11 Visual Fields

DAVID P CRABB

Summary

Modern automated perimetry is the current standard for assessing visual field defects in glaucoma. Despite the problem with measurement variability they should remain the benchmark by which we interpret glaucoma because they directly assess what the patient can see, as opposed to indirect measures such as imaging or intraocular pressure measurements. Their role as the most important outcome measure in clinical trials of different new treatments for glaucoma should be established. Systematically and correctly examining the statistical analysis accompanying visual field plots assists in deciding whether physiological field loss is present or worsening. However, the wealth of statistical information on the visual field chart is no substitute for careful clinical interpretation.

Introduction

This chapter summarizes the use of standard visual field measures that are most likely used in modern glaucoma detection and management. For the interested reader there are some excellent complete texts on the subject, notably Henson,[1] Cubbidge,[2] and also chapters in Edgar and Rudnicka.[3]

The visual field is simply the portion of space from which light can enter the eye, reach the retina, stimulate the photoreceptors and evoke a sensation of light. Perimetry is a diagnostic examination technique for recognizing disturbances in the visual field. It is of basic importance for ophthalmologists and optometrists, and extends to other medical specialties, notably neurology and neurosurgery. In current clinical practice perimetry remains central to the detection and monitoring of visual function in glaucoma.

Perimetry normally tests the light-difference sensitivity across the visual field. This sensitivity reflects the capability of the eye to perceive a brightness difference between a test target and its background. Light-difference sensitivity depends upon the tested location on the retina and upon the parameters of the measurement technique, such as intensity of background luminance and target size. The normal visual field extends further away from fixation temporally and inferiorly than superiorly and nasally. The physiological blind spot corresponds to the location where the optic nerve enters the eye and its center is located about 15° temporal from fixation. From the center of the retina this sensitivity decreases towards the periphery, evoking the classically defined 'hill of vision': a three-dimensional representation of retinal light sensitivity. In this analogy there is a peak at the center of the hill of vision which represents the increasing sensitivity to light from the retinal periphery to the fovea. A visual field defect is any departure from the normal topography of the hill of vision (Fig. 11-1).

The history of the recognition of visual field defects is a fascinating one and the interested reader is directed towards a short review by Atchison (1979).[4] The first true clinical description of a perimetric technique to examine and quantify the visual field was by von Graefe in the mid-19th century. A chalk board with a central fixation point was used in conjunction with a large, moving illuminated object. Marks were recorded on the board as the object moved from seen to unseen areas. One of von Graefe's early figures crudely illustrated a peripheral field defect in a patient with glaucoma. In 1857 Aubert and Foerster introduced a perimetric technique where a test stimulus was presented on an arc. Several directions or meridians could be examined by rotating the arc. In the late 1800s Landesberg used similar methods to define as scotomas visual field defects that are surrounded by areas with more normal sensitivity and Bjerrum developed a tangent screen examination whereby a subject fixates the center of a flat observation surface: this was used to establish the characteristic arcuate distribution of glaucomatous visual field loss that still bears his name. In the early 20th century Rönne used this type of perimetry to define the glaucomatous nasal step, relating it to the anatomical arrangement of the retinal nerve fiber layer.

Manual Visual Field Testing

Perimetry, using stimuli moving across a background surface, was advanced significantly by Goldmann in the 1930s with the development of standardized kinetic perimetry: this elegantly designed device allowed control of the luminance of both the background and stimuli with the latter projected onto a hemispheric bowl, being moved from 'not seen' areas to sites where it was first perceived. The stimuli devised at that time have become standards: the smallest being Goldmann Size 0, with a diameter of 0.43° and area of 1/16 mm^2. On the Goldmann scale the diameter size doubles each time; the standard used in both manual and automated perimetry is Goldmann III (0.05° and area of 4 mm^2). In Goldmann perimetry, lines called isopters are drawn to connect points which exhibit the same sensitivity to differences between stimulus and background luminance. These isopters generate a type of contour map of the sensitivity of the visual field. The direct mechanical link between the stimulus control and a plotting pen provided the first visual field measurement with a degree of reproducibility and accuracy.

Goldmann perimetry is still widely used today, including in some centers in glaucoma diagnosis and management

(Fig. 11-2). The high-resolution shape information obtained by the 'improvization' of kinetic testing in real time allows for detailed delineation of visual field defects that can be invaluable for neuro-ophthalmologic diagnosis. However, kinetic or manual perimetry is subjective, being heavily reliant on training and experience, and colloquially bears resemblance more to an 'art' rather than a standardized scientific measurement. There are serious technical limitations: especially with regards to the psychophysical response to the moving target and spatial summation effects, along with the subject's response time to the examiner. More simply, the examiner may simply overlook areas of the field which are not thought to be important and the configuration of field defects may be biased to fulfill preconceived ideas. Moreover, kinetic testing gives poorly reproducible results in the central field and at the edges of gradually deepening scotomas such as those found in glaucoma. Therefore, when quantifiable, reproducible results are required, automated perimetry is preferred.

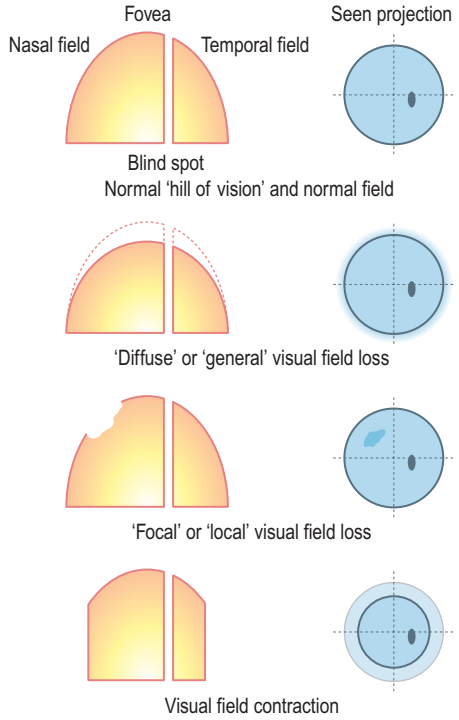

Figure 11-1 Schematic showing 'hill of vision' representation and 'projected' form of the visual field. Early glaucomatous defects are typically diffuse or focal (scotomas).

Automated Visual Field Testing

The modern benchmark used for measuring the visual field in glaucoma is standard automated perimetry (SAP) (Fig. 11-3). Considerable research evidence has established that glaucomatous loss is detected and managed much more reliably with automated perimetry as compared to Goldmann perimetry. In contrast to the kinetic strategy used in manual Goldmann perimetry these automated devices are examples of static perimetry: the stimuli presented to the subject do not move. Luminance sensitivity is established at a fixed matrix of test points by varying the stimulus intensity until each test location is just seen: this point is known as the threshold. A light stimulus presented below the threshold will not be detected by the subject, whereas a stimulus above the threshold will be detected by the subject. The threshold sensitivity at each test location, which is the reciprocal of the threshold, is typically presented in decibels (dB) indicating the logarithmic nature of light intensity on a linear scale where, for example, 0 dB would represent the brightest stimulus intensity on the perimeter, with, very approximately, values around 30 dB being 'normal' values. These values are a relative scale and are not directly comparable across different makes of perimeter.

SAP is the modern clinical standard for measuring glaucomatous visual field defects: it is mainly operator-independent and yields clinically measurable numerical data relating to the measured threshold at a grid of points

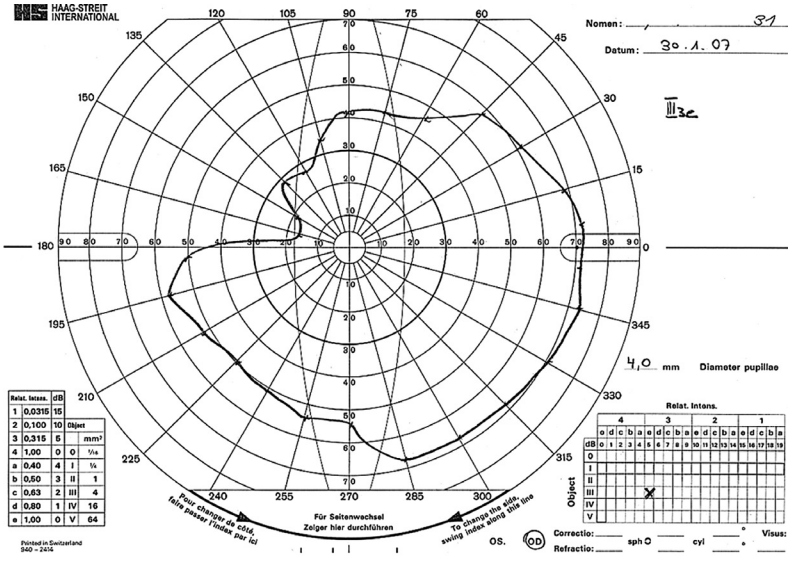

Figure 11-2 Example printout from Goldman perimetry for a glaucomatous patient (right eye) with a significant defect using a Goldman size III stimulus. The area within the contour line is the 'seeing' part of the field.

