the 51 NTG subjects with initially unilateral field loss, 17 eyes with initially normal fields demonstrated at least one location fulfilling the definition of deterioration. Within the OHT group, 12 eyes of 12 patients were defined as deteriorating. The mean age of the NTG 17 patients was 59 6 (range 44–78). The mean age of the OHT subjects was 64.4 (range 47–79). The mean follow-up for the NTG was 5.2 years (SD 2 1) range (1.7–7 3) years and for the OHT groups was 4.9 years (SD 1.5) range (3.7–7 8) years. Examples of deteriorating OHT and NTG eyes are shown in Figures 1 and 2.

The median number of locations showing the earliest simultaneous onset of field deterioration in the NTG group was two (range 1–4), and four (range 1–8) in the OHT group. There was a statistically significant difference between the two groups (Mann Whitney Rank Sum $p < 0.01$) Figure 3 shows these results as a histogram.

Analysis of the spatial distribution of deteriorating locations is shown as a cumulative frequency map (Fig. 4). There was a higher proportion of progressing location within the central ten degrees of field in the NTG eyes (41%) compared to 25% for OHT.

The NTG eyes were untreated throughout the field series studied. OHT were either untreated or treated with combinations of beta-blockers, pilocarpine or adrenaline No OHT subject underwent drainage surgery or laser treatment during the field series. Table 1 shows the 12 subjects and respective treatments It can be seen that only two subjects were treated with pilocarpine One of these subjects showed four progressing locations, *i e.*, relatively "diffuse" progression onset This may be related to pilocarpine use: to explore this possibility the frequency of progressing locations in this case was changed from four locations to one and the analysis repeated. The significant difference between the groups as a whole persists but is less significant ($p < 0.05$ Mann Whitney Rank Sum).

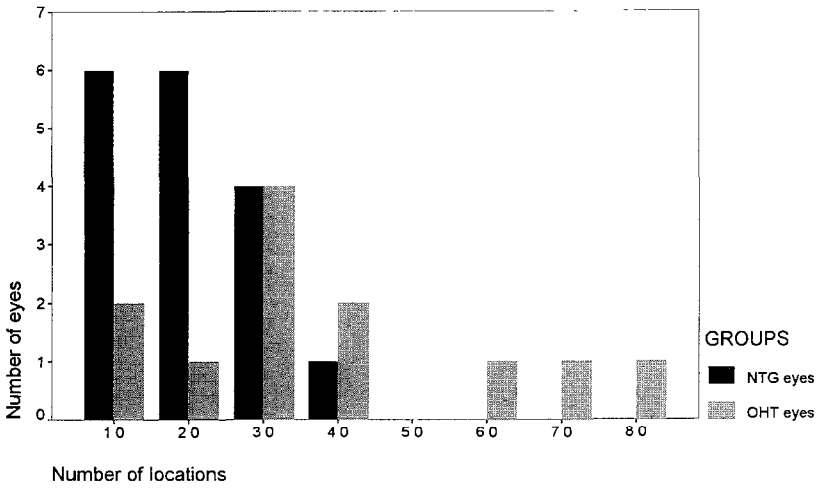


Fig 3 Histogram indicating the frequency distribution of locations in the two groups showing the earliest evidence of progression

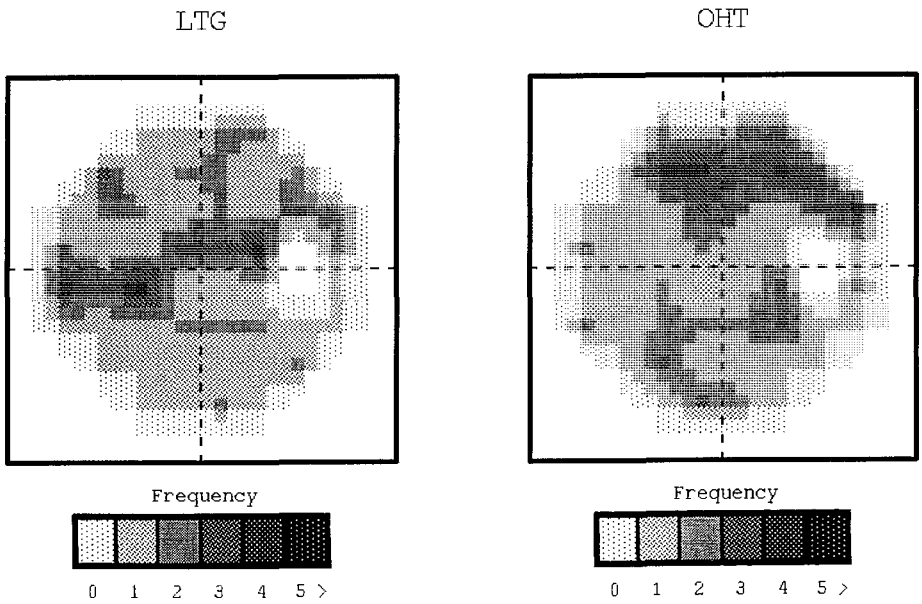


Fig 4 The spatial distribution of the Humphrey locations where the earliest visual field progression occurred in high- and normal-tension subjects (cumulative frequency map: left eyes laterally inverted) The grey scale indicates the cumulative frequency of deteriorating locations from each eye of both groups: darker greys indicate locations most frequently involved in the earliest deterioration

Discussion

This retrospective study has shown that ocular hypertensive eyes showed the earliest evidence of visual field progression at more locations simultaneously than a normal-tension group. This significant difference remained even after correction for pharmacologic pupil miosis in the OHT group The analysis method used for visual field progression performs lin-

Table 1

Subject	*Number of points*	*Treatment*
1	1	untreated
2	1	beta-blockers, pilocarpine, adrenaline
3	2	beta-blockers
4	3	beta-blockers
5	3	beta-blockers
6	3	beta-blockers
7	3	beta-blockers
8	4	beta-blockers, pilocarpine
9	4	untreated
10	6	beta-blockers
11	7	untreated
12	8	beta-blockers

ear regression at each location in the visual field and did not use global indices, this allows high sensitivity for the detection of both focal change as well as more diffuse losses. There was a tendency for the earliest progression in NTG to occur at locations closer to fixation than in the OHT group. Both groups showed a similar spatial pattern of early progression at locations arranged in a superior and inferior arcuate pattern. Other authors have described differences in early field loss in high- and normal-tension glaucoma. Levene[13] showed that visual field defects in normal-tension glaucoma were closer to fixation than in high-tension glaucoma and Hitchings and Anderton[14] have reported that the defects in advanced NTG were steeper and nearer fixation This study further suggests that the early defects in NTG also tend to have deeper, more localized defects while HTG tends to have more shallow defects.

Examination of the histogram in Figure 3 shows a broadly similar distribution of number of involved locations between the two groups but there is a skew in the right part of the distribution for the high-tension subjects This may indicate that a few subjects in each group are showing relatively clear evidence of either focal or diffuse change but that for most subjects there are many similarities in the early onset of field change. The findings from our study taken together with the work of other workers suggest that there are differences in early functional losses in high- and normal-tension subjects. There may be a tendency for a more diffuse pattern of loss in high-tension subjects with more focal losses in normal-tension subjects. However, these differences are only marked in a relatively small proportion of either group, with the majority of the subjects showing broadly similar changes This study suggests more than one pathogenic mechanism underlying the functional loss in glaucoma suspects

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Diagnostic value of asymmetric optic disk parameters in patients with unilateral glaucoma

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Abstract

The authors wanted to know how well intra-individual asymmetries in optic disk parameters can indicate glaucomatous damage Fifty-six patients with unilateral or highly asymmetric glaucoma (Octopus G1: ΔMD> 2 dB or ΔIOP > 5 mmHg) were examined with the Rodenstock Optic Nerve Head Analyzer (ONHA) and/or the Heidelberg Retina Tomograph (HRT) Forty-two healthy volunteers served as controls For each parameter the distribution of the intra-individual differences in the normal group was compared with the distribution in the unilateral glaucoma group

The best separation between normal and unilateral glaucoma was possible with the parameters "rim area" and "CD ratio", both obtained with the ONHA (p = 0 0001) "Cup volume" (HRT) had a smaller separation power (p = 0 007) but indicated unilateral glaucomatous damage better than the other parameters, measured with the HRT: "cup area" (p = 0 01), "disk area" (p = 0 05) and "max depth" (of the cup, p = 0 5)

Introduction

Comparative evaluation of both optic disks of the same patient may undoubtedly indicate glaucomatous damage Even in ocular hypertensives optic disk asymmetries are more pronounced than in normals[1] On biomicroscopic examination a couple of parameters (disk size, pallor, cupping etc.) are evaluated subjectively and simultaneously. It has to be taken into account that for each single parameter there are marked asymmetries in normal persons as well For example, Funk *et al* [2] found differences in the cup disk ratio between the left and right eye of healthy subjects up to 0 6! In this study we wanted to evaluate whether asymmetries in single optic disk parameters allow at all a separation between unilateral glaucoma and normal Secondly we wanted to show which parameter allows the best differentiation.

Methods

We examined both eyes of 56 patients (mean age 57 ± 15 years) with unilateral or highly asymmetric open-angle glaucoma (two of them had pigment dispersion syndrome) All had a difference in the mean defect (Octopus G1 program[3]) of more than 2 dB between both eyes or a difference in intraocular pressure of more than 5 mmHg. Exclusion criteria were: anisometropia > 2 dpt, ocular diseases other than glaucoma, mean defect (MD) of the better eye > 2 dB (except for eight cases with a slightly subnormal MD in the better eye but a ΔMD > ten dB)

Forty-two healthy volunteers (mean age 30 ± 6 years, ΔMD < 2 dB, normal visual fields) served as controls

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The optic disk structure was examined with two different methods: Rim area and cup disk ratio were measured with the Rodenstock Optic Nerve Head Analyzer (ONHA), which analyzes the three-dimensional shape of the disk using stereophotographs[4]. Cup volume ("volume below surface"), disk area, cup area (*i e*, area above the cup, "effective area") and the maximum depth of the excavation were determined with the Heidelberg Retina Tomograph (HRT). The latter uses a scanning laser camera to build up a three-dimensional image of the disk[5] Due to technical reasons not every patient was examined with both devices: 39 patients with unilateral glaucoma and 28 normals were examined with the ONHA, 42 patients and 23 normals with the HRT For each pair of eyes and parameter the intra-individual difference "healthy eye (with the better visual field or the lower IOP) minus affected eye" was calculated.

For each parameter the distribution of the intra-individual differences in the normal group was compared to the distribution in the unilateral glaucoma group. Statistical comparison was performed using the unpaired two-tailed *t* test.

Results

Mean differences (± standard deviation) for each distribution, *p* values and the number of patients with the (paradoxically) better values in the affected eye are given in Table 1. Sensitivities and specificities of the separation between our normal and our unilateral glaucoma group were calculated for the most powerful parameters (Table 1).

All distributions are summarized in a box plot diagram (Fig 1), giving the 10th, 25th, 50th (median), 75th and 90th percentiles. Separation power decreases from the left to the right. The two parameters measured with the ONHA ("rim area" and "CD ratio") showed a highly significant separation between normal and unilateral glaucoma. "Cup volume" and "cup area" were less powerful. "Disk area" and "max. depth" could not separate between both distributions

Discussion

From our data we conclude that marked optic disk asymmetries appear also in healthy persons. They can however, if pronounced enough, support the diagnosis of unilateral glaucoma. Glaucomatous damage may well be indicated by asymmetries in the rim area exceeding 0.3 mm^2, the CD ratio exceeding 0 2 and the cup volume exceeding 0 2 mm^3 These values lie far beyond the 90th or 10th percentile of the distributions of the normal controls (Fig 1).

Table 1 Mean differences (healthy eye-affected eye) in the unilateral glaucoma and the normal group (± standard deviation) and *p* values (*t* test) Sensitivities and specificities are calculated for an "optimal discrimination line" (0 16 mm^2 for the rim area, –0 07 for the CD ratio and –0 06 mm^3 for the cup volume) The right column shows the number of patients with the better ("healthier") values in the glaucoma eye

Parameter	*Mean ± SD*		*t test*	*Sensitivity*	*Specificity*	*Glauc eye better*
ONHA:	*Glaucoma*	*Normal*				
Δrim area	0 32±0 18 mm^2	0 01±0 17 mm^2	p=0 0001	85%	86%	1/39
Δcup disk ratio	–0 14±0 1	–0 01±0 11	p=0 0001	77%	79%	1/39
HRT						
Δcup volume	–0 2 ±0 28 mm^3	–0 02±0 16 mm^3	p=0 007	67%	70%	10/42
Δcup area	–0 19±0 34 mm^2	0 03±0 32 mm^2	p=0 01	–	–	12/42
Δdisk area	–0 04±0.19 mm^2	0 05±0 15 mm^2	p=0 05	–	–	16/42
Δmax depth	–0.04±0 16 mm	–0 01±0 2 mm	p=0.5	–	–	18/42

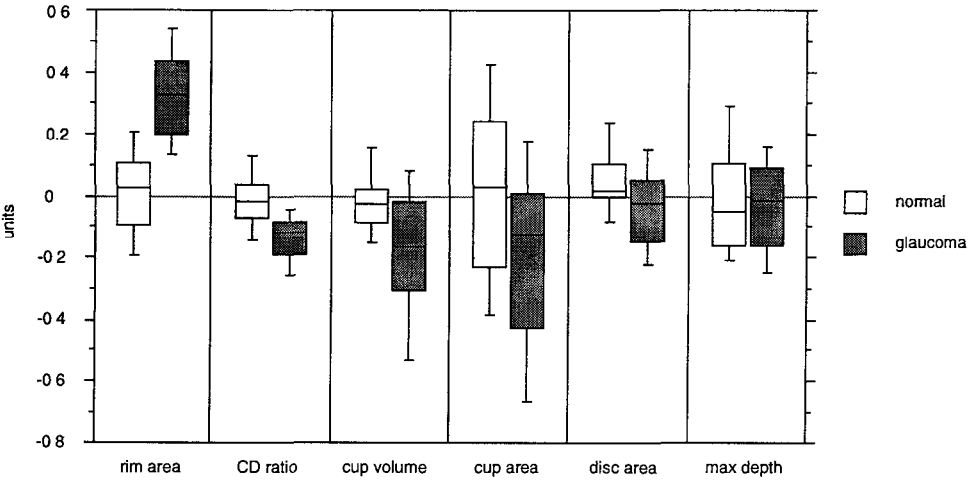

Fig 1 Box plot diagram showing the 10th, 25th, 50th, 75th and 90th percentile for each distribution Normals white, unilateral glaucoma patients grey Units are the same as in Table 1

Comparing the cup area of both disks is not as useful, differences in disk area and maximum depth are not useful at all

All glaucoma eyes in our study had a more or less advanced damage, we therefore cannot say which of the parameters tested *will change first* in the beginning of glaucoma The sensitivity and specificity values given above (Table 1) cannot be directly related to the detection of early glaucomatous damage, respectively. On the other hand we may draw the conclusion that disk area and maximum cup depth, measured with the HRT, do not change significantly in ongoing glaucoma, while rim area and CD ratio do The latter has already been demonstrated in a longitudinal study[6] using the ONHA.

O'Brien *et al*[7] showed that the most consistent and significant correlation between visual field loss and structural damage occurs at the disk surface, namely cup area In contrast correlation between visual field loss and nerve fiber layer thickness or area of pallor was poor[8].

Jonas *et al.* showed that disk size (area), measured by two-dimensional analysis, does not differ significantly between normals and glaucoma patients[9] Though the difference for disk area turned out to be borderline significant in our study, we believe that (with regard to this parameter only) statistics may be misleading: By definition the eye with the worse visual field was subtracted from the better one, though they are almost equal in normals. In the normal group it should be allowed to do this the other way round, leading to a change of the sign of all difference values (Table 1) All values in the glaucoma group would then remain similarly different from the corresponding value of the normal group, except Δ disc area. We therefore do not disagree with Jonas.

Definition of the parameters is different with the ONHA (based on stereophotographs[4]) and the HRT (a laser scanner[5]) Moreover the groups examined with the HRT and the ONHA differ slightly. Both may account for the better separation power of rim area compared to cup area, though for theoretical reasons the distributions for rim area and cup area should be similar (rim area + cup area = disk area)

Due to the marked overlap between normal and glaucomatous disk parameters, which has also been shown using other techniques[10,11], early glaucoma cannot be proven by a single measurement Longitudinal monitoring should be more appropriate[2].

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GLAUCOMA THERAPY

Brovincamine fumarate, Ca^{2+} blocker, favorably influences the prognosis of visual field defects of normal-tension glaucoma

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Abstract

In an attempt to evaluate the effects of brovincamine fumarate, a Ca^{2+} blocker, on the visual field defects (VFD) in NTG patients, we carried out a randomized, controlled study comprising 28 NTG patients (28 eyes) Fourteen received brovincamine 20 mg t i d p o and another 14 did placebo t i d p o. for at least two years Twenty-two were females and six were males Their age ranged from 42 3 to 71 2 years (52 9 ± 7 6, mean ± SD) The mean follow-up period was 37 9 months (SD: ± 9 9) Visual field was tested by Humphrey Field Analyzer (program 30-2) at least six times every four to six months during the study The changes over time in VFD were judged according to the significance level of MD slope calculated by Statpac 2 The change with p value less than 0 05 was taken as the significant, namely either improvement or aggravation The significant improvement of visual fields was observed in six eyes of six patients (42 9%) of the brovincamine treatment and visual field changes over time were statistically significant (p= 0 012, c^2 test with correction) Also the significant deterioration of VFD was seen in two patients (14 3%) in the placebo-treated group and in none in the brovincamine-treated group Stepwise discriminant analysis was carried out to identify prognosticating factors, demonstrating that brovincamine treatment, better cold recovery, and higher systolic blood pressure are significant factors and discriminant efficacy is 92 9% when the three factors are combined The drug seems to deserve further investigation as therapeutic means of NTG

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The acute and chronic effect of B_1-selective and non-selective beta-blockers on macular blood flow and contrast sensitivity in glaucoma

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Abstract

Macular blood flow (blue field entoptic simulation technique), contrast sensitivity (Pelli-Robson and Vistech) and intraocular pressure were measured in 20 patients with primary open-angle glaucoma in a double-masked, cross-over protocol Measurements were performed after a three-week washout period (baseline), after two hours and after three weeks of topical timolol and betaxolol administration in two treatment arms Placebo measurements were performed at baseline and two hours after a single dose Repeated measures analysis of variance, two-tailed paired *t* test and the Wilcoxon signed rank test were used to assess statistical significance

As expected, IOP was significantly lower after a single dose and after three weeks of timolol and betaxolol compared to baseline ($p < 0\ 001$) There was no significant change in leukocyte velocity (vel) or density (den) after acute or chronic dosing of timolol or betaxolol There was a small improvement in Pelli-Robson contrast sensitivity (cs) after acute dosing of betaxolol ($p = 0\ 076$) but not after timolol ($p = 0\ 377$) No significant change in contrast sensitivity was detected with the Vistech charts There was no significant difference in the change from baseline in vel, den or cs after three weeks of timolol versus betaxolol ($p > 0\ 05$)

B_1-selective and non-selective topical beta-blockers did not have a significant effect on macular blood flow in glaucomatous eyes Betaxolol exerted a small favorable effect of borderline significance on cs

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Is the visual field of patients with advanced POAG protected by lowering the IOP?

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Abstract

The authors evaluated the effect of a large decrease of IOP, obtained surgically, on the VF of patients with advanced glaucomatous damage Selection criteria were as follows: preoperative IOP > 21 mmHg; postoperative IOP < 16 mmHg on no medications; stable visual acuity and pupil size; preoperative visual field with MD > 6 dB (Humphrey 30-2); minimum follow-up of eight months Of the 27 patients who met the above criteria 14 had postoperative IOP < 12 and > 4 mmHg VF data were analyzed using the Statpac 2 glaucoma probability change program and the Wilcoxon Rank-Sum Test Median follow-up is 14 (range 6–25) months Results were:

Group	*N*	*MD changes**	*SF changes**
IOP 4–12	14	$p < 0.06$	NS
IOP 12–16	10	NS	NS
Total	24	$p < 0\ 000$	NS

* Wilcoxon Rank-Sum Test

Seven out of 25 (29%) cases showed an improvement of the MD with the Statpac 2 program ($p < 0\ 5$) Our data support the protective effect of a stable and large reduction of IOP against the progression of severe glaucomatous damage

Introduction

Lowering the intraocular pressure (IOP) is the only available treatment for primary open-angle glaucoma (POAG). A decrease in IOP can be accomplished by medications, laser therapy or surgery, with the hope of obtaining an IOP level compatible with long-term maintenance of the visual field. How to identify a "safe" IOP is controversial, and even more so is the ability of any given IOP to stop the progression of the disease. Several authors support the idea of the need of "low" IOPs for patients presenting with advanced glaucomatous damage[1–11] and propose as desirable targets values between 5 and 15 mmHg. Since the success of surgical procedures for glaucoma is usually measured by their ability to obtain an IOP below 21 mmHg, surgery defined as "successful" might in some cases not be lowering the IOP

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enough to preserve the visual field Purpose of our study is to evaluate prospectively the effect of a large decrease of IOP, obtained surgically, on the visual field of patients with advanced glaucomatous damage

Patients and methods

Selection of candidates

To be included in our prospective study, patients were selected as follows:

a) Preoperative criteria
– POAG with advanced damage, defined as mean defect (MD) ≥ 6 dB by Humphrey perimetry using program 30-2
– age > 60 years
– experience with automated perimetry (at least four previous field exams)
– preoperative IOP > 21 mmHg with maximum treatment despite ALT
b) Postoperative criteria
– postoperative IOP always ≤ 16 mmHg on no medications
– stable pupil size (≤ 1 mm change) and visual acuity (≤ 1 Snellen line change)
– minimum follow-up after surgery of six months

Twenty-five patients met all the criteria, with a median follow-up of 14 months and a maximum of 24 months. All patients were judged to be good candidates for filtration surgery. In none of the cases was the IOP < 4 mmHg after treatment.

Surgical technique

In all cases *ab externo* photoablative filtration surgery was performed with the excimer laser, the technique is detailed elsewhere[12,13]. In brief, after topical and subconjunctival anesthesia with 2% plain xylocaine, a bridle suture is passed under the superior rectus or transcorneally and a limbus-based conjunctival flap is dissected After cleaning and cautherizing the sclera, the laser beam is directed *ab externo* to the limbal area overlying Schlemm's canal, while the globe is rotated downwards In order to obtain a rectangularly shaped beam, photoablation is performed through a custom-made metal mask, and is carried until acqueous percolates at the bottom of the photoablative crater. The conjunctiva is then sutured water-tight with 8-0 running virgin silk We used a Summit Technology Excimed LA 200 excimer laser emitting at 193 nm with a fluence of 180 mj × sq\cm at 10 Hz Our early clinical results are characterized by final IOPs in the low teens, with minimal inflammation and low complication rate[12,13].

Visual field testing

All patients underwent Humphrey computerized perimetry using program 30-2. The parameters mean defect (MD), pattern standard deviation (PSD) and short-term fluctuation (SF) were measured and compared using Wilcoxon's Rank-Sum Test. The visual fields were also analyzed using the Statpac 2 program

Results

The results of visual field analysis are detailed in the tables. On the whole sample ($n = 25$) the MD showed a statistically significant decrease; this was not confirmed on a subset of pa-

Table 1 Median F U 14 months (min 6–max 25) Mean defect pre- vs post IOP lowering

min F U 6 months $n = 25$ $w = 191$ $z = 3.31$ $p < 0\ 000$ Significant improvement	IOP < 12 Hg $n = 14$ $w = 81$ $p < 0\ 06$ Significant improvement
min. F U ≥ 12 months $n = 14$ $w = 57$ $p > 0\ 06$ No significant change	IOP ≥ 12 mmHg $n = 11$ $w = 57$ $p < 0\ 06$ No significant change

Wilcoxon Rank-Sum Test

Table 2 Statpac 2

Total No 25	
	7 (29%) improved 16 (64%) not significant 2 (8%) worsened
IOP ≥ 12 mmHg 10 patients 2 (20%) improved 6 (60%) no significant change 2 (20%) worsened	IOP < 12 mmHg 15 patients 5 (34%) improved 10 (66%) no significant change

$\chi^2 = 3.42$; $p = 0\ 18$

tients ($n = 14$) with minimum F.U ≥ 12 months When separated into two groups according to the IOP levels, patients maintaining IOP levels < 12 mmHg ($n = 15$) showed a significant decrease of their MD (Table 1). Using the Statpac 2, our total sample showed an improvement in seven (29%) cases and a worsening in two (8%) cases; although the subgroup with IOPs < 12 mmHg performed better than those with IOPs between 12 and 16 mmHg the difference was not statistically significant (Table 2). Short-term fluctuation and pattern standard deviation did not vary significantly.

Discussion

The favorable effect of lowering the IOP in glaucomatous patients is supported by several authors[1–11]. The idea of individualizing the target IOP for each patient, thus identifying the desirable pressure is gaining acceptance[14–15]. The concept of target pressure changes the approach of our management for glaucoma; instead of aiming to a percentage decrease from baseline IOP or rather more commonly to a non-specific level below 21 mmHg, the ophthalmologist should decide beforehand the IOP level considered safe for the individual being treated, and proceed upwards along the therapeutic stepladder until the target is eventually reached. Obviously, risk factors besides the IOP will need to be considered[16]. Our data show an overall decrease of the mean defect occurring after glaucoma surgery lowered the IOP to levels never exceeding 16 mmHg on no treatment It is interesting to note that in the subgroup with relatively higher IOPs this change was not significant. When evaluated with the Statpac 2 program, visual field improvements were 3 5 times more frequent than worsening This compares favorably with the reported course of advanced POAG[3,5] We have no explanations for those eyes showing a worsening by Statpac 2, despite stable IOPs below 16 mmHg. Our study has several drawbacks; first of all our results are short-term, especially considering the chronic nature of POAG We did not attempt to define target pressures for each individual nor for the group as a whole; even though some authors are indicating similar IOP values as reasonable for patients with advanced disease, the cut-off at 16 mmHg was chosen arbitrarily. In conclusion, we cannot yet explain why in some patients the visual field continues to deterio-

rate despite an IOP ≤ 20 mmHg: is it because some POAG are pressure-lowering insensitive or because the IOP was not lowered enough? Our data support the hypothesis of a protective effect of a drastic and stable reduction of IOP on the visual field of patients with advanced POAG.

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Influence of trabeculectomy with mitomycin C on the visual field

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Abstract

The authors present their experience with trabeculectomy combined with mitomycin C and its influence on visual field and visual acuity Mitomycin C was applied (0 28 mg/ml) during two to five minutes intraoperatively in 32 eyes from 31 patients The visual field was measured with Octopus program G1 several times before and at least once six months after surgery As expected, six months after surgery the mean intraocular pressure was markedly and statistically significantly decreased Despite frequent hypotony, the visual field and the visual acuity recovered to preoperative values in this six-month follow-up and were on the average even slightly but statistically not significantly improved

In glaucoma patients with uncertain prognosis for intraocular pressure, the intraoperative application of mitomycin C definitely and considerably improves the intraocular pressure prognosis It did not produce major adverse effects on visual field and visual acuity during a six-month follow-up However, long-term studies on a larger group of patients are necessary to confirm the present results

Introduction

Patients with excessive fibrosis have a poor prognosis for the outcome of ocular surgery. Due to this fact, during the last years many different substances, such as steroids, beta irradiation, and antimetabolites, have been applied to modulate this wound-healing process Of the latter, one of the latest is 5-fluorouracil, which normally needs to be injected several times in the postoperative phase Its complications are already known[1,2].

However, encouraging results with the application of mitomycin C in ophthalmology have been reported[3–5] Mitomycin C is especially effective in trabeculectomy[3, 4], where modulation of the wound-healing process is desirable to improve the surgical success, especially in glaucoma patients associated with risk factors for failure in trabeculectomy, such as congenital, juvenile, neovascular, secondary, and black race, among others.

Mitomycin C is an antibiotic which also has an alkylating cytostatic effect[6]. It inhibits DNA synthesis secondary to alkylation and proliferation of cultured animal and human subconjunctival fibroblasts, to an extent 100 times higher than that of 5-fluorouracil[7].

However, complications, such as hypotony characterized by maculopathy, disk edema, vascular tortuosity, and chorioretinal folds, which do not always improve with the resolution of the hypotony, have been described[8–10] The purpose of the present study was to evaluate the influence of trabeculectomy with mitomycin C on the outcome of visual function, particularly visual fields and visual acuity. Of special interest was the question whether early complications, such as hypotony, flat anterior chamber, choroidal effusion, or either disk or macula edema, have any influence on the functional outcome

Subjects and methods

From June 1992 until May 1994, 121 eyes from 109 patients underwent trabeculectomy with intraoperative application of mitomycin C in our clinic. At present we have a six-month

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Table 1 Patients and diagnoses

Diagnosis	*No of patients*	*No ALT*	*Prior surgery*	*Refractory glaucoma*
POAG	22	8	8	4
Pigmentary	3			1
Pseudoexfoliation	3	1	1	1
Juvenile	3	1	2	2
Normal tension	1			

No ALT: number of patients who had had argon laser trabeculoplasty before surgery

perimetric follow-up in 32 eyes from 31 patients. The mean age±SD was 60±14 (27 to 84) years The indications for trabeculectomy with application of mitomycin C were: young age, prior surgery, and refractory glaucomas (intolerance to long-term treatment with antiglaucomatous therapy or progression of visual field under maximal therapy). The diagnoses are listed in Table 1

Informed consent was obtained from all patients All trabeculectomies of the included cases were performed by the same surgeon (JF) and with the same technique. A limbal-based conjunctival flap was created, and a saturated sponge with mitomycin C (0 28 mg/ml) was applied intraoperatively between tenon's capsule and episclera. The application time varied between two and five minutes. Abundant rinsing with balanced salt solution was performed After preparation of a corneo-scleral flap, a trabeculectomy with a punch and iridectomy with scissors were performed A suture of the corneo-scleral flap and, finally, a separate closure of tenon and conjunctiva were performed.

All patients had had previous experience in Octopus automated perimetry. The visual field was measured with Octopus program G1[11] several times before and at least once six months after surgery Mean defect (MD) and square root of loss variance (SQRT-LV) were taken as perimetric variables for statistical analysis. The paired *t* test as well as the non-parametric Wilcoxon test were performed for statistical analysis.

Results

Six months after the surgery, the mean intraocular pressure (±SEM) was markedly and statistically significantly decreased from 24±0.9 mmHg to 11±0.8 mmHg ($p<0.001$). Despite frequent hypotony, the mean MD±SEM in the visual field tended to improve from 10.9±1 3 dB to 10 2±1 2 dB ($p= 09$); as well as the mean SQRT-LV±SEM from 5.9±0 5 dB to 5.8±0.5 dB; the improvements were statistically not significant (Figs 1, 2, 3) The visual acuity recovered to preoperative values in this six-month follow-up

In our population, the frequency of early postoperative complications, such as hyphema, mild inflammation, and flat anterior chamber was about the same in patients with trabeculectomy with and without mitomycin C. The most frequent complications were hypotony ($n=6$) and extensive choroidal effusion ($n=3$) in this particular series, which normally resolved spontaneously

Healon GV was applied postoperatively to deepen the anterior chamber in two cases. One myopic patient developed hypotonic maculopathy with disk edema and chorioretinal folds; all these signs disappeared without any treatment. The visual acuity recovered totally within a few months

Discussion

From these results we can confirm that, in glaucoma patients with uncertain prognosis for intraocular pressure, the intraoperative application of mitomycin C definitely and considerably improves the intraocular pressure prognosis. Many studies report frequent hypotonic

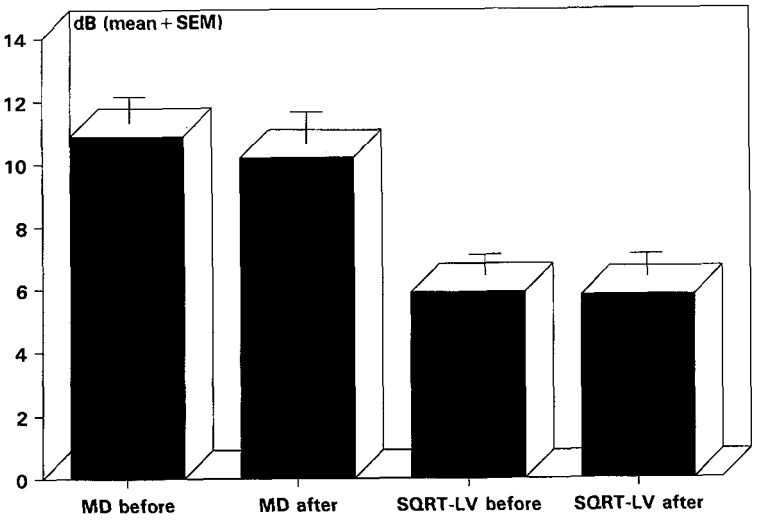

Fig 1 Mean visual field indices, MD and SQRT-LV, before and six months after surgery Slight improvement can be observed.

