Visual screening for blinding diseases in the community using computer controlled video perimetry

by

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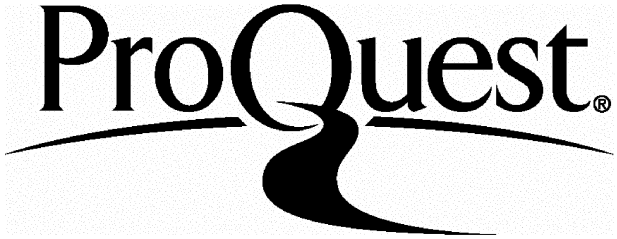

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Abstract

Detecting early visual impairment in a community-based approach is difficult because of the variety of light contrast in which measurements have to be made. Finding ways which are functionally efficient, and yet cost-effective, could lead to important improvements to health and quality of life. To select an appropriate visual screening test for use in *multicontrast* situations, requires an understanding of the interface between clinical epidemiology, visual field technology and the environment in the community where the tests are to take place. Four issues have been taken into account in the study: basic *multicontrast* characteristics; aspects of clinical application of motion stimuli; discriminative ability, reliability and validity to detect early visual loss, and the acceptability of the test.

The study included the development of a group of software programmes called collectively Computer Controlled Video Perimetry (CCVP). The Motion Sensitivity Tests (MSTs) were developed as a part of CCVP in collaboration with Dr Fitzke for early glaucoma detection. The Motion Sensitivity Screening Test (MSST) was finally developed by using a low cost and portable **notebook** computer to assess acceptability. The tests were carried out on 2632 individuals, from whom 5129 CCVP tests were recorded. Testing was undertaken in a wide variety of situations that included a glaucoma clinic in an eye hospital; an eye health survey in inner city community; a glaucoma survey in an Irish rural community; mass screening for optic nerve disease in region of meso-endemic for onchocerciasis in Nigeria and a self-testing programme set up during a clinical meeting in the USA.

CCVP showed that it was possible to detect early visual function loss in a wide variety of situations, whether in clinic or in the community. The results from my study provide a framework for clinical application of using CCVP technology and motion testing to be made with respect to glaucoma and optic nerve disease screening.

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"Screening is the practice of investigating apparently healthy individuals with the object of detecting unrecognized disease or its precursors in order that measures can be taken that will prevent or delay the development of disease or improve the prognosis when it is already present."

R Farmer & D Miller(1991, p155)

Chapter 1 Background

1-1 Screening for blinding diseases in the community

Blindness is one of the world's major human disabilities(Wilson, 1980). According to the World Health Organization, between 27 and 35 million people are suffering from blindness(WHO, 1987a). The number will double by the year 2000 unless rapid action is taken to identify and treat the main causes of avoidable blindness (Thylefors, 1982). More than 90% of the above blindness occurs in developing countries and 80% of the blindness discovered in developing countries could be prevented if early preventive actions were undertaken (Thylefors, 1990). Yet, it is obvious that to identify blinding diseases in the community there is clear dependence on risk factors such as age and geographic location.

For children in Africa and Asia, identification is directed toward nutritional problems and ocular infections which cause more than half of all childhood blindness(Foster and Sommer, 1986). However, in Western countries, genetic factors account for half of the serious visual impairment in children(WHO, 1984). In adults, the main blinding diseases are cataract in developing countries, and age-related macular degeneration in developed countries. Glaucoma and optic nerve disease are important in both developed and developing countries(Thylefors, 1990).

While case-finding of cataracts is part of cataract programs, there is no particular value in population-based screening program directed towards early cataract(WHO/PBL, 1987a). But, we do need to screen for glaucoma, and for retinopathy in diabetics, in many western countries(Hitchings 1986; Sommer 1987, 1989 and Power, 1989) and to screen for optic nerve disease in onchocercal endemic areas(WHO, 1987a). Glaucoma, with other optic nerve diseases is responsible for approximately 10% of all blindness in the world, and this problem will rise with an increase of life expectancy(Thylefors, 1990).

This study focuses on glaucoma case finding in the U.K. and optic nerve disease screening in Nigeria.

1-1-1 Prevention of blindness due to primary open angle glaucoma

The primary open angle glaucoma(POAG) is a group of diseases involved in optic nerve head damage with loss of the visual field and glaucomatous cupping(Quigley et al, 1982, 1987ab, 1988ab). Some of the patients with glaucoma have an intra-ocular pressure(IOP) exceeding the upper limit of normal(Hitchings, 1986). Glaucoma affected at least 0.4% of adults over 40 years in Wales (Hollows, et al, 1972), 0.99-2.16% depending on age in Framingham(Leibowitz et al, 1980). Glaucoma accounts was 14% of all blind registration in Britain(Perkins, 1978; Aclimandos and Galloway, 1988; Grey et al, 1989 and Thompson et al, 1989).

A recent survey has estimated the prevalence of glaucoma as ranging between 0.92% to 2.16% in whites aged 40 years over and 1.23% to 11.26% in blacks aged 40 to 80 years or over(Tielsch et al, 1991).

Although the prevalence of glaucoma is lower than the cataract, the economic burden from glaucoma is considerable because of the expense of medical management. In the United States, the estimated annual expenditure for glaucoma treatment was $1.9 billion - in other words, $1000 per one glaucoma patient per year(Guzman, 1992).

Glaucoma is the second most common cause of blind registration in industrialized countries.

It is less common than age related macular degeneration but more common than cataract, myopia or diabetes(Miller et al, 1974; Ghafour et al 1983; Hitchings 1986; Thompson et al, 1989). In the United States, it has been suggested that 1.9 million Americans have open angle glaucoma and 116,000 are blind due to glaucoma(Guzman et al., 1992). In UK,it was estimated that there were 100-120 thousands persons with POAG in the population over 40 (Graham 1978). Because established glaucomatous damage is irreversible, early treatment is needed to slow or arrest the progress of the disease(Sponsel et al, 1983; Jay et al, 1989), and yet between one third of those patients(McMurdo & Baines 1988) and "roughly half of all subjects with optic nerve damage from primary open angle glaucoma"(Tielsch et al, 1991) were unaware that they had glaucoma. Earlier detection therefore is undoubtedly important.

Two different strategies; screening and case finding may be applied to the early detection of glaucoma. First, all members of the population at risk are invited to undergo a screening test such as measuring intra-ocular pressure(IOP) in order to separate them into those with higher and lower risk of having glaucoma(Levi et al, 1983).

The second strategy relies on physicians or optometrists measuring the IOP and/or examining the optic disc of all patients who come to them with a problem irrespective of whether it may be related to glaucoma. Until recently, For instance, in the U.K. almost 100% of elderly people have seen an optician(Vernon et al, 1989) in the last 7-9 years and most new cases of glaucoma were referred from opticians(Brittain et al, 1988). Both case finding and screening rely on either tonometry or optic disk observation. Neither test has been formally assessed for validity, in terms of sensitivity and specificity (Foreman, 1990). Tielsch(1991) has recently reported that" more than half of all glaucomatous eyes would have been missed by a screening criterion of 21 mm Hg. ... Tonometry, by itself, is neither an effective nor an efficient screening tool."

The role of the visual field in glaucoma diagnosis has recently been emphasized (Sternbuch and Gutzwiller,1991 and Tielsch et al, 1991). However, there are two substantial problems. Firstly, although automated perimetry has made considerable progress in detecting visual field defects in recent years (Heijl 1988), the reliable determination of a glaucomatous abnormality

depends upon detecting a threshold rise of at least 5 Db(Harrington and Drake, 1990). By this time a substantial number of ganglion cells may have been damaged(Quigley et al, 1989).

Secondly, in the U.K. there are few general practitioners who are equipped with semi-automated or automated perimeters(Tuck, 1991), and it seems unlikely that the use of such machines by opticians will increase much, because of the expense(Reeves and Hill, 1989; Strong, 1992). Glaucoma screening programmes with visual field testing would cost $100-300 million each year in the United States(Power et al, 1988). Therefore, a lower cost visual field screening test with higher sensitivity is urgently needed.

Two recent important advances in research into early glaucoma may help to solve these problems. First, Quigley et. al., (1989) indicated that the earliest ganglion cell axons to be damaged in glaucoma belong to the large fibre group. Psychophysically, this corresponds to loss of sensitivity at high frequency detection to motion or flicker(Tyler, 1981; Trick 1985; Fitzke et al, 1984, 1988; Bassi and Lehmkuhle, 1990; Silverman et al 1990 and Bullimore et al, 1991). This test aimed at measuring magnocellular mediated function may provide a more sensitive test for early glaucoma detection. Many of psychophysical studies have suggested that the properties attributable to the large ganglion cells are significantly affected early in chronic human and experimental glaucoma(Tyler, 1981; Trick, 1985; Marx et al, 1986; Johnson et al, 1978, 1989; Drum et al, 1986; Fitzke et al, 1986,1988; Silverman et al, 1990). Therefore, a test stimulus which selects magnocellular function is needed.

Secondly, Minckler(1989) found the earliest location of glaucoma damage in the lamina cribrosa, the scleral portion of the optic nerve head, not at the retina level(Anderson, 1974; Quigley et al 1981). In addition, in chronic glaucoma, the superior and inferior parts of the optic nerve undergo more rapid atrophy than the nasal and temporal parts (Quigley et al, 1982,1989). Radius et al(1979) and Minckler(1980) indicated that those parts most affected contain axons of ganglion cells whose receptive fields are located in the mid-peripheral retina. More recently, Sanchez et al(1986) suggested that there is a higher proportion of large axons in those parts. Quigley(1987c) has also indicated that the "entire" optic nerve was damaged in an eye with early glaucoma and that the superior, inferior and temporal sectors had more

damage than the nasal. These findings have been confirmed recently when Glovinskey(1993) studied the pattern of foveal ganglion cell loss in experimental glaucoma. It was shown that there was selective loss of larger ganglion cells in the glaucomatous eye in the foveal and peripheral receptive field in the same eye.

In practice, it is necessary to rethink this concept in a screening test based upon CCVP. Should we test a sensitivity function covering part or all the visual field? Should the screening strategy be aimed at detection of diffuse or focal damage?

1-1-2 Prevention of blindness due to optic nerve disease in onchocerciasis

In many developing countries a programme of screening for infectious disease (e.g., trachoma, onchocerciasis) is still needed to prevent blindness. Onchocerciasis, or "river blindness," is one of the major endemic, parasitic diseases that in addition to causing untold human suffering, is a major obstacle to socioeconomic development. It is estimated that somewhere between 20 and 30 million people are infected by onchocerciasis throughout the world(WHO, 1985). Contrary to some older text book descriptions, the main cause of blindness in an onchocercal semi-endemic population is not anterior segment but posterior segment disease(Smith, 1986 and Semba et al,1990). Screening for posterior segment disease requires more than the simple technology needed to find cataract, such as testing visual acuity, and as using a torch. Ideally, it should be possible to identify early cases of optic nerve disease in Onchocerciasis patients, so that treatment can be given and further loss of visual function prevented(Abiose et al, 1993).

A recent survey in Nigeria, using conventional visual function tests has shown that optic neuritis occurs in up to 10 % of the whole population aged over 15 years in an onchocerciasis meso-endemic area(Murdoch et al, 1991). The most common cause of bilateral blindness was from optic atrophy and the next was glaucoma(Murdoch et al, 1991). Patients who are at risk of optic nerve disease are not easy to screen by simple conventional visual function tests (e.g., visual acuity or confrontation test). Most of the time, conventional tests can only identify optic nerve disease when it is in an advanced stage. Testing for visual acuity alone

would detect less than 40% of functional impairment of vision in that community(Abiose et al, 1990).

Nigeria has virtually no modernized perimetry facilities(Abiose, 1989). The provision of scientifically sound, relative low cost, simple technology for developing countries is a priority(International Agency for the Prevention of Blindness(IAPB), 1980; Thylefors, 1990).

1-2 The validity of a screening test

All of the considerations for a screening test emphasise that the aim of screening is for control of disease that is not yet evident to the patient and the ultimate goal is to prevent the development of disease in healthy persons(Farmer and Miller, 1991). A screening program should also consider the following issues:

> "Importance of the disease;
> natural history of the disease;
> effectiveness of early treatment;
> characteristics of the test;
> acceptability of the test;
> population to be screened;
> cost of screening."
>
> (Farmer R & Miller D, 1991 p158.)

An effective screening program is highly dependent on the characteristics of the test. For any clinical test it is necessary to know its specificity (which is how accurately it identifies those without the disease) and its sensitivity (which is how accurately it detects those with the disease). A high specificity and high sensitivity indicate that the test has a high validity. However, it is not only the validity of the test is that important.

Reliability is also an important aspect. Reliability is the degree to which the result of the test is stable or reproducible. It is well known that validity and reliability are not necessarily

correlated with each other(Fletcher et al, 1982). The results from a test with high validity may be widely scattered about the true value. On the other hand, the results from a test with high reliability do not necessarily correspond to the true value(Fletcher et al, 1982).

1-2-1 Test Validity

To establish validity, a test is compared to some accepted standard. However, the validity of the test may vary in different clinical situations(Sackett and Holland(1975), and Henson(1988)). **Table 1-1** lists four different clinical situations, and their purposes and subjects. The validity of tests will vary in such different sittings.

In theory, clinical tests have at least three different purposes(Feinstein 1977): discovery of a disease, confirmation of a disease, exclusion of a disease. Tests can be used for one of these purposes, sometimes two and sometimes all three. For a test with many potential purposes, the exact purpose of the test is dependent on the sittings in which the test will be used. For example, the purpose of a visual field test in a glaucoma clinic is to confirm a diagnosis of glaucoma and to monitor its progression.

In contrast, if the visual field test is used in a mass screening program its purpose is to identify those individuals at high risk of having glaucoma. If the test is used in a case finding situation, as in a G.P. surgery or optician premises, its purpose is to exclude glaucoma as an opportunistic diagnosis when the patient is attending for another complaint(Crick and Daubs, 1980ab; Hitchings 1989).

The emphasis on sensitivity or specificity of a visual field test varies in different clinical situations(Sommer, 1990). The test in order to confirm the diagnosis of glaucoma must have high specificity. The sensitivity is less important because other clinical findings can be used to confirm or refute the diagnosis.

A confirmatory test is not the same as a diagnostic test. Health workers may prefer a diagnostic test for etiological assessment which makes use of the laboratory(Fletcher et al,

1982). A diagnostic test which makes use of a psychophysical test alone may be criticized because of the subjective bias in measurements (Proenza et al, 1981; Fletcher et al, 1982; Fitzke, 1988.) However, because there is no single acceptable and reliable objective test for some clinical situations, such as glaucoma diagnosis (e.g., IOP (Sommer, 1990)), a visual field test has been commonly used as part of the diagnostic procedure.

Table 1-1 Distinctions of clinical tests.

Situations	Purpose	Subjects
Survey	Community diagnosis	A random sample from a representative population.
Mass Screening	Early detection for effective treatment	Voluntary responders from a defined population at risk.
Case finding	Opportunistic testing of patients presenting with other complaints	Patients in first-contact with health provider[1]
Diagnosis	Identify the exact cause of the presenting complaint	Referred with a provisional diagnosis of disease for confirmation and treatment.

If a visual field test is designed for glaucoma case finding, the test (as an exclusion test) should have a high sensitivity, with few false negatives. A negative result will virtually exclude a diagnosis of glaucoma at that time although a positive test does not establish the diagnosis. Unlike a test for mass screening, a case finding test does not necessarily aim to influence the outcome favourably by early detection and treatment and it may be only considered necessary to document the suspicion of an abnormality(Sackett and Holland, 1975). With these documented results, it may be possible to perform a confirmatory test later on after a number of retests confirm that the abnormality is consistently found (Abramson 1990).

[1] From the point of view of community health, the first contact health service can be part of primary health. For example, almost 100% people aged over 50 see an optician in Britain(Vernon, 1989). As a result, the optician does not need to call for volunteers, but can simply routinely detect early cases when patients come to him for their vision test. About two-thirds of glaucoma and glaucoma suspects have been found by examination by opticians (Tuck & Crick, 1989).

If a visual field test is used in a screening programme for glaucoma, the test must have high sensitivity. It is also desirable that it has a fairly high specificity. Low sensitivity will decrease the value of the screening test. Low specificity will increase the number of 'false positive' cases requiring further investigation. It will also increase the cost.

Table 1-2 Principal properties in relation to the importance of a test used for different clinical situation

Property	Population survey	Screen	Case finding	Diagnosis
Simplicity	++++	+++	+	0
Acceptability	++++	+++	++	0
Speed	++++	++++	++++	0
Cost low	++	+++	++	0
Reliability	++++	++	++++	++++
Sensitivity	++	++++	++++	++++
Specificity	++++	++++	++	++++
Positive predictive value	+	++++	++	++++

Key to important: 0 =irrelevant.

\+ =minor.

\++ =moderate.

\+++ =major.

\++++ =crucial.

(After Sackett and Holland, 1975; Henson, 1989ab)

In comparison with a test used in a survey, a screening test is seeking early asymptomatic disease in the individual rather than evaluation of the community. Unlike a test in a survey, the object of a test in a screening program must be early detection, which carries an implicit promise that will benefit the participants by follow up with diagnosis, and that early treatment will be available if required. Furthermore, the results of screening need to be available for further evaluation by a subsequent diagnostic test, or follow-up of suspects. Because negative tests are not followed up(Fletcher et al, 1982), a screening test must have high sensitivity as well as high specificity as needed for a survey.

Validity is not the only consideration for a screening test. Table 1-2 lists the differences in

properties when a test is used for different situations. The simplicity, acceptability, test speed, cost and predictive value all have to be taken into account(Damato, 1985ab). To simplify these criteria for a screening test rather than a screening program, Henson(1989ab) has suggested that the aim of a screening test should be to meet the criteria of "speed, sensitivity, specificity and suitability for all patients."

1-2-2 Methods for determining the validity of a test

The validity of a screening test should be measured in the population in which the test is to be used. There are two main reasons that make it essential to test validity in different clinical situations. It is an advantage to use hospital-based data to determine the sensitivity of a given exclusion test by routine checking in the clinic, because all of the individuals have, or will have, well documented clinical data for comparison. "False negatives" can be determined by other clinical findings or follow up tests.

In contrast, it is virtually impossible to re-examine all subjects with a diagnostic test after undergoing a screening test. Logically, if a diagnostic test can be available for all e.g., detecting cataract by a torch, it is not necessary to create a screening test. Furthermore, it is often not convenient to have a further diagnostic examination for people who had negative results from a screening program. This situation leaves us unable to determine the false negative rate for a screening test. It is too risky and expensive to attempt to have an immediate evaluation of the negative rate in a mass screening program (Fletcher et al, 1982).

However, for diseases that are always progressing, the early stages become obvious in a matter of a few years after they are first suspected. The results of follow-up can determine the real negative rate. Many chronic diseases fall into this situation including glaucoma. All that is required is follow-up testing. The specificity of the test in a mass screening program can be examined because all of the people identified by a screening test will be referred for a diagnostic test. The false positives among all referrals can be found.

The validity of a screening test is also dependent on acceptability and simplicity, which vary

according to testing conditions e.g., a hospital-based or a community based sitting. The validity resulting from a hospital based study may be misleading when the results are generalized to a population based study. This is because of sampling bias which can occur when information collection from one clinic is generalized to many other clinics(Fletcher et al, 1982)..

The role of measuring intra-ocular pressure(IOP) as a screening test for glaucoma has been debated for many years(Crick, 1982ab; Hitchings, 1986; Foreman, 1990). Based on hospital data, Crick(1982ab) found that it had such low sensitivity and specificity for glaucoma diagnosis that it was concluded that no useful information could be obtained from IOP. More recently, Tuck and Crick(1989) in a study on IOP as a case-finding test (from 5% of all sight tests performed by optometrists in England and Wales over six months,) suggested that measurements of IOP can provide very important information in glaucoma-case finding, because 41% of confirmed glaucoma can be initially detected by abnormal IOP(> =30 mmhg). But this did not take account of cases missed by IOP testing.

In another example, Arden and Jacobson developed a simple contrast sensitivity test in 1978 that showed a high sensitivity and specificity for detecting glaucoma based on a small controlled clinical population and they suggested the test could be a very good screening test(1978). But this view was immediately opposed by other clinicians(Atkin et al, 1979; Ginsburg, 1981), because a number of conditions can alter contrast-sensitivity function; these include reflecting environments, refractive error, and the selection of optimum hardware(Ginsburg, 1981). Most recently, Yu(1991) concluded that the test "was not valuable for screening."

These scenarios exemplify that the validity of a test varies in different clinical circumstances. Therefore, to avoid this problem, it is essential to undertake comprehensive studies of a new screening tool looking at different populations with "an appropriate spectrum of mild and severe, treated and untreated disease, plus individuals with different but commonly confused disorders"(Sackett et al 1985, p49).

1-3 Computer Controlled Video Perimetry

1-3-1 History of Computer Controlled Video Perimetry

Almost since the inception of the cathode-ray-tube(CRT) display industry, psychophysical researchers have applied the CRT as a visual stimulus device(Barlow and Levic, 1965). Over the last few years, considerable progress has been made on how we can use a psychophysical stimulus on the CRT(Mayzner, 1969, Sekuler and Armstrong, 1971; Dyer and Schelderup, 1973; Polit, 1976; Shapley and Rossetto, 1976; Milkman et al, 1978; Reed 1979; Cavanagh and Anstis, 1980; King-Smith et al, 1983; Hisdal, 1985; Cowan and Rowell, 1987; Taylor and Murch, 1986; Lollo and Finley, 1986; Vingrys and King-Smith, 1986; Buchsbaum, 1987; Brill and Derefeldt, 1991). One of the most important advantages of using CRT is that it provides great flexibility in generating stimuli of different form, spatial configuration, and spectral composition without extensive hardware changes(Fitzke, 1988).

In 1978, Flocks introduced the first application of CRT for a visual field test in visual field screening via closed-circuit television or television broadcast. The test consisted of a 10-minute videotape including three parts: eye health education, visual acuity using Snellen-type letters and the visual field using the Harrington-Flocks Multiple Pattern Method with self contained instructions.

However, complex visual stimuli varying spatially, temporally, chromatically, and in intensity cannot be fully controlled by video tape or a mechanical system. Computer controlled stimuli for CRT display have literally revolutionized psychophysical testing in the field of visual science and clinical research in the last twenty years. Braunstein(1976) developed a computer-based methodology for creating complex motion stimuli. Cutting(1978) created software for generating point-light measurements. Timberlake, Mainster and Schepens(1980) wrote a program for automated clinical visual acuity testing and Arden et al developed the color vision test(Arden et al, 1988).

After the introduction of personal computers, Friendly and Weiss(1985) created an automated visual acuity testing computer program using the Apple. Bertenthal, Proffitt, and Keller(1985)

wrote a program for visual function tests for a personal computer such as the Apple micro-computer. Anstis et al(1986) developed a computer-generated screening test for colour blindness. In addition, a great number of visual science researchers have made computer programmes for generating complex visual stimuli(Braunstein et al, 1982; Ramachandran, 1973; Friendly and Weiss, 1985; Meyer and Greenberg, 1986; Wong and Plumb, 1986 and Brainard 1989.)

Personal computers with graphic displays have only been available for a few years, but several advantages over the traditional methods in ophthalmic services were soon demonstrated. It has not been questioned whether to use the computer(Wu and Huang, 1986a) but how efficiently we can use controlled graphic displays as visual stimuli. Several studies have illustrated the basic characteristics related to visual psychophysical tests in the different personal computer systems, such as IBM PC(Heathcote, 1988; Greeger et al, 1990; Graves and Bradley, 1988), Macintosh(Blumenthal and Cooper, 1990), and Amiga(Anstis and Paradiso, 1989). Many limitations in CRT that were summarized by MacLeod(1986) have been overcome with the improvement of computer software, (Mulligan, 1986; Heathcote, 1988; Graves and Bradley, 1988; Moulden and Kingdom, 1988; Greeger et al, 1990; Crosbie, 1990; Gabrielsson and Jarvella, 1990; Segalowitz and Graves, 1990; and Paredes et al, 1990).

Moreover, researchers have proposed *software-based* visual psychophysics by which a whole experiment can be easily made ready for implementation by a single software package. Landy et al(1989) created the EVE software package for several different visual function tests. Wenderoth(1990) wrote the package for visual psychophysical research in using the Commodore Amiga computer. The important advantage of using software-based visual function tests is that they allow implementation of a whole test in only minutes without knowledge of computers or programming languages(Wenderoth, 1990). The same kind of achievement has been contributed by many other researchers (Dlhopolsky, 1983; Ostrander et al, 1989; Landy et al, 1989; Washburn, 1990 and Crosbie, 1990). This indicates that a complex psychophysical test can be simplified by the use of computer controlled graphics.

These successful applications have encouraged us to use a personal microcomputer for

visual field assessment for clinical purposes. For example, Accornero (1984), and Huang and Wu et al(See publication) used an Apple II for the central 21 degree field; Hart and Gordon(1984) created the colour perimetry and Hart and Burde(1985) developed the colour contrast perimetry using a personal computer; Fitzke (1986, 1987) used a BBC computer for detecting light sensitivity in the central field in patients with central serous retinopathy with his fine matrix perimetry; and Frisen et al(1987) used a high-pass resolution perimetry(HRP) driven by an IBM personal computer(PC) to test the central 30 degree field. A number of visual psychophysical studies(reviewed by Fitzke 1988) have also used a micro-computer and display system but they were not of direct application for looking at the entire central or peripheral field.

More recently, the new electronic displays such as the liquid crystal display(LCD) in laptop or notebook computers, have shown potential advantages. These include a portable flat screen monitor, even contrast, absolute freedom from flicker and no radiation(Bosman, 1989). There are also problems, such as lower contrast, varying brightness, narrow viewing angle, more limited range of luminance, less flexibility of pixel size and limited response speed. However, such problems will be solved by the electronic industry and the advantages over CRT are certainly anticipated.

Unfortunately, there is no report about the application of this technology in visual science. I will demonstrate the preliminary application of CCVP based on this technology to provide a potential alternative way for developing a portable automated perimeter. All the above examples for visual field testing are software-based. With the aid of software for a visual field test, a personal computer can be adapted as a visual field device easily without changing or adding any hardware(HighTech manual, 1990; Frisen, 1987).

The definition of CCVP is that the method of testing visual fields can be done on a conventional video, such as a computer monitor or TV monitor. The software is specific but it is not an additional requirement to have dedicated hardware. Obviously, the software needs a computer in order to run but the exact specification of the hardware is flexible and can be used for other purposes.

1-3-2 Implementing CCVP

CCVP has two applications: As a sophisticated visual function test in a dedicated background e.g., examining room in laboratory and hospital with a dedicated computer; and as a screening test without a dedicated testing room in a waiting room or ordinary house where a personal computer is available. Each application has different advantages for visual science and for clinical management. A sophisticated visual function test provides a reproducible and accurate measurement but it requires a dedicated test background.

Several applications of CCVP already mentioned are of the former type that requires a dedicated background and a dedicated computer. For example, in high-pass resolution perimetry(Frisen 1987), the test uses a new type of stimulus that generates ring targets on the high-resolution display to determine a high-pass spatial frequency. This application was not possible in the traditional perimetry industry. The test has reduced the effect of several artifacts such as the learning effect and refractive blur(Frisen, 1991). It has also provided speed, sensitivity and specificity (Gavanagh et al, 1986; Chauhan, 1990; Lindblom, 1990; Lachenmayr et al, 1990; Wall et al, 1991) but the test has no resistance to a reflecting background. Thus the essential requirement for the test is that "The test area should be COMPLETELY DARK to ensure constant contrast conditions and freedom from reflexes from the test display surface"(HighTech Vision Manual, 1990).

In contrast, a CCVP screening test aims to provide a software-based screening program run by personal computer users for early detection of visual field abnormality. This application is ideal for use with any computer display device in a health care sitting (e.g general practitioner(GP) surgery, an optician's premises), by reducing the expense of dedicated hardware, and for mass screening in areas outside a hospital, such as a public hall or waiting room. However, this raises the problem of test-reproducibility with different computers and different reflecting environments even though are run by the same software.

The experience from TV screening tests(Flocks 1978) suggested that there was much potential variation in its application in a residential sitting. To examine the validity of this test Flocks(1983) stated that no criteria were established for passing or failing the test under

different conditions and "no claim for extreme accuracy can be made." The response might be affected by either "a subjective test involving a process unfamiliar to the person being screened" (Flocks, 1983) or a test sitting affecting individual contrast level requirements that can vary enormously no matter how carefully the examination is done(Taylor and Murch, 1986; The London Hazards Centre Trust Ltd(LHCTL), 1987).

It is well known that the choice of contrast level for a television program is highly dependent on the audience. Some audiences prefer higher contrast than others. The contrast level tends to change as the ambient light intensity changes, due to light or dark adaptation in the visual system. As a result, there is a tendency to use higher contrast in a TV room with higher lighting than with lower one(LHCTL, 1987). The same TV program can be received with different contrast under different ambient light conditions. This problem is also found in computer displays(Bosman, 1989).

The problem of unfamiliarity with the test can be solved by training, but the variable contrast level in each individual test, which can cause a fundamental reproducibility problem, cannot be easily eliminated. It is always an essential requirement to have a stable ambient light in the testing room for conventional field tests(Greve, 1973; Harrington, 1990), but it is not always possible to have this in a TV room. In addition, there is no calibrated system to maintain a standard contrast level for any electronic display set(Brill and Derefeldt, 1991) even though the colour can be adjusted by matching the reference pattern provided by the TV programmer. With low sensitivity and substantial variability, the TV screening test has not been accepted for either clinical use or for mass screening, even though the program has the potential for screening thousands of people simultaneously (Keltner & Johnson, 1983).

In order to apply a standard test in CCVP, it is necessary to be able to control the parameters of all stimuli generated by the hardware, namely; amplitude, colour, size, eccentricity, meridian(i.e., position on the screen) and duration. This applies both in the dedicated background of the laboratory and in a waiting room as might be used in mass screening. However it is not easy to determine a standard stimulus over a great number of different types of hardware(both computers and displays). The problems are as follows:

1. Different standard resolution in terms of pixels (MacLeod, 1986; Moulden and Kingdom, 1988).
2. Different chromatic aberration depending on the phosphors(Brill and Derefeldt, 1991).
3. Difference in the convergence of the three chromatic components from the guns onto the screen(e.g., the image at the periphery may appear blue due to incorrect convergence)(MacLeod, 1986).
4. Different in temporal control due to phosphor persistence and the raster scanning speed (MacLeod, 1986; Fitzke, 1988).
5. Non-linear light output from the phosphors(Lollo and Finley, 1986; Mulligan, 1986; Fitzke, 1988.)
6. Different dynamic range of contrast in different computer systems (MacLeod, 1986).
7. Different types of video adapters(Heathcote, 1988; Paredes et al, 1990).
8. Limitation the size of visual field(Proffitt and Kaiser, 1986; Paredes et al, 1990).
9. Different temporal control due to the computer's internal timer(Heathcote, 1988; Gabrielsson and Jarvella, 1990 and Greeger et al,1990).
10. Different response systems in terms of the use of keyboard or mouse(Gabrielsson and Jarvella, 1990; Crosbie, 1990; Greeger et al, 1990 and Segalowitz and Graves, 1990)

This thesis will not cover all the above hardware problems because many of them have to be solved by the industry. Some problems due to hardware could be automatically solved with the simultaneous development of a computer and a display device, but not all of them, particularly the problem of *multicontrast* environments(Prager, 1990). "*Multicontrast* " is not as the same as contrast sensitivity which discriminates the minimum difference in the luminances between stimuli and background. The term used in this thesis includes any conditions that will similarly disturb a stable and standard contrast of CCVP stimuli. These consist of the unstable ambient light in the testing environment(Bosman, 1989; Prager, 1990); the variable reflection from the electronic display surface(Parry 1941, 1942ab; Bosman 1989); the different contrast sittings in each video display and un-even contrast level across the display(MacLeod, 1986; Livingstone and Hubel, 1987); the non-linear correlation between contrast and digitally-controlled CRT displays(Mulligan 1986); and the different dynamic contrast range being used between different types of display(e.g., CRT or Liquid Crystal

Display).

The use of the concept of *multicontrast* environment takes into account the fact that there are endless ways to affect the contrast level in CCVP if used in the community without dedicated hardware. This thesis concentrates on the difficulties caused by the *multicontrast* environment on the delivery of standard psychophysical screening test. Implementing CCVP outside a hospital or laboratory will be expected to be associated with more serious problems from the *multicontrast* environment than in the first application in a controlled environment. Some solutions will be demonstrated.

1-4 Clinical Implications of parallel visual pathways

One of the most important problems in developing psychophysical tests to classify different visual mechanisms is that of establishing appropriate and selective experimental conditions to dissociate the compounded phenomena. For example, visual researchers have discovered a number of noninvasive tests to isolate the separate contribution of the three cone systems, using an appropriate wavelength that would otherwise be contaminated by the responses of the others.

Present knowledge suggests that the primate visual system from a lower level(between the retina and the geniculate body) to higher level(primary visual cortex) consists of two major visual pathways that differ in their selective processing of colour, contrast sensitivity, speed, and spatial resolution(Livingstone & Hubel, 1987). The role of parallel pathways at the higher level is mainly of interest to visual science; here I will be concerned with the lower level of the parallel pathways, which seems to have direct clinical application with regard to prevention of the blinding diseases.

Although classification methods are based on many different criteria, I will choose the method of using the destination in the lateral geniculate nucleus(LGN) for low level pathways introduced by Livingstone and Hubel(1987) i.e. visual motion, stereopsis and high sensitivity to low-contrast stimuli seem to be driven mainly from the *magnocellular* pathway(M-cell), and colour,

form, visual acuity seem to be driven mainly from the *parvocellular* pathway(P-cell). Comprehensive discussion of parallel visual pathways and of various classification methods is available(Lennie, 1980; Livingstone et al 1987). In this study, I will emphasise the contrast, spatial and temporal sensitivities of each pathway revealed in physiological experiments. An even more serious form of contamination than failure to separate different types of cones, appears to be lack of knowledge of whether discrimination of spatial and temporal sensitivity takes place in the retina, or the retina plus brain(Sekuler et al, 1990). Nevertheless, knowledge of the parallel pathways may help in the early diagnosis of some blinding diseases.

Table 1-3: Characteristics of ganglion cells in the retina*

	X cell	Y cell
Distribution	Mainly central	Uniform
Connecting axons	Small	Large
Conduction Velocity	Slow	Fast
Location in LGN	Parvocellular	Magnocellular
Receptive field	0.5^{o}	2.5^{o}
Response to		
brief light	Delayed & sustained	Rapid & transient
grating light	Yes	No
sustained light	Sustained	Transient
Response to movement	No	Yes
Linear spatial summation	Yes	No**
Tolerance of brief IOP elevation***	Lower	Higher

* Modified based on Livingstone Hubel(1987) and Bassi and Lehmkuhle(1990).
** Cleland et al(1971)
*** Shou and Zhou(1989).

Two initial types of ganglion cells (X, Y) were distinguished in the cat according to differing morphological and physiological characteristics(Table 1-3)[2]. The distinction between the two

[2] There are also W-ganglion cells described in many visual science text books but these are not relevant to clinical application. For this study, I will focus strictly on X- and Y-cells.

parallel visual pathways is not based on the absolute cell size because an X-cell in the periphery can be the same size as a Y-cell near the fovea(Shapley, 1990). Further important evidence for two clear visual pathways will be found in the LGN although the cortical pathways show anatomical cross-talk(Van Essen et al, 1992).

In many primates, including humans, a physical segregation of neurons differing in their physiological properties can be clearly found in the lateral geniculate nucleus. The LGN is a six-layered structure, with two physically visible subdivisions: the four dorsal, small-cell (parvocellular) layers and the two ventral, large-cell(magnocellular) layers(Hickey & Guillery, 1979). The two LGN subdivisions receive input from the two distinct types of retinal ganglion cells: the X cells project to the parvocellular division, and the Y cells project to the magnocellular division. These two linked-relations that are distinguishable both anatomically and physiologically(**Table 1-4**) will be refereed to as P-cell function and M-cell function in this study.

Table 1-4: Characteristics of P-cell and M-cell functions*

Characteristics	P-cell	M-cell
	Anatomical	
Receptive field	Small	Large
Distribution	Mainly central	Uniform
Percent of total cells**	90	10
Ganglion cell	X-cell	Y-cell
	Physiological	
Colour	Yes	No
Spatial resolution	High	Lower
Temporal resolution	Slow	Fast
Motion discharge rate	Low	High
Defocussing	High	Low
Responding stimulus	Small	Large

* Modified after Livingstone and Hubel(1987), Bassi and Lehmkuhle(1990)
** Kaplan and Shapley(1982)

1-5 Visual field implications of parallel visual pathways

According to the above discoveries of the parallel pathways, the visual field function will be influenced by following the separation between M-cell function and P-cell function in the retina(Fig. 1-1). This will help us to outline the choice of conditions of a visual field test(e.g., physical stimulus size, presenting time, type of stimulus) in relation to different properties of the parallel visual pathways.

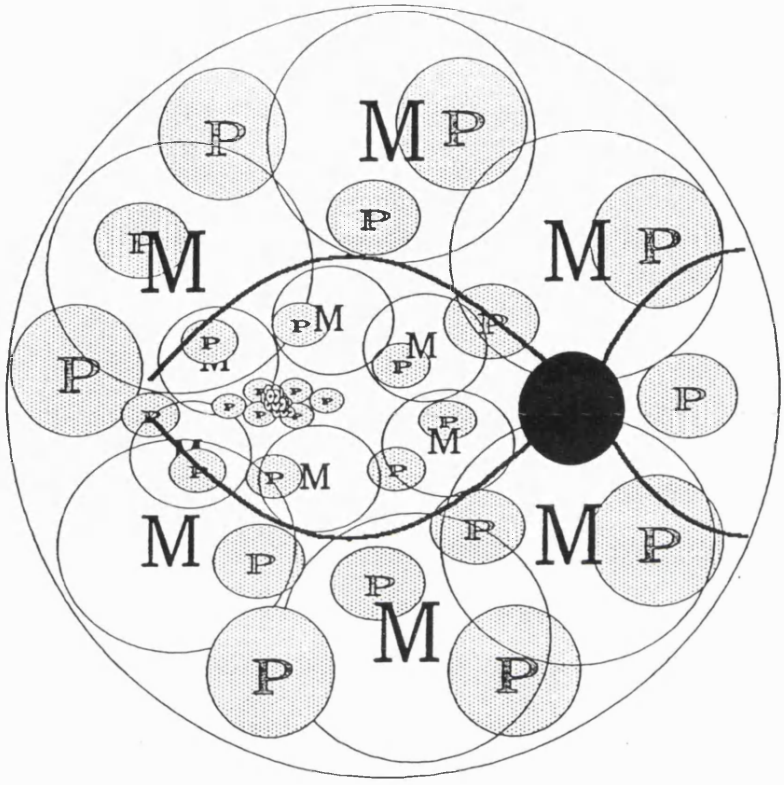


Fig.1-1. Schematic diagram of the correlation of P-cell function and M-cell function at the retinal level (modified from Kaplan and Shapley, 1982, Livingstone and Hubel, 1987; Bassi CJ and Lehmkuhle S, 1990): Note 1)P-cell function has a much larger number of receptive fields but a smaller size of field than M-cell function at any given retinal eccentricity; 2)Large overlap of P-cell function in the fovea and uniform distribution of M-cell function across the retina; 3)Both functions are linked.

1-5-1 Spatial frequency

Since the sizes of the receptive fields in the two pathways are different, various spatial frequencies will differentially stimulate the two pathways(Kaplan and Shapley, 1982). That is, M-cell function has larger receptive fields, which means it will respond to larger stimuli or lower spatial frequencies, whereas P-cell function will respond to smaller stimuli or higher spatial frequencies.

Since P-cell function has a high spatial resolution, it is believed that P-cell function serves visual acuity responses (Livingstone and Hubel, 1987). The object of all visual acuity test is to determine the least spatial resolution of the stimulus.

Schiller et al(1990) reported on Rhesus monkeys in which visual functions of the parvocellular layers or magnocellular layers were selectively damaged by the neurotoxin ibotenic acid. The monkeys with a parvocellular lesion exhibited absent responses to spatial frequencies over the whole range, especially high spatial frequencies at high contrast level. But the monkeys with a magnocellular lesion showed no difference compared with normal monkeys. Moreover, an important feature of these experiments was that the retinal location corresponding to the parvocellular lesion was found near the fovea. This suggests that the smaller the size with higher contrast stimuli and the closer to the fovea, the more likely are the responses to be due to P-cell function.

1-5-2 Temporal frequency

Since the sizes of cell bodies and axons in the two pathways are different, the M-cells, whose axons are thickly myelinated, conduct more quickly than the P-cells, whose axons are more thinly myelinated(Kaplan and Shapley, 1982). This difference in conduction speed is probably insignificant in static perimetry which measures light sensitivity. But it may be more important in detecting loss of M-cell function because critical flicker fusion or motion stimuli depend on conduction speed. Schiller et al(1990) found that if the monkeys had only a magnocellular lesion the capacity for flicker detection and motion detection was separately damaged, with normal P-cell function.

1-5-3 Contrast sensitivity

From a psychophysical point of view, Livingstone et al suggested that the steeper curve of motion detection against contrast is based on the magnocellular pathway. Their conclusion has been confirmed by Sclar et al(1990). A similar analysis, based on early saturation of contrast in the magnocellular system, suggests that this system is more sensitive than the parvocellular system to low contrast.

However, there is a debate about whether the property is caused by the magnocellular system

or by both pathways. Psychophysical studies show that the higher the level within the brain, the more independent are the two systems(Livingstone and Hubel, 1988). Neurons in the cortex are very selective for given stimuli such as contrast, spatial frequency and colour but neurons in the retina or even the ganglion cells are not always so selective. The earlier saturation to contrast in the magnocellular system is one of its important characteristic features compared with the parvocellular system. But this feature does not appear clearly at the optic nerve level or before the LGN(Sclar, 1990). Livingstone and Hubel(1988) have suggested that "though they differ significantly in their response characteristics, the magno and parvo systems do share some basic physiological properties."

Because contrast sensitivity seems to be mediated by both pathways, depending upon spatial frequency, temporal frequency, and retinal eccentricity, it cannot be separated at a low level of the parallel visual pathways (Post et al, 1984; Derrington and Goddard, 1989). It may be difficult to say which pathway has better responses to contrast gain. The M-cells, because they have superior low spatial frequency and high temporal frequency function, would be expected to mediate contrast threshold at low and intermediate spatial frequencies or at high temporal frequencies. The contrast thresholds at very high spatial frequencies or low temporal frequencies would presumably be subserved by the P-cell function.

In fact, recent reports(Merigan et al, 1989; Schiller et al, 1990) showed that a parvocellular lesion seems to cause a more serious contrast sensitivity loss than a magnocellular lesion in monkeys. In other words, the P-cell might give better responses to contrast sensitivity function than expected. The role of contrast in motion stimulation is also unclear. Various studies have shown that contrast has little or no effect on motion sensitivity provided it is *saturated* or *above* some critical value(Watt and Morgan, 1983; Nakayama & Silverman, 1985a, McKee).

There is also evidence that there is a difference of effect of contrast between motion detection and motion discrimination (Derrington and Goddard, 1989). Motion discrimination means identifying the orientation of the movement.

Despite these arguments in visual science terms, the author is in practice more interested in

early saturation of contrast in motion stimulation rather than anything else. Analysis of the physical characteristics of motion stimulation can be divided into three stages by level of contrast. This is based on the findings of Livingstone and Hubel (1987):

In Stage One (insensitivity), contrast below 5%, no apparent movement was seen regardless of displacement interval size. In Stage Two(sensitivity), contrast between 5% to 20%, motion sensitivity rapidly increased as a function of contrast and was associated with displacement interval size. In Stage Three (saturation), motion sensitivity was flat and less affected by increase of contrast(Livingstone and Hubel, 1987). Several investigations in this study, experimental, clinical and community based, will demonstrate how important it is to recognise the correlation between these three stages of contrast sensitivity in motion sensitivity testing. Furthermore, a number of projects will provide evidence that stage three is the most important for community based visual psychophysical tests.

Several studies have reported that the best performance on motion tasks occurs at low contrast, not high luminance contrast(Derrington&Goddard 1989; Boulton and Hess, 1990b). But this difference of dependence on luminance contrast is thought to be "due to the physiology of the visual system, rather than the physics of the stimulus" (Boulton and Hess, 1990). It is found with motion discrimination tasks but not motion detection tasks (Derrington & Goddard, 1989).

1-5-4 Selection of motion stimulus

Two types of motion stimulation have been described for observing visual motion detection in glaucoma: a moving bar(Fitzke et al, 1986, 1989; Watkins and Buckingham, 1991) and a random dot pattern(Silverman et al, 1990; Joffe et al, 1991; Bullimore et al, 1991; Wood et al, 1992 and Bayer et al, 1992). The first type that was the first application of a motion test for glaucoma detection was a peripheral displacement threshold(PDT), which was introduced by Fitzke (1986). The displacement threshold was measured for a two minute by 2 degree vertical line generated by micro-computer on a green phosphor display screen. The contrast of the stimulus was set high (the luminance of the stimulus 27 cd/m sq and the luminance of the background was 7 cd m/sq). The motion detection threshold was determined by constant

stimulus methods. The number of trials was small(10 times). The range of displacement threshold was from 0 to 18 minutes of arc. The line moved from side to side for a 2 second period. No reference line was presented but a warning tone sounds before each stimulus. The subject then simply pressed the button to respond to movement stimulus seen.