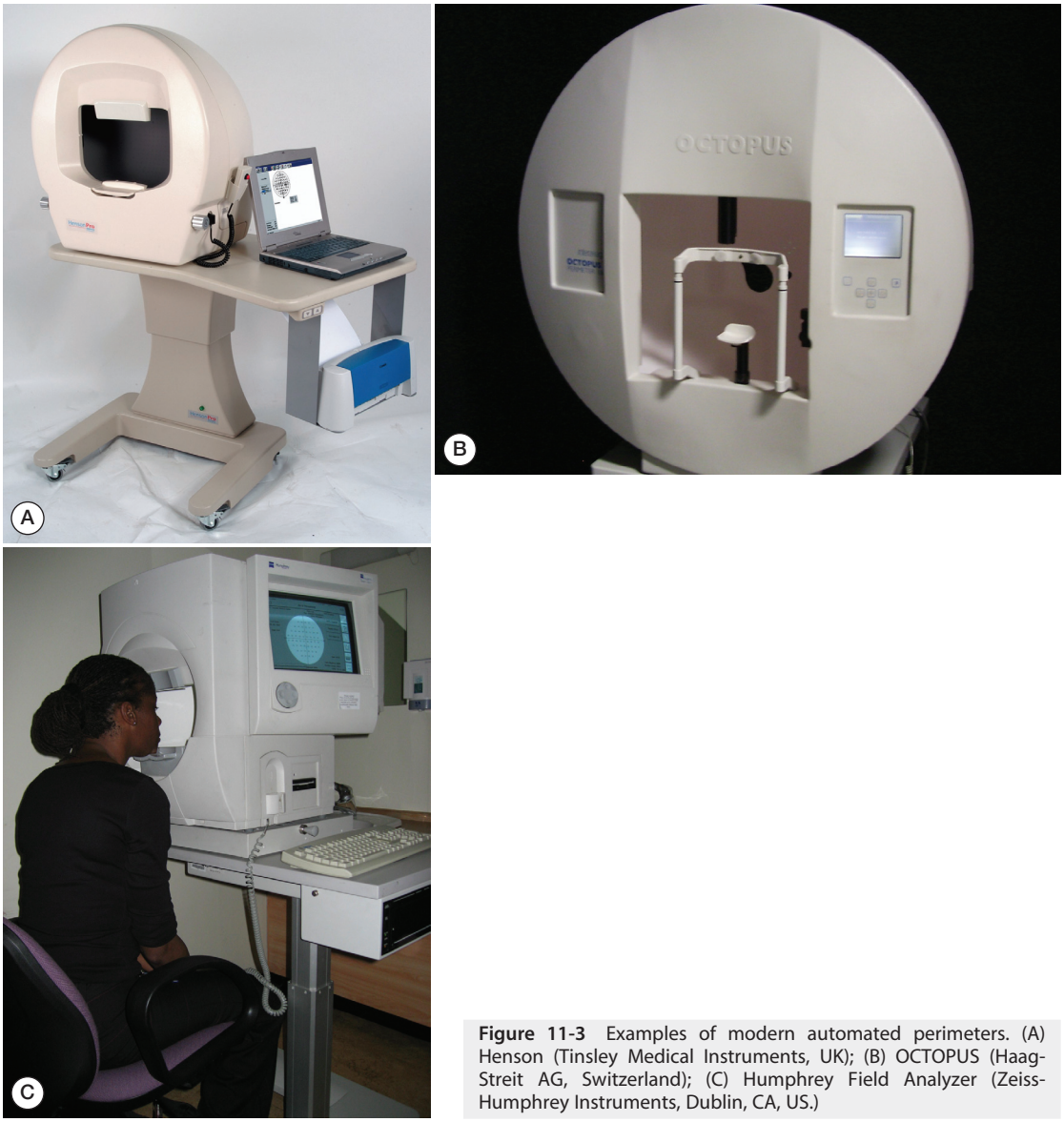

Figure 11-3 Examples of modern automated perimeters. (A) Henson (Tinsley Medical Instruments, UK); (B) OCTOPUS (Haag-Streit AG, Switzerland); (C) Humphrey Field Analyzer (Zeiss-Humphrey Instruments, Dublin, CA, US.)

in the visual field. SAP can be divided into suprathreshold strategies, typically used in glaucoma detection and screening, and full-threshold strategies, mainly used for more detailed testing and monitoring disease worsening or glaucomatous progression.

Suprathreshold techniques are relatively quick to administer: they simply record whether a location is normal (stimulus seen) or abnormal (stimulus not seen). This is done by presenting a stimulus calculated to be slightly more intense than the subject's threshold (suprathreshold increment), normally set between 4 dB and 6 dB higher. Most suprathreshold tests take account of the fact that sensitivity declines with age and also varies by location with, for example, relatively reduced sensitivity of the peripheral visual field compared to the central field. These suprathreshold tests therefore use a list of values held as a database from which the testing threshold is determined.

Some suprathreshold tests attempt to determine the subject's unique overall threshold, usually by means of a full-threshold examination using a few selected test points and then use this information. The Henson perimeter is an exemplar of suprathreshold instruments: these have recently incorporated other improved types of suprathreshold testing including the HEART algorithm[5] and multisampling techniques.[6]

Full-threshold techniques provide more detailed information than suprathreshold strategies since they indicate the depth of scotomas rather than merely their presence or absence. However, full-threshold testing is much more protracted, which has important implications in the clinical setting and in terms of the demand on the patient. In full-threshold testing each location is examined using a staircase or bracketing technique. An example of this is the widely employed 4-2 staircase strategy used, for example, in Octopus (Haag-Streit AG, Switzerland) and Humphrey (Zeiss-Humphrey Instruments, US) perimetry (Fig. 11-4). The intensity of the initial stimulus depends on age-matched normal values: if this is seen, the next presentation at that location is 4 dB less intense. If this is also seen, the following stimulus at that location is reduced by a further 4 dB in

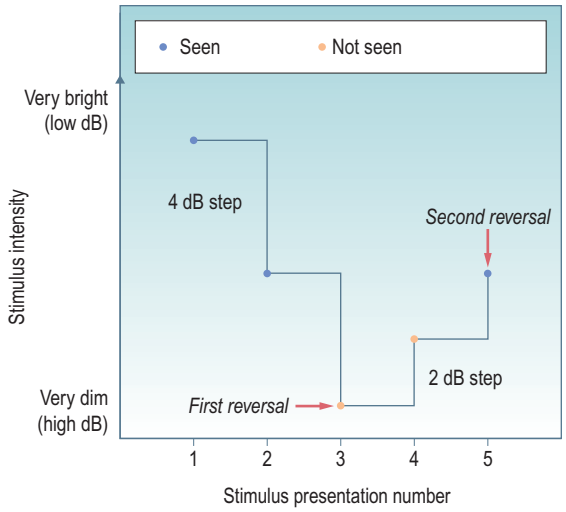

Figure 11-4 Schematic illustrating the staircase algorithm for standard full-threshold perimetry. The stimulus intensity is varied in 'steps' of 4 dB until the first reversal occurs and subsequently in steps of 2 dB. With the Humphrey, intensity of the last seen presentation is taken as the final threshold estimate, after a second response reversal has occurred.

intensity, and so on until the subject fails to see a stimulus presentation: this is the 'first reversal'. The stimuli following this are increased in intensity by 2 dB each time until the subject now reports a stimulus as seen: this is the 'second reversal'. The threshold is typically estimated as the mean of the final and the penultimate presentation intensities, but this final calculation varies between instruments with, for example, the Octopus applying a final correction. If the initial presentation is not seen, intensities of subsequent presentations are increased by 4 dB until one is seen ('first reversal') then decreased by 2 dB until one is missed ('second reversal').

Thresholds are initially estimated in this manner at four locations in the visual field, one in each quadrant at approximately 9° from the fovea. Although each of the four 'seed' locations is measured in turn, the perimeter does this in random order, so that the position on the staircase is different for each location and the observer is not preconditioned to the location of the next stimulus presentation. Points adjacent to the seed points are tested next: the initial stimulus presentation is set at the brightness determined from the threshold previously obtained at the seed point. This testing of contiguous points 'spirals' outwards such that all points in the grid are eventually measured.

The threshold is a peculiar measurement: it isn't measured directly, and is based on a probability of 'yes' and 'no' sequences. Moreover, the physiological nature of the threshold varies during a test (short-term fluctuation) and between tests (long-term fluctuation). In psychophysics, staircase testing is often designed so that the threshold is crossed many times, so that the threshold can be estimated with acceptable precision but at the cost of lengthy examination. This time luxury cannot be afforded in the clinic. Over the years much research has been aimed at developing clinically useful perimetric testing strategies that reduce the test time; in the mid-1990s, the Swedish Interactive Testing Algorithm (SITA) developed by Heijl and colleagues[7] accomplished the task of reducing time whilst maintaining the standard of accuracy observed in 4-2 full-threshold testing.