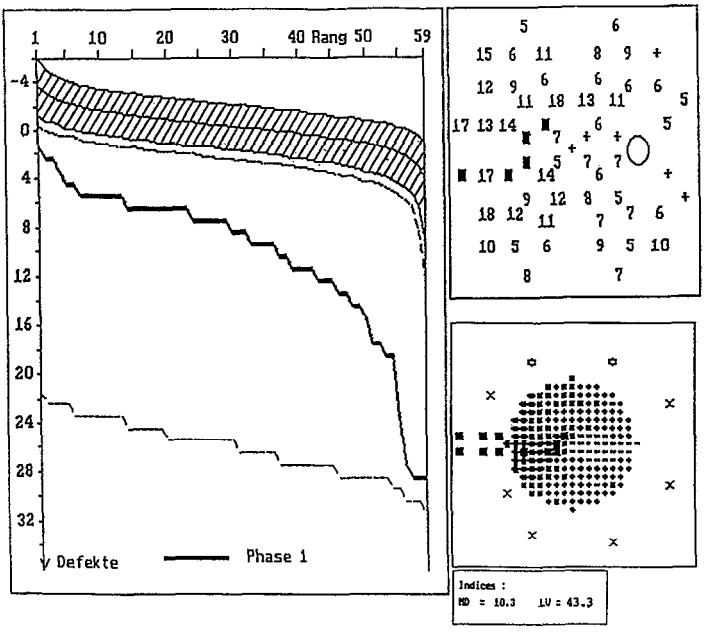

Fig 2 Typical example of a visual field of a glaucomatous patient represented with the Bebie curve, CO print out and grey scale before surgery

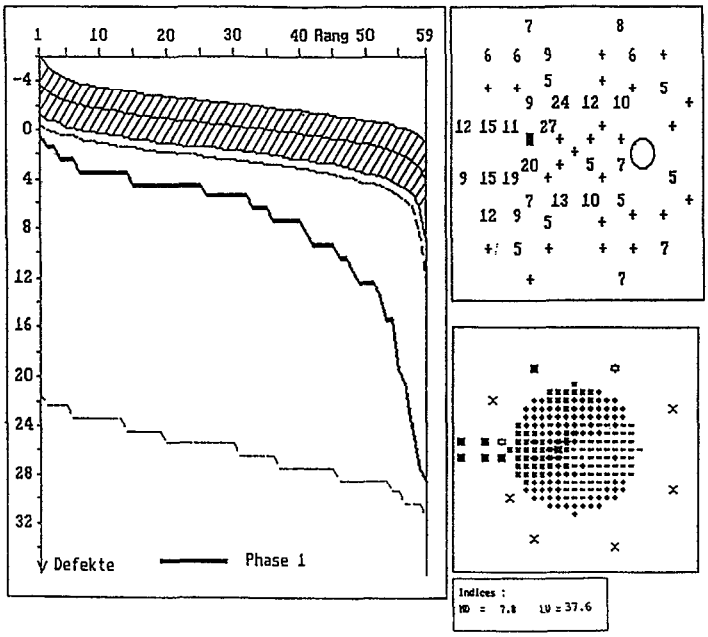

Fig 3 Same eye as in Figure 2, six months after surgery.

maculopathy However, the application time and the concentration of the drug differ considerably from one study to another In our population, it did not produce major adverse effects on visual field and visual acuity during a six-month follow-up period. However, long-term studies on a larger group of patients are necessary to confirm the present results.

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SCREENING

Vision assessment behind dense cataracts in developing nations

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Abstract

An advanced design, precision Vernier acuity (hyperacuity) test instrument is being tested at Aravind Eye Hospital, Madurai, India This device has evolved from earlier forms A high luminance orange three-point display is used The patient sets the moveable central stimulus in line with two vertically disposed fixed stimuli This instrument is a precursor to a field device to be used later in a clinical study Both central and non-central points can be tested (although here only tests of central vision are considered) We seek to predict post-surgical vision outcomes for the ophthalmic surgeon This is a critical issue in developing nations where 20–30% of cataract surgeries do not result in a satisfactory visual result.

Here, two challenging sets of problems are considered The experiments conducted are of interest in their own right; and some difficulties associated with translating a laboratory finding to a developing world setting are detailed

Introduction

Using high luminance, small visual stimuli (Fig 1), Vernier judgments (a hyperacuity test) can be made in the presence of markedly degraded retinal imagery Without coaching, observers perform center-of-gravity assessments of the relative locations of these degraded images. Utilizing this principle, we seek to define, pre-surgery, those individuals who will derive most benefit from cataract removal; and, because two eyes are rarely treated in a developing world setting, we want to determine which of two cataractous eyes has the better post-surgical visual prognosis Given very large backlogs of patients awaiting treatment in developing nations, these tests are very useful, particularly for triage.

We conducted preliminary research on the defined hyperacuity test at Berkeley[1]. Later, added studies were performed at the Aravind (Free) Eye Hospital, Madurai, India[2,3] This research is preliminary to a planned clinical study at Aravind.

At Berkeley, we sought to determine the number of repeat trials necessary; to compare a two-point and a three-point Vernier display; to determine the shape of the measured response function at large gap (or feature) separations between test stimuli, to define optimal test distance and stimulus dimensions; to assess the effect(s) of a broad range of uncorrected

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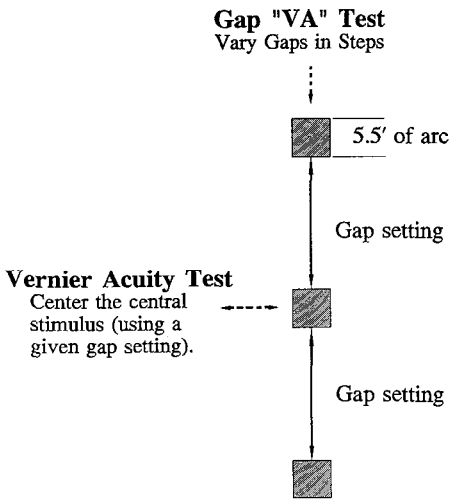


Fig 1 A schematic drawing of the three stimulus array Both the "in-line" array (variable gap separations) devised for the Gap "VA" test, and the variable center stimulus position used in the Vernier acuity test are shown.

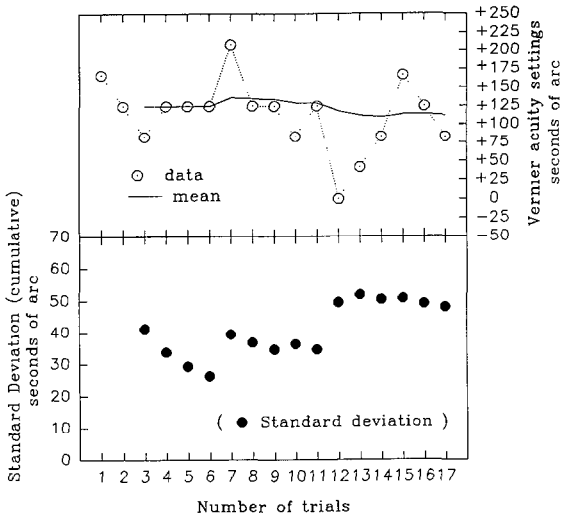


Fig 2 Sample plot of cumulative mean and standard deviation determinations obtained during a single Vernier acuity test run using a two-point test array at Berkeley For each trial, the moveable point is located + or – (right or left in arc seconds, open dots) relative to the vertical location of the stationary stimulus point (position zero on the right-hand ordinate) After the first two determinations, as each data point is acquired (here, a total of 17), a new mean value (line, refer to right ordinate) and standard deviation (filled dots, refer to left ordinate, lower graph) are determined Clearly, a single determination can markedly influence resultant standard deviation, particularly if a limited number of trials are used

refractive errors upon outcomes, and to consider means to minimize refraction-based errors by using a pinhole, a vision correction, and/or spatial filtering. And we correlated a new mechanical hyperacuity test device controlled by computer (since delivered to Aravind Hospital – "the India instrument") with current laboratory equipment (CRT/VDT based,

computer controlled) providing comparable stimuli – "the Berkeley instrument" (used in all studies mentioned above). The Berkeley instrument has lower liminous emittance than the India instrument Adjustment of luminance settings permitted correlation of the two devices College age adult normal subjects were used in the studies, wore their usual visual corrections, and were tested with and without simulated dense nuclear cataracts.

Based upon results of these studies and prior research[1], a preliminary "hyperacuity study protocol" (HASP) was defined. HASP was then tested upon the advanced cataract population at the Aravind (Free) Eye Hospital using the India instrument. Meaningful difficulties were encountered, and substantial changes had to be made in the proposed protocol This paper considers briefly the results of the Berkeley-based experiments[1], conditions causing alterations in the planned protocol, approaches taken to resolve problems encountered, and the current status of the modified HASP protocol[1–3].

Apparatus

We distinguish four instruments Both instruments 2 and 3 will be used in conjunction with the HASP protocol

1 "The Berkeley instrument" This is a computer-driven instrument located at Berkeley used for testing hyperacuity functions with emphasis upon clinical applications[1]. It utilizes a cathode ray tube (CRT) display and a "mouse" for response (see results, Figs. 2–5)

2. "The India instrument": Instrument 2 is computer-driven, and contains a high luminous emittance quartz/halogen source and orange filter which illuminate a triple fiber optics bundle (which provides the three stimuli now used) The locations of the stimuli are mechanically controlled by a computer which drives precision translation and position readout devices. This device is now in India (see results, Figs. 5–7). The instrument is sturdy, and its remarkable versatility allows us to determine properly final instrument parameters for conduct of both the clinical study (instruments 2 and 3) and for design of a device suitable for developing world applications (instrument 4). The stimulus displays used for both the Gap "VA" test (see below) and the Vernier acuity (hyperacuity) test are presented in Figure 1 Instrument 2 will be used for added preliminary studies, correlated with instrument 3, and post-surgical testing (and as back-up) in the clinical study

3. The clinical study instrument, instrument 3, is an intermediate-stage field test device. It is a greatly scaled down and simplified version of instrument 2. It is much less costly, it is still more rugged, it has only rudimentary data processing capacity, and one moving part. This is the field triage hyperacuity device planned for use in the clinical study. Parameter range selections are restricted, and it is designed for, but not limited to pre-surgical testing. High intensity quartz/halogen lamps are used as light sources in instrument 3

4. The hyperacuity triage instrument, instrument 4, will be used in the field in developing nations. We distinguish between instruments 3 and 4 (which are similar), because the planned clinical study will include large numbers of patients examined pre- and post-cataract surgery Instrument 3 has added computer readout capability in order to facilitate large volume data handling. Instrument 4 will be easy to use, and will provide the data necessary for individual patient evaluations.

Parameters defined in these studies will be incorporated into the design of instruments 3 and 4. No problems are anticipated relative to realization of design goals

Preliminary findings: U.C. Berkeley

1. Based upon analyses of cumulative mean and standard deviation determinations of data sets (see sample data set in Fig. 2) and reliability studies, 8–10 repetitions of the Vernier acuity test were deemed acceptable. The highest and lowest values recorded in each data set were dropped prior to data processing. This resulted in satisfactory stability in a data set (defined as less than 5% change in standard deviation)

2. Data obtained using a two-point Vernier acuity display ("Line up one point exactly above

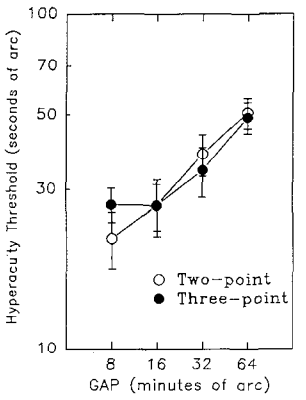


Fig 3 Vernier acuity data (the "gap function") were obtained for a two-point and a three-point Vernier acuity test array (combined data of ten subjects) No real differences in response emerged in the normal young adult subjects tested with and without (data presented here) a ground glass plate [GG] being interposed (1) GG was set to simulate a 6/60 (20/200) nuclear cataract (these data are not shown in this figure). On the ordinate, Vernier acuity thresholds (measurements of standard deviation in seconds of arc, scaled logarithmically) are indicated, and on the abscissa gap settings utilized for these tests (in minutes of arc, scaled logarithmically and varied in octave steps) are presented.

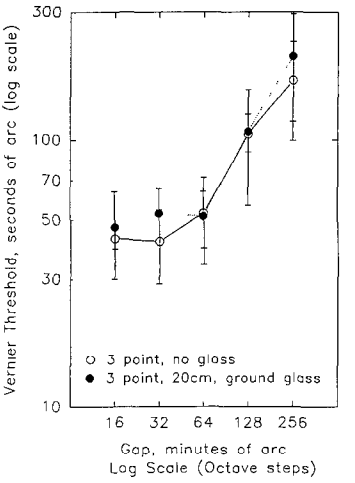


Fig 4. Does the Vernier acuity gap function flatten at large gap settings such as might be necessary for measurements conducted upon the advanced cataract population at Aravind? And is there an effect of image degradation? Both questions were tested on four normal subjects at Berkeley Mean data presented here show little or no flattening at large gaps, and image degradation did not alter this result So saying, in the individual data set, occasionally modest flattening is recorded (*e.g.*, see Fig 2 in Ref. 3) Ordinate and abscissa as in Fig. 3.

the other".) or a three-point display ("Locate the central point exactly in line with the two end points".) provided essentially equivalent results whether the image was sharp (Fig. 3), or degraded The three-point display is much easier to describe to an individual with limited education and was adopted for use in this program.

3 The shape of the gap function (Vernier threshold vs gap separation) is not altered for large gaps (Fig 4), although there is modest upper end flattening of the curve in some normal subjects[1–3] Also, see Aravind advanced cataract patient data in Figure 7

4. Because of size considerations associated with physical gap dimensions, and limited space available in developing world examination areas, test distance was set at two meters.

5 Gaps selected for use were 2′, 4′, 8′, 16′, 32′, 64′, 91′*, 128′, 181′*, 256′, 362′* (of arc). Octave steps (0 3 log unit) are used At large gaps, half-octave steps (*) are employed.

6 The measured hyperacuity estimate is improved when refraction is corrected. If this is not possible, a 2.0 or 2.2 mm pinhole markedly improves visual performance.

7 High spatial frequency noise often causes spurious resolution, *e g*, patients with posterior subcapsular cataract frequently report multiple images of a point object, or individuals with uncorrected astigmatism experience lineal distortion(s) of a point source. Removal of high spatial frequencies from stimuli in such situations improves measured hyperacuity responses[4,5] A ground glass plate (GG) separated from the stimuli serves as a spatial filter, and while it affects all spatial frequencies, it most affects high frequencies.

8. The India instrument correlated satisfactorily (correlation coefficient +0.70) with the Berkeley instrument set at the same retinal illuminance setting[1]. In Figure 5, these same data are plotted in the format used in Figures 3 and 4. Performance on the India instrument was slightly better, partly because when using that instrument we did not encounter the pixel size limitation inherent in the CRT display of the Berkeley instrument. The pixel size problem was

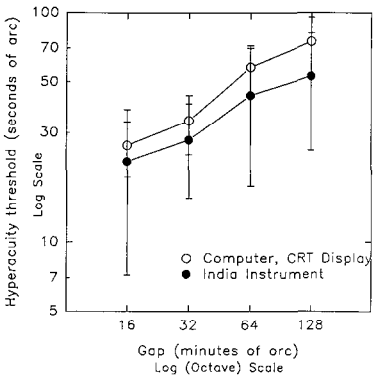


Fig 5 Combined data of eight subjects obtained on both the Berkeley and India instruments are plotted using near identical conditions at a test distance of 2 meters These mean data have essentially the same slope, but performance on the India instrument is slightly better (see text) Ordinate and abscissa as in Fig 3.

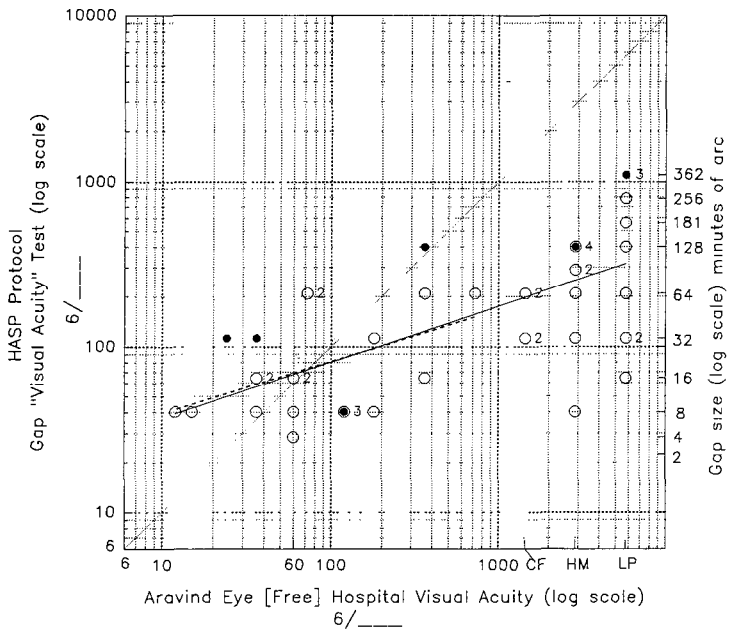
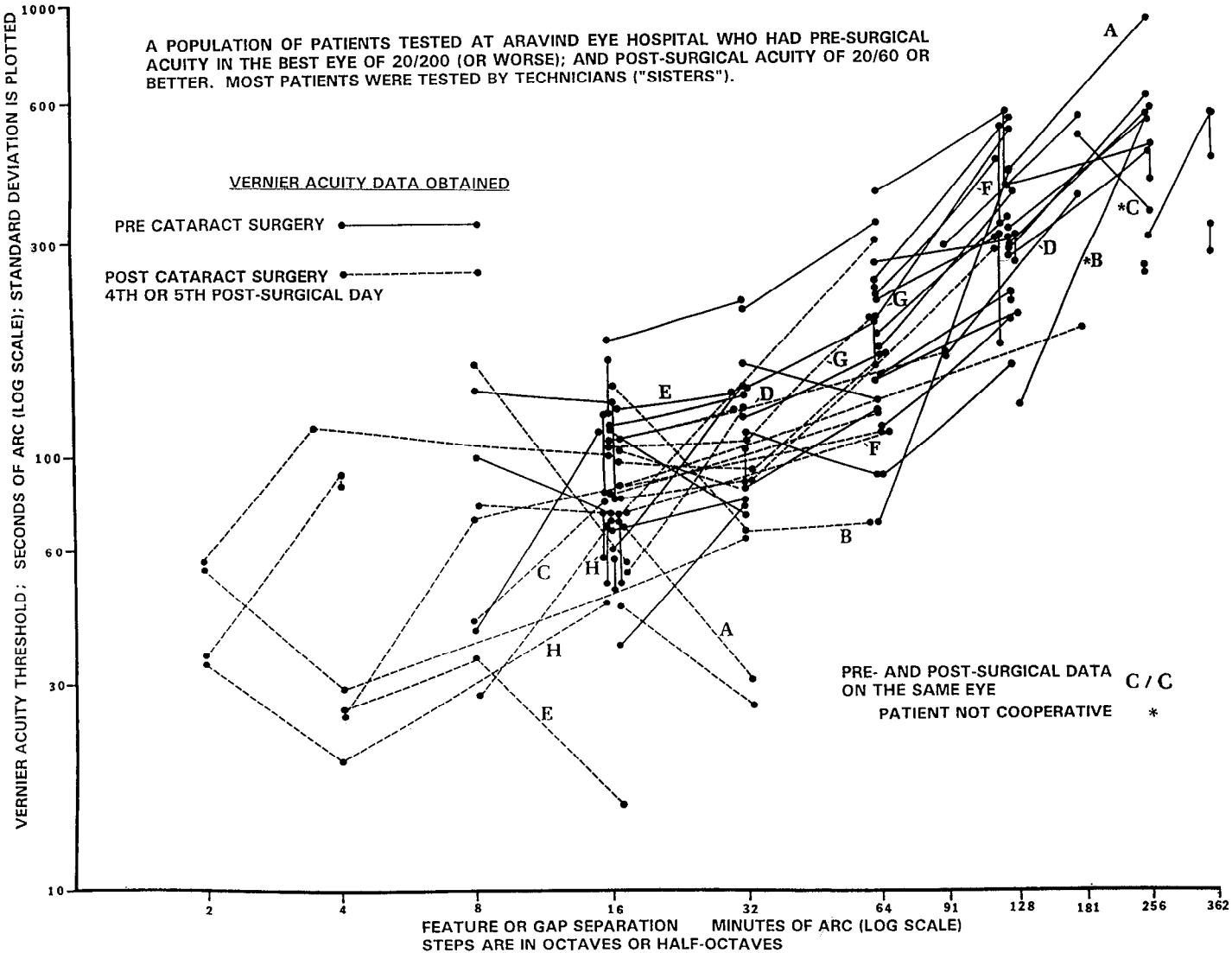


Fig 6. These visual acuity data were obtained preoperatively on a population manifesting advanced cataracts at the Aravind (Free) Eye Hospital. Gap "VA" measurements (ordinate) are compared with Aravind VA determinations (abscissa) Log scaling is used The denominator of the Snellen fractions, English system, is plotted, *e g* , 6/12 is plotted as 12 The X,Y origin is set at the equivalent of LogMAR = 0 0, or Snellen VA 6/6 Each dot represents data obtained on both tests for the same eye; unfilled dots are data obtained from eye of cooperative patients, and black dots, from uncooperative patients; points with numbers appended indicate the sum of overlapping data points, and a symbol with a filled circle within an unfilled one indicates that both cooperative and uncooperative patients shared this value. The two regression lines presented, and the location of CF, HM, and LP on the abscissa are discussed in the text Note the non-linear scaling of gap values on the right ordinate (see "duty cycle", Ref 2)

aggravated by use of a 2 meter test distance for this experiment. Previously, using a 4 meter test distance, the Berkeley instrument compared well with other apparatuses used in this laboratory, and with Westheimer's instrument[6–11]

9 To simplify data recovery by technicians (or computers) in developing countries, Mitutoyo digital readout indicators are used instead of micrometers


A POPULATION OF PATIENTS TESTED AT ARAVIND EYE HOSPITAL WHO HAD PRE-SURGICAL ACUITY IN THE BEST EYE OF 20/200 (OR WORSE); AND POST-SURGICAL ACUITY OF 20/60 OR BETTER. MOST PATIENTS WERE TESTED BY TECHNICIANS ("SISTERS").
VERNIER ACUITY DATA OBTAINED
PRE CATARACT SURGERY
POST CATARACT SURGERY
4TH OR 5TH POST-SURGICAL DAY
PRE- AND POST-SURGICAL DATA ON THE SAME EYE C / C
PATIENT NOT COOPERATIVE *
VERNIER ACUITY THRESHOLD: SECONDS OF ARC (LOG SCALE); STANDARD DEVIATION IS PLOTTED
1000
600
300
100
60
30
10
2
4
8
16
32
64
91
128
181
256
362
FEATURE OR GAP SEPARATION MINUTES OF ARC (LOG SCALE)
STEPS ARE IN OCTAVES OR HALF-OCTAVES

Fundamental changes in protocol required as a result of preliminary studies conducted in India

1 At Aravind, it was not feasible to use head restraints, nor fixed pinholes on this patient population. Trial frames could be used (but not with inserted pinholes)

2. These advanced cataract patients cannot manage joystick, trackball or mouse control devices. For response, they will tap a washer or coin with their right hand

3 Technicians ("sisters") operate the response device Almost all patients broadcast their readiness to respond by raising the washer/coin some seconds before responding (this reaction is carefully observed) And patients will only respond to one-direction tracking of a moving point of light (*i.e* , they will not refine measurements back-and-forth). For improved control of responses, technicians were taught to make intermittent, but near continuous, the motor-driven translation of the stimulus (so the stimulus does not pass through the judgment area at a rate too rapid for response by these patients)

4 The sisters performed refractions and VA assessments of eyes of patients with advanced cataracts. An analysis of patient records indicates that either refractions could not be conducted on many of these eyes, or the refractions tended to be rudimentary. This created uncertainty in interpretation of refraction data and Aravind VA measurements

A number of these patients believed that if they gave evidence of other than marginal sight (or any sight) in an eye, they would not receive surgery The eye with worst Aravind VA was operated, but if VA was equal in both eyes, the patients selected the treated eye.

Given these and other factors[2], a rapid and simple additional visual acuity test was developed for use in the HASP protocol. This was termed the Gap "VA" test It provided a rational basis for selection of gaps for Vernier acuity testing

For Gap "VA" assessment, we used the three-point instrument display in-line as a resolution test (Fig 1) and asked how many points could be seen. If three points of light were detected, gap separations were reduced by 1 octave (for gaps above 64′ of arc, 1/2 octave steps were used). When only one or two points of light were reported as seen, gap separations were comparably increased. The smallest resolved gaps were recorded as the Gap "VA" for the eye tested. This test was repeated (two common readings were required). Note, the three stimuli used in the Gap "VA" test were intensely illuminated (see below), and unequal stimulus separation steps occurred as a result of octave (or half-octave) step changes in gap settings[2]. The latter effect is seen on the right ordinate of Figure 6

Figure 6 provides visual acuity (VA) data obtained prior to surgery on the advanced cataract population at Aravind; both eyes were tested. This figure compares routine Aravind VA data with Gap "VA" results. Two regression lines are plotted in this figure The dashed

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←

Fig 7 Vernier acuity data were obtained pre- and post-cataract surgery from eyes of patients who had advanced cataracts and Aravind VA equal to, or poorer than 6/60 (20/200) in both eyes prior to surgery. All patients reported here had post-surgical Aravind VA of 6/18 (20/60) or better (most had 6/12) in the operated eye measured at discharge 4 or 5 days after surgery. For the population defined in this figure, this implies that visual response in the central retinal area was most probably relatively normal in both eyes prior to cataract surgery Pre-surgical Vernier acuity measurements are designated with solid lines, and post-surgical determinations are indicated by dashed lines. Fewer Vernier acuity data points were recorded post-surgery than pre-surgery Surgery was performed on only one eye, and some problems of patient access were encountered For easy comparison of results, some pre- and post-surgical data from the same eye are identified by letters A and A, B and B, etc , and an asterisk indicates a non-cooperative patient.

Vernier acuity thresholds, plotted on the ordinate, were obtained from individual data runs The gap setting used for each test run is plotted on the abscissa Gap steps are expressed in octaves or half-octaves, and 1 octave = 0 3 log unit. A small proportion of pre-surgical patients wore a refractive correction during the test, most did not. Some data were taken by Enoch, most by the sisters (but supervised by Enoch). Included are the sister's training trials (except the first trial) Some data were obtained during development of the protocol In spite of inconsistencies in this data set, a highly coherent picture of response emerges. Data were acquired during a one-month period

line includes data on all patients except those with Aravind VA determinations of count fingers (CF), hand motion (HM), and light perception (LP). The darker line includes all data. The latter assessment was a test for appropriateness of placement of CF, HM, and LP designations on the abscissa. A Gap "VA" measurement could be made on all patient eyes (Fig. 6; for details see [2]), and provided a superior estimate of VA in more advanced cataract cases (Fig. 6) Filled circles indicate less cooperative patients. They generally had poorest performance on Gap "VA" measurements.

Afterwards, when examining Vernier acuity, the first gap selected for evaluation was set one octave larger than the measured Gap "VA". After conducting two trial runs at this setting, the gaps were reduced by one octave and one additional trial was run.

5 Figure 7 provides results of Vernier acuity measurements made on patients prior to (solid lines) and after (dashed lines) cataract surgery Both eyes of patients included in Figure 7 had Aravind VA prior to surgery equal to or worse than 6/60 (20/200); the eye with poorest Aravind VA was operated upon; and, after surgery, that eye had to have Aravind VA of 6/18 (20/60) or better.

6. Poor hyperacuity response (high measured standard deviations) when using central fixation has five possible causes (a) Inexperience or inattention during testing on the part of the technician This is resolvable. (b) Inattention on the part of the patient This is variable, but addressable through training, rests, or refreshments. (c) Improper refraction. In some cases this can be resolved. Even if not resolvable, this is a constant during testing. (d) Image degradation caused by the cataract or other media opacity. This is a constant. There is one exception, *i e* , in the presence of a Morgagnian cataract, head movement induced translation of the eye lens nucleus within the largely liquified hypermature cataract cortex could transiently alter the optical properties of the eye. Stability of head position can be monitored. (e) Poor central fixation caused by a macular disorder This is a variable

Prior to surgery in these patients, one of the conditions we seek to determine is the presence of a central macular disorder behind the cataract We predict poor fixation or macular function to be revealed by higher variance when testing the Vernier threshold in the presence of such a disorder. We expect more variable outcomes on test-retest in such patients if non-stable fixation or eccentric viewing are present, *i.e* , condition 6 (e) pertains. Thus, the primary gap setting selected for use in testing Vernier acuity is tested twice. Added data are needed in order to test further this hypothesis.

7. Grading of cataracts· In order that appropriate instrument settings could be utilized in individual patients, an easily applied and rapid grading scheme for cataracts was developed for this project at Aravind by Drs N.V. Projna and G Rohini, ophthalmologists. The following catagories of cataracts are defined: (a) hypermature, (b) mature, (c) immature cortical, (d) nuclear, (e) posterior subcortical, (f) mixed (order of importance and types specified), and (g) other (type[s] specified) Degree of cataract is graded in four steps based on distant direct ophthalmoscopy (1 meter), and customary direct ophthalmoscopy[3] Entrance pupils are dilated to at least 6 mm diameter for purposes of grading. Emphasis is placed on the effect of the cataract upon vision

Test conditions currently defined for HASP[2,3]

1. An orange filter (Schott Glass filter, # OG 570) is used, because longer wavelengths of light are less affected by the yellow pigments of the eye; longer wavelength stimuli do not fluoresce in the visible spectrum; this pass-band is absorbed less by hemoglobin and oxyhemoglobin; longer wavelengths are not markedly affected by Raleigh scatter (a minor factor here); and removing shorter wavelengths of light does not markedly affect luminance.

2. Three luminance levels were selected after extensive trials on patients.

Normals, cataract grade 1, and post-cataract.	$6\,0 \times 10^3$ c/m^2
Cataracts grades 2–3	2.3×10^5 c/m^2
Cataracts grade 4 (includes most mature and all hypermature cataracts):	$5\,6 \times 10^5$ c/m^2

Note, because only 4 patients with hypermature cataracts have been seen to date (only two measured), we have not yet fully assessed the effects of the position of the lens nucleus in Morgagnian cataracts; nor have we determined the affects of calcium deposits on Vernier

responses; nor the effects of (or need for) pupil dilation in these patients; nor whether, in some cases, a different test distance (1 m?) or added luminance is preferable; etc.