Silverman et al(1990) worked with a random dot pattern. Each dot was 16 minutes in diameter and the contrast was 99.2% in a dark room with 0.034 cd m/sq^2 background. The testing field was 60 degrees in width. To determinate the threshold, a constant stimulus method was used with a four-alternative, forced choice technique. The threshold for abnormality of motion detection was defined as 75% correct responses.

Despite differences of techniques of test procedures between these two independent groups, both included subjects with glaucoma, ocular hypertension and a small number of normal people. It is difficult to compare the results within the hypertensive groups because of difference of case definition. Despite this, the sensitivity for finding glaucoma with the bar stimulus was less than with a random dot pattern.

With the bar stimulus, there was an abnormal motion detection of 56% with a cut-off threshold at 8 minutes of arc. In contrast, Silverman et al(1990) found 71% abnormal motion detection. Silverman et al(1990) indicated that the higher sensitivity of finding glaucoma in comparison with the Fitzke et al study, was related to the choice of motion stimulus. Further they suggested that the random dot pattern "allows for the intensity of the motion signal to be precisely varied." On the other hand, the bar stimulus "cannot be assumed to reflect only motion sensitivity since form- and position-dependent mechanisms also may be involved."

However, the random dot pattern may not be better than the bar stimulus for detecting large ganglion cell damage. Theoretically, it is unclear whether a random dot pattern is better than a bar stimulus to isolate motion function from other visual functions such as colour, or form. Since Braddick(1974) introduced the concept of short range and long range motion processes, it has been questioned whether the moving bar stimulates solely the motion sensitive processes. It has been accepted that the random dot pattern probably can distinguish

between short range and long range motion processes. Perhaps for this reason, many clinical reports using the motion process were based on the random dot pattern.

However, there is a great deal of confusion in the experimental studies concerning short- and long range processes(Petersik, 1989).

Table 1-5
Summary of the characteristics of the random dot pattern and un-random dot pattern in apparent motion

Condition	Apparent Motion in Random Dot Pattern	Apparent Motion in Bar or Spots
Isoluminance	slow (2,3) stop (1)	slow and stop (4) stop (2)
High contrast	early saturated(6) not constant (10,12,15)	early saturated (4,8) later saturated (11)
Low contrast	favourable(5)	favourable (7)
Difference between Dim and bright background	favourable(17)	irrelevant (9)
Low spatial resolution	favourable (13, 17) unfavourable (14) favourable with optimal spatial frequency(12,18)	favourable (4)
High spatial resolution	unfavourable (19)	unfavourable (4)

1. Ramachandran & Gregory 1978; 2. Simpson 1990; 3. Cavanagh et al 1984; 4 Livingstone and Hubel 1988; 5. Braddick 1980; 6. Nakayam and Silverman 1985; 7. Petersik and Pantle 1979;8.Sclar et al, 1990; 9. Caelli and Finlay 1981;10. Cleary 1990; 11.Raymond and Darcangelo, 1990; 12. Boulton and Hess 1990b; 13. Petersik & Grassmuck, 1981; 14. Braddick, 1974; 15. Cleary and Braddick, 1990; 16. Lappin JS & Bell HH, 1976; 17. Chang JJ & Julesz B 1983; 18. Boulton and Hess 1990a and 19. Turano and Wang, 1992.

Table 1-5 shows a selective list of favourable conditions of apparent motion that has been proposed for the bar and random pattern dot tests. The two different types of motion stimuli had the same responses to the different conditions. The list is not exhaustive, especially in terms of characteristics of the spatial resolution because there are so few studies to compare characteristics with both types of stimuli.

Table 1-5 presents the evidence that there is no specific difference between the two stimuli in detecting apparent motion. Despite the above arguments and from a practical point of view,

the random dots pattern requires more sophisticated technological supplements than the bar stimulus(Chang, 1986). The bar chosen in the present study, instead of random dots pattern, was largely for simplicity and the greater possibility of application to available computer displays in the community.

To sum up, deciding what kind of motion stimulus to use for clinical application should not be solely dependent on evidence from experimental situations. It is important to bear in mind that the clinical situation is much more complex. Thus, in this clinical epidemiological study, the most important objective is to determine what is the optimal motion stimulation to be used in a community setting with regard to acceptability and validity.

1-5-5 Selection of testing location

It is unclear which retinal locations should be tested for M-cell function. Under the assumption that M-cell function is uniformly distributed across the retina including the fovea(Glovinsky 1993), it is reasonable to assume that any area can be tested. Schiller et al(1990) found that a M-cell lesion in Rhesus monkeys affected a visual area 3 to 15 degrees from fixation and P-cell lesions affected 0.5-9 degrees of eccentricity. It seems that there is an increase of segregation between the two pathways with increased eccentricity. Therefore, if these observations can be applied to human beings, the measurement of M-cell function should take place at least beyond 10 degrees of eccentricity. Glovinsky(1993) has recently found that he could also find abnormalities in the fovea in terms of larger retinal ganglion cell function in experimental glaucoma.

In summary, it is probably more effective to measure M-cell function rather than P-cell function in a visual field test. There are at least two reasons:(1) uniform M-cell function across the field and (2) a large receptive field. In the first case, an investigator can use a single amplitude stimulus for the entire field. In other words, there may be very little amplitude-effect on eccentricity. In the second case, the investigator can save a great deal of time by reducing the number of test locations because large stimuli can be used.

1-6 Conclusion

An effective screening test is highly dependent on its speed, acceptability, validity and reliability. The validity and the acceptability of a screening test should be measured together in different clinical situations and in different populations. It is an advantage to use experimental data or hospital data to determine the sensitivity of a screening test, when all "false negatives" could be determined by sophisticated follow up tests. On the other hand, it is an advantage to investigate the specificity in a population outside hospital. The best way to find out the acceptability for a screening test is in a community, not in a hospital(Hennekens et al, 1987).

CCVP is specifically devised for efficient visual field testing under different testing conditions without the drudgery of conventional tests. All that is needed to adapt a personal computer as a visual function test is to design software. There are two main applications of CCVP: as a sophisticated test with a specific computer and monitor in a hospital based examination room; and as a screening test run by any available computer display in a public place.

An important problem when implementing CCVP in a community sitting is the *multicontrast* environment. The *multicontrast* environment refers to any factors that can disturb a standard, stable contrast level in CCVP during a given test(Proenza et al, 1981). These include the unstable ambient light in the testing environment(Bosman, 1989); reflecting environment on the display surface(Parry 1941, 1942; Bosman 1989); different contrast sitting in each video display; un-even contrast level across the display(Livingstone and Hubel, 1987); non-linear correlation between contrast and digitally-controlled CRT display(Mulligan, 1986) and a different dynamic contrast range being used between different hardware. Unfortunately, no simple replacement has been found for any visual function test which does not involve these problems.

This study addresses the *multicontrast* environment issue by documenting the *multicontrast* effect in different clinical environments, in order to understand how to overcome the *multicontrast* problem in the further application of CCVP. If CCVP can avoid the problem of

contrast, for example by using motion stimulation with saturation to contrast, it may overcome one of these major problems. Yet, underlying this assumption, I should raise three unanswered questions:

1- What is the variation across the visual field tested in a multi-contrast background?

2- Is it possible to increase the sensitivity for detecting early field defects by using differential motion sensitivity rather than differential light sensitivity ?

3- What is a correct testing strategy for CCVP ?

Knowledge of the parallel visual pathways is better understood than ever before. The use of computer controlled video graphics has provided a great opportunity to detect spatial and temporal differences in the parallel pathways, but only in the laboratory or research centre sitting. Perhaps, there is a lack of interaction between the scientist and clinicians because clinicians often cannot appreciate the experimental results, and basic scientists rarely understand the more complex clinical situation (Enoch and Proenza, 1981).

A great effort is made in this study to join basic psychophysical science with clinical epidemiology. From the basic science point of view, the results of the *multicontrast* effect in terms of variation of light intensity from the hardware, testing background, and basic features of motion stimulus as a target in the visual field, especially in glaucoma patients, are described. Based on experimental findings, a visual field testing program package has been developed. From a clinical and epidemiological point of view, detection of M-cell function loss may be more efficient than detecting P-cell function loss in a community sitting for the early detection of glaucoma or other ocular diseases.

Chapter 2 Method

2-1 Introduction

There were three stages of development to create a screening test. The first stage was to investigate basic properties of visual motion function in the visual field. This work evolved into a basic visual science investigation. The major part of this aspect of the study was carried out in the Department of Visual Science, Institute of Ophthalmology. In the second stage, a software package of visual field tests for clinical application was progressively developed and evaluated in a preliminary laboratory test program and then in hospital based clinical investigations. The objectives included: 1) the software specification techniques by using existing computers 2) the interface of CCVP software usability between operator and patient implementing CCVP in a community setting and 3) the variation of applications in different clinical settings such as the glaucoma unit in Moorfields Eye Hospital, the Inner City Eye Survey(ICES)(Wormald et al, 1992) and the Roscommon Glaucoma Survey(RGS)(Coffey et al, 1993). During the third stage, two main objectives were: 1) to see how early we can detect glaucomatous visual field defects, 2) to optimize the motion function test as an effective screening test.

Finally, a motion sensitivity screening test(MSST) was developed for a notebook computer. This new version of the test has been transferred to a battery supported computer for practical use in the field. This allows the test to be used in areas without electricity. MSST was tested in different clinical situations, such as screening for glaucoma in Moorfields Eye Hospital, optic nerve disease screening in West Africa and self-testing in U.S.A..

2-2 Methodology of *multicontrast* measurements

2-2-1 Equipment

In order to investigate the *multicontrast* environment, the light intensity was measured by a digital photometer (Hagner Model EC1, Sweden) which provides a *lux* unit for the photometric value. The detecting range is from 1 to 10,000 *lux*. The diameter of the detector is 10 mm.

Most of the experimental studies were carried out on a single standard VGA(Video Graphics Array) (IBM 8514) driven by IBM computer(P/S2 Model 50Z). The diagonal picture size of the VGA monitor is 16". The pixel size is 0.42 X 0.42 mm^2. The maximum resolution is 640 X 480 pixel in 256 colours. The computer processor unit(CPU) was a 286 without a co-processor. The CPU running speed was at 12 Mhz under DOS operating system. This is called the *primary computer* in this study. Other displays were later used outside the laboratory. In addition, five other desktop computers such as one PC/XT(Amstrad 5121) with colour generator adaptor(CGA), four Ats(Opus, Olivetti, IBM model 60 and PC-III) with VGA display and 3 portable computers with LCD display were all involved in this part of the study.

2-2-2 Process

The modern electronic display, such as VGA provides digitally- controlled light intensity. This is done by a fast digital-to-analog converter(DAC) to vary the voltage-intensity relationships of the three phosphors(Brainard, 1989). The advantage is that it allows the use of a simple software programme to control light intensity of stimuli without changing the hardware. It was felt that it could be a great advantage to use digitized numbers for controlling light intensity for the light sensitivity test in CCVP. But the disadvantage is that there is no standardized DAC in the electronic display industry and it is necessary to have a fine calibration. (Mulligan, 1986; Bosman, 1989).

CALIBRATION

The Red, Green and Blue digital values in the VGA display were set to 29 in the program written by Dr. Fitzke so that the luminance of the display corresponded most closely to the standard Goldmann background(10 cd/m^2). In addition, when the digital value was 29 the reading from the light meter in 1989 and 1990 was 134 and 107 respectively(Table 2-1). According to instructions of the manual(Ophthimus System Manual Version 2, HighTech Vision), 100 lux in the Hagner EC is equal to 10 cd/m^2 but this was only valid for the Ophthimus system. This confirmed the recommendation in the lightmeter instruction that it may be incorrect for other applications(HightTech, 1989). For this reason, I did not consider 100 lux equivalent to 10 cd/m^2 here. The light meter readings were used to determine the

variation of illumination. Because this study does not attempt to investigate what photometric unit should be used for calculating variation of illumination, the photometric unit read from the light meter was used. In this study, the ratio of the stimulus intensity of light source to the background is arbitrary as the *contrast* which differs from the concept of *multicontrast*. Therefore, it is not necessary to limit the concept of the contrast to the Michelson definition.

Table 2-1 Look-table of calibration to digital photometric value and contrast

VGA (reading)	SEI* (unit)	Hagner* (Lux)	Contrast* (%)	SEI** (unit)	Hagner** (Lux)	Contrast** (%)
29	6.8	134		5.9	107	
31	8.2	151	6	.9	120	6
33	9.8	199	10	7.8	154	9
35	10.6	249	15	9.8	202	15
37	12.5	310	20	10.6	237	19
40	13.8	402	25	12.9	298	24
44	19.9	514	29	13.4	381	28
49	23.5	680	33	20.1	512	33
63	27.4	1145	40	24.3	890	39

* June, 1989

** June, 1990

LOOK-UP TABLE

Because the temporal stability of the ratios in a colour monitor is very short(Cowan and Rowell, 1987), a re-calibration is required each time. The re-calibration over time will make another variation in CCVP application (from the *multicontrast* point of view). For the above reason, the present study has kept away from measuring precise visual function in a community. Nevertheless, an understanding of this problem is essential for the application of CCVP. It was also felt better to find a single look-up table no matter which different types of displays were used because it could save a complicated calibration(Brainard, 1989). However, this would

depend on how many variations there were in different display sets. Thus, not only was the variation of the relationship between digital-value intensity and luminance investigated for different display sets, but also the variations of light intensities as a function of digital value within different locations on a given display were measured.

There were two ways to apply the digitally-controlled intensity in the present study. One depended on built-in DAC without CCVP software correction and one used a look-table with CCVP software correction(See appendix I). In the former, there were 64 steps of digitized intensity values in the VGA system by DAC but there was a non-linear relation between digital value and light intensity(Cowan and Rowell, 1987; Mulligan, 1986; Brainard 1989 and Brill and Derefeldt, 1991). In the latter, a correction for the non-linearity was required by using a look-up table (**Table 2-1**). This allowed approximately equal steps of contrast(in 8 contrast levels in this study). However, there was one disadvantage of using a look-up table which required calibrating for each individual display set.

To simplify this calibration problem, I used Table A1(see Appendix I) which was prepared by Dr. Fitzke and included his original program(Table A2). In the table it lists that the relation between digital input(from 4 to 62) and photometric unit reading, which is based on independent measurements of the luminance of 8514A video graphic display by the use of an SEI photometer. When the background of CCVP was set at the standard background(10 cd/m^2) a measuring range was 0.64 logarithms from 30 to 63 digital input value. 0.08 logarithm was chosen as step in measurements of light sensitivity. The digital input value: 31,33, 35, 37, 40, 44, 49 and 63 were therefore selected to build a look-up table(Table 2-1). After the initial measurement was done, the contrast controller and the brightness controller were covered on the VGA display in order to maintain the initial sitting.

ABSOLUTE INTENSITY

The measurements of the *multicontrast* environments were combined from separately - made measurements of the "absolute intensity" from the screen of the computer display, and the "ambient light intensity" from the examination room e.g. laboratory room or residential living

room. Measurements of the absolute intensity were made for different positions on the VGA display sets. The different values of the analogue input voltage to the VGA input, and variation as a function of time were also observed. Because it was felt that there was large intra-display variation of the intensity across VGA displays, the measurements were taken at 48 points around the entire display.

After an initial warming up period and clearing the accumulated dust from the screen, the detector head of the light meter was put directly on the surface over one of 48 rectangles on the display. The rectangles were drawn by a program "Cali.exe". One rectangle consisted of 48 pixels on the VGA display. The physical size of each rectangle was almost even in the same display but varied between different displays. These variations ranged from 18 X 18 mm to 20 X 20 mm which is almost 4 times bigger than the size of the detector(10 X 10 mm). Each rectangle was measured three times and the readings were recorded. Then, a similar procedure was done for the next rectangle. The value for each rectangle was an average of the three readings. The value for each display was an average of the 48 values from 48 rectangles corresponding to a given VGA unit. Measurement started from digital input value of 29. 7 VGA units of 31,35,40,44,49 and 63 were separately used to create the rectangles luminances and their contrasts were measured.

'THE INITIAL CONTRAST' AND 'THE MAXIMUM CONTRAST'

The term ' the *initial contrast* ' was that default contrast level on a given display which had been selected by a computer user through the contrast controller before the measurement took place. The term ' the *maximum contrast'* in this study was estimated after adjusting the computer contrast controller and the bright controller.

A survey of the initial contrast and the maximum contrast was conducted over 8 computer displays in the Department of Preventive Ophthalmology, Institute of Ophthalmology. Five CRT displays and three Liquid Crystal Displays(LCD) were measured. The luminances of 48 stimuli which were drawn by the "Cali.exe". The background was measured and the contrasts were calculated.

Digitally-controlled inputs in the "cali.exe" program were used and the digital input values for background and stimulus was 29 and 62, respectively. The luminances were directly measured by the light meter three times before and after adjusting the contrast controller and the bright controller.

There are several ways to calculate the contrast in a psychophysical stimulus. In the present study, the expression of difference of light unit between the stimulus and background used the Michelson contrast[3], that is,

$$(L_{stimulus} - L_{background})/(L_{stimulus} + L_{background}) \ X\ 100 \ . \qquad (2\text{-}1)$$

For light decrements or increments the method of Livingstone and Hubel(1987) was used, that is

$$(L_{stimulus} - L_{background})/(L_{stimulus} + L_{background})/2\ X\ 100 \ . \qquad (2\text{-}2)$$

In addition, averages of the overall luminances of the 48 testing points as a function of digital inputs were calculated for each VGA CRT display set. The variation of contrast within an individual display, and the variation of contrast between different displays were also determined in terms of mean and standard error. The 95% confidence intervals of contrast around estimates of mean for each display as a function of digital input were made(CIA program, British Medical Journal).

VARIATION OF AMBIENT LIGHT

For measuring ambient light, the detector was put in front of the display set at a distance that was equivalent to the width of the display set. The detector of the photometer was fixed on a chin rest(when it was available) and directed towards the centre of the display. The reading from the light meter was done when the display was off. These variations over time were measured in different sittings. These included the laboratory in Judd street, the glaucoma clinic in Moorfields Eye Hospital, a Day Centre in the Inner City of London, residents' homes in London, community health centres in Roscommon, and several compounds in northern Nigeria. The test was also made in the largest exhibition hall at the Association of Research for Visual and Ophthalmology(ARVO) Annual Meeting, in Sarasota, USA, 1991.

[3] More detail can be seen in Spillmann & Werner(1990), page 56-59.

2-3 Testing strategy in CCVP

Because it requires a long time to do a constant strategy for any visual field test, test strategies consisting of only the *stair-case* and the *single amplitude trial* were used in the study.

Stair-case(SC): This presents the initial stimulus, which assumes a slightly supra-threshold level at a given point(Rose et al, 1970). If the subject sees the stimulus, CCVP decreases the amplitude of the subsequent stimulus at the same location until the subject does not see it. Then the amplitude is increased until the subject sees the stimulus. The last seen amplitude is identified as the subject's threshold at that location. The advantage of SC is to have precise reproducible measurements(1982; Lieberman, 1987; Heijl, 1986 and Simpson, 1990). However this has been debated by others(Watson and Fitzhugh, 1990 and Johnson et al, 1992)

Single Amplitude Trial(SAT): Unlike the above strategy, SAT has only one amplitude to be tested but many repeat tests or trials. The score at a given location is the fraction seen in a given number of trials. For example, if one stimulus is seen out of two trials, the score is 1/2. However, if there are 5 seen among 10 trials, the score is 5/10 and it is equivalent to 1/2. The advantage of SAT is to reduce the effects of extraneous noise in a test(Swets 1979; Swanson, 1990). This improves the reliability at a given amplitude.

2-4 Motion stimulation

CCVP program was written to make several visual function tests easy for both experimental and clinical observers. Table 2-2 lists only the 5 models of motion stimulation programme in CCVP, which were written in the QuickBasic Version 4.5 under the DOS operating system in respect of application periods and clinical situations. It required no additional programming by the user for different applications, but several options extended its capabilities by changing testing parameters. For experimental observation, CCVP provided a highly flexible model which was called "*Init-5*". In *Init-5*, one could easily change stimuli to flash, movement, or flicker, and change test location when required. All information, including routine data entry e.g.,

name, age, and identification, false response, reaction time, and test duration are recorded.

Table 2-2:Summary of developments of the motion models in CCVP

Model	Period*	Stimuli	Features and hardware involved	Test Strategy	Application	Setting
Init-5	1987-1988	option	Preliminary model on IBM 50Z with VGA CRT display.	SC/SAT	Basic features of motion stimuli	Laboratory
MT	1988-1989	48	Menu driven, determining motion threshold as a function of eccentricity and as a function of contrast.	SC	Preliminary applications	Institute & Hospital
MST	1989-1990	16/18	Menu driven, fewer locations tested, desktop computer	SAT	Detection of visual function loss in unselected population	Community Health Centres
MF	1989-	6	with 4 amplitudes of displacement threshold and 3 frequencies of flicker, Desk top computer	SAT	An case finding test for M-cell function abnormal detection	Glaucoma Unit in the hospital
MSST	1990-	6	Motion Sensitivity Screen Test, LCD, VGA model, notebook computer.	SAT	Validate the capacity of the test	Hospital and community based clinics

* The years for application of the model.

The visual fields obtained with CCVP are saved in ASCII code which can be directly transmitted into many other commercial data processing programs such as Dbase III and Lotus 123 and can be also printed on a printer. The motion sensitivity was measured by the primary computer by three different parameters - namely variable pixel, variable contrast, and variable length of bar. The size of stimulus was based on the display pixel in this study. In order to compare with other studies, the visual angle of the stimulus can be converted according to the formula:

$$\text{Visual angle} = tan^{-1}(\text{length of pixel/viewing distance}). \qquad (2\text{-}3a)$$

Because the CRT displays were not absolutely flat, the visual angle per pixel decreases with increasing eccentricity. To translate a pixel into visual angles, the $\cos^2$ effect was considered(Drum and Bissett, 1991). The equation for translating a pixel into a visual angle in CRT was according to the formula:

Visual angle= tan^{-1}(length of pixel/viewing distance) X cos(eccentricity) (2-3b)

If the length of a pixel is 0.42 mm and the viewing distance is 273 mm, the visual angles of the pixel at fixation and 15° from the fixation are equivalent to 5.28 min of arc and 4.9 min of arc, respectively. For most conditions, the width of the stimulus was 2 pixel(0.86 mm.), and the length of bar varied from the central to peripheral field. The equation for changing the length of bar was according to the formula:

Length(pixel) = 4 + *integer*(eccentricity/6-0.5) (2-4)

Because, several experimental protocols were used at this stage and the size of bar varied with the type of observation made, this will be described more fully with the method for each particular observation.

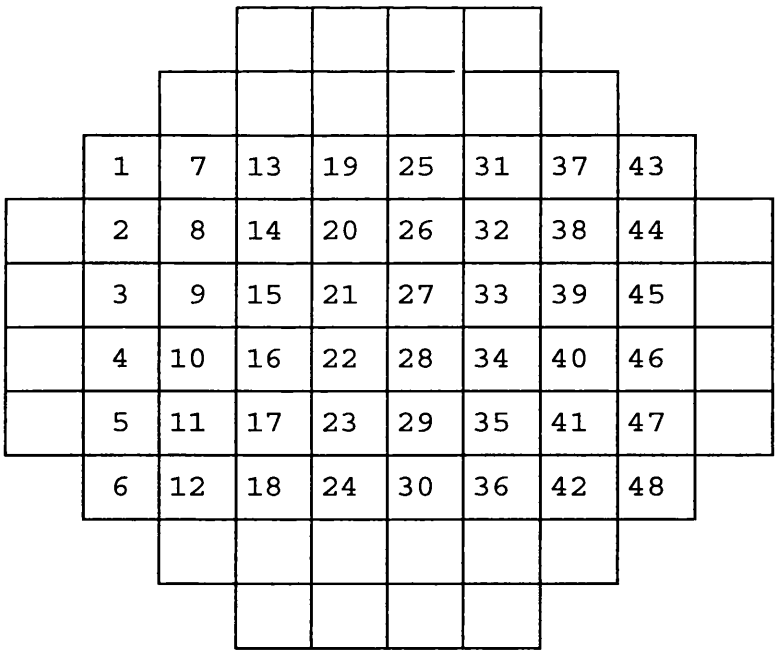


Fig. 2-1 Distribution of 48 locations in fixed method. At standard distance, each location is separated by 6 degrees.

There was no pre-stimulus interval. The presenting time for displacement movement from side to side time was 200 msec for each side. The post stimulus interval was 1.5 sec. The timing is controlled by the system-time-of-day clock. This clock contains four components: hours,

minutes, seconds, and hundreds of seconds. Because IBM 80286 CPU works in 12 Mhz and information is updated every 83 msec(Reed, 1979), the times of successive presentation can vary between 201 to 283 msec[4].

In *Init-5*, the sequence of location selected was according the order of location number. It always started from location 1 to the last number of location(**Fig. 2-1**). For each displacement measurement trial, the stimulus was stationary at its starting position and was then moved to the left or the right side of the starting position, then back to the starting position where it again remained stationary. The threshold determination used a modified stair-case method(Cornsweet, 1962 and Fitzke, 1985). The endpoint of the staircase was defined as the displacement threshold.

The fixation target in MT and MST consisted of red horizontal and vertical cross hairs with a total length of 10 pixels in each orientation. In MF and MSST, the fixation target was a circle, whose diameter was 5 pixel. The automatic successive presentation of the next stimulus is linked to the individual reaction time of the patient. In other words, if the subject presses the response key quickly, the interval before the subsequent presentation will be shorter. If the subject presses the key slowly, the next presentation will be delayed.

There were two methods used for selection of locations. One was the customized method in which the geography of locations tested could be defined by the operator. The resolution of testing location could range from 1 pixel up to 640 pixels in the horizontal field and up to 480 in the vertical field in the VGA display.

To detect the blind spot and an angioscotoma with high resolution testing, two 10 X 10 testing patterns were generated on the blind spot area based on this method(see section below). Other clinical applications had a fixed method in which the distances between loci were pre-designed and fixed in a given pattern. For example, to allow comparison with conventional automated perimetry, the method was matched to the Humphrey 24-2 program(**Fig. 2-1**) and each location was separated by 6 degrees at the standard viewing distance.

[4] This is account 200 msec for presenting time plus minimum of delay time 1 or maximum of delay time 83

In the laboratory, a subject sat in the dark at a table, with the chin rest, and the monitor screen was placed 273 mm from his/her cornea. In the clinic, to eliminate the effect of ambient light, a special monitor cover was used. A subject watched the monitor through a 10 cm diameter hole in the cover. In such a case, there was no chin-rest but the subject could rely on the cover to support his/her head. Subjects were instructed to press a response key whenever they saw the stimuli while they fixated the fixation target. The proportion of correct responses per displacement magnitude was calculated for each individual location and different colours, lengths of bar and displacement intervals. All original ASCII data from CCVP were transferred into a database. For this and the subsequent data analysis, the statistical work was always based on the SPSS/PC package(SPSS inc. 444N. Michigan Avenue, Chicago, Illinois 60611, U.S.A.) unless otherwise noted.

2-5 Motion Sensitivity Measurement in laboratory

2-5-1 Stimulus

Hardware

The motion sensitivity measurement for most situations was done on the primary computer as described earlier. The 16" test display with VGA 8514/A card was set to 480 X 640 picture elements. It was free from flicker. The IBM mouse was used as a response key. A chin-rest was used. It was fixed at the standard viewing distance.

Software

In previous studies (Fitzke et al, 1986, 1989 et al), the stimulus appears and remains stationary for some time, then begins to move after a beep. After a given time it stops moving and remains stationary until its disappearance. Therefore, no reference line precedes the stimulus. This procedure was called a stop-go-stop procedure(Bonnet, 1984).

Unlike the previous studies, all models of the motion test in the present study have presented reference lines at test locations before a test starts. The effect of reference line has been considered(Johnson and Scobey, 1982). The width of the all lines is 2 pixels. All reference lines remain stationary throughout the test until it is selected as a stimulus. When a reference

line becomes a stimulus, it moves either to the left then to the right or to the right then to the left of its' static position at a constant rate(0.2 sec). After moving, it returns the original position . No warning beep is made before an object moves.

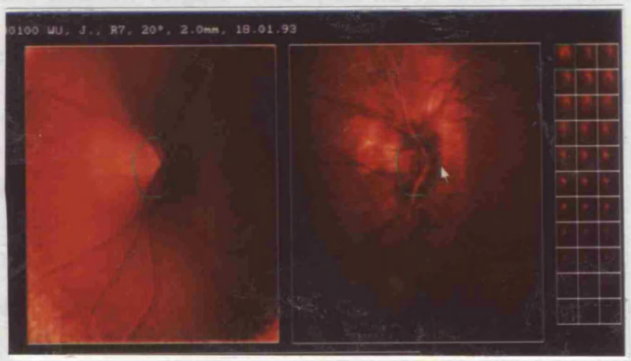
2-5-2 Contrast effect

The displacement threshold as a function of contrast was measured by Motion Threshold(*MT*)(**Table 2-2**). It measured 48 locations(**Fig. 2-1**). In each session, 48 displacement thresholds corresponding to 48 retinal loci across the central of 20° were determined with the stair-case at one given contrast level. Therefore, in order to see the contrast effect, 8 levels of contrast in the range from 3% to 40%(Table 2-1) were separately measured in each session. The display background luminance was closely to 10 cd/m^2. The illumination in testing room varied from 35 lux to 114 lux.

To complete this part of the study, each volunteer had to have 8 sessions in the whole trial. There was approximately 5 minutes break for a rest between sessions. Five subjects (DW aged 7, GW aged 36, JW aged 34, CB aged 34 and YZ aged 70) were involved in this experiment. All of them were free from any ocular or systemic disease, did not use medication and were experienced observers in the displacement threshold detection test(Fitzke et al, 1987). The experimental tests were done on the right eye of each individual, following a full explanation of the experimental procedures. In each person, wearing spectacles if necessary, Snellen acuity was 6/6 or over. None of them wore contact lenses.

2-5-3 Effect of fundus features

In order to find whether the motion sensitivity test was affected by visible retinal features, namely a blind spot and central retinal vessels, the author's right eye was measured by using the model *Init-5* at the standard viewing distance. Two customized test location patterns for field were created by this model in CCVP(**Fig. 2-3ab**). The patterns for detecting the blind spot and vessels were from degree coordinates (x, y)=(12, -8) to (30, 10) degrees, coordinates (x, y) =(14, 6) to (23, 15) degrees in a 10 X 10 square matrix, respectively. For detecting the blind spot, the total testing visual angle was nearly 20° square reached 15° from fixation in the temporal field. This represents an area of 5.5 mm. by 5.5 mm. on the



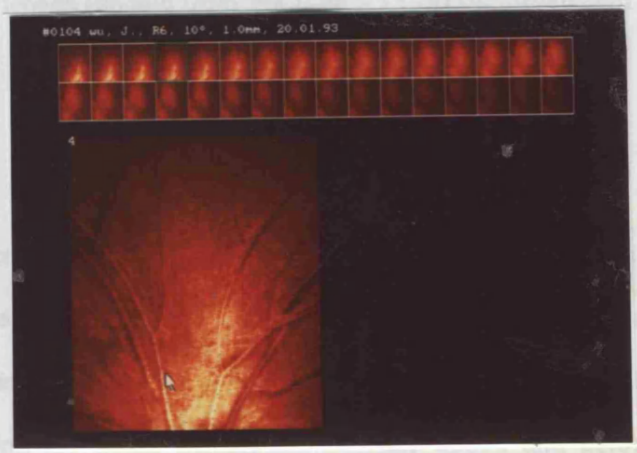


Fig. 2-2 Fundus photographs of the observer(JW) were made by Laser Scanning Tomography(Heidelberg Engineering, D-6900 Heidelberg, Germany). The above image of the optic nerve head(A) was taken under 20 degrees field of view which is matched to the testing area in **Fig. 2-3a**. The green contour line is interactively drawn around the excavation of the optic nerve head. This provides reproducible measurements. The image below of the central retinal vessels(B) was taken under 10 degrees of field of view that is matched to the testing area in **Fig. 2-3b**. The arrow indicates the vessel that caused a angioscotoma(see section 3-3-2).

retina(276 microns on retinal per 1° visual angle(Fitzke, 1985). For detecting the vessels, the total testing visual angle was nearly 10° square reached 15° from fixation in the temporal field. This represents an area of 2.7 mm. by 2.7 mm. on the retina. The number of retinal positions for each pattern was 100. The testing positions for detecting blind spot and retinal vessels were separated by 2.0°, 1.0°, respectively, in terms of the visual angle. The author's right eye was -2.5 Dioptres of Sphereid(DS). The test was done in a dark room. A chin rest was used. The author looked at the fixation target. The optic nerve head and the central retina at the upper margin of optic nerve head were measured.

2-5-5 Effect of Defocus

The effect of defocussing was partially investigated. This part of the study was based on a series of observations by two trained observers(JW 34 and GW 34 yr). The test procedure was similar to that described earlier. The bar contrast was 80%. Two amplitudes(4 pixel and 8 pixel) were measured to see the difference of any defocussing effect between amplitudes. A series of defocussing lenses ranging from +1.0 to +11.00 Dioptres(HightTech, 1989) were used.

2-5-6 Data analysis

Data analysis of displacement threshold as a function of contrast effect was calculated by the mean and 95% confidence interval of 46 locations. Two locations in the blind spot were excluded in data analysis. Displacement threshold as a function of eccentricity was calculated separately for 12 testing locations, namely immediately above and below the horizontal meridian (No. 3,4,9,10 ,15, 16, 21, 22, 27, 28 33 and 34 in **Fig. 2-1**), which were drawn from 48 locations for data analysis. Data from the study on the effect of fundus features was transferred to a main frame computer. The three dimensional topography and the contour and breadth of the blind spot or vessel were plotted by using the software supplied by F W Fitzke (1986). This provided a 3-dimensional graph and a contour map for each method of measuring motion. Data from the study of the effect of defocus was based on the fraction of motion seen over all 46 locations as a function of defocus.

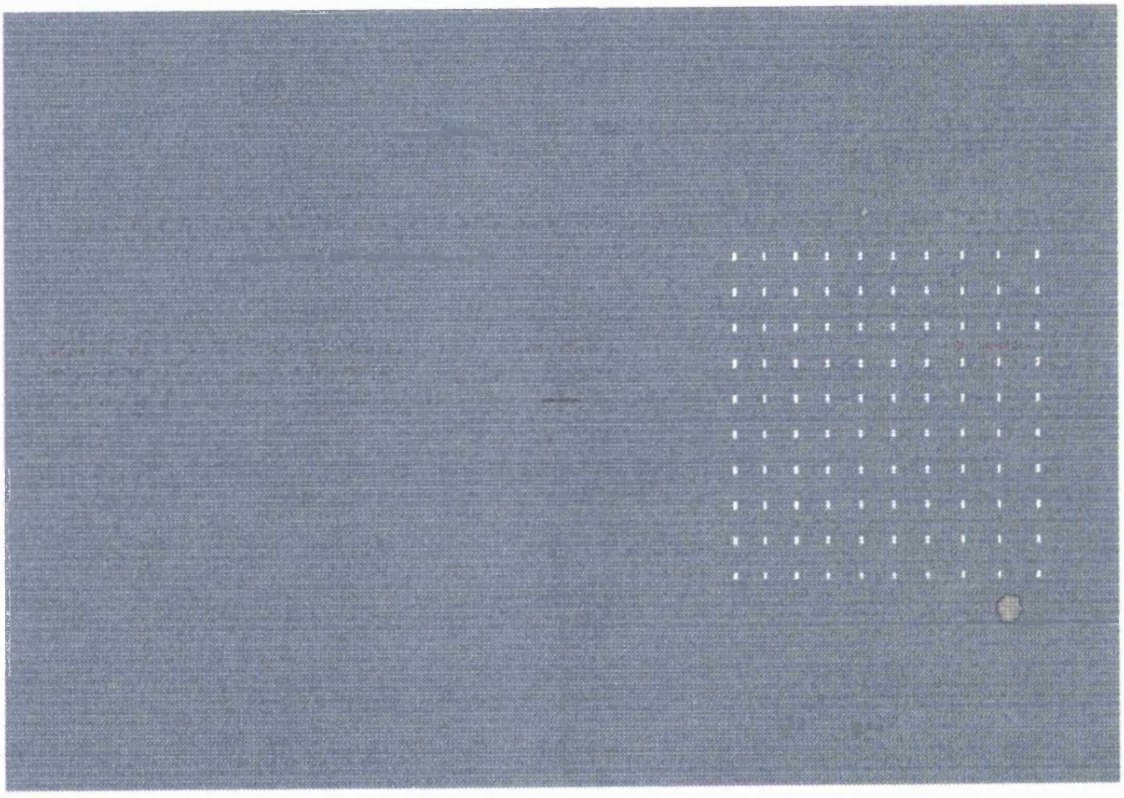


Fig. 2-3a The test pattern for detecting the blind spot. The red cross is a fixation point.

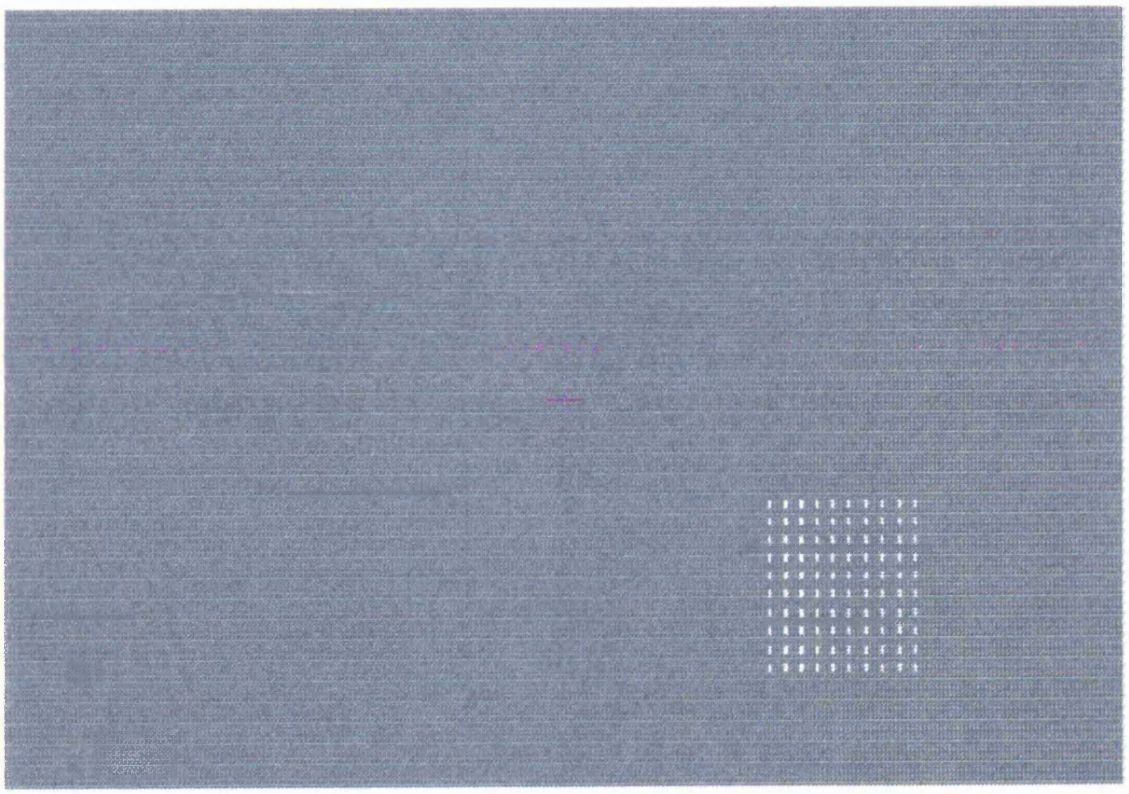


Fig. 2-3b The testing pattern for detecting the angioscotoma

2-6 Motion sensitivity measurements in glaucoma case finding

In this section, the motion sensitivity test was investigated within a hospital clinic and a community based clinic in order to determine its capacity for early glaucoma detection.

2-6-1 Stimuli

Hardware

The Motion Screening Test(MST) was run on four IBM or IBM compatible computers. These consisted of one primary IBM computer(model 50 Z) with 16" VGA, one(NEC) portable computer connected to a 11" TAXAN super Vision EGA display, and two desktop computers(AST and NTS) with 11' EGA monitors. The AST computer with 386c processor can run at 33 mHz but for the purposes of this study it ran at 12 mHz. MF test was only run on the IBM Model 65. Calibration of all the different computers was done by using the light meter in order to achieve the highest contrast level that the computer was capable of. A chin-rest was not always used.

Software

Four different models of motion test were used in this part of the study(**Table 2-2**). All lines are presented at "maximum contrast" in order to be sufficiently visible at all eccentricities. The lengths of the line increase by approximately 2 pixels(11 min arc) with each increase 6° of eccentricity(**Fig. 2-4**).

Motion Sensitivity Test(MST)

MST randomly examined 16 locations with the SAT testing strategy(**Fig. 2-4**). The number of trials was 10. The background luminance varied in the four displays and all were above 10 cd/m^2 in the central screen. Only one amplitude was used in MST. The motion stimulus colour was white on a black background. The stimulus(bar) would move from side to side for a 0.2 second period. The displacement distance(amplitude) from side to side in eccentricity of 3°, 9° 15° to 20° was 10, 9.8, 9.6 and 9.1 min arc, respectively. Because several different computer displays with different display sizes were involved in this part of the study, the viewing distance varied according to the display size. MST took 5 to 8 minutes, based on subjects' response times and number of defects. The results were printed and saved. Abnormal motion for the case finding procedure was any fraction of motion seen below 0.8 over 14 testing points(excluding 2 close points to the blind spot).

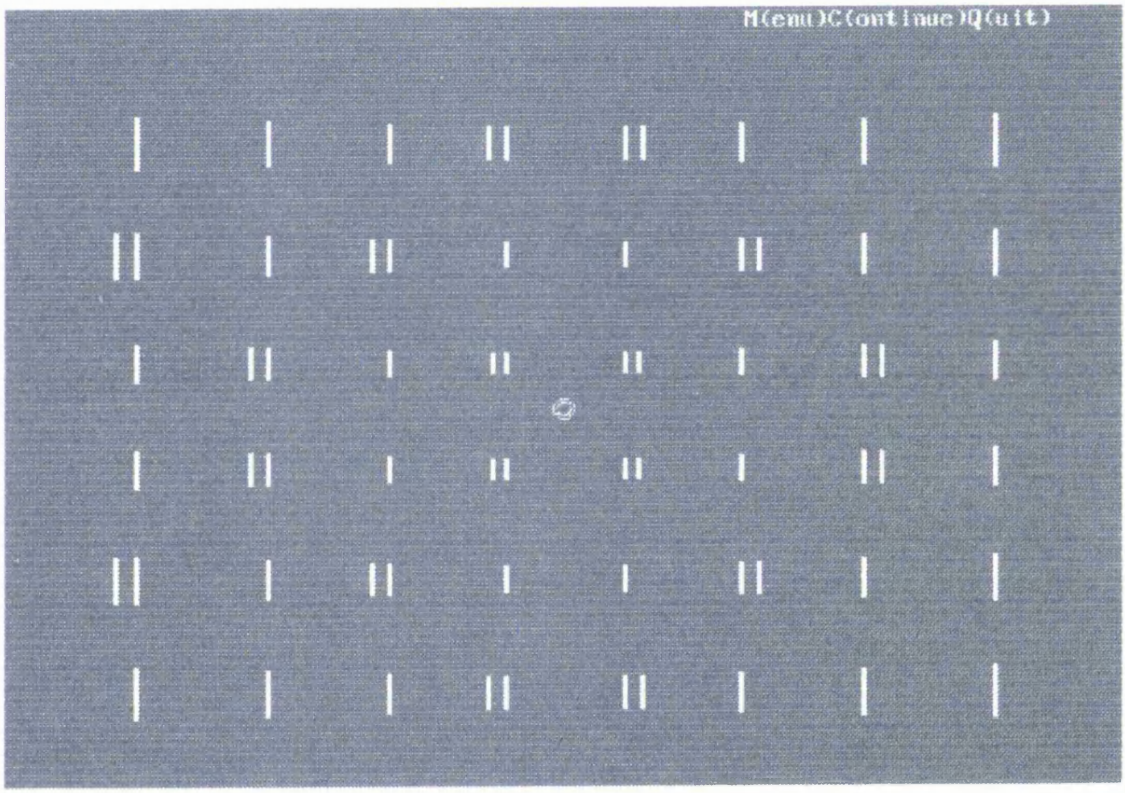


Fig. 2-4 Distribution of 16 locations tested (double lines) for right eye in Motion Sensitivity Test(MST). Note that the displacement intervals increase by approximately 1 pixel(5.5 min. arc) with each 6° increase of eccentricity.

Motion and Flicker(MF)

The MF was intended to provide a M-cell function test. The test consists of both motion and flicker stimuli. It was only used in the Glaucoma Unit, Moorfields Eyes Hospital, and the program was only run or the primary computer. Three digital voltage numbers corresponding to green, blue and red elements were used for background luminance, which were 62, 20 and 20 respectively. The other three digital voltage numbers for the lines were 62, 20 and 20 for green, blue and red elements, respectively. The background was green and the luminance was close to 7 cd/m^2. The Michelson contrast was 58.8% with a green colour((formula 2-1, see section 2-2). The test examines 6 locations, which are named 1, 6, 43, 48, plus 20 and 23 for right eye, or plus 26 and 29 for left eye (Fig. 2-1). The viewing distance is 75 cm. Therefore, four test locations furthest from the fixation are at 15 degrees in four quadrants and the two testing locations closest to the fixation are at 7 degrees from the fixation.