SITA reduces the actual number of stimulus exposures required by measuring closer to the patient's true seeing threshold using a principle of Bayesian probability: this can be explained with a simple analogy. In horseracing certain animals have a higher probability of winning than others and this is reflected in the different odds offered by a bookmaker covering the 'favorite' to 'outsiders' or 'long shots': these probabilities are adjusted before the race commences to account for previous winning form, quality of the jockey and other factors. Similarly, at the start of SITA testing (before the subject presses the response button!) not all thresholds are assumed to have an equal probability of occurring; they are adjusted based on the expected response (using factors like the patient's age, location in the field and previous normal reference data). Moreover, like a fluctuating betting market, the probability of establishing the final response varies as the test progresses: as the patient responds to seeing different thresholds with 'yes' and 'no' answers, the underlying probability of a particular measured threshold being the final outcome is adjusted during the test. The range of possible outcomes is summarized by likelihood functions which can be thought of as graphs of all the likely final thresholds with the final position and shape of the graphs giving the estimated threshold (see Fig 11-5). Moreover, SITA uses prior information about sensitivity values at neighboring locations using a physiological map of the expected relationship between the sensitivity at points in the field that adjusts the testing sequence at points and quickens the examination.

SITA testing takes approximately half the time (about 7 minutes per eye) to complete than examination with the standard 4-2 algorithm. Very noteworthy is the main reduction in test time is a result of novel features for monitoring patient attention and reliability during the visual field examination, reviewed later. These techniques tailor the pacing of the test to the individual and save as much testing time as the clever mathematics of the testing strategy.

SITA testing has become something of a reference standard test algorithm but it should be remembered that it was designed for glaucoma and use with other clinical conditions should only be considered with caution. 'SITA Fast' is a different algorithm to 'SITA standard': the former deliberately uses larger step sizes in stimulus presentation and is, therefore, quicker still. SITA Fast may have a role in testing subjects that find longer tests impossible to complete but it has higher measurement variability. Other supposedly more efficient visual field testing algorithms have remained on the pages of the research journals and have yet to translate to the commercial instruments. For example, a very recent development allows researchers to develop algorithms that work seamlessly with one commercially available instrument,[8] whilst other research suggest more adaptive tests,[9] especially when areas of the visual field are already blind.[10]

Sometimes binocular visual field testing is required for the assessment of true functional disability or for socio-legal reasons. For example, in the UK the binocular Esterman Test is currently used for assessing the visual fields component in terms of legal fitness to drive. The Esterman is a

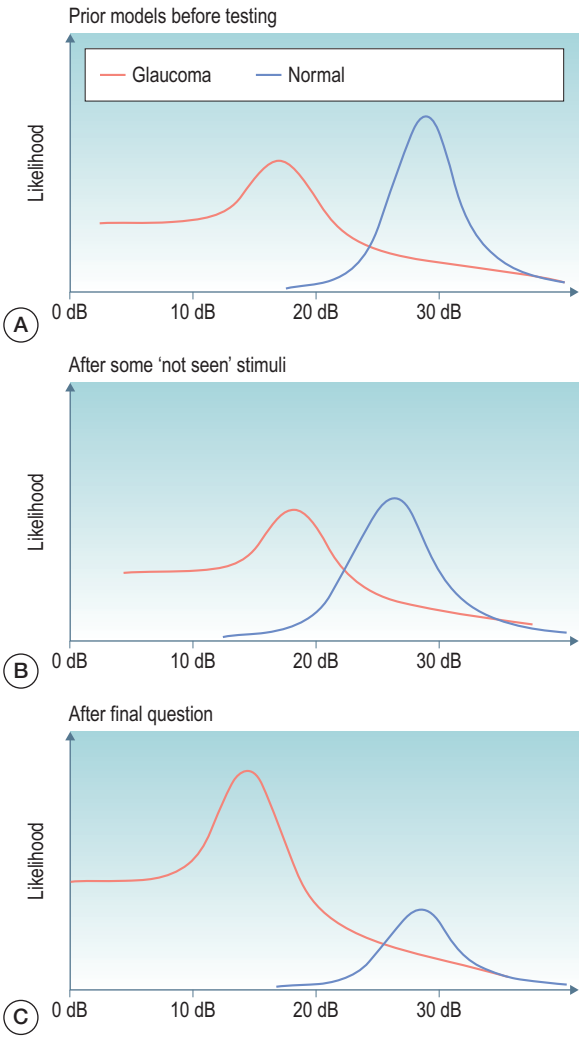

Figure 11-5 Schematic illustrating the use of likelihood functions for efficiently estimating thresholds in SITA. Each point in the visual field has two starting likelihood functions as illustrated in panel (A). (In full-threshold testing the 'curves' would simply be rectangles with all responses equally likely.) The curve for the normal response has the higher peak to start with but the shape of both functions alters as a patient responds to the stimulus at different intensities. For example, (B) illustrates what the curves look like after a series of stimuli are not seen, thus indicating that the patient's response is more likely to fall within the curve for glaucoma. After more unseen responses the glaucoma likelihood function 'dominates' and the threshold is estimated from some location on the curve, normally the peak of the curve but this can be further adjusted when compared to neighboring locations (C).

suprathreshold test where patients simply have both eyes open and is available on automated perimeters. It seems that equivalent information can be gleaned by merging monocular results.[11] At this stage it is worth emphasizing the difficulty that some patients have with perceiving their visual field defects and the importance of binocular assessment. Although it is critical to assess the function of each eye individually to determine the presence, severity and progression status of glaucoma, the visual world is determined by the input from both eyes to the brain. Patient's perception of the severity of their visual field loss is often difficult because an unaffected eye essentially fills in for the other.[12] The idea that a binocular estimate using results from monocular measurements is a better representation of visual function compared to the person's 'better eye' is being underpinned by research evidence.[13] The interested reader is directed towards a wider discussion on the visual field and functional correlates by Spaeth, Ramulu and Glen.[14–16]

Patterns of Visual Field Loss in Glaucoma

There is no simple blueprint for the pattern of visual field loss in glaucoma. However, typical loss is directed by the arrangement of the retinal nerve fiber layers as they congregate on entry into the optic disc, with those fibers from the temporal retina usually most susceptible to damage, resulting in defects occurring more frequently in the superior hemifield. The damaged nerve fiber layers typically give isolated damage in the paracentral areas (10° to 20°) eventually forming arcuate scotomas. Another important configuration of early loss can be the 'nasal step', resulting in asymmetry in retinal sensitivity either side of the temporal horizontal midline. As the disease advances both hemifields may become involved (Fig. 11-6). Other patterns of loss are thought to occur, including baring or enlargement of the blind spot and generalized depression of the sensitivity of the field, but these are more typically non-specific signs of glaucomatous loss. For example, diffuse loss can occur in many diseases affecting visual function, such as opacification of the lens and cataract, with the latter sometimes causing difficulty when trying to establish if a visual field defect is worsening on follow-up.

Various spatial grids are available in automated static perimetry to detect these patterns of loss. A common testing

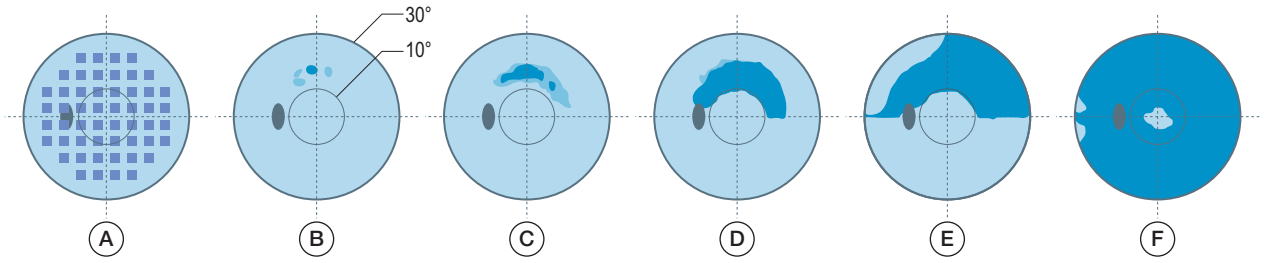

Figure 11-6 Schematic showing worsening patterns of visual field loss in open-angle glaucoma. (A) Location of testing points of the 24-2 Humphrey visual field. (B) Isolated defects in paracentral area. (C) Small isolated defects combine to form larger defect. (D, E) Arcuate defect forms and worsens and eventually breaks through to the periphery. (F) End-stage defect, with only small functional macular area remaining.

pattern used for general visual field testing involves a 'square' grid of 6° separated points tested out to 30° on the Humphrey instrument (called the 30-2), or the slightly more constricted 24-2 pattern shown in Figure 11-6A. (This only tests to 30° in the region of the nasal defect.) Various different configurations are used for screening algorithms on suprathreshold perimetry, where it is important to assess the spatial extent of the defect and Henson[1] provides a good discussion of this. The Octopus perimeters use regular spatial grids similar to the Humphrey, but the stimulus separation varies a little. In end-stage glaucoma the 10-2 spatial grid is sometimes used on the Humphrey perimeters covering the macular area to 10° with points separated by 2°. The main point here is that defect detection is determined by the size of the scotomas and the resolution of the visual field examination; certain testing patterns have become fixed 'quasi' standards for testing in glaucoma because fewer test points mean shorter tests. Other types of visual field testing, examining areas in the mid- to far-periphery (beyond 30°), are applicable to a wide range of retinal and optic nerve pathologies, including retinal dystrophies and late glaucoma. There is renewed recent interest here in developing automated clinically useful tests for these regions of the visual field.[17]