3. The eye with best Aravind VA is tested first and the patient is instructed

4. For operational applicability, 8 repetitions of response are determined per trial run; the high and low settings are dropped; and mean and standard deviation are computed.

5. For hyperacuity assessment, the first gap setting examined is 1 octave larger than the best measured Gap "VA" determination Vernier acuity response is tested twice at this setting. Then, the gaps are set 1 octave smaller and the Vernier acuity test is repeated

6 The ground glass is set 1 mm from contact with the fiber optics bundles in all cases except in patients with high uncorrected astigmatism and/or dominant posterior subcapsular cataract. In those cases, the ground glass is set at 2 cm from the ends of the fiber bundles[3–5] The ground glass used in India ([1–3], and Figs. 5–7) was ground more deeply, and had a coarser grind than that used in research conducted at Berkeley ([1], and Figs. 2–4)

7 When testing Vernier acuity, the rate of translation of the moveable stimulus varies with gap separation: (a) 12 or 6 mm/sec for gaps 128′ of arc or larger, (b) 4 mm/sec for gaps 16′ of arc to 91′ of arc, (c) 2 mm/sec for gaps 8′ of arc or smaller (minimum setting, 2′ of arc) Note, a translation of 1 mm/sec = 1 72 minutes of arc per sec.

8 Stimuli· 5.5′ × 5.5′ square, at the 2 m test distance used 3 luminous stimuli disposed vertically.

Current status of the hyperacuity project: brief summary

Very good progress has been made in the development of both the apparatus and a technique for assessment of vision in the presence of dense media opacities. Currently, no difficulty is encountered when assessing vision through mature cataracts No window is needed. However, there are questions which need resolution which will be addressed further during a future trip to Aravind (Free) Eye Hospital. We expect to construct shortly instrument 3, a field device suitable for triage, which closely approximates a final apparatus (instrument 4), and to subject instrument 3 to clinical study in the field.

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Oculokinetic perimetry in a health screening program

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Abstract

This was a preliminary attempt to evaluate the ability of oculokinetic perimetry (OKP) to detect eye diseases in a public health care program which does not employ ophthalmologists The OKP glaucoma screener was used in 941 subjects (1882 eyes) as a part of the health screening in Gifu-ken Industrial Health Center.

Twenty-two subjects (24 eyes) who had abnormal OKP results underwent ophthalmological examinations including funduscopy, tonometry and perimetry with the Humphrey Visual Field Analyzer Abnormal OKP results were attributable to open-angle glaucoma in seven patients (nine eyes), retinal vein occlusion in four (four eyes), macular degeneration in three (three eyes), optic atrophy secondary to optic neuritis in one (one eye), brain tumor in one (one eye), and myopic chorioretinal atrophy in one (one eye), respectively In three patients (five eyes) they were false-positives

OKP is worthwhile to include in ophthalmic health care screening, particularly when funduscopy or fundus photography is not feasible.

Introduction

The glaucoma screener of oculokinetic perimetry (OKP) or OKP glaucoma screener was developed for the detection of glaucomatous visual field loss by Dr Damato[1] It has 26 examination points, and the points are distributed in the area where glaucomatous visual field defects frequently occur. We reported that the OKP glaucoma screener seems to be an effective method for detecting moderately advanced, glaucomatous visual field changes. In an attempt to evaluate the ability of the OKP glaucoma screener to detect eye diseases in public health care screening, we tested the subjects with OKP who were examined in a public health care screening program which did not employ ophthalmologists.

Patients and methods

Nine hundred and forty-one subjects, 1882 eyes (702 males and 239 females) were tested with OKP as a part of the Health Screening Program at the Industrial Health Center in Gifu prefecture. The mean age was 47 1 years, ranging from 27 years to 65 years.

In the first step, at the Industrial Health Center, all of the subjects were tested for visual acuity, intraocular pressure (IOP) by means of a non-contact tonometer (Topcon, Tokyo), and fundus photography by a non-mydriatic fundus camera (Topcon, Tokyo) prior to OKP. During OKP, they used their own spectacles or ready-made ones (+1D, +1.5D, +2D, +2.5D, +3D, +3.5D), as needed to clearly see the blue numbers and the black point on the OKP chart. Oph-

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Washington DC, USA, July 3–7, 1994
edited by R P Mills and M Wall

Table 1 Criteria for abnormality in the first step

(1)	OKP: Abnormal point exit
(2)	IOP ≥ 20 mmHg
(3)	Fundus photograph: read by ophthalmologist
(4)	Visual acuity < 20/20

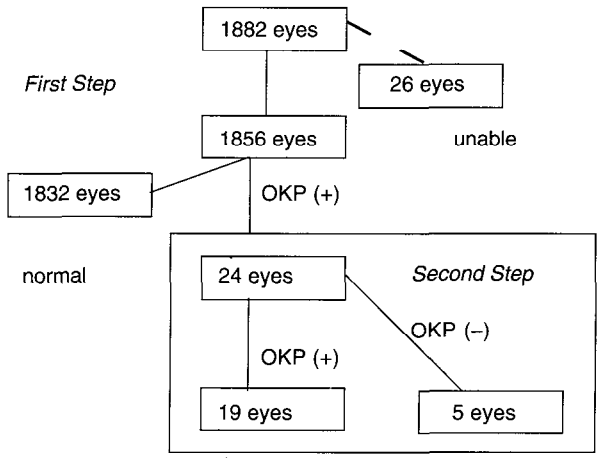


Fig 1 Results of OKP

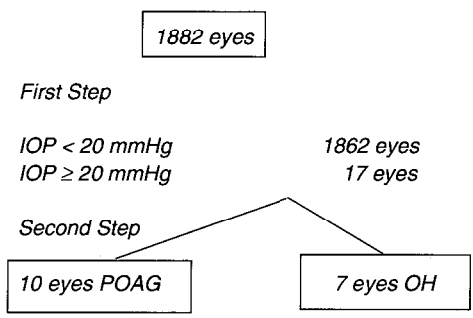


Fig 2 Results of tonometry

thalmologists were usually not present, and a physician and nurses who work in this center performed examinations The presence of eye diseases was judged by an ophthalmologist based upon fundus photographs, visual acuity and IOP. In the second step, subjects with any suspected ocular abnormality in the first step were examined in our eye clinic Ophthalmological examinations included direct fundoscopy, tonometry with a Goldmann tonometer and perimetry by the Humphrey Visual Field Analyzer (program 30-2, model 630). The criteria for abnormality in the first step and enrollment into the second step are shown in Table 1 The first step was a mass screening and the second step was a thorough examination.

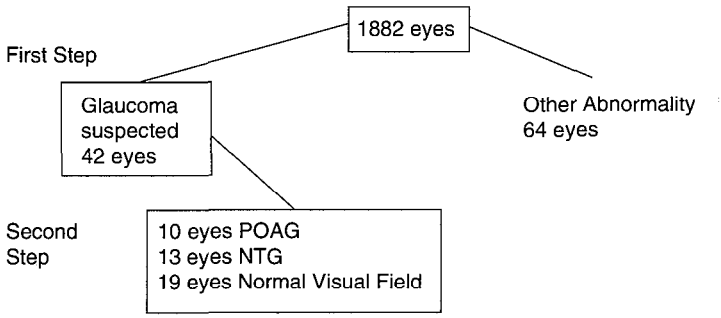


Fig 3 Results of fundus photography

Table 2 The glaucomatous eyes – detected by OKP

	Aulhorn Greve's classification						
	0–I	*I*	*II*	*III*	*IV*	*V*	*Total (%)*
	xx	xx	o	o			
POAG		xx					10
		xx					(20 0)
NTG	xx	oo	xx	oo			13
		oo	x	o			(53 8)
		x					
	(0%)	(36 4%)	(25 0%)	(100%)			

o: detected; x: not detected

Results

In the first step, among 1882 eyes of 941 subjects, 26 eyes of 15 subjects could not be tested with OKP. The causes of the failure to test were low vision (< 0.4) in 21 eyes and were not clear in five eyes. Twenty-two subjects (24 eyes) had abnormal OKP results In the second step, 19 eyes had reproducible OKP results and five eyes were judged to be false-positives (Fig. 1). The results of tonometry are shown in Figure 2 In the first step, 17 eyes had IOP greater than 20 mmHg, and in the second step examinations, ten eyes were diagnosed as primary open-angle glaucoma (POAG) and seven eyes as ocular hypertension The results of reading of the fundus photographs are shown in Figure 3; 42 eyes were judged to be glaucoma suspects. In addition, other abnormalities were suspected in 64 eyes.

The second step examinations found that eyes with abnormal OKP results had open-angle glaucoma in seven patients (nine eyes), retinal branch vein occlusion in four patients (four eyes), macular degeneration in three patients (three eyes), optic atrophy secondary to optic neuritis in one patient (one eye), brain tumor in one patient (one eye) and myopic chorioretinal atrophy in one patient (one eye), respectively

In addition to the nine open-angle glaucoma eyes, eight POAG eyes and six normal-tension glaucoma (NTG) eyes were identified in the second step, based upon elevated IOP, optic disk changes or perimetric findings Using Aulhorn-Greve's glaucoma visual field classification, the severity of glaucomatous changes found in this study are shown in Table 2. OKP detected defects in 20% of these with POAG and in 53.8% of these with NTG. Thus, the ability of the OKP glaucoma screener to detect early changes was low and 100% in stage III. These results conform well with those of our previous report[2]

OKP緑内障
スクリーニング
検査シート

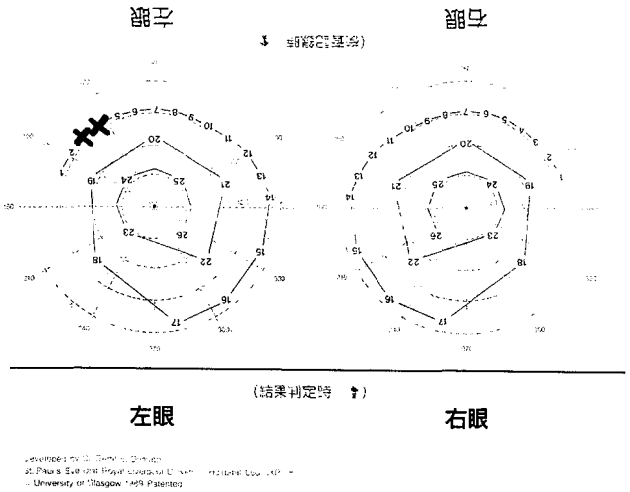
☆氏 名. C H
☆ I D
☆性 別: (男) 女)
☆生年月日・年齢:
M・T・S・H 年 (19 年)
月 日生 (才)

〈眼 所 見〉

	右眼	左眼
☆矯正視力: (40cm)	1.0	1.0
☆レンズ: (屈折)	S +3.5 D	S +3.5 D
	C −0.5 D	C −0.5 D
	A 70°	A 110°
☆瞳孔径:	mm	mm

〈備 考〉

検査時間:
検査日: 1992年 9月 7日
検 者:



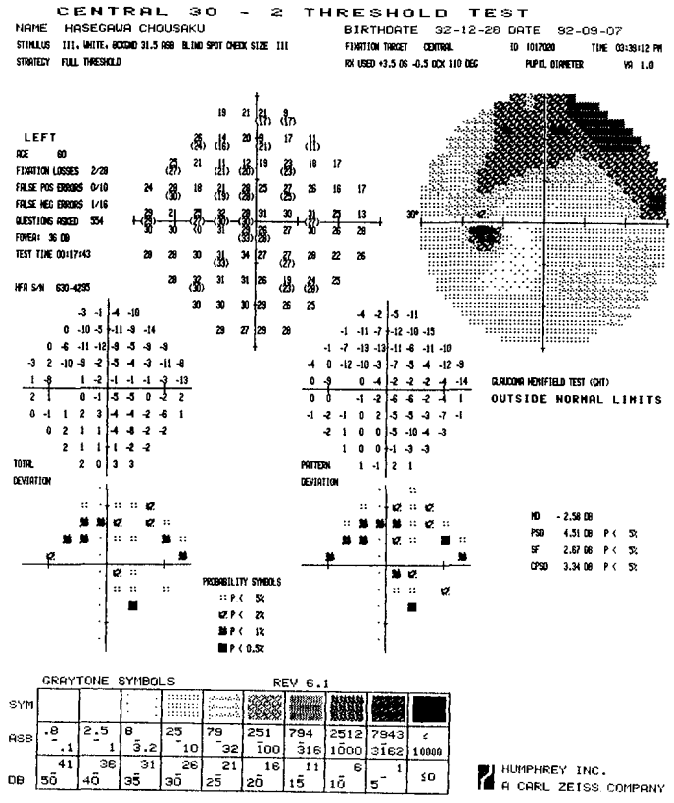
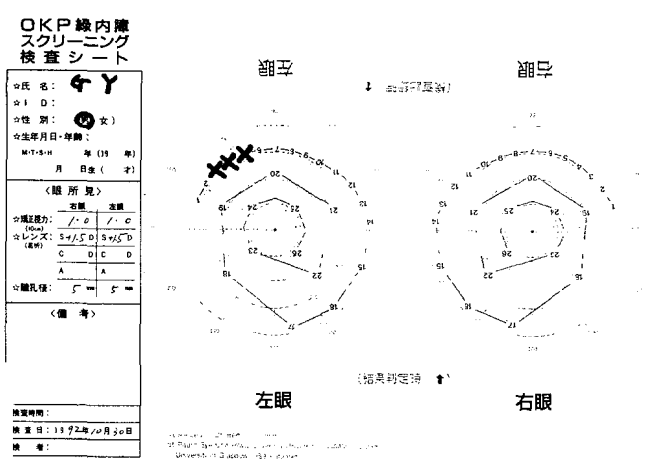


Fig. 4. Case 1.


OKP緑内障
スクリーニング
検査シート
☆氏 名：
☆ I D：
☆性 別：
☆生年月日・年齢：
〈眼 所 見〉
右眼
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☆矯正視力：
☆レンズ：
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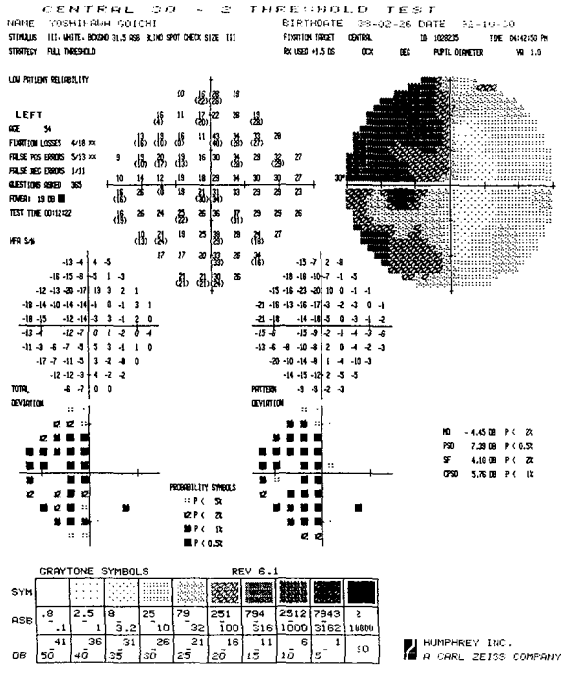
CENTRAL 30 - 2 THRESHOLD TEST
NAME YOSHIKAWA GOICHI
BIRTHDATE 38-02-26 DATE 92-10-30
STIMULUS III, WHITE, GOLDND 31.5 ASB BLIND SPOT CHECK SIZE III
STRATEGY FULL THRESHOLD
FIXATION TARGET CENTRAL
RX USED +1.5 DS
DCX
DEG
PUPIL DIAMETER
VA 1.0
LOW PATIENT RELIABILITY
LEFT
AGE 54
FIXATION LOSSES 4/18 XX
FALSE POS ERRORS 5/13 XX
FALSE NEG ERRORS 1/13
QUESTIONS ASKED 365
FOVEA: 18 DB
TEST TIME 00:12:22
HFA S-N
TOTAL DEVIATION
PATTERN DEVIATION
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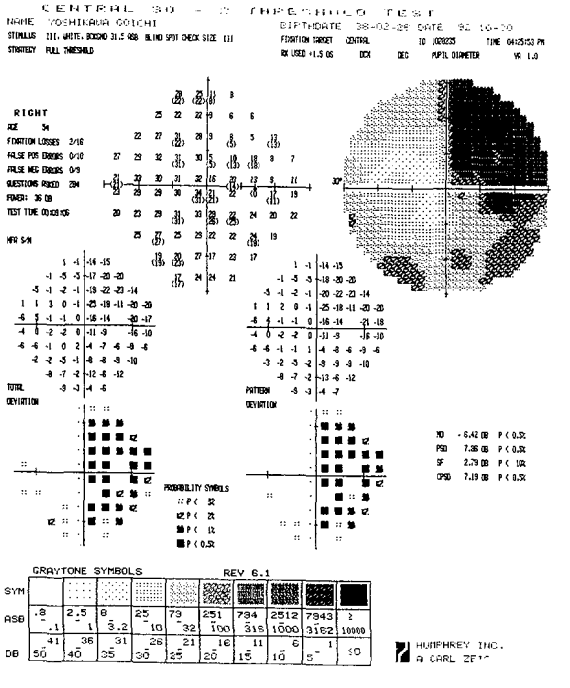
PSD 7.28 DB P(0.5%
SF 4.10 DB P(2%
CPSD 5.76 DB P(1%
GRAYTONE SYMBOLS
REV 6.1
SYM
ASB
DB
HUMPHREY INC.
A CARL ZEISS COMPANY


CENTRAL 30 - 2 THRESHOLD TEST
NAME YOSHIKAWA GOICHI
BIRTHDATE 38-02-26 DATE 92-10-30
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STRATEGY FULL THRESHOLD
FIXATION TARGET CENTRAL
RX USED +1.5 DS
DCX
DEG
PUPIL DIAMETER
VA 1.0
RIGHT
AGE 54
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FALSE NEG ERRORS 0/9
QUESTIONS ASKED 294
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HFA S-N
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PATTERN DEVIATION
PROBABILITY SYMBOLS
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PSD 7.85 DB P(0.5%
SF 2.79 DB P(10%
CPSD 7.19 DB P(0.5%
GRAYTONE SYMBOLS
REV 6.1
SYM
ASB
DB
HUMPHREY INC.

Fig. 5. Case 2.

Case 1 was POAG with an abnormal visual field Sensitivity was decreased in his upper visual field At the screening examination, OKP detected defects in the same location (Fig 4). Case 2 was a taxi driver with no subjective symptoms, visual acuity of 1.0 with normal fundus OKP disclosed a visual field abnormality in the first step. In the second step, perimetric examination with a Humphrey Visual Field Analyzer showed hemifield defects in both eyes, and pituitary adenoma was found by computed tomography The visual field of the right eye was normal by OKP (Fig 5)

Discussion

OKP can be an important examination method in mass screening or in a routine health care program. It may even detect early abnormalities, if the test points happen to coincide with the area of visual field abnormality.

For early detection of glaucoma in a large population sample, it is not practical to incorporate perimetric examination. Thus, in the vast majority of previous reports, subjects were screened by IOP and optic disk findings. Visual field evaluation by OKP may be a useful part of a screening program for detecting glaucoma or ocular diseases. However, OKP has its limitations. OKP is not designed to detect early visual field changes. Nevertheless, the false-positive rate was low and the abnormal results of OKP testing were attributable to vision threatening diseases in 80% of the cases screened at the first step. It should be emphasized that none of the cases detected by the present screening had been aware of their ocular diseases In conclusion, the OKP glaucoma screener is a particularly worthwhile test to be included in ophthalmic health care screening where funduscopy or fundus photography is not feasible

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Motion sensitivity testing in occupational health screening

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Abstract

Since the UK Health and Safety Executive directive on workers using a visual display unit (VDU) was instituted as a result of EC legislation, departments of occupational health in industry, commerce and public services have been obliged to provide free sight testing should their employees request it The occupational health department of Cable and Wireless plc, a large multinational company, has exploited this opportunity to screen employees for ocular abnormalities and vision defects as part of a general health assessment A software package was developed at the Institute of Ophthalmology for the delivery of the intermediate distance visual acuity test and motion sensitivity screening test on a "notebook" computer with monochrome Liquid Crystal Display The results of screening of the first 1680 individuals, aged 29.5 years SD 12 7 (range from 18 to 61 years), over a year are presented 135 repeat tests have been carried out and to date 29 referrals for further ophthalmological assessment have been made to several centers across the UK Amblyopia, and persons with cataract have so far been detected but only one unconfirmed glaucoma suspect has been identified The acceptability of the test to the work force and occupational health physicians and nurses is good

Background

The use of VDUs in the workplace has brought about enormous changes, most of which have been of benefit to both the employee and employer Adverse effects of their use, mainly in the ergonomic area have been reported[1,2,3], but this prompted a response by the Health and Safety Executive[4] followed by a directive from the European Community[5] and these regulations became law in January 1993

Under the regulations[5] all VDU users are entitled to an eye sight test, at the employer's expense, and the right to a pair of spectacles when they are *specifically* required to perform VDU work (also at the employer's expense). Since free sight tests for all were abandoned in the UK in April 1989[6] it was anticipated that there would be a high acceptance of a free eye sight test offered within these regulations.

The regulations state that those conducting the eyesight screening tests should have a basic knowledge of the eye and its functions. Some companies opted for a vision screening facility within their own occupational health set-up, with referral to an optometrist or ophthalmologist if any problem or defect was identified. The occupational health department of Cable and Wireless plc decided to optimize this opportunity to screen their work force for any ocular abnormality or visual defect as part of an already provided general health assessment. Cable and

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Wireless plc asked advice from the Institute of Ophthalmology in London regarding the vision testing. An existing software package, developed at the Institute of Ophthalmology for use on a "notebook" computer with a 12" monochrome Liquid Crystal Display, was modified and set up for use on their portable "Compaq" computers at various testing sites throughout the UK.

The package featured an intermediate distance visual acuity test and a motion sensitivity screening test. The motion sensitivity testing (MST)[7] is not dependant on standardized testing conditions such as contrast, brightness or refractive error, and since the test viewing distance is not critical, it appears ideal for the occupational health situation

Method

The system first presents a visual acuity (VA) test based on a LogMAR (minimum angle of resolution) "E" test. This is conducted monocularly with the subject wearing any appropriate optical correction. Because the viewing distance is relatively short (approximately 60 to 70 cm) it limits the best visual acuity level to 0.19 LogMAR, 6/9 Snellen equivalent. The system then makes allowance for the VA which is recorded before commencing the MST because poor VA can influence the MST results.

The strategy in the "package" supplied is to specifically test for large ganglion cell damage with the motion stimulus and to identify and locate abnormal zones of the optic nerve head. Therefore the MST may detect any defect although it was originally designed specifically to detect glaucoma defects. The system generates 48 vertical lines in six zones (central 20 degree area) around a fixation target Only six of the 48 targets are tested, and these are tested repeatedly The moving stimuli are vertical lines with a horizontal displacement, the length of the vertical bars and distance of displacement between the bars is automatically adjusted according to the result of the visual acuity testing

It is known that any psychophysical test which takes longer than five minutes to complete results in reduction in the subject's concentration and therefore accuracy. The fact that this test takes less than five minutes to test both eyes independently means that there is the opportunity to repeat any test in which the reliability is suspect. The test is explained to the subject, and a training exercise is carried out binocularly, one key serving as the response key. Each time one of the lines is seen to move the key is pressed. One eye is then occluded and the subject is instructed to fixate the fixation circle On appreciating movement of any of the horizontal lines in the periphery, the key is pressed. A suitable cut-off for discriminating normal from abnormal was taken at 50% mean motion detection score for all age groups. All those not gaining 50% on the first test were recalled for a repeat test.

Subjects

All the employees of Cable and Wireless plc are eligible for the test. 1718 tests (some duplicate) have been carried out in the first year of the system being set up, on 827 females and 891 males The average age was 29 5 years (standard deviation 12 7, ranges from 18 to 61 years), 1257 being between the ages of under 20 to 40 years. Only 14% of the employees tested were over the age of 40 and would be in the age group where they may be at risk of developing glaucoma. 132 of the subjects had duplicate tests and three had three tests carried out. These repeat tests were carried out to check interobserver variation in those with good results. In others, repeat tests were carried out to test for improvement either due to the learning effect or change of situation such as wearing spectacles or contact lenses (CL) Employees who showed no improvement on repeat testing, where no known legitimate cause (such as amblyopia or cataract) for the reduction in the MST could be determined, were referred for further evaluation

Results

1590 (95%) of the subjects had visual acuity of 6/9 or better 528 had 100% on the MST correlating with good VA, as 509 of these had a vision of 6/9 or better in either eye

Only 29 of the 1680 individuals tested were referred for further testing and investigation by the ophthalmologist. The average age of those referred was 38 years (8.5 years older than the average work force age). The referral rate of 1.7% is low but, the population tested was a young, healthy, working one.

Any subject who did not obtain 50% on the first MST test had a repeat test – and if they improved to 50% they were not referred A few who still did not reach 50% on MST did not get referred where an adequate reason for the poor result was apparent, such as known amblyopia or cataract.

The results of the full ophthalmological investigation of five referrals are not yet known

Only one of the referrals was suspected of having glaucoma and is being followed up as she has a positive family history of glaucoma and is in the older age group (58 years). There were 248 over the age of 40 years so this gives a glaucoma referral rate of 0.4% in the older age group The Bedford and Ferndale[8,9] studies on similar white UK populations over the age of 40 years have prevalences of primary open angle glaucoma (POAG) of 0.71% and 0 43% respectively

One referral from this study had tilted disks but otherwise the full ophthalmological investigation was normal As there was a positive family history of glaucoma she will be reassessed in a year.

Two referrals have dry eyes and mild ocular surface disease, not requiring any treatment, but this may account for the abnormal MST.

436 of the subjects wore spectacles and 135 (8%) wore contact lenses (CL), ten said they wore both – presumably interchanged Seven referrals (24%) wore soft or gas-permeable CL. One of these had poor fitting CL but otherwise a normal ophthalmological investigation Three of the CL wearers had large myopic disks and this may have been the origin of the abnormal MST response. The full ophthalmological examination was normal in these three. The remaining three CL wearers were normal on further investigation We considered the abnormality might be due to reduction in blinking while carrying out the MST Alternatively the age of the lenses may have been a factor

Four referrals had squint and/or amblyopia (one of these also had nystagmus) and this could have caused the reduction in the MST Full ophthalmological investigations were otherwise normal.

In nine referrals, no reason for the reduced MST could be found, as full ophthalmological examination was normal. The results mirror this company's work force as a young, healthy, working population

Discussion

The young age distribution and the intermediate working distance for the VDU would mean that very few subjects should require a special optical correction for use at the VDU In a young, healthy, working population the need for optical correction is normally known and this is supported by the fact that 33% of the work force presented for examination already wearing a spectacle or CL correction. It has been suggested that the wearing of CL may aggravate the asthenopic ocular symptoms[10] reported in VDU workers, but this may be contributed to a dry atmosphere and reduced blink rate which appears to occur[11]. In one study[3] 33 7% of those questioned complained about eye problems, but these were non-specific asthenopic symptoms and no eye examination was carried out to confirm the self-reported problems

In a small hospital-based study carried out by optometrists within a visual assessment department[12], 3% of those tested were referred as at risk of developing glaucoma or having definite glaucoma but 33% of this population were over the age of 40 years.

The use of the MST as a tool in early diagnosis of glaucoma, before visual field defects are apparent on conventional assessment, has been documented[13] The use of the MST in screen-

ing a young, healthy, working population for any type of ocular defect has not been reported before.

The test was well accepted by the occupational health physician and nurses carrying out the test and by the employees of the company who were examined In this study an occupational health nurse, who had been trained in the use of the system, assisted the participant throughout the test – although the system has the potential to be integrated onto the employee's own computer work station in the future, facilitating self-testing within the working environment This quick and simple method of assessment should be considered in the future

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OPTIC DISK IMAGING

Inter-operator variability in laser ellipsometry of the nerve fiber layer

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Abstract

Laser ellipsometry of the nerve fiber layer is a new imaging technique which estimates thickness of the nerve fiber layer by using the fact that it is birefringent A commercial device, the Nerve Fiber Analyzer™, uses a dedicated scanning laser ophthalmoscope to produce an image of the nerve fiber layer adjacent to the optic nerve head To study operator-related variability in nerve fiber layer thickness measurements, we had four trained operators test 11 subjects twice, resulting in 88 nerve fiber layer images. We analyzed five indices computed from these images: mean thickness in each of four quadrants, and overall mean thickness Repeated-measures ANOVAs showed significant operator effects for four of these indices (from $p = 0.002$ to $p = 0.016$ across indices) The average test-retest variability across operators was 3 0 μm for the overall mean thickness, and ranged from 4 0–4 9 μm for the four quadrants For each index, inter-operator differences as large as 42% of the average value were noted The clinical usefulness of the device will be limited until it has been modified to reduce inter-operator variability Research studies should try to have the same operator test all subjects, and mask the group identity of each subject

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Reproducibility of optic disk measurements with the "Heidelberg Retina Tomograph"

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Abstract

Four examiners evaluated the optic disk of one eye of 12 subjects with the "Heidelberg Retina Tomograph" 6–10 times. One observer was experienced in data acquisition with this instrument, the others were trained within a few days Six optic disk parameters were evaluated A *t* test showed significant differences between the measurements of each examiner in seven eyes, highly significant differences in four eyes. Outlying sets of data were found for each one of the four observers The coefficient of variation was falling in the range of 1 3–61 1%, and it showed significant inter-observer differences in five eyes These eyes were not coinciding with the ones with increased inter-observer differences of disk parameters, however. Obvious high variation happened in each of the observers, and was more prominent in some of the subjects Deviation and fluctuation of values independently occur in all disk parameters and cannot clearly be attributed to insufficient examiner's training A quality parameter for each single examination might help to reject improper tests and thus improve reproducibility

Introduction

The analysis of trends in the topometric follow-up of the optic disk requires high reproducibility Older equipment was less satisfying in this respect[1] We tested a newer instrument, the "Heidelberg Retina Tomograph" (HRT) with special emphasis on inter-observer and inter-subject variability of repeated measurements.

Materials and methods

Four observers evaluated the optic disk of one eye of 12 subjects between 21 and 62 years of age with the HRT 6–10 times with an undilated pupil. One examiner was experienced in data acquisition with this instrument (J R S), the others were trained within a few days The contour line around the disk of each eye was marked once by one of us (F D) and transposed to all available measurements. Six highly characteristic disk parameters were evaluated: cup area, cup volume, mean depth of disk, mean depth of cup, "height variation contour" (height differences along the disk edge), and "third moment inside contour" (slope of the cup). The repeated examinations were analysed separately and as mean topography image for each observer and each subject (software version 1.08)

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Results

Mean image. The mean standard deviation as given by the instrument for each mean topography image ranged between 20.73 and 85.46 microns with a mean of 39 68 ± 17.58 microns SD for the 12 eyes and four observers (Fig. 1). Values were predominantly between 20 and 40 in ten eyes and between 40 and 85 microns in the other two. The value of one observer is missing in subjects No. 1–4, since these subjects were the observers An outlying value was apparent in subject 2 and 3 for observer "Icag", represented by a white bar. The profile of values for the observers in the other subjects did not disclose any trend. A comparison of the performance of the four observers by a *t* test when pooling these data for all subjects did not show significant differences Highly significant differences existed between the 12 subjects, however Subject No 9 was the most prominent outlier: Each one of the examiners had problems in obtaining good pictures for this moderately myopic eye. Three other eyes presented with considerably high values of standard deviation.

Single images. The analysis of each picture separately resulted in individual values for each subject and each observer. This approach gives values for each optic disk parameter. Disk area was kept constant by the study design Cup area, cup volume, cup depth and cup slope are the most meaningful ones and will be described in detail. The values for these four parameters are presented in Figure 2a–2d, the coefficient of variation in Figure 3a–3d.