Four displacement amplitudes were measured (**Table 2-3**). From a practical point of view, the unit of amplitude for displacement used was the *pixel* instead of the visual angle. In MF, one pixel[5] converts int a visual angle of 1.92 min. With the *cos* effect(Drum et al, 1990), the visual angles per pixel are reduce as function of eccentricity in a CRT display. In MF, one pixel approximately converts into a visual angle of 2 min., 1.96 min., 1.87 min. and 1.7 min. at 10°, 20° and 30° respective eccentricities of fixation (Formula 2-3b). 2 min. per pixel were assessed in MF test with regardless of eccentricity.

Table 2-3 Sequence of testing motion amplitudes in MF programme by location****

Sequence	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24
Pixel	8	8	8	8	8	8	2	2	2	2	2	2	4	4	4	4	4	4	6	6	6	6	6	6
Amplitude*	-------A1-------						------A2---------						-----A3---------						--------A4--------					
Location**	20	23	1	6	43	48	23	6	48	20	1	43	20	23	1	6	43	48	23	6	48	20	1	43
Pattern***	-------P1-------						-------P2--------						------P1---------						-------P2-------					

* Displacement amplitude used to indicate the parameter indexes were 4 min arc(A1), 8 min.arc(A2), 12 min.arc(A3) and 16 min.arc(A4). ** Test location indexes for right eye based on Fig 2-1.

*** Testing pattern indexes.

**** The whole sequence for MF is (A1P1 +A2P2 +A3P1 +A4P2) X Number of trial

[5] The display pixel in the IBM was 0.42 mm, which translate into visual angles of 1.92 min arc at a view distance 750 mm.

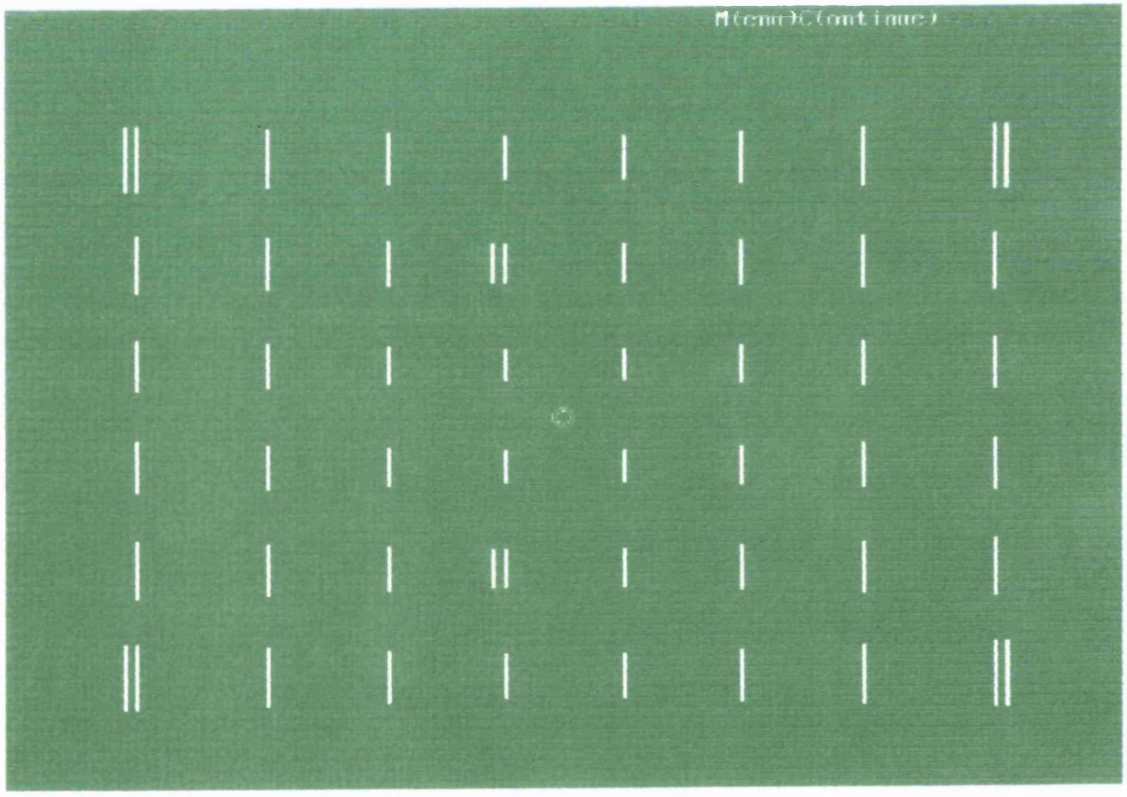


Fig. 2-5 Distribution of 6 locations tested (double lines) for right eye in Motion and Flicker test(MF).

In order to have a standard testing procedure for all 4 amplitudes and all 6 locations, the sequences of testing points and the sequences of amplitude of displacement movement measured were always kept the same, controlled by computer according to a look-table(**Table 2-3**). There was no feedback system for testing sequence.

Table 2-3 shows that in one trial the first amplitude was 8 pixel, then 2, 4 and 6 pixels. This sequence was repeated during the test. The locations selected for testing were determined by a look-up table. There were two testing patterns, each of which had 6 test locations. In the first pattern(P1), the sequence of test location was at location 20, 23, 1, 6, 43 and 48. Then the sequence changed according to the second pattern(P2) to be at 23, 6, 48, 20, 1 and 43. The subsequent trials repeat the sequences.

The advantage of using a standard testing sequence instead of a randomized order is to provide a reproducible test procedure. One main reason that a fixed sequence of locations was used was because I expected to see a fatigue effect after a given time and a number of trials. In this case, each amplitude and location tested was treated as an "independent" parameter in the MF. Therefore, the MF provided 24 fractions of stimuli seen for each test location to correspond to 4 amplitudes tested in 6 locations.

The interval for the next presentation after a positive response(pressing the button) and after a negative response(not pressing the button) is 0.65 sec and 2 sec, respectively. The minimum and maximum of time of waiting before the response was approximately 1 to 2 sec.. The interval could be modified after first 25 responses. For example, if the average of the first *group of responding times* is 1 second, the interval can be changed to 1.5 rather 0.65 sec. in order to provide enough time for the response. This approach was particularly designed for elderly people. If a patient has many negative responses, the testing time extends to 14 minutes. If a patient can see all presentations, the testing time is 7 minutes.

To make the test efficient, MF had a switch to stop the test automatically if the number of targets seen after first 18 presentations are less than 9. The computer then beeps and prints the message: "Uncompleted test". In order to detect the false positive response, there is a

1.2 second break with no presentation. After eight consecutive responses (seen target). If the computer receives any response during this break, it notes a false positive response.

2-6-2 Setting and Subjects

Testing for the first part of this study was performed at three places; the Glaucoma Unit in the hospital, the Inner City Eye Study(ICES)(Wormald et al, 1992) in the Goodinge Health Centre, Islington, London and the Roscommon Glaucoma Survey in an Irish rural community(Coffey et al, 1993).

Glaucoma Unit and the Institute

The 81 proven glaucoma patients, 119 glaucoma suspects and 76 normal subjects were from the Glaucoma Unit in Moorfields Eye Hospital. All glaucoma patients and glaucoma suspects underwent standard ophthalmic examination and their visual fields had been documented by the HFA.

ICES

In the ICES, 784 individuals, 65 years of age and over, were examined from the lists of selected G.Ps(Wormald et al 1992). All these people were invited by letter by the members of the group practice to participate in a survey of eye health. Therefore, the population examined in the ICES did not particularly relate to glaucoma but included all other ocular disorders e.g., cataract. The visual field was mainly tested with the Henson CFS 2000(Keeler), using the 132-point suprathreshold programme(Henson, 1988). The participants included in the study were randomly sent by the ophthalmologist for glaucoma case finding. No test results were removed from the original database which consists of 591 subjects(768 files) who were examined by CCVP. Of them, only 151 had MST and rest of them had different CCVP tests that did not measure motion sensitivity[6].

[6] A rapid screener based on multi-pattern flashing light CCVP was used in the early part of the study. Because clinical data in ICES was not always complete (Wormald, 1992), this data was not processed. Despite that, clinical experience of the test gave author useful practice in CCVP program design.

Table 2-4
Summary of subjects performed CCVP

Study place	No of Examined (individual)	No of records (eye)
Glaucoma Case finding		
Moorfields Eye Hospital & Institute of Ophthalmology	276	414
Inner City Study	591@	768
Roscommon Glaucoma Survey	210Ω	246
Subtotal	1077	1428
Motion function screening		
Moorfields Eye Hospital & Institute of Ophthalmology	272	680
WHO project in Nigeria *	375	1238
Mass screening in Nigeria**	834	1076
ARVO meeting***	74	77
Subtotal	1555	3071
Total	2632	5129

@ Only 151 had a motion test. The remainder had other CCVP tests.
Ω Only 156 had a motion test. The remainder had other CCVP tests.
* One third retested after one year period. The data in the second visit are not included here.

** Thirty-two subjects could not do MSST because there was no movement seen.
***: Association for Research in Vision and Ophthalmology(Wu et al, 1991)

RGS

The majority of glaucoma suspects whose problem had not previously been recognized was from the Roscommon Glaucoma Survey(RGS). This survey was conducted from 1988 to 1991 in county Roscommon in the West of Ireland, a rural county whose population of 34,000 is served by 2 community medical ophthalmologists and 3 optometrists. A crude prevalence of 1.89% for glaucoma was found(Coffey et al, 1993). 1660 subjects over the age of 50 had already been examined before the motion test was available in 1990.

The 210 subjects who attended this part of the study were divided into 1) a recall group from the 1660 screened by the standard tests 2) a first call group which had not yet been screened by the standard tests. The criteria for the recall group were a raised IOP or a cup/disk ratio greater than 0.5 but without proven field defects. Standard visual function tests included visual acuity and Henson CFS2000. All participants were further divided into normal, glaucoma suspects, and glaucoma groups. The definitions are as follows.

2-6-3 Clinical Definition

Normal subjects

There was no standard definition for "normal," because different clinical situations had their own definition of "normal." This was mainly determined by the test facility. For example, in the Glaucoma Unit, to consider the patients spouse as a control required several exclusion tests, including Humphrey perimetry. In the surveys, all the people who by the survey criteria did not have glaucoma were considered as controls regardless of other ocular disease.

Glaucoma and Glaucoma suspect

Primary glaucoma is a group of diseases that share characteristic visual field defects and degenerative changes at the optic nerve head. The ocular pressure can be raised, but not necessarily(Tielsch et al, 1991). Glaucoma diagnosis is mainly based on visual field results(Drance, 1967). The classification of glaucoma for this study varied slightly in different clinical situations. This related to the use of different visual field testing strategies. Glaucoma patients from Moorfields Eye Hospital were tested with the Humphrey Field Analyzer but the patients from the population based on surveys(e.g., RGS or ICES) had Henson CF2000.

Table 2-5

Classification of glaucomatous visual field defects

	Shin	HFA	dB loss
Normal/Full	1, 2,	Full.	0-3.7*
Early Defect	3, 4, 5	Slight depress, Relative defect depression.	3.8-8
Defect	6 to 11, 13	Nasal defect, Double arcuate depression, Breakthrough.	8.1-15
Advance defect	12, 14 to 16	Double arcuate defect, Double breakthrough, Central/or temporal rest.	> 15

* Using 4 dB instead of 5 dB corresponded to the abnormality found by the motion sensitivity test. dB loss calculation was based on the corrected pattern standard deviation(CPSD), which has weighted age effect(Heijl, 1986).

Table 2-6

Inclusion criteria for primary open-angle glaucoma, early glaucoma, glaucoma suspect and ocular hypertension groups

Clinic	Case finding*	Screening***	Survey
Proven glaucoma	Defect or above C/D > 0.6	Symptoms C/D > 0.8	Henson Survival**** =< 94% and C/D > 0.8
Early glaucoma	Early Defect C/D >0.5	IOP > 22 mmHg, C/D>0.6	
Glaucoma suspect**	Full Field C/D > 0.5	C/D > 0.5	Henson Survival > 94% and C/D >0.5
Ocular Hypertension	Full Field IOP(at initial diagnosis) 21 mmHg or above C/D =<0.5		Full Field IOP 22 mmHg C/D =< 0.5

* Hospital based glaucoma service

** For all of asymmetrical glaucoma cases who had only one eye with glaucoma, fellow eyes were included as glaucoma suspect's eye.

*** Conventional field test was not available for every person when the study was performed in Nigeria.

**** See section 3-4-5

Therefore, if the patients had the Humphrey visual field, I used the classifications(Table 2-5) modified from the methods proposed by Heijl(1986) and Shin (1991). If the patients had only

the Henson, the classification of field results was based on survival score(Henson, 1986bc). All potential glaucoma patients were further divided into four subgroups; proven glaucoma, early glaucoma, glaucoma suspects and ocular hypertension. The summary of criteria for glaucoma diagnosis is presented in **Table 2-6**. These criteria were used for the screening test in the later section(see section 3-4).

2-6-4 Ethical considerations

Four major ethical principles have been applied in the screening project(Mant and Fowler,1990).

1. It is unethical to provide any recommendation to the clinician or patient based on the result of the new test being investigated alone unless the test has been validated.
2. It is unethical to investigate people who do not wish to participate.
3. It is unethical to make any clinical decision without consulting the clinician concerned.
4. The data base in this study does not include the patient's address and other private information. No named data will be included.

2-6-5 Procedure

The procedure varied between the different clinical sittings.

Hospital clinic

People with glaucoma and glaucoma suspects were drawn from patients in the Glaucoma Unit of Moorfields Eye Hospital. Individuals referred from the unit for psychophysical testing between 1990 and 1991, were taken as potential cases. The programme, ICEPACK(Sommer et al. , 1987) was used to classify the automated perimetry field to determine whether it was abnormal and normal. After ICEPACK analysis, all potential glaucoma cases were further determined as group 1 with normal HFA, group 2 suspects and group 3 with abnormal HFA.

The decision of one eye, one person in this study was based on the analysis of the better eye. The reason for this characterization that person was not just to avoid the problem of correlation between pairs of eyes in the same individual(Newcombe and Duff, 1987) but also to include

more early glaucoma cases in this population. With this classification, a proven glaucoma patient who had asymmetry of visual field damage between two eyes could be in the glaucoma suspect group if one eye had a normal visual field.

Two testing models, namely MST and MF, were used in this part of the study. In MST, because the different clinical sittings used and the ambient light in each room was different, the cover to protect the screen from the reflecting environment in the clinic (see section 2-2) was used. In addition, several different computers were used from clinic to clinic. One displacement amplitude(5 pixel) and 16 locations were tested(Fig. 2-4). The chin rest was used when this was available. Other aspects of the procedure were similar to that for MF. The average testing time was 8.5 minutes.

In MF, the test was done in a dark room in Glaucoma Unit, Moorfields Eye Hospital. The background and stimuli were green and the contrast was 58%. The reason for using the green colour and this contrast was that these were the same testing conditions which could be compared with other motion sensitivity tests(Fitzke et al., 1986). The average testing time was 14 minutes for each eye. The fractions of seen motion at given amplitude were calculated. The MF originally tested 4 motion amplitudes and 3 flickers. Because testing time was too long, the program was modified to test 3 motion amplitudes and one flicker.

Community based sittings

Only MST model of CCVP was used in community based sittings. In ICES, the test was located in a community hall. The computer display's cover which was used in the early study was also used in ICES. In RGS, the test was located in a suitably darkened "visual field examination room".

Because the ICES was a survey of eye health in elderly people rather than a dedicated glaucoma survey full ocular examination was involved. This included binocular Snellen 6 metre visual acuity, near vision, and Henson CFS2000 to assess visual fields. IOP was tested with the Perkins Mark 2 applanation tonometer; the pupil size and reactions were recorded; the optic

disc and the retinal periphery were examined with a Volk aspheric 90 dioptre lens and a binocular indirect ophthalmoscope with a 28 dioptre aspheric lens.

Patients who were found to have an ocular abnormality (e.g., cataract, glaucoma) in ICES requiring further assessment and/or treatment were referred to a hospital. All early glaucoma patients or glaucoma suspects were referred to the glaucoma unit in the Moorfields Eye Hospital. After routine examination in ICES which usually took about 20-40 minutes(not including Henson), the subjects came to the Henson CF2000 and MST. The sequence of the two field tests was randomly arranged.

In RGS, because the community based sittings in Roscommon were sited in different community health centres, different computer displays were used. The examination rooms varied from place to place. Thus, the initial contrast level for each display varied. To have standardised testing conditions, the contrast of MST was kept at the highest level in each set.

Glaucoma suspects from the recall group and those sampled from the first call group all had both MST and the conventional clinical examination. The conventional clinical examination included: (a) visual acuity using 6 meter Snellen chart; (b) applanation tonometry by Goldmann tonometer or Perkins Mk 2 hand held applanation tonometry; (c) assessment of anterior chamber angle by slit-lamp bio-microscopy; (d) cup disc ratio estimation using slit-lamp bio-microscopy and the 90 dioptre fundus lens and (e) central visual field analysis using the Henson CFS 2000 semi-automated perimeter (132 Point Screening Strategy(Henson, 1988a)).

All glaucoma patients and suspects requiring confirmation were referred to an ophthalmologist who was also one of the principle investigators in the ICES. The criteria of defining glaucoma were similar to the ICES(Coffey et al, 1993).

2-6-6 Data analysis

In MF, frequencies of response to a given amplitude or a given trial were calculated and transferred to ROC.wq1. The program was written by the author for Receive Operating Characteristic(ROC) curve analysis based on Hanely and McNeil's method(1982) in Quattro

2.0(Borland, 1800 Green Hills Road, P.O.Box 660001,CA 95067-0001,U.S.A). The final results were made by ROC.spg in Sigmaplot Scientific Graphing System(CopyRight Jandel Cor. 1986-1990).

ROC curve analysis was done in two steps: 1. Frequencies of a given parameter in "normal" and "abnormal" groups made by "Freq.exe" program in Quick basic language, 2. sensitivity and false positive rate (1-specificity) were plotted by "ROC.XMF" in the Sigmaplot. The areas under the ROC curve were tested with the Hanley & McNeil method for statistically determining differences in the accuracy of detection procedures(Hanely and McNeil, 1982).

In MST, points in blind spot area (location 39 and 40 in the right eye or 9 and 10 in the left eye) were eliminated in data analysis. Light sensitivity was calculated according to a pattern deviation in which dB loss was compared to results with an age matched normal population by the Humphrey Field Analyzer(Heijl, 1987ac). This was initially recorded for each point, which had been tested by MST. However, it showed that there was no constant relationship between the motion and light tests by point location. Therefore, the comparison was done zone-by-zone. The central field was thus divided into 5 zones (4 quadrants and one foveal area) as in **Fig. 2-6**. The mean of the fraction seen in motion and the mean of decibel loss(Pattern Standard Deviation) in light were calculated for each zone. The Chi square statistic was used to test the significance of association between loss of light sensitivity or motion sensitivity for each zone within each diagnostic category. Partial Pearson correlation was used to evaluate the association between the target variable and other variables.

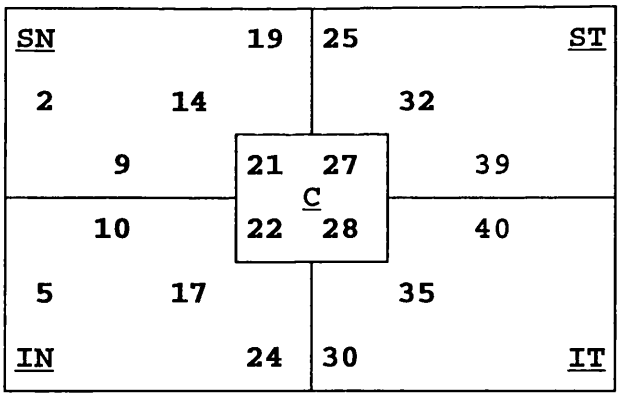


Fig. 2-6 Distribution of 5 zones for the right eye. Each zone consists of 2, 3 or 4 testing locations which are indicated by the number. These were centre(*C*), superior temporal(*ST*), superior nasal(*SN*), Inferior temporal(*IT*) and Inferior nasal(*IN*). Test location 39 and 40 are excluded for data analysis because they are in the blind spot area.

2-7 Application of the Motion Sensitivity Screening Test(MSST) in mass screening

2-7-1 Stimuli

Hardware

MSST was modified from MF and produced on four low cost notebook computers(Sharp PC 6220) with a 10" Liquid Crystal Display. The display was 'paper white' TST(triple supertwist technology) with cold cathode fluorescent tube backlighting, 16 shades of grey, 640 X 480 pixel resolution, VGA emulation(Sharp Co, 1990). It weighs 4.4 pounds and the dimension are 1.4 X 11 X 8.5-inch. Three notebook computers(Sharp PC 6220) were used in this study.

Software

6 locations are tested with one amplitude(8 minutes of arc) which was assumed to be an optimal amplitude for the screening test(see section 3-4-2). The sizes of the four peripheral lines were 10 X 2 pixels and the two central lines were 5 X 2 pixels(**Fig. 2-7**). In a dark room(no reflecting environment), the average light intensity for the reference lines was 41.3 cd/m^2 and the background was 9.5 cd/m^2. Michelson contrast was 62.5% (Formula 2-1). Each computer contrast was calibrated. Other features were kept the same as MF. Each test

point had 11 trials. The percentage of motion seen was calculated from the last 10 trials, the first trial being discounted. The result was displayed on the screen, stored to disc, and printed out(Fig. 2-8).

2-7-2 Subjects

Over 3071 files(1555 subjects) were recorded in 32 screening clinics in 13 different sites in the present study(Table 2-4). These sites included two hospital based sittings: one in the Glaucoma Unit, one in the National Eye Centre, Kaduna, Nigeria; eight community based sittings in rural Northern Nigeria; and self-testing by participants at the ARVO annual meeting in 1991 in the Sarasota Civic Centre Exhibition Hall, U.S.A..

No data in the original data base were excluded but there were excluding criteria for further data analysis regarding different clinical issues. Those files of individuals without complete information such as age, sex, visual acuity and ID number(WHO, 1987b) have not been included in the comparison study with WHO project data.

Abnormal Motion Case finding

In the Glaucoma Unit, I aimed to detect any case who had abnormal motion with MSST in the part of the field that had conventional visual field loss. Five clinics were held weekly. The study was conducted over one year. Subjects were invited from patients attending the clinic by receptionists and a glaucoma technician. Two hundred and twenty patients were recruited to have MSST. Most patients underwent a complete ophthalmic examination that included visual acuity, applanation tonometry, gonioscopy, the visual field 24-2 program, and stereo optic disc photography on the same day. In all, 52 eyes from 52 normal controls underwent routine eye examination by experienced ophthalmologists as well as MSST. The controls included spouses of glaucoma patients, or relatives, and also included students who attended the course for the Diploma in Community Eye Health in the International Center for Eye Health.

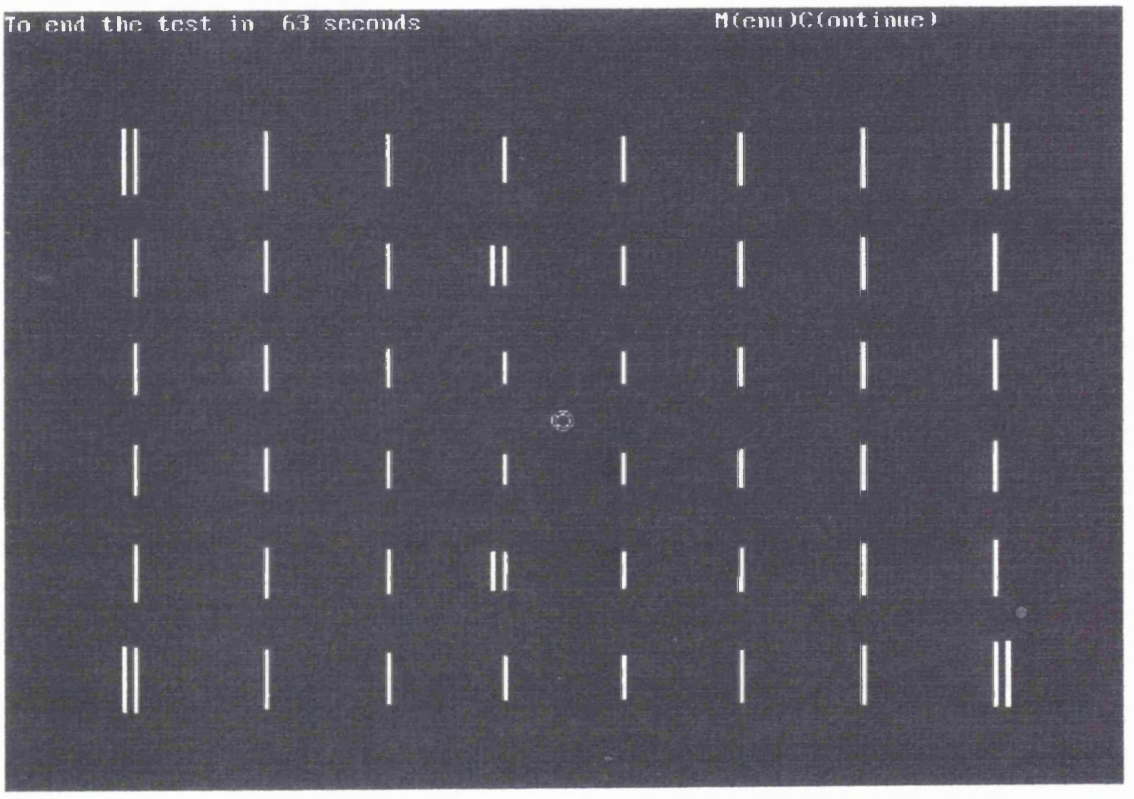
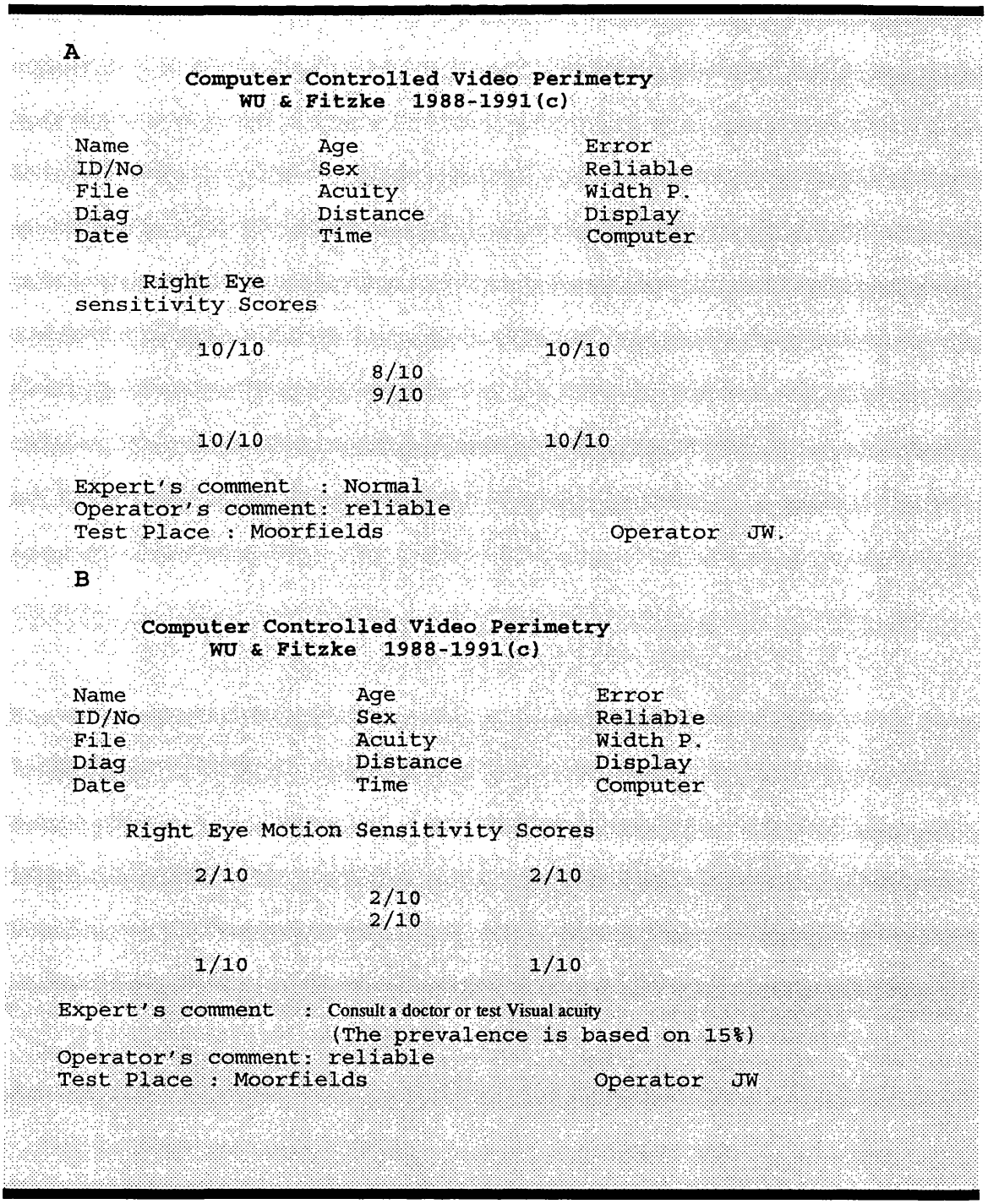


Fig. 2-7: Testing Pattern For Motion Sensitivity Screening Test on the Sharp PC 6200.



A

```
        Computer Controlled Video Perimetry
           WU & Fitzke  1988-1991(c)

Name                Age                 Error
ID/No               Sex                 Reliable
File                Acuity              Width P.
Diag                Distance            Display
Date                Time                Computer

     Right Eye
sensitivity Scores

          10/10                    10/10
                      8/10
                      9/10

          10/10                    10/10

Expert's comment   : Normal
Operator's comment: reliable
Test Place : Moorfields                  Operator  JW.
```

B

```
        Computer Controlled Video Perimetry
           WU & Fitzke  1988-1991(c)

Name                Age                 Error
ID/No               Sex                 Reliable
File                Acuity              Width P.
Diag                Distance            Display
Date                Time                Computer

     Right Eye Motion Sensitivity Scores

          2/10                     2/10
                      2/10
                      2/10

          1/10                     1/10

Expert's comment   : Consult a doctor or test Visual acuity
                     (The prevalence is based on 15%)
Operator's comment: reliable
Test Place : Moorfields                  Operator  JW
```

Fig. 2-8: The example of Print outs (A) Normal case, (B) Abnormal

Because the purpose of MSST is to detect early glaucoma in the community,patients who had surgery in the last 6 months, a constricted pupil, cataract, amblyopia, high myopia(>-5.D), aged over 80 years or had visual field damages greater than stage 4(Shin et al, 1990) were thus excluded. Patients were also excluded from the study if they met the following criteria:(1) visual acuity of 6/12 or less (2) a low reliability as indicated by the Humphrey reliability index(False negative error, false positive error, and fixation losses)(Katz and Sommer, 1988), (3) a foveal threshold less than 27 dB and negative mean deviation more than 15 dB. In addition, according to the Glaucoma Hemifield Test(GHT) in STATPAC II(Heijl et al, 1991b), the patients who had "General reduction of sensitivity" or "Abnormally High Sensitivity" were not included. 30 patients were excluded. The remainder were 55 low tension glaucoma patients, 67 primary open angle glaucoma patients and 68 glaucoma suspects or ocular hypertensives.

The fields in the better eye of all the patients were classified into three visual field groups based on Glaucoma Hemifield Test(GHT)(Heijl, 1991b): (1) Normal fields(80 eyes from 80 individuals) had normal GHT and the average age was 55.47 years old with 95% C.I. 52, 58. (2) Suspect fields(35 eyes from 35 individuals) had borderline GHT, mean aged 56.85 years with 95% C.I. 53,60.6. (3) Abnormal fields(75 eyes from 75 individuals) had GHT outside normal limits, mean aged 58.16 years with 95 C.I. 55.9, 60.5.

Screening For Optic Nerve Disease(OND)

In the Nigerian community, I aimed to use MSST 1) to assess relation between motion sensitivity and onchocerciasis, in terms of optic nerve disease caused by onchocerciasis(Abiose et al, 1993), 2) to assess OND risk between two different treatment groups: one with ivermectin and one without; and 3) to assess the acceptability and reproducibility of MSST. The study area is in Kuduna state which is mesoendemic for onchocerciasis.

The overall prevalence of onchocercal infection was 49% among those aged below 20 years and 72% for those aged above 20 years(Abiose et al, 1993). The initial study was carried out in March to April, 1990. After one year the study was repeated in the same area. Most

participants were illiterate rural people. Two different populations were tested.

Fig. 2-9 MSST test setting in Nigeria

First, MSST was carried out on 403 consenting subjects[7] aged 15 and over in the Kaduna randomized controlled trial of *ivermectin* for onchocerciasis, which was carried out by a WHO team. In this project all subjects had been taking either ivermectin or placebo annually for three years. MSST was performed after standard visual function tests had been carried out by one of 6 ophthalmic nurses. After MSST, people who were abnormal (positive from either the nurses tests or MSST) were examined by an ophthalmologist in a mobile clinic equipped with a slit-lamp biomicroscope and a retinal fundus camera. Second, MSSTs were then carried out on 834 Nigerians(1533 eyes) who volunteered for MSST but who were not in the WHO project. This consisted of subjects from communities in the meso-endemic area in the far east and far west of Kaduna city and subjects from non-endemic areas around Kaduna City.

Self-testing

In the self-testing episode in the U.S.A. I aimed to assess how well MSST can be done by volunteers themselves. The volunteers were ARVO's members. ARVO's membership consists of both clinical and basic visual researchers. Approximately 44% were ophthalmologists, 33% were Ph.D.'s, and 25% were others, e.g., optometrists(ARVO, 1992).

2-7-3 Procedure

Although MSST has been carried out in different clinical situations, the basic procedure was the same. That is, the subject covers the eye not being tested with one hand and the elbow resting on the desk(**Fig. 2-9**). The viewing distance was approximately equivalent to the width of display. However, if the subject reported that he/she could not clearly see the vertical lines, they can either wear the glasses that they usually wear or slightly shift the viewing distance. The latter approach was mainly used in rural Nigeria where few people had glasses. The subject was instructed to press the space bar (In the U.K. and U.S.A.) or the button (In the WHO project in Nigeria) whenever moving stimuli were seen while they fixated on the fixation circle. The reason that Nigerians used the button was that village people pressed the space

[7] The subjects included most people who had MSST in 1991. However, 112 new subjects who had inter or intra observations in second test in 1992 were added. The majority of new cases tested in 1992 (approximately 800) were not included.

bar too forcefully, which could damage the keyboard.

Except at ARVO, participants were required to repeat MSST on the other eye. A retest was then done on the right eye after the left eye had been tested. In the U.K., the MSST was usually operated by the author, otherwise by technicians and receptionists. In Nigeria, 65% of MSSTs were performed by trained nurses and village helpers. Table 2-7 shows that the frequency of tests performed by local helpers.

Table 2-7
The proportion of MSST done by different operators

	n	%
Ophthalmologist (JW)	702	31.9
Ophthalmic nurse (PD)	213	9.6
Other ophthalmic nurses	45	2.3
9 village helpers	1173	53.4
Ophthalmic nurse students*	63	2.8
Total	2196**	100

* The measurements by ophthalmic nurse were for training tests.
** 118 files without operator's name were not included here.

In Nigeria, because many Muslim women did not attend the WHO project, home visits to Muslim homes were attempted. Five compounds were visited. A home-visit was conducted by two village helpers with the author. The normal population from a non-endemic area was drawn from the National Eye Center(NEC) in Kaduna City, Northern Nigeria. The vast majority of participants were eye patients with an abnormality in the anterior segment such as trachoma or conjunctivitis. Relatives were also tested. All the participants did MSST and had disc evaluation before having other conventional eye tests. In self-testing, MSST was by definition done by the subjects themselves.

In order to assess the acceptance of MSST, a brief introduction of aim, method and results were presented by a poster. Observers were invited to test themselves. They then were

required to fill a form which consisted of three questions : 1) Name and address, 2) Interests and 3) Comments. The form did not include question on whether people wore contact lens when they performed the test.

The testing procedure was similar to the early applications except no routine data entry in terms of name, age, sex and ID number was recorded. In addition, there was one test per individual instead of three tests per one individual. No test was repeated. These modifications of the previous procedures were mainly in order to save time. Two Sharp PC 6220 notebook computers were placed on a desk in front of the poster. By that means, MSST tests could be performed by two volunteers at the same time.

2-7-4 Gold Standard

Because MSST was used in different clinical situations, the "gold standard" test also had to varied. In the Glaucoma Unit, a standardized and codified visual field interpretation of a single HFA result according to the GHT in Statpac II was used(Heijl et al, 1991b). In Nigeria, the "gold standard" test was based on the biomedical data which was available as a result of the World Health Organization(WHO) project: "Community acceptance and incidence of serious adverse effects of Ivermectin for Onchocerciasis in Nigeria"(ID 870456, WHO, 1987b).

In self-testing at ARVO, I was aware that this part of the study could not evaluate the validity of MSST but the purpose was to see that there was no serious problem with acceptance of MSST in these volunteers.

2-7-5 Data analysis

In Nigeria, because data entry was by villagers who had no keyboard skills, it was necessary to check the quality of data entry before analysis. Therefore, data files in MSST were examined against the data base of the WHO project when possible. The data of each subject was also analyzed with respect to the minimum and mean percentage of movement seen at each of the six testing points. This was defined as the motion sensitivity(MS) and Average of motion sensitivity(AMS) for that eye.

ROC analysis which is not only a method that has provided information about all possible pairs of specificity and sensitivity, but also offers a comprehensive way for comparing different scoring procedures for one test(Hanely and McNeil, 1982) was used as the basic approach to assess the validity of MSST.

In order to observe the agreement of MSST findings within and between observers, analysis was based on the limits of agreement(Bland and Altman, 1986) and the intra-class correction coefficient(Jamart, 1992). A plot of the intra-observer agreement against the mean of two observers was produced to illustrate the range of disagreement in MSST with retest values. A similar analysis was done for the inter-observer agreement.

Chapter 3 RESULTS

3-1 Introduction

The object of this study is the practical use of CCVP in the community. I will present the results of observation of the physical testing environment and how *multicontrast* nature affects a visual function test. This can result from the use of different computer devices, lack of constant ambient light and lack of uniformity of background luminance. This will provide information about the kinds of testing environments in which CCVP could be used and the solutions we can find for difficult testing environments.

The results, based on initial studies of a displacement stimulus, will tell us what characteristics of the stimulus would be suitable for CCVP. The present study measures several parameters of the sensitivity profile of normal observers with emphasis on the effect of light sensitivity, fundus features, and displacement intervals.

Development stages of the present motion sensitivity test, took place in several different types of clinics. The results presented will show how I evaluated a rapid motion sensitivity screening test from its experimental to its clinical stage, particularly for early glaucoma detection. The results will emphasize the clinical aspects of a new psychophysical test: the motion sensitivity test.

According to the clinical aspects, a motion sensitivity screening test for a mass screening program was finally developed. The major aim of this part of the study was to assess MSST as an efficient test in various clinical situations, particularly in Nigerian rural areas. A low cost computer(notebook computer) was used for MSST. The acceptability and reliability of MSST were evaluated in such rural area.

3-2 A *multicontrast* environment

3-2-1 The effect of ambient light on CCVP applications

Table 3-1 shows the variation of the ambient light throughout one day when CCVP was performed in one of the screening clinics in a Nigerian rural area. The causes of changing illumination were also recorded. The maximum range of ambient light was 340 lux.

Table 3-2 shows the variations of the illuminance level within a given testing period by clinic. Small variations were found in the laboratory and in the hospital clinic. Large variations were found in many community-based clinics. The largest variation was found in one of the screening clinics in Nigeria . The illuminances ranged from zero to 4500 lux.

Table 3-1

Time	Background (lux)	Mark
9:10	75	MSST set up in the village room
9:20	120	First patient coming, door opening
9:22	75	Examine first patient's right eye
9:26	75	Examine first patient's left eye
9:35	85	Sunshine through holes in the roof
10:00	200	Doors opened by children
10:10	90	Examine fifth patient's left eye
14:00	123	Sunshine through holes in the door
14:10	340	Door opened by 24th patient
15:00	110	Examine 25th patient, more than 10 people standing by. Because the temperature was high, one window and the door had to be opened
19:00	0 =<*	Finishing last patient(68th). It Was sunset.
		Range of Ambient light was 0<to 340

* The minimum of measurement of illumination by the light meter was 0 lux.

Large variation in ambient light can disturb the contrast of stimuli on the display. It is well known that increasing ambient light can reduce stimulus contrast due to reflection from the surface of the display(Bosman et al, 1989). However, the magnitude of the effect depends on

the direction of the lighting, type of screen surface, position on the screen and luminance of the display.

Table 3-2
Variation of illuminance level within a given testing period

Setting	Range of Intensity (lux)
Lab	<0.0*to 12
Eye clinical room	7 to 8
GP clinic	10 to 150
Roscommon glaucoma survey	<0.0 to 100
Eye Clinic in Roscommon	10 to 100
Compounds in Nigeria	<0.0 to 4500**
Waiting Room in Nigeria	80 to 1000
Glaucoma unit	2 to 20
Residential living Room	200
Exhibition Hall in Sarasota	400
Total range	<0.0 to 4500

* The minimum of measurement of illuminance by the light meter is 0.0 lux.
**. The 4500 lux was caused by the sunshine through a window.

From Table 3-2, it can be seen that the influences on the constancy of ambient light can be subdivided into the following two groups:

1. **Dedicated dark room not used;**
2. **Door or window opening unexpectedly during the test.**

The ambient light can be significantly different day and night or between testing rooms(Table 3-1). The large variations of ambient light in Nigeria resulted partly from different testing times throughout the day(Table 3-1). In a dark room situation, the variation was mainly caused by the door opening unexpectedly. This was also very common during a rapid screening test in a community based sitting because a lot of people had to come through one door into the room. In a temporary dedicated dark room outside a hospital, the sunshine was often seen to come through several tiny holes increasing the ambient light.

3-2-2 The variation of contrast on the display

The measurements of inter-display variation of contrast were obtained from different types of display: 5 cathode ray tubes and 3 liquid crystal displays(See section 2-2). Table 3-3 shows the *initial contrast* with 95% confidence intervals, and the maximum contrast. It can be seen that there were slight differences between all 5 CRT sets but the widths of 95% confidence intervals overlapped. The highest *initial contrast* in the CRTs was found on the Epson display. The lowest one was on the PCIV(Table 3-3). The average *initial contrast* level over 5 CRTs was 80%.

In LCDs, the highest *initial contrast* was found on the Sharp PC. The lowest contrast was on the Zenith. The average *initial contrast* level over 3 LCD displays was 49%. The findings are supported by a report that the Sharp PC with supertwist screen provided the highest contrast level among all the notebook computers at the time(Poor, 1990). Moreover, in Table 3-3,it can be seen that each *initial contrast* was almost equivalent to its maximum contrast, particularly in LCD screens.

In comparison with the CRT, LCD showed fewer differences in contrast level between central and peripheral fields. LCDs had narrower 95% confidence intervals than CRTs. It suggests there were smaller variations of contrast across the entire surface of the LCD display(Table 3-3). However, the dynamic range(only 12 grey levels) of contrast was significantly narrower in the LCDs than in the CRTs(t-Test, $p < 0.001$).

Table 3-3

Variation of contrast across the different type of display

Computer Name	Display Type	Initial Contrast* (%)	95% C.I.	Maximum Contrast* (%)
	********* CRT**********			
IBM	VGA	80	77.4, 82.4	86
IBM	VGA	82	80.1, 84.2	86
Epson	EGA	86	82.0, 89.6	86
PCIV	VGA	78	75.0, 80.8	78
Amstrad	CGA	84	80.4, 87.4	86
	********* LCD *********			
Sharp PC	VGA	62	60.4, 73.2	68
NEC	CGA	46	44.8, 48.8	46
Zenith	EGA	42	41.6, 44.4	42

*: Initial contrast and maximum contrast(see 2-2-2)

3-2-3 The variation of digitized contrast value

The effect of a digitized contrast value was measured on 4 different qualities of VGA CRT displays(see section 2-2). Including two high quality VGA displays(IBM, 8514/a), and three low quality VGA displays: one Viglen, one Olivetti and one PC-V VGA display. All have 64 digitized values that control 64 different light intensities or grey levels. However, the same digital value does not generate the same contrast in different display devices. Fig. 3-1 shows that there were differences of contrast corresponding to the same digital number[8]. With

[8] The contrast control or brightness control could be used to adjust those four computers to the same luminance level at digital number 30. These adjustments are not used in practice because the measurement of light intensity is a complicated job. It should not be necessary to do this for the application of CCVP.

increasing digital numbers (from 31 to 60), the differences between contrasts generated by five computers increased rapidly. The 95% confidence limits did not overlap. None of the five VGA displays shows consistent stepwise increase of contrast with digital number.

Non-linearity of contrast corresponding to digital number was found in all the displays. This suggests that the exact stimulus'contrast on CCVP can not based on digital value only. Calibration for each display set is essential if CCVP test is highly dependent on contrast sensitivity. However,calibration for each display is difficult and impracticable for wider use of CCVP(MacLeod et al, 1986). Because of the findings above, I decided to avoid using the digital value in CCVP for any clinical application.