Measurement Variability

Visual field testing examines the impact of a defect on visual function and is therefore the cornerstone of glaucoma assessment. However, despite the advances in automated perimetry the subjective nature of the test remains – after all, it is completely reliant on a subject reliably answering questions and pressing a button! The variability in response or measurement noise is overwhelmingly multifactorial. To start with there is variability within a single examination (short-term fluctuation): this is influenced by physiological factors, such as the magnitude of visual sensitivity itself, with lower thresholds manifesting greater fluctuation. In short, patients with defects are considerably more variable than subjects with normal fields. Short-term fluctuation also appears to vary in different parts of the field with, for example, noise increasing with eccentricity. Moreover, the fatigue effect, which tends to increase variability in response with examination duration is a widely accepted contributor to short-term fluctuation and is difficult to control or measure. Other factors that influence measurement variability, including refractive error, lens artefacts, pupil size and even droopy eyelids are, to a certain extent, controllable with diligent testing. Media opacity also affects measurements but a tweak in the analysis of results attempts to correct for this. Unsurprisingly, short-term fluctuation also varies with the reliability of the subject's response: inattentiveness (false-negative errors); 'trigger happy' reactions (false-positive errors); loss of fixation – for these the automated perimeter attempts (sometimes quite cleverly) to measure patient reliability. To cap it all, there is the problem of long-term fluctuation encountered when tests are performed on separate occasions; this in turn is influenced by the learning effect, where subjects simply get better at the examination and more reliable with experience, yielding an improvement in sensitivity, with defects falsely appearing to get better! A number of investigators believe most of the learning to be complete after the performance of the first two fields, whilst some published studies indicate that improvements in performance remain beyond this especially when baseline sensitivity is very low. In general, it is good practice to allow at least one training visual field test per eye to account for most of the learning effect, especially if establishing a baseline measurement for follow-up.

Interpretation of Visual Field Results

Results for automated perimetry are typically presented as printouts which vary from instrument to instrument but almost all automated perimeters have some features in common (Fig. 11-7). A grid of numbers representing the 'raw' thresholds measured at all the test locations are typically displayed as a grid of values. The grayscale of the visual field provides an image which is more readily interpreted with darker areas representing defects. For suprathreshold tests there is normally only one of two categories being represented by a symbol indicating whether the stimulus at that location was seen or not (Fig. 11-8).

Since automated perimetry generates numerical results, a vast array of statistical analyses has been applied to visual fields. Quantification procedures applied to visual field results can be put into three main categories: single field analysis, analysis of patient response reliability and series of visual field results (analysis of progression).

SINGLE FIELD ANALYSIS

Analyses based on a single field test typically compare a visual field with results from a normal population or by using within-eye comparisons. This section briefly summarizes single visual field analysis with the emphasis on results from automated perimetry, specifically the Humphrey. Reviews of the single field analysis of results from other types of perimetry and other automated instruments, including the widely used Octopus can be found in Henson.[1]

The difficulty of interpreting the stand-alone raw values and grayscale is compounded by the existence of sensitivity threshold values that decrease with increasing age and eccentricity in the normal field. Hence, to further aid the interpretation of the raw data, age-corrected normal values have been established and are stored in the Humphrey (Fig. 11-9). These can be subtracted from the recorded sensitivity threshold at each test location to give a defect depth representation, usefully displayed as a total deviation plot. This is expressed in dB, and charted as symbols representing the different levels of probability with which the particular value would occur in a normal population. The symbols beneath indicate probability statements about the measured threshold at each test location when compared with a normal database.[18] For example, a black symbol indicates that the deviation from normal at that point occurs in less than 0.5% of normal subjects and, therefore, must be regarded as highly suspect. The pattern deviation grids are similar to the total deviation plots, but a possible shift in the

direction of a general reduction in retinal sensitivity is mathematically removed. This essentially makes this representation more sensitive to localized defects. It is worth emphasizing that in glaucoma detection the pattern deviation plot is by far the most useful graphical display on the entire printout.

Information relating to the amount of visual field loss, and whether the loss is generalized or focal, is summarized in a set of summary measures known as global indices. For the Octopus perimeter the main indices are mean defect and loss variance. The corresponding measures for the Humphrey perimeter are now described in more detail. The mean deviation (MD) is simply the average deviation from the age-corrected normal reference field. It is an estimate of the total field loss, both general and localized. Pattern standard deviation (PSD) is the standard deviation of the differences between the measured thresholds and the normal reference values at individual test locations. PSD estimates the non-uniform part of the deviation. A small value for PSD indicates close agreement in shape between the subject's field and the normal reference field. Conversely, a high value of PSD indicates an irregular hill of vision and a field with localized defects. Limits for normal subjects have been evaluated for all the indices and if a calculated value falls outside these limits a probability statement is given. These levels of probability are associated with the distribution of the value of the particular index in a normal population. Therefore, in this instance $p < 5\%$ simply means that less than 5% of the normal population demonstrate a larger value for the calculated index. It does not equate to a 5% chance that the result is normal. Like all summary measures, global indices are a form of data reduction, and whilst useful in giving an overall numerical value to the field, should always be considered secondary to the deviation plots, especially in the early detection of glaucomatous defects.

Additionally, the Humphrey printout gives the results of the Glaucoma Hemifield Test (GHT) used to determine whether a single field is normal or has a suspected glaucomatous defect (Fig. 11-10).[19] It was devised to detect field loss that is asymmetric about the horizontal meridian – a characteristic of glaucomatous loss. Analysis is performed in five corresponding pairs of sectors that are based on the normal anatomy of the retinal nerve fiber layer. Deviations from the age-corrected normal threshold in the most sensitive areas of the field are used to detect overall glaucomatous loss. Fields are classified as outside or within normal limits, borderline, or as having a general reduction in retinal sensitivity. This automated algorithm has been proven to give good levels of sensitivity and specificity for separating glaucomatous from normal fields,[20] especially if a repeated GHT was considered. In Octopus perimetry, the Bebie curve is a cumulative distribution of the defect depth at each location and, like the GHT, is designed to separate normal visual fields from those with early diffuse loss.

RELIABILITY INDICES

In practice, consideration of the reliability measures should be the first step when examining the printout from automated perimetry. The full-threshold program on the Humphrey is typical of modern automated perimeters in performing 'catch trials' throughout the test to determine subject reliability. These are known as false-positive (FP) trials, false-negative (FN) trials, and fixation losses (FL).

The movement of the stimulus projection system used by the Humphrey is audible to the subject. Periodically during each test, the projector moves as if to present a stimulus but does not do so. If the subject responds, a FP error is recorded. At other times a stimulus which is much brighter than threshold is presented at a site where sensitivity has already been determined. If the patient does not respond, a FN error is recorded. Hence, a large number of FP errors may denote a 'trigger happy' subject, whilst a large proportion of FN errors may indicate an inattentive or fatigued subject. Fixation is monitored throughout the test by the Heijl–Krakau method: this presents stimuli at the site of the predetermined blind spot. If seen, there is an indication that fixation has been lost, and a FL error is recorded. Visual fields which have a large proportion of fixation losses, false-negatives, or especially false-positives are likely to be unreliable. Automated perimeters may alert the examiner to this: for example, the Humphrey displays a 'low patient reliability' message.

An additional indicator for patient response reliability or measurement variability is assessed, by the short-term fluctuation (SF) index in full-threshold testing programs in the Humphrey and the Octopus. On the Humphrey, SF is calculated as a weighted mean of the standard deviations at ten pre-determined test points where the threshold is measured twice during the examination. This procedure is costly in terms of test time, offers limited precision and may not be useful because of the nature of the points being pre-selected: for example, they may be in defect areas where the response variability is known to be greater.

In Humphrey SITA testing the reliability measures are estimated differently and are completed without the need for extra catch trials, thus significantly reducing test time. For example, FP rates are estimated by use of the patient's reaction time, with overly quick responses disregarded and re-tested. This procedure does more than estimate FP responses but tailors the pacing of the test to the individual's reaction time and makes a significant contribution towards the quicker test times in SITA. Furthermore, FN is estimated in SITA by examining the subject's sequence of responses and again no extra testing is required. It is recognized that the Heijl–Krakau method is limited by correct initial mapping of the blind-spot area and the fact that the stimuli are relatively small in comparison to the area that it is projected on the optic disc, meaning that the patient's fixation will have to move a long way for the stimulus to fall outside the blind spot. For these reasons, newer instruments have abandoned this method and provide gaze tracking to monitor eye movements using an infra-red camera projected onto the cornea. This provides a trace or gaze graph that can be assessed by the examiner at the end of the test (Fig. 11-11). In the Octopus version the test is automatically interrupted if fixation is lost during examination. In summary, the reliability indices are important, but often the examiner's qualitative judgment is as useful in determining if a subject has preformed the test well. Technician experience, time of day, and the percentage of false-positive