Cup area. Absolute mean values were grouped quite closely for all subjects and within each subject (Fig. 2a) When comparing the data by a *t* test, six eyes disclosed significant inter-observer differences, however, marked with asterisk for their level of significance. Eyes No. 4 and 6 were leading in this respect. The *coefficient of variation* (Fig 3a) was markedly elevated in three subjects, who did not coincide with those with large inter-observer variations: Nos 3, 9 and 11 were falling out of the general trend The profile of values of the four observers disclosed no systematic characteristics.

Cup volume (Fig 2b) presented with more inter-subject variation, subjects 3 and 9 demonstrating the smallest, subject 1 and 10 the highest values A *t* test revealed inter-observer differences in six eyes, this time subject 6 and 10 being the greatest The *coefficient of variation* (Fig 3b) was not highest in these, but in three other subjects: Nos. 3, 9 and 11, as for cup area. The profile for the observers in each subject did not indicate any trend.

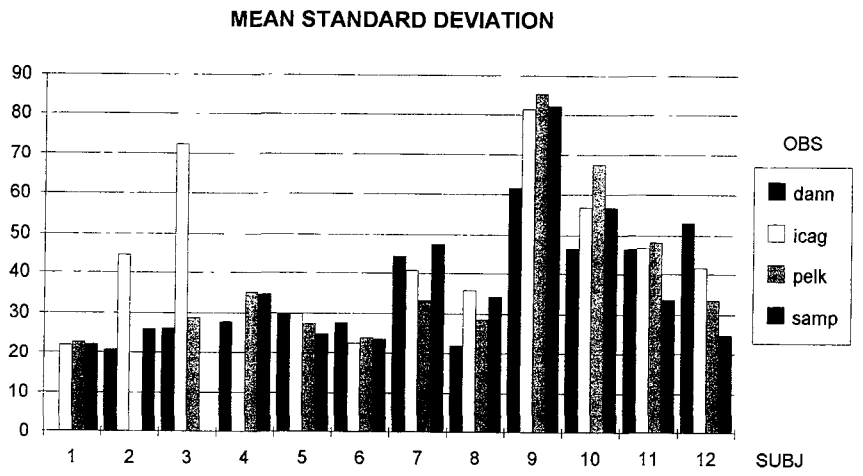
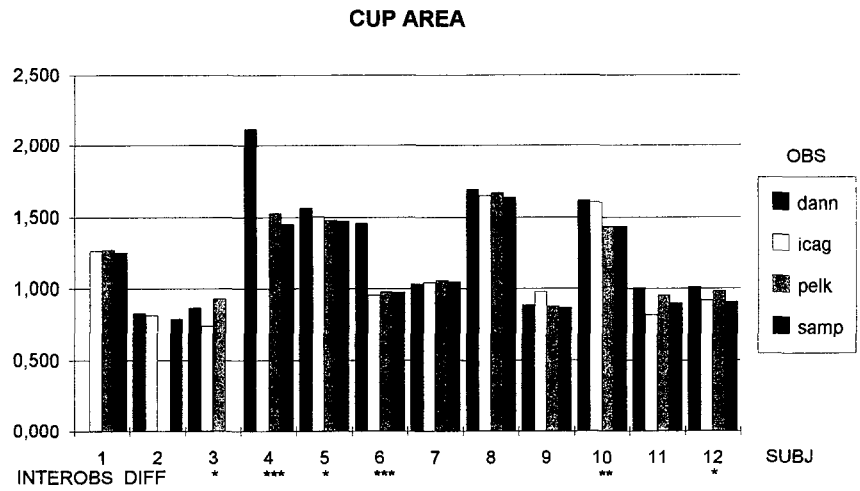


Fig 1 Mean standard deviation of a mean picture from six to ten combined pictures in microns (y axis) for subject 1 through 12 (x axis). Data in each subject consist of four bars representing the values of each one of the four observers (legend on the right) One bar is missing in the first four subjects, since there were also the observers


CUP AREA
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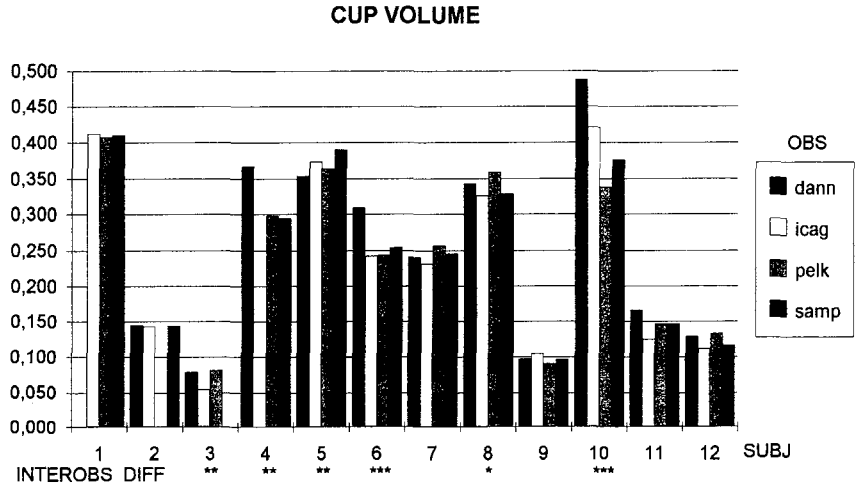
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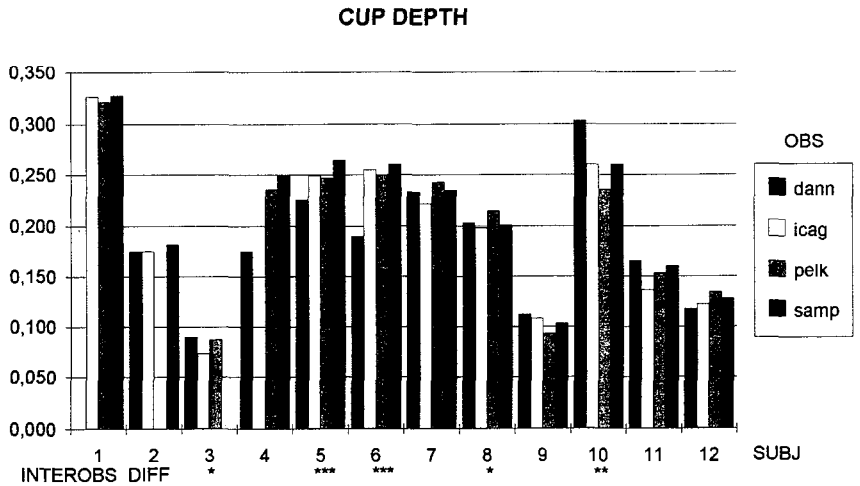
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Figs 2a-c

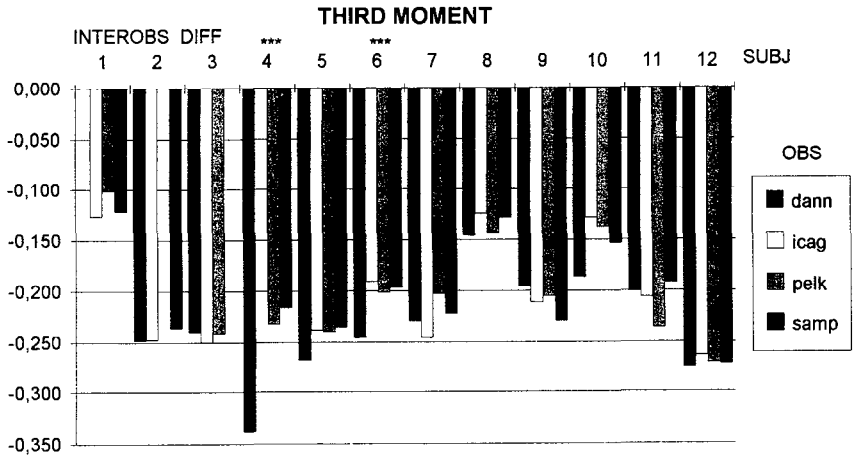

Fig 2 Mean values of four disk parameters (y axis) from six to ten single pictures for subject 1 through 12 (x axis) Data in each subject consist of four bars representing the values for each one of the four observers as in Figure 1 Subjects in which significant differences occurred between the four observers are marked with asterisk underneath the subject number for level of significance (* < 0.05, ** < 0 01, *** < 0 001). a) Cup area in mm^2 b) Cup volume in mm^3. c) Cup depth in mm. d) Third central moment of frequency distribution of depth values

Cup depth (Fig 2c) showed the expected inter-subject differences. Significant inter-observer differences were present in five eyes, this time subjects 5 and 6 being outstanding The *coefficient of variation* (Fig. 3c) was most markedly elevated in subject 4, followed by 9 and 11, resembling the two other parameters in this respect

Third moment (Fig 2d), defined as the parameter of slope, revealed negative values, indicating soft sloping cups in all eyes. Two eyes, No 4 and 6, had highly significant inter-observer differences. The *coefficient of variation* (Fig 3d) revealed high values in subject 8, 10 and 11, whereas subject 9, which was prominent for all other parameters, behaved somewhat better for this index.

The *coefficient of variation*, when separately calculated for each index, subject and observer, was lying in the range between 1.3 and 61% When all data were pooled for the four observers (Fig. 4), we found a common mean of 16%. The profile of values for the six parameters was slightly different in each subject, and highest values occurred in subjects 4 and 9 There were no differences between the disk parameters when pooling the data on variation for all 12 subjects. When we analysed the measurements of each examiner separately by pooling the different disk parameter, we found high inter-observer differences in five subjects, marked by asterisk for their level of significance

The overall result of the inter-observer differences for all parameters and subjects is given in Table 1: Seven eyes revealed significant differences in some of the disk parameters, four eyes with the highest level of significance Each one of the four observers produced nearly equally frequent outlying results. The coefficient of variation was different for the four observers in five eyes, when taking all parameters together (right column). These eyes were not the same ones as those with deviating measurements, however. Outlying values of variation again occurred for each one of the examiners Eye No. 9 had the highest mean standard deviation and the highest coefficient of variation for most of the disk parameters. Even then the mean values of all disk parameters coincided favorably in this subject for all observers

There was no statistically significant correlation between inter-observer differences, ex-

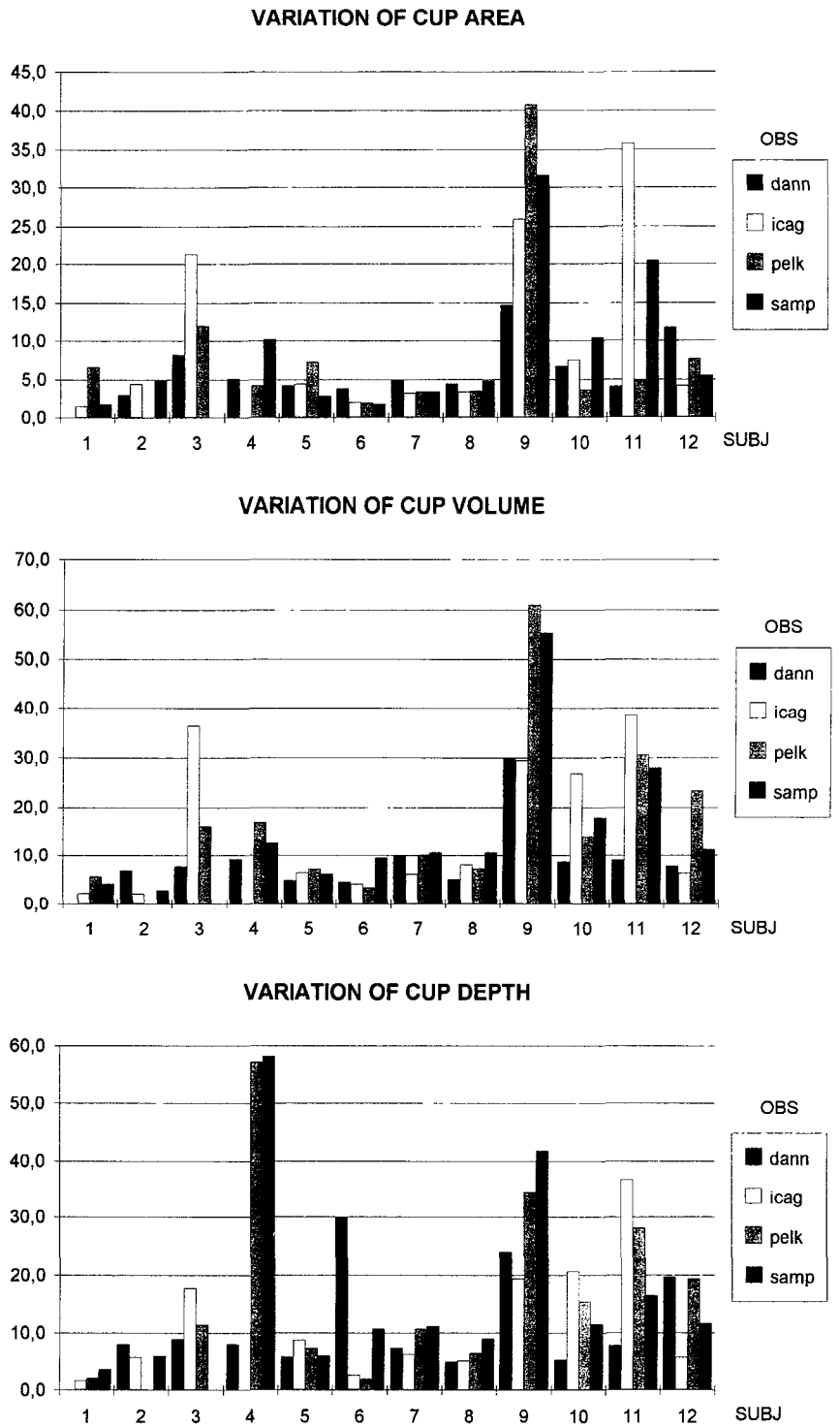

Fig 3 Coefficient of variation of six to ten measurements of four disk parameters (a–d) in % (y axis) for subject 1 through 12 (x axis) Data in each subject consist of four bars for the four observers, as in Figures 1 and 2 a) Cup area b) Cup volume. c) Cup depth d) Third moment

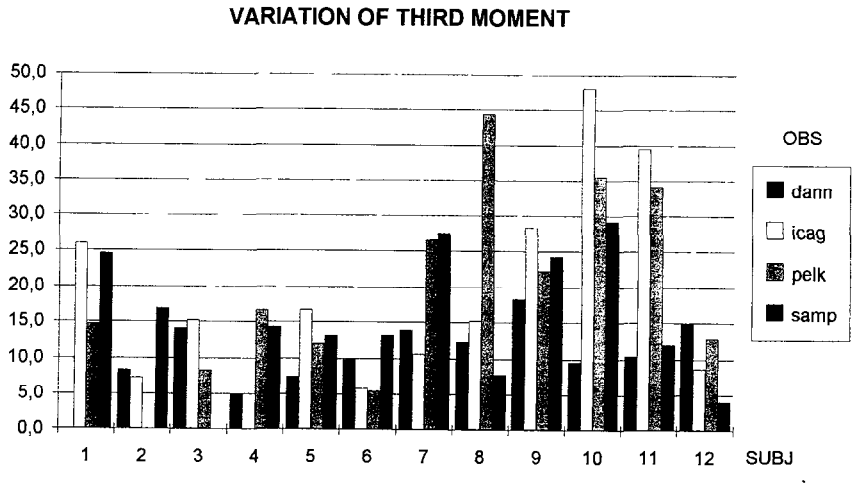

Fig 3d

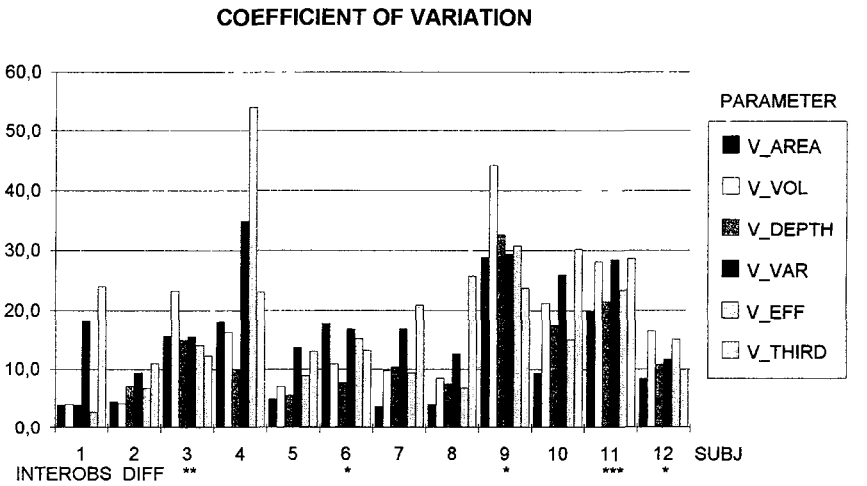

Fig 4 Coefficient of variation of six to ten measurements of four observers pooled together (y axis) for subject 1 through 12 (y axis). Data in each subject consist of six bars representing the values for each one of the six disk parameters: Cup area, cup volume, disk depth, contour variation, cup depth, third moment (legend on the right). Subjects in which significant differences occurred between the four observers are marked with asterisk underneath the subject number for level of significance as in Figure 2

pressed by the p value of the t test, and the coefficient of variation. Inter-observer differences were, however, more pronounced in subjects with a small coefficient of variation (*e.g.*, subject 3, 5 and 12 for cup area) Increased variation was noted in parameters with individually high and low values.

Table 1. Inter-observer differences in their repeated measurements of six optic disk parameters: cup area (V_area), cup volume (V_vol), disk depth (V_depth), contour variation (V_var), cup depth (V_eff), third moment (V_third) for each one of 12 subjects (P1–12) Level of significance marked with asterisks as in Figure 2. Right column represents inter-observer differences in coefficient of variation between the disk parameters as in Figure 4

	Differences between examiners							V different
P	area	vol	depth	var	eff	third		
1								
2								
3	*	**	*		*			**
4	***	**		***		***		
5	*	**	***		***			
6	***	***			***	***		*
7								
8		*	*	*	*			
9								*
10	**	***	***		**			
11								***
12	*							*

Comment

The variation of single measurements of optic disk parameters in our clinical set-up turned out to be higher than in previous reports[2,3,4], and expectedly higher than in a model eye[2,5]. The reason for this observation could be that we had by chance included some subjects who produced consistently high variation. Deviating values of disk parameters between observers occur for all disk parameters independently from increased variation of values, and they cannot clearly be attributed to insufficient examiner's training Single pictures are definitely not sufficient, and five or more might be helpful to increase reliability[6,7,8,9].

This material probably includes a considerable proportion of poor pictures Our software version did not yet provide a quality check for single pictures Such a quality parameter for each examination might help to reject improper tests and thus improve reproducibility. A reevaluation of our data with the latest software is under way

Acknowledgments

The Heidelberg Retina Tomograph has been provided by the manufacturer for this study We have no proprietary or developmental interest in this instrument We are indebted to George Brinnig, PhD, MD, for revision of this manuscript

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Accuracy and reproductibility of the Heidelberg Retina Tomograph – results of volume measurements in a model eye

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Introduction

The Heidelberg Retina Tomograph (HRT) and its predecessor, the laser tomographic scanner, were primarily designed for the examination of the optic disk[1,2,3] The HRT can, however, also be used for measuring fundus elevations such as in macular edema or macular hole[4,5] We wanted to quantify the accuracy of the HRT in measuring elevations and depressions

Methods

Details of the HRT confocal image acquisition and processing have been described elsewhere[3]

A model eye was constructed consisting of two cylinders which could be slipped into one another The front cylinder carried a +20D lens, the back cylinder with its artificial "retina" (50 mm away from the front lens) had a hole for the insertion of various buttons They served as artificial cups and elevations of known geometry The model eye was air filled Its optical data differed from Gullstrand's model eye which is programmed into the HRT. Therefore, correction factors had to be applied[6] The visual angle of Gullstrand's eye was divided by the visual angle of the model eye giving a factor k. The real volumes of the buttons were divided by the fourth power of k^6 k depended on where the focal plane of the HRT was In the case of depressions the focal plane was on the artificial retina (k = 2.9) and in the case of elevations a +2.5D lens was shifted in front of the model eye so that all of the elevations could be measured (k = 2 555).

Each of the artificial disks and elevations was measured three times. 10° scans were used for the depressions (as is usually done in examining the optic disk of patients) and 20° scans for the measurement of the elevations (as is necessary for the analysis of macular edema or a tumor). The scan depth was 2 0 mm The parameters "volume below surface" and "volume above surface" were taken for further analysis.

The mean value and standard deviation of three repeated measurements were used to calculate the relative error and the coefficient of variation

The relative error was defined as[7]:

$$\text{relative error} = \left(\frac{\text{mean of the measured values}}{\text{actual value*}} \times 100 - 100 \right)\%$$

*after correction for dimensions (Gullstrand data)

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The coefficient of variation was defined as:

$$\text{coefficient of variation} = \left(\frac{\text{standard deviation of the measured values}}{\text{mean of the measured values}} \times 100 \right)\%.$$

Table 1 Real volumes as compared to measured volumes, relative error and coefficient of variation of HRT measurements in a model eye

Type of artificial depression or elevation	*Real volume (mm^3)*	*Measured volume (mm^3)*	*Relative error (%)*	*Coefficient of variation (%)*
	1 39	1.63	17 6	0.86
	0.78	0 87	12.1	0.81
	0 40	0 36	9 7	3 61
	2 30	2 34	1 5	1 91
	0 98	0.90	8 0	2 34
	1 54	1 52	0.8	4 02

Results

Qualitatively The profiles of the artificial depressions and elevations were correctly scanned. The edges were sharp; there was not much electronic noise.

Quantitatively (Table 1): The relative error ranged from 0.8% to 17 6% with a mean of 8 3%. The elevations were recorded more accurately.

The coefficient of variation ranged from 0.81% to 4.02% with a mean of 2 3%. There was not much difference between the elevations and the depressions

Discussion

The relative error in measuring the volumes of the elevations was smaller than in measuring the artificial cups One reason for this may be that the volumes of the artificial cups were smaller than the volumes of the elevations. To compare the measured to the real volumes of the depressions and elevations a factor k was calculated, because our model eye differed from Gullstrand's eye (the optical data for which are programmed into the HRT). k was significantly smaller in the case of elevations, as the focal plane of the HRT was shifted into the vitreous by an additional front lens. As the real volumes of the elevations and depressions were divided by the fourth power of k, rounding errors contributed more in the case of depressions than in the case of elevations. This may be another reason why the relative error was larger in measuring depressions On the other hand, the mathematical model seems to be correct, as there was no systematic error (some volumes were measured too large, some too small) Furthermore, it is much more difficult to build a Gullstrand eye Such a delicate piece of optics would have many more errors than were caused by the mathematical adjustments we made

As yet there are no reports about the accuracy of volume measurements with the HRT for elevations. Dreher and Weinreb[7,8] report accuracies for the Laser Tomographic Scanner. Weinreb[8] measured an 0.3 to 3 1% accuracy for the one dimensional "cup diameter" in a phakic model eye Dreher[7] found the accuracy to be 2.0% for areas and 11.7% for depth measurements. If we use this 2 0% accuracy for areas and the 11 7% accuracy for depth measurements for calculating $\sqrt{(2^2 + 11\ 7^2)}$, the resulting 11 9% agrees well with our data (compare Sachs[9])

Our coefficient of variation was 2 3% Lusky *et al* 's data[10] cannot be compared to our data, as they refer to one dimensional parameters The reproducibility in the model eye was better than in patients[3,11–13] This is not surprising. The optical irregularities of the human eye are larger than those in a model eye Furthermore, the coefficient of variation is influenced by eye movements and the pulsation of the retina

In conclusion, the HRT can also be used for the measurement of fundus elevations Its performance here is at least as good as its performance in measuring fundus excavations The accuracy of less than 10% for a three-dimensional parameter is excellent. This accuracy should be sufficient for the follow-up of macular edema or of a small retinal tumor.

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Intervisit reproducibility of the Glaucoma-Scope optic disk imaging system

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Abstract

Intervisit reproducibility of the Glaucoma-Scope was assessed using criteria practical for the clinical setting One eye of 33 consecutive glaucoma and glaucoma suspect patients was imaged with the Glaucoma-Scope (software version 3 12) on two separate occasions on the same day These images were analyzed and digitally compared Reproducibility was graded as good when ≤ 10 contiguous pixels within one pixel of the disk rim and at least two pixels from major retinal vessels showed 100 m depth change We felt most clinicians would not suspect clinically significant change at that level Borderline (11–25 such pixels showing 100 m change) and poor (> 25 such pixels showing 100 m change) reproducibility would elicit greater clinical concern 91% of image-pairs showed good, 6% showed borderline and 3% showed poor reproducibility The Glaucoma-Scope has an acceptable level of reproducibility to warrant sequentially following those patients on whom good quality images can be obtained, taking care to confirm apparent change until longitudinal validation studies have been performed

The authors have no financial interest in Ophthalmic Systems or the Glaucoma-Scope.

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Topographic change in the optic nerve head following acute reduction of IOP in glaucoma

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Abstract

Purpose: To investigate topographic change in the morphology of the optic nerve head using the Heidelberg Retinal Tomograph (HRT), following acute reduction of IOP in a glaucomatous population

Method: The HRT was used to record baseline and post-therapeutic images in 18 patients undergoing trabeculectomy or Diamox therapy Seven trabeculectomy subjects and five Diamox subjects met the rigorous inclusion criteria for image quality and IOP reduction A minimum of three images (10° field) were recorded in each session and mean topography (MT) files were generated

Results: The topographic difference (TD) utility was used to analyze pre- and post-therapy images Only one subject with trabeculectomy demonstrated a significant and repeatable difference (NoCP = 0 44) When further analyzed using custom software within the limits of the optic nerve seven of the 12 subjects demonstrated significant change

Conclusions: Gross change in the morphology of the optic nerve is required for the TD utility of the HRT to designate such change as significant When analysis was restricted to the optic nerve (*i e* , the area of interest) seven of 12 subjects demonstrated topographic change in morphology following acute IOP reduction The change generally consisted of a shallowing of cup depth and/or increase in neural rim

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Correlation of visual field indices with scanning laser tomographic imaging in glaucoma

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Background

Morphological examination of the optic disk and psychophysical testing are important ways to monitor the progression of glaucoma. In recent years confocal scanning laser ophthalmoscopy has been proposed as an accurate method for optic disk and nerve fiber layer analysis. Despite the very different nature of morphological and psychophysical tests, a correlation between them is expected since they both address the issue of glaucoma progression

Purpose

To assess the correlation between automated static visual field indices and structural optic disk data obtained with a confocal laser tomographic imaging system

Subjects

One eye of 46 patients (mean age 63 ± 10 years) with early to moderate glaucoma (mean defect 4.8 ± 6 2 dB) was randomly selected.

Methods

Static automated perimetry (Octopus G1 program or Humphrey 24-2) and confocal retinal tomography (Heidelberg) was performed on all eyes. The visual field indices mean defect and corrected pattern standard deviation were calculated for the analysis. On the tomographic images, a circular contour line was traced immediately outside the border of the disk rim to delimit the optic disk The following morphological data were calculated: area (mm^2) within the contour line; effective area and volume (mm^2 and mm^3) of the structure located below the plane of the contour line (corresponding to the "cup area" and "cup volume") and volume above that plane (mm^3); area (mm^2) and volume (mm^3) of the structure below the relative "0" reference retina height and volume above that plane (mm^3); radius of the contour line (mm); mean height of contour (mm) representing the mean nerve fiber layer height along the contour line; height variation contour (mm) which is the difference between the highest and the lowest nerve fiber layer height; mean and maximum depth of the structure inside the contour line and of those below the reference plane (mm). The same data are provided stratified for sector of the optic disk Other information provided are the third moment of the distribution of the

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structure delimited by the contour line and below its plane and the x, y and z coordinates of the gravity center of the cup

Statistical analysis

The correlation between the morphological data and the visual field indices was evaluated with Pearson's correlation coefficient (r) with Systat for Windows (Systat Inc , Evanston, IL, USA).

Results

The height of the peripapillary nerve fiber layer showed a statistically significant correlation ($p < 0.05$) with the corrected pattern standard deviation (CPSD): $r = 0.30$, 0 43 and 0.44 for the global, inferonasal and inferotemporal quadrants The cup depth also showed a significant correlation with both mean defect (MD) and CPSD ($r = 0.36$ and $r = 0.33$ respectively) The highest correlation was found between the third central moment of the frequency distribution of the depth values and the visual field indices. Pearson's correlation coefficient was $r = 0.66$ and $r = 0.56$ for MD and CPSD respectively.

Discussion

The third moment of the frequency distribution is related to the skewness of the frequency distribution of heights and to the overall structure of the optic disk as points with depth values far from the average (as can be found in disks with deep cups and steep cup borders) make the third moment value higher than that of disks with points of relatively uniform depth (small or no cup) The third central moment of the depth distribution may be considered a good indicator of the degree of damage of an optic nerve. An increasing value over a series of follow-up visits is highly suggestive of glaucoma

A study of an integrated glaucoma analysis system using computer-assisted image processing techniques

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Abstract

The authors developed an integrated glaucoma analysis system using computer-assisted image processing techniques, in order to evaluate the visual field, optic nerve head and retinal nerve fiber layer This consists of a nerve fiber coordinate system on color fundus image and five analyses to serve glaucoma parameters: visual field, erosion between the optic disk edge and the pallor edge, NFBD, bend of optic cup vessels, and evaluation of four parameters in a nerve fiber coordinate system The system was applied to eyes with glaucoma There were overlaps of parameter peaks in some directions This system is considered to be useful for diagnosis of glaucoma

Introduction

In diagnosis of glaucoma, the importance of examining visual field defects, optic disk excavation, and retinal nerve fiber layer defects is well known. In recent years, we have seen a growing application of image-processing techniques to fundus analysis[1,2] Such techniques have contributed greatly to advancing research on quantitative representation of glaucomatous changes

Let us consider the examination of a fundus image or visual field. Generally, the examiner employs a procedure wherein he or she examines the subject while comparing multiple data, since it is difficult to evaluate a case based on a single datum

With the objective of developing a new method of analyzing glaucoma, we have been engaged since 1991 in studying computer-assisted methods of performing integrated glaucoma analysis. Presently, we have developed a prototype system This report focusses on this system's basic functions. We intend to report the technical contents of the system at a future date

Methods

In order to develop an integrated analysis method, it is necessary to construct a computerized relationship map of the multiple parts involved. Based on the premise that glaucomatous changes are involved in the course of nerve fibers, we developed a nerve fiber coordinate system, or NFC, as a standard map. The NFC descriptions not only enable parameter magnitudes to be evaluated, but also permit the positional correlation among glaucomatous changes to be quantitatively represented. This method of analysis also allows effective evaluation of minor glaucomatous changes.