3-3 Basic physical characteristics of motion stimulation in a visual field test

3-3-1 Effect of contrast

There were 5 subjects in whom displacement sensitivity was measured in the right eye. The age distribution of the subjects ranged from 7 to 70(36.2 SD 20). Fig. 3-2 summarized the displacement threshold as a function of contrast. When the contrast was less than 10%, most subjects had less sensitivity to motion, except YZ(aged 70 years), in whom the motion sensitivity was higher than in the young age group. The 7-year-old boy had no data at 6% contrast because of no response at that contrast. When the contrast was increased to more than 10%, the motion sensitivity sharply improved. The boy, however, did not have the same response curve as a function of contrast as the adults did. The motion sensitivity in that boy did not reach the highest level until the contrast level was 29%.

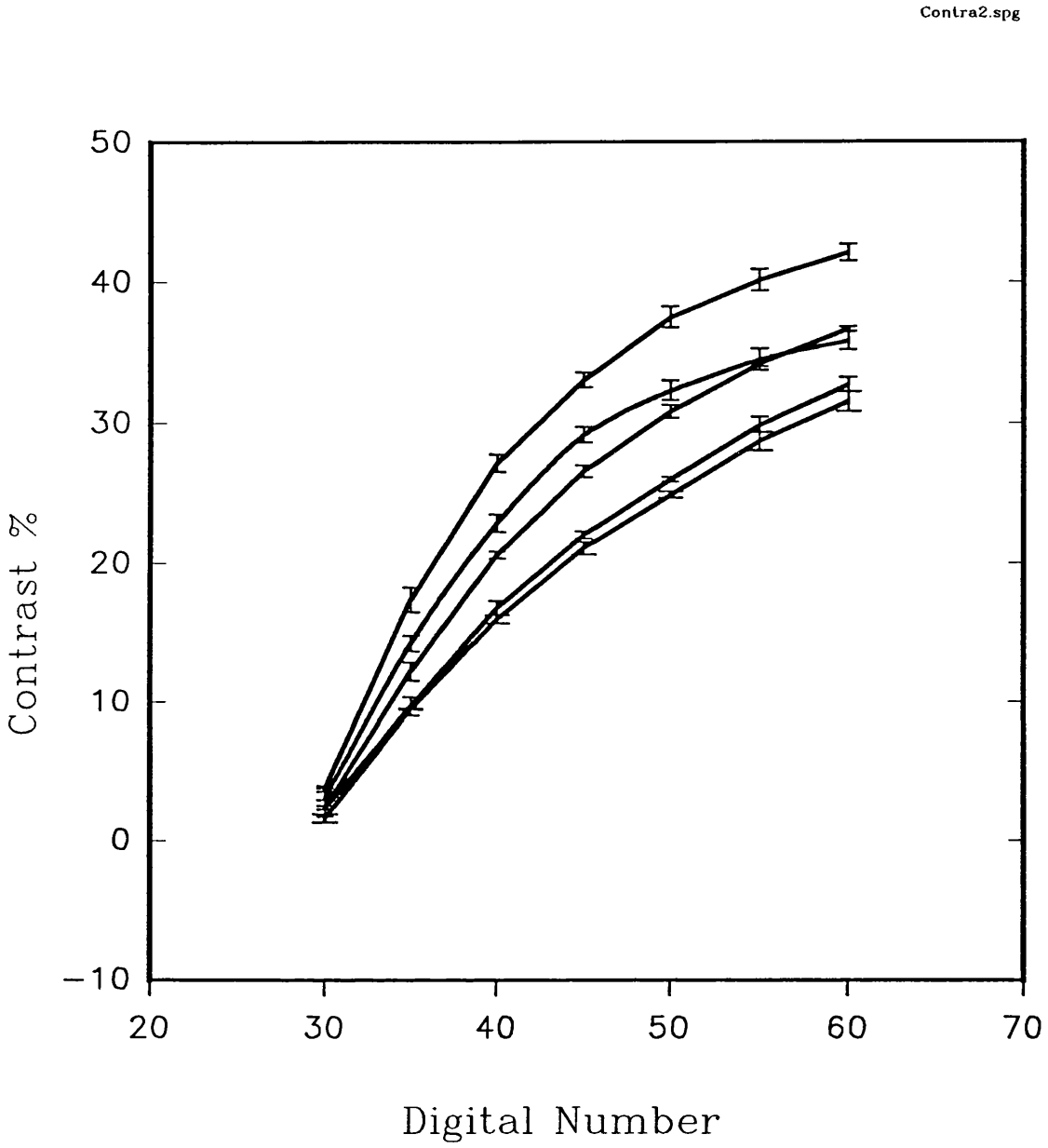


Fig. 3-1 Differences of contrast for a given digital value between different computer display sets. Each point represents the mean of contrast, and the vertical bars represent 95% confidence intervals over all 46 test locations. The same digital number does not generate the same contrast in different display devices. Non-linearity of contrast for responding to the digital number existed.

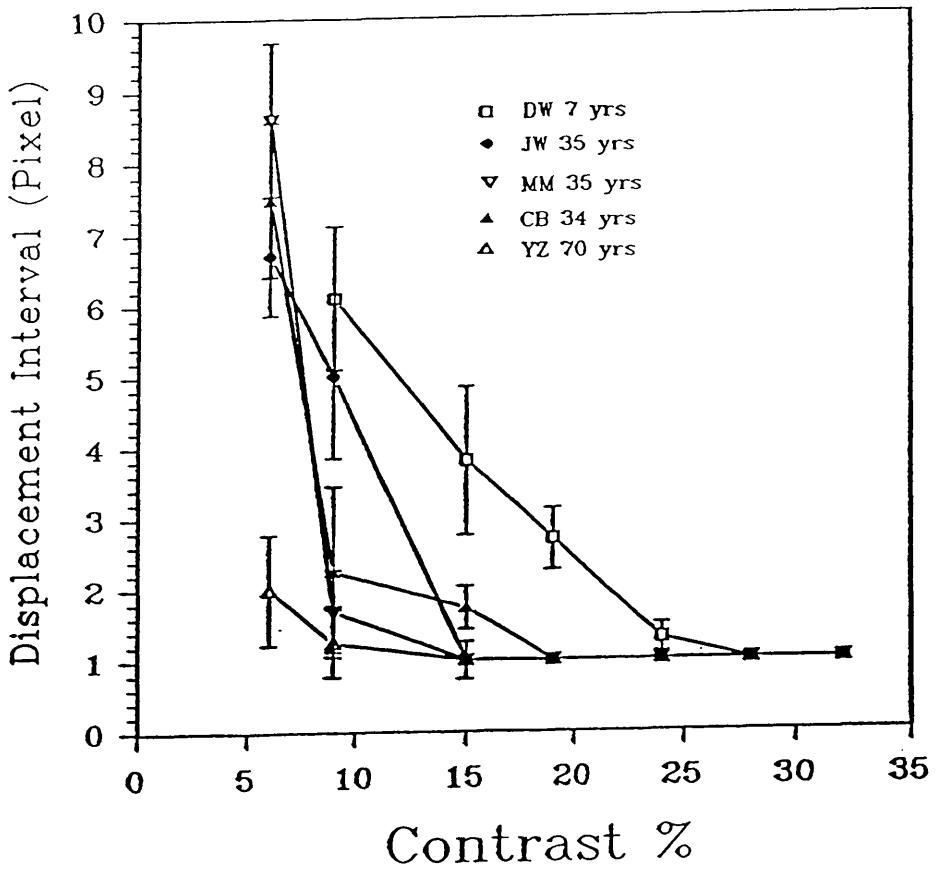


Fig. 3-2 Motion Sensitivity as a function of contrast. Each point represents the mean of sensitivity and the vertical bar represents 95% confidence intervals over 46 loci.

A trend was observed whereby both the variation of motion sensitivity between 46 loci and the variation of the motion sensitivity between 5 subjects was less when the contrast increased. No difference in motion sensitivity was found when the contrast was at 20% or over in respect of both loci and subjects. This may suggest that there were different offsets with respect to the displacement interval values below the 20% contrast but not beyond 20% contrast. Possible explanations for this will be given in the Chapter 4. The variation of motion sensitivity as a function of eccentricity in the central field was also examined on one subject (JW, 35 years). The results were drawn from 6 test points(named 3, 9, 15, 21, 27 and 33 in **Fig. 2-1**), and shown in **Fig. 3-3**. Similar findings were found in another normal subject. With 6% contrast(**Fig. 3-4a**), there was a significant difference between the central (4 degrees from the fovea) and peripheral points(22 degrees from the fovea). There was no significant difference of motion sensitivity between central and peripheral loci when the contrast level was over 6%(**Fig. 3-4bc**). The variation within 46 test locations was eliminated when the contrast reached high levels.

A uniform motion sensitivity across the entire central field was established when the contrast level reached 15% or over(**Fig. 3-4c**). The mechanism of this uniform motion sensitivity is unclear. However, the use of high contrast stimuli in any motion test has been emphasized in the present study.

3-3-2 Fundus features

a. Absolute scotoma

Fig. 3-5 summarises the mapping of the blind spot from the same subject which was determined by the use of three different parameters of motion stimulation. For variance in the length of the bar, **Fig. 3-5a** shows a narrow border whose the length increases from low to the maximum(30 pixel), mapping the optic nerve head in the contour graph. This demonstrates a sharp border around the optic disc defined by motion stimulation. It also displays an inferior extension, which might be due to a central retinal vessel. There may also be short-term fluctuation near the border(Gaefliger & Flammer, 1989).

Other parameters such as the variable contrast of the bar and the variable displacement interval of the stimuli failed to plot a clear border of the optic disc (Fig. 3-5bc). Among 100 testing points, there were 19 points that were absolutely non-responsive to motion stimuli despite increasing the length of the bars.

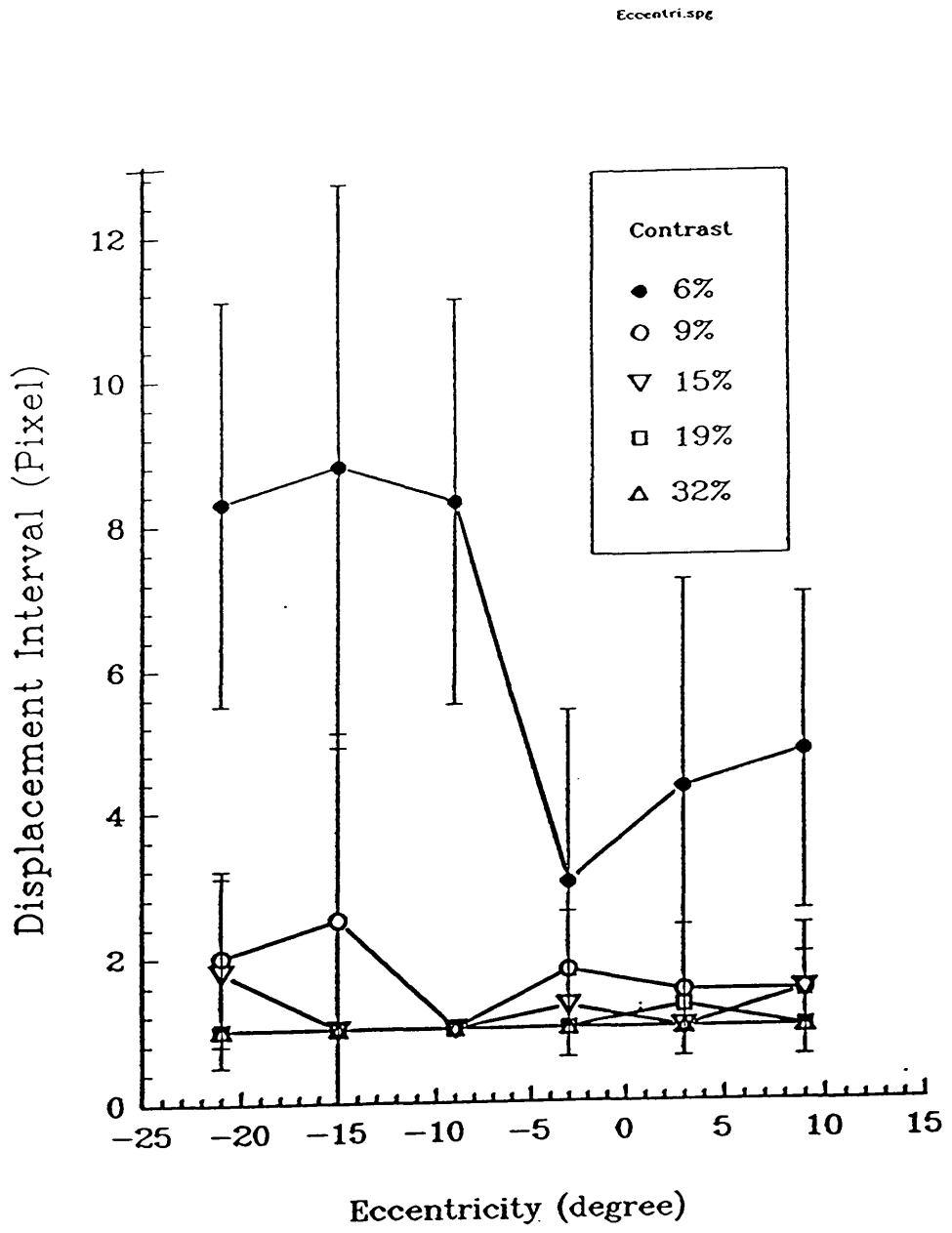


Fig. 3-3. Motion Sensitivity as a function of eccentricity by contrast. Each point represents the mean of sensitivity and the vertical bar represents 95% confidence intervals from loci 3,9,15,21,27 and 33 after 8 trials (see Fig. 2-1).

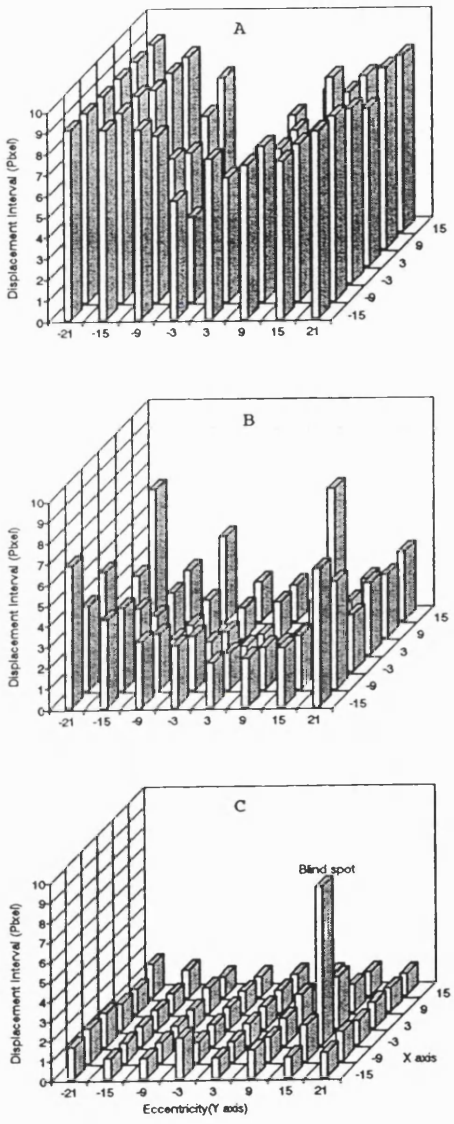


Fig. 3-4. Motion sensitivity over 48 test locations by using contrast bar tested with 6%(a), 9%(b) and 15%(c) contrasts. Note that a uniform motion sensitivity over 48 testing loci is approached when the contrast is 15%.

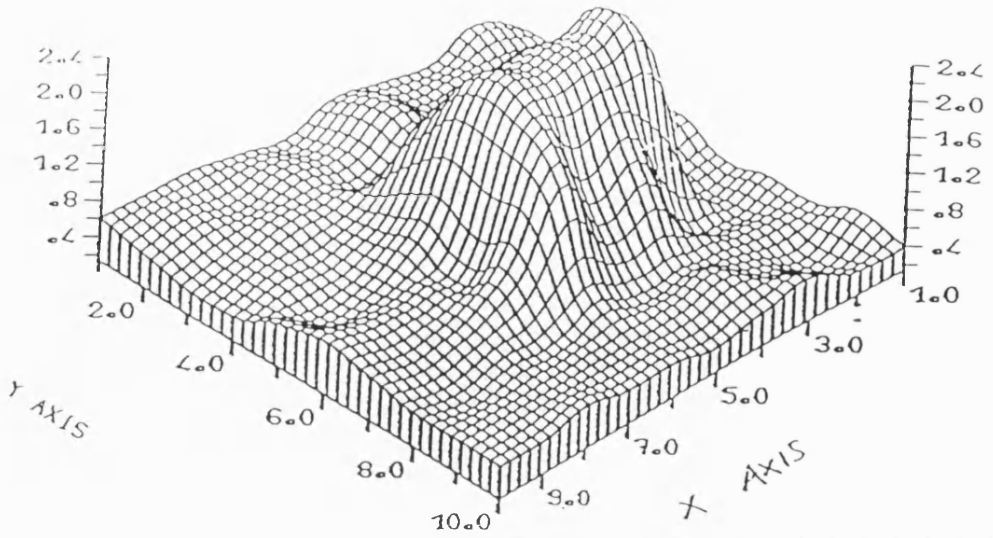
4%(n=4) were absolutely non-responsive points to stimuli with variable contrast and 3%(n=3) to stimuli with variable displacement intervals. A one sample x^2 test for three different proportions of missing points was used. It shows that there was a statistically significant difference between those three displacement stimulations(X^2 = 20.3, n=300, p < 0.00 1) to detect missing points. Thresholds were determined using a method of ascending limits to all of three elements measured for two measurements in two separate sessions. The X and Y axes in the subsequent 3 dimensional and contour figures represent eccentricities that varied with different experiments. The Z axis is length of the bar x 10 in pixels in Fig. 3-5a, intensity of stimuli in digital value x 10 in Fig. 3-5b and the displacement interval in pixels x 2 in Fig. 3-5c.

b: Relative scotoma

A series of measurements for detecting angioscotomata (relative scotoma) was made near the upper edge of the optic nerve head (Fig. 2-2, 2-3). In order to locate the course of the angioscotomata, light stimulation was used. A map of the angioscotoma(reverted) of the branching central retinal vessels from the blind spot(BS) is shown in Fig. 3-6a. It was reproducible after one week(Fig. 3-6b). By comparison with Fig. 2-2(B), the course of the angioscotomata can be matched to the course of the central retinal vessels. It shows that there were some areas of threshold with a drop-off on the course of the retinal vessels. It should be noted in Fig. 2-2b that a few other retinal vessels in the testing area were not detected by light stimulation. Other small vessels were ignored during the measurement.

With the same procedure, two different parameters for motion stimulation such as variable length and variable displacement intervals were tested. In Fig. 3-7a, the Z axis is the length of the bar(x 10). No course of angioscotoma was recognized. Near the optic disc edge, there was elevation of the threshold (Indicated "A"), then a drop-off towards the periphery.

In Fig. 3-7b, the Z axis is the displacement interval (pixels). It shows that there was a region of threshold increase on the one side of central retinal vein where the value of the increase was apparently higher than on the edge of the optic head disc (Indicated "A").



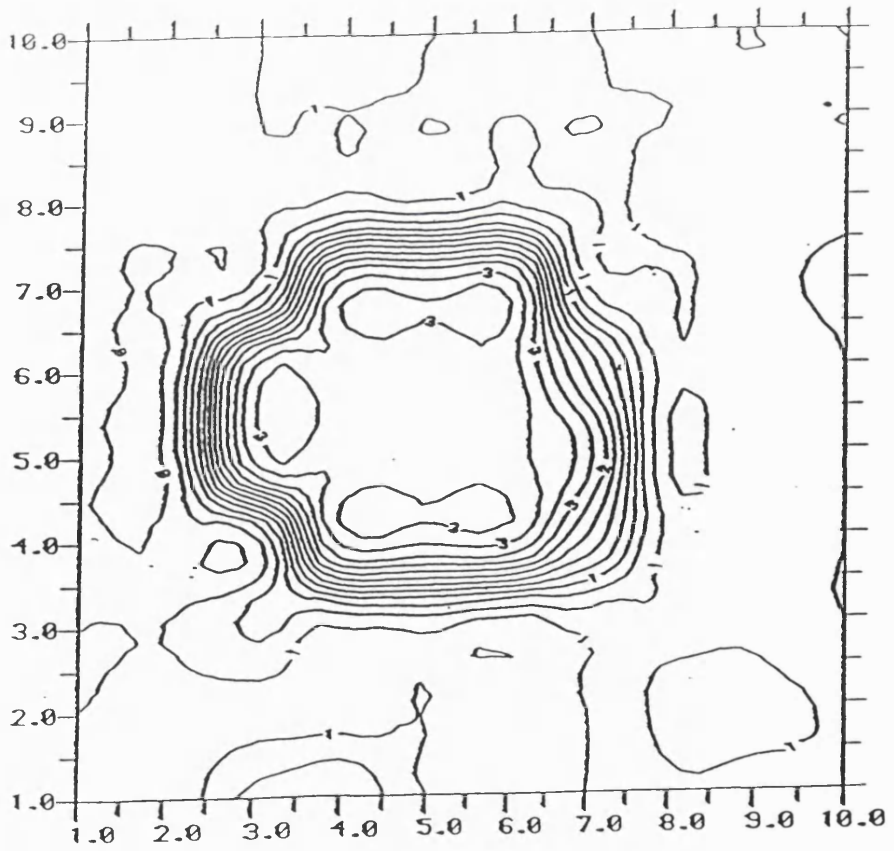
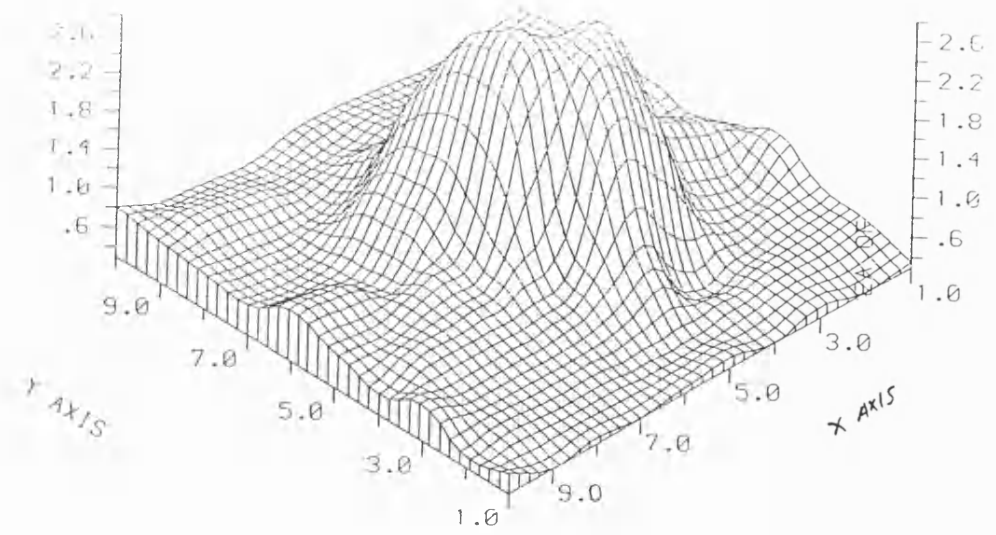


Fig. 3-5a Blind spot border and area detected by motion stimulation with variable length of the bar. Each tick on the X and Y axes in 3 dimensional and contour figures represent eccentricity in 26.6 minutes' arc. Z axes represent the length of the bar in pixel X 10. A narrow border around the optic nerve head is mapped in the contour graph. This shows a sharp border around the optic disc defined by motion stimulation. It also demonstrates an inferior extension, which might be due to a central retinal vessel.



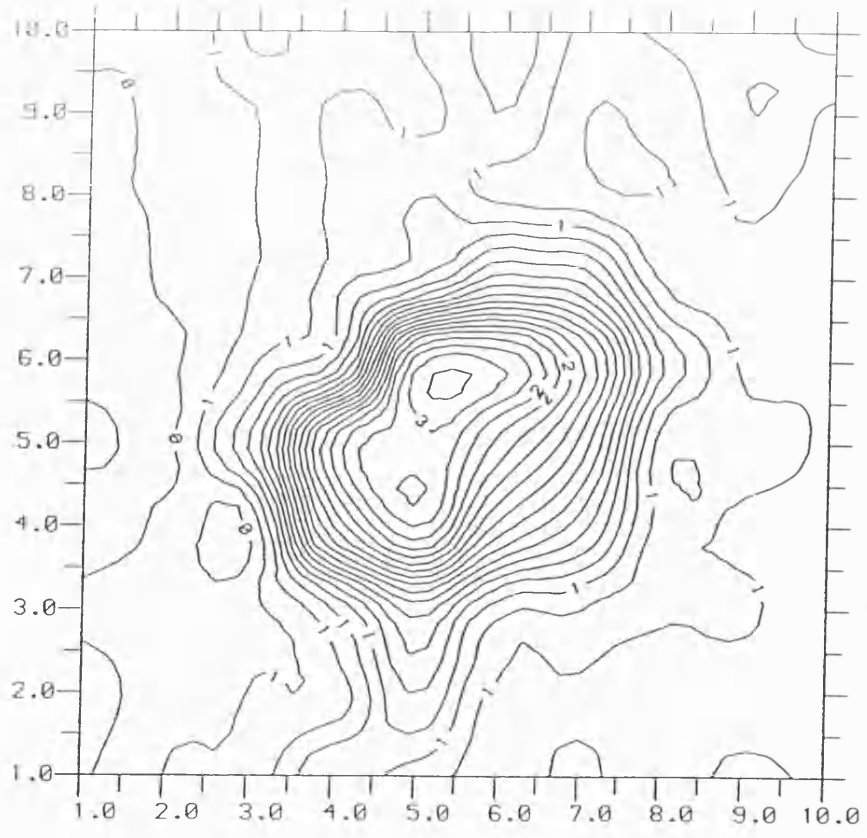
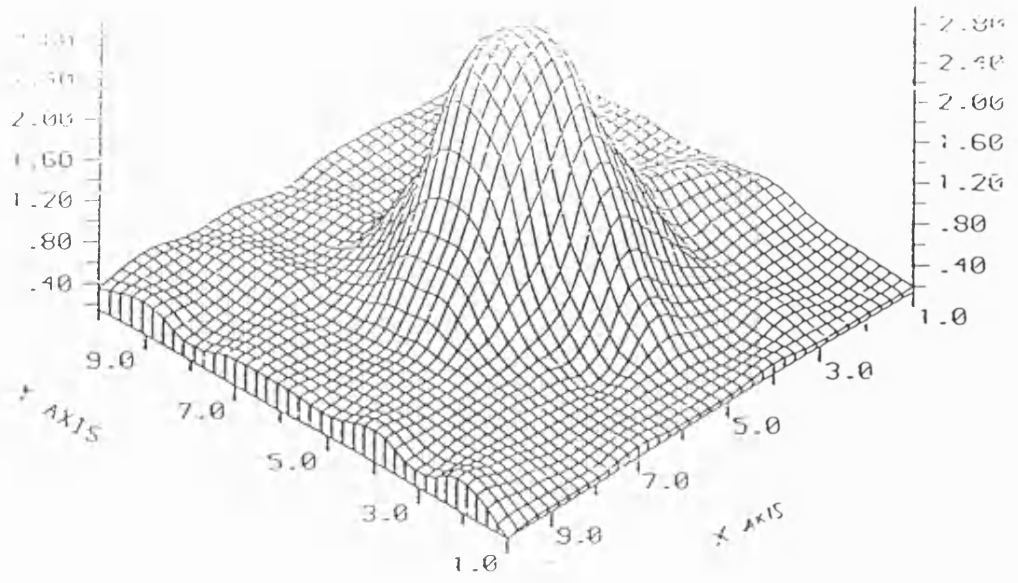


Fig. 3-5b Blind spot border and area detected by motion stimulation with variable contrast. Each tick on the X and Y axes in 3 dimensional and contour figures represents eccentricity in 26.6 minutes arc. Z axes represent the digital number X 10. The digital number for the background was 4. A wider border on the optic nerve head is mapped in the contour graph.



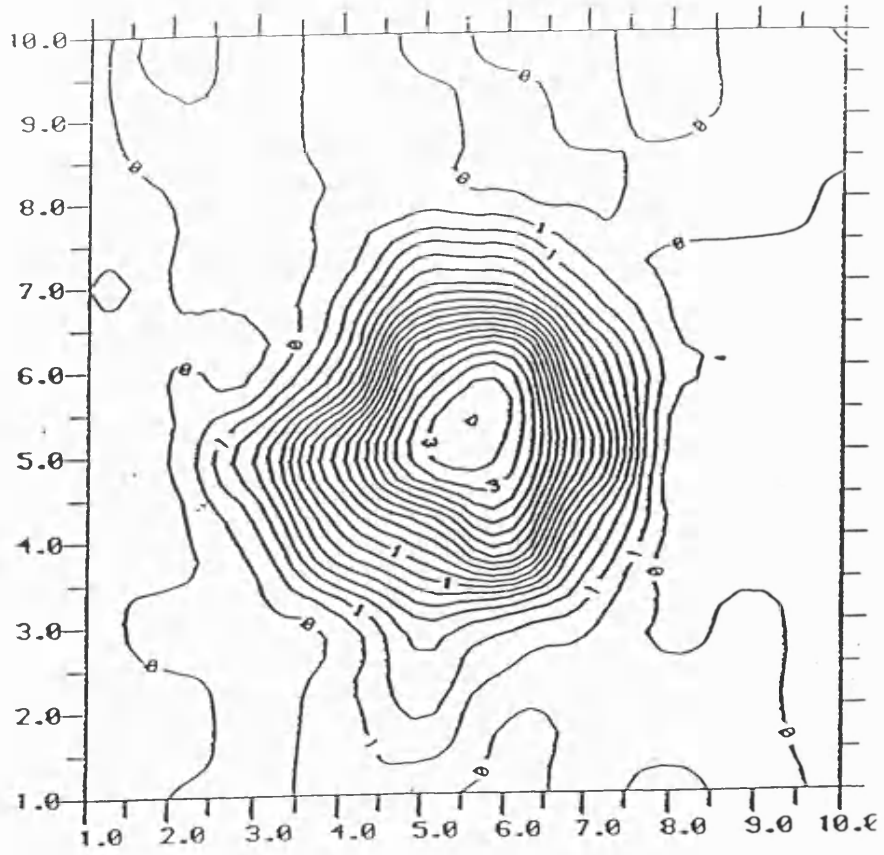
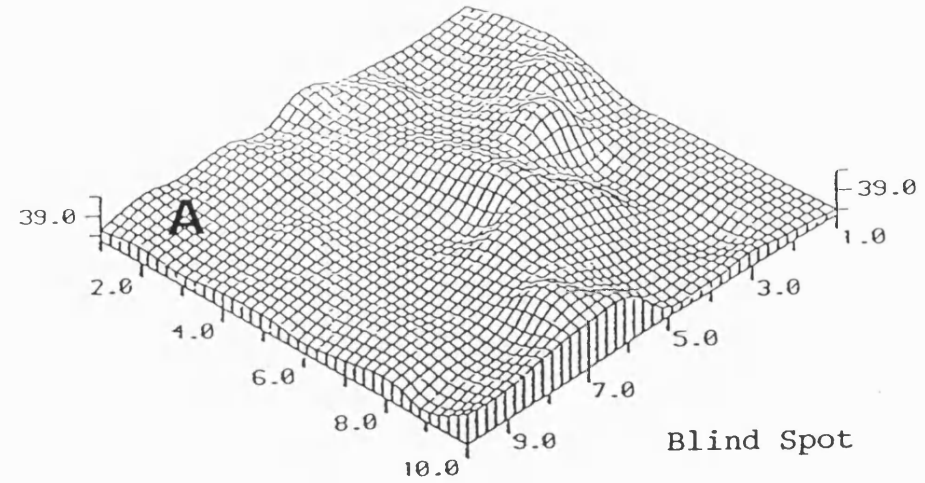


Fig. 3-5c Blind spot border and area detected by motion stimulation with variable displacement interval. Each tick on the X and Y axes in 3 dimensional and contour figures represents eccentricity in 26.6 minutes arc. Z axes represent the displacement interval in pixel X 2. The range of displacement interval was 2 to 12 pixel. A wider border on the optic nerve head was mapped in the contour graph.



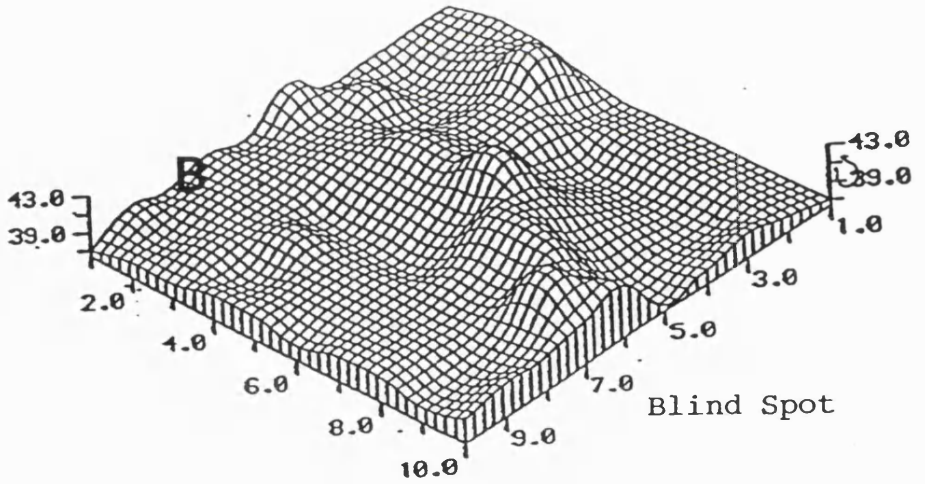


Fig. 3-6. A light threshold map at the inferior edge of the blind spot with the map inverted to allow comparison with fundus. Measurements were made by using variable light intensities on the test (A) occasion and the retest (B) occasion. Each tick on the X and Y axes in 3 dimensional figures represents eccentricity in 13.3 minutes arc. Thresholds were determined by a method of the ascending limits to length of the bar. The Z axis is the digital value for light intensity which ranges from 37 to 64.

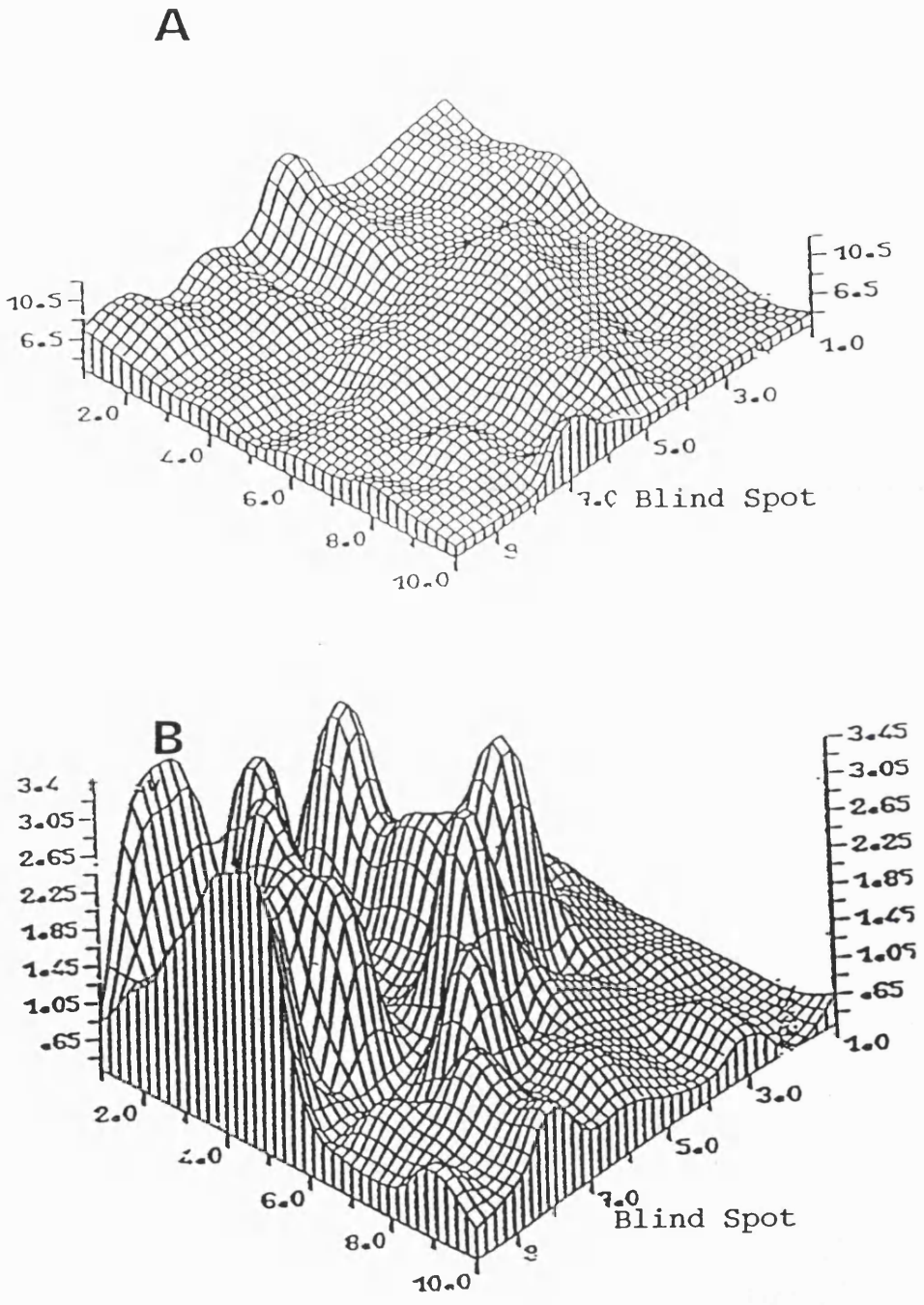


Fig. 3-7 Angioscotoma detected by motion stimulation.

Each tick on the X and Y axes in 3 dimensional figures represents eccentricity in 13.3 minutes arc. Thresholds were determined by a method of the ascending limits to length of the bar(A) and the displacement interval(B). The Z axes in A and B are the length of the bar (pixels) and the displacement interval(pixels), respectively. No clear course of the angioscotoma was recognized by any motion stimuli that were tested in the study.

The displacement thresholds were inconsistently elevated on the side of the vein, where there are several branches of the vessel. On the other side of the vein, where there is no branching, the thresholds were almost uniform.

3-3-3 Defocus

It is difficult to measure the exact defocussing power in a visual field because several factors can influence the defocussing power e.g. eccentricity, illuminance background and pupil size (Atchison, 1987; Leibowitz et al, 1972). To simplify the measurement in a comparable clinical situation, this part of the study emphasises the difference between large and small amplitudes as a function of the lens power. The results are plotted in Fig. 3-8.

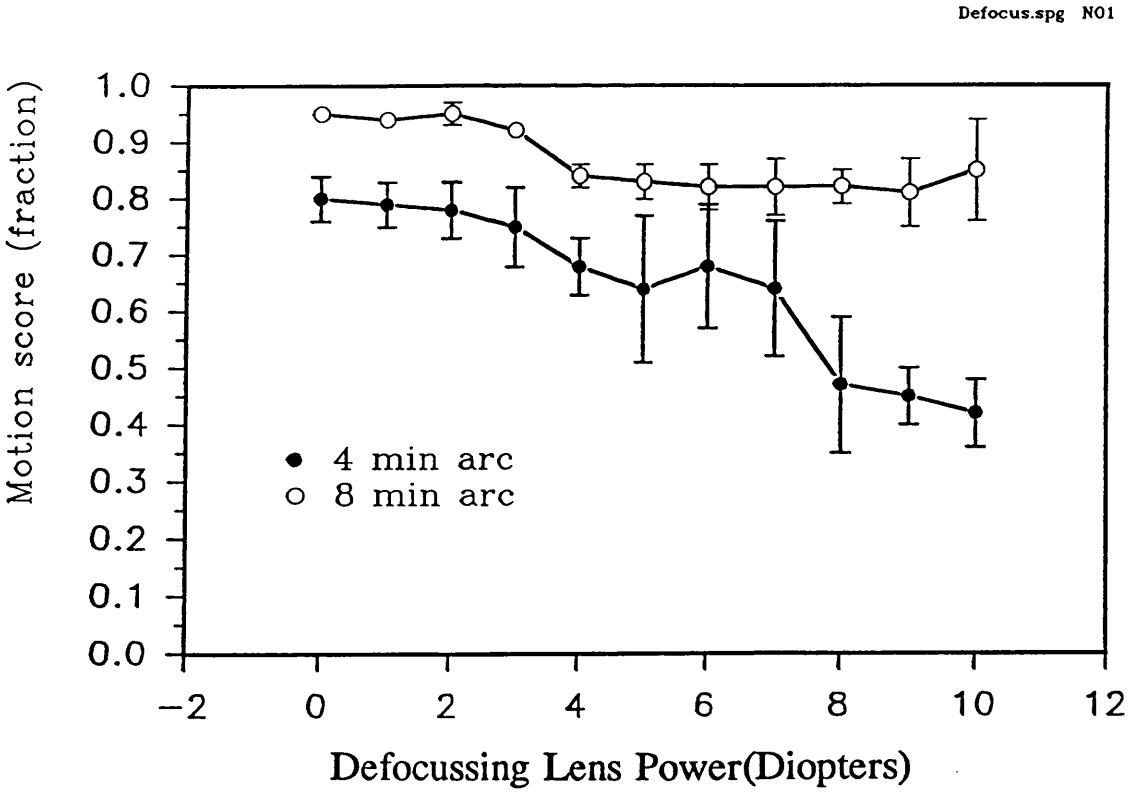


Fig. 3-8: Effect of defocus. Points show the mean of motion sensitivity scores by two observers as a function of the lens power. The motion sensitivity was determined by the fraction of motion seen at a given amplitude for 10 trials. The given amplitudes were 4 and 8 pixels. The mean of fractions of motion seen and 95% confidence intervals were calculated for each lens power. The error bars indicate 95% confidence intervals over a total of 92 loci of two young subjects (34 yrs and 33 yrs). Both pupil sizes were at 3 mm.

It shows that the motion sensitivity to large movement displacement (16 min arc) did not decline as a function of defocus. However, the motion sensitivity to small movements (8 min arc) fell gradually until a steeper reduction of sensitivity occurred when the defocus power was +7.0 dioptre. The range of accommodation of young subjects can be more than 6.0 D (Swaine, 1925). In order to exclude the effect of accommodation in the two young observers, definite defocussing occurs from +6 dioptres.

3-4. Motion Sensitivity in Glaucoma Detection

3-4-1 Normal sensitivity

A total of 76 normal controls had the Motion Flicker(MF) test. Most of these were patients' spouses. No control cases had signs of visual function loss in their tested eyes. The average age in this group was 49 with 95% CI 45.2 to 57.6 years. For data analysis, the subjects were divided into two age groups: a young group, those 17-59 yrs of age(n=47: mean 40, SD ± 18 yrs) and old group;those 60-80 yrs of age(n=29; mean 67, SD ± 3.8 yrs). In addition, I grouped the 46 locations into two areas; a central area which included location 15,16,20 to 23, 26 to 29,33 and 34 in a central 15° zone, and a peripheral area which included the rest of them in central 16° to 24° zone. Because the right eye was always tested first, I separated them in order to see a fatigue effect or learning effect(Finlay et al, 1987).

The mean motion sensitivity value for each age group, for each testing zone and for the right and left eyes are shown in Table 3-4. The mean motion sensitivity to the smallest amplitude (2 pixels) was depressed relative to the other three amplitudes. There were no statistical differences between the central and the peripheral locations (P = 0.067), and between the right eyes and the left eyes(P = 0.162). With the smallest amplitude, there was a trend seen in the older age group whereby the left eye had higher sensitivity and lower standard deviation than the right but this was not statistically significant($p > 0.1$).

In the young age group, the situation was reversed. There was no statistically significant difference ($p > 0.3$). Motion sensitivity did not increase constantly with grating displacement

interval(interaction P = 0.089). An age-related reduction in motion sensitivity was only found by testing the smallest amplitude(interaction P = 0.091).

Table 3-4

Normal motion sensitivity by age and eye (Mean in fraction of seen±1SD)

	Centre of field				Periphery of field			
	Right Eye		Left Eye		Right Eye		Left Eye	
	< 59 yrs	> 59 yrs	<59 yrs	>59 yrs	<59 yrs	> 59 yrs	<59 yrs	> 59yr
Displacement interval (pixel)								
2	.68±.26	.77±.17	.70±.17	.69±.17	.54±.44	.75±.26	.56±.17	.67±.17
4	.86±.17	.89±.09	.86±.09	.89±.09	.89±.17	.91±.09	.93±.09	.90±.09
6	.91±.17	.92±.09	.84±.09	.91±.09	.93±.09	.96±.09	.93±.09	.94±.09
8	.92±.09	.92±.09	.87±.09	.93±.09	.93±.09	.93±.09	.88±.09	.93±.09

Tab e 3-5

Pearson Regression by amplitude by age

pixel	Centre F.	Peripheral F.	Entire F.
2	-.48 **	-.25	-.32*
4	-.22	-.16	-.17
6	-.03	-.09	-.05
8	-.13	-.05	-.07

* P < 0.05
** P < 0.001

For variability of motion sensitivity, as calculated by standard deviation, **Table 3-4** shows that the smaller the amplitude used, the larger the variability regardless of eye, age and testing zone. When the displacement interval was 4 pixels or over, the variability was no different for the testing zone, for the eye group and for the age group. **Table 3-5** shows a series of Pearson regressions of this data between different amplitudes and different test locations by age. The motion sensitivity was correlated with age in the central field only if the smallest

amplitude of motion stimulation was tested (r=-0.48, $P < 0.001$).