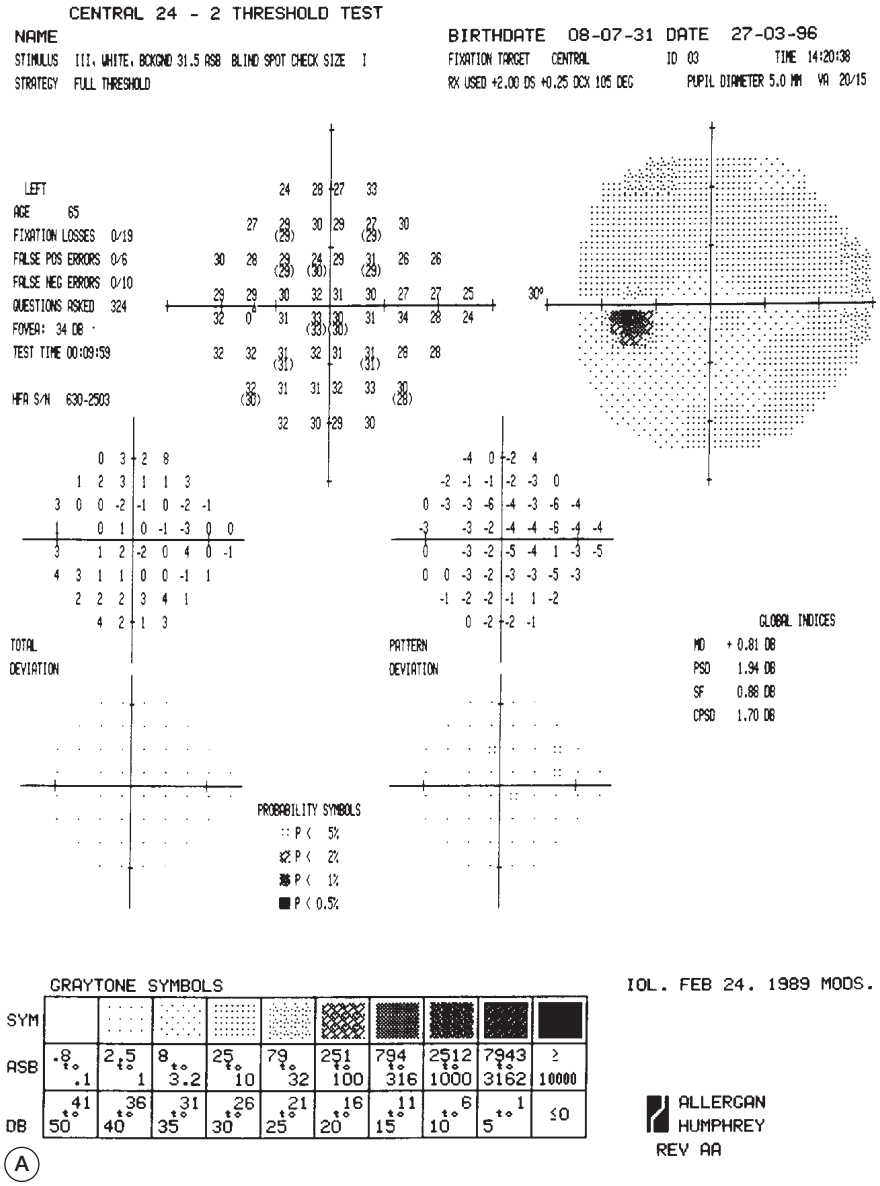

Figure 11-7 Humphrey Field Analyser output showing a single field analysis of results from a normal subject (A)

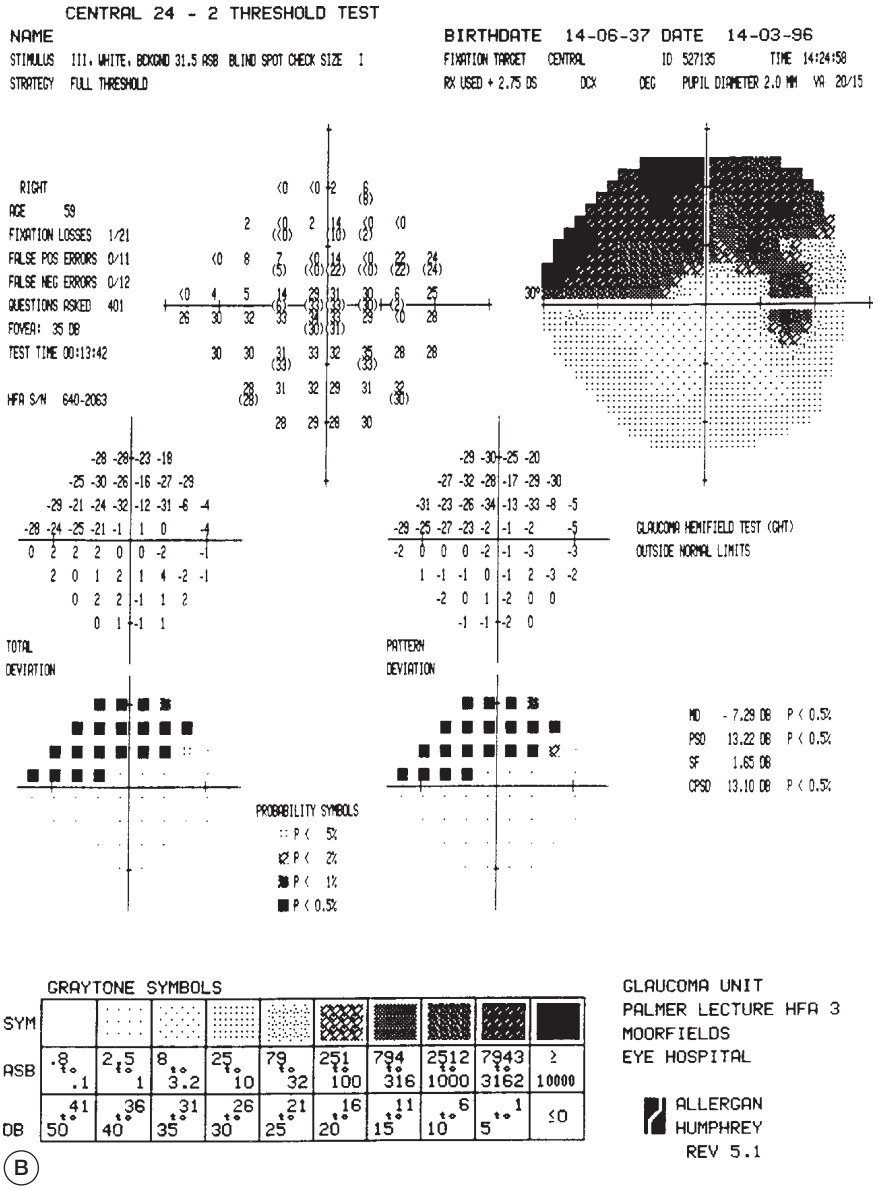

Figure 11-7 *Continued* and a glaucomatous patient (B) using the full-threshold 24-2 program.