We would now like to explain the composition of the system Roughly, the system is composed of an input part, NFC setting part, image analysis part, and an integrated analysis part

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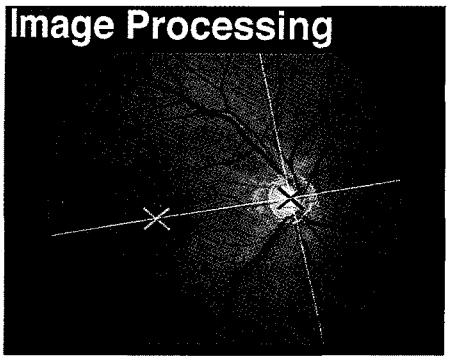

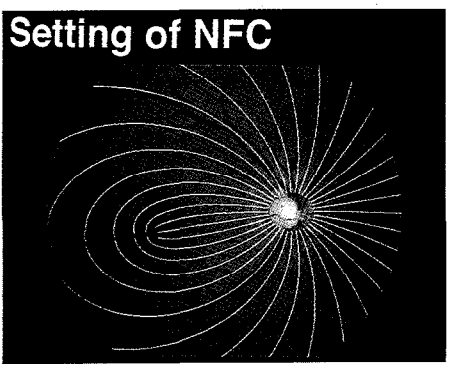

Fig 1

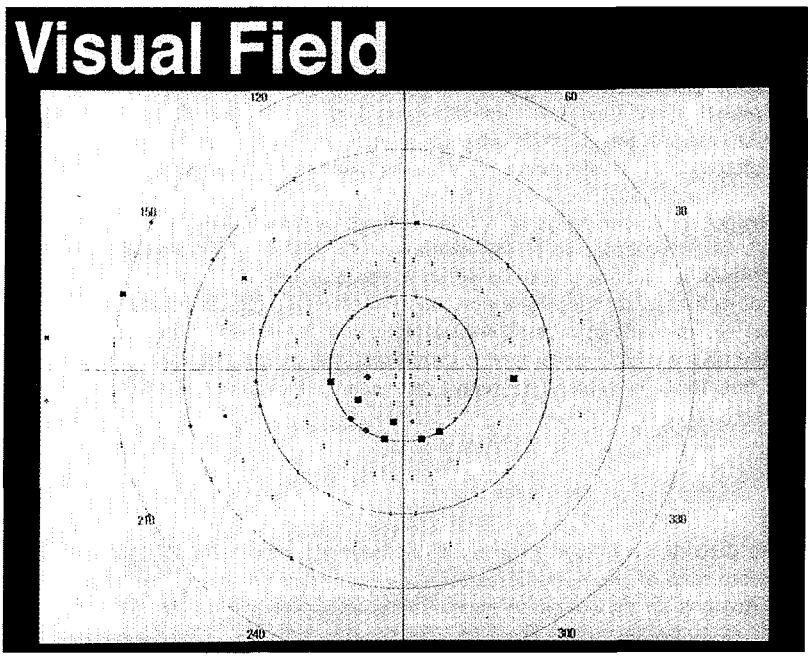

Fig 2

For the input part, we use the TOPCON SBP-2020 and the TOPCON IMAGEnet as input devices for the visual field and the fundus

In NFC setting, two pieces of data are processed: the optic disk and the retinal macula in a fundus photograph. The first step is to detect the center of the disk, edge of the disk, and center of the macula by use of image processing The next step is to simulate the pathway of the nerve fiber layer based on the defected locations of these sites. The final step is to derive an NFC system which has its original point in the center of the disk and describes the fundus at a nerve fiber layer angle θ and a distance R (Fig 1).

In our study, the image analysis part was composed of analyses of four parts the visual field, nerve fiber layer defects, or NFBD analysis, optic disk edge-pallor erosion, and optic cup blood-vessel bend analysis.

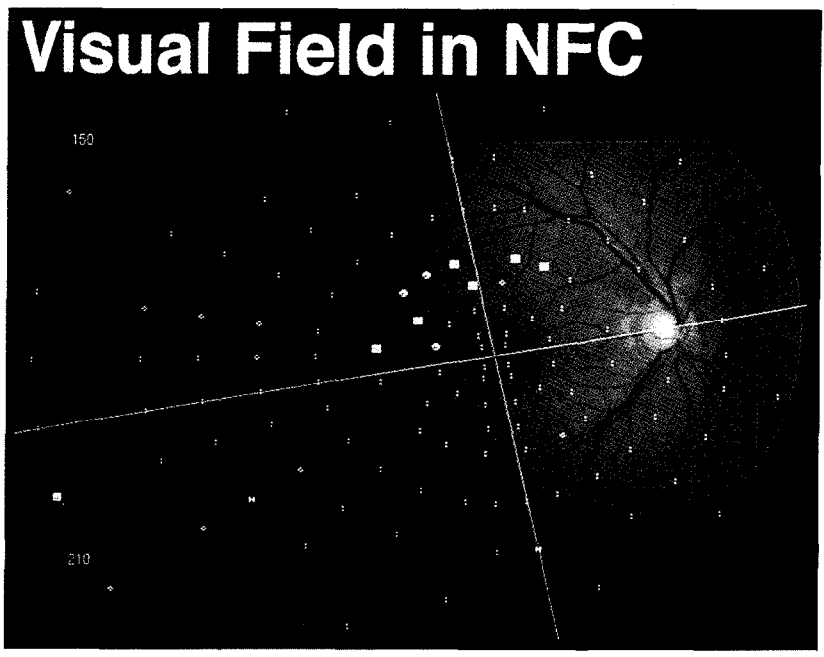

Fig 3

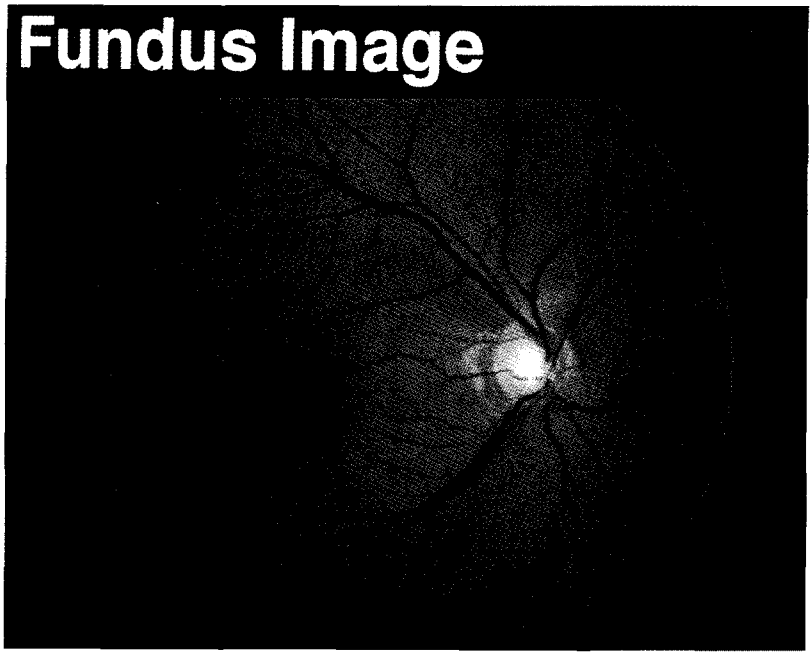

Fig 4

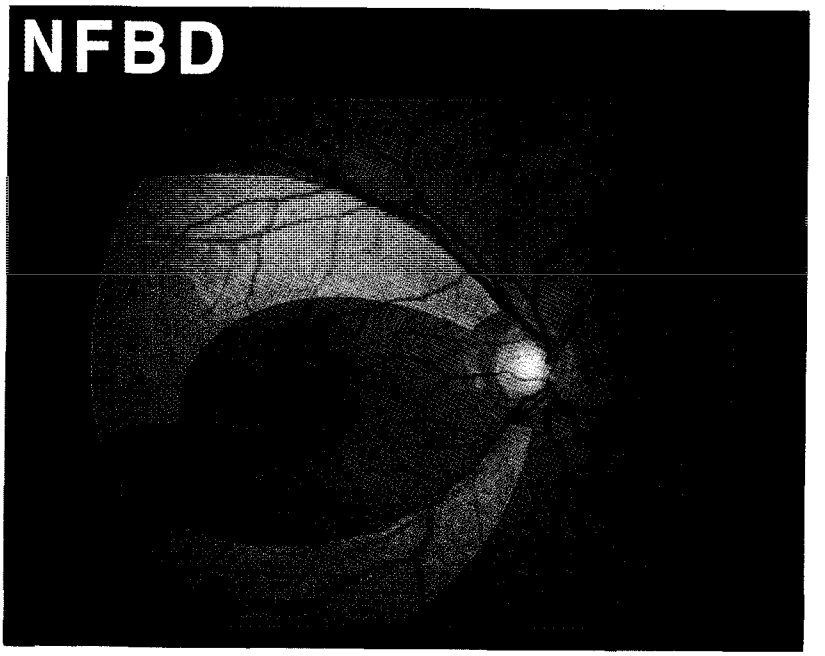

Fig 5.

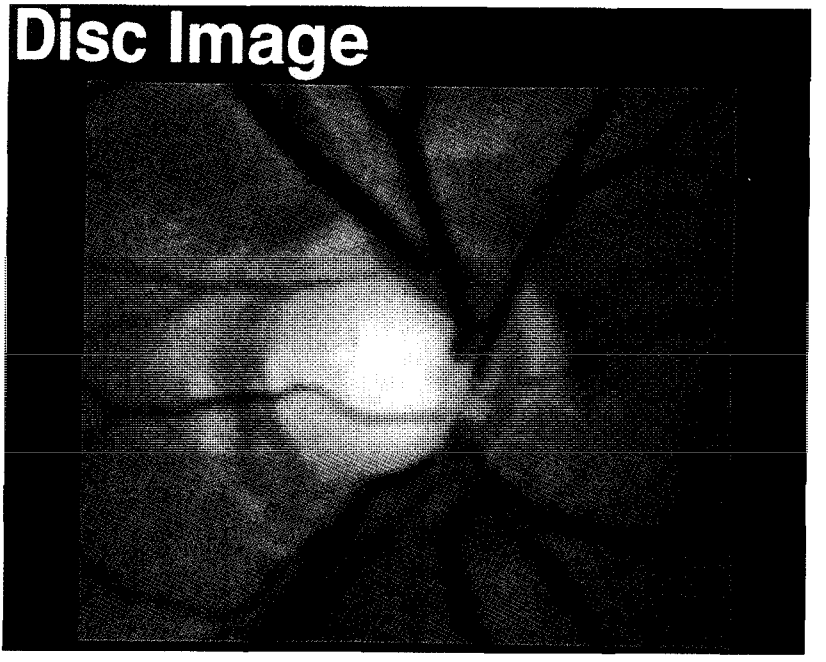

Fig 6

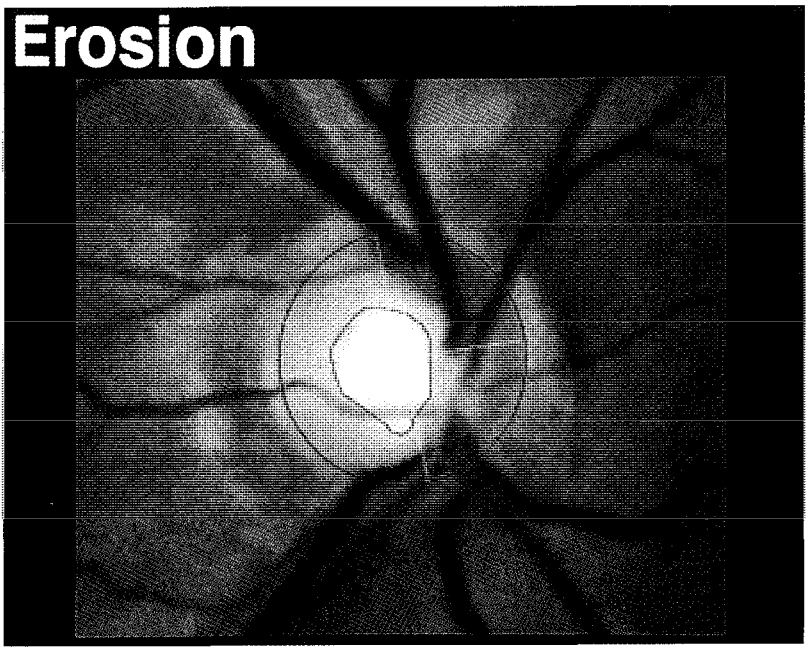

Fig. 7

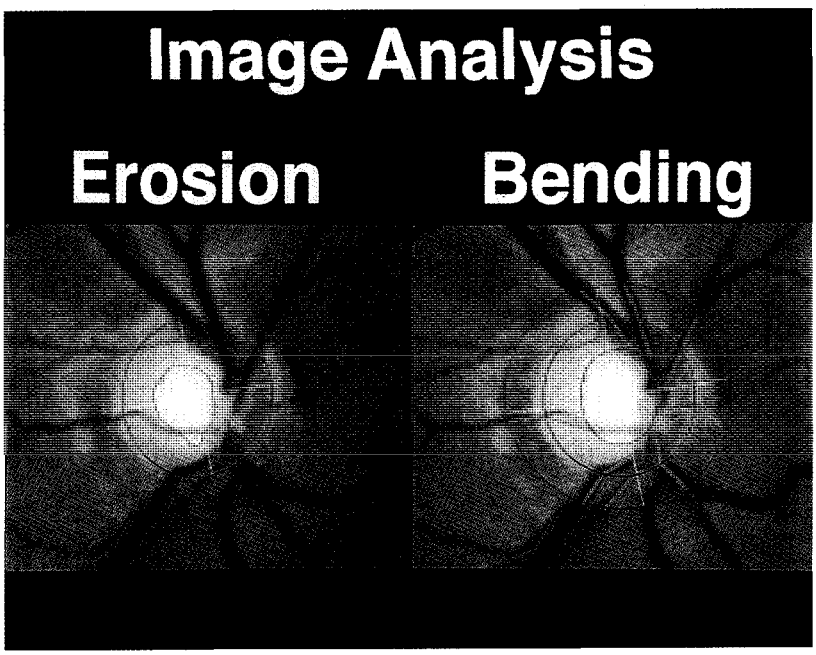

Fig 8.

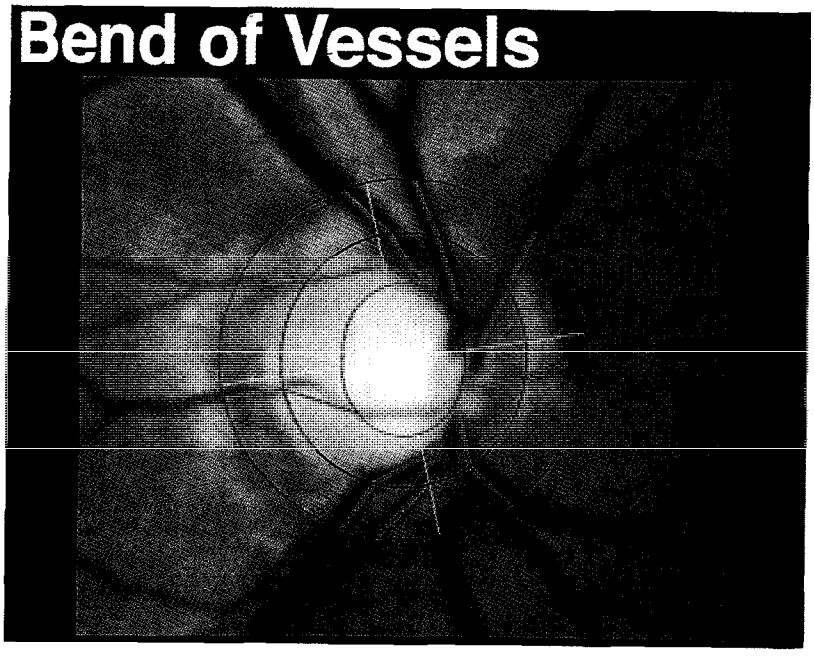

Fig 9

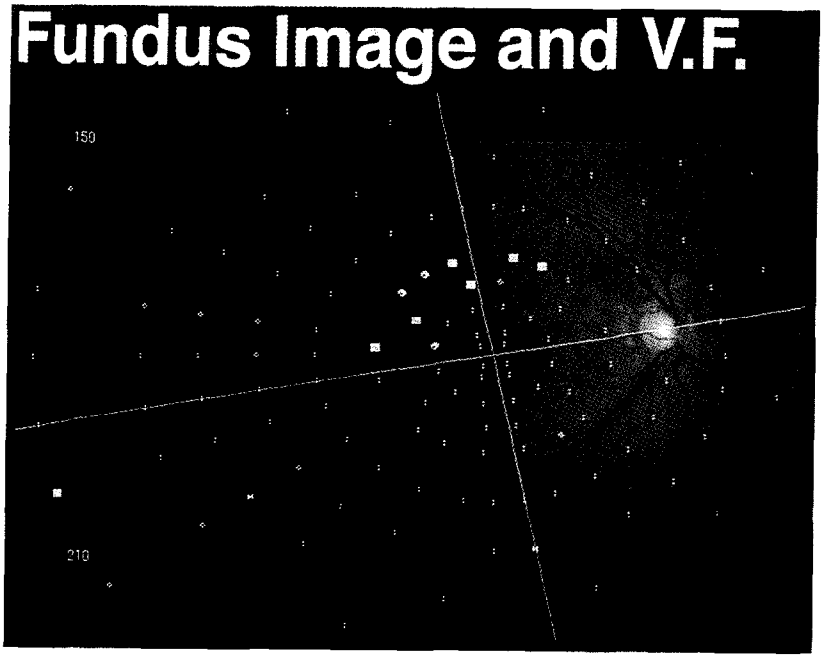

Fig 10

tion. Further, we see an overlapping distribution of shallow visual field defect, erosion between the optic disk edge and the pallor edge, NFBD and blood-vessel bend in the 7 o'clock direction. The similar orientation of these parameters probably indicates that particular attention is warranted.

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MISCELLANEOUS

Fluorescein filling defects of glaucomatous optic disks and visual field changes

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Abstract

Fluorescein angiography of 20 eyes with glaucoma was performed with a scanning laser ophthalmoscope Disk filling defects corresponded with visual field defects and their density No difference was observed between normal-tension glaucoma and primary open-angle glaucoma in this small series

Introduction

A scanning laser ophthalmoscope (SLO)[1,2] is a device that scans the fundus of the eye using a laser while the images obtained are shown on a video monitor

The SLO has the following advantages

1. It allows detailed observation of retinal hemodynamics in real time.
2. It permits detailed observation of the lamina cribrosa and retinal nerve fiber layer
3. Since the microscopic objective of the SLO has a wide range, it is easy to focus In addition, the intensity of the light used is far lower (approx. 1/20) than for conventional funduscopes Thus, the SLO causes less discomfort during examination and enables observation to be continued for a long time

The mechanism of optic nerve damage in glaucoma has yet to be clarified. The mechanical theory proposes that optic nerve damage is due to ocular hypertension[3], while the vascular theory suggests that ischemia of the optic disk is responsible[4–6] Thus it is important to evaluate the circulatory status of the optic disk when investigating the pathology underlying glaucoma

In the present study, fluorescein angiography of glaucomatous eyes was performed using the recently developed scanning laser ophthalmoscope (SLO), and the relationship between absolute filling defects and visual field changes was investigated

Subjects and methods

The subjects included seven patients (ten eyes) with primary open-angle glaucoma (POAG) and nine patients (ten eyes) with normal-tension glaucoma (NTG). Fluorescein angiography of the optic disk was performed at an imaging angle of 20°. An argon blue laser (488 nm) was used for the excitation light source The relationship between fluorescein filling defects[7] of the disk and visual fields was analyzed. The visual fields were compared with those fluorescein angiographic images in which disk filling defects were most clearly observed, and the percentage of the disk area occupied by filling defects was calculated utilizing a digitizer (filling defect area/total disk area %)

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Table 1

		NTG	*POAG*	*Unpaired t test*
	mean	57 40	60 00	
Age	SD	12 74	14 14	
	n	10	10	$p = 0\ 671$
	mean	23 63	18 28	
% disk area of filling defects	SD	13 52	7 57	
	n	10	10	$p = 0\ 293$
	mean	28 99	20 17	
I-2-e isopter (cm^2)	SD	21 35	13 64	
	n	10	10	$p = 0\ 285$
	mean	127 45	133 20	
I-4-e isopter (cm^2)	SD	39 71	22 61	
	n	10	10	$p = 0\ 695$
	mean	–6 85	–5 69	
Mean deviation (dB)	SD	7 11	4 86	
	n	10	10	$p = 0\ 673$
Mean deviation for test points	mean	–9 25	–6 04	
corresponding to filling defect	SD	9 37	6 05	
(dB)	n	10	10	$p = 0\ 812$
Mean deviation for test points	mean	–4 58	–3 41	
not corresponding to filling	SD	5 12	3 21	
defect (dB)	n	10	10	$p = 0\ 829$

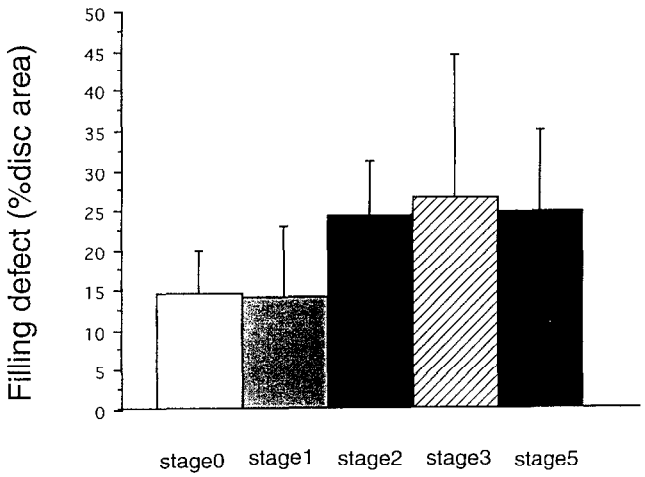


Fig 1 Stage of glaucomatous visual field defects by Greves' modified classification

The following points were evaluated

1 The relationship between percentage disk area of fluorescein filling defects and the area of intact visual field for the I-4-e and I-2-e isopters by Goldmann perimetry.
2 The relationship between percentage disk area of fluorescein filling defects and the mean deviation obtained by the Humphrey Field Analyzer.
3 Using the method of Wirtschafter *et al* [8], those test points (out of a total of 74) in program 30-2 that corresponded to those disk filling defects were identified. The mean deviation for these corresponding test points was then compared to that for the remaining non-corresponding test points

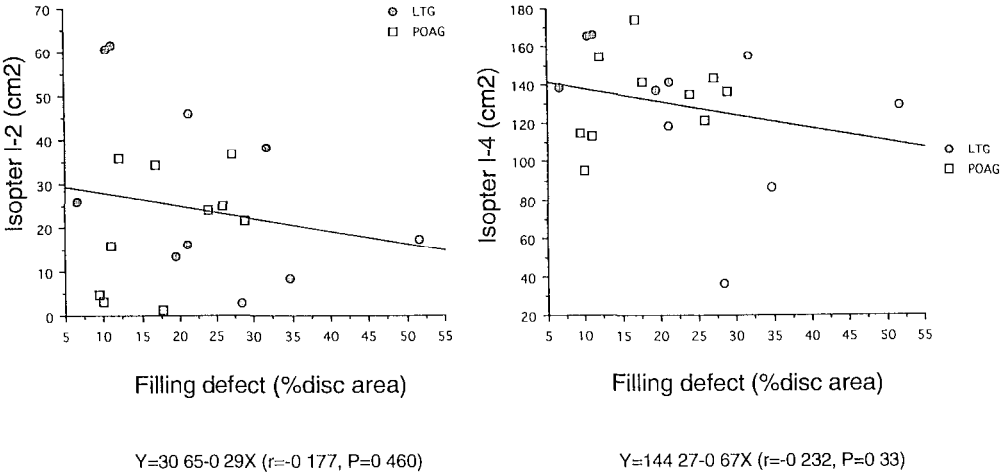


Fig 2

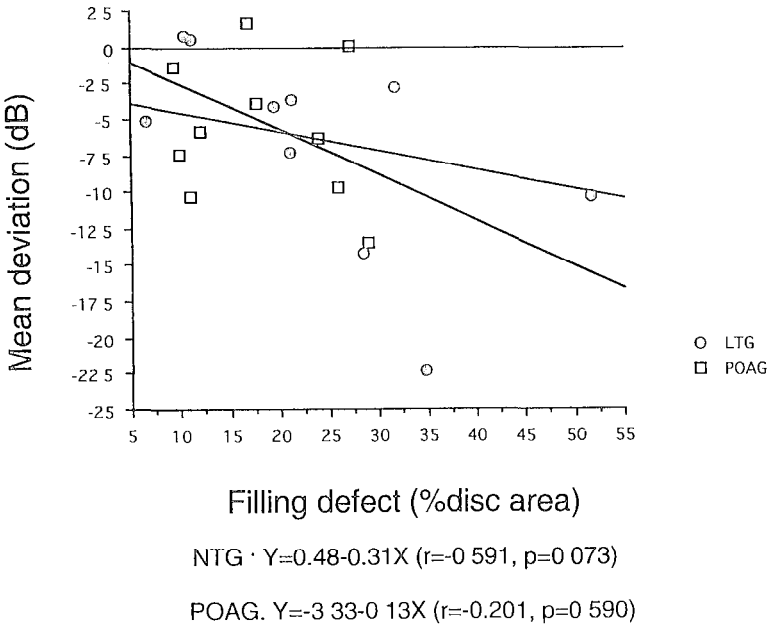
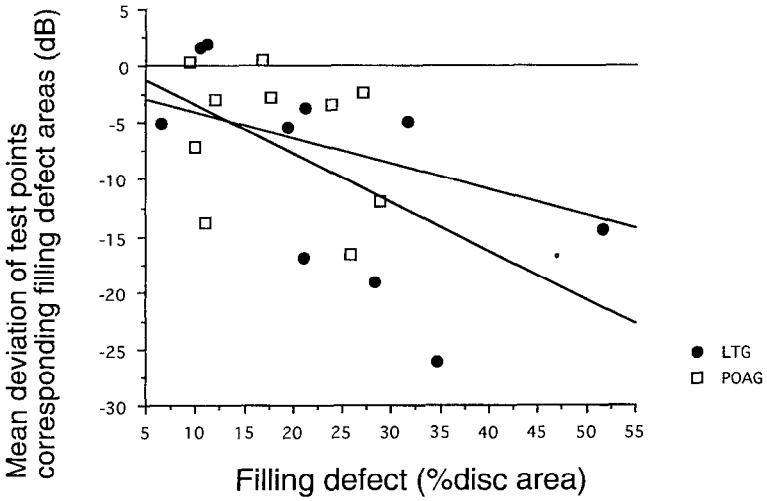


Fig 3

Results

Disk filling defects were detected in all cases having visual field changes, with most corresponding in location to the visual field defects Furthermore, the size of the filling defects was found to increase with severity of the visual field changes (Fig 1) There was no difference between NTG and POAG groups in terms of average percentage area of fluorescein filling defects, average area of I-4-e and I-2-e isopters, and average mean deviations and average age (Table 1)



NTG : Y=0.87-0.43X (r=-0.619, p=0.559)

POAG: Y=-1.91-0.23X (r=-0.283, p=0.442)

Fig 4

Relationships between percentage disk area of fluorescein filling defects and area of intact visual field, for I-4-e and I-2-e isopters; both the areas for the I-4-e and I-2-e isopters showed a tendency to decrease with increasing size of disk filling defects The correlation coefficients between visual field area, and percentage disk area of filling defects were $r = -0\,232$ ($p = 0\,33$) for the I-4-e isopter, and $r = -0\,177$ ($p = 0.460$) for the I-2-e isopter, respectively (Fig. 2)

The relationship between percentage disk area of fluorescein filling defects and mean deviation· The percentage disk area of filling defects was compared with the mean deviation in order to evaluate the relationship between retinal sensitivity of the central visual field and disk perfusion Mean deviations were observed to decrease with enlargement of filling defect areas The correlation coefficients were $r = -0.488$ ($p = 0.028$) for all cases together, $r = -0.591$ ($p= 0.070$) for NTG cases only, and $r = -0\,201$ ($p= 0.201$) for POAG cases only (Fig. 3)

There was a statistically significant difference (paired t test, $p = 0.006$) between the average mean deviations for test points corresponding to filling defects ($-7.65 \pm 7\,85$ dB) and those not corresponding to filling defects ($-4\,00 \pm 4.20$ dB), when all cases were considered together Mean deviations for test points corresponding to filling defects showed deterioration with increasing percentage disk area of filling defects (Fig 4). The difference between NTG and POAG was not statistically significant due to the limited number of cases in each group

Discussion

A number of authors have stated that the primary event in the development of visual field defects in glaucoma is papillary circulatory impairment. In contrast, other investigators believe the primary event to be degeneration of optic nerve fiber bundles, with regression of the papillary capillary network occurring secondarily Thus, the role of disk filling defects in the pathogenesis of the visual field defects of glaucoma remains unclear

Absolute filling defects of the optic disk corresponding to visual field defects were noted in

all cases, with the percentage area of filling defects increasing with decreasing retinal sensitivity. Mean deviations for test points corresponding to areas of absolute filling defects were lower than that for non-corresponding test points These findings suggest that absolute filling defects of the disk may accompany retinal sensitivity loss in established glaucoma

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Correlation between intraocular circulatory dynamics and visual field defect in normal-tension glaucoma

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Abstract

The blood flow velocity of ophthalmic artery was analyzed in normal subjects and patients with normal-tension glaucoma (NTG) to investigate the relationship between the change of intraocular circulatory dynamics and visual field defect Thirty-five normal subjects and 25 NTG patients were examined using color Doppler imaging Visual field testing was performed with program central 30-2 of the Humphrey Field Analyzer and intraocular pressure with a Goldmann applanation tonometer Resting systemic blood pressure and heart rate were examined prior to the measurement of the blood flow velocity of the ophthalmic artery

There were no significant differences in systemic blood pressure, pulse rate, intraocular pressure between normal subjects and patients with NTG The NTG patients showed a significant reduction in the blood flow velocities ($p < 0\ 01$), and a significant increase in resistivity index ($p < 0\ 01$) compared with normal subjects The linear regression of resistivity index on mean deviation was statistically significant in NTG patients ($r = 0\ 558$, $p < 0\ 01$) ·

The results indicate that circulatory dynamics of ophthalmic arterial perfusion might be related to the progression of the visual field defect in patients with NTG

Introduction

The mechanism of damage in visual function in glaucoma is unclear. Damage to the optic nerve can be caused by elevated intraocular pressure (IOP) alone However, vascular factors with or without an elevated IOP have been implicated in the development of glaucomatous damage. Many vascular diseases have been reported to be related to glaucoma including diabetes[1], hypertension[2] and migraine[3]. Spasm of peripheral vessels has been found to be more common in patients with normal-tension glaucoma (NTG) than in normals[4]. Disk hemorrhage, which is proposed to be an ocular vasospastic sign, has a higher prevalence in patients with NTG compared with high-tension glaucoma (HTG). This suggests that circulatory disturbances may play a role in development of glaucomatous damage[5] However, it remains difficult to study the ocular circulation in human eyes by direct examination

Color Doppler imaging (CDI) is a recent advance in diagnostic imaging for the study of vascular disorders[6–10]. CDI enables a detection of blood flow velocity at specific locations by simultaneous B-mode imaging The technique has been described as a means of investigating orbital arterial blood flow velocity in the eye and orbit by identifying waveforms from specific sites.

In this study, we compared the blood flow velocity of the ophthalmic artery in patients with NTG and normal subjects

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Subjects and methods

We studied 60 subjects comprising of 25 patients with NTG and 35 normal subjects. Diagnostic criteria for NTG were consistently lower IOP than 21 mmHg including diurnal tension studies, and characteristic glaucomatous optic disk cupping along with visual field defects. Patients with a history of intraocular surgery, cardiovascular disease, systemic hypertension or hypotension, diabetes mellitus, and collagen vascular disease were excluded in this study.

Methods

This study was approved by the Ethics Committee of the Nihon University School of Medicine Informed, written consent was obtained from each subject after the procedure has been fully explained. The flow velocity of ophthalmic artery was measured with CDI unit The CDI scanner (SSA-160A®, Toshiba, Tokyo) was used in this study, with a 5 0-mHz sector-phased transducer (PVF-50FT®, Toshiba, Tokyo). The estimated peak temporal intensity at 3.5 cm depth in the spectrum analysis mode is approximately 93 mW/cm^2. Although this intensity exceeds the guidelines for ophthalmic application by current Japanese Industrial Standards, the Doppler power was set at 15% of maximum

Color Doppler examinations were performed by an observer who was masked from the clinical diagnosis of the subjects. Velocity readings were obtained within the branch of the ophthalmic artery that enters the ethmoid air cells adjacent to the medial orbital wall and 15 mm posterior to the globe.

The peak systolic flow velocity (peak), the mean envelope velocity (mean E), and end diastolic flow velocity (diastolic) were determined, and resistivity index was calculated according to the following formula: RI was equal to peak velocity minus diastolic velocity over peak velocity.