3-4-2 Optimal motion criteria for glaucoma detection by MF

50 proven early glaucoma patients who had 'early defects' or 'defects' (Table 2-5) underwent MF. Of these, 43(86%) were classified as low tension glaucoma(LTG) and 7 were primary open angle glaucoma(POAG) patients. In order to establish the baseline for normal motion, 76 normal subjects were included as a *control group*. There were no significant age differences between the patient group and the control group (mean age, 95%CI age, 56, 52 to 59 vs 49, 45 to 57). However, there were significant cup/disc ratio differences between the patient group and the control group (mean cup/disc ratio, 95% CI, .55, .38 to .72 vs .23, .14 to .32).

a. Optimal amplitude

In this part of the study, fractions of motion seen over 6 test locations for each eye were recruited for ROC analysis. Results from each single displacement were separately plotted on the ROC curves. In Fig. 3-9, points along the curve represent different cut-off criteria for a given location tested. All potential pairs of sensitivity and specificity values are indicated as potential cut-offs when the curves are shift from higher to lower thresholds. The more the ROC curve moves towards the upper left corner of the graph, the higher the discriminating power. The diagonal line in the graph is the "line of no information." It can be seen that the curve for 8 min arc is close to the left upper corner of the graph. None of the other curves overlap that for 8 min arc and none of the curves are close to the diagonal line. Table 3-6 summarises these basic features related to sensitivity, specificity, the area under curve(AUC) and 95% confidence intervals.

Table 3-6
Sensitivity and specificity by amplitudes

Amplitude	Cutoff	Sensitivity	Specificity	AUC	95% CI
4 MA	4/10	72%	70%	0.75	.65, .81
8 MA	5/10	92%	73%	0.92	.88, 1.0
12 MA	7/10	82%	58%	0.72	.62, .78
16 MA	8/10	88%	59%	0.75	.65, .81

The sensitivities and specificities of motion stimuli show considerable powers to differentiate between the glaucoma and normal group for all amplitudes. AUCs ranged from .72 to .92. The highest detection power, namely an AUC of 0.92, was defined by 8 minutes of arc, and the best sensitivity-specificity combination was 92% and 73%.

An important finding was that there was the same discriminating power, in terms of the AUC, between the smallest amplitude and the largest amplitude(mean and 95% CI 0.75 and .65 to .81). The smallest amplitude was expected to have greater sensitivity than the largest one, but the 95% confidence limits for the AUC overlap. It can be seen that the cutoff for the best combination of sensitivity-specificity varied between amplitudes; in the smallest amplitude, it was 4/10 but in the largest it was 8/10. In summary, there was no trend to show better detection power towards either the smallest amplitude or the largest amplitude and there was, therefore, no single cutoff for the best detection power with regard to different amplitudes used. 8 min arc was selected as optimal amplitude for future tests.

b. Optimal number of hemi-fields

I was aware that all the glaucomatous fields included here had asymmetry of visual field defects according to the early glaucoma diagnostic criteria(Heijl, 1991b). In order to exclude this *selection bias*, the results for ROC analysis on optimal locations were based on horizontal hemifield results. This is to see whether the result in one hemifield is enough to detect all abnormality. **Fig. 3-10** shows that the best detection power was from the whole field, when the amplitude was 8 minutes of arc and the number of trials was 10 as described earlier. The best sensitivity-specificity combinations for the whole field were 92% and 73%. If the superior or inferior hemifield had the same specificity(73%), the sensitivity in the superior and inferior hemifield was 65% and 50%, respectively. the inferior hemi-field (AUC, 95% confidence

interval;0.74, 0.64 to 0.78 vs 0.66, 0.54 to 0.72). But there was a difference between the results from one hemi-field compared with the whole field which had an AUC of 0.92(95% CI .88 to 1.0). There was no difference between the superior and inferior hemi-fields. Therefore for future tests, I always tested both superior and inferior hemi-fields.

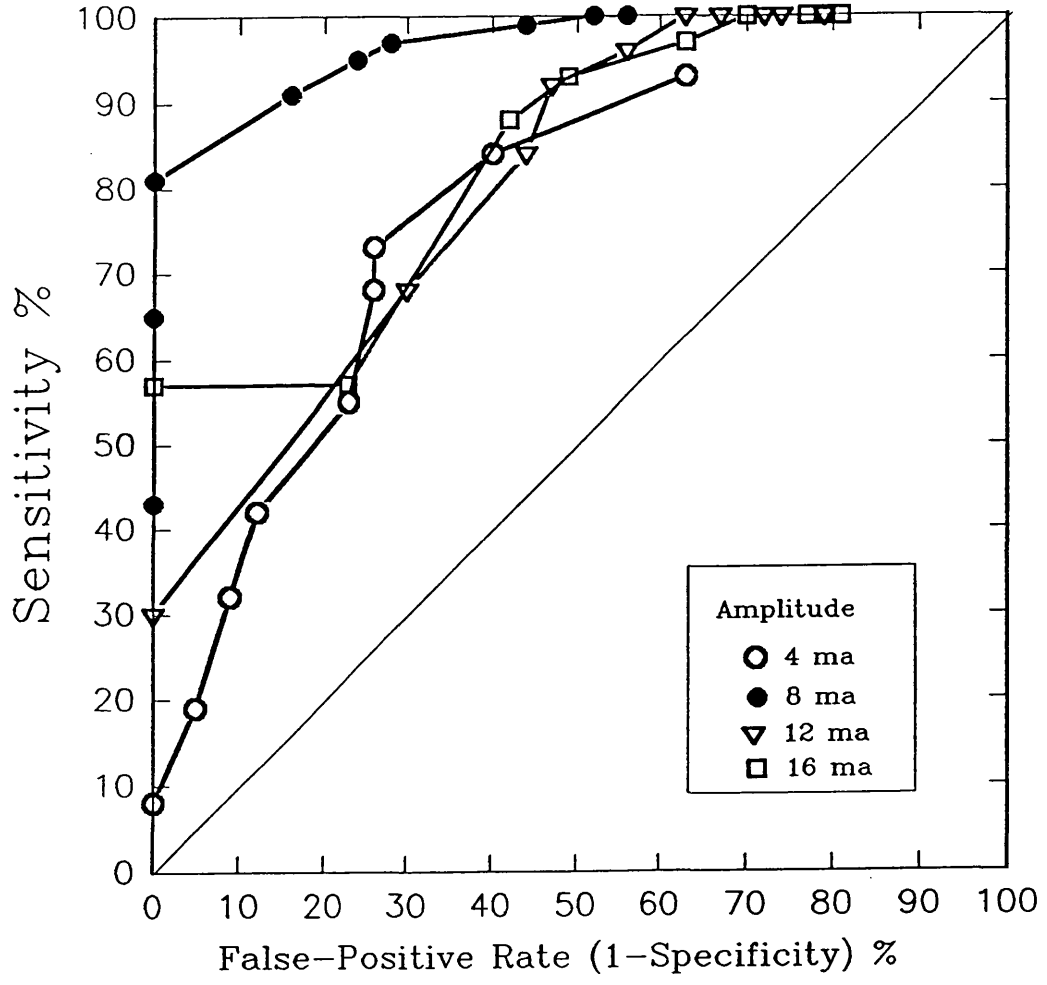


Fig. 3-9: Optimal amplitude in the whole field: Each point along the curve represents different cut-off criterion. All potential pairs of sensitivity and specificity values are indicated as the potential cut-off points when the curves are shifting from higher to lower thresholds. The more the ROC is toward the left upper corner of the graph the higher the discriminating power. The diagonal line in the graph is the "line of no information." The curve for 8 min arc is closest to the left upper corner. None of the other curves overlap the curve for 8 min arc and none of the curves are close to the diagonal line.

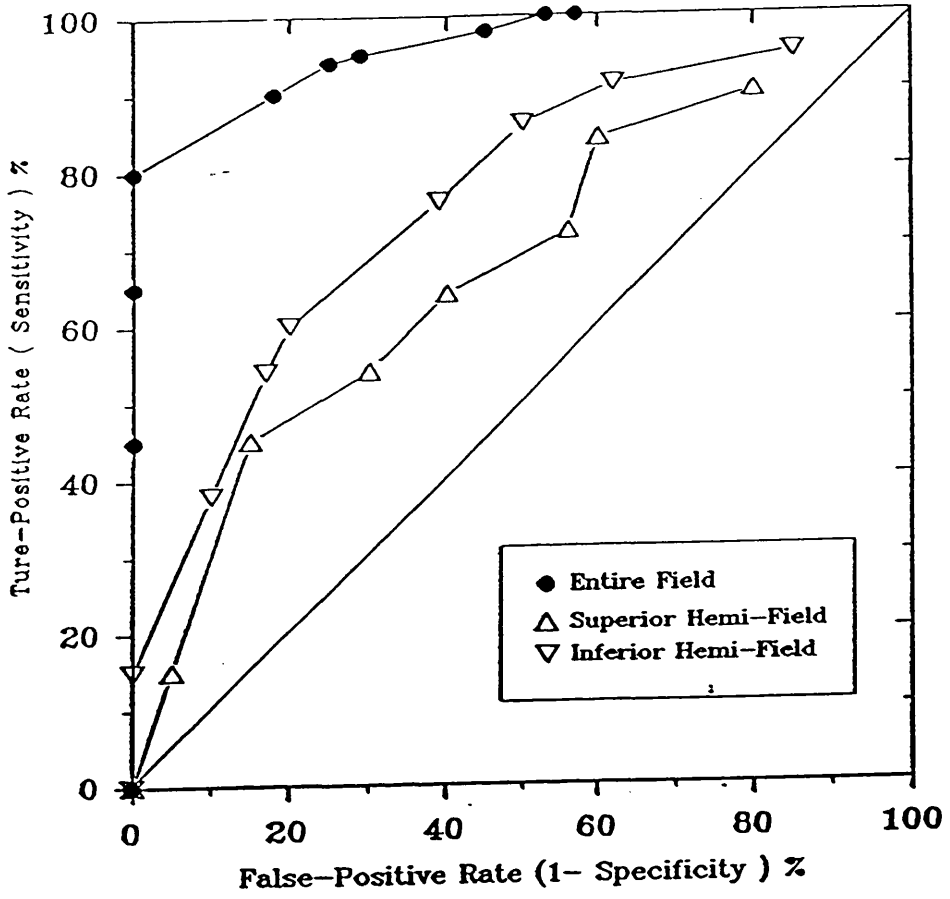


Fig. 3-10 Optimal number of locations
The curve for the whole field is closest to the left upper corner. The best sensitivity-specificity combinations for the whole field was 92% and 73%, respectively. If the superior or inferior hemifield had the same specificity(73%), the sensitivity was 65% and 50%, respectively.

c. Optimal number of trials

The data analysis for the optimal number of trials was based on the assumption of using the optimal amplitude and optimal test locations i.e. 8 min arc and full field. The purpose of this data analysis was to see what was the detection power was as a function of number of repeats. **Fig. 3-11** shows that there are a number of ROC curves for different numbers of trials in MF. The closest to the top left corner among ROC curves was the curve for 10 trials. The

best combination was 10 trials with 92% sensitivity and 73% specificity. There was only a slight trend that the detection power improved with an increase in the number of trials.

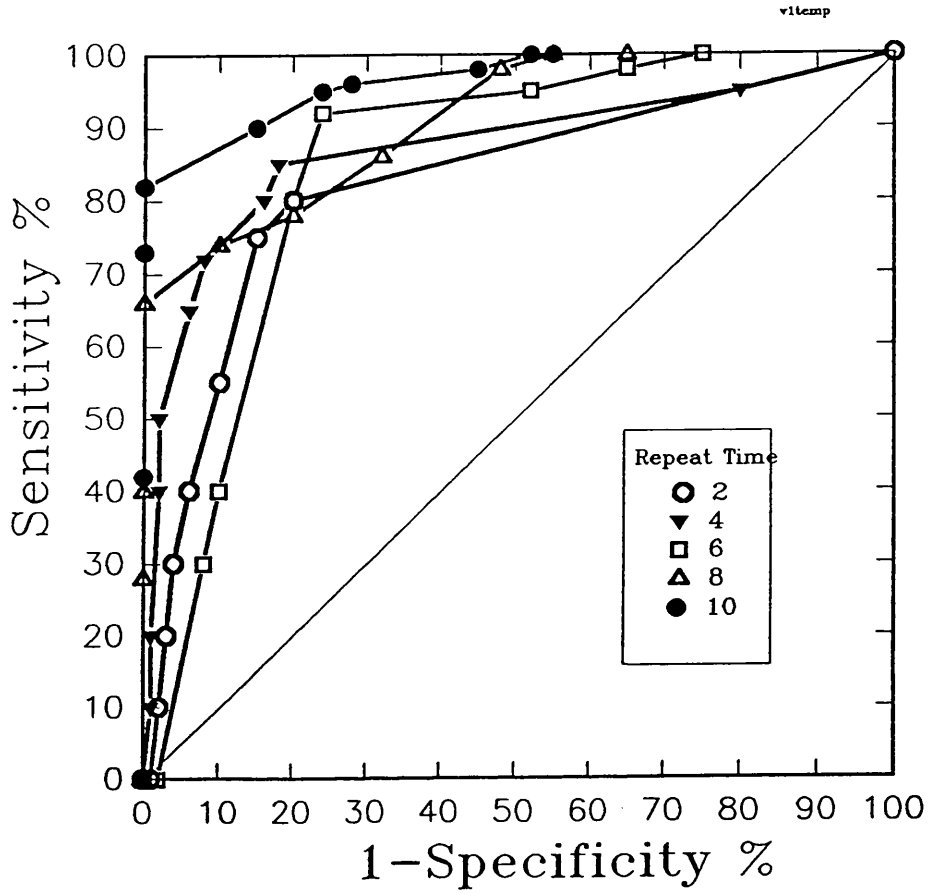


Fig. 3-11 Optimal number of trials.

The curve for the 10 trials is closest to the left upper corner. The best sensitivity-specificity combinations for the 10 trials was 92% and 73%, respectively.

3-4-3 Correlation of visual function loss: motion and light

The numerical values for the thresholds obtained with MST and Humphrey were not directly comparable because of differences in stimulation and testing strategy. To provide an approximation, MST motion scores and Humphrey thresholds were calculated by summing the

average of each anatomic region of the field. The anatomic sectors used were based on the 4 field quadrants plus the central area so that there were 5 sectors in each field(Fig. 2-6). The 2 locations in the blind spot in each test were not included(see section 2-6-6). A total of 16 locations were tested in MST.

Thirty-one proven glaucoma patients(all POAG) and 26 ocular hypertensive patients who had documented Humphrey Field results and MST were included. In addition, 29 normal people who underwent Humphrey Field and MST also were recruited in this part of data analysis. The mean age of the glaucoma group was 61.8 ± 11.93(1SD) years, of the hypertensive group 56 ± 13.1(1SD) years, and the normal group 57 ± 15.4(1SD). All eyes with refractive error(spherical equivalents equal or greater than to ± 3.5 dioptres) or with Mean Deviations(MD) greater than -15 dB were also excluded.

Fig. 3-12 shows the overall distribution for all sectors by three specific groups in MST. A vertical cut-off line is laid over those three groups. The measurements were obtained from 145 sectors in the left eyes of normal volunteers, 155 sectors in the better eyes of glaucomatous patients, and 130 sectors in ocular hypertensive left eyes. It is possible to shift the line from left to right until 95% of the normal sectors are on the left side. So that, the cut off for screening motion sensitivity loss is beyond 5%. This means, the chance of detecting abnormal motion at any single glaucomatous sector was 75% when the chance of detecting false abnormal motion at any normal sector was 5%. The chance of detecting abnormal motion at OHT sector was 7%.

Furthermore, all glaucoma cases had at least one abnormal MST sector. Nine out 26 hypertensive eyes(34%) and 5 out 29 normal eyes(17%) had one abnormal MST sector. There was no statistically significant difference of motion sensitivity between normal group and OHT group(X^2 1.77 n = 1 $p > 0.1$). Twenty four-glaucomatous eyes(64%) had more than one abnormal sector. There was no normal subject who had an abnormal MST in more than one sector.

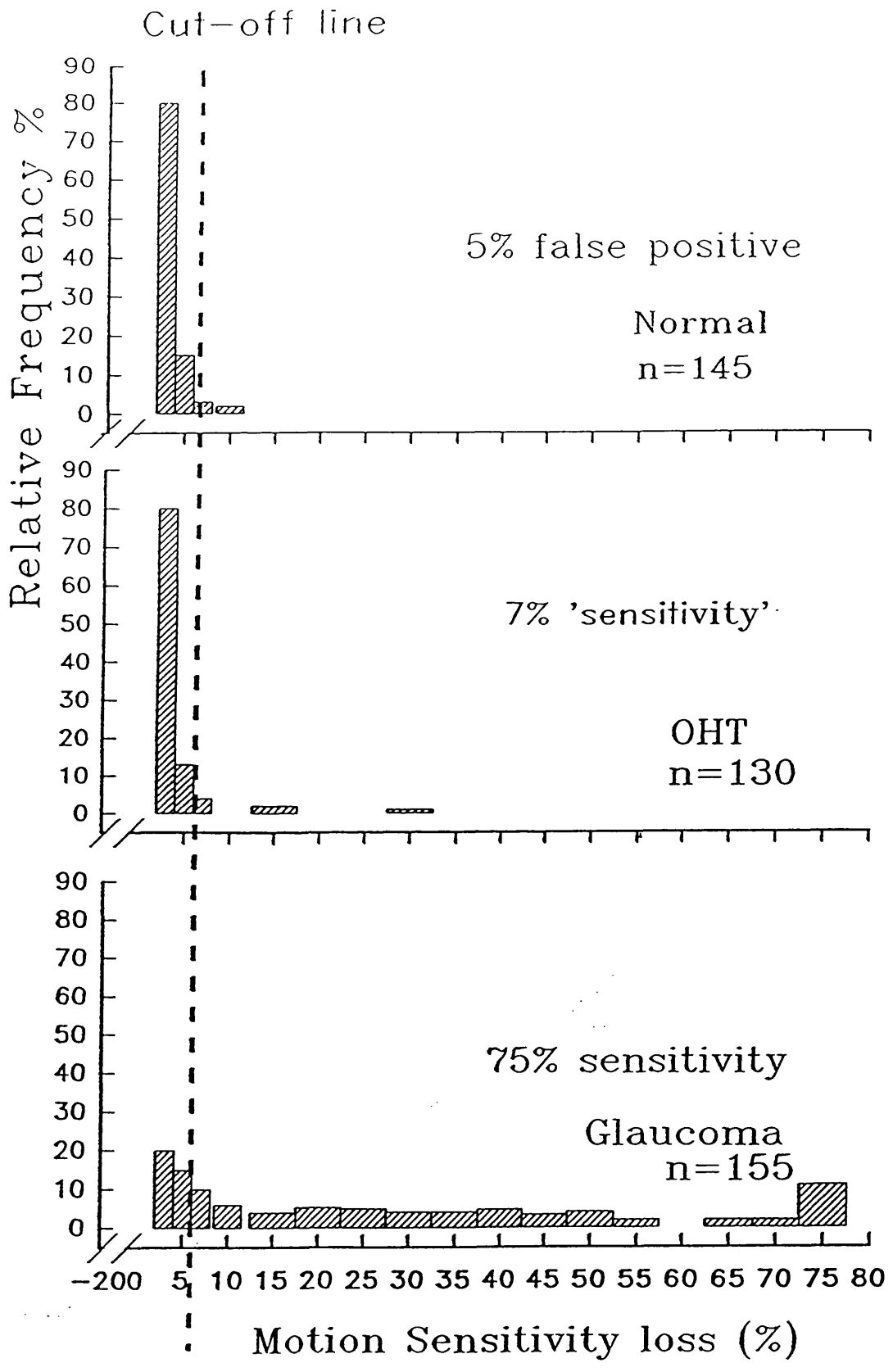


Fig. 3-12 Overall distribution of motion sensitivity loss from all "sectors" by three specific groups in MST. A vertical cut-off line is laid across the three groups. Measurements were obtained from 145 sectors in the left eyes of normal volunteers, 155 sectors in the better eyes of glaucomatous patients, and 130 sectors in ocular hypertensive left eyes. It is possible to shift the line from left to right until 95% of the normal sectors are on the left side. So that, the cutoff point for screening motion sensitivity loss is beyond 5%. glaucoma group.

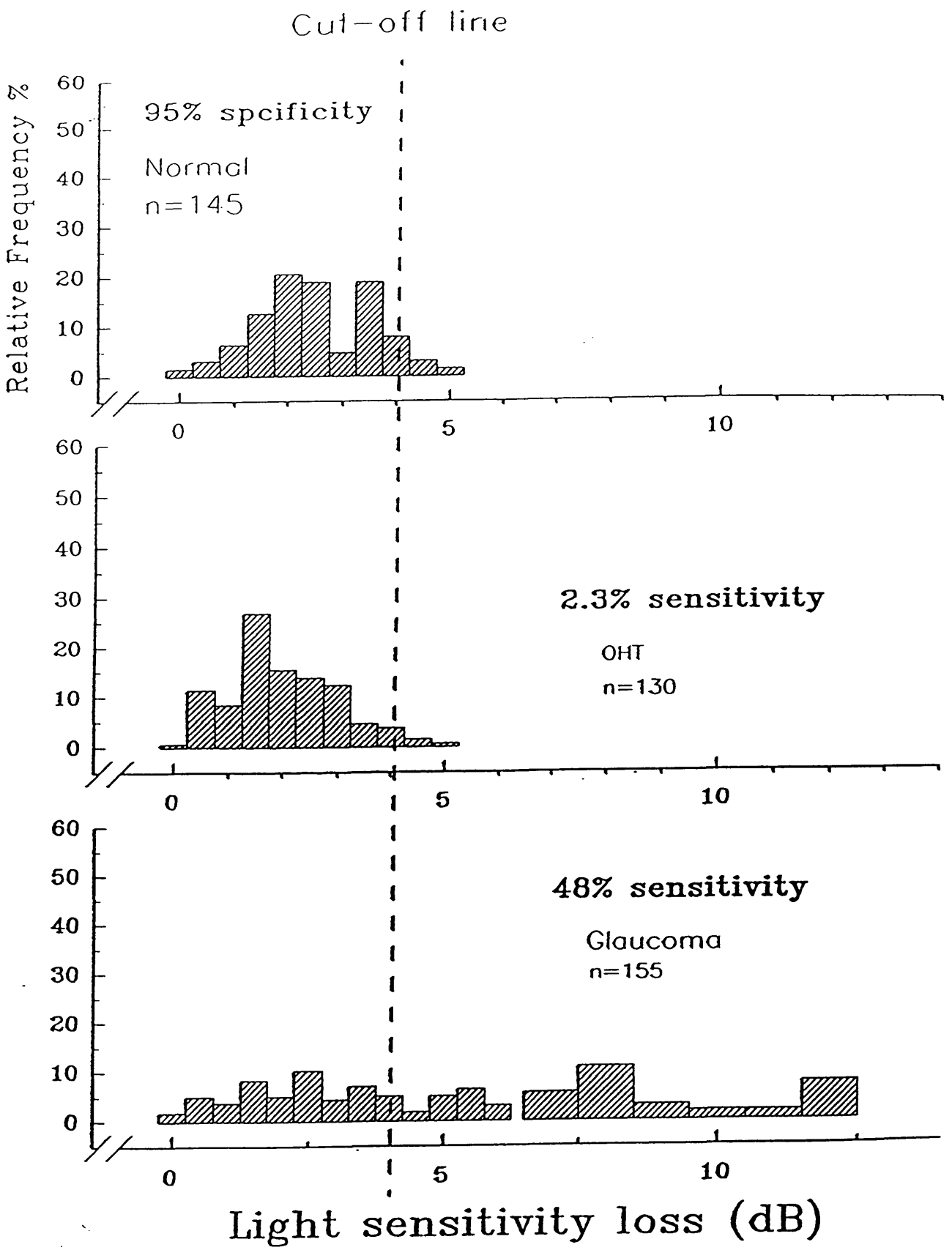


Fig. 3-13 Overall distribution of light sensitivities for all sectors by three specific groups in MST. A vertical cut-off line is across the three groups. The measurements were obtained from 145 sectors in the left eyes of normal volunteers, 155 sectors in the better eyes of glaucomatous patients, and 130 sectors in ocular hypertensive left eyes. It is possible to shift the line from left to right until 95% of the normal sectors is on the left side. The cut off point for screening light sensitivity loss are beyond 4 dB loss. This allows only 5% of abnormal sectors out of the overall sectors in the normal group and 48% of sectors with abnormal light sensitivity on the right side in the glaucoma group.

The same process was done on the HFA results to see whether light sensitivity can be effective in discriminating between normal, glaucoma cases and ocular hypertensives. It was very difficult,however, to find the best combination of sensitivity and specificity. Distributions of light sensitivity threshold results for overall sectors are illustrated in **Fig. 3-13.**

If specificity was fixed at 95% level, in which 95% of normal sectors were on the left side of the cutoff line, the sensitivity in glaucomatous eyes was 48%. This corresponds to light sensitivity loss at 4 dB. To increase sensitivity, the line could be shifted to the left i.e. 3 dB, the sensitivity could have been slightly improved but it could also have suffered from a large loss of specificity. To increase specificity, the line was shifted to 5 dB, specificity could be 100% but sensitivity could be further reduced.

When comparison was made of results of light detection with motion detection in each sector, there was a trend observed whereby the more the motion loss the more the light sensitivity loss in the glaucoma group. The correlation coefficient between motion and light sensitivity over all sectors was 0.49($p < 0.001$). If one looks at frequency of abnormal motion sensitivity (cut off was at 6% of motion seen) as a function of the severity of light sensitivity loss in glaucoma patients, the correlation between frequency of motion sensitivity loss(Y) and light sensitivity loss (X) is as following:

$$Y\,(\%) = 0.81 + 8.81 \times X(dB) \qquad (3\text{-}1)$$

A very strong correlation was found between frequency of motion sensitivity loss and the light sensitivity loss($r = .95$, $p < 0.001$) in the glaucoma group(**Fig. 3-14**). By contrast, if the same comparison was done by the point-wise correlation in 434 pairs from all glaucomatous eyes, the correlation coefficient was unexpectedly low(0.16, $p > 0.1$). This contradiction will be discussed in Chapter 4.

3-4-4 MST in the elderly population

307 people in ICES(151 individuals) and RGS(156 individuals) performed MST. For purposes of analysis, 19 outside the age range, 5 with visual acuity less than 6/18, 7 with advanced

visual field loss, 11 with unreliable Henson field tests, 6 with incomplete MST were excluded from the study. In all, two hundred and fifty-nine individuals were included in this part of the study. Among them, were 10 cases of glaucoma; 71 were glaucoma suspects and 178 did not have glaucoma. The average age was 65 years old.

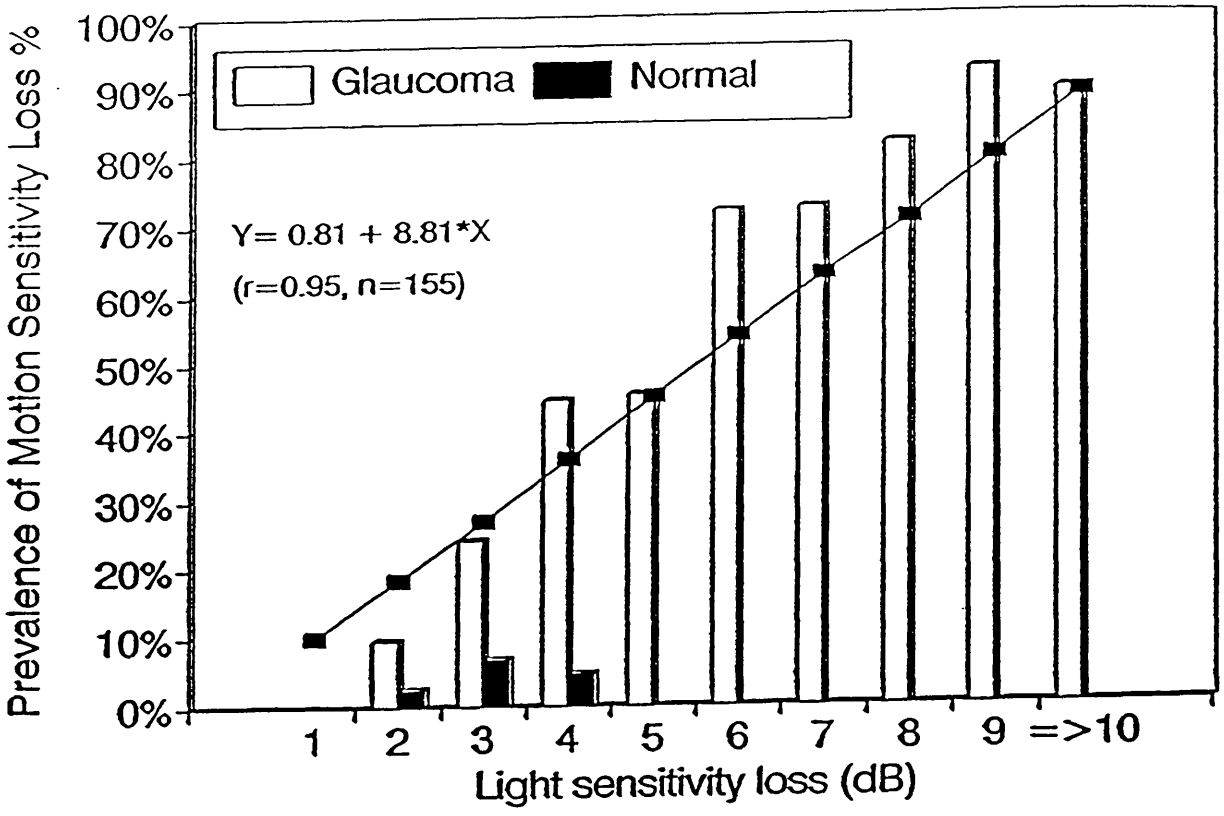


Fig. 3-14 For 155 sectors from 31 glaucoma patients and 145 sectors from normal control eyes, the prevalence of motion sensitivity loss is plotted against the light sensitivity loss (dB) by specific diagnosis. When significant motion sensitivity loss compared to light sensitivity loss is considered, 25% motion loss has been established for 3-dB loss sectors. The linear regression line suggest strong correlation between motion sensitivity loss and light sensitivity loss in the fields of glaucoma patients. However there is no similar correlation found in normal persons(55 sectors from 11 normal persons).

Table 3-7

Proportion of major eye problems in ICES & RGS

	n	(%)
Normal	93	36
Glaucoma	10	4
Glaucoma suspect	71	27
Cataract	48	19
ARMD suspect	23	9
Amblyopia	9	3
Retinopathy	5	2
Total	259	100%

Table 3-7 lists major eye problems in these two populations sub-sample tested by MST. Only 36% of the participants(93 individuals) had an entirely normal eye examination. The second largest group of participants consisted of glaucoma suspects(27%) and then cataract(19%).

Before this part of the study began, I considered MST to be normal if at least 8/10 stimuli were seen (except 2 loci in the blind spot area). This criterion was based on the hospital study , described earlier, which could provide almost 100% specificity and 100% sensitivity to detect early glaucoma cases(see 3-4-3). The result was regarded as "unreliable" if both two stimuli in the blind spot were seen in 6 out of 10 presentations. MST was considered abnormal if (1) the blind spot was detectable and (2) any stimulus missed more than twice times in any location tested.

After testing the first 48 elderly subjects, I realized that many elderly people without glaucoma often missed one or more stimuli more than twice. 16 individuals(35%) had an unreliable test because the blind spot could be detected. This suggested that preestablished criteria were not specific enough: 32 subjects(71%) would have been considered abnormal. I, therefore, changed the criteria for an abnormal MST. They became 1) any stimuli missed 5 or more times after 10 presentations 2) fixation loss not more than 10 times after 20 presentations.

Table 3-8

The distributions of MST score

Score	n	%	cumulative%
10/10	25	10	..
9/10	98	38	48
8/10	44	17	65
7/10	20	8	73
6/10	12	5	78
5/10	5	2	80
4/10	5	2	82
3/10	5	2	84
2/10	12	5	89
1/10	10	4	93
0/10	18	7	100
Total	259	100%	

Distribution of MST based on the worst eye from 259 individuals is shown in Table 3-8. By comparison (Table 3-8), of the 259 people tested with MST, 187(72%) had normal MST and 72(28%) had abnormal MST when the cut off was at 7/10. In this case, all proven glaucoma cases(10 individuals) and 23 glaucoma suspects were abnormal. If MST is considered abnormal, the eye may have glaucomatous damage(or at least receivers further diagnostic evaluation), the calculated sensitivity of MST was 100% with these 10 proven glaucoma cases.

If the rest of the abnormal MST's(33 individuals) found in 178 non-glaucomatous subjects were false positives, the specificity was an 82%. So, although MST is sensitive in detecting proven glaucoma, the problem is 18% "false positive rate." In comparison with earlier findings (section 3-4-3), the greater the MST cut off point the greater "false positive rate" in this community based survey which suggests other ocular abnormalities can affect motion sensitivity. MST, like a visual field test, is not specific for glaucoma.

As a result of quantifying distributions of abnormal MST in relation to other ocular abnormalities when the validity of MST for detecting glaucoma was similar to the Henson, the cutoff point of MST was from compared 7/10 to 6/10 in order to achieve a similar sensitivity and

specificity (Table 3-9). A total of 52(20%) had an abnormal MST in that population(Table 3-9). Of these, 10 eyes (19%) had glaucoma, 17 eyes(33%) were glaucoma suspects, 6 eyes (12%) had cataracts, 6 eyes (12%) were amblyopic, 6 eyes (12%) had retinopathy , 2 eyes(4%) had age related macular degeneration(ARMD) and 8 eyes(15%) were normal. If an abnormal MST found with any ocular abnormality but without glaucoma was not regarded as a false positive, the calculated specificity of MST was 91%(8/93). This finding would suggest that almost 50% of motion abnormalities were unrelated to glaucoma.

Table 3-9

Distribution of abnormal MST and Henson by diagnoses

		Abnormal MS		Abnormal Henson*	
Diagnosis	No	No. Test Positive	Test Positive%	No. Test Positive	Test Positive%
Glaucoma suspect	71	17	23	8	11
Glaucoma	10	10	100	9	90
Cataract	48	6	13	10	22
Amblyopia	9	6	67	0	0
ARMD	23	2	9	8	34
Retinopathy	5	3	60	3	60
Normal	93	8	9	7	8
Total	259	52		45	

* The survival score less than 96%

3-4-5 Comparison with Henson CFS 2000

Acceptability

186 elderly people aged over 65 years were examined by both MST and the Henson in a random order on the same day during the two surveys(ICE and RGS). A few people were unable to do either MST or the Henson. Two people could do neither MST nor the Henson because they were too sick. 3 people did not understand MST even with extended training and another 3 could not press the response button. There were 3 people who did not understand the Henson, four had difficulty counting the stimuli, and two could not speak or indicate the points they had seen. The acceptability of MST and the Henson was 98%(280/286) and

96%(275/286), respectively. This is not a statistically significant difference(Chi^2 1.356, p >0.05).

Validity

To compare the validity of the tests, unconfirmed early glaucoma cases and people with unreliable results in the Henson or MST were excluded. A total of 93 entirely normal participants and 10 manifest glaucoma patients who had both MST and Henson records were included from the ICES and the RGS. To achieve an objective comparison, the field survival score in the Henson CFS 2000 was used for a standard screening test in this study.

The results from MST and the Henson are shown in **Table 3-10** and **Table 3-11**, respectively. The best combination of sensitivity-specificity for MST was 100% sensitivity and 91% specificity when the cutoff was 6/10. For Henson, the cutoff point for the best combination was 96% survival. This provided 100% sensitivity and 98% specificity. It appears that the specificity in Henson was better than MST.

Table 3-10

Performance of MST expressed as fraction of motion seen in glaucoma detection

	Proven Glaucoma Case			Persons without Glaucoma		
no of times target seen in 10 repeats	no of patients (out of 10 patients)	Sensitivity	%	no of persons (out of 90 persons)	Specificity	%
10	0	10/10	100%	52	52/90	58%
9	0	10/10	100%	68	68/90	76%
8	0	10/10	100%	80	80/90	88%
7	0	10/10	100%	82	82/90	91%
6 *	0	10/10	100%	84	84/90	93%
5	1	9/10	90%	86	86/90	96%
4	2	8/10	80%	88	88/90	98%
3	4	6/10	60%	88	88/90	98%
2	6	4/10	40%	88	88/90	98%
1	10	0/10	0%	90	90/90	100%

Table 3-11

Performance of HENSON 2000 in relation to the survival score in glaucoma detection

	Proven Glaucoma Case			Persons without Glaucoma		
Henson CFS2000 Survival score %	no of patients (out of 10 patients)	Sensitivity	%	no of persons (out of 90* persons)	Specificity	%
100	0	10/10	100%	74	74/90	82%
99	0	10/10	100%	79	79/90	87%
98	0	10/10	100%	84	84/90	92%
96	2	8/10	80%	88	88/90	98%
93*	3	7/10	70%	90	90/90	100%
90	5	5/10	50%	0	90/90	100%
85	6	4/10	40%	0	90/90	100%
80	8	2/10	20%	0	90/90	100%
70	8	2/10	20%	0	90/90	100%
=<30	10	0/10	0%	0	90/90	100%

* Three Henson CFS2000 field results had no blind spot were excluded.

However, there were no statistical differences in terms of AUC analysis (AUC 0.95, 95% CI 0.90 to, 1.0 for MST versus AUC 0.98, 95% C.I. 0.95 to 1.0 for Henson). The comparison of the two tests applied when their optimal cut-offs had been selected(**Table 3-10** and **Table 3-11**). This avoided selection bias in such a comparative study. The agreement between the Henson and MST in discrimination between normal and advanced glaucoma was good (Kappa=0.5394, SE=0.0936). It should be noted that the analysis was limited as there were few glaucoma cases.

3-5 Applications of Motion Sensitivity Screening Test(MSST)

After a number of experimental studies and several clinical observations, the validity of the motion sensitivity test, and the optimal testing strategy for CCVP application was established. However, it remained to be shown that CCVP technology could easily provide a high sensitivity and specificity without a dedicated visual field instruments and without a dedicated visual field environment.

3-5-1 Abnormal motion case finding in glaucoma clinic

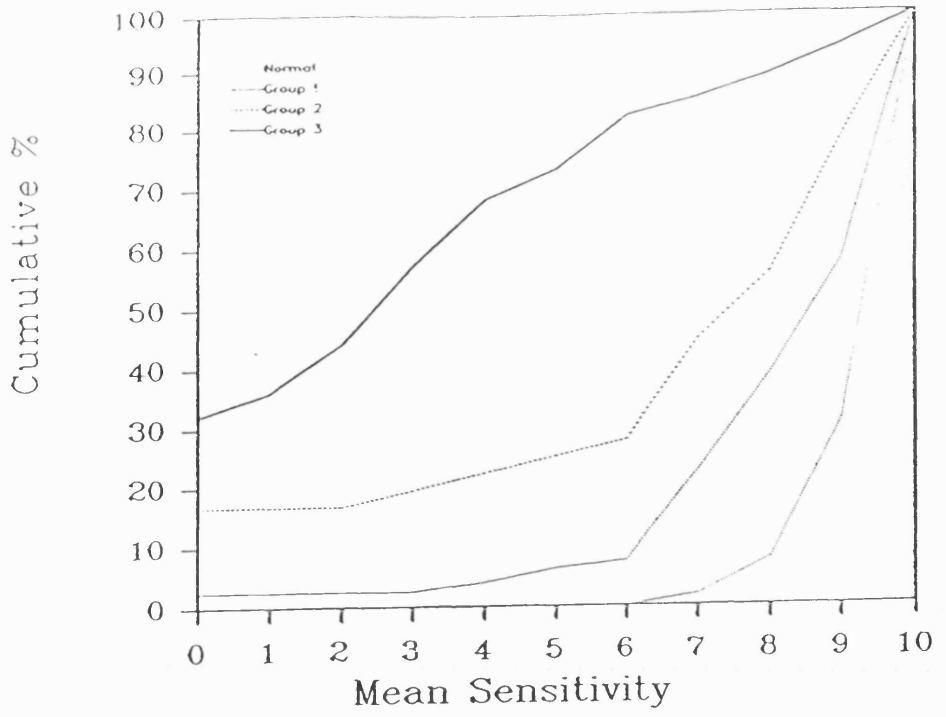
For abnormal motion case finding, 190 subjects who attended the glaucoma unit were recruited by clinic receptionists. Those subjects who had amblyopia, serious cataract, or posterior segment ocular abnormalities were excluded. Based on the GHT classification of light sensitivity loss(Heijl, 1990), the better eyes of all patients were further graded into three groups: Group 1(within normal limits; Group 2: Borderline; Group 3:Outside normal limits(see page 72). In addition, 52 eyes from 52 volunteers served as a control group and underwent routine eye examination and MSST.

Table 3-12 Motion Detection for patients and controls showing 95% confidence interval(C.I.)*

status	Eyes	Average Motion Seen		Motion Sensitivity	
	n.	mean	95% C.I.	mean	95% C.I.
Normal	52	9.32	9.1 to 9.5	8.28	7.9 to 8.7
GHT Group 1	80	8.36	7.7 to 8.9	6.58	6.0 to 7.2
GHT Group 2	35	6.39	5.3 to 7.1	4.05	3.0 to 5.1
GHT Group 3	75	3.06	2.4 to 3.7	1.17	0.7 to 1.7

*: Calculated by CIA software. When the sample was small the exact method was used(BMJ, 1990).

Both average motion seen(AMS) and motion sensitivity(MS) were distributed with differences between the normal subjects and the patients with regard GHT results(Table 3-12). For AMS, only 4 eyes(7.7%) in normal controls had AMS less than 9. In contrast, AMS less than 9 in group 1, group 2 and group 3 were 31 eyes(38%), 20 eyes(56%) and 67 eyes(89%), respectively. MS less than 6/10 or 60% were found in 3 normal eyes(5.8%) but 26(33%) in the group 1, 23 eyes(64%) in group 2 and 71 eyes(92%) in group 3, respectively. There was no overlap between normal subjects and the other three patients' groups in terms of 95% confidence intervals(Table 3-12). Motion sensitivities were distributed differently among the groups(Fig. 3-15). The ROC curves are shown in Fig. 3-16.



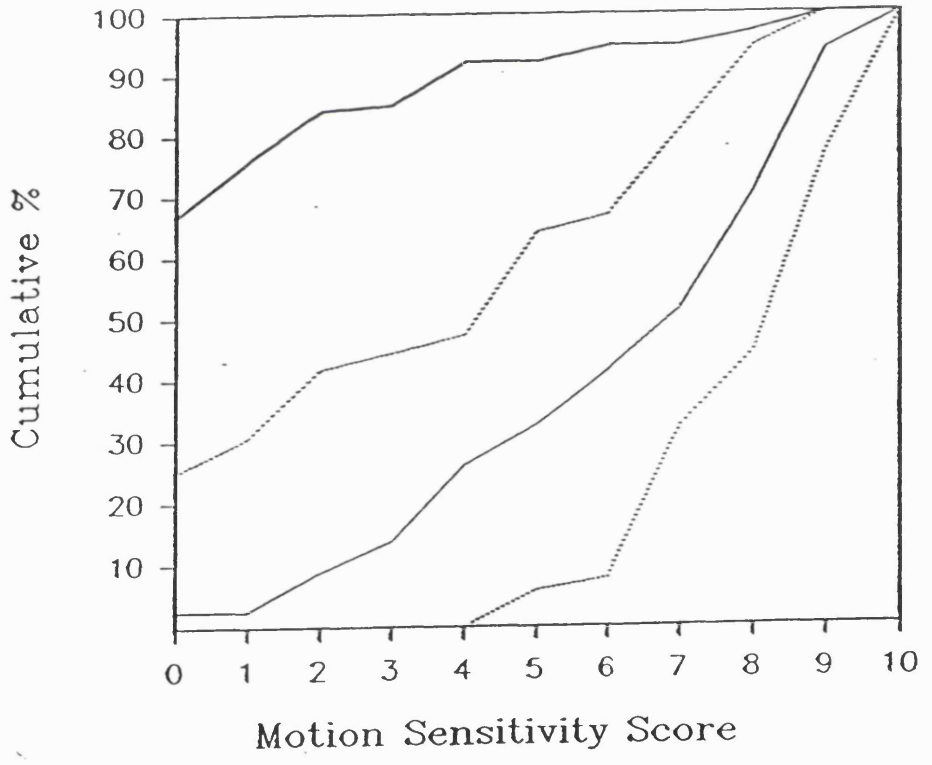


Fig. 3-15 Distribution of AMS(above) and MS(below) by group.
For abnormal motion case finding in glaucoma patients, 190 glaucoma patients were recruited by receptionists. Based on the Glaucoma Hemifield Test(GHT) classification of light sensitivity loss(Heijl, 1990), the better eyes of all patients were further graded into three groups: Group 1(within normal limits; Group 2: Borderline; Group 3:Outside normal limits). In addition, 52 eyes from 52 volunteers served as a control group and underwent routine eye examinations and MSST. The motion sensitivity decreased in all glaucoma patients($P < 0.0001$) irrespective of the presence of absence of light sensitivity loss.