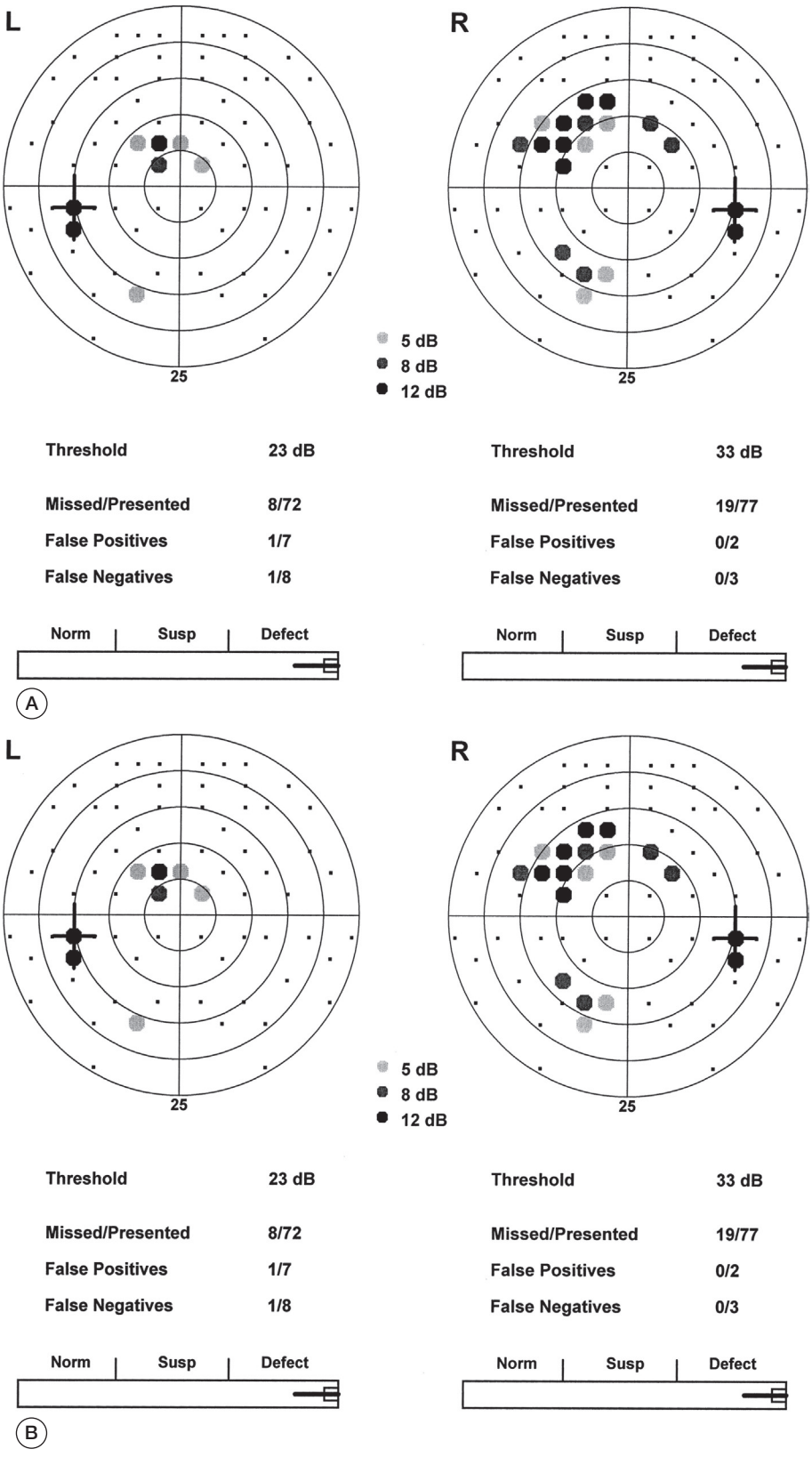

Figure 11-8 Results from a single stimulus suprathreshold test with the Henson Pro perimeter. In the right eye there is a superior arcuate defect and an inferior paracentral defect while in the left eye there is a paracentral defect that is close to fixation. Each visual field is quantified, based upon the number of missed stimuli, their depth and clustering properties. The results of this analysis are given on the scales at the bottom of the chart. The box represents the value and the horizontal line the confidence limits.

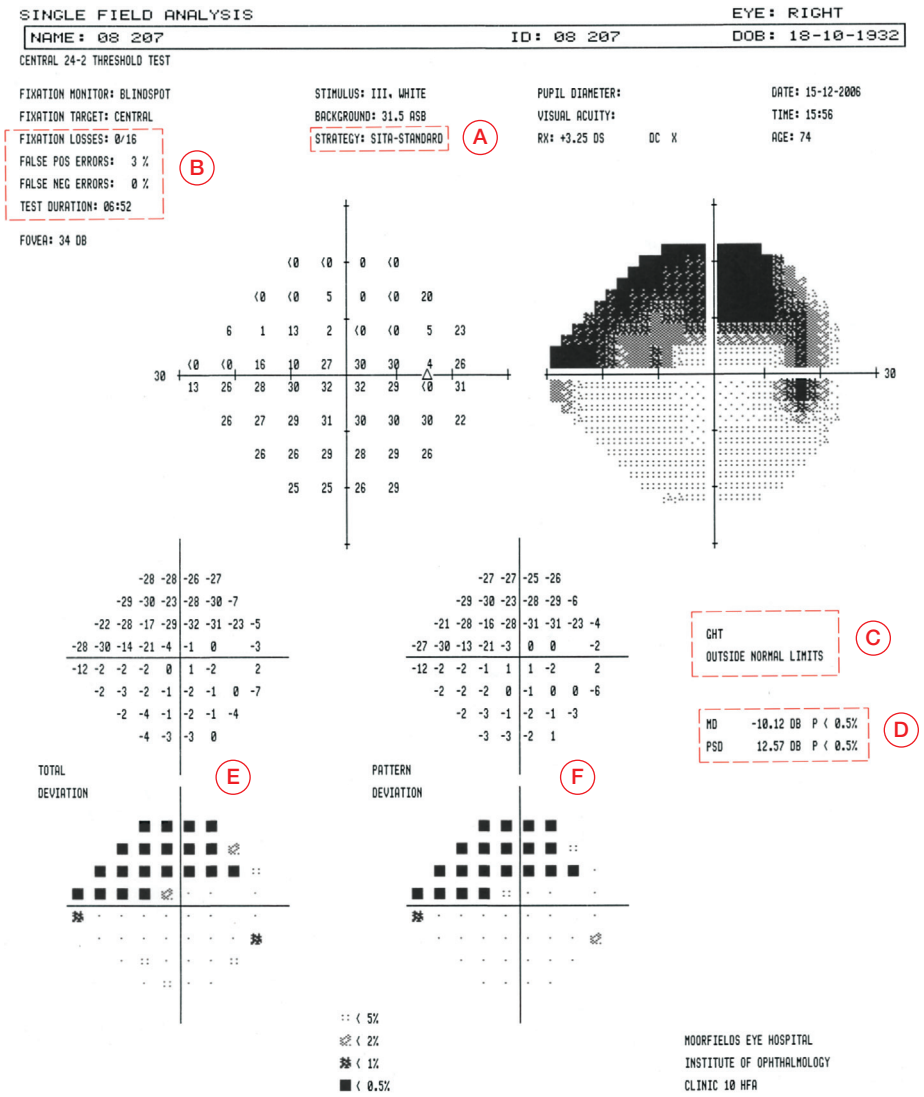

Figure 11-9 Humphrey Field Analyser output showing a single field analysis of results from a glaucomatous patient using the SITA standard program (A). Reliability indices and test duration are shown in the top left-hand corner (B). The results for the GHT (C) and global indices (D) are shown below the main grayscale. For this subject there is little difference in the appearance of the total deviation plot (E) and the pattern deviation plot (F). Nevertheless, the latter is the most important defect plot on the chart for assessing glaucomatous defects because this attempts to correct for any general loss of sensitivity that may be present because of media opacity or cataract.

answers have recently been shown to be the main predictors of measurement reliability.[21]

VISUAL FIELD PROGRESSION

The accurate detection of glaucomatous change in a series of visual field results is important in the clinical management of a patient, and in the evaluation of which treatments are most effective in arresting progression. The slow, often equivocal rate of sensitivity loss, and the variability that exists between field results, makes this a difficult task. Sometimes with sufficient follow-up it is easy to determine even though it might be difficult to exactly quantify (Fig. 11-12). Often, however, it is normally much more difficult: take a quick look at the grayscale representation of a baseline field and follow-up for the glaucomatous patient shown in Figure 11-13 and make a judgment about whether the field defect has worsened without looking at the details in the legend! Separating any physiological change (signal) from the between-test measurement variability (noise) is a real challenge.

There is certainly no gold-standard method for determining visual field progression.[22] Moreover, there is no direct or external measure of disease progression in glaucoma that can be used to validate visual field changes: current clinical devices for measuring structural deficits using optical imaging techniques still only provide a surrogate measure of the biological variable of real interest, namely retinal ganglion cell count and function. In practice, visual field progression is often determined by clinical 'judgment' and 'experience' in looking at series of visual field charts. For research purposes, a 'panel' of such expertise is often used as a surrogate gold standard. However, agreement between experts has been shown to be spectacularly poor[23] and this approach provides only qualitative information rather than a numerical value for change or the probability of change.

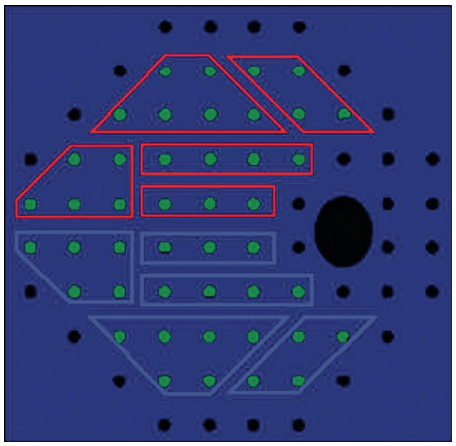

Figure 11-10 For the Glaucoma Hemifield Test (GHT) five anatomical sectors (red) in the superior visual field are superimposed on the Humphrey test pattern selected according to the normal arrangement of the retinal nerve fiber layers. Within each sector, the sum of the probability scores is calculated and the difference compared with the mirror image sector (green) in the inferior hemifield. If there are significant differences between the sectors then the GHT is 'outside normal limits'. GHT is a reasonably precise diagnostic procedure for early glaucomatous loss.

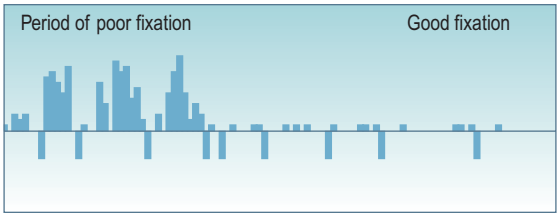

Figure 11-11 An example of a graph indicating eye movements, with upward spikes indicating eye movements and downward spikes indicating blinking during stimulus presentation. This is typically given as a trace on the bottom of the results printout that can be reviewed at the end of the examination.