We compared each of the four indices between one randomly selected eye of the 35 normal subjects and 25 patients with NTG. Systemic blood pressure, heart rate and intraocular pressure were also recorded prior to the CDI examination The visual field of patients with NTG was examined using program central 30-2 by the Humphrey Field Analyzer (Allergan-Humphrey, San Leandro, CA). Using a statistical analysis package (Statpac [Allergan-Humphrey, San Leandro, CA]), we calculated the mean deviation (MD) and the corrected pattern standard deviation (CPSD) as indices for visual field defects.

Student's t test was used for statistical evaluation

Results

The general clinical measures in normal subjects and patients with NTG is shown in Table 1. There were no statistically significant differences in age, systolic, diastolic blood pressure, heart rate and intraocular pressure between the two groups at the time of examination.

Table 2 demonstrates the results of the four indices of normal subjects and patients with NTG NTG patients had a significant reduction in peak, mean E, diastolic velocities of the ophthalmic arterial blood flow ($p < 0\ 01$), and a significant increase in the resistivity index ($p < 0\ 01$) compared with normal subjects The relationships between blood flow indices and visual field indices were examined between both groups using linear regression The linear regression of resistivity index on MD was highly statistically significant in patients with NTG ($r = 0.558$, $p < 0\ 01$), however, values for peak, mean E and diastolic velocity had no correlation with MD and CPSD

Discussion

The advent of Doppler ultrasound, which enables a reliable non-invasive measurement of the blood flow velocity in the ophthalmic artery, was the impetus for comparing the ophthal-

Table 1 General measures of normal subjects and normal-tension glaucoma

	Normal subjects (n = 35) mean ± SD	*Normal-tension glaucoma (n = 25) mean ± SD*
Age (years)	56 3 ± 9 7	58 8 ± 11 2
Systolic BP (mmHg)	125 3 ± 16 5	125 6 ± 12 1
Diastolic BP (mmHg)	74 9 ± 11 7	71 4 ± 7 4
Heart rate (beat/min)	80.1 ± 9 4	81 1 ± 8 5
IOP (mmHg)	14 2 ± 2 6	13.6 ± 2 0

SD = standard deviation; BP = blood pressure; IOP = intraocular pressure

Table 2 Ophthalmic flow velocities in normal subjects and normal-tension glaucoma

	Normal subjects (n = 35) mean ± SD	*Normal-tension glaucoma (n = 25) mean ± SD*	*p value*
Peak velocity (cm/sec)	42.2 ± 10 2	34 9 ± 12 0	< 0.01
Mean E velocity (cm/sec)	27 0 ± 9.4	20 8 ± 9 3	< 0 01
Diastolic velocity (cm/sec)	10 9 ± 4 9	7 6 ± 4.6	< 0 01
Resistivity index	0 73 ± 0 07	0 79 ± 0 07	< 0 01

SD = standard deviation

mic arterial flow velocity of normal subjects and patients with NTG. We found that NTG patients showed a significant reduction in all three indices of velocity and a significant increase in resistivity index compared with normal subjects. We found that resistivity index showed a significant increase with an increase of MD in patients with NTG However, there were no significant differences in general systemic clinical measures between normal subjects and patients with NTG. These findings indicate the possibility that the change of circulatory dynamics of the ophthalmic artery in patients with NTG may be related to the progression of the visual field defect.

Ocular vasospasm has been proposed as a risk factor in the pathogenesis of NTG. Recently it was reported that vasospasm plays a significant role in the development of visual field defects in some cases of NTG[11], and that the oral administration of a calcium channel blocker may cause visual field improvement by reversing the vasospastic events[12] The blood supply to the tissue is determined by perfusion pressure, vascular resistance and blood viscosity The arteriolar vascular bed is the focus of maximum vascular resistance. The arterioles mainly determine the local diameter throughout a vascular region by changes in the smooth muscle tone. If vasospasm occurs for pathophysiological reasons, ischemia of the tissue to be supplied can occur.

The blood supply of the optic nerve depends much more on the choroidal circulation than the retinal circulation, *i e* , the main blood supply of the optic nerve comes from the short posterior ciliary arteries[13]. Therefore, vascular resistance of small vessels in optic nerve head and peripapillary choroid may be important in the pathogenesis of NTG.

Therefore, the measurements of the present study do not directly reflect the circulatory dynamics of the optic disk. However, we conclude that the vascular resistance of the ophthalmic artery plays a role in the progression of visual field defect in patients with NTG This finding suggests that the circulatory dynamics of the ophthalmic artery might be related to the visual field defect in patients with NTG

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The visual field in diabetic retinopathy

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Abstract

The authors performed automated static threshold perimetry (Humphrey 30-2 full threshold program) in 63 diabetic patients at all stages of diabetic retinopathy Each eye was tested three times giving a total of 378 visual fields The study was designed in this way to limit disturbing effects of random field variability and lack of perimetric experience, MD, PSD and Statpac total deviation probability maps were used in the analysis of the results

No evidence of visual field loss was found in eyes without retinopathy or with very mild and mild disease (levels 20–35 in the ETDRS final scale) Significantly increased field loss started in moderate diabetic retinopathy and increased with the severity of the disease However, field loss was usually mild or at most moderate also at later stages of retinopathy

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Threshold fluctuation in clinically stable age-related macular degeneration

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Abstract

Clinical evolution of age-related macular degeneration (ARMD) is usually evaluated by means of visual acuity and fluoroangiography The perimetric evaluation of differential light sensitivity changes in macular diseases may be difficult owing to threshold fluctuation To estimate the magnitude of non-progressive long-term light threshold fluctuation (LF), 18 eyes of clinically stable ARMD patients were studied by repeated perimetric examinations (Humphrey 640 VFA central 10–2 program)

The mean long-term fluctuation for all test locations was 2 15 ± 0 69 dB and was correlated neither with eccentricity nor with visual field gradient LF was inversely related to sensitivity: in test location where sensitivity is higher than 20 dB a loss of light sensitivity of 4 dB or more is due to random fluctuation only in 2 5% of stable ARMD patients

Introduction

Age-related macular degeneration (ARMD) is characterized by acquired modifications of the retinal pigment epithelium and photoreceptors[1]

The evolution of ARMD may be variable and unpredictable, some macular ophthalmoscopic signs, as drusen, are evident in 30% of the elderly population[2] and may be considered as a marker of risk for deterioration

In 12% of the patients ARMD shows the exudative form which leads to severe damage and even to legal blindness· the atrophic form (88%) only in 5–10% of cases presents this risk.[3]

A follow-up of ARMD is extremely important in order to find the earliest signs of subretinal neovascular membranes that can benefit from laser treatment. Usually the follow-up of ARMD is carried out by measuring far and near visual acuity, by ophthalmoscopy, fluoroangiography, indocyanine green digital angiography, Amsler grid autoexamination and perimetry.

Perimetry has often been used to evaluate both visual function and laser treatment effect in ARMD[4–12] Perimetry represents a non-invasive and easy technique to evaluate the modifications of macular light sensitivity in ARMD.

In the advanced stages of ARMD, a decrease of sensitivity is mainly related to sensorial retinal damage This loss of sensitivity is characteristic of the observed areas of atrophy and pigment epithelium detachment, while no sensitivity reduction can be found in either soft or hard drusen areas[5] The presence of drusen in ARMD does not cause local loss of sensitivity and leaves the way open to survey the development of small relative scotomas as an early sign of an atrophic or exudative process[5].

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Light threshold, as measured by automated perimetry, is subjected to physiologically well-defined short-term and long-term fluctuations[14] Furthermore these fluctuations are increased in pathological conditions, and in clinically stable diseases Threshold fluctuations have been studied in clinically stable glaucoma patients in order to establish statistical significant criteria to evaluate real sensitivity changes[15–19]

The availability of normal age-matched sensitivity values allows us to detect the earliest visul field defects in glaucoma as in other diseases, like maculopathies[20]. An extended statistical package for the assessment of multiple successive fields defects in glaucoma (Statpac 2 glaucoma change probability) has been implemented in the Humphrey VFA[21]. Nevertheless, evaluation of sequential perimetric examinations to detect progressive damage in both glaucoma and ARMD is a difficult and important problem.

The aim of this study was the measurement of threshold and its long-term fluctuation in a group of clinically stable ARMD patients in order to evaluate its relationship with depth and topography of the visual field defects. This allows identification of significant criteria to evaluate real sensitivity changes not due to random threshold fluctuation.

Materials and methods

The clinical charts of 53 ARMD patients followed in the Retina Service of the University Eye Clinic of Genoa were reviewed. Thirty-four subjects who met the following criteria were included in the study.

1) Diagnosis of ARMD based on typical ophthalmoscopic and fluoroangiographic findings, excluding exudative changes.
2) At least two available automated visual field examinations and at least nine months follow-up after the first examination.
3) Good reliability indices (fixation losses $\leq$ 10%; false positive and negative answers $\leq$ 10%).
4) Visual field defects inside 10° eccentricity.
5) Visual acuity of 0.5 or better (E.T.D.R.S. visual acuity charts), without change during the follow-up period[22].
6) Near visual acuity of 2nd De Wecker or better without changes of "metamorphopsia" during the follow-up period.
7) Refraction ± 4 00 D without changes during the follow-up time.
8) No other eye disease (cataract, glaucoma), neither laser nor surgical treatment.
9) No change in medical therapy during the follow-up period.

All the subjects included in this study were successively examined at least three times by automated perimetry The time interval between examinations was at least three weeks.

All visual fields were performed with the Humphrey 640 VFA using the central 10–2 program (full threshold strategy), the central fixation point and the foveal threshold measurement At the end of the follow-up period all subjects underwent a fluoroangiographic examination

Sixteen subjects were excluded from our study for the following reasons (1) appearance of exudative changes or subretinal neovascular membranes; (2) visual acuity decay; (3) reliability indices deterioration; (4) voluntary withdrawal; (5) excessive tiredness; (6) refractive modifications

At the end of the study 18 eyes of 18 patients were included in the statistical analysis

In every patient, light threshold values in each series of examination were compared point by point and the long-term fluctuations were measured.

The long-term fluctuation (LF) was defined as the statistical variance of the repeated measurements of the differential light sensitivity at each test location

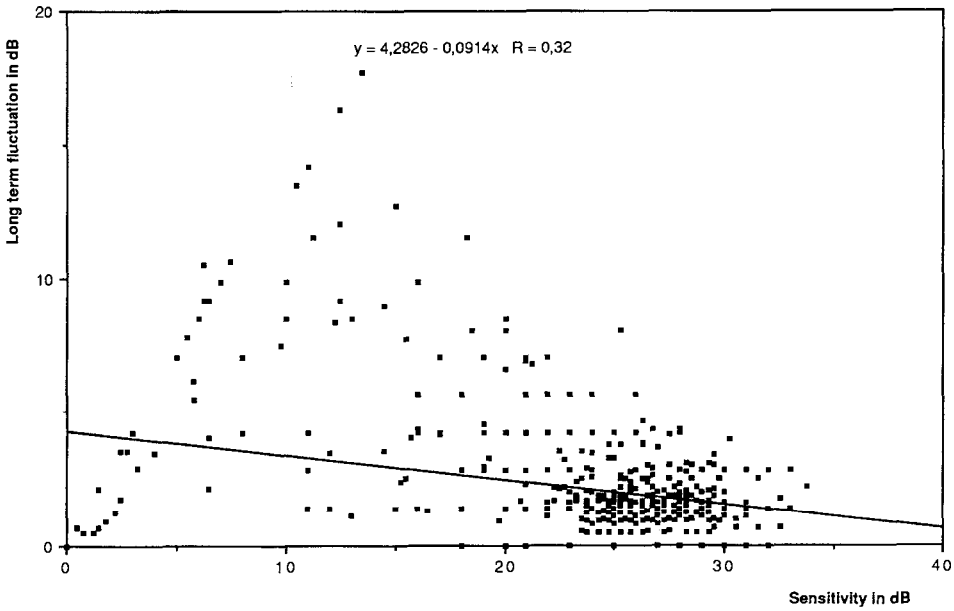

Fig 1 Scatterplot of the long-term fluctuation versus differential light sensitivity

Results

Seventy-six visual fields of 18 eyes of 18 patients were qualified for the study Each patient had an average of 4 2 visual field examinations (range 3–5). The mean time interval between examinations was 27.5 days ranging from 17 to 34 days

The patient's mean age (± SD) was 57 3 (± 8 3) years (range 48–71). The mean light sensitivity of all visual fields was 23.51 ± 5 07 dB (range 15.70–30 dB) and the mean (± SD) LF for all test locations of the entire sample was 2.15 ± 0 69 dB with the 95% confidence limits between 0 77 and 3.53 dB

The linear regression analysis of LF with differential light sensitivity showed a statistically significant negative correlation (r=0.32; $p \leq 0\ 001$); however, no significant correlation was found between LF and test location (eccentricity and visual field quadrants) (Fig 1).

The percentage coefficient of variation (CV%) (LF to light sensitivity per cent ratio) was 32 68%.

Discussion

The LF in stable ARMD patients was studied The mean LF (± SD) was 2.15 ± 0 69 dB This value is not statistically related to location· neither to eccentricity nor visual field quadrant. This can be explained if we consider that visual field examinations were carried out only in the central 10°, and in ARMD there are no specific sites with higher risk of damage

In our sample of 4968 light threshold measurements we tried to define the upper limits of threshold change in VF which might be considered a result of random fluctuation. Our results suggest, in an ARMD patient we should consider as suspect of clinical deterioration a test location sensitivity decrease of more than 3 53 dB; this change is due to random fluctuations in 5% or fewer of locations even with low differential light sensitivity

The LF correlation with light sensitivity revealed the same characteristics of other diseases like glaucoma[15–17] Test locations with good sensitivity showed low LF

A change of more than 3 dB in a single test location with light sensitivity better than 20 dB is due to random fluctuation only in 8% of our examinations, while a change of 4 dB or more is seen only in 5% The evidence that locations with very low light sensitivity frequently correspond to chorioretinal atrophic areas, may explain the reason why we found a paradoxically low LF there

These threshold changes are much more important when they are present in many locations, especially if clustered

These data provide us a practical guideline for the evaluation of progressive visual field loss in ARMD The implementation of a computerized statistical program for the assessment of the ARMD visual field probability change seems to be extremely useful and desirable.

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The feasibility of automated visual field examination in children between five and eight years of age

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Abstract

To investigate how young children develop the ability to undergo a visual field evaluation using regular automated perimetry, 42 normal girls, aged five, six, seven, and eight years, were tested Using the Octopus 2000R with a two-level strategy, 12 locations in the central 15-degree area were evaluated False-positive presentations appeared randomly in 50% of the tests, but no more than twice in succession, whereas false-negative presentations occurred in each examination session The procedure was conducted three times in succession

Before being tested, the children were given a systematic explanation of the procedure using a specially designed program This consisted of a step-by-step introduction, with successive demonstration of (1) light stimuli of different intensities projected into the central 15-degree area of the visual field, while the subject was attempting to gaze at the center of the field; (2) the same as the preceding phase, plus inclusion of false-positive presentations; (3) the same as phase two, with additional request to press the buzzer when the light stimulus was perceived; and (4) a rest period

With the exception of only one five-year-old child, all tested subjects were able to complete the planned procedure The mean proportion of false-positive answers was 17 9% (0–75%) during the first examination procedure, and 7 4% (0–51%) during the third procedure There were five negative answers in a total 308 false-negative catch trials Four five-year-old children each gave one false-negative answer

Children did remarkably well regarding both the duration of the examination and the reliability of the answers A preliminary familiarization phase with a specially designed adaptation program was found to be mandatory with children aged seven or under.

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A.R.G.U.S. – A model for an interactive perimetric and functional neuroanatomic atlas*

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Abstract

A R G U S is a data base that connects scotomata directly with possible sites of lesions in the visual pathways and vice versa

Visual field defects can be depicted on a VDU by means of a touch-screen or a "mouse" while on a second monitor the computer program simultaneously shows the resulting defects in the visual pathways and the specific patterns of optic atrophy It is possible to page through different sections of the visual system; the lesion is most probably located in that section where on the one hand the affected fibers lie most closely to each other and on the other hand the non-affected fibers are maximally apart, respectively Additionally, the VDU depicting the visual pathways can show the surrounding anatomic structures in the form of brain sections Even in these sections, lesions can be superimposed interactively; the resulting scotomata are simultaneously depicted on the "visual field VDU" Anatomic and functional details can be displayed by touching the structure of interest. For educational reasons, a video clip (demonstrating neuro-ophthalmological symptoms like refraction scotoma, afferent pupillary defect, different types of nystagmus,) can be activated in the same way New anatomic findings can be considered by modifying the course of fibers of the visual pathways. This new technique is especially helpful in distributing comprehensive neuro-ophthalmological knowledge

Introduction

A perimetric atlas has the difficult task to provide a didactically impressive link between a functional defect (scotoma) and the causal morphological pathology (lesion of the visual pathways).

Previous publications on this subject meet this expectation only in a quite incomplete manner. Nearly always there is only a unidirectional link between functional loss and a morphological lesion: mostly, the sites of lesions are handled along the course of the visual pathways and the resulting scotomata are demonstrated step by step

In contrast to this method, the physician is usually confronted with quite a different procedure: he has detected a visual field defect and now is looking for the most probable localization of the lesion This access sometimes leads to several solutions; this may be the reason that this clinically important approach is only rarely chosen.

A R G U S , a software model based on a personal computer, is able to link all the features mentioned above in an *intuitive, interactive, bidirectional* way.

*Essential parts of this manuscript were taken from a prior publication in the German language[30]

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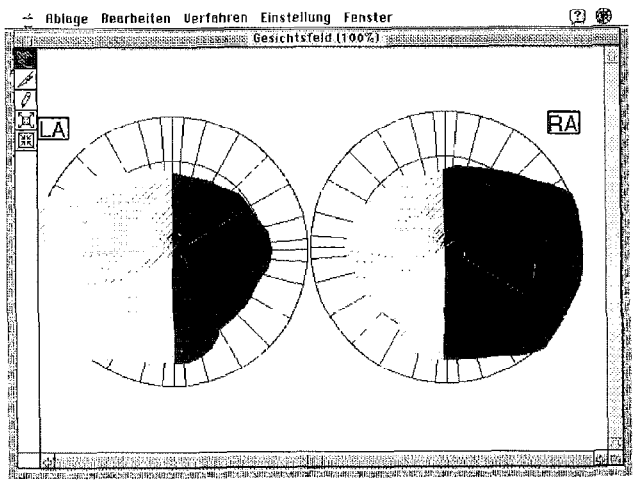

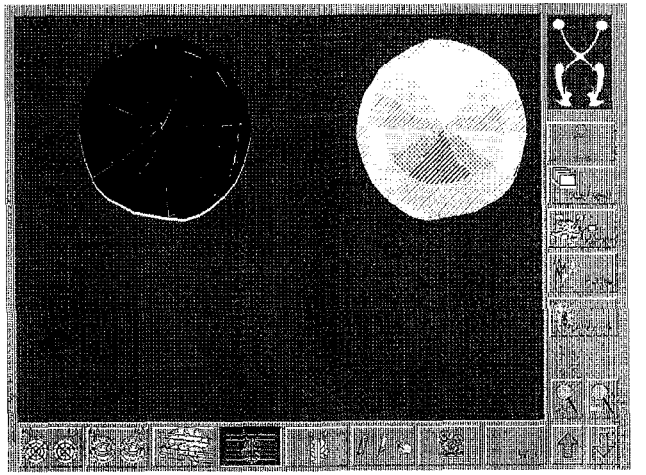

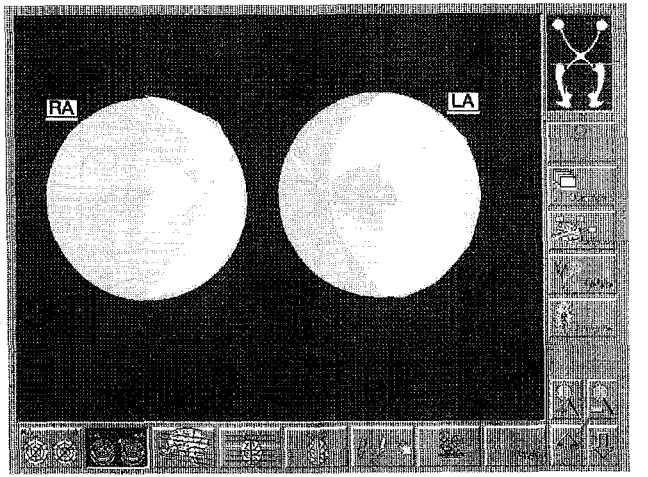

Fig. 1. Homonymous hemianopia to the right, caused by a lesion of the left optic tract. Depiction of the combination of VDUs realizing A.R.G.U.S.. *Top left*: "Visual field VDU": scotomata are represented by black areas; *Top right*: "Anatomic monitor" depicting a coronal section of the visual pathways at the level of the optic chiasm; the actual position of the sectional plane is symbolized by the line in the small window at the right upper corner. Affected fiber bundels are shown in black. *Bottom*: Additionally, the retinal nerve fiber pattern can be shown: affected nerve fiber bundles are depicted in white – analogous to optic disk pallor (view through the direct ophthalmoscope).

Methods

A Quadra 840 av personal computer (Apple Inc , Munich, Germany, Motorola 68040 CPU, 40 mHz, with 68882 mathematical co-processor, 16 MB RAM and an internal 1 GB hard disk) is the central part of this prototype. Additionally, further external storage media (hard disks, magneto-optical disks) can be installed without any problems

The computer is connected with two VDUs (Fig 1)

- The "perimetric" VDU (Fig 1, top, left) is a conventional 13"-color monitor (Apple Inc.).
- The "menu" or "anatomic" VDU (Fig. 1, top, right) is a high resolution (75 dpi, 1024 pixel × 768 pixel; 20" diagonal diameter) color monitor, driven by a special graphic board (miroChroma/CALIBRATOR, German distributor: Fa. Miro Datensysteme GmbH, Braunschweig).

The user is guided by continuously visible "icon keys". These can be activated by a mouse click or even more simply by touching the monitor with the finger tip. The latter is realized by a touch screen, sensitive to changes of capacity (TouchScreen ClearTek, German distributor· IQ 2000 AUTOMATION Inc , Freising)

The software allows an interactive, bidirectional visualization of defects of the visual field or lesions of the visual pathways, respectively. Additionally, the user can call for further information (Fig. 2), *e g*

- windows with activatable text passages,
- detailed anatomic figures (in different sectional planes),
- visualization of affected nerve fiber layers and patterns of optic disk atrophy according to a special visual field defect (Fig. 1, bottom),
- movie-like sequences (realized by a recent Apple software development, called QuickTime™, working with special compression routines, Fig. 3)

Discussion

It is a primary task of a (neuro-)anatomic atlas to provide the user with correct information about naming, size, shape, and position of anatomic structures relative to neighboring tissue[1–6]. In this context, some publications try to give an illustrative pseudo-3D illustration, additionally concerning functional, patho-physiological, and patho-morphological facts[7,8].

According to requirements of computerized imaging techniques, modern neuroanatomic or neuroradiologic publications depict structures of interest not only by one view but provide the user with different relevant sections (coronal, axial, sagittal, .)[9–15] Recently, anatomic data stored on electronic or magneto-optical media are used High-end (personal) computers with special graphic performance allow the construction of optional sectional planes[16–19]

Conventional textbooks confront a reader searching for special information with a rigid strategy of knowledge transformation in the form of a list of keywords or an arrangement of chapters. This method is acceptable as long as pure facts have to be transferred However, this strategy comes to its limits as soon as graphic data are of particular interest. An anatomic atlas and a textbook both claim to inform the users as completely as possible Their rigidity, combined with their aim at completeness are responsible for the fact that in most cases they answer questions that have not been asked by the user at all.

In the case of a perimetric atlas there occurs the additional problem that it has to elucidate the link between a *functional* loss (scotoma, described by graphic data) and a *morphological* defect (again, characterized by pictorial information). Due to limitations of the size of a publication, this link normally is *unidirectional* only: in most cases, typical lesions of the visual pathways (sometimes in a quite simplifying matter) and the resulting visual field defects are shown[20–24] This method is particularly informative in structures with complicated course of the visual fibers as this is the case in the chiasmatic region[25 29], for example. In the case of a

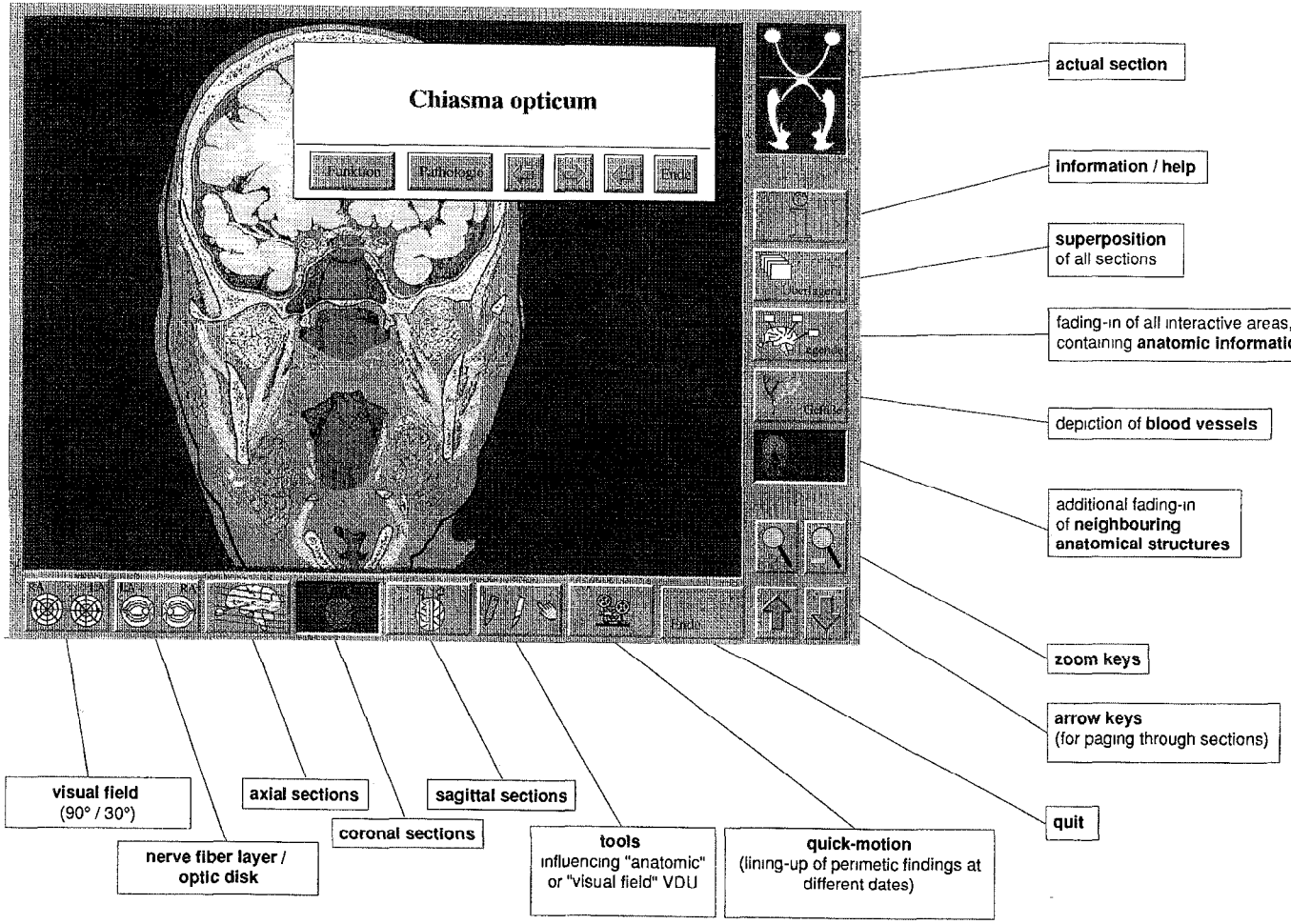

Fig. 2. Graphical user interface of the "anatomic monitor" (schematic view). Touching a structure of interest induces opening of a pop-up menu showing its anatomic name. Additional keys provide the user with further information about *function* or *pathological changes* of this structure.

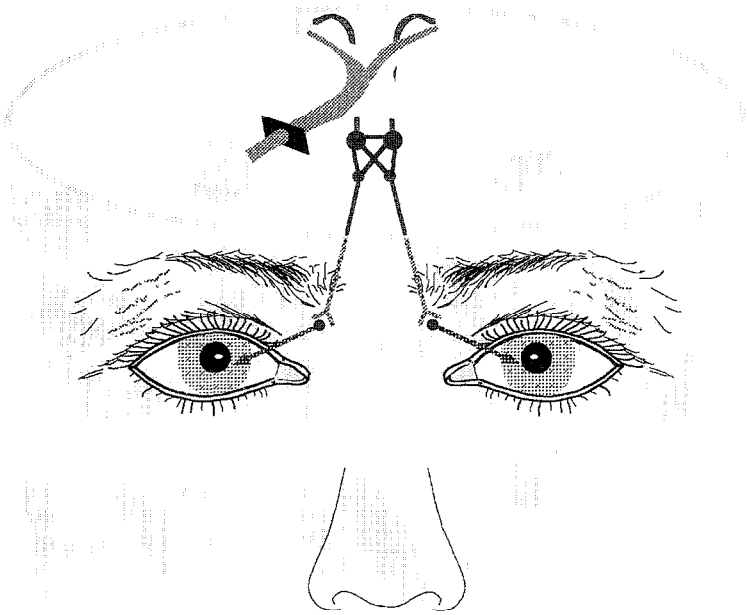

Fig. 3 Single frame taken from a movie-like audiovisual sequence (QuickTime™) illustrating the term "afferent pupillary defect"

known site of a lesion this is without doubt an adequate and effective procedure However, in most cases the ophthalmologist has to face just the opposite situation: he is confronted with a visual field defect and has to reconstruct the exact localization of the underlying lesion.

The *interactive, bidirectional* procedure of A R G.U.S satisfies both requirements mentioned above: it does not matter whether the morphological or the functional defect is taken as the leading factor[30] Just entering this lesion on one VDU induces a depiction of its results on a second monitor at the same time, this is an additional remarkable didactic advantage Furthermore, affected retinal nerve fiber bundles can be highlighted to facilitate early recognition of special patterns of optic disk pallor. Another feature of A R G U S. allows to page step by step through all sections of the visual pathways after entering the visual field defect. In that way, the most probable localization of the lesion can be delineated the site of the morphological defect is most probably situated in that section where the lesions lie most closely together and have maximal distance from normal fiber bundles (principally, the software could run this procedure automatically) Having found this special section of the visual pathways, the user can additionally fade in the surrounding anatomic structures (depicted in different sectional views) All anatomical images are primarily free from any superfluous, disturbing labels. Only aiming at a structure of interest with a mouse-click or finger tip activates a pop-up menu showing the exact anatomic name and if necessary the function of the structure of interest. In that way a carefully directed search for a functional loss in other systems can be induced. Several parameters of functional importance can be demonstrated in an impressive manner by audio-visual sequences. Thus, complex disorders of ocular motility can be shown or complex functional tests can be elucidated, for example. This is of additional importance in education and patient information Of course, the final stage of such a program shall overlap many special disciplines and therefore will demand remarkable storage capacity. On the other hand, this is enabled by an enormous decline of prices especially in this computer sector

A R G U.S. is designed as an electronic educational and teaching device and thus can be rated as an interesting alternative to a conventional textbook or atlas there are no printing ef-

forts for the primary and especially any subsequent editions. Corrections of mistakes, revised editions can be simply shipped as update-disks This procedure is surely much more comfortable than sending around loose-leaf editions and guarantees a more actual flow of information. Additionally, electronic textbooks allow more complex and effective searching strategies. Several publishers have already realized these facts and are preparing a shift from printed to electronic media[31]

In contrast to a rigid conventional textbook, A.R G.U S is individually flexible: the user can bring in his own knowledge, skills and experiences by individual modifications (*e g* , of the nerve fiber pattern) – in a printed medium there is only the possibility of a marginal note or a letter to the author.