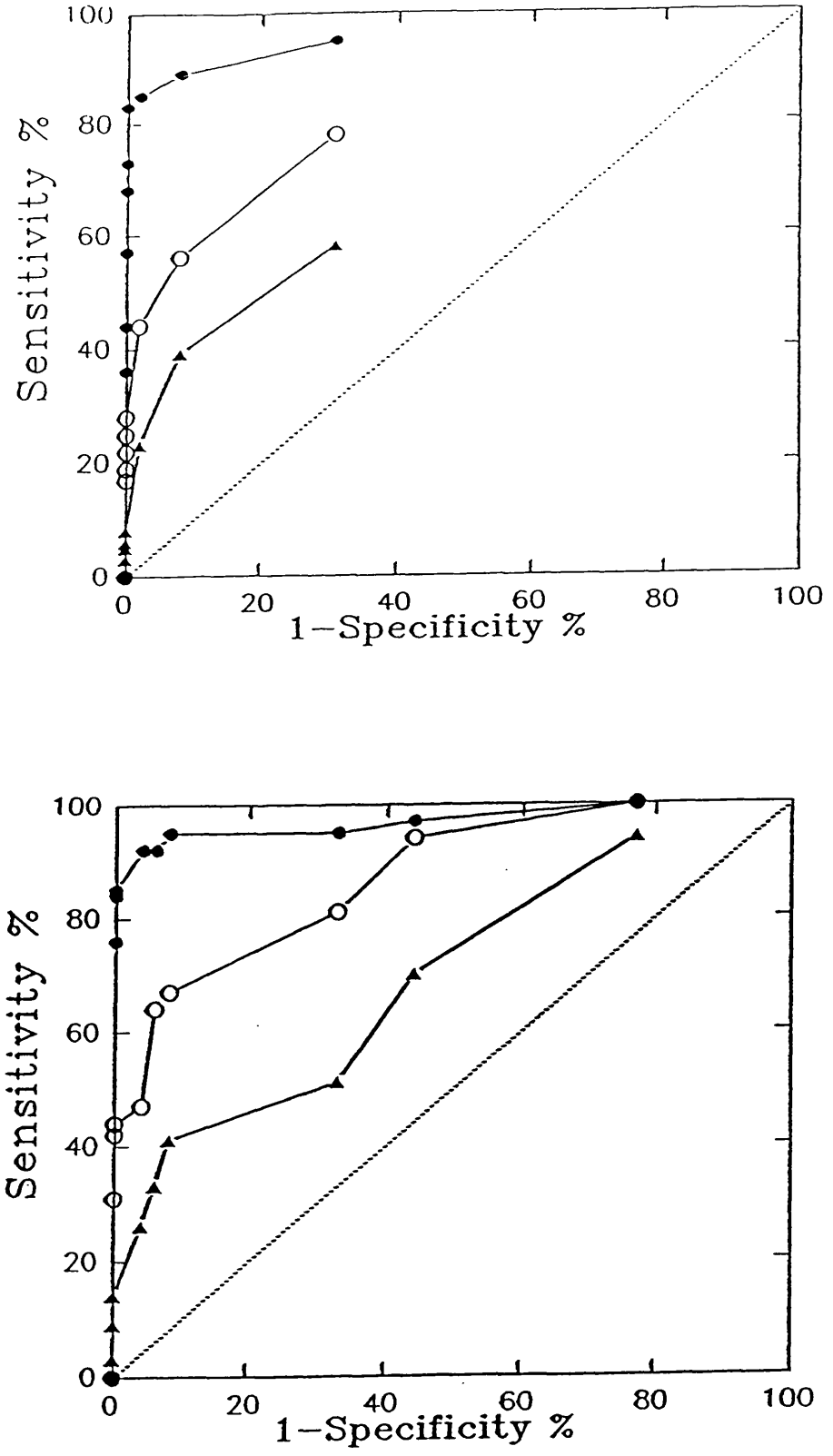


Fig. 3-16 ROC Curves. Upper: Average Motion Seen; Below:Motion Sensitivity. Solid triangles represent patients from group 1; open circles represent patients from group 2 and closed circles represent patients from group 3.

Both average motion seen(AMS) and motion sensitivity(MS) were distributed with differences between the normal subjects and the patients with regard GHT results(Table 3-12). For AMS, only 4 eyes(7.7%) in normal controls had AMS less than 9. In contrast, AMS less than 9 in group 1, group 2 and group 3 were 31 eyes(38%), 20 eyes(56%) and 67 eyes(89%), respectively. MS less than 6/10 or 60% were found in 3 normal eyes(5.8%) but 26(33%) in the group 1, 23 eyes(64%) in group 2 and 71 eyes(92%) in group 3, respectively. There was no overlap between normal subjects and the other three patients' groups in terms of 95% confidence intervals(Table 3-12). Motion sensitivities were distributed differently among the groups(Fig. 3-15). The ROC curves are shown in Fig. 3-16.

The areas under the ROC and their 95% confidence intervals for each group are given in Table 3-13. A perfect MSST based on MS has an AUC probability of 1 for discriminating normals from the group 3. By the way comparison, Group 1 seems to have no light sense loss as defined by GHT and both AMS and MS were limited to provide discriminating power between normals and the patients.

Table 3-13 Area under the ROC for discriminating light sensitivity loss in the patients

GHT Status	Average Motion Seen			Motion Sensitivity		
	area	SE	95% C. I.	area	SE	95% C.I.
Group 1	0.66	0.04	0.57, 0.75	0.7	0.05	0.61, 0.76
Group 2	0.75	0.06	0.64, 0.86	0.9	0.04	0.8, 0.95
Group 3	0.94	0.02	0.90, 0.98	1.0	0.02	0.94, 1.00

*Power for testing one side test of significance with p=0.05 (Colton, 1974)

There were no significant differences between AMS and MS for detecting the same group patients in terms of AUC, despite the fact that MS seems to provide more potential cutoffs to improve the sensitivity while the specificity is not seriously reduced. For example, in Group 3, a cut-off point of 8/10 to 10/10 would give a sensitivity of 80% for AMS and 95% for MS, respectively. For the same cut off point, specificity of 65% was obtained for AMS compared

to a specificity of 30% for MS. The sensitivities and the specificities corresponding to the optimized cut-off point are given in **Table 3-14.**

Table 3-14 Sensitivity and specificity with the optimized cut-off

GHT Group	Average Motion Seen cutoff	Sensitivity	Specificity	Motion Sensitivity cutoff	Sensitivity	Specif.
Group 1	9.0	39%	92%	8/10	51%	67%
Group 2	9.0	56%	92%	7/10	67%	92%
Group 3	8.0	85%	98%	6/10	92%	94%

3-5-2 Application in screening for ocular diseases in Nigeria

This part of the study was repeated one year later after the initial examination. Because the data from Second visit was incomplete at the end of 1992, the results presented here were mainly based on the initial examination data. There were two population samples tested by MSST. One was in Kaduna city which has been considered to be a non-endemic area for onchocercal optic nerve disease. The second population was in the meso-endemic onchocercal communities which consisted of isolated and illiterate rural village people.

2314 MSST files were originally recorded: 1238 from the WHO project and 1076 from others. Except 454 individuals, all were from the endemic area. Because the data from outside the WHO project did not include a complete eye examination, they were only used for assessment of risk of motion loss based upon a population rather than an individual(see section 1-2-1). In the WHO project, forty-four files were excluded because of unreliable data, such as missing identification, age and sex in their data files. Of the remaining total, there were 375 individuals from the WHO survey.

Simplicity & Acceptance

There were ten village helpers and 11 ophthalmic nurses trained to perform MSST. Among village helpers, one was a trainee from a church, 8 were primary school graduates and one had no school background. The training time was approximately 1 hour for village helpers. All ophthalmic nurses were students attending an ophthalmic nurse training course at the ABU Teaching Hospital, except 2 who were members of the WHO project. All had a half hour training for MSST in the hospital. Except for one village helper, all of them could conduct the test satisfactorily. This allowed 68% of MSST to be done by local people or paramedics(Table 2-7). Since MSST is less affected by the *multicontrast* environment, no special effort was made to have a dark room for the test. Public rooms, such as school rooms and the waiting room in the hospital and huts in each village were used. The vast majority of the subjects understood what they should do during the test after they had seen other people tested(see below). Few tests(2.1%) were incomplete due to lack of understanding. The rural communities had no objection to home visits.

In the hospital, MSST was used for 6 days. A large number of patients or patients relatives or their friends from the out-patient department were waiting to have MSST examination. There were always two queues in front of each computer. In addition, there was a 100% response rate from 160 individuals who were required to be retested with MSST on more than two different occasions. No one complained that the test was uncomfortable. Rather, the test attracted many people even though they did not know what the test was for. Although there was no advertisement for MSST, many people wanted to have MSST because they had heard about it from friends, colleagues and children.

Rapid screening test

To start MSST, it is necessary only to switch on the computer. A batch file manages MSST and generates the stimuli for the test. The testing time per eye for 5 repeats and 10 repeats were 98 seconds and 167 seconds, respectively. The testing time for 5 repeats for both eyes including training was 5.5 minutes. For most subjects additional training was not necessary because they quickly became confident to do the test from observing other people doing it. The maximum number of visual fields screened in one day was 225 with two Sharp

computers. It was always possible to retest immediately if this was required(e.g. for intra-subject variation).

Motion sensitivity vs Microfilarial Load

When the cut off point of MSST was 6/10, the sensitivity of detecting OND was 91% in 56 OND cases defined by the WHO project and the specificity was 75% in 319 Nigerians without OND. When 25 cases were excluded: 9 with low vision(VA < 6/18), 7 with early cataract and 9 potential glaucoma cases (cup/disc ratio > 0.5 and/or intra-ocular pressure > 21 mmhg), the specificity was still lower(82%) than was found in abnormal motion case finding in hospital.

Table 3-15 Distribution of microfilarial load by clinical status

	'Normal'Nigerian* n= 255 MSST		OND n=56 MSST		Total n=311 MSST	
	Neg.	Pos.	Neg.	Pos	Neg.	Pos.
Microfilarial Load (mf/mg)	n=201	n=54	n=5	n=51	n=206	n=105
< 10 (n=224)	188	21	4	11	192	32
10.1-30 (n= 46)	8	17	1	20	9	37
>30 (n= 41)	5	16		20	5	36
p value	0.0000				0.0000	

* 25 cases with other ocular abnormalities and 39 Nigerians who had no microfilarial load record were excluded

The relationship between Motion sensitivity versus Microfilarial load was therefore studied. Table 3-15 shows the distribution of MSST by clinical group according to their microfilarial load. Among subjects with normal ocular examination and with a microfilarial load greater than 10 mf/mg, the prevalence of abnormal MSST was roughly 7 times higher than subjects who had a microfilarial load less 10 mf/mg($p < 0.000$). If these cases a the microfilarial load greater than 10 mf/mg were excluded, the specificity became 90% (188/209).

Observer agreement

Intra-observer agreement on MSST was measured by repeating MSST immediately at the same sitting. Inter-observer agreement for each subject on MSST was separately measured on two different MSST sittings using different computers and different operators in the same testing room after 5 minutes break. Each of the 112 eyes(71 individuals) was examined twice by each of three operators for inter-observer variation.

40 controls and 72 persons from endemic populations were tested. These results are presented in Fig. 3-17. The limits of agreement were from -0.198 to 0.18 in intra-observer agreement(Fig. 3-17A). The inter-observer agreement, also showed very good agreement(Fig. 3-17B), the limits of agreement being from -0.25 to 0.27. The mean differences(test-retest), For inter- and intra- observation were 0.01 SD o.13 and -0.02 SD 0.11 in Table 3-16.

For the proposed British Standard for the test(Bland, 1986), there were 6(5.3%) differences of more than 2 SD in intra-observer agreement and 3(3.3%) differences of more than 2SD in the inter-observer agreement. Both the intra-observer and inter-observer differences were uniform across the whole range of motion sensitivity and were not related to the mean (correlation coefficient r= -0.026, p > 0.05 and r=-0.181 p> 0.05, respectively). The intraclass correlation coefficients are shown in Table 3-16.

Table 3-16 Limits of agreements (LOA) and Intraclass Correlation Coefficients (ICC) of MSST

	Control			Endemic			Total		
	n	mean(SD)	ICC	n	mean(SD)	ICC	n	mean(SD)	ICC
		LOA			LOA			LOA	
Inter	40	0.01(0.16)	40%	72	0.01(0.12)	90%	112	.01(.13)	78.9%
		(-0.039,0.059)			(-0.017,0.0377)			(-0.01,0.034)	
intra	37	-0.02(0.07)	98%	53	-0.02(0.13)	60%	90	-.02(.10)	95.5%
		(-0.064,0.0241)			(-0.054,0.014)			(-0.04,0)	

ICC = $(S^2(X) + S^2(Y)-S^2(D))/(S^2(X) + S^2(Y) + d^2-(S^2(D)/n))$
n= number of subjects
$S^2(X)$ and $S^2(Y)$ are the variances of measures for observers.
D and $S^2(D)$ are the mean of differences and the mean variance of differences between measures of both observers, respectively(Bland, 1986).

Motion sensitivity

A total of 158 randomly sampled individuals underwent MSST(74 controls and 84 onchocerciasis endemic subjects). The average of age in the controls and onchocercal populations was 31.2 SE 0.24 and 31.9 SE 0.57, respectively. The correlation coefficient between MSST and age was -0.50(p <0.001) in the control group. After excluding all cataract cases(5 individuals), no significant correlation was found(r=-0.24, p > 0.05). For the meso-endemic onchocerciasis population sample, the overall correlation coefficient between age and MSST was -0.21(p<0.01).

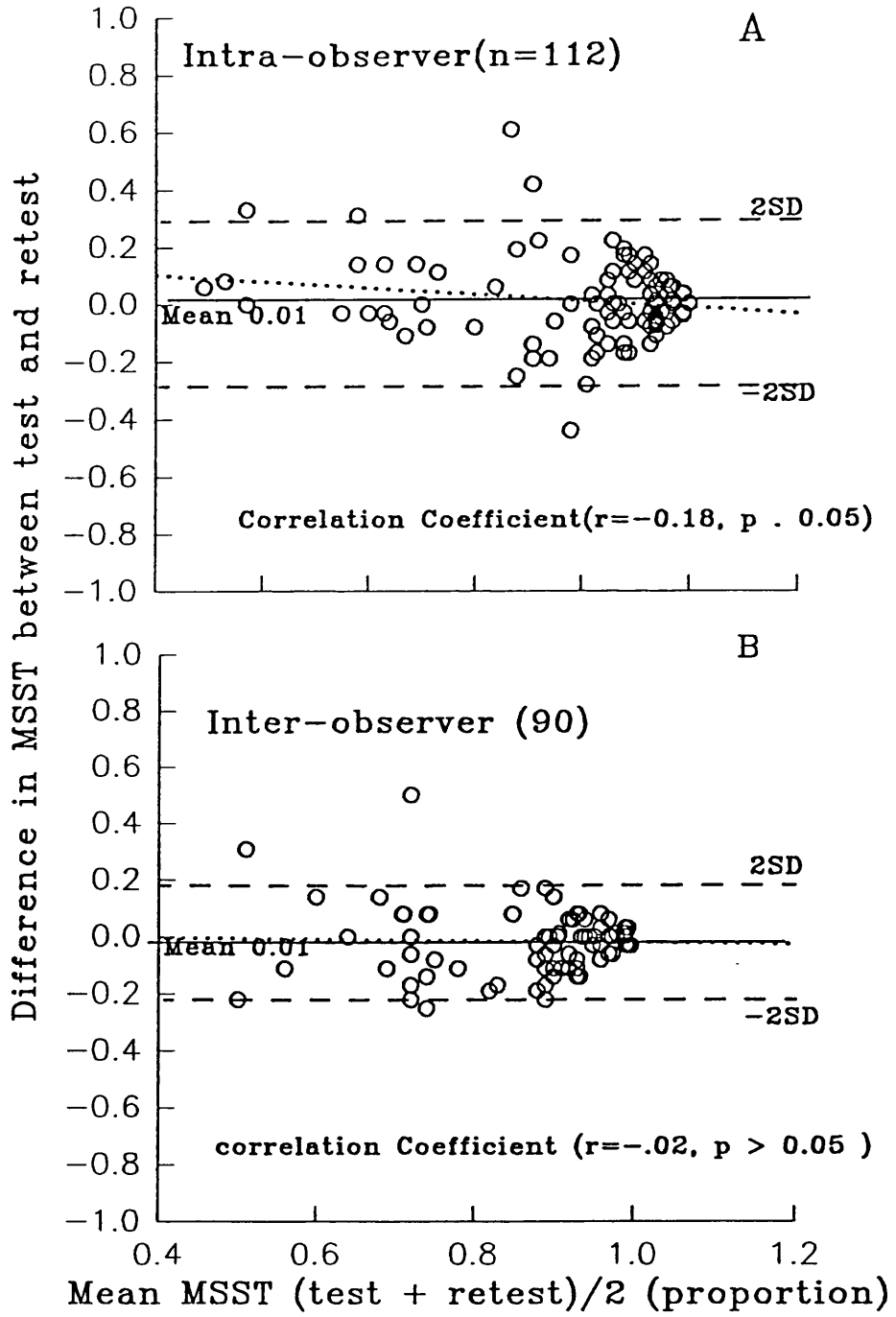


Fig. 3-17: Range of disagreements by retesting 40 persons from the control community(Fatika) and 72 from meso-endemic onchocercal community for intra-observer variation(A) and retesting 92 eyes of 52 persons for inter-observer variation(B).

MSST results were plotted as a function of percent of response by different populations(Fig. 3-18). If the cutoff criterion of normal motion was set at 50%, 23% of the onchocerciasis endemic population in Nigeria had reduced motion sensitivity, while only 5% was found in the non-endemic Nigerian population. The prevalence of motion sensitivity loss in the sample of the endemic population was more than 4 times the rate in this non-endemic population. If the cut off was selected at 70%, 33% of the onchocerciasis endemic population had abnormal MSST.

Validity of follow up test

One third(102 individuals) were retested after one year, mostly by the WHO project staff. All the procedures were the same as the initial ones in 1991 except there were new operators, a chin-rest and a dark room used. A training program and computerized peripheral flash and flicker screening tests had been added. For data analysis, only the left eye was used because MSST on the right eye in 1991 were regarded as a "training test."[9] Six people without left eye results in either the first test or the second test, 5 people with undetectable motion sensitivity and 3 people with unreliable tests were excluded. 88 left eyes were included in the final data analysis. Of these 88 eyes, 44 were treated by ivermectin and 44 by placebo. There was no age or sex difference between the two groups. A comparison of MSST results on persons in the ivermectin trial in 1991, repeated in 1992 is shown in **Table 3-17.** The result shows that the placebo treated group has developed an unmatched "tail" worsening in 1992 and the ivermectin treated group has developed an unmatched "tail" of improvement(**Fig. 3-19**).

Cost

Because the two Sharp computers used for the field study were not initially bought for this study and the travel cost for the author between London and Nigeria would not be necessary for a local user, these costs have not been included. The only specific cost for the first trip in 1991 was £26 for recruiting 5 local helpers for ten days work at a rate of N10(exchange

[9] Testing the right eye was treated as a training test because there was no training program. In the second screen, there was an added training program.

rate at that time was N16/£1) and £62 for recruiting one ophthalmic nurse at a rate of 100 Nairas per day. The average cost would be only £ 44 per thousand MSST tests.

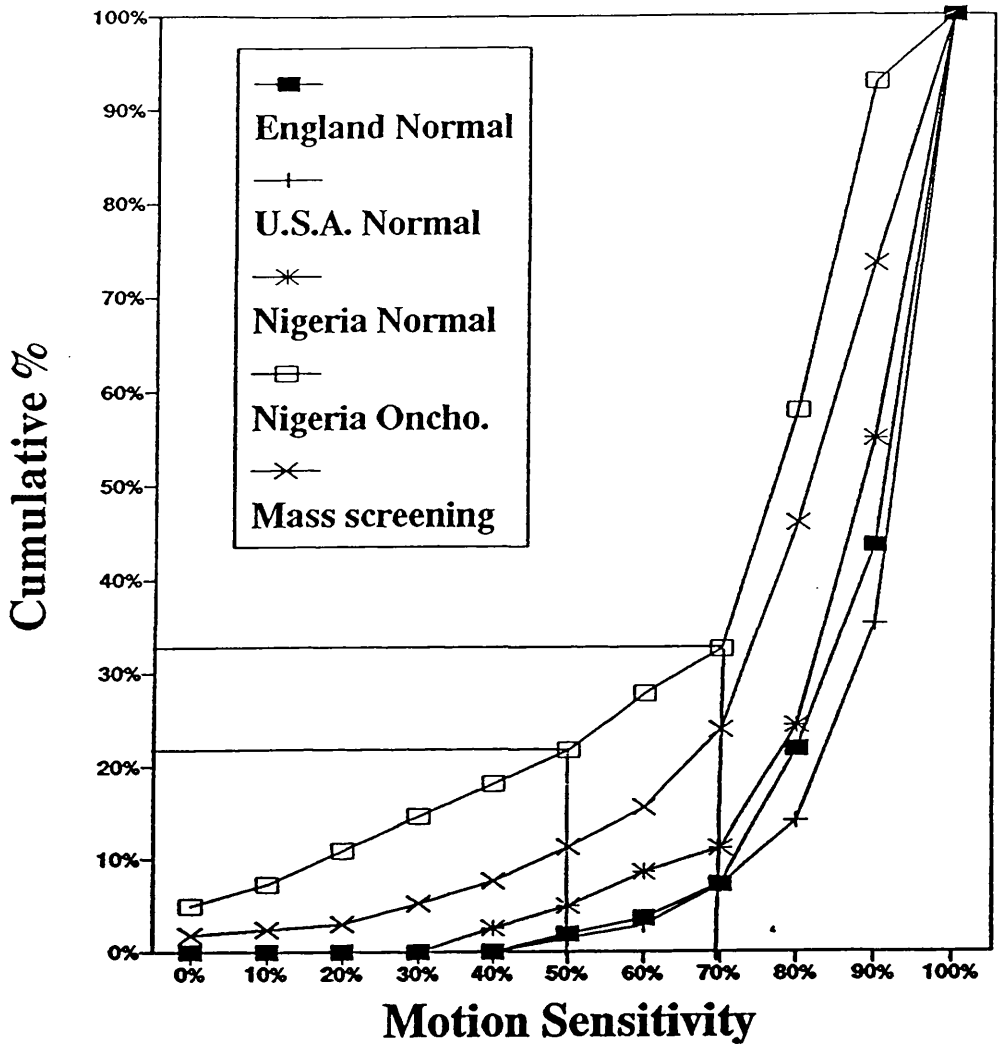


Fig. 3-18: Cumulative frequencies of MSST results in 3 putatively normal groups and 1 meso-endemic onchocercal group and 1 mass screening population including non-endemic and endemic populations. English Normal : 91 staff, student and 121 glaucoma patients' spouse volunteers, Institute of Ophthalmology, London; U.S.A. Normal : 74 volunteers for MSST at ARVO Meeting 1991, Sarasota; Nigeria Oncho.: 84 persons from meso-onchocerciasis communities in which visual failure was due mainly to optic nerve or retinal disease.; Nigeria Normal(Randomized) : 74 persons from Fatika(non-endemic for autochthonous onchocerciasis. Similar in ethnic, cultural, geographic, and economic background to the onchocercal communities.); Mass Screening : 802 persons' left eyes from mass screening in Kuduna State.

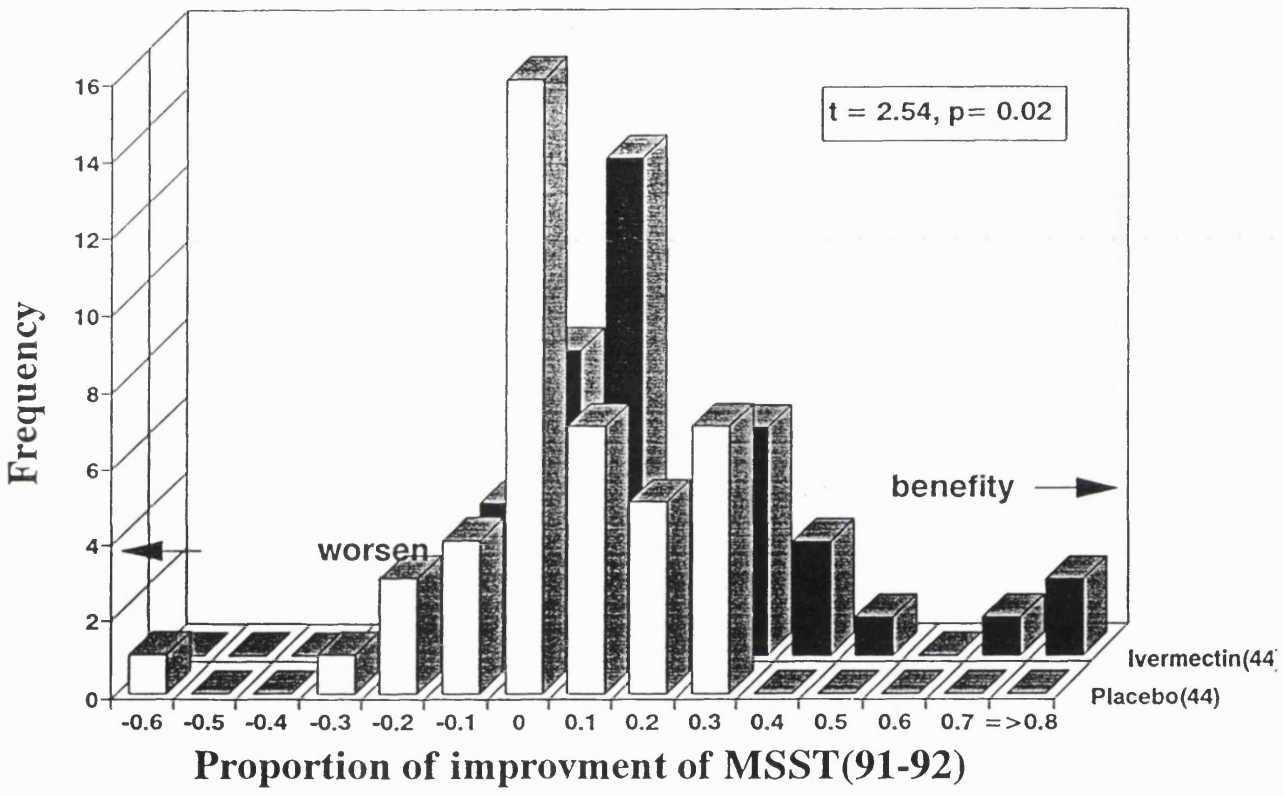


Fig. 3-19: Proportionate change in MSST after 1 year compared with initial MSST(91) for left eyes of 44 persons receiving annual ivermectin and 44 persons receiving placebo(MSST1992-MSST1991)/(MSST91).

Table 3-17
Distribution of improving scale by groups

Improving Scale*	Ivermectin		Placebo	
	n	%	n	%
-0.60	0	0.0	1	2.3
-0.50	0	0.0	0	0.0
-0.40	0	0.0	0	0.0
-0.30	0	0.0	1	2.3
-0.20	2	4.5	3	6.8
-0.10	4	9.1	4	9.1
0.00	8	18.2	16	36.4
0.10	13	29.5	7	15.9
0.20	4	9.1	5	11.4
0.30	6	13.6	7	15.9
0.40	3	6.8	0	0.0
0.50	1	2.3	0	0.0
0.60	0	0.0	0	0.0
0.70	1	2.3	0	0.0
0.80	2	4.5	0	0.0
Total	44	100	44	100

*: (MSST91-MSST92)/MSST91

3-5-3 Self Testing

MSST self testing was set in the ARVO meeting where 74 ARVO members participated. The majority of subjects could perform the test without any training. Two persons did not complete the test. And one person pretended to be abnormal by deliberately not to seeing certain targets. These three eyes were excluded in the present data analysis.

The distributions of average motion seen(AMS) and motion sensitivity(MS) are given in Table 3-18. It can be seen that both AMS and MS were quite similar. If the test is expected to have a 5 percent abnormality the cut offs for AMS and MS were both at less than 60% seen. Thus there were 4 individuals outside the 95% range of normal MSST. Of these, two cases were amblyopic, one had a retinopathy and one was wearing a contact lens which may reduce the contrast of motion stimuli(Nadle, 1990). The average testing time for each eye was 56.6 seconds with 95% CI 61.8, 50.9 according to the built-in time record in computer.

Table 3-18 Distribution of AMS and MS

Seen Rate* %	Average of Motion			Minimum of Motion		
	No of eye	Cumulative	%	No of eye	Cumulative	%
100	10	10/71	14	10	10/71	14
90	42	52/71	73	24	34/71	47
80	11	63/71	89	20	54/71	76
70	3	66/71	93	9	63/71	88
60	3	69/71	97	4	67/71	94
50	1	70/71	98	3	70/71	98
40	1	71/71	100	1	71/71	100
30	0	71/71	100	0	71/71	100
20	0	71/71	100	0	71/71	100
10	0	71/71	100	0	71/71	100
0	0	71/71	100	0	71/71	100

*** In Average of Motion, the seen rate is the average of number of times target seen in 60 repeats over 6 test locations; in Minimum of Motion, the minimum seen rate is the minimum number of 10 repeats for all locations(see text).**

Chapter 4 Discussion

4-1 Introduction

One of the objects in this study was to determine the fundamental principles of applying computer controlled video perimetry in the community. Several different applications of CCVP based on motion stimulation were subsequently investigated in the laboratory, the hospital, community based surveys, and mass screening in a rural area. In this chapter, I will stress several clinically important aspects of CCVP application in respect of motion detection which combined new and old findings.

4-2 Selecting testing conditions for CCVP

4-2-1 *Multicontrast* effect

CCVP, which aims to test visual function with un-dedicated hardware under unstable background lighting, has to solve a fundamental problem. That is the *multicontrast* condition in a CCVP test, which gives variable contrasts in different situations (Table 3-1), testing periods (Table 3-2) and hardware used(Table 3-3). There is no simple method to eliminate the *multicontrast* condition since we cannot have the same background or ambient light in different settings, and cannot have the same hardware for different computer systems that already exist as resource in the community, e.g., a computer system for medical records in a general practitioner's survey.

Because there is no simple calibration method to standardize this *multicontrast* environment(Cowan, 1985, Kingdom and Moulden, 1986), the question of how a standard CCVP test can ever be achieved arises. Without a satisfactory solution to this question, it would be unmeasurable to expect CCVP to work as an efficient visual function test in the community. For instance, if a CCVP program was highly dependent on a stimulus contrast, it would be difficult to run the test precisely in a *multicontrast* environment, such as a Nigerian rural area(Wu et al, 1992/1993; Cassels-Brown et al, 1993). Because all contrast sensitivity , colour and light differential tests are highly dependent on contrast sensitivity function, there

is no question that these conventional tests are not suitable for accurate application of CCVP.

With increasing knowledge of the fundamental characteristics of visual pathways in recent years, it might be expected that new types of stimuli may be less dependent on contrast function in varying situations. From the pioneering work of Wiesel and Hubel(1966) and the review of Shapley(1990), evidence suggests that there are many independent pathways for transmitting information from the retina to the brain. The significance of using multi- parallel pathways in a clinical application has been discussed by Bassi & Lehmkuhle(1990). In that discussion, the question addressed by the authors was whether new types of stimuli, using spatial or temporal parameters, could raise the sensitivity of a clinical test without having to overcome the contrast problem.

I have aimed to identify the ideal properties of a visual function test which are least affected by contrast. The results from Fig. 3-2, Fig. 3-3 and Fig. 3-4 support the view that there is an early saturation of contrast in the measurement of motion parameters (Livingstone and Hubel, 1987). The effects of contrast on the measurement of motion parameters may be reduced because of early contrast saturation. Alternatively, it may indirectly indicate that a motion test may have greater ability to resist to *multicontrast effects* than differential light tests when the motion test is measured above 15% contrast level. However, this would limit CCVP's ability to detect a relative scotoma. For example, Fig 3-7 show that motion stimulus was unable to detect angioscotoma when CCVP used a high contrast stimulus.

4-2-2 Spatial frequency effect

The original IBM PC provides two different graphic interface boards. One is monochrome, which was limited to text with some graphic characters. The another is a colour graphic adapter(CGA), which supplies two colours at 600 X 200 pixel resolution. After CGA, IBM introduced its enhanced graphic adapter(EGA) in 1984, which provides a resolution of 640 X 350 pixels. In 1987 they introduced the Video Graphics Array (VGA) with 640 X 480 pixels and with 256 colours(Washburn, 1990). High spatial resolution on the display provides high quality graphic characters but the variation between different display sets is greater (Ostrander

, 1989). In addition, the angle of a pixel, in terms of visual function, is not only based on the resolution of the display but also on the physical size of a display set.

Since the pixel is not square in the lower spatial resolution graphic adaptors such as CGA and EGA, horizontal and vertical lines which consist of the same number of pixels can have different lengths(Paredes, 1990). The physical size of a pixel varies with different CRT monitors, which means that size of a stimulus composed of the same number of pixels varies from one displays to another. CCVP software provides a "converter" programme for the CRT. It allows a CCVP test to be run by different display sets e.g., CGA, EGA and VGA, with a standard physical size of stimulus. Therefore, the same size of stimulus can be generated on different computers without the problem of changing or adding hardware.

Table 4-1
Degree of testing point shift from expected point with unstable viewing distance by eccentricity
(Standard view distance = 450 mm)

Viewing distance change (mm)	Expected Eccentricity Tested* (Degree)				
	1	5	10	15	20
-200	0.8	4.0	7.6	10.7	13.0
-100	0.5	2.5	2.7	4.0	4.9
100	-0.18	-0.9	-1.7	-2.6	-3.3
200	-0.31	-1.5	-3.0	-4.5	-5.7

* The condition for expected eccentricity tested was based on the testing points far from fixation 8 mm, 40 mm, 80 mm, 120 mm and 160 mm on CRT display, respectively. The *cos* effect was considered.

One of the most important elements in CCVP is the relationship between the visual angle and the display pixel when the test attempts to measure spatial frequency. Although CCVP can automatically adjust the stimulus size according to the size of pixel, it cannot control the exact visual angle on each pixel,because it is affected by unstable viewing distances and eccentricity effects(Parades et al.,1990) or *cos* effect(Drum et al 1991). The *cos* effect can be eliminated when CCVP uses LCD instead of CRT(Bosman, 1989) but the viewing distance effect cannot

be eliminated. An unstable viewing distance can change the test location and visual angle of the target. Without control of the viewing distance, the subject's head can move, and the visual angles of the pixel and the testing field will vary. This study did not systematically investigate this issue which is a potential problem in CCVP. Instead, I calculated this effect in terms of theory. The results are shown in Table 4-2.

It can be calculated that there is approximately one degree of difference at 1 degree from the fixation point whenever the head moves forward 200 mm or backward 200 mm. However, there is a great difference at 20 degree eccentricity , particularly when the head is forward.

Table 4-2
Visual angle(min arc) of one pixel changed in respect of the unstable viewing distance by eccentricity (Standard viewing distance = 450 mm)*

Viewing distance change(mm)	Eccentricity of the pixel position (Degree) 1	5	10	15	20
-200	2.6	2.5	2.3	2.1	1.8
-100	0.9	0.9	0.8	0.8	0.72
100	-0.58	-0.57	-0.56	-0.53	-0.50
200	-0.98	-0.98	-0.95	-0.91	-0.86

* The size of pixel was 0.42 mm. The *cos* effect(Drum, 1991) was also considered. There is a trend that with increasing eccentricity, the smaller the min arc changed was made. It can be seen that increasing the viewing distance had a greater effect on the visual angle changes than reducing the viewing distance.

From a clinical point of view, if we cannot maintain a stable viewing distance, the solution may be to avoid situations in which the test results are affected by the spacial frequency of a stimulus or related to field topography. It was, therefore, decided not to test fine matrix points in the visual field. Each test location was limited to one quadrant or cluster of the field in the motion test. One location to one quadrant was thought to be enough to detect any neuron abnormality in that quadrant. Any shift in the test locations as a result of an unstable viewing distance is unlikely to move the target more than 10 degrees outside that quadrant(Table 4-1).

One test location to one quadrant of the field does not eliminate all the effects of unstable visual angle due to an unstable viewing distance(Table 4-2). Table 4-2 shows that the visual angle of the target can be still changed. To minimise the problem, I have avoided measuring the motion threshold defined by the **smallest** displacement seen which can be greatly affected by the spatial frequency or the visual angle effect, (King-Smith, 1978; Snowden and Braddick, 1990). In addition, the test loci are removed from the fixation point where the displacement interval can be easily changed when the viewing distance is unstable(**Table 4-2**). Such efforts seem to benefit CCVP application in MSST in the Nigeria study.

One might ask whether CCVP can be a topographical perimeter if it does not distinguish information from different locations in the field or indeed whether CCVP is sensitive enough to detect small visual field defects. I cannot, from my study, answer either question except that several successful applications of CCVP have shown that early abnormalities in patients with glaucoma and optic nerve disease can be detected.

4-2-3 Temporal frequency effect

There are several advantages in measuring temporal frequency in CCVP. First, it is easy to manage temporal frequency by use of the computer's real time clock(Heathcote, 1988 and Paredes, 1990). Second, the temporal frequency of a formed image on the display can be purely dependent on the computer clock if the image is not too complicated(Dihopolsky, 1983; Lollo and Finley, 1986; Greeger et al, 1990 and Paredes et al, 1990). Third, there is homogenous speed of appearance or disappearance of stimuli even if their positions on a given display are different(Bosman, 1989). Fourth, processing time events in current micro-computers, e.g., PC 286, 386 and over, and PS/2 is highly accurate (at millisecond-level) even though there are many sources of time error. This includes a video refresh rate, keyboard scanning rate, disk I/O time(Greeger et al, 1990, Segalowitz and Graves, 1990).

Finally, temporal sensitivity is less independent of spatial frequency in the visual system(Bassi et al, 1990; Bassi and Lehmkuhle S, 1990; Grigsby et al, 1991). In other words, it is relatively unaffected by the viewing distance effect which can change the spatial frequency of the size

of stimulus. Although there are no experimental results from this study to support the above advantages, the results of measuring temporal sensitivities such as MF, MST and MSST have provided some positive evidence in favour.

The disadvantage is that a motion test may not efficiently detect angioscotomas(**Fig. 3-7**) and small defects(**Table 3-9**). This suggests that the measurement of temporal sensitivity would not be sensitive for some diseases causing as focal retinal damage in the retina. For example, in ICES,the motion test was unable to detect several cases of retinopathy which were detected by Henson CFS 2000. Despite this disadvantage, it would appear that temporal frequency(motion)is useful for detecting optic nerve disease using CCVP.

4-2-4 Conclusion

Most psychophysical experiments using video displays have no direct application in the *multicontrast* environment. Either they use a dedicated testing room or a very sophisticated computer system. In this study, an essential test condition has been to emphasize effectiveness in respect of the *multicontrast* environment. To guide the further design of a standard visual function test for the use in community screening, the three general requirements for the application of CCVP stimulation are summarized:

1. CCVP should be minimally affected by contrast.
2. CCVP should be minimally affected by spatial frequency.
3. CCVP should mainly use temporal frequency.

4-3 Basic aspects of clinical application of motion stimulation

A sense of motion is a fundamental visual function beside light, and colour(Nakayama, 1985). Since motion plays so many different roles in vision, appreciation of the extent to which motion is capable of stimulating a visual response requires consideration of the psychophysical

properties of human vision(Lennie, 1980; Chang & Julesz, 1983, Bonnet, 1984; Chang, 1986; Petersik, 1989).

In theory, motion detection is more complex than a light detection (Legge and Campbell, 1981; Nakayama and Silverman, 1985; Johnston & Wright, 1985). Motion detection requires closer communication between the retinal cell and the cortical neural system than light detection(See Appendix II, Borst and Egelhaaf, 1989).

In practice, not only is motion stimulus more sensitive in detecting glaucoma defects than light stimulation(Fitzke et al. , 1988; Quigley et al. 1988; Silverman et al. 1990), but it can be more efficient than a light stimulus as a CCVP target. It is negligibly affected by pupil size and luminance (Fitzke et al, 1989); it can be relatively free from effects of contrast when a motion test is performed at high contrast level(Nakayama, 1985; Livingstone and Hubel, 1988; Derrington and Goddard, 1989; Boulton & Hess, 1990a; Bassi and Lehmkuhle, 1990) and it is less sensitive to degeneration of the optical media than a light stimulus(Whitaker and Buckingham, 1987; Whitaker and Deady, 1989 and Fitzke et al 1989) Finally, it can be less affected by refractive error, as found in this study(**Fig. 3-8**). The above results are mainly based on specific experiments with selected populations. It is still not clear whether the motion sensitivity test is efficient for use in an unselected population or in a community based setting.

4-3-1 Advantages and problems of using high contrast

Motion sensitivity is highly dependent on the contrast at a level of 15% or below(Livingstone and Hubel, 1987; Derrington and Goddard, 1989; Boulton and Hess, 1990b). It is minimally affected by contrast above 15%(**Fig. 3-2**). If we do not want a motion sensitivity test to be much affected by contrast, then the test should be conducted at the high contrast level.

There are several advantages to using a high contrast level for a motion test in CCVP. First, high contrast can reduce the *multicontrast* effect. Ambient light can easily change the contrast level in a public place(**Table 3-2**). If the contrast of a motion stimulus shifts from 10% to 15% or the reverse, the motion sensitivity test will be strongly affected, up or down (Fig.

3-2). If the contrast shifts from 15% to 32%, which is within the high contrast range, the sensitivities show little change(Fig. 3-2).

Second, there is small individual variation. The higher the contrast, the less the variation is. (Barlow 1957, 1965 and 1977; Teich et al., 1982). We have seen that there is great variation in motion sensitivity with low contrast levels(10 to 15%) but this is not so between each individual(Fig. 3-2) or between different eccentricities(Fig. 3-3&3-4) when the contrast level is high. Since different individuals have different contrast sensitivities, the actual contrast sensitivity required for motion stimuli may vary, particularly in elderly population((American Association of Optics(AAO), 1990). If we use low contrast, and also want to be free of the *multicontrast* effect, we would need to know precisely the contrast sensitivity for each individual and for ambient lighting in the room before a motion test was applied. This is not practical in a mass screening situation. It is not a new idea to use high contrast stimuli in a visual function test. Many studies have addressed the idea that in order to eliminate measurement error it is important to use high contrast(Barlow, 1957, 1977; Greve, 1973 and Barlow & Pelli, 1987).

Not all agree with this. 1) Larger ganglion cells have large receptive fields and form the principal pathway for rod signals(Bassi and Lehmkuhle, 1990), 2) clinical evidence in scotopic perimetry has supported the view that the larger ganglion cells are damaged in early glaucoma(Goldthwait et al, 1976; Drum et al, 1986; Glovinsky et al, 1990; Quigley et al, 1991). It is, therefore argued that it is very important to measure motion sensitivity with a dim background, at low contrast, in order to selectively test M-cell function(Quigley et al, 1992).

One must be cautious in extrapolating psychophysical findings related to M-cell function to real clinical situation. In this study, I found no evidence that the motion test only tests the M-cell function. I also found no evidence that M-cell function is specifically affected by either glaucoma or other optic nerve diseases. Others(Folkert et al, 1992) have not supported the idea that the scotopic background and low contrast are essential for improving the sensitivity of the test as Quigley suggests(1991). I can assume that there is not only a high sensitivity for the motion sensitivity test in detecting glaucoma but also for detecting optic nerve

diseases(Abiose et al, 1993) which may be influenced by M-cell function while an ordinal visual function test was still normal. However, this should be also affected by P-cell function which I will describe later(**see Fig 4-1**).

4-3-2 Eccentricity

Most measurements of visual sensitivity show a decline with retinal eccentricity. The sensitivities for contrast, binocular disparity, vernier offset, colour and spatial resolution are all highest in the parafoveal region (Fendick and Westheimer, 1983; Westheimer, 1983 and Johnson et al. , 1978, 1979 and 1980). There has been occasional speculation that the periphery might be particularly sensitive to motion, but absolute motion thresholds rise with eccentricity(Johnson et al 1985). This is comparable to the change which depends on the spatial frequency involved (Tyler and Torres ,1972; Johnson and Leibowitz, 1976 and Post et al 986). It has been shown that thresholds for displacements with high spatial frequency, in terms of the smallest displacement interval, rise faster with eccentricity than visual resolution thresholds(Livingstone and Hubel, 1987).

Conversely, when measuring low spatial frequency(the maximum of displacement threshold) the threshold reduces as eccentricity increases(Wright et al., 1987). Levy-Schoen(1977) has reported that there is increasing homogeneity of the visual system for larger stimulus sizes as a function of eccentricity. Johnson and Scobey(1980 and 1982) indicated that motion sensitivity improved with increase in line length in the periphery but not with foveal viewing after they observed the smallest displacement threshold as a function of the length of moving line stimulus presented either foveally or peripherally.

More recently, Wright et al(1985) suggest that displacement threshold is essentially independent of eccentricity if the stimulus size is scaled such that the number of stimulated ganglion cells or the size of stimulated cortical areas is almost the same at any eccentricity. In addition, Wright(1987) suggests that the displacement sensitivity can be similar in the centre and in the periphery if the measurement is made by a low spatial frequency grading system.

These findings justified my aim to have a homogenous motion sensitivity across the 21° central field by using different lengths of the bar, and by measuring a large displacement interval. However, the question of the size of line in respect of eccentricity remains. The grading system of the line in this study was mainly based on the resolution of the display. Thus we cannot exactly follow the spatial frequency grading system in the visual system(Wright et al, 1985).