One set of methods relies on estimates of change in the global indices of the field such as the mean defect value (Fig. 11-14). However, summary measures largely or completely ignore detailed spatial information contained within a visual field and are insensitive to early localized change. They do, however, provide a very specific method for determining change: meaning that if a patient is showing change with the global indices then they are almost certainly progressing, with the caveat that overall depression in the visual field may also simply be a sign of the onset or worsening concomitant cataract. Other methods for 'scoring' visual fields (for example AGIS criteria) have been used in clinical trials but these 'scores' share similar attributes to analysis of the global indices. Still, monitoring a single measure, like the mean defect, provides useful information about the overall change in the visual field and can provide useful information about the speed, or rate, of visual field loss. Moreover, a relatively new metric, called the Visual Field Index (VFI), is now available on the Humphrey for estimating rates of change in glaucoma.[24] The VFI expresses the amount of visual field loss as a percentage relative to the sensitivity of a reference group of people with normal vision. A completely normal visual field would be associated with a VFI of 100% while a perimetrically blind field would have a VFI of 0%. To reduce the potentially confounding effects of cataract, the VFI disregards reductions in sensitivity unless they are associated with pattern deviation probability outside normal limits. In addition, locations in the center of the visual field are more heavily weighted. The VFI is a welcome recent addition to the Humphrey software; its advantages and disadvantages have been recently discussed by Artes et al.[25]

Methods that consider the change in sensitivity at individual test locations have been suggested as a means of more accurately estimating visual field progression in glaucoma. These pointwise methods are becoming more readily used because of available software and are generally thought to be sensitive to change. A good example of these methods is the Glaucoma Progression Analysis (GPA) which was used to quantify progression in the first large, controlled, randomized clinical trial to evaluate the effect of lowering the intraocular pressure on changes in defects in newly detected, open-angle glaucoma.[26] The method has been adopted by other more recent clinical trials too.[27] GPA is designed to evaluate change in sensitivity from baseline data, and evaluates the amount of change with respect to empirical results of repeated tests derived from a population of patients with stable glaucomatous field loss (Fig. 11-15). Two of the first three fields in a series are automatically selected and averaged to give a merged baseline field. The change from baseline (dB) is evaluated and displayed at each test location. The objective is to highlight locations where sensitivity changes by more than is typically observed in the stable glaucoma patient database. The analysis takes into consideration the location of the test point within the field, the initial amount of sensitivity loss and the MD of the field as a whole. These results are given as symbols on a GPA plot with a triangle indicating a degree of deterioration found less than 5% of the time at that location in the group of stable glaucoma patients. Other symbols indicate confirmed change in subsequent follow-up, and an overall statement of change is also provided (Fig. 11-16). GPA is an 'event'-type analysis with each individual follow-up field compared with baseline and intermediate tests are not used. It is also dependent on the population-based reference data it uses to adequately describe the variability that needs to be exceeded to flag change.

A different approach is afforded by using linear regression of sensitivity values at each location. (This provides a clinically useful rate of loss at each point which is estimated by how well the sensitivity values follow the trend over time.) This method is solely based on the subject's own data with more variable patients requiring a greater rate of loss before significance can be assumed; equally points which are slowly deteriorating with little noise are likely to be flagged earlier. The PROGRESSOR visual field analysis software (Medisoft Ltd., Leeds, UK) uses this method and additionally presents the results in a useful and easily interpretable way (Fig. 11-17). Each test location is represented as a small bar graph, with one bar for each test. The length of each bar corresponds to the sensitivity of the location at that test: the longer the bar, the lower the sensitivity. The color of the bar relates to the significance of the slope of the regression line at that test. Thus undamaged locations are seen as series of short gray bars, damaged but stable

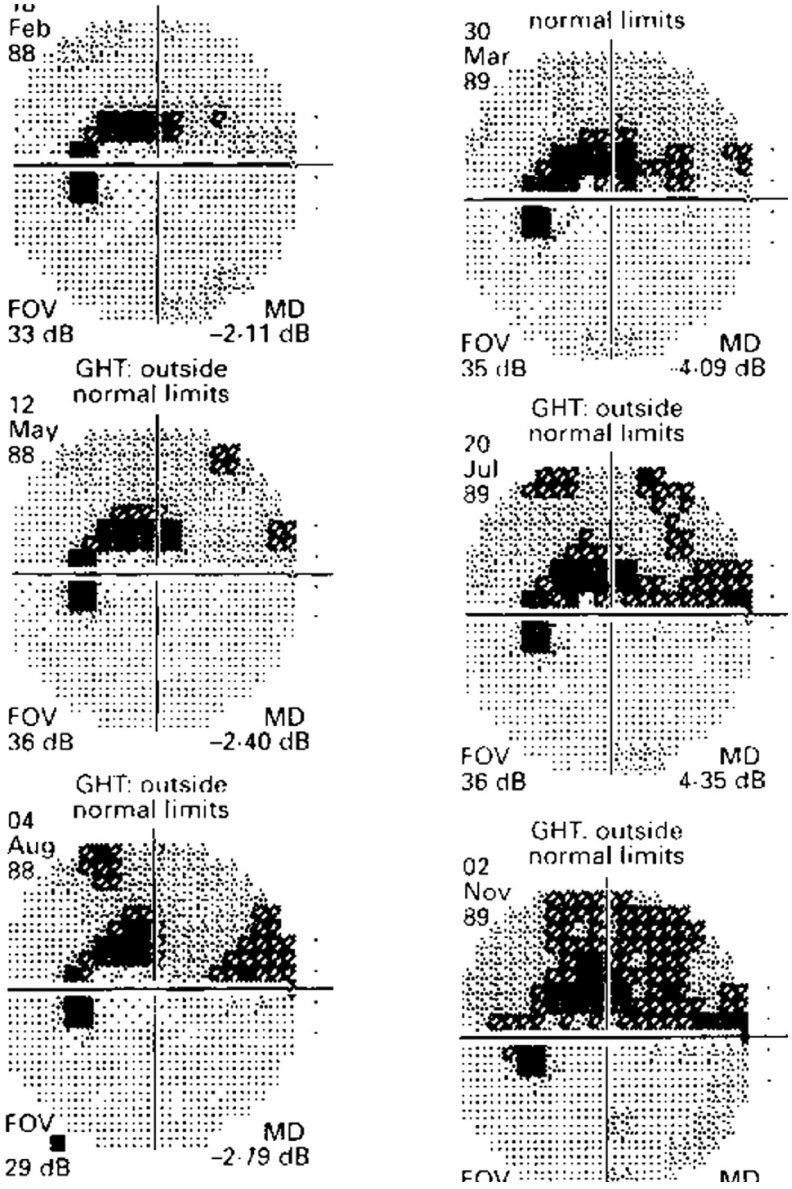

Figure 11-12 Series of Humphrey visual fields (grayscales) of the same eye showing clear and obvious progression of a superior hemifield defect.

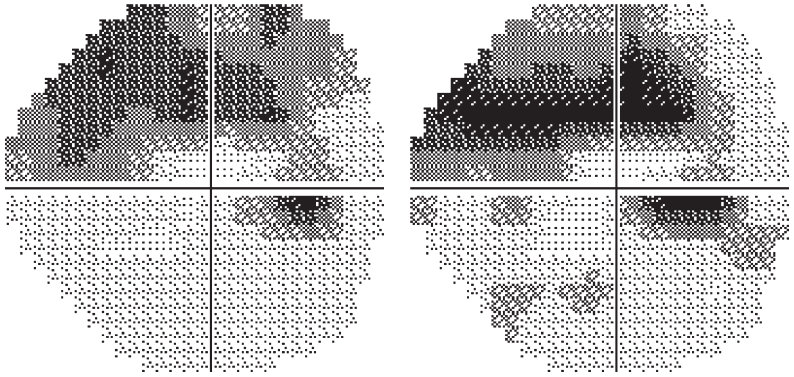

Figure 11-13 Baseline and follow-up Humphrey visual fields (grayscales) for a patient with glaucoma. Has the visual field defect worsened and progression occurred? No! Both visual fields were measured on the same morning in a very reliable patient! The difference between the two fields illustrates the typical level of between-test variability. Separating true physiological change from this noise is a challenging task in detecting visual field progression.

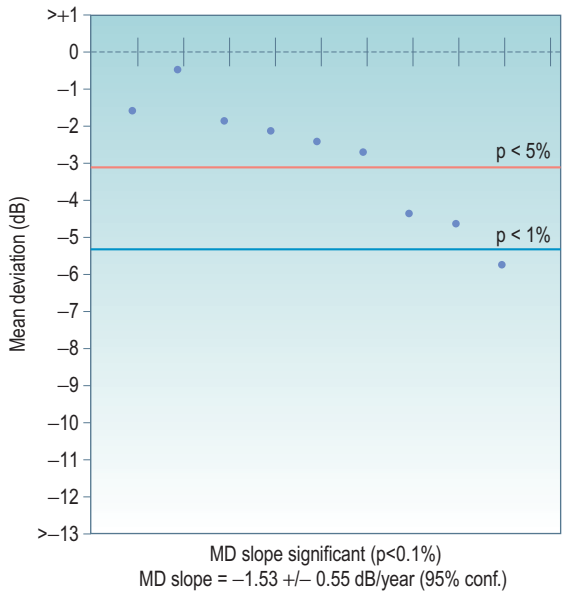

Figure 11-14 A plot of MD against time extracted from a Humphrey printout of serial analysis. Each symbol represents the MD at a different visit in follow-up. Worsening of MD can be assessed as the point falls below population reference values or a trend analysis such as linear regression of MD against time of follow-up. In this case there is clear evidence that the patient's overall visual field sensitivity is deteriorating.