The program presented here is a functioning platform, primarily designed to handle questions of neuro-ophthalmological relevance. Cooperation with other disciplines (neurology, neurosurgery, neuroradiology, endocrinology, ...) can expand knowledge transfer and range of application of this new softwarc in a modular way.

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Influence on the visual field after photocoagulation or cryotherapy in children with retinopathy of prematurity

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Abstract

Many investigators reported the visual function after retinopathy of prematurity, but the development of the central visual field was not well reported previously The authors retrospectively studied the visual field within the central 30 degrees in 30 eyes of 16 children who had a history of retinopathy of prematurity Nineteen eyes were treated with photocoagulation and/or cryotherapy (treated group); the other 11 eyes had no therapy (untreated group) Perimetry was performed with the Octopus 201 program 31 in children with an average age of 12 5 years, and total loss of the visual field was studied

The total loss of the treated group was 403 9 ± 361.6 dB (mean ± SD), and that of the untreated group was 146 1 ± 130 5 dB The total loss of the treated group was larger than the untreated group, and the difference was statistically significant ($p = 0.03$)

These results not only suggest the direct influence of photocoagulation and/or cryotherapy on the visual field, but also on the baseline prematurity of retinal development

Introduction

In 1968, Nagata *et al* [1] reported that photocoagulation (PC) treatment was effective in preventing the progression of retinopathy of prematurity (ROP) In Japan, PC therapy or cryotherapy is popular for ROP, and it has brought marked reduction of the incidence of ROP-induced blindness[2,3,4]

PC or cryotherapy causes large chorioretinal atrophic lesions, which are thought to induce visual dysfunction including visual field defects corresponding to the lesions Both PC and cryotherapy tend to overcoagulate, and they could damage a larger area of retina than the scar lesion, including the posterior pole that looks intact by examination with the ophthalmoscope

Some investigators reported visual field defects with the Goldman perimeter after PC and/or cryotherapy[5,6], showing that the nasal side defect corresponds to both the severity of ROP and the coagulation scar, and in some cases, depression of sensitivity over the entire field However, little is known about the influence of treatment and ROP on central visual field with static perimetry We studied sensitivity of patients who had had ROP and influence of such therapy on the central visual field with static perimeter.

Patients and methods

The final sample consisted of two groups of children with mean age and standard deviation of 12.5 ± 3.3 years. Patients who had undergone photocoagulation (PC) with the xenon laser (O'Malley Xenon Light Coagulator, Clinitex, Inc., Danvers, MA, USA and/or cryotherapy

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(Alcon Crio-Ophthalmic Unit, Alcon Surgical Dynatech, Alexandria, VA, USA) are regarded as the treated group, and those who had had no therapy as the untreated group The average age of the former group (19 eyes) was 12.0 ± 3 4 years, and the latter (11 eyes), 13 3 ± 3 1 years, the difference of which was statistically not significant (p = 0 32)

PC was performed with scattered spots over the retina, including the demarcation line and avascular zone (power level, neutral; diaphragm, 3-4-5; duration, 0.3–0.5 seconds). Cryotherapy (temperature –55°C, duration 5 seconds) was used in addition to PC in cases of advanced proliferation or alone in cases in which treatment with PC was impossible.

All patients underwent visual acuity testing and funduscopy We selected patients with visual acuity better than 16/20 and retinopathy in cicatricial stage grade 1, with no posterior pole abnormality, including dragged disk, in funduscopy

Static perimetry, Octopus 201 program 31 (default parameters) was performed to study the visual field under full spectacle correction, with care taken to the fixation of patients It was done at least twice to obtain stable data Using the comparison program, the differences between normal sensitivity (dB) stocked with age-matching and sensitivity of patients at each point were summed up (total loss).

Results

The total loss of the treated group was 403.9 ± 361.6 dB (mean ± SD), and that of the untreated group was 146 1 ± 130 5 dB. The total loss of the treated group was larger than that of the untreated group, and the difference was statistically significant (p = 0 03; Fig 1)

In some cases, one eye was treated and the other eye untreated Figures 2 and 3 show one of such cases PC and/or cryotherapy was administered when ROP was progressing to the proliferative stage, usually active phase stage 3 It is known that even lesions of stage 3 could recover spontaneously Thus, we sometimes treated only one eye, which was slightly worse than or the same as the other The Goldman perimeter showed a nasal defect in both treated and untreated eyes The total loss of the treated eye was much larger than that of the untreated, although untreated eyes also showed depression of sensitivity from the stocked normal data.

Discussion

Many authors reported that xenon PC for ROP was effective in preventing progression of extraretinal fibrovascular proliferation when it was applied in an appropriate manner at the third stage of the active phase[2,3,7,8] In significant cases with poorly dilated pupil and/or with fair opacities in the optic media, technical difficulties required supplemental cryotherapy. The number of extremely premature infants who should be treated with PC or cryotherapy is increasing, probably due to the improvement of neonatal care. In our hospital, 4–10% of ROP patients have been treated with PC and/or cryotherapy in the past 5 years.

Both PC and cryotherapy tend to overcoagulate, and a coagulated retinal burn tends to be relatively oversize for ROP lesion, resulting in large chorioretinal atrophic lesions which are thought to be a remote cause of visual dysfunction including visual field defects and poor visual outcome[9].

Some investigators reported visual field defects by the Goldman kinetic perimetry after PC and/or cryotherapy, showing the nasal-side defect corresponding to both the severity of ROP and the coagulation scar, and in some cases, depression of sensitivity over the entire field[3,5]. In our cases, four eyes of the untreated group (total = 11 eyes) and 18 eyes of the treated group (total = 19 eyes) showed a nasal defect by Goldmann kinetic perimetry. Figure 1 shows depression of sensitivity of both treated and untreated groups in the visual field within the central 30 degrees. The total loss of the treated group was larger than that in the untreated group, and the difference was statically significant (p= 0.03)

On the basis of these results, PC and/or cryotherapy caused depression of sensitivity at the central visual field, although all of our cases belonged to cicatricial stage 1, with no remarkable scar at the posterior pole with examination by ophthalmoscope, in addition to depression

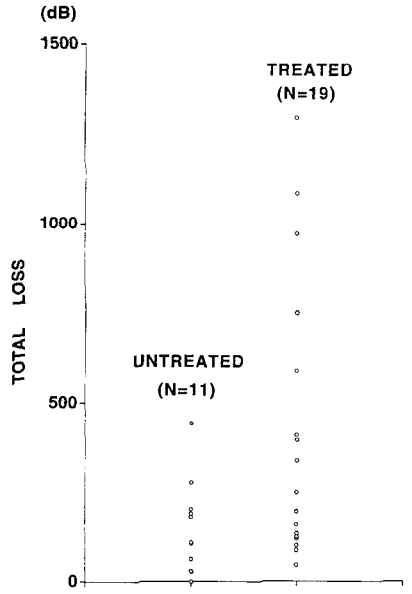

Fig 1

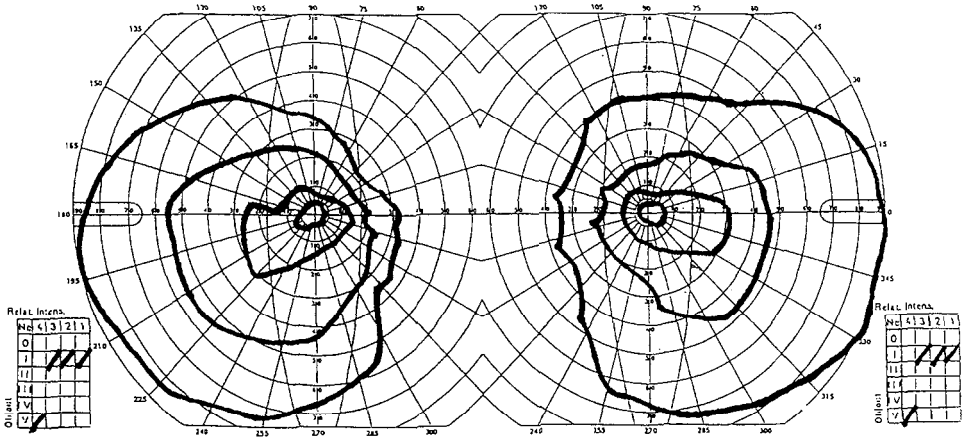

Fig 2 The girl was born with a birthweight of 1140 g at 27 weeks When ROP was progressing to the proliferative stage (active phase stage 3, zone 2) in both her eyes, PC (360° circumferential) and cryotherapy (on temporal half of retina) was administered to her left eye

for degeneration of retina for ROP itself and incompleteness of the avascular fovea in children with ROP[10–12].

It is true that PC and/or cryotherapy were very effective[13] in preventing progression to a more advanced proliferate stage, and they have brought marked reduction of the incidence of ROP-induced blindness, but we have to note that xenon PC and/or cryotherapy tend to overcoagulate, and the coagulation spots are large, which cause damage to local retinal pigment epithelium and all the retinal layers[9], not only in peripheral field but central field, causing depression of sensitivity Our results indicate that the use of xenon PC and/or cryotherapy should be minimized to prevent depression of sensitivity in the central visual field

OCTOPUS®
Form C

Surname, given names:
Date of birth: 06.02.1984
Patient number/eye: K010.91R
Examination numbers: 2 12.07.1993 16.00
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Size of stimulus: 3
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Program numbers: 31

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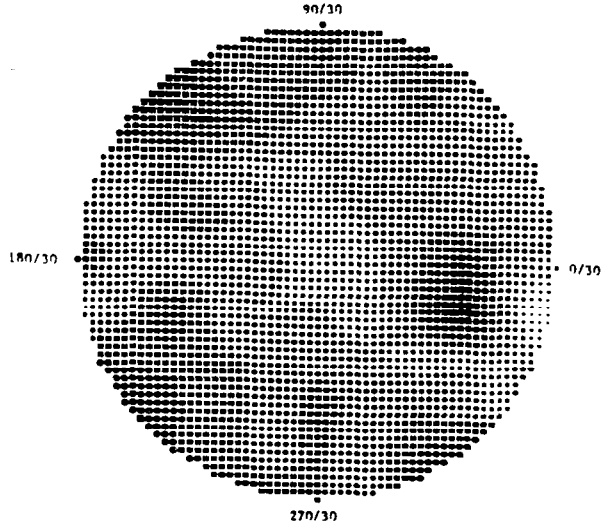
Date of printout: 2.01.1994



FLUCTUATIONS (R.M.S.): 2.4 DB LUM. INTERVAL: 2

OCTOPUS®

06.02.1984
K010.91R
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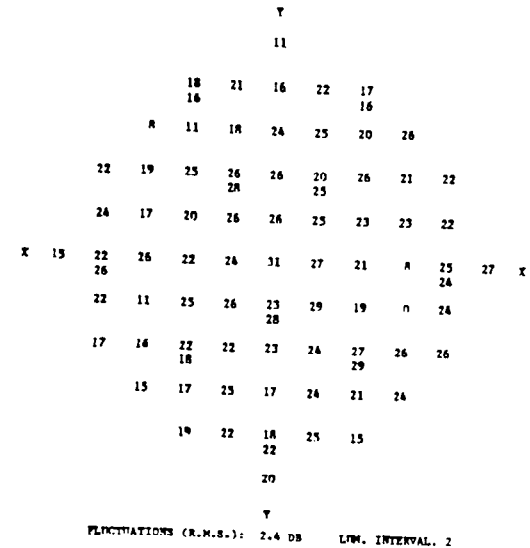

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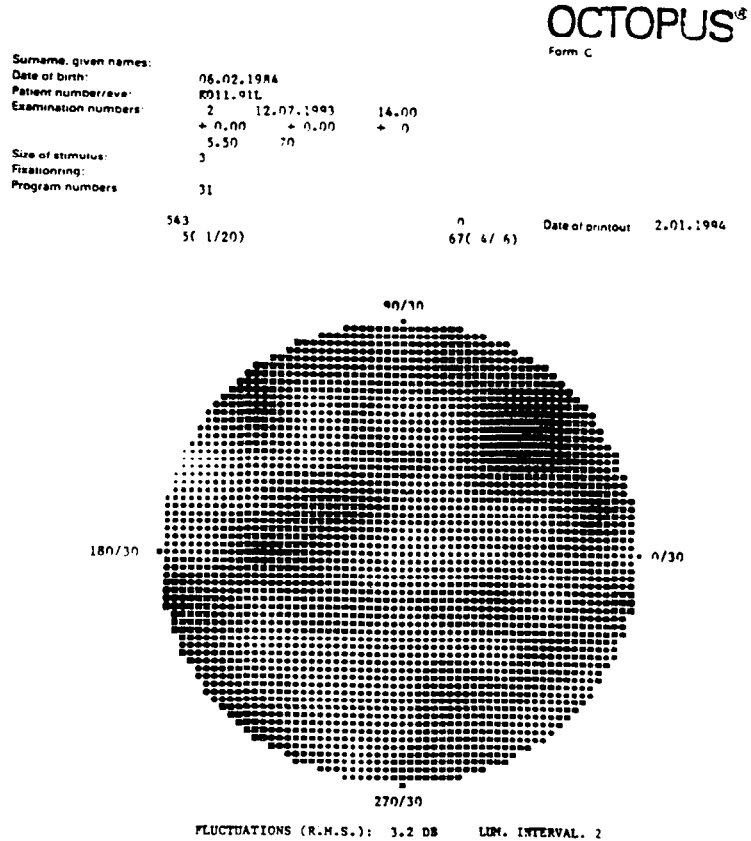
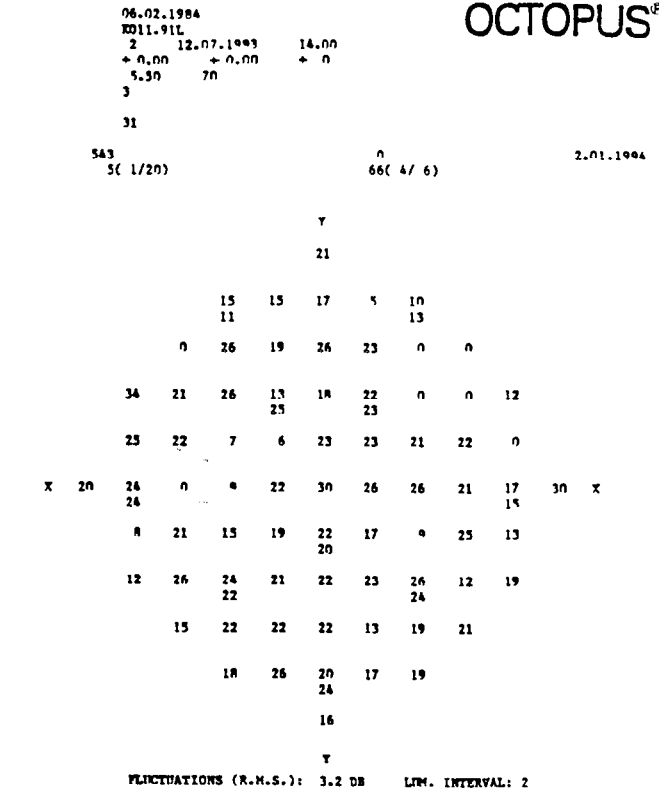
Fig. 3.





Total loss (dB)	
Right eye (untreated)	442
Left eye (treated)	750

Fig. 3.

Recently, the argon laser system has been adopted at some institutions for treatment of ROP The system enables us to attain optimal size and power output of PC in fundus areas, as intended. We are planning to investigate the influence of the argon system on the visual field and whether damage to the retina can be minimized by means of converting from xenon PC and/or cryotherapy to argon laser

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Is the Esterman binocular field sensitive enough?

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Abstract

In this study we tested 34 patients with moderate to severe glaucomatous visual field loss, to see how the severity of the disease related to the binocular Esterman field score Patients were recruited from the glaucoma clinics of two London hospitals, all were experienced on the autoperimeter Standard Humphrey 24-2 fields were performed for each eye, followed by the binocular Esterman test The average mean deviation ((left MD+ right MD)/2) was used to give an indication of the severity of glaucomatous field loss All of the average mean deviations were negative (range –7 54 to –26.57), the range of the Esterman scores was 50 to 100 The correlation between the average mean deviation and the Esterman score was $r = 0\ 751$ However, the Esterman score never fell below 50, suggesting that the sensitivity could be increased

Introduction

The International Perimetric Society has long been conscious of the shortcomings of standard visual field testing when assessing patient's functional ability Perhaps, most commonly, this type of assessment is performed for the evaluation of the individual's suitability to drive motor vehicles. The regulations on driving vary from country to country, but are based on tests of visual acuity and visual field alone In an international survey representing twenty countries Gandolfo *et al* [1] found that the requirements were either "normal visual fields" or a horizontal minimum. Only in Great Britain was an additional vertical limit stipulated The Esterman visual field test is an internationally accepted test of binocular function and is being used routinely for these assessments

We have formed the clinical impression that the Esterman field score is unexpectedly high in glaucoma patients who have established defects of their central visual field In this study we examine the relationship between the glaucomatous field loss and the Esterman score

Method

Patients were recruited from the glaucoma clinics of two London hospitals Eligible patients were those who had bilateral glaucomatous field loss and had performed a minimum of three automated field tests on the Humphrey Field Analyzer In all, 34 patients were recruited After routine follow-up, field testing using the 24-2 algorithm, a standard explanation of the binocular Esterman field test was given. The patients then each performed an Esterman binocular field test.

To give an indication of the severity of the binocular glaucomatous field loss from the 24-2 data, the mean deviations from each eye were averaged This measure has been compared to the Esterman field score.

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Results

The range of the averaged mean deviations were all negative as expected in a group of glaucoma patients, the range was –7.54 to –27.59. This measure was plotted against the Esterman visual field score Correlation was analysed using the Pearson coefficient

The correlation between the combined 24-2 field score and the Esterman score was 0 751 This is represented graphically in Figure 1.

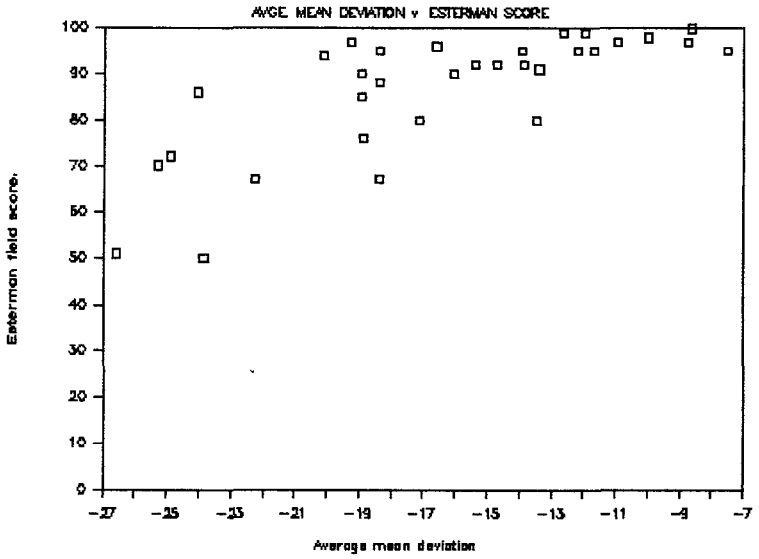

Fig 1

Discussion

In this group of patients we have found a reasonable correlation between the field defects as measured by the average mean deviations and the Esterman field score. However, the Esterman score was always above 50, including the most severely affected patients. Such a finding may be partly explained by the phenomenon of binocular summation. Interestingly, Calabria *et al.*[2] found that glaucoma patients showed a sensitivity summation less efficient than other patients when tested binocularly. To expand the useful range of scores the stimulus intensity used in the Esterman test could be decreased.

The Esterman binocular field test was originally devised to determine how useful the patient's visual field is[3]. It was not developed specifically as a test for driving Altering the parameters of the field score may render it less valuable in other medico-social and medico-economic settings. If this is felt to be the case then a binocular field test tailored to international driving requirements may have a place

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The phantom contour illusion letter test: a new psychophysical test for glaucoma?

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Abstract

Purpose: To validate the phantom contour illusion letter test (pCILT) in a glaucomatous population

Method: The pCILT is a low spatial, high temporal frequency test generated using a phase-reversing textured border of random dots to define the ten standard Sloan optotypes The phase contrast threshold was determined using two subject groups: Group 1 had 99 high-risk OHTs and glaucoma patients all without visual field loss and Group 2 consisted of 29 glaucoma patients with repeatable visual field loss The study was incorporated into the five-year prospective Toronto Hospital Glaucoma Detection Study

Results: Thirty-seven of the 99 Group 1 patients were outside the normal, age-matched 95% confidence limits. Twenty-six of the 29 Group 2 patients were classified as abnormal, with the remaining three being within normal limits Results will be compared to prospective results for blue-on-yellow perimetry and peripheral displacement thresholds

Conclusion: The pCILT is a rapid, simple test that in this cross-sectional study appeared capable of detecting early glaucoma prior to standard automated perimetry Prospective studies have been instigated to determine the test's ability to correctly predict those subjects that will develop glaucomatous visual field abnormality

Introduction

The phantom contour illusion letter test (pCILT) was developed to provide a high temporal, low spatial frequency stimulus in order to preferentially stimulate those mechanisms that subserve such visual characteristics[1,2]. Livingstone and Hubel[3] first described the use of a phase-reversing edge of high frequency and Rogers-Ramachandran and Ramachandran[4,5] suggested the use of a textured border to eliminate edge artifacts (Mach bands) that could arise from spatial non-linearities.

The repeatability and validity of pCILT has been investigated over a range of temporal frequencies and dot densities to determine the optimum stimulus characteristics The pCILT was found to have good repeatability and to give additional information about the visual system with respect to that achieved by high and low contrast letter charts and the Pelli-Robson chart[1,2]. Normal values were established for a healthy young population[1,2] and have since been established over a range of ages (see Fig. 1).

The aim of this study was to validate the pCILT in both a high risk and a glaucomatous population.

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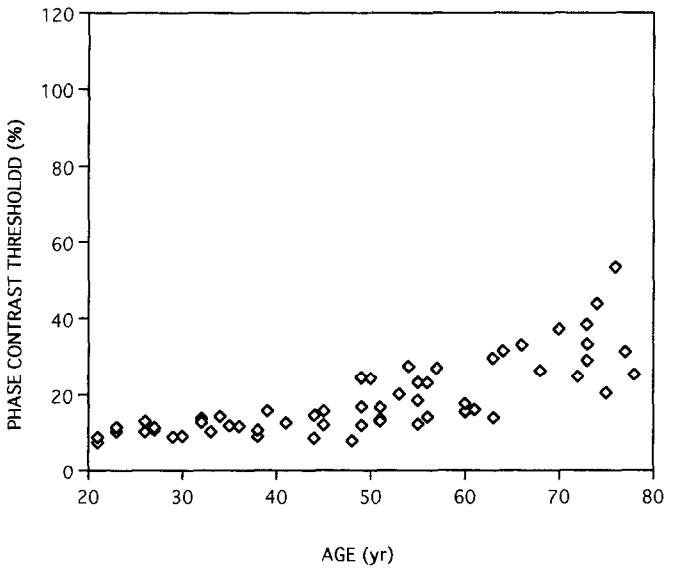

Fig 1 Normal age data for the phase contrast threshold for the phantom contour illusion letter test.

Methods

The sample consisted of two patient groups which were recruited from the on-going five-year prospective Toronto Hospital Glaucoma Detection Study[6]. Group 1 comprised 99 high-risk ocular hypertensives and glaucoma patients without visual field loss, as assessed by the Humphrey Field Analyzer (HFA), program 30-2, full-threshold strategy. There were 44 females and 55 males The mean age was 58 (SD 13 8) years with a range between 30 and 78 years. Forty-eight were diagnosed as having POAG, 40 as high-risk OHTs, 14 with pigmentary dispersion syndrome and nine with pseudoexfoliation.

Group 2 comprised 29 glaucoma patients with repeatable visual field loss by HFA, program 30-2, full-threshold strategy. There were 11 females and 18 males The mean age was 62.2 (SD 11.0) years with a range between 31 and 79 years. Eight were diagnosed as having POAG and 11 as pigmentary glaucoma

Exclusion criteria included an age of less than 30 years, visual acuity worse than 6/18, macular disease, optic nerve disease, congenital anomalies of the optic nerve, aphakia and pseudophakia, ocular trauma, ocular inflammation, the use of topical or systemic steroids, the use of central nervous system depressants and poor general health

The pCILT was generated using an ATI VGA Wonder Excel display adapter and high-resolution, non-interlaced monitor. The ten standard Sloan optotypes (D, O, C, H, N, K, S, V, R, X) were generated at a size translating to a 3/60 (100 min of arc) Snellen letter within 4000 random dots The random dot size was between four and 14 min of arc at three m. The optotypes were defined within the random dot presentation by ensuring dots inside the edge of the letter were out of phase with the dots outside (Figs. 2 and 3) The two phases were alternated at a rate of 30 Hz. Percentage contrast was calculated between L_{max}, the white dots, and L_{min}, the black dots. The background was maintained at a mean luminance of 63 cdm^{-2}.

The advantages of using a letter test are that it is criterion independent[7,8], accepted and used by clinicians[7], readily understood by patients[7] and, as a recognition task, it can negate peripheral artifacts[2]

At the beginning of each test session the monitor was calibrated to ensure the 63 cdm^{-2} background luminance. The test was demonstrated using letters with a 50% phase contrast level One eye of each subject was randomly assigned and assessed Ten contrast levels were

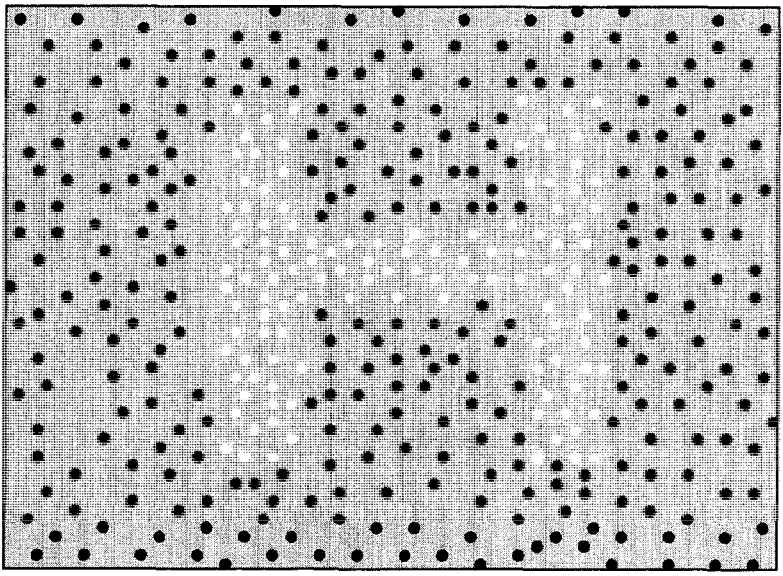

Fig 2 Illustration of Phase One of the pCILT stimulus showing a letter H

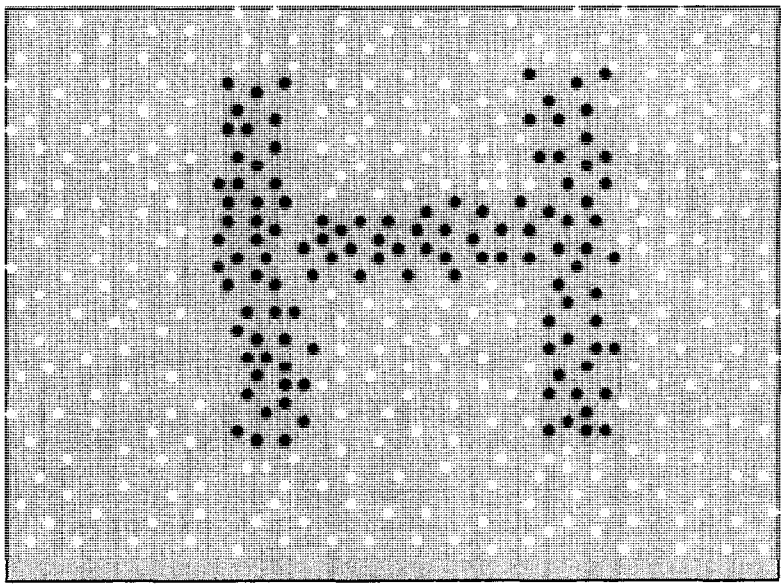

Fig 3 Illustration of Phase Two of the pCILT stimulus showing a letter H

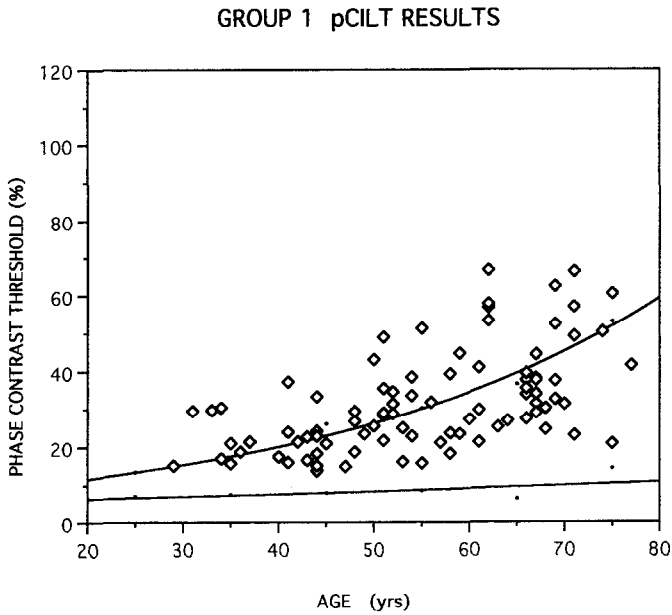

Fig 4 Group 1 phase contrast threshold results compared to the upper and lower confidence limits of the normal sample (solid lines).

tested and presented in a pseudo-random order. Ten randomized letter presentations were assessed for each contrast level using a ten-alternative forced choice paradigm. All tests were performed at a working distance of three m. The 55% phase contrast threshold was determined from the frequency of seeing curve using a logit function Data were discarded or re-assessed if the logit function had a regression coefficient with an R^2 of less than 0 85

Analysis

Ninety-five percent confidence limits were established for a normal population with an age range between 20 and 79 years (Fig 1). Patients from both groups with results that were outside of the established normal limits were identified and collated.

Results

Thirty-seven of the 99 Group 1 patients were outside normal limits (Fig. 4) whilst 26 of the 29 Group 2 patients were outside normal limits.

Of the 99 Group 1 patients 20 had demonstrated abnormal blue-on-yellow visual fields one year previously and 27 were abnormal by year two of the Toronto Hospital Glaucoma Detection Study when the cross-sectional pCILT data were recorded Twenty-four of the 99 Group 1 patients demonstrated abnormal peripheral displacement thresholds Ten Group 1 patients had converted to abnormal white-on-white visual fields by year two of the study

Discussion

The pCILT is a rapid, simple test In a cross-sectional study it identified 37% of a sample of high-risk OHT and glaucomatous patients with normal visual fields, as being abnormal

pCILT demonstrates potential as a simple screening test for early glaucoma. Prospective studies are underway to determine the test's ability to correctly predict those subjects that will develop glaucomatous visual field abnormality pCILT is a central test Contour illusion-based tests of peripheral vision are currently being developed.