Finally, **Fig. 3-3, 3-4** demonstrate that there were larger intra-test variations as a function of eccentricity in the contrast **Sensitivity Stage** than the contrast **Saturation Stage.** There was no homogenous motion sensitivity across the central 21° field until the contrast reached the **Saturation Stage.**

From a visual science point of view, it is unclear whether this homogenous motion sensitivity across the central field is due to a "suprathreshold" stimulus; in other words, that the intensity of the motion target is too strong to demonstrate small differences between the central and peripheral fields (Leventhal et al. , 1981; Perry et al. , 1981, 1984). Alternatively, the problem may be due to the small sample involved in this part of the study. Despite the above arguments, from the point of view of an efficient screening test, it is important to have a uniform target in order to have a simplified test procedure(Greve, 1973).

4-3-3 Age-related motion sensitivity

Visual function, whether measured by acuity, colour vision, or automated perimetry, has been shown to decline with age. However, the findings from histological studies are conflicting(Glooratapper, 1950; Weleber, 1981; Hess, Flammer and Schneider, 1986, Morrison et al, 1990 and Balazsi et al, 1984). Although previous anatomical studies suggest that there is a linear decline with age in the number of optic nerve fibres, only two studies have demonstrated that this change is statistically significant(Devaney and Johnson, 1980).

Repka and Quigley attempted to determine whether there is a selective loss with age of optic nerve fibres of certain sizes in humans(Repka et al, 1989). There was a statistically significant trend of reduction of the diameter of the optic nerve in elderly people($p < 0.01$). Older people

seemed to have relatively more small fibres and fewer large ones. They suggested that there may be a selective loss of large fibres in that population.

Recently, with a computerized counting system, Morrison et al(1990) have assessed the effects of age on the optic nerves of 28 rhesus monkey eyes. The conclusion was that age did not have any significant effect on mean axonal diameter even though there was a slight increase in diameter in elderly monkeys, and even though there was a slight decline of axon number with age, this was not statistically significant.

Minckler has reported that age related ganglion cell loss is 689,500 per year but it is mainly from small ganglion cells. The proportion of large ganglion cells can increase with age(Minckler, 1991). These findings support the view that visual acuity begins to decline after age 50(Greene and Madden 1987); the magnocellular system function is expected to be less affected. Moreover, Tyler(1991) has reported that elderly people had improved sensitivity in low spatial contrast.

Few experiments have observed the relationship between age and motion detection. It has been shown that motion sensitivity, defined by the displacement threshold, is age-related (Buckingham et al, 1987 and Shilds et al 1992) but the results were based on the smallest displacement threshold. This is not surprising, because Owsley(1983) has suggested that if one carefully eliminates the visual acuity factor, most visual function tests show no tendency to decline progressively with age. This could be demonstrated in contrast sensitivity function with the lowest spatial frequencies(Owsley et al, 1983), flicker sensitivity with high temporal frequencies(Tyler et al, 1991), and electroretinography for scotopic a-wave amplitude(Weleber, 1981, Wright et al, 1985).

There is strong evidence that the higher the spatial frequency the higher the likelihood of an age effect. From the point of view of a screening test, if one wants to eliminate the age factor, the smallest displacement amplitude which is dependent on age(Table 3-4) should not be included. This does not mean that we should not test the smallest displacement interval under well controlled testing conditions such as at a research centre or a hospital based setting.

4-3-4 Fundus features

The blind spot in the visual field is caused by the optic disc. The average horizontal diameter of the optic disc is 1.61 mm. and the average vertical diameter is 1.79 mm.(Duke Elder, 1938). If 1 mm. on the retina corresponds with 3.6 degrees in the visual field(Fitzke, 1985), the average diameter of the blind spot should be 5.8° in horizontal diameter and 6.4° in the vertical diameter. The blind spot measured by conventional perimetry has nucleus of absolute intensity loss surrounded by a margin of relatively reduced light sensitivity.

It has been said that the margin surrounding the nucleus is due to angioscotomas (Greve, 1973). The size of the margin shows high individual variation and depends on the method of measurement(Gramer et al, 1979). However, the actual blind spot size varies from 7.5 to 10 degrees depending on stimulus size(Armaly, 1969) and testing procedure. Bek and Lund-Andersen(1989) showed that a nucleus of absolute loss of sensitivity in a blind spot can be fully replaced by the margin when the largest size of stimulus(Goldmann V) was applied.

In this study, the main findings may be summarized as follows. **Fig. 3-5abc** demonstrate the blind-spot detected by using different parameters, and different methods in relation to motion stimuli. The larger the border of the blind spot, the larger were the variations in the measurements made. With a variable stimulus length, the nucleus of the blind spot clearly appeared. However, when other parameters were used (e.g., variable contrast and variable displacement interval) the right size of the nucleus of the blind spot did not appear. The large border of the blind spot cannot simply be due to the stimulus overlap, which is shown in the **Fig. 4-1**. With increasing bar length, movement cannot be seen until the bar is seen(**Fig. 4-1A**). With increasing contrast, the movement can not be seen until the contrast is over 15%.

However, if there are substantial variations in low contrast(**Fig 3-2**) a large border around the nucleus can be expected. **Fig. 4-1C** shows the fact that increasing the displacement interval does not always result in an increase of the intensity of displacement stimulus. It can be seen that the intensity was not increased until substantial part of the bar stimulus fell outside the region of blind spot. This phenomenon could occur when the visual field already has many

absolute scotomas. In such a condition, the motion test is substantially affected by local retinal sensitivity rather than measurement of the conduction speed.

It is unclear why the border was so large when the motion sensitivity test was based on contrast sensitivity. The wider border of blind spot area could be due to the reflection from the optic head of the light source, when one input was located in the retinal area and an other input located at the optic nerve head (Bek and Lund-Andersen, 1989).

For the stimulus with variable contrast sensitivity, in which there were no overlapped stimuli, a large border around the nucleus of the blind-spot appeared. This suggests that measurement of contrast sensitivity may have more variation than measurement of spatial frequency motion tests.

Where there are substantial variations in low contrast(**Fig. 3-2**) a large border around the nucleus can be expected. **Fig. 4-1C** shows the fact that the intensity of motion stimuli did not always increase with a greater displacement interval.

None of the motion stimuli can distinguish the course of angioscotomata(**Fig. 3-7**). A low density stimulus pattern is an unlikely explanation for this finding because the course of the retinal vessels has been clearly demonstrated by light stimulation using the same stimulus pattern(**Fig. 3-6**). It is also unlikely that the large variation was due to pathology because other types of motion stimulus did not show any abnormality.

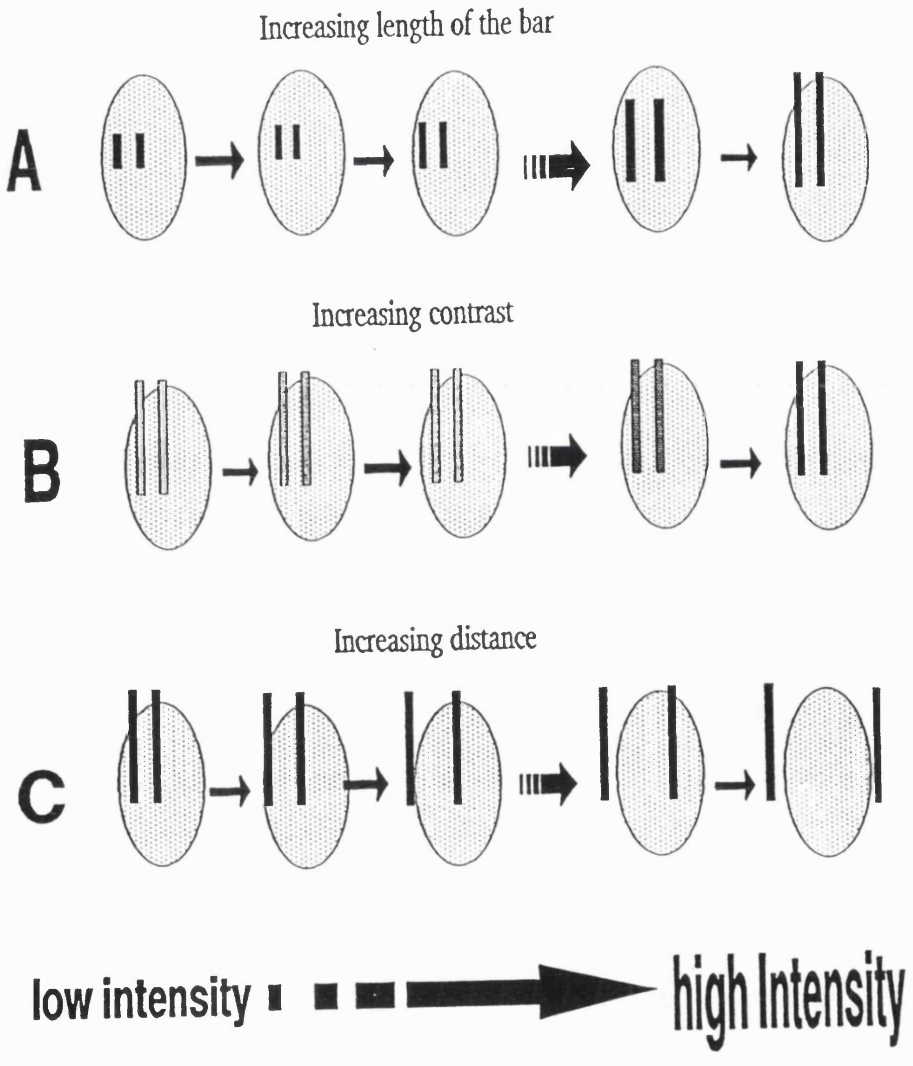


Fig. 4-1 Dynamic range of testing area

The steps of increase of motion stimulus size are not even when the length of the bar increased, the contrast and the displacement interval of the motion stimulus are increased. For an increasing length of the bar, the movement could not be seen until the bar is seen(**Fig. 4-1A**). For an increasing contrast the movement could not be seen until the contrast is over a given point(**Fig. 4-1B**). For increase of the displacement interval the movement could not be seen until the bar is seen(**Fig. 4-1C**).

The reason for failing to detect the course of vessels may be either the relatively high intensity, or the large stimulus used when I used the maximum contrast or the longest bar in this part of study. The finding that motion stimulus was not effectively detecting angioscotomata by the use of variable intervals or bars may, however, simply reflect lack of systematically observing the relationship between the fundus feature and the characteristics of motion stimulus. I have no real explanation for this finding, other than to accept the assumption that a large stimulus with high contrast may reduce the sensitivity of detecting a relative scotoma.

Furthermore, it can be seen that there was an inconsistent retinal effect on the right side of Fig 3-7b where there were several vessels(Fig 2-2). The motion sensitivity was reduced. This indicated the motion sensitivity may be affected by the vessels. If a displacement threshold can be affected by retinal vessels, it implies that the displacement interval will be affected by light sensitivity in some situations. Therefore, M-cell function measurement will be certainly influenced by light sensitivity. And, light sensitivity loss, and perhaps other causes of incomplete receptor function, such as media opacity, must be expected to influence M-cell function measurements(Turano and Wang,1992). Turano and Wang(1992) suggested that the elevation of displacement sensitivity can be caused from the photoreceptor dropout, particularly using a minimum amplitude of motion.

As stated in an earlier section, it is important to correctly select the parameters used for motion stimuli, which can eliminate the effect of light sensitivity and isolate motion sensitivity from other visual functions. I therefore ceased to measure the minimum motion sensitivity based on the minimum displacement interval.

Based on experimental data(**Fig 3-6** and **Fig 3-7**), it is clear that understanding the basic characteristics of the motion stimulus in clinical circumstances is essential. It is important to be careful in selecting the parameters for the motion stimulus. I found that the choice of parameter of stimulus is important in motion stimulation as is commonly inferred from perimetric studies involving the processing of light stimulation (Greve, 1973; Heijl, 1983ab, 1987ab, 1989ab and 1991ab).

4-3-5 Conclusion:

1. Motion sensitivity is less dependent on the *multicontrast* environment if the test contrast is at the Saturation Stage.

2. A relationship between motion sensitivity and age was not found when the smallest displacement intervals were excluded.

3. With the aid of high contrast and a scaled length of bar corresponding to eccentricity, and excluding the minimum displacement magnitude, homogenous motion sensitivity across the central field can be obtained.

4. The motion stimulus may not be as effective in detecting a small focal defect as a light differential test.

4-4 Motion sensitivity test in glaucoma detection

It seems that the test location effect, the learning effect, the fatigue effect and the age effect in motion sensitivity could all be aggravated by selecting a small amplitude of displacement as the motion target(Table 3-4 and Table 3-5). In other words, if the small amplitudes are not included, those differences due to age, eyes and test locations could be reduced. This potential property of motion stimulus was one important advantage to simplify visual function tests without common problems found in light differential test.

4-4-1 The Sensitivity

Quigley's findings that early light sensitivity loss cannot be found unless the defect is at least 5 dB or when more than 20% of the total ganglion cell fibres have been lost(Quigley et al.,1989), suggests that a 4 dB sensitivity loss corresponds to 10% cell death(Fig. 4-2). 10% ganglion cell death could mean very little if it is compared with large variations in the total ganglion cell population in normal individuals(Devaney and Johnson, 1980).

Supposing 10% cell death was predominantly M cell(large ganglion cell), there would be substantial M cell function loss, such as absolute motion sensitivity loss, because only 10% of the optic nerve fibres are M cell axons (Leventhal et al. 1981; Perry and Cowey, 1981; Kaplan and Shapley, 1982). By analogy, it would be expected that the M cell function damage would be detected more efficiently than P cell function damage. In fact, in this study, there was only 45% of abnormal motion sectors with light sensitivity loss of 4 dB. This indicates that either the motion sensitivity test cannot always predict early visual function damage or M cell axons were predominantly damaged in glaucomatous optic atrophy. At this stage, it is not possible to assess these two alternatives. It is not surprising that motion sensitivity is not as sensitive as expected.

Firstly, there is no evidence to show that all early damaged optic fibres are large ganglion cells, even in the monkey model(Quigley and Hendrickson, 1984). Secondly, there is no evidence to show all human glaucoma has the same mechanism as the monkey model. Thus, caution

is needed. If human glaucoma does not have predominately M-cell function damage, the motion test will still be normal.

According Fig 3-12, it seems likely that motion tests identify people with optic nerve fibre loss but not ocular hypertension. There were a small number of hypertensives with abnormal motion sensitivity(Fig. 3-12). The finding here that there was a low sensitivity to OHT is in disagreement with other studies(see section 1-1-1). The reason for this is unclear. It may reflect lack of power because of the small number of hypertensives,few of whom may progress to glaucoma.

Finally, I ask whether there is any residual retinal ganglion cell death not detected by the motion sensitivity test? Can we find a more sensitive test than motion sensitivity test? The question addressed here anticipates the problem relating to a "gold standard." If a new test has reached the sensitivity which is greater than old test, it might be difficult to find a "gold standard" test to prove the new finding.

The definition of visual impairment recommended by The World Health Organisation(1973) does not effectively recognise that people with 0.3 visual acuity have already lost 95% of their normal channels(Frisen, 1980). A recognized visual field defect in automated perimetry in the central field needs 50% of the ganglion cells to be damaged (Quigley et al, 1989). Therefore, it is to be expected that many cases would be abnormal with motion sensitivity, but not with these old tests.

On the other hand, motion sensitivity could be normal because there is no evidence to show all early glaucoma is associated with M-cell damage. It could be expected that the motion test will miss cases in which only P-cells are damaged. In order to determine the real validity of motion sensitivity to early detection of glaucoma, a long term follow up study(Poinoosawmy et al, 1992, Wu et al, 1993) is required rather than just comparing it with the light sensitivity loss in a cross sectional study. Because cases of glaucoma found in RGS and ICES were so few, one is limited to making further conclusions(Wormald et al, 1992 and Coffey et al, 1993). The question of the real sensitivity of the motion test to early glaucoma therefore remains in

this study.

4-4-2 The specificity

It is not surprising that the sensitivity of MST was 100% for detecting glaucoma when MST was applied in the two surveys, namely ICES and RGS. According to the conservative definition of glaucoma in these two surveys(Wormald et al, 1993; Coffey et al, 1993), all glaucoma cases have substantial visual field defects. These were defined by conventional visual field tests(see **Table 2-6**). Since the motion sensitivity test may have high sensitivity in patients with early glaucomatous defects, which was proven in the hospital based study, there is no question that MST can detect these glaucoma patients with advanced defects.

In undertaking a community-based survey for visual field impairment, an efficient, fast, sensitive, specific and easily administered test is required. The specificity of a clinical test is influenced by the choice of cut-off criteria and efficiency of the test. In this study, because The Henson CF2000 was used as the "gold standard" test during the surveys, the sensitivity was determined by the Henson and may be of little relevance to real motion sensitivity. The specificity of MST could be also affected when I reduced its sensitivity in order to achieve the same sensitivity as Henson. One must be cautious in transferring the specificity of MST found in this study to other clinical situations. Many very elderly subjects had a problem pressing the response key. They might press the response key before a stimulus were presented or after next stimulus was presented. This may reduce the fraction seen for the motion test and increase the false positive rate. Clearly, this problem will be limited when such elderly people are few in a general community-based screening situations.

The fact that 27(52%) cases among the 52 people with abnormal MST had evidence of glaucoma, suggests that MST has a high false- positive rate for glaucoma, and that other factors also cause abnormal motion sensitivity.

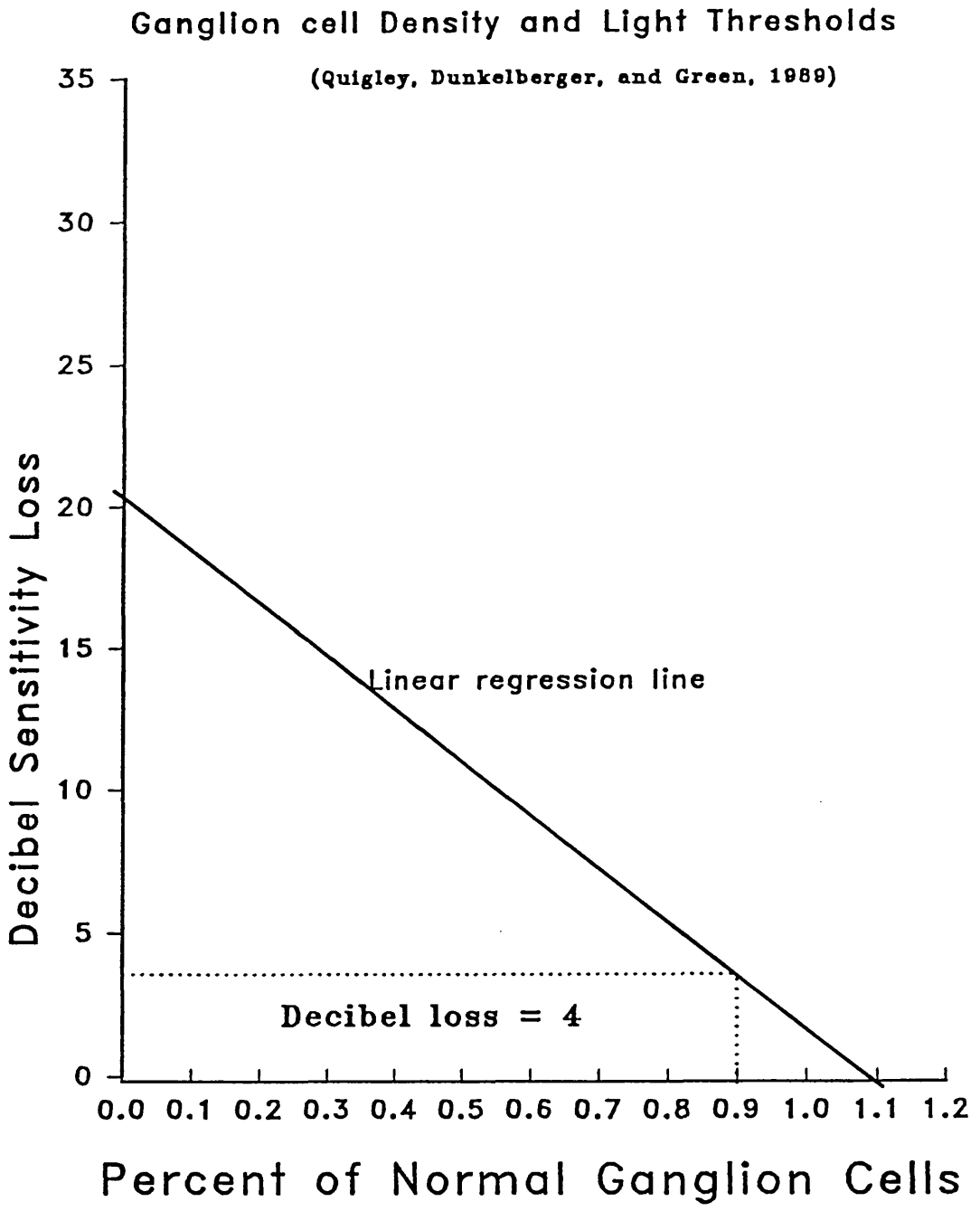


Fig. 4-2: Correlation between the decibel loss and motion loss

Although absolute motion sensitivity loss(motion-blind) is extremely rare(Hess et al., 1989), several examples of reduction of motion sensitivity due to other ocular disorders have appeared in recent clinical reports. Whitaker (1989) has found that the displacement threshold was correlated with poorer acuity levels ($r=0.37$ $p<0.05$) but it had a very weak correlation with the grade of cataract($r=.32$ $p<0.1$).

Trick and Silverman(1990), and Gary et al(1990) have observed patients with Alzheimer's disease who have optic nerve damage(Sadun and Bassi, 1990). All the patients had motion detection loss at an early stage. Koth et al(1990) found that multiple sclerosis patients had abnormal motion sensitivity, and Watkins et al(1991) suggested that there is substantial loss of motion sensitivity in other causes of optic neuritis. Ziel and Schmeisser(1990) report that some cases of amblyopia show apparent temporal frequency loss and Bassi and Lehmkuhle(1-990) further suggest that amblyopia could cause motion sensitivity loss when other visual functions remain normal. This was the case in the present study when 67% of people with amblyopia had abnormal MST.

The findings in the Nigerian part of the study show that more than 80% of Nigerian people with more than 10 mf/mg had abnormal Motion sensitivity. The majority of people(89%) with less than 10 mf/mg seems to have no motion sensitivity loss. I have no explanation for this finding but, it is clear that motion sensitivity loss is not only due to glaucoma or established optic nerve diseases.

Finally, it would be interesting to see whether there is a specific pattern of motion loss when glaucoma is compared with other disorders. This aspect has not been fully investigated at this stage. With the limited number of early glaucoma patients involved, no pattern of motion sensitivity loss that was specific for glaucoma could be detected. The types of MST loss in a patient with a diagnosis of glaucoma were similar to MST loss measured in a patient with serious cataract or a posterior segment disorder. Detailed analyses with targets of different displacement interval, or at different retinal eccentricities may help distinguish between various causes.

All this suggests that the motion sensitivity test cannot simply be considered as a diagnostic test alone. In other words, a patient with abnormal motion sensitivity cannot automatically be diagnosed as glaucoma but also necessarily cannot be treated as a "false positive."

In summary, the motion test, like many other psychophysical tests should "never be interpreted in the absence of other clinical information"(Caprioli, 1991). We have to bear in mind that motion sensitivity loss cannot just be considered as due to glaucomatous damage. The motion test with its high sensitivity, may be good as a case finding procedure to exclude patients with a glaucoma risk.

4-4-3 The acceptability

In order to have an objective standard test for assessment of the acceptability of a visual field screening test, the Henson CF2000 was considered in this study because it is a reasonably fast test, acceptable for every one and suitable as a screening test (Marraffa et al, 1989; Patchett et al, 1989; Martone et al, 1990; Vernon et al 1990ab; Costagliola et al 1991 and Brady et al, 1992). In trying to compare the acceptability of the two tests, I calculated that the two tests had the same sensitivity and specificity. There were conflicting results on the validity of the Henson from the literature review(**Table 4-3**).

Although there is no established definition of glaucomatous visual field defects for the Henson. The Henson provides two quantification systems to indicate the result of each examination(Henson, 1986). The results may simply reflect the choice of cutoff criteria for visual field defects. Therefore, I decided to find out what objective criteria gave the optimal interpretation from the Henson instrument. I also eliminated the operator factor because a testing procedure of the Henson can be easily affected by a different operators. In order to avoid the operator effect, the Henson data was drawn from two linked studies (ICES and RGS) where the tests were performed by two well trained operators.

Table 4-3. Sensitivity and Specificity for Henson CFS2000

Author	year	Eye	Sensitivity	Specificity
Henson et al+	1991*	?	92%	93%
Henson et al+	1986	91	90%	88%
Martone et al+	1990	92	78%	94%
Marraffa et al+	1989	182	59%	88%
Patchett et al+	1989	99	40%	100%
Vernon et al&	1990	855	25%	91%
Costagliola et al+	1991	710	66%	100%
Brady et al&	1992	123		95%

*: Definition of Visual field defect is of 2 or more absolute defects or 4 relative defects in any single quadrant

\+ Case finding test

& Screening

I assumed that the lower sensitivity found by other users(Vernon et al, 1990a) could be caused by few test locations. I, therefore, used data only from the test program with 132 points. The average time for the 132 locations testing program is 5 to 8 minutes per eye, which was the same test time for performing one motion test. With such efforts, it is not surprising that there was no statistical difference between the two tests in terms of AUC (Fig. 3-16).

Under these situations, the results from this comparison cannot really estimate the validity of both tests in mass screening for early detection of glaucoma. Many advantages of CCVP(motion test), such as a low cost, easy administration and full automation were not taken into account in the comparison. The equivalent testing time in both tests was the subject. However, the point stressed here is that the motion test in CCVP can have the same acceptability as the Henson when it is applied in an epidemiological survey. Elderly people had no substantial difficulty in performing CCVP.

4-4-4 Conclusion

1. It has been estimated that almost 50% of retinal locations which have a 4 dB light sensitivity loss show abnormal motion sensitivity. A motion test which measures conduction speed has low sensitivity to ocular hypertensive patients.

2. There is no specific pattern of motion loss for glaucoma as defined by the motion test. Other diseases such as cataract, amblyopia and optic atrophy may also cause an abnormal motion sensitivity.

3. The measurement of motion sensitivity cannot provide a diagnostic test for glaucoma but normal motion sensitivity indicates that a standard glaucomatous visual field defect(more than 5 dB loss) can confidently be excluded.

4-5 Methodology of Motion Sensitivity Test

4-5-1 Single Amplitude Trial

In principle, any visual psychophysical test is safe. This is one reason that visual function tests have been commonly used for mass screening, for example visual acuity, colour, and visual fields. However, a psychophysical test is a subjective measurement. The endpoint of the test is not directly found out. For this, a threshold test is usually required, but this is time consuming(Green et al, 1966). In research laboratories, the displacement threshold test is usually done using a constant stimulus on a cathode-ray tube. With this strategy, a motion threshold can be measured at as many closely-spaced spatial frequencies as desired beyond the hyperacuity range. The sensitivity plotted as a function of the displacement interval gives the threshold that is required to estimate 50% correctly seen. It is also possible in a research laboratory or hospital clinic, to use good psychophysical procedures(e.g., a two-alternative forced-choice or a four-alternative forced-choice staircase method, with randomly interleaved stimuli of

different intensity). But extra time is required. For laboratory based observations, there is no doubt that these are psychophysically "correct" methods for obtaining a displacement threshold or motion sensitivity.

However, for clinical application, particularly in a rapid screening test, there is debate whether we should adopt the methods of measurement which have been successful in the research setting. Four major factors undermine the use of these methods outside the laboratory. First, subjects find it difficult to report on faint, near-threshold stimuli(Green, 1966). They might say "no" to seeing stimuli that fall below 90% of points on their underlying sensitivity function. Second, they are not trained, highly motivated psychophysical observers who may be very cautious in their responses (Fletcher et al., 1982). Conversely, a positive labelling effect may occur when a patient is told that if the test is abnormal, treatment will follow. Third, a visual field screening test usually requires 2 to 5 minutes per eye(Keltner and Johnson, 1983). To satisfactorily estimate one single threshold by traditional strategies, e.g., constant stimuli or the stair case method, more than 60 trials are needed(Johnson et al, 1992).
Finally, fluctuation is a common problem existing in all threshold tests involving psychophysical methods, whether the constant or adaptive method is used(Swets and Tanner, 1964; Enoch et al, 1990). The current testing strategy applied in light differential tests in automated perimetry has not been satisfactory in providing an efficient visual field test(Heijl, 1989d, 1990): One of the major problems is ignored - namely, short term fluctuation of the threshold in light detection(Lynn et al, 1986).

Werner and Drance(1977) first noted a relation between fluctuation and glaucoma. They investigated one glaucoma patient who was initially ocular hypertensive for ten years. The visual field defects developed several years later. They concluded that the increased fluctuation of the threshold may be an early sign of glaucomatous damage. In 1984, Flammer et al (1984)reported that the earliest detectable change of glaucoma was short term fluctuation when they used automated perimetry. These findings were confirmed by other studies(Heijl et al, 1986, 1989b, 1990; Werner et al 1977; Flammer et al, 1983, 1984; Whalen, 1985). It has been suggested that the threshold fluctuation in early glaucomatous visual field defects can range between 0 dB and a normal value (> 20 dB) during an individual test(Heijl et al, 1987b).

It is unclear how the frequency of these short term fluctuations is distributed during a given period. A staircase testing strategy, cannot determine these short term fluctuations(Krakau, 1990). As a result of such large fluctuations during the test, it is difficult to assume that the threshold at a given point is stable for a conventional testing strategy(Lynn et al, 1986).

The single amplitude trial(SAT) takes the fluctuation into account when there is no attempt to determine the threshold in its measurement. The assumption in SAT is that, for a normal observer, there is such small fluctuation that the response to the given amplitude will be constant; for an abnormal observer, it either cannot be seen at any time or is unstable, and sometimes can be seen, sometimes not. The unstable status is considered as a sign of the abnormality for whatever reason. The fraction of motion decreases if the motion is not always seen.

Another advantage of using SAT is reduction of measurement noise. Swanson et al(1990) studied the effects of extraneous noise on threshold estimates from 306 healthy, untrained infants. They found that the measurement of threshold is particularly difficult when the"frequency-of-seeing" has a shallow slope and the number of trials is small at a constant stimulus. They reported that the stair-case is limited in its effectiveness when there is substantial extraneous noise. They used a suprathreshold stimulus under a "Free" trial, which is similar to the Single Amplitude Trial in this study, in order to try and protect against extraneous noise. The result suggested that when extraneous noise is large the precision(standard deviation of the estimate) is better with a "Free" trial than with other testing strategies, although the accuracy is slightly worse. When considering a mass screening programme, it is anticipated that there will be more noise than when the test is performed by trained patients in a hospital. The SAT should be used in a screening test situation to minimise measurement noise.

4-5-2 Optimal parameters for a screening test

Size of stimulus

Fig. 3-10 demonstrates that the optimal amplitude is at 4 pixels(8 min. in arc). Interestingly, neither the smallest displacement interval nor the largest measured as number of pixels demonstrated the highest power for discriminating between normal and glaucoma in terms of ROC curve analysis. As reviewed earlier, elderly people tended to have loss of visual acuity through small ganglion cell degeneration, loss of contrast sensitivity through media opacity, and increased visual blur through loss of accommodation. All of these optical dysfunctions can somehow interact with given amplitude of motion stimulation. However, a large displacement interval would be expected to be less affected by early cataract which causes high frequency loss(Hess and Woo, 1978).

My findings indicate that the use of a large displacement interval reduces the sensitivity but increases the specificity. This suggestion has been partly supported by Wood and his colleagues(1992). They developed a versatile random dot motion test on the Macintosh II computer with 0.35 mm white dots on a dark background. The dots were displayed across the entire screen, but the motion dot pattern was restricted to the central 1.5° area. The viewing distance was at 6 meters. The minimum displacement threshold and the maximum displacement threshold were measured in 18 glaucoma patients, 20 glaucoma suspects and 24 normals. Their results show that testing the minimum displacement threshold can be statistically significant in discriminating between the glaucoma patients and the normal($p < 0.001$). In contrast, testing the maximum displacement threshold seems to discriminate less well between glaucoma and normal($p < 0.05$) but with less variation.

Number of trials

The initial aim was to determine the optimal number of trials to be used in this study, which would detect the abnormalities exhibited by patients with diseases of the optic nerve and pathway(Enoch et al, 1981) in the least amount of time. The findings from the optimal number of trials from the hospital based setting of the present study did show that there was slight improvement of discriminating power as the number of trials increased but it was not statistically significant in terms of AUC(see section 3-4-5).

This is in disagreement with many previous studies on fluctuation and fatigue in glaucoma(Flammer et al 1984,and Heijl 1990) but it is in agreement with Enoch's study(1981). The reason for a non-significant time related motion threshold may reflect small the sample size or that the test time was not long enough to show this function.

The findings of the community-based study in Nigeria did show a statistically significant reduction of motion sensitivity related to the number of trials, in people with high risk of optic neuritis in the meso-endemic onchocerciasis area (3-5-2). People with optic neuritis have appear to have a marked fatigue effect in motion sensitivity during a prolonged test(**Table 3-16**), the greater the number of trials the higher the motion loss with OND. This was less obvious in the non-endemic area(**Table 3-16**).

The mechanism of the fatigue effect has never been clearly explained since Enoch first reported it in 1979 but it is common finding in optic nerve diseases(Enoch, 1981; Hess and Plant, 1986). With a traditional Flashing Repeat Static Test, the test time needed to detect fatigue , is usually more than 5 minutes at one location(Enoch, 1981). This would not apply for a rapid screening test in which multiple-locations are tested. However, an early visual fatigue-like effect was exhibited in patients with optic nerve diseases in my study after 5 trials in each location. This may suggest that the minimum number of trials should be 5 for screening for OND in such endemic area(Wu et al, 1992/1993).

Another main purpose of increasing the number of trials in a psychophysical test is to reduce the amount of measurement error(Klein and Manny, 1989; Swanson and Birch, 1990). If patients show less cooperation than normal, one would not expect any improvement in detection rate with an increase in the number of trials. This explains the finding that there was no significant difference between the number of repeats in glaucoma patients but not in the general public in Nigeria. This could be attributed to several other factors; for example the use of "professional" observers under well controlled testing conditions or because the majority had undergone different motion threshold tests many times(Fitzke et al, 1987). Many normal controls or Nigerian farmers had no more experience of the motion sensitivity test than the patients had.

Number of Test location

The arcuate scotoma was found by Bjerrum one century ago. Localized variation with a small cluster of points that differed from their neighbours by more than 2 or 3 dB, has been widely accepted as representing an early glaucomatous visual field defect(Hoskins et al, 1989). The development of modern automated perimeters achieves detection of more than twice the number of such early defects than manual perimetry(Heijl, 1991a). Perhaps, one fundamental advantage of using automated perimetry is to find small scotomas. However, King et al(1986) has indicated that automated perimetry can still miss 20% of small scotomas because the distance between two test locations is not small enough(6 degrees).

The statistical probability of identifying 4° defects when using a standard testing pattern (6° testing loci) is only 35%(Fankhauser and Bebie, 1979). Therefore, it has often been thought that the poor sensitivity might result from an insufficient test point density, and scotomas could be missed between tested points (Greve 1973; Gramer 1979 and Lieberman and Drak 1987). It has been debated whether it is possible to increase the number of retinal points tested in order to improve detection of early defects(Rabin and Kolesar, 1978; Henson, 1988). According to these investigators' suggestions, by optimizing distribution of test locations in the area where defects most often appear, the number of test locations can be reduced.

It is well known that a small defect is not specific to glaucoma. It is fully documented that a small scotoma can be caused by chorioretinal lesions(Harrington and Drake, 1990), optic disc lesions, optic nerve lesions e.g., ischaemic optic neuropathy(Hess and Plant, 1986) and angioscotomas(Greve, 1973). Therefore, people with small defects without other abnormalities cannot be classified as glaucoma(Heijl et al, 1989d). Nevertheless, there is a trend towards higher density of testing points in order to find such relative scotomata, "in an attempt to find the earliest glaucomatous scotoma"(Whalen et al, 1985).

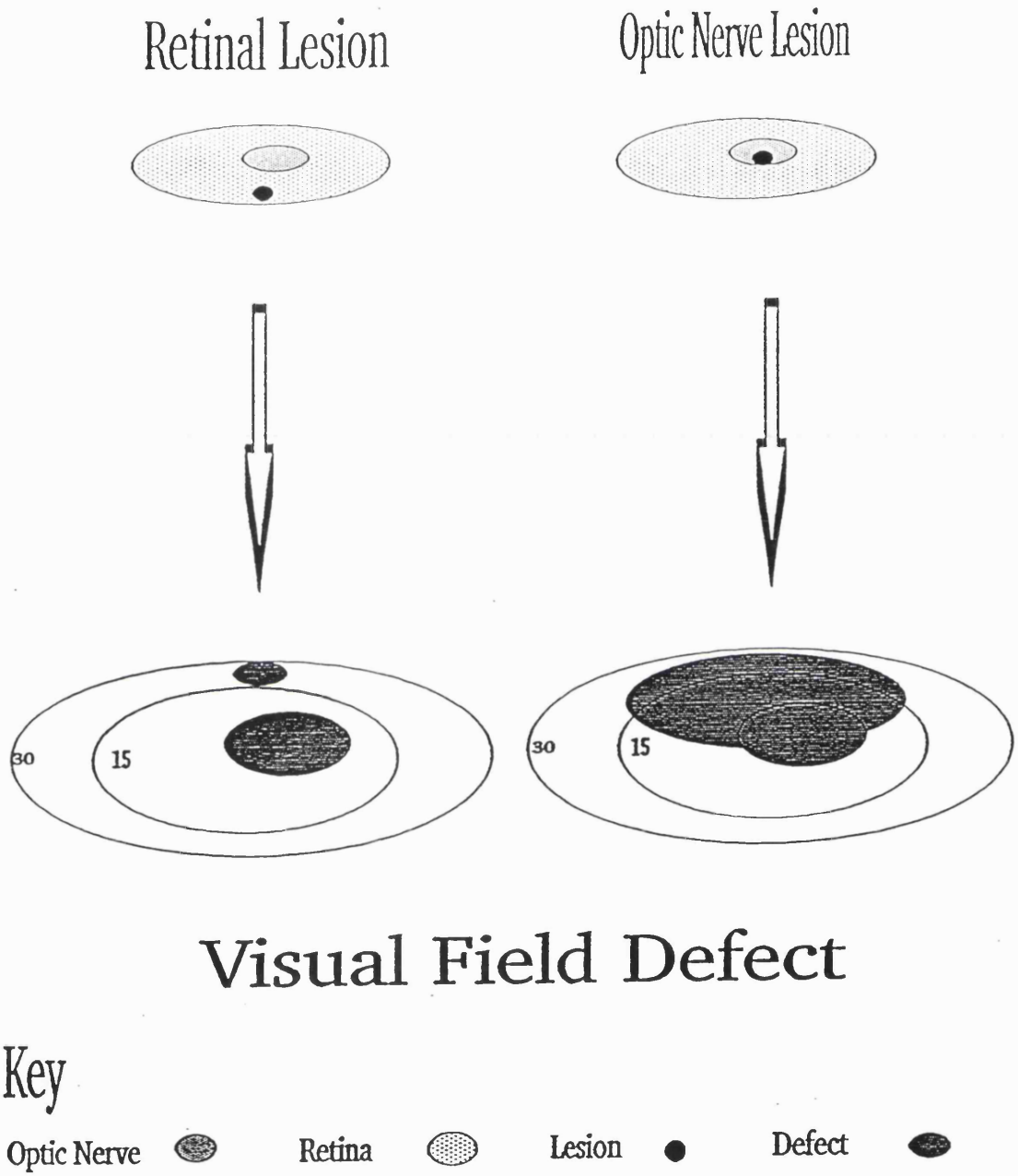


Fig. 4-3 Basic differences of scheme of detection between retinal lesion and optic nerve lesion in visual field test

higher levels of the neurological system (Henson et al, 1988). As the diameter of the scotoma becomes smaller the chance of detection decreases. Greve(1973) stated that in the 30 degree field, with 150 locations and 10′ stimulus diameter, the chance of detecting a 6° scotoma is 100% but the chance of detecting a 1° scotoma is 5.7%.

In contrast, if the visual field defects are due to lesions of the optic nerve, no matter how small the damage in the optic nerve, the size of corresponding defects will rarely be smaller than the blind-spot because the distribution of ganglion cell axons passing through the same area of the optic disc spread widely from the centre to the periphery(Minckler 1980; Minckler and Ogden 1987). An involved area of damaged optic nerve corresponds to a much larger visual field than an equivalent area of damage in the retina(**Fig. 4-3**). Therefore, it may not be necessary to have many points to detect a neuro-ophthalmological disorder(Haley, 1987).

The current evidence from histological studies suggests that the earliest pathological lesion in glaucoma seems to be slight to the optic nerve damage (Minckeler and Ogden, 1987) not of lesions at the retinal level(Anderson et al, 1974). One would therefore expect more diffuse defects in a large receptive field.

However, there is no evidence that all glaucoma patients have diffuse defects. Although Quigley et al(1988a) found that the optic nerve is "entirely" damaged in an early glaucomatous eye, I found no evidence to show that motion sensitivity was entirely abnormal regardless of location. One test location would not be sufficient to give a sensitive test for early glaucoma detection(Quigley 1989; Heijl, 1991a). Asymmetry of motion loss between hemifields further suggests that multiple locations in different hemifields in the entire central field might raise the rate of detection of loss of motion sensitivity. It is important to test at least two hemifields, or four quadrants, even though the field size related to motion defects is unknown.

To date, we do not know exactly the distribution of M-cell receptive fields in the human being. One is unlikely to be able to detect a motion sensitivity scotoma as small as the blind spot in size,because the M-cells are diffusely distributed throughout the entire field. A topographical change of visual field may be an unlikely finding in M-cell function loss.

If the motion test is dominated by M-cell function, the variation of visual function from measuring large receptive field function will be expected to be less than when measuring small receptive fields(See table 1-3). Because the distribution of M-cells is uniform, uniform motion sensitivity across the fields might be expected(Fig 1-1). When the receptive field is large, the necessary number of test locations can be reduced.

In summary, traditional *glaucoma* field screening is intended to detect small scotomas. One argument against this philosophy is that the earliest visual dysfunction in a glaucoma patient may be diffuse, at least as far as M-cell function is concerned. I cannot verify whether there is diffuse damage to M-cell function since I did not systematically address this question. The current criteria for abnormal motion sensitivity were highly influenced by data from patients with established glaucoma. Despite this, the same sensitivity was found in the motion sensitivity test, with only 12% of test the locations used in current screening tests. This may indirectly indicate that it is more efficient to measure M-cell function than P-cell function in glaucoma patients.

4-5-3 Conclusion:

The present study indicates that the measurement of motion sensitivity in glaucoma, namely temporal sensitivity may be more efficient than other visual stimuli in CCVP. It is worthwhile using a single amplitude trial in CCVP.

From a practical point of view, an optimal displacement interval as the target for a screening test is neither the minimum displacement threshold nor the maximum displacement threshold. The optimal number of trials and optimal number of test points and position in a motion test may vary depending mainly on the pathology to be detected.

4-6 Screening for optic nerve-diseases with MSST by notebook computer

4-6-1 Application by notebook computer perimetry

The techniques of automated perimetry need a specific stimulus generating system, data input and output, experienced technicians and a dedicated work space. Using computer display devices to generate visual stimuli, a new type of perimetry has been developed which no longer requires specific hardware. With development of personal computers, CCVP can be made smaller if a notebook computer is used.

There are numerous psychophysical tests generated by desktop computers in research centres , but no clinical application has been previously reported of the transfer of the test to a notebook computer. It is unclear why this has not happened. The technological problem of LCD hardware could be a major obstacle because of the small dynamic range of contrast.

However, there was no serious difficulty in implementing MSST from a desktop into a

notebook computer. It was possible because motion test requires a small range of contrast and was less affected by the *multicontrast* environment.

4-6-2 Characteristics of an efficient screening test

Rapid test

One of the most important qualities of an efficient screening test is a short testing time. There are many ways to speed up the test, e.g., by reducing the number of test locations or using a single threshold instead of multi-threshold, without being at the expense of the validity of the test for an ordinal visual field instrument. CCVP (motion test) can do this in order to speed up the test time. For example, the number of locations tested in motion testing was reduced from 48 to 18, then 16,and finally to 6. The test time was significantly reduced but the sensitivity and specificity was *not* reduced.

It must be pointed out that a potential way to achieve a rapid test in CCVP is to have several CCVP sets. This was done in the Nigeria study. Three Sharp notebook computers which were initially intended for field data entry, were used for CCVP.

Reproducibility

Reproducibility is an important characteristic of relatively stable measurements repeated in quick succession. MSST results based on the minimum motion seen for glaucoma detection has shown greater validity, in terms of specificity and sensitivity than the results based on the mean of motion seen. However, the "minimum motion" seen had low reproducibility when the test was used outside a hospital. This lower reproducibility does not appear to be due to a chin-rest being used in the second visit because the mean of motion sensitivity should have been affected also. The most likely possibility is that it is due to poor fixation. The "minimum motion seen" is based on one given test location which has the lowest score. To have highly reproducible motion sensitivity in a given test location, it is necessary to have good fixation. However, no claim has been made, that MSST can improve fixation. For example, it is

expected that many subjects who performed MSST in Nigeria did not have had good fixation because they were not perfectly trained "observers." Many women attended the study with their babies. During the test, their eyes were still glancing at their babies even though their heads did not move.

It is interesting to find that the reproducibility of "mean of motion sensitivity," is high despite poor fixation. This would be mainly due to using the same target over all test locations and all testing times. Therefore, even if the fixation is lost and the test location shifts from one place to other, the intensity of target seems not to change and the probability of seeing motion will remain the same within certain ranges(**Table 4-1, 4-2**).