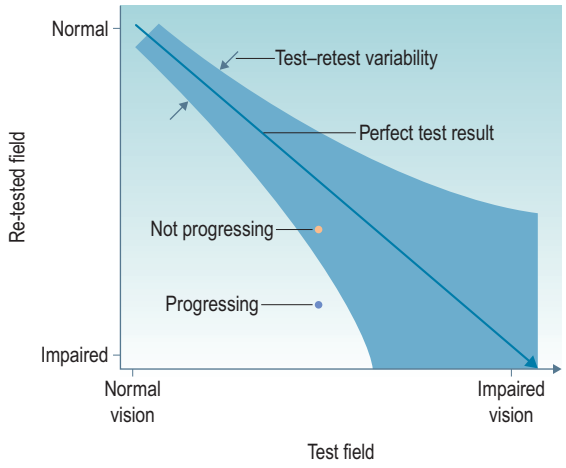

Figure 11-15 GPA quantifies change in relation to the between visual field test measurement error. On retest the 'perfect' test result would be on the diagonal; the shaded areas around the line represent the variably in 'stable' glaucoma. A point is only declared progressing if it falls beyond this expected error. The shaded area increases as the sensitivity of the visual field declines: a greater magnitude of change is required in a field with low sensitivity, whereas more subtle differences between baseline and follow-up are flagged as change in fields with higher overall sensitivity. These limits are derived from a population data set and do not account for the patient's own level of measurement variability.

locations are seen as long series of long gray bars, and progressing locations are seen as series of progressively lengthening bars which change color as the regression slope becomes more significant. Other pointwise methods for detecting change have been recently proposed.[28]

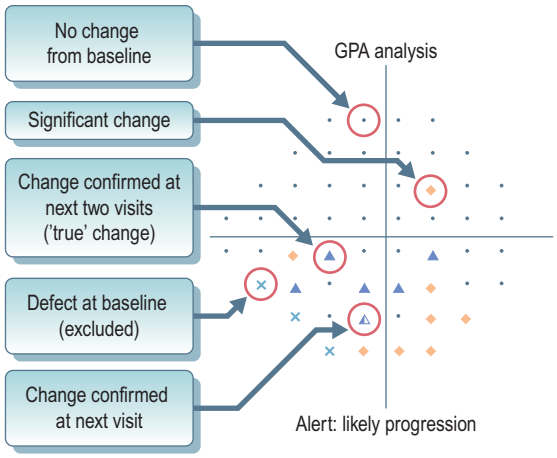

Figure 11-16 Interpretation of the GPA symbols. A significant change from baseline in the same three or more locations in three consecutive follow-up tests generates a 'likely progression' alert (three filled black triangles).

Pointwise methods are certainly more sensitive than using global measures but are not so specific; there is no evidence of consensus on what level of pointwise change constitutes 'real' progression, or whether there should be a requirement for contiguous points to show this behavior and whether it should be maintained in subsequent fields. The latter is important because no decision should be made on progression at the very first signs of it. Developing better methods for quantifying progression will continue to occupy the researchers in the field with the hope that these will be blended with structural measures to improve the clinically useful data management tools available.[29]

Recent interest in visual field testing for detecting progression has centered on the important question about how often examinations should be carried out to detect changes. Frequent visual field tests after initial diagnosis not only help to detect clinical changes, but could also determine the speed of disease progression in each individual patient, which subsequently allows the management to be appropriately tailored. It is important to note that the speed (rate) of VF progression varies widely between patients and timely detection of progression requires accurate and consistent measurement of VFs over years. Useful discussion about this can be found elsewhere.[30,31]

Technical Tips for Users

Automated visual field examination is an easy procedure, but the examiner should be aware of a number of factors when setting up the subject for testing. These are briefly summarized here.

Patients should be set up comfortably and be instructed to keep the occluded eye open. Importantly subjects should be encouraged to blink normally: too often subjects will unnaturally stare without blinking, this inhibits good test performance. One should remember that although the test is automated, good results are achieved if the patient is counseled carefully and the test is carefully explained, especially the importance of fixation. An important message is

that it is better to stop the test and re-instruct rather than wait for obvious flags appearing on the reliability indices on the printout after the test has been done. Other aspects to testing that have a real bearing on the quality of the results are rims of frames if subjects use their own correction and correct refraction. Good practical advice is offered on the latter in Henson,[1] Cubbidge,[2] and Chauhan et al.[30]

Patient fatigue is a big problem with visual field testing. The classic presentation of the fatigue effect on visual field outcome is the clover leaf pattern, where patients have tired after the four primary points have been tested at the beginning of the test (Fig. 11-18A). For this reason, the second eye examined will generally perform slightly worse than the first eye. It is therefore useful to remember, when carrying out series of visual fields during follow-up, that the eye testing order remains constant. In elderly patients, lid ptosis (Fig. 11-18B) may be present and this often manifests an artefact in the final field – precautions in these cases using comfortable taping should be instituted before testing.

The most important technical tip in terms of interpreting visual field results is to never make a clinical decision based on one test result! Repeated fields and follow-up fields must be done to confirm or verify any kind of clinical decision. Remember, for glaucoma, the pattern deviation plot is by far the most useful graphical tool on the printout and that all statistical analysis should be interpreted in conjunction with the subject's reliability indices and the examiner's overall feel for how well the subject has performed the test.

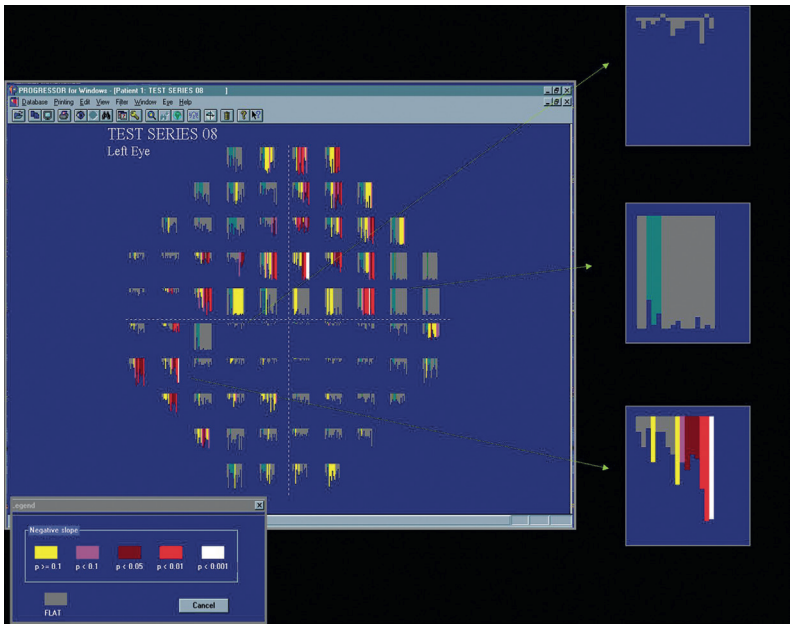

Figure 11-17 PROGRESSOR software showing an analysis of a series of 16 visual fields from the left eye of a patient with progressive field loss. Each location is represented by a bar graph with each bar representing, from left to right, a visual field in the series. Longer bars are defects and shorter bars are nearer to normal sensitivity. The 'hotter' colors indicate that the rate of loss at that point is statistically significant. There is considerable evidence of widespread progression mainly in the superior hemifield and at inferior points close to the blind spot location.

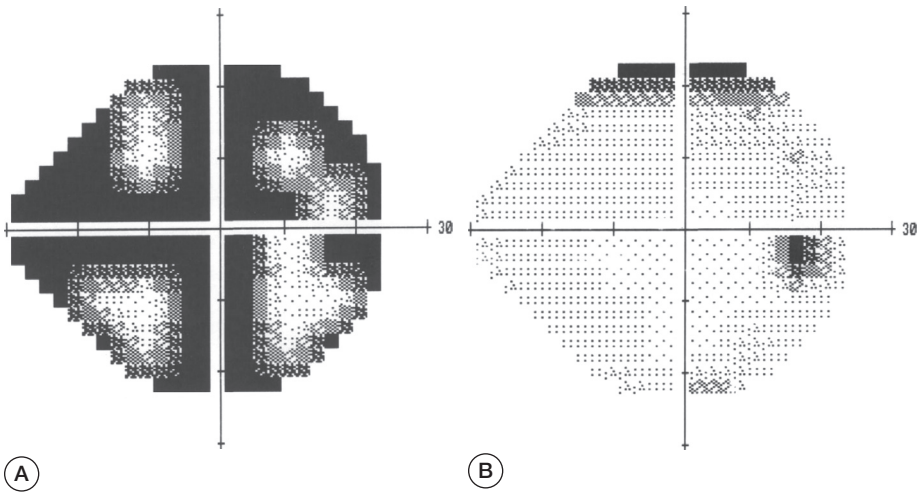

Figure 11-18 (A) Grayscale of a visual field showing an obvious clover leaf pattern, indicating fatigue during testing. (B) Grayscale of a visual field where the subject has a superior lid artefact.

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