Acknowlegdments

We thank M Nelson for assistance in establishing the age normal data illustrated in Figure 1, K Weed and J Simpson for assistance in the development of the technique, and J Cassidy of Microsystem Technologies for software development

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Evaluation of the difference in sensitivity between the upper and lower visual field by computerized perimetry and event-related potentials

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Abstract

Human visual evoked potentials (VEP) from upper and lower hemifield stimulation are thought to reflect the anatomical and functional differences between the hemiretinas and corresponding visual pathways

Conflicting results have been reported in topographic studies on the putative cortical generators The authors have compared the differential input sensitivity (Octopus 2000R) of the lower and upper hemifields of the retina in 12 healthy, cooperative subjects with no history or evidence of visual or neurological diseases A visual p300 was recorded in an odd-ball paradigm with monocular presentation (at 20° eccentricity in each hemifield) of high contrast checkerboards at two different spatial frequencies (frequent stimulus: 1 25 c/deg; infrequent stimulus; 2 5 c/deg) VEP and p300 were recorded at O_1 and O_2 and at C_z respectively, through 0 1–100 Hz and 0 1–50 0 Hz bandwidths. Lower thresholds were found, and higher p300 amplitude values were obtained when stimulating the lower compared to the upper visual hemifield The results are consistent with previous findings and available anatomical and physiological evidence in animals and man Interactions between perceptive processes in the visual system and higher cognitive functions are conceivable

Introduction

The term event-related potentials (ERP) refers to a class of (usually) small, scalp-recorded phasic potentials elicited in conjunction with sensory, cognitive or motor events As opposed to responses to sensory stimulation, ERP reflect neither properties of the stimulus nor sensory input, but rather depend on situational links such as significant convergence, interaction, association or omission, or uneven incidence of events (eventually sensory stimuli), and are concomitants of information processing and cognition ERP are in this respect specific to the investigated neuropsychological or cognitive processes, while sharing the sensitivity of electrophysiological measurements. By contrast, and unlike stimulus-dependent phenomena, ERP are reliably recorded only when subjects are fully cooperative, although studies in psychiatric or dementia patients and in animals have been successfully completed[1–13]

The p300 is the principal component of the ERP and it is successfully recorded with visual stimuli. The stimuli are presented in the same sensory modality, but with different physical characteristics or different temporal incidences.

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Subjects are requested to pay attention to the infrequent stimuli The different incidence of frequent vs rare stimuli is crucial to the occurrence of p300 which is a late positive component peaking at approximately 210–550 msec of latency[14–18]

A good recording of p300 must involve the emotional participation of the patient which will be linked to the degree of attention To obtain the optimum cooperation of the examined subject it is convenient to request that the different stimuli are counted. This task is quite easy, and involves all three cortical functions that influence the ERP· attention, memory and, if the target stimuli are infrequent, the expectation that, as already known[19–23], increases the level of arousal

Upper and lower hemifields stimulation generate different visual evoked potentials (VEP) which it is thought to reflect the anatomical and functional differences between the hemiretinas and corresponding visual pathways[24–26].

Subjective examinations such as computerized measurement of the visual field show this difference[27–29], but conflicting results have been reported in topographic studies on the putative cortical generators[30–36] ERP are probably another expression of these differences since interactions between perceptive processes in the visual system and higher cognitive functions are conceivable

The aim of this study was to evaluate the different perceptions between the upper and lower visual hemifield firstly by a subjective examination (computerized perimetry) and secondly by VEP and ERP.

Material and methods

Twelve healthy volunteers (seven males and five females) ranging in age between 21 and 36 years (mean 27.1 ± 4 3 yr) underwent a complete ophthalmological and orthoptic examination to exclude ocular diseases and refractive errors greater than ± 0.75 D Computerized perimetry was performed with the Octopus 2000R, program 32. This program examines 76 points situated in a regular grid in the central 30° visual field, by means of a full threshold strategy All the examined subjects were acquainted with automatic perimetry.

The VEP was recorded by dermal Ag/AgCl electrodes positioned at the O_2 and O_1 locations of the 10–20 International System. The reference electrode was the midfrontal (Fpz) and the ground was at Fz Amplifiers (Amplaid SD15) were set at 1–100 Hz, 100 epochs of 300 msec each, free of artefacts, were averaged. A checkerboard pattern subtending 10° (viewing distance: 1.5 m), with 2 5 c/deg spatial frequency and 80% contrast and reversing at 2 Hz served as stimulus. It was positioned in anyone of three positions, such that the center of the pattern corresponded to the primary position or to 20° of eccentricity in the upper and lower hemifields respectively.

The p300 was elicited in an odd-ball visual paradigm, in which a checkerboard pattern (ten deg; 80% contrast; viewing distance: 1.5 m) was displayed for 0.25 sec with a spatial frequency of either 2.5 c/deg or 1.25 c/deg. The appearance of the rare (2.5 c/deg) stimulus was random, with an average proportion of one rare stimulus every five frequent stimuli. Subjects were requested to count the number of rare stimuli Active dermal Ag/AgCl electrodes were positioned at C_z The reference was at Fpz; the linked ear lobes served as ground. The amplifier bandpass was 0 1–50 Hz Two hundred and twenty-five epochs of 500 msec following the frequent stimulus and 50 epochs following the rare stimulus were independently averaged.

The amplitude and latency values of waves n70, p100 and n145 of the pattern-VEP and of p300 were measured. Amplitude measures were peak-to-peak to minimize errors in the definition of the baselines.

The mean thresholds detected in the upper and lower visual hemifields and the amplitudes and latencies of pattern-VEP and visual p300 after stimulation of the upper and lower hemifields were statistically compared by the paired *t* test

Table 1.

TAB. 1: V E P RESULTS

	N75 implicit time			P100 implicit time			N145 implicit time			N75-P100 amplitude		
	UP	PP	DOWN	UP	PP	DOWN	UP	PP	DOWN	UP	PP	DOWN
1	89.93	74.12	87 18	128.35	101 16	121.35	167.51	143.48	160.15	6.51	14.28	7.84
2	91.17	78.35	88.46	126.51	99.87	119.83	168.00	139.51	158.58	4.38	15.71	6.19
3	92.45	75.61	85.91	131.38	102.41	126.45	168.19	147.54	161.32	7 12	12.15	7.20
4	98.36	77 17	90.19	130.47	103.53	123.21	165.50	148.31	159.57	4.15	16.14	6.05
5	94.51	73.44	91.36	129.31	100.21	127.36	160.15	145.65	158.84	4.08	13.27	5.94
6	92.57	76.03	88.57	133.18	98.91	121.84	165.19	148.91	163.27	5.31	15.31	7.01
7	90.15	76.13	89.92	130.51	100.32	125.35	166.17	137.38	160.15	6.19	11.28	7.33
8	93.99	75.05	91.86	129.99	99.83	129.18	160.15	145.44	156.84	7.02	16.84	8.04
9	94.00	74.81	93.45	126.68	102.51	122.45	163.26	148.35	162.19	5.14	15.32	7 19
10	97 45	72.90	90.19	120.55	103.38	120.38	168.68	142.31	166.48	4.84	14.68	7.31
11	90.19	78.07	88.90	131.41	100.31	123.84	166.15	143.85	164.53	4.92	12.35	6.98
12	96.51	76.43	94.38	128.38	98.93	125.89	169.13	139.54	161.37	5.01	13.46	7.33
m	93.44	75.68	90.03	128.89	100.95	123.93	165.67	144.19	161.11	5.39	14.23	7.03
s	2.89	1.71	2.46	3.28	1.63	2.93	3.07	3.88	2.70	1.07	1.74	0.66

Table 2.

TAB. 2: E R P RESULTS

	N200 IMPLICIT TIME						P300 IMPLICIT TIME						N200-P300 AMPLITUDE					
	RARE STIMULUS			FREQUENT STIMULUS			RARE STIMULUS			FREQUENT STIMULUS			RARE STIMULUS			FREQUENT STIMULUS		
	UP	P.P	DOWN	UP	P.P	DOWN	UP	P.P	DOWN	UP	P.P	DOWN	UP	P.P	DOWN	UP	P.P	DOWN
1	268.31	201.53	251.33	281.38	212.31	272.84	309.15	281.17	302.18	320.12	302.33	318.37	19.33	48.19	27.63	16.02	37.39	23.94
2	259.40	215.86	242.38	268.93	223.84	268.76	333.86	268.72	331.54	339.31	283.76	338.76	21.36	57.33	35.18	19.91	41 13	31.72
3	262.37	198.83	236.53	269.96	201.19	241.19	319.07	269.15	300.81	328.18	291 18	315.03	11.72	32.15	13.15	10.55	28.36	12.12
4	266.31	223.71	248.49	275.34	248.57	249.13	341.38	302.51	330.38	353.36	324.86	341.16	20.19	69.18	40.05	13.37	50.13	38.88
5	242.38	219.54	239.93	260.19	233.42	254.38	373.84	321.15	368.36	386.51	325.32	375.84	51.38	80.31	60.16	49.46	63.72	51.38
6	236.51	202.38	228.54	241.12	209.17	233.94	360.08	286.33	351.33	372.19	312.15	360.13	33.70	77 13	41 42	28.06	61 19	36.67
7	267.77	233.50	241.41	273.84	246.07	251.28	369.13	342.15	359.19	372.36	346.03	367 16	17.08	48.54	21.18	12.31	37 15	19.92
8	243.53	198.20	239.51	250.19	211.09	243.76	364.15	281 18	359.86	379.89	300.02	373.76	26.61	66.34	27.38	20.18	48.96	23.55
9	259.94	216.52	253.59	266.72	232.26	262.74	347 19	308.36	338.36	351.34	331 19	350.18	31.34	72.36	35.39	29.92	70.19	31.13
10	261.33	209.48	248.12	264.18	215.19	251.36	366.69	318.31	363.72	383.33	320.13	378.15	31.37	81.39	40.61	30.18	67.54	36.73
11	258.13	212.33	241.36	277.34	231.67	252.84	361 17	309.84	359.18	376.20	315.77	367.84	29.56	67.70	33.12	27.34	54.72	29.29
12	264.36	205.81	252.93	271.19	212.03	270.36	352.15	294.96	351.53	363.32	309.84	356.59	39.49	72.03	42.54	33.12	68.15	40.17
m	257.53	211.47	243.68	266.70	223.07	254.38	349.82	298.65	343.04	360.51	313.55	353.58	27.76	64.39	34.82	24.20	52.39	31.29
s	10.70	10.87	7 44	11.54	15.26	12.16	20.48	22.49	22.93	22.08	17.56	21 44	10.88	14.98	11.96	11 11	14.09	10.50

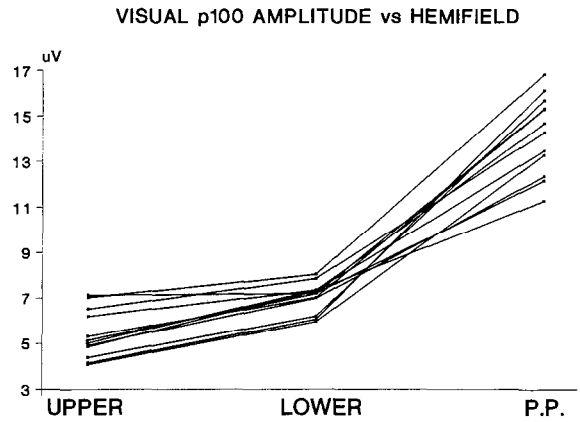

Fig 1 The amplitude of p100 after stimulation in the primary position (P P), and in the upper and lower hemifields

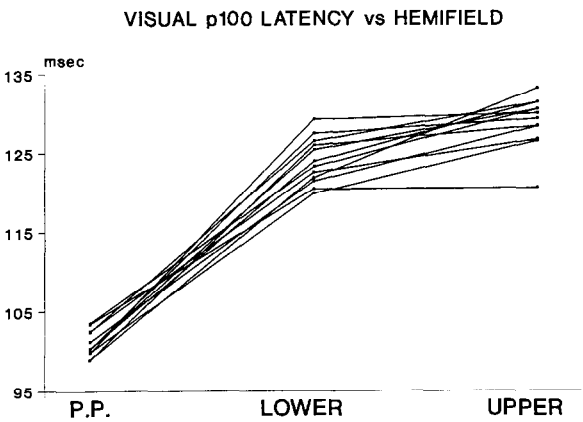

Fig 2 The latency of p100 after stimulation in the primary position (P P), and in the upper and lower hemifields

Results

Visual field

The mean thresholds detected in the upper (mean: 25 35 ± 0.95 dB) and lower (25.84 ± 0.89 dB) visual hemifields differed statistically (paired t test: $t = 3\,206$, $p < 0.005$), indicating a significant altitudinal threshold difference.

Pattern-VEP

A pattern-VEP with latencies and amplitudes of waves n70, p100, n145, all within normal limits were recorded in all cases (Table 1) The amplitudes of the VEP resulting from stimulation in the upper and lower hemifields were significantly ($p < 0\ 01$) smaller than that resulting from stimulation in the primary position, whereas the latencies were longer (Table 1). Significant differences were also observed between the responses of the upper and lower hemifields Namely, amplitudes were higher and latencies shorter in the lower hemifield compared to the upper hemifield (Table 2, Figs. 1, 2)

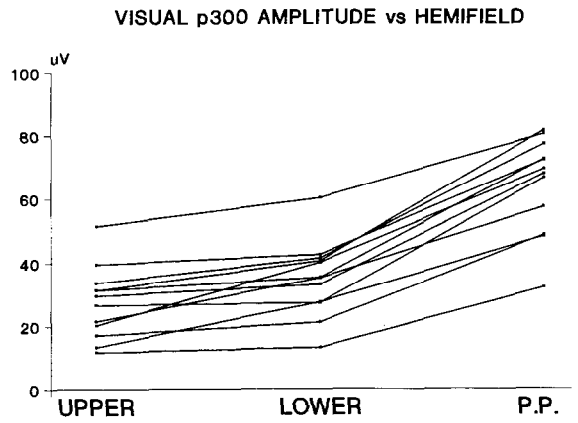

Fig 3 The amplitude of p300 after stimulation in the primary position (P P), and in the upper and lower hemifields

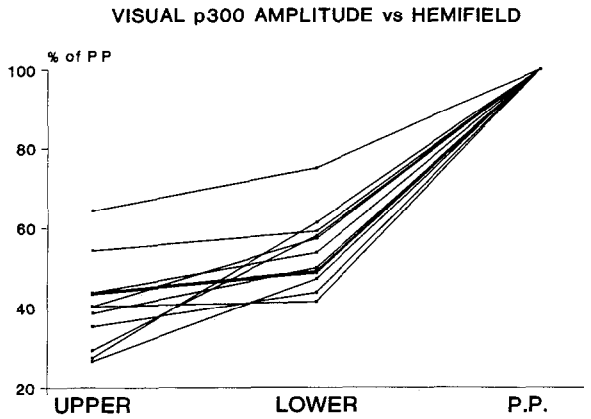

Fig 4 The amplitude of p300 after stimulation in the upper and lower hemifields expressed as a percentage of the corresponding value after stimulation in the primary position (P.P) in order to reduce the variability between subjects

p300

A visual p300 in response to the target stimulus was recorded in all subjects in the experimental conditions selected for the study, after stimulation in the three positions in the visual field. The mean latency in the primary position was 298 6 ± 22.4 msec (range: 268.7–342.1); the mean amplitude was 64 39 ± 14 98 μV (range: 32.1–81.3). The p300 amplitudes after stimulation in the upper and lower hemifields were significantly ($p < 0.01$) smaller than after stimulation in the primary position, and differed from each other (Table 2, Figs. 3, 4), with the amplitude after stimulation in the lower hemifield being higher compared to that of the upper hemifield

Discussion

It should be emphasized that the results are not meant to provide any inference about the structure(s) potentially involved in the generation of the visual p300. Detailed topographic studies, with identification of putative dipole-equivalent generators are mandatory in this regard However, the results do confirm the reported differences between responses to foveal and peripheral stimulation while also suggesting differences in the differential light threshold (computerized perimetry) and in the amplitude and latency of the pattern-VEP and the p300 between the upper and lower hemifields. Latencies and amplitudes of pattern-VEP waves were found to be respectively shorter and larger after stimulation in the lower compared to the upper hemifield This difference is consistent with the described anatomical, perceptual and electrophysiological differences between upper and lower retinal hemifields and the cortical distribution of the VEP corresponding to stimulation of selective portions of the visual field. A comparable difference between hemifields was also observed in the amplitude of p300, therefore suggesting dissimilarities in visual data processing that apparently exceed the structures and mechanisms involved in the generation of the VEP after selective stimulation of the fovea and through the striate papillogeniculate pathway and which conceivably involve cognitive processes.

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Perimetric follow-up of patients affected by vitamin A deficiency

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Abstract

In a previous preliminary report (X IPS Congress) the authors presented a study on perimetric alterations due to hypovitaminosis A In the present paper the authors report a longitudinal study in a larger group of patients

Functional and morphological parameters were evaluated in 20 patients (12 females and eight males) with automated perimetry, dark adaptation testing and impression cytology of the conjunctiva (Wittpenn's method) All had undergone a surgical biliopancreatic diversion Ten normal subjects (five females and five males) of comparable age were examined as a control group Significant perimetric alterations were found, particularly in the upper visual field, when low vit A levels were present Dark adaptation and conjunctival cytological abnormalities were also found The severity of defects was correlated with the blood retinol level rates The findings were reversed with vitamin therapy

Introduction

Vitamin A (dehydro-3-retinol) which has an epithelium-protective role in diverse organs and tissues is indispensable to the integrity of the corneal and conjunctival epithelium It also controls the function of the retina, in particular the peripheral vision, and the adaptability to darkness[1].

Hypovitaminosis A has been observed in patients undergoing surgery for biliopancreatic diversion[2], a therapy for pathological obesity

The aim of the present work is to evaluate the retinal function by adaptometry, automated perimetry, and the conditions of the ocular surface in a group of patients affected by post surgical hypovitaminosis A before and after therapy

Materials and methods

Twenty patients (12 females, average age 42.84 ± 12.85; eight males, average age 45.04 ± 16 11) operated on for biliopancreatic diversion (BPD) (over an average period of three years ± 1.5) were observed for ocular disturbances such as hemeralopia and ocular burning. Ten patients matched for age were chosen as a control group

All the patients underwent a complete ophthalmological examination (biomicroscopy, visual acuity, tonometry, funduscopy). In particular, dark adaptometry (Goldmann-Weekers adaptometer)[3], automated perimetry (Perikon DSK program.)[4], and impression cytology of the conjunctiva (Wittpenn's method)[5] were carried out.

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Table 1

MD	*CPSD*	*FT dB*	*KIA degrees*
1 = 0–1 5 (20%)	1 = 0–1 (22 5%)	1 = > 37 (40%)	1 = 55–67 (27 5%)
2 = 1 6–3 5 (27 5%)	2 = 1–2 (27 5%)	2 = 33–36 (37 5%)	2 = 48–54 (60%)
3 = > 3 5 (52 5%)	3 = > 2 (50%)	3 = < 33 (22 5%)	3 = 36–47 (12 5%)

Plasma levels of retinol were determined by high performance liquid chromatography (HPLC)[6].

All the examinations were done before and at the 30th, 60th and 90th day after therapy with vitamin A (300,000 IU i m daily)

The results were statistically analyzed using Student's t test and the Cochran Q test)

Results

The average visual acuity was 0.98 ± 0.04 in the BPD patients which was not statistically different from the control group (0.91 ± 0.17)

Adaptation curve to darkness showed significant alterations compared to the normal group: average cone-rod breakpoint was 21 37 ± 6 71 min versus 4 45 ± 0 66 min ($p < 0.0001$) and average absolute rod threshold was 4 10 ± 0.8 log U picostilb (psb) versus 2.85 ± 0 10 log U psb ($p < 0$ 0001). Three types of curves have been considered:

1 biphasic with cone-rod breakpoint prolonged more than 9 min and absolute threshold within 3.5 log U psb (no case);
2. biphasic with cone-rod breakpoint prolonged more than 9 min and absolute threshold between 3.5 and 4.5 log U psb (15% of cases);
3. monophasic, with absolute threshold between 4.5 and 5 log U psb (85% of cases).

Visual field alterations in the BPD patients versus the normal patients were the following:

Mean defect (MD) average = –3.90 ± 3 21 versus –0.09 ±1.28 ($p < 0.000001$)

Corrected pattern standard deviation (CPSD) average = 2 49 ± 2.09 versus 1 19 ± 0.89 ($p < 0.0001$)

Foveal threshold (FT) average = 32 98 ± 4.58 dB versus 37.08 ± 2.37 dB ($p < 0$ 000001).

The kinetic isopter average (KIA) average = 51.72 ± 4.27 degrees versus 57.16 ± 2.98 degrees ($p < 0.00001$)

Three levels of alterations were considered in the perimetric parameters (see Table 1). The topographic analysis of the perimetric alterations showed that the defects were situated mainly in the upper nasal part of the visual field.

The findings of the *conjunctival surface* were the following:

Type 1 nucleous/cytoplasm (N/C) ratio of the epithelial cells more than 1/2, presence of more than 200 goblet cells in the microscopic observation field Type 2: N/C ratio from 1/2 to 1/3 in the epithelium and presence of less than 150 goblet cells for field Type 3: N/C ratio less than 1/4 in the epithelium, less than 20 goblet cells for field (squamous metaplasia).

In our sample of BPD patients Type 2 (20% of cases) and Type 3 (80% of cases) alterations were found Bitot's spots in three cases of squamous metaplasia of conjunctiva were observed.

The *plasma levels of vitamin A* were greatly reduced in the patients who had undergone BPD surgery compared to the control group (60.75 ± 41 49 ng/ml versus 632 ± 168 ng/ml).

Follow-up

In Tables 2–5 we report the percentage variations of adaptometric, perimetric, and cytological alterations, after substitutive therapy with vitamin A, during a follow-up of 3 months, and the relative levels of plasma retinol

Table 2 Adaptometric alterations

Level	T_0	T_1 *(30th day)*	T_2 *(60th day)*	T_3 *(90th day)*	*p*
Type 1	0	0	15 (75%)	17 (85%)	
Type 2	3 (15%)	9 (45%)	4 (20%)	2 (10%)	< 0 001
Type 3	17 (85%)	11 (55%)	1 (5%)	1 (5%)	

Table 3 Perimetric alterations

	Level	T_0	T_1 *(30th day)*	T_2 *(60th day)*	*T3 (90th day)*	*p*
MD	1	8 (20%)	10 (25%)	11 (27 5%)	15 (37 5%)	
	2	11 (27 5%)	10 (25%)	12 (30%)	11 (27 5%)	< 0 01
	3	21 (52 5%)	20 (50%)	17 (42 5%)	14 (35%)	
CPSD	1	9 (22 5%)	11 (27 5%)	12 (30%)	16 (40%)	
	2	11 (27 5%)	12 (30%)	12 (30%)	11 (27 5%)	< 0 01
	3	20 (50%)	17 (42 5%)	16 (40%)	13 (32 5%)	
FT	1	16 (40%)	18 (45%)	18 (45%)	19 (47 5%)	
(dB)	2	15 (37 5%)	16 (40%)	16 (40%)	16 (40%)	< 0 01
	3	9 (22 5%)	3 (15%)	3 (15%)	5 (12 5%)	
KIA	1	11 (27 5%)	11 (27 5%)	13 (32 5%)	16 (40%)	
(degrees)	2	24 (60%)	26 (65%)	24 (60%)	23 (57 5%)	NS
	3	5 (12 5%)	3 (7 5%)	3 (7 5%)	1 (2 5%)	

Table 4 Impression cytology alterations

Level	T_0	T_1 *(30th day)*	T_2 *(60th day)*	T_3 *(90th day)*	*p*
Type 1	0	0	8 (20%)	20 (50%)	
Type 2	8 (20%)	18 (45%)	24 (60%)	16 (40%)	< 0 001
Type 3	32 (80%)	22 (55%)	8 (20%)	4 (10%)	

Table 5 Plasma retinol levels (ng/ml)

T_0	T_1 *(30th day)*	T_2 *(60th day)*	T_3 *(90th day)*
60 ± 41	198 ± 37	368 ± 60	532 ± 98

Discussion

The aim of this paper was to carry out a functional and morphological ocular study in a group of patients affected by a malabsorption syndrome in which vitamin A deficit played a central role

At first, our BPD patients showed severe alterations especially in adaptation to darkness (85% cases) and in impression cytology of conjunctiva (80% cases), that are typical of hypovitaminosis A.

The alterations of perimetric parameters were most frequent in mean defect (54%) and corrected pattern standard deviation (50%), less, frequent in foveal threshold (22.5%) and kinetic isopters average (12%).

The topographic analysis of the perimetric defects demonstrated that they are typically located in the nasal field, suggesting an anatomical correspondence with the critical watershed area of the retina

The results of the study during the follow-up revealed the reversibility of the lesions observed. In fact, after treatment with vitamin A the alterations of the adaptation curve, the contraction of the peripheral isopters and also the conjunctival cytological lesions practically disappeared This confirms their correlation with the retinol levels However, the perimetric indices showed only improvement, but not complete remission

These data support the hypothesis that the deficiency of other factors plays an important role in the development and continuation of perimetric damage. It must be remembered that in this malabsorption syndrome not only all the liposoluble vitamins but also some of those hydrosoluble, the proteins and ions are involved. Therefore the etiopathogenesis of the perimetric damage observed might have a more complex mechanism, not yet completely investigated

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Perimetric and electrophysiological tests in hypovitaminosis A: their significance and biological correlations

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Abstract

Fifty-one patients affected by mild hypovitaminosis A caused by the use of fenretinide (4-HPR), a synthetic retinoid antimetabolite, were examined Twenty-eight subjects, not treated with 4-HPR, were examined as a control group

During a study of several years, the patients have shown perimetric alterations (absolute scotomas, fascicular relative defects and global threshold elevation) and ERG (increase of delta between a_1 and a_2 wave latency and increase of amplitude of B wave) The results of the tests were correlated with plasma retinol levels

The effects on the visual field were reversed within one month after discontinuing therapy

Introduction

Fenretinide (4-HPR) a synthetic retinoid, used in cancer chemotherapy, can induce a condition of hypovitaminosis A[1,2]

In our previous report[3] we noticed the presence of adaptometric, ERG, visual field and ocular surface alterations in a small number of patients who had undergone HPR treatment

The aim of the present paper is to present the perimetric and electrophysiological results, and their correlations with plasma retinol levels, of a wider group of subjects

Material and method

Fifty-one female patients (average age 57 7 ± 4 6 yr), who had undergone surgery for breast cancer and had 4-HPR treatment (200 mg/day) for an average period of 32 ± 8 months were examined.

Twenty-eight female patients (average age 56.12 ± 5.74 yr), who had undergone the same type of surgery, but had not had 4-HPR therapy, were chosen as a control group.

All the subjects had undergone complete ophthalmological examination, by means of biomicroscopy, tonometry and retinoscopy, to exclude cases with pre-existing ocular diseases

All the subjects were examined before they were asked if they were receiving the therapy and the time of the last dose (average 13.5 hr ± 1)

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The following parameters were determined:
- visual acuity;
- refraction;
- visual field, using DSK strategy of the Perikon PCL 90[4], that allows both kinetic and static testing, in order to find the foveal threshold (FT), the mean deviation (MD), the corrected pattern standard deviation (CPSD) and the average of kinetic isopters (KIA);
- ERG, at photopic and scotopic levels, were recorded using skin electrodes located on the border of the inferior lids, connected to an Amplaid amplifier[5]: latencies and amplitude of a_1, a_2 and B photopic and scotopic waves and their difference (delta) were evaluated;
- VEPs were recorded by dermal electrodes (Ag/AgCl) located at O2-O1 according to the 10–20 International System[6]: the latency of the p100 wave was evaluated;
- plasma levels of retinol, 4-HPR and its metabolite 4-MPR were determined by means of high performance liquid chromatography (HPLC)[7].

Statistical analysis of the results was performed using Student's t test and the χ^2 test.

Results

No statistical difference in age existed in the 4-HPR patients compared to the control group (57.75 vs 56.12 yr, $p = 0.21$). The corrected visual acuity and the refraction (0.95 ± 0.05 vs 0 93 ± 0.08 and +0.54 ± 0.50 vs +0.41 ± 0 75) were not statistically significant ($p = 0.79$ and 0.68 respectively).

The analysis of the visual field revealed the following data.
- the MD in 4-HPR-treated subjects was 1.24 ± 3.52, while in the control group it was 0 ± 0.40 ($p = 0.07$)
- the CPSD in 4-HPR patients was 2.25 ± 2.36 as opposed to 1.05 ± 0.79 in the control group ($p = 0.008$)
- the FT in 4-HPR-treated patients was 34.96 ± 4.58 dB and 37.38 ± 2.54 dB in the control group ($p = 0.01$)
- the KIA was 52.21 ± 6.54 degrees in the 4-HPR treated patients vs 56.09 ± 4.98 degrees in the untreated patients ($p = 0.003$)

Analysis of the different parameters of ERG provided the following results:
- delta a_1L (difference between the latency of the a_1 wave and a_2 wave under photopic conditions) = –0.35 ± 2.32 msec in 4-HPR patients vs –0 96 2.52 msec in the normals ($p = 0.04$)
- delta a_2L (difference between the latency of the a_1 wave and a_2 wave under scotopic conditions) = 1.51 ± 1.36 msec in the 4-HPR patients vs 0.83 ± 0.75 msec in the normal controls ($p = 0.04$)
- the amplitude of the B wave under scotopic conditions was 70.53 ± 18.96 μV in the 4-HPR patients vs 66.18 ± 14.99 μV in the normal controls ($p = 0.05$).

The p100 latency of the VEP did not show a significant difference between the two groups.

The plasma level of vitamin A, 4-HPR and 4-MPR results were:
- vitamin A· 156.25 ± 102.59 ng/ml in 4-HPR-treated patients vs 565.467 ± 75.28 ng/ml in the control group ($p = 0.0001$)
- 4-HPR: 387 ± 360 ng/ml
- 4-MPR: 295 ± 230 ng/ml

The correlation between the duration of the therapy and 4-HPR and 4-MPR plasma levels was not significant ($p = 0.735$ for 4-HPR and $p = 0.66$ for 4-MPR).

The correlation with plasma vitamin A levels was statistically significant for:
- average of kinetic isopters ($p = 0.01$)
- CPSD ($p = 0.001$)
- delta a_2L ($p = 0.05$).

Reversibility of the alterations

The 4-HPR-treated patients were examined 3, 7, 15 and 30 days after the discontinuance of the therapy

The alterations found in perimetry and in ERG gradually disappeared from the 15th to the 30th day after the suspension of 4-HPR therapy

Discussion

Fenretinide is a synthetic derivative of retinoic acid that causes a deficit of the plasma concentration of vitamin A, through a competitive process with retinol[8]

It has been demonstrated that 4-HPR partially inhibits secretion of the retinol binding protein (RBP) of the liver and other tissues, simultaneously lowering the plasma concentration of vitamin A and RBP[9] Hypovitaminosis is produced, in a direct way, by competition for vitamin A, and in a secondary and indirect way by functional alterations of its binding protein[10]. Our study has confirmed that this therapy causes electrophysiological and psychophysical alterations in relation to the plasma level of vitamin A

The contraction of the peripheral isopters of the visual field is the expression of the functional alteration of the rods These data are confirmed by the increase of the latency of the a_2 wave of ERG

The reduction of the foveal threshold is instead a sign of impaired function of the cones These data are confirmed by the increase of the latency of the a_1 wave of ERG The electrophysiology showed an increase of the amplitude of the B scotopic wave that is generated mainly by the Müller cells In fact these cells contain RBP and are a source of retinoic acid in the retina. In a condition caused by a lack of vitamin A the secretion of RBP is inhibited and its biosynthesis does not take place

The presence of fascicular defects nevertheless suggests a wider involvement of the light perception transmission chain, but VEP results do not confirm the involvement of the visual neuron chain

The strict correlation with vitamin A plasma levels and not with those of HPR or its metabolite, confirms that hypovitaminosis A is the cause of the psychophysical and electrophysiological changes observed.

The alterations seem to be reversible with the suspension of the therapy. In conclusion 4-HPR therapy induces visual psychophysical and electrofunctional alterations, because changes occur at the photoreceptor and Müller cell levels Subsequently neuronal alterations take place.

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