Validity of CCVP

One might incorrectly estimate the validity of CCVP based on the results from mass screening in Nigeria because (1) the vast majority of participants in the screening program did not have the chance to be rechecked by the "gold standard" test; (2) the "gold standards" of Basic Eye Examination(BEE) and Special Eye Examination (SEE) were mainly for diagnostic purposes, by which many early OND cases might be treated as 'false positive cases' or normal; (3) the data from BEE and SEE was not available for all people who had MSST.

Instead, the studies of relation between MSST and microfilarial load and comparison with the follow-up data at one year are considered to be the basis of the evaluation of the validity of MSST in this study. Thus fewer influences after BEE and SEE would have held over the criteria for abnormal MSST. However, since MSST in the Nigerian study was not as well done as those tests done in the clinic in London, different operators and different testing situations may affect MSST results. It was found that the test was more difficult for Nigerian farmers than people in London. The response buttons were frequently damaged because of excess force in pressing the button. It was also found that the viewing distance for MSST was not well controlled when the local helpers were just beginning on the first day in the team. These factors would tend to reduce the sensitivity and specificity of MSST and to increase the number of unreliable tests. Neither poor sensitivity and specificity or poor reliability can explain

the strong relationship between microfilarial load and motion sensitivity loss.

Such a relationship between visual function and microfilarial load has never been reported in other studies, even though here is no doubt that visual function can be damaged by a high microfilarial load(Kirkwood et al, 1983 and Burnham et al, 1991). I did not discover whether age or sex are confounding factors in this study or whether there is some relationship between optic nerve disease and glaucoma. Whatever the other factors existed here, the finding of isolated abnormal motion sensitivity with normal ocular examination defined by BEE and SEE in many people with onchocercal infection by the motion test, was consistent. It might suggest that MSST will be useful in estimating the risk of onchocercal infection or provide a new method of monitoring onchocercal communities in order to detect and potentially prevent further optic nerve damage.

A comparison of MSST results on persons in the ivermectin trial in 1991, repeated in 1992, shows a significant benefit from ivermectin. This difference has been confirmed by the WHO project(Abiose et al, 1993). In contrast, the main WHO trial of ivermectin on optic nerve disease using standard methods required *three years* follow up on 3522 persons to prove a statistically significant benefit(Abiose et al, 1993). If this difference holds up for all participants in the WHO project, this impressive phenomenon will give a measure of the advance that MSST offers in assessing the benefit from various regimens of ivermectin in trials of onchocerciasis.

Low cost test

I wished to assess the cost-effectiveness of performing a motion sensitivity test compared with a total basic eye examination in detecting optic nerve diseases. Such a study should include 1) expenditure on this study ; 2) the effectiveness of impact on health outcomes;3) it should have an adequate input data base. To simplify the calculation, from the salary costs for the WHO project, there were 6 trained ophthalmic nurses to do basic eye examinations and 2 data entry operators for data input(WHO, 1987b). But CCVP required only one ophthalmic nurse, because most of the jobs could be done by local people operating the computer, with supervision from the ophthalmic nurse. The salary for local people was less than for

ophthalmic nurses. Based on these numbers, if the screen was conducted by 6 nurses with conventional tests the average amount spent on screening was £ 16 for each individual for 6000 people. In contrast, it was approximately 10 pence by the MSST when the test is conducted by village people.

Universal Application

The advantage in using CCVP technology is that it provides not only a single test, which is uniquely independent of the *multicontrast* environment, but it can also promise to provide a multitude of other types of visual function tests(e.g., vision acuity, contrast test). It can perform an exclusion test, or a confirmatory test for different clinical situations. For instance, suppose one had an abnormality with the screening test by CCVP, the next test could be a more specific test on the same computer, controlled by different software. Therefore it would not be necessary for person to go to a hospital to confirm the screening test results.

In addition, the tests can be done in people's homes which will ensure that an adequate sample for a survey is obtained. 3.5% of people failed CCVP due to an unreliable test or were unable to be tested in the first screening by MSST. This was significantly lower than the failure rate for the BEE which ranged from 10 to 30%.

4-6-3 Conclusion

MSST is a visual field screening test which is fast, has few test locations, has a high validity, is simple, safe and acceptable for every one. The present work demonstrates a successful application of motion testing in CCVP which can easily adapt to a real *multicontrast* environment with different hardware sets and community settings.

The development of the motion test or CCVP is still a very early stage as a screening test because we do not know about the frequency of motion sensitivity loss in the general population. Further investigation will be needed with a follow-up study in a large population.

4-7 CCVP versus automated perimetry

In comparison with automated perimetry, the two different technologies have different approaches to determine visual field function. This comparison is most complex, and the objections focus on the most common aspects

1) Stimulus generator

2) Calibration

3) Control of test reliability

4-7-1 Stimulus generator

A stimulus generator is used in the commercial video display in CCVP. As mentioned earlier, it can be varied to provide many different stimuli as visual field targets. Automated perimetry uses three different forms of stimulus generation: projection, light emitting diode and fibre-optic

stimuli. All traditional perimetry has a fundamental problem in that it cannot provide a complex stimulus e.g. bar, or text. By contrast, all types of stimuli found in automated perimetry can be used in CCVP, and more. One might conclude that the size of visual field in CCVP is limited by the video size. From a technical point of view it is impossible to make CRT in CCVP like a bowl as in automated perimeters. However, it should be pointed out that with the development of the electronic display industry, the CRT display is not the only video system for CCVP. The notebook computer provides a potential application of the LCD display system instead of CRT. With LCD, there is no fundamental problem in making any shape or type of display set(Kaneko, 1987 and Bosman, 1989) for a computer screen.

From a biomedical point of view, it may be not necessary to examine the far periphery when the information from the central field is entirely sufficient. Evidence already shows that all confirmed cases have motion sensitivity loss in the central field.

4-7-2 Calibration

To have a standard test, it is important to calibrate the stimulus intensity and the test conditions. However, calibration does not necessarily mean that the test is standardized. For example, all automated perimeters have been calibrated, but not standardized between each other(Wild, 1988). The background or adaptive levels are between 4 and 31.5 Asb and the results with these different perimeters cannot be compared quantitatively(Wild, 1988). It would be impossible to calibrate CCVP applied in the community with dedicated instruments. If a test is integrated into a computer network for all computer operators, each terminal in the network will not have the same calibrated contrast on their displays. But it does not mean they cannot have a standardized test.

CCVP has its own standardized test requirements. Using a viewing distance corresponding to the width of a video display provides a standardized size of stimulus regardless of the different video size, as has been suggested by Flocks(1978). A CCVP test using motion sensitivity is relatively independent of contrast sensitivity.

4-7-3 Reliability control

The developers of automated perimetry have expended much effort to produce a reliable test. This includes fixation control, a monitor system, a blind spot checking procedure and using a chin rest to control head movements(Wild, 1988). All these require additional hardware and are time consuming. The fact that CCVP does not have these features does not mean that CCVP necessarily lacks reliability. The results from Nigerians retested after a one year interval indicated that a reliable test had been achieved using MSST based on the "mean of motion sensitivity." A number of procedures can contribute to the reliability of CCVP. These include a dynamic fixation point to attract the subject's attention, a feedback system to indicate performance, speeding up the test time to reduce the fatigue effect and simplifying the test to minimize the learning effect.

4-7-4 Conclusion

1. With developments of the computer and electronic display industry, CCVP could provide an alternative way to do a visual field test with low cost and high efficiency.

2. To develop a standardised and reliable CCVP test, one should aim for a software system which allows individual users to add specialized functions in respect of "*multicontrast*" environment.

Chapter 5 General conclusion and further investigation

The advantages of computer controlled video perimetry over traditional visual field technology are many. First, it provides a simplified approach to the release of sophisticated, expensive, and complicated visual function tests from the research laboratories into primary eye care through personal computers and television programmes.

Second, the method provides great opportunities to break the traditional limitations of standard perimetry, and to take advantage of rapid developments in modern technology. For example, the notebook computer arrived on the commercial market only 2 years ago, and notebook perimetry based on CCVP technology was developed within a year(Wu et al 1991). This has been accepted by other investigators(Quigley et al, 1992). Third, the method has great potential to increase the range of effective visual field testing. The motion test generated in CCVP has provided a relatively valid and reliable screening test. Fourth, the method is familiar to most patients who have used computers or a keyboard. This allows them to test themselves.

Finally, and perhaps most importantly for primary eye care, CCVP is low in cost and highly feasible. If CCVP software is to be integrated into general practitioners' computer systems, a visual function test would be available throughout primary care services without financial constraint.

Although the motion sensitivity test has not yet demonstrated a specific pattern for the purpose of glaucoma diagnosis,its high sensitivity will allow confident exclusion of many false positive cases defined by traditional screening tests. Evaluating effectiveness is most important in any screening test, some of which has been done for CCVP, for instance, the evaluation of the application of notebook perimetry in a population based-survey. This provided lower cost screening when compared with standard screening tests.

However, the most important evaluation will be to see whether CCVP can be effective in reducing morbidity and blindness. This will require a large scale clinical trial to compare blindness rates among a population screened by CCVP and a population not screened. It is important to start such a trial at the earliest opportunity, both in an industrialized country and in a developing country setting.

There are several disadvantages of CCVP based on a motion test. The major disadvantage of a high contrast stimulus is the impossibility of detecting small relative scotomas located on the retina. The motion test does not provide a topographical map of motion sensitivity, which may limit CCVP in documenting field damage quantitatively. However, it is unclear whether topographical information in the field is important in early detection when M-cell function is more likely to be diffuse. The third problem is the physical constraint of the size of the testing field. Some problems can be solved by the new type of CCVP but not others. Thus, CCVP cannot replace the current visual field test but it will certainly provide a new approach to screening for visual function loss in the community.

Finally, as I mentioned before, a comprehensive CCVP test should provide a simplified way of interpreting the result when there is no expert opinion. Several studies have attempted to use an expert system(Krakau, 1986) or a neural network utilizing visual field results(Shields et al, 1990; Goldbaum et al, 1990; Shalom et al, 1990; Nagata et al, 1991; Keating et al,1992). Unfortunately, there is no practical way to do this at the moment.

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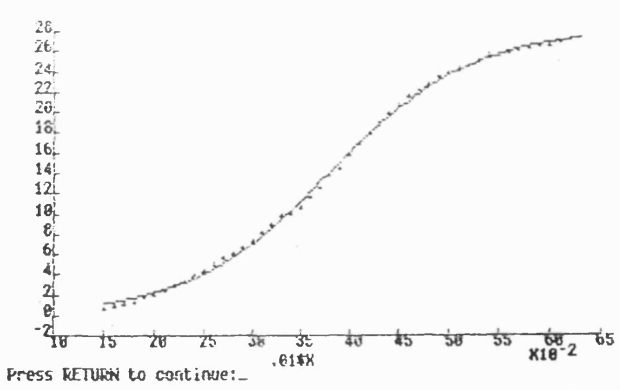
Appendix I Table A1 Calibration

```
* Press RETURN to continue:2

esults from fitting :-  Hyperbolic tangent : Y = b + b*TANH(c + d*X)
----------------------
ile:- .IBM  -  13 Jan 1989 11:52:50
---

-variable is  .01*X
-variable is  .01*Y

arameter       Value          Std Err
--------       -----          -------
              14.171        0.63716E-01
              -2.5971       0.69508E-01
               6.8301       0.98960E-01

in =     0.00000E+01
ax =      28.343
 for 50% of Ymax   =     0.38024
lope at this point =      96.792

S =      5.1152          d.f. =    46      MSE =     0.11120

* Press RETURN to continue:_
```



Appendix I Table A2 Fitzke data

Values for hyperbolic tangent b,c,d
14.117 -2.6319 6.9325

VGA units	measured	log	diff(log)	fit	log	diff(log)
4	0.011	-1.959	0.073	0.252	-0.598	0.060
5	0.013	-1.886	0.090	0.289	-0.539	0.060
6	0.016	-1.796	0.194	0.332	-0.479	0.059
7	0.025	-1.602	0.274	0.380	-0.420	0.059
8	0.047	-1.328	0.226	0.436	-0.360	0.059
9	0.079	-1.102	0.199	0.500	-0.301	0.059
10	0.125	-0.903	0.204	0.573	-0.242	0.059
11	0.200	-0.699	0.169	0.656	-0.183	0.059
12	0.295	-0.530	0.153	0.751	-0.124	0.058
13	0.420	-0.377	0.140	0.859	-0.066	0.058
14	0.580	-0.237	0.120	0.983	-0.008	0.058
15	0.765	-0.116	0.096	1.123	0.050	0.058
16	0.955	-0.020	0.061	1.282	0.108	0.057
17	1.100	0.041	0.105	1.463	0.165	0.057
18	1.400	0.146	0.084	1.668	0.222	0.056
19	1.700	0.230	0.081	1.899	0.279	0.056
20	2.050	0.312	0.068	2.160	0.334	0.055
21	2.400	0.380	0.075	2.453	0.390	0.055
22	2.850	0.455	0.064	2.782	0.444	0.054
23	3.300	0.519	0.073	3.150	0.498	0.053
24	3.900	0.591	0.052	3.559	0.551	0.052
25	4.400	0.643	0.056	4.013	0.604	0.051
26	5.000	0.699	0.049	4.515	0.655	0.050
27	5.600	0.748	0.044	5.066	0.705	0.049
28	6.200	0.792	0.040	5.668	0.753	0.047
29	6.800	0.833	0.043	6.322	0.801	0.046
30	7.500	0.875	0.039	7.028	0.847	0.044
31	8.200	0.914	0.040	7.785	0.891	0.043
32	9.000	0.954	0.037	8.591	0.934	0.041
33	9.800	0.991	0.009	9.441	0.975	0.039
34	10.000	1.000	0.025	10.332	1.014	0.037
35	10.600	1.025	0.047	11.256	1.051	0.035
36	11.800	1.072	0.025	12.206	1.087	0.033
37	12.500	1.097	0.043	13.174	1.120	0.031
38	13.800	1.140	0.021	14.152	1.151	0.029
39	14.500	1.161	0.037	15.129	1.180	0.027
40	15.800	1.199	0.027	16.096	1.207	0.025
41	16.800	1.225	0.028	17.044	1.232	0.023
42	17.900	1.253	0.024	17.966	1.254	0.021
43	18.900	1.276	0.022	18.854	1.275	0.019
44	19.900	1.299	0.019	19.701	1.294	0.017
45	20.800	1.318	0.018	20.504	1.312	0.016
46	21.700	1.336	0.010	21.257	1.328	0.014
47	22.200	1.346	0.012	21.960	1.342	0.013
48	22.800	1.358	0.013	22.610	1.354	0.011
49	23.500	1.371	0.007	23.209	1.366	0.010
50	23.900	1.378	0.009	23.756	1.376	0.009
51	24.400	1.387	0.004	24.254	1.385	0.008
52	24.600	1.391	0.010	24.705	1.393	0.007
53	25.200	1.401	0.009	25.111	1.400	0.006
54	25.700	1.410	0.002	25.476	1.406	0.006
55	25.800	1.412	0.002	25.802	1.412	0.005
56	25.900	1.413	0.003	26.093	1.417	0.004
57	26.100	1.417	0.005	26.352	1.421	0.004
58	26.400	1.422	0.003	26.581	1.425	0.003
59	26.600	1.425	0.002	26.784	1.428	0.003
60	26.700	1.427	0.006	26.964	1.431	0.003
61	27.100	1.433	0.003	27.122	1.433	0.002
62	27.300	1.436	0.005	27.261	1.436	0.002

Values for hyperbolic tangent b,c,d

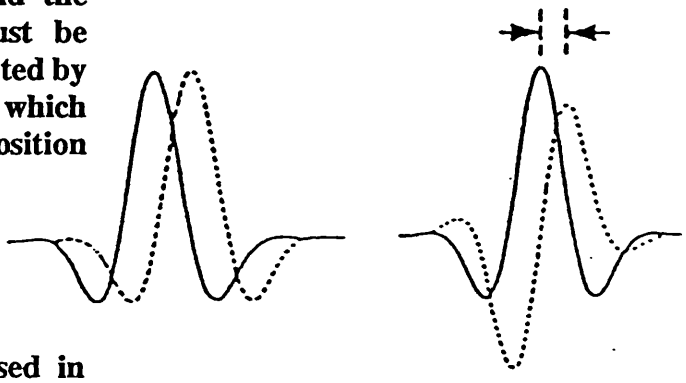
Appendix II Motion Detection

General Requirements of Motion Detection

(Basic scheme of motion detector)

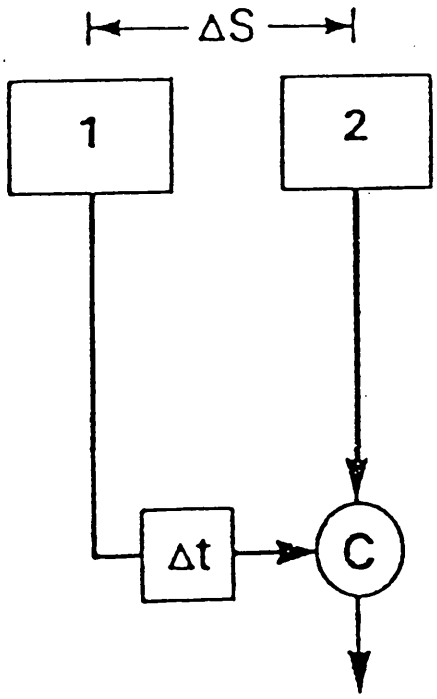
Two receptors

The stimulus can be one if it stimulated the first receptor and then, with △t, did the second one. But two receptors must be necessary since motion has to be computed by two-dimensional array of receptor, which provide brightness based on time and position of retinal(Bors A & Egelhaaf, 1988)



Two differences, △S & △t

The two receptors have to be processed in asymmetry way, with space difference(△S) and time difference (△t). If there is no asymmetrical, it is then no longer to discriminate difference which receptor was excited first and which later. Limitation of △S may be based on *spatial frequency* ranges(Blakemore & Compbell, 1969) in size of stimulus and image scale. Limitation of △t may be based on *temporal frequency*, which delays the signals before.



One centre

The △S and △t have to been sent one centre (C) to be computerized. Without a final stage of integration of both spatial and temporal information, the *apparent motion* would not be generalized (Nakayama, 1985).

It should be pointed out that if any of five elements is deficit the motion sensitivity would be declined or no longer be.

Publications(Abstract)

A list of old and present researched papers which have been used the CCVP technology or motion tests and I have involved during last 5 years.

Laptop computer perimetry for glaucoma screening

X.WU, R.Wormald, F. Fitzke, D.Poinoosawmy, S. Nagasubramanian and R.Hitchings.

A computer controlled video perimetry(CCVP)-laptop model has been developed for early detection of glaucomatous field defects. This test is specifically designed for detecting large ganglion cell damage with a displacement stimulus. It identifies zonal optic nerve damage by analysing motion detection asymmetry across the horizontal raphe. The moving stimuli were vertical lines generated by the computer on 10 " Liquid Crystal Display at six locations across the central visual field. The lateral displacement distance was 4 pixels. The viewing distance varied between 20 cm to 65 cm. The software package was tested in a group of 17 patients with glaucoma (mean age 60.8 yrs.), 16 ocular hypertensive patients (mean age 58.7 yrs) and an age matched control group of 26 normal subjects. There was absolute motion detection loss for all glaucomatous eyes. Using receiver operator characteristic analysis, the optimum out-off for motion asymmetry between superior and inferior hemi-fields of mean motion detected was 0.6 (the difference in mean motion detected between the hemifields as a proportion of the overall mean motion detected), which could provide 65 % sensitivity and 75 % specificity to discriminate glaucoma suspects from normals.

(Invest Ophthal Vis Sci, 32(4):810, 1991)

PREVALENCE OF GLAUCOMA IN THE WEST OF IRELAND

Michele Coffey, Angela Reidy, Richard Wormald, Wu Xing-Wang, Lesley Wright, Parul Courtney

County Roscommon in the West of Ireland is a relatively remote rural area whose population of 55000 is served by 2 community medical ophthalmologists and 3 optometrists. Eye surgical services are not available within the county. In order to assess the needs of the community for prevention of blindness from glaucoma, a simple random sample of the population of County Roscommon was taken for a community based glaucoma survey. 2186 people over the age of 50 were examined which represented a 99.5% response rate. The high response rate was achieved by the community basis of the study and vigorous follow up of non-attenders. Intra-ocular pressure was measured using both Schiotz and Applanation tonometry, disc evaluation by both direct ophthalmoscopy and stereoscopic biomicroscopy, and visual field analysis using the Henson CFS 2000 and experimental **computer controlled video perimetry**. Diagnostic criteria were consistent with the Preferred Practice Pattern of the American Academy of Ophthalmology. A crude prevalence of approximately 2% for primary open angle and normal tension glaucoma was found. The population profile of intraocular pressure showed a pattern which decreased with increasing age unlike the Framingham and Ferndale studies but similar to Japanese data.

(Br J Ophthalmol 77:17-21,1993)

VARIABILITY IN GLAUCOMATOUS VISUAL DAMAGE MEASURED WITH MOTION DETECTION.

J.X.Wu, F. W. Fitzke, P. Poinoosawmy, R. Hitchings and G Johnson

Purpose. To determine if motion detection threshold(MDT) would show less fluctuation than light differential test in glaucoma patients. Methods. We have developed motion sensitivity perimetry(MSP)(Fitzke 1987, 1991) and measured 3 displacement amplitudes(0.8, 1.2 and 1.4 log minarc) in 6 locations over the central 20°. 171 glaucoma patients (342 eyes) were prospectively followed for 11 to 22 months with MSP. For analysis of these data, we considered all possible combinations of test results, and grouped the data according to the differences between the initial and the follow up based on eccentricity, over all sensitivity, trial number and magnitude of displacement. We used the Glaucoma HemiField Test(GHT) in Humphrey full threshold to determine if the visual field is progressing. Agreement between repeated measurement was analyzed using the limits of agreement and intraclass correction coefficient(Bland & Altman, 1986). Results. The eyes were divided into two groups: (A) 144 eyes (42%) had progressing visual field, and (B) 198 eyes(58%) that had no progressing visual field. Initially, abnormal MSP for all 3 amplitudes was found for 103 eye in Group A and no eyes in Group B.

Table Limits of agreements (LOA) and Intraclass Correlation Coefficients (ICC) of MSP*

		Motion Sensitivity Perimetry					
Eye		0.8 log minarc		1.2 log minarc		1.4 log minarc	
		LOA	**ICC**	**LOA**	**ICC**	**LOA**	**ICC**
	(n)	mean(SD)		mean(SD)		mean(SD)	
Group A	144	4.2 (5.5)	34%	2.24(4.3)	45%	1.35(2.34)	68%
Group B	198	0.58(2.2)	66%	0.24(0.9)	90%	0.31(1.17)	92%

For Group A, the agreement of repeated MSP was low resulting in ICC of 34% to 68%(Table). For Group B, the small amplitude of displacement has lower agreement than the larger($p < 0.01$) but the agreement from all three amplitude is higher than Group A($p < 0.01$). Conclusion. The MDP proved to be useful and reliable measurements of glaucoma progressing for the early glaucoma patients

(Invest Ophthal Vis Sci, 34(4): No 1475, 1993).

MOTION DETECTION THRESHOLDS MAY BE USED TO PREDICT CONVENTIONAL VISUAL FIELD LOSS IN LOW TENSION GLAUCOMA SUSPECTS. D. Poinoosawmy FW Fitzke, JX Wu and RA Hitchings

Thirty four normal tension glaucoma suspects were prospectively investigated over a three years period using Humphrey computerised visual field analysis(HFA) and motion detection testing(MDT). At the onset, HFA thresholds showed normal visual fields in all 34 patients using the LTG multi-center study protocol criteria of a nucleus with 10 dB loss with a surrounding cluster of 3 points of 5 dB loss. All had a cup disc ratio of more than 0.6. At the test location for motion detection(15 degrees visual angle on the 330 degree meridian) the mean of the cluster of 4 surrounding points from the HFA was within 5 dB of normal using the corrected pattern standard deviation(CPSD) for all 34 patients. This will be referred to as the MDT cluster. MDT values were considered abnormal if they were beyond two standard deviations of the values of the control group comprised of patient spouses(IPS 1986 and IPS 1988). These patients were divided into two groups on the basis of the MDT results. At the onset of the study, group I had normal MDT(n=11) and group 2 had abnormal MDT(n=23). By the third year 1/11 (9%) in group 1 had losses in the MDT cluster of more than 5 dB. This was also the sole patient with an abnormal MDT by the third year. In contrast, 13/20(65%) who began with an abnormal MDT acquired losses of more than 5 dB in the MDT cluster.

(Invest Ophthal Vis Sci, 33(4):1278, 1992)

ASSESSMENT OF VISUAL IMPAIRMENT USING A MOTION SENSITIVITY SCREENING TEST (MSST) IN A COMMUNITY MESOENDEMIC FOR ONCHOCERCIASIS.

A.Cassels-Brown, J.X.Wu, B.R.Jones, G. Johnson, B.Adeniyi, A Abiose.

Purpose: To determine the efficacy of motion sensitivity test (MSST) in assessing visual impairment from optic nerve and chorioretinal disease in a community mesoendemic for onchocerciasis. **Method.** MSST (Wu et al 1990) was applied to a total of 1274 individuals, in Kaduna state,North Nigeria using three Sharp notebook computers operated by trained village helpers. These individuals also underwent ophthalmic examination by four trained ophthalmic nurses including assessment of visual acuity, four quadrant counting fingers visual field pupillary light response and optic disc evaluation. Individuals who failed the MSST or ophthalmic nurse examination and a pre-selected random sample, subsequently underwent Friedman visual field analysis and examination by an ophthalmologist which included; slitlamp biomicroscopy, applanation tonometry, direct and indirect ophthalmoscopy and fundus fluorescein angiography. **Results:** A total of 256 individuals in the mesoendemic community underwent MSST, Ophthalmic nurse examination, Friedmann field analysis and ophthalmologist examination to provide a "gold standard". of these; 123 individuals (243 eyes) were normal, 49 individuals (90 eyes) had both optic nerve and chorioretinal disease (OND+CRD), 55 (105 eyes) had pure optic nerve disease (OND) and 22 (42 eyes) had pure chorioretinal disease (CRD). MSST reproducibility was found to be good (Eu et al 1992). If the MSST specificity is fixed at 70% against the "gold standard", the sensitivities for detecting mixed OND+CRD, pure OND and pure CRD are 98%, 80% and 55% respectively. If the MSST specificity is fixed at 90%, the sensitivities for detecting mixed OND+CRD, pure OND and pure CRD are 84%, 76% and 40% respectively. If the sensitivity of the MSST in detecting any onchocercal posterior segment disease is set at 89% a specificity of 70% is achieved. Intraclass correlation between MSST and conventional test were mainly good, but were found to depend on both the different disease patterns (OND+CRD, pure OND and pure CRD) and the conventional test studied. **Conclusion**: We conclude that the MSST is highly effective in assessing visual impairment due to onchocercal optic nerve and chorioretinal disease and compares very well with the conventional test. It can therefore be used to detect communities at risk of blindness from onchocerciasis, requiring ivermectin mass chemotherapy.

(Invest Ophthal Vis Sci, 34(4): No 3407, 1993)

The Universal Visual Acuity(UVAT):performance in illiterate rural Nigerians.
B.Adeniyi, J X Wu, A.Cassels-Brown, B.r.Jones,A.Abiose ,S Nagasubramania

Purpose. To determine the efficacy of new computerized visual acuity:UVAT in routine application. Method. UVAT is a fast reliable standardised test covering the full range of acuities. The target presented to the observer on the Liquid Crystal Display is a single E optotype of varying sizes. The step between each size was approximately 0.1 log. Each size of optotype E is presented in one of only two orientations(to right or left). The subject was instructed to indicate the direction of the E type. The operator pressed the arrow key corresponding to the subjects' indication. A built-in statistical method deals with guessing. The results are displayed on screen and storied on hard disc. Results. It was measured during an onchocerciasis research programme on a population of over 4297 illiterate rural persons aged 15-65 years in Northern Nigeria. A total of 1201 individuals were screened with both ophthalmic nurses' single E optotype Snellen acuity test and the UVAT. Good agreement was found(Kappa 0.88 SE 0.07). The UVAT appears to be a higher sensitively, reproducibility and acceptability than the nurses' visual acuity test. Conclusion. The results suggest CVAT many be useful visual function test for visual screening, especially, when combined with the Motion Sensitivity Screening Test (visual field test).

(Invest Ophthal Vis Sci, 34(4): No 1201, 1993)

PILOT STUDY FOR GLAUCOMA CASE FINDING BY MOTION SENSITIVITY SCREENING IN NEPAL E.Raithel; J.X Wu; F.W.Fitzke, S.Kaminski and G.J.Johnson.

Purpose. To determine the efficiency of motion sensitivity screening testing for glaucoma case finding. Method. Three local ophthalmologists from the Nepal Eye Hospital were asked to refer patients. From their case-load they referred glaucoma suspects, and randomly selected non-glaucoma patients. Referral criteria of glaucoma suspect cases were the following: 1) glaucoma family history, 2) symptoms related to glaucoma such as pain, redness, blurring of vision, 3) IOP more than 23 mmHg (SchiÜtz) or 4) Cup/disc ratio > 0.5. Those selected perfomed the motion sensitivity screening test(MSST) generated by a SHARP 6220 notebook computer(Wu, 1991). Before the MSST, foveal visual acuity was measured by computerized visual acuity test. Results. Out of 10,500 patients seen by the ophthalmologists during the study period(36 days), 97 people were referred for MSST. Of these, 38 individuals(73 eyes) were glaucoma suspects and 59(116 eyes) were non-glaucoma patients. There was no age difference between glaucoma suspects(44.32 yrs) and non-glaucoma patients(42.13 yrs)(p=0.325). Glaucoma suspects had better visual acuity(0.16 LogMAR) than non-glaucoma patients(0.33 LogMAR) (p=0.002). 29(76%) glaucoma suspects had abnormal MSST and 4(6%) of the non-glaucoma patients had abnormal MSST. The correlation coefficient between motion sensitivity and visual acuity in glaucoma and non-glaucoma groups was -0.426 (p=0.001) and -0.145 (p=0.1), respectively. The mean test time including training, the visual acuity test and MSST in both eyes was 9.38 minutes and a single MSST was 1.76 minutes. Conclusions. The low cost notebook computer for motion detection testing was a quick and efficient method of screening for glaucoma.

(Invest Ophthal Vis Sci, 34(4): No 3640, 1993)

Discrimination between progression and nono-progression visual field loss in low-tension glauocoma. D Poinoosawmy, John X. Wu , Frederick W Fitzke, and Roger A. Hitchings.

Low tension glaucoma patients who had good sensitivity in at least one portion of the visual field measured by the Humphrey Field Analyser were followed over a period between 1986 and 1992. Motion Detection Thresholds (MDT) were measured in the more normal part of the visual field and visual field progression was analysed by pointwise linear regression analysis using Progressor software. The patients were divided into those with initially normal MDT (22 patients) and those with initially abnormal MDT (40 patients). Significant progression was found after four years in 10/22 (45%) with initially normal MDT while 30/40 (75%) with initially abnormal MDT showed significant progression. MDT and pointwise linear regression analysis may be helpful in following these patients.

(*Perimetry Update 1992/1993, in press*).

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·技术改进·

微型计算机对眼压描记数据的处理

湖南省人民医院眼科 吴兴旺

用Grant氏眼压描记图测定C值的方法对青光眼诊断、预后、手术选择、药物降压机理的研究及发病机理分析等方面都具有重要价值，但该项检查误差因素多，临床价值受到影响[1]。其中误差因素之一是采用查表以代替繁琐运算C值所致。目前电子计算机已广泛应用于科学计算、数据处理和过程控制之中，其优越性已众所周知。因此，我们采用Sharp PC-1500袖珍计算机(图1)，用扩展BASIC语言，将C值、E值、F值、Po/C及校正C值、F值及眼球压迫试验等10个计算公式，按照程序图编成15个子程序，以通用程序使其连接成一个青光眼应用软件系统，并命名为"Glaucoma-2"系统(图2)。该系统可在半分钟内迅速完成上述10个公式的运算，并通过显示器显示、打印和录入磁带永久保存。显示和打印方式可根据临床需要确定。例如打印C值报告分供临床医生和科研两种。临床用的报告(图1)只提供E值为0.0215时的C值、F值、Po/C值及眼压，科研用报告将全部运算结果均打印提供。若读报告者未知这些数据的正常值时，

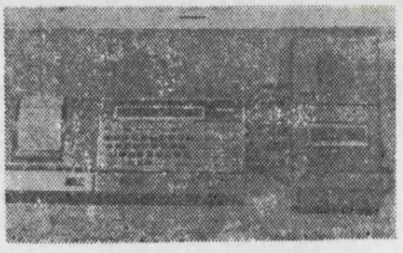

图1 Sharp PC-1500袖珍计算机

可根据打印报告的颜色确定是否异常。磁带储存目的是为临床复诊对照和科研统计提供资料。复诊病人只要提供报告编号、姓名、年龄、

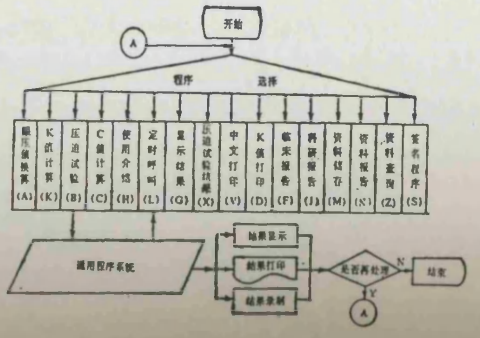

图2 "Glaucoma-2"系统程序

临床诊断及检查日期中任何一项，就可由计算机自动查找初查结果，并提供查询结果报告。本系统操作方便，未学计算机者也易迅速掌握，所设的15个子程序都有其相关键代替，操作者只需按DEF键后，再按自己选定的子程序键即可运行，运行时通过人机对话指导操作。

"Glaucoma-2"系统是运用微型机解决眼科日常繁琐计算工作的初步尝试，它同OPL(Ophthalmology Program Library)系统一样[2]，编写程序人员不是计算机专业人员而是临床工作者自己。这种临床工作者编写的眼科应用软件常可收到立竿见影的效果，并在临床应用中随时修改逐渐完善。本系统的程序编写仅用一个月时间，但自1984年3月应用于临床后曾作多次修改，为使其向着C值检查全自动化方面发展创造条件。

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to Dr. John Wu FAX: 0044-071-250-3201
（吴兴旺）

则b波消失。

2、视网膜中央静脉阻塞：检查了6只眼，3只眼ERG正常；2只眼ERG振幅降低，峰潜伏期正常；一例陈旧性病变病人表现熄灭型。EOG均异常。许多学者认为对视网膜中央静脉阻塞的病人，用ERG检测，尤其是对b波振幅的观察，在了解视网膜功能，估计病人的预后方面是有意义的。

六、视网膜脱离：检查7只眼。ERG表现为a波、b波均减小（4只眼）或熄灭（3只眼），EOG异常。Lebes认为EOG比值下降的程度与视网膜脱离的范围有关，而视网膜复位后平均90天EOG恢复正常。

七、糖尿病性视网膜病变：检查了12只眼，既有眼底尚无明显改变的糖尿病患者，也有玻璃体积血，眼底已窥不见的病人。眼底尚无明显改变者ERG正常，振荡电位振幅降低。眼底出血者，ERG振幅降低，振荡电位消失。

对糖尿病性视网膜病变的诊断和预后是一个重要的问题。电生理检查，尤其是振荡电位检测对糖尿病性视网病变患者有早期诊断价值。目前有许多学者，通过电生理检查对糖尿病性视网膜病变的诊断、分期、指导治疗及治疗评价进行了较深的探讨。

八、视神经、视路疾患：检查了各种类型的视神经炎、视神经萎缩及视路中占位性病变共28只眼。视神经疾患，闪光ERG正常，模型ERG和VEP可异常。视神经交叉及视交叉以后视路的占位性病变，多导VEP可出现相应的定位性改变。

九、屈光间质混浊，眼底不能窥见时可用视觉电生理方法来评价视网膜功能。我们检查了13只眼，视网膜、视路正常者ERG、VEP正常。

十、其它：检查了各种类型的青光眼（11只眼），视网膜脉管炎、眼外伤、高度近视、脉络膜黑色素瘤等共32只眼。青光眼组6只眼ERG正常，5只眼ERG有不同程度振幅下降，3只眼模型ERG异常。眼外伤组，有一例眼球挫伤、外伤性虹膜炎、视网膜震荡者ERG表现b波超常，峰潜伏正常，EOG光峰降低。球内异物表现ERG b波振幅下降。这些病例的视觉电生理改变尚待进一步观察、探讨。

To Dr. John. Wu（吴兴旺）

微电脑在电视视野计中的应用

吴兴旺* 黄家林** 胡建荣* 周耀曾*

随着人民生活水平提高，老年人增加，作视野检查的人次也明显增加，但基本上保持近二个世纪以前的手工视野检查，无论从检查数量还是质量都不能满足现代医疗质量要求。近10年来国外广泛使用了自动化视野计（Automated Perimeters，AP）。这种AP最大的特点是检查质量提高，需要受技术员操作的机会明显减少，每次测试时间也有缩短。然而这种AP造价还未都高，有的可达10万美元，这对我国大多数单位来讲，[illegible]

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的。对此，我组从1985年9月开展了微型个人计算机在电视视野计中应用的研究工作，旨在建立一种适合广大基层单位使用的自动化视野计，为我国防盲治盲工作提供一种有效的视野检查系统。经过8个多月的研制和临床应用，现对其研究结果总结如下。

我们研究的主要方法就是利用我院现有一台用Apple—Ⅱ个人微电脑控制的电眼压描记上的计算机，在不另加任何其它附加设备情况下通过设计一个作视野检查的软件而完成视野检查，经过临床应用反复测试，修改而达到研究目的，该软件系统被称之为WHA电脑电视视野系统，其特点：

（1）造价便宜：系统是在Apple—Ⅱ国内最流行应用的微型计算机上实现，该微型计算机是与浙江大学生产的眼电生理仪使用的电脑完全一致，故也是国内眼科使用最广泛的一种微机，正由如此，这些单位使用本系统基本上可不花钱就可实现（因为本系统只是一个能够考贝的软件磁盘）。另外，单购苹果机（Apple—Ⅱ）也只需几千元。

（2）结构简单：一台Apple个人微型计算机配上标准配件，例如9寸绿色电视屏（可用黑白电视代替），即可完成视野检查，如果再配上磁盘驱动器和打印机，那么检查结果就可永久储存并打出报告。

（3）检查方便：对操作者来讲，只需熟悉键盘位置，通过菜单式提问即可完成WHA系统各操作要求。对被检查者来讲，他只要面对计算机上的监视器或电视屏，保持头在检查时与电视屏距离不变（通常固定在一个托架上），眼球固视注视点不转动，当看到屏幕上出现任何一点就按计算机键盘中任意一键即可按照规定的程序完成距中心固视点5°—45°不同范围的静态视野检查。大部分病人都能顺利完成此检查，对儿童来讲，常常是在玩“星球大战”电子游戏感觉下完成检查，对其刺激强度和背景光照度分别采用计算机自动确定测试刺激强度和永久固定背景光照度，以便简化操作，提高测试精度。

（4）检查时间减少：正常人每只眼作60个刺激检查只需2分钟左右，而200刺激亦只要3—9分钟，通常20°视野范围检查是5—6分钟。由于WHA系统对视野检查的每个刺激点都是随机在屏幕不同部位出现，每一范围刺激点数出现频率都几乎相同，所以在检查生理盲点时，尽管刺激点出现不象手工视野检查，事先就在相应生理盲点周围多次检查，而是整个检查视野范围均匀出现刺激视标，但结果几乎是100%的能够查到生理盲点。这样做避免了原技术员主观方面造成的误差，使视野暗点检出率明显提高，对18例有WHA视野报告又有Goldman视野或Humphrey电脑视野结果的32只眼作统计分析表明：WHA视野发现暗点或视野缺损与Goldman视野检查结果对照符合率[illegible]

计件的磁盘外，不再需要其它特别设计的装置及操作熟练的技术员。故对能够借用Apple—算使用的单位或个人都可有机会完成WHA视野检查，作为个人自我检查来讲这对许多病人是有益的。实际上本组从85年底就分别向一些单位和个人推广了这种视野检查方法，在推广中无论是推广者还是被推广者都基本上在不花钱情况下完成的，这与国内微型计算机已有一定基础是分不开的。

（8）检查费低：在本组18例曾作过Goldmann视野计或Humphrey电脑视野计检查病人的检查费统计分析表明，采用WHA电脑电视视野检查加上手工周边视野检查全部费用也只是Goldman的1/2～1/3，而Humphrey则只有其1/10价格。

二、问题及解决方法

同任何新仪器一样，这种WHA电脑电视视野亦存在某些不足之处急待解决，例如：

（1）结果不容易分析：WHA测试结果尽管可提供视野平面图和定量用的立体图，但评价这些图象时如果不了解分析这些结果的标准，而按照传统的手工视野方法分析必将造成错误结果。事实上对WHA没有经验的人分析视野图，可造成假阳性率达21%或者更高，而熟悉WHA者可使假阳性率在8%以下。

（2）标准化困难：WHA是利用现有的个人微型计算机完成视野检查，这与国外为视野检查设计做的AP在标准化方面是截然不同的，因为前者测试时光刺激强度，背景光照度都是随机性，没有固定的标准，而后者有为这些专门设计的装置，所以能够有固定的标准对应，由于标准化困难，对同一测试对象在不同时间，不同地方的WHA结果在对照分析时会带来困难。

（3）检查范围不够大：WHA尽管通过移动固视点扩大了视野检查范围可达45°，但这需要延长检查时间，对一些病人来讲延长时间常造成假性暗点增多。

（4）临床使用时间太短：WHA还没有大量临床工作中得到应用，该视野对不同情况下测试的正常标准还未能一一产生，故现对临床广泛应用带来困难。

对于WHA视野结果不容易分析问题，近期只能通过广泛地临床试用，尽早建立评价这种视野结果的一整套标准，除此外不断的改善测试方案，对不同疾病采用不同的测试策略等等措施给予解决，而最终解决则是在上述基础上，利用人工智能技术，让计算机自己模拟视野专家对视野结果作分析。

标准化问题可以通过测试单位或个人在对照分析前先建立自己的标准值，这需要做一定的群体调查，但标准化后有助结果正确辨别。

电脑电视视野由于采用电视屏，所以每次检查时不能一次性的完成30°中心视野检查，这尤其是在小电视屏，例如9英寸屏幕时，不能单纯用通过将眼球与固视点距离缩短方法扩大视野检查，因为距离太近部分病人有不良的反应影响测试结果，对此移动固视点，扩大某一方向检查范围是可行的，今后则是根据病情扩大检查范围。

综上所述，我们认为WHA这种电脑电视视野计是符合我国国情的一种自动化视野机，为了使这种视野计功能更加全面，暗点发现率增高，这就需临床广泛实践，因此本组愿同对视野感兴趣的各方面专家，学者共同研究这方面问题，并将WHA软件供大家应用，故凡需WHA系统软件者可寄一张51/4英寸的磁盘作考贝软件用，望在使用中提出意见，以求逐日完善WHA系统。

（来信请寄：湖南省人民医院 吴兴旺医师）

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一种便于推广的电脑视野计

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近一个世纪以来，视野检查一般都要求有特定的仪器设备才能得到检查结果，主要操作都是依靠手工，检查时间长，检查者与被检查者都感到负担重，由此造成了检查精度不高。近年来，随着微电子技术的发展，一些新型的电脑视野计陆续问世，使得视野检查的精度大为提高，操作也比较方便。但是由于电脑视野计本身也还处在发展阶段，检查标准尚未统一，而且价格昂贵，对于我国广大的基层医院来说，一时还难以负担。所以，发展一种既具有现代自动化视野计的功能和特点，价格又便宜的电脑视野计是很有必要的。我们研制的WHA电脑视野计系统，就是为了达到上述目的。

WHA电脑视野计采用APPLE Ⅱ微型计算机，只需基本配置即可。由于受到显示器的限制，本视野计只能对中心视野进行检查（中心视野为固视点周围30°范围以内）。当计算机启动后，自动引导主程序进入计算机运行，并在屏幕上显示主选菜单。当医生根据菜单的提示回答有关问题，并选定了检查方法后，计算机就在显示器屏幕上随机地出现刺激点（即视标），被检查者如果看见了，就按一下键盘上的任意一键，否则不按键，直到完成对预定范围的检查，计算机又在屏幕上出现主选菜单。这时可以选择有关功能把检查结果保存在磁盘上，以备对照检查、分析、打印检查结果时调用。

由于WHA系统利用了APPLE Ⅱ的较高分辨率的作图方式，而且在一次检查过程中还要保留最多达240个刺激点的坐标、阈值等数据，因此APPLE Ⅱ的内存显得不够。为此，我们按不同的功能把系统软件分成了引导、主选菜单、测阈值、测试、图形处理、打印、资料库管理等7个功能模块。除常用的几个模块常驻内存以外，其余的模块分别存放在磁盘上。

由于视野检查对于不同的患者有不同的要求，所以我们在软件设计时都尽可能地加以考虑，以满足视野检查的需要。

1. 确定被检查者的眼睛与屏幕中心之间的距离

这对于保证检查结果的精度和重复对照检查的可信性有着重要的意义。所以我们专门设计了一种画面（如图1所示），用来确定眼与屏幕中心的距离。当被检查者的眼与固视点平行且对准了屏幕中心时，通过头部的前后平行移动，总能找到一个位置，看不见屏幕上的块状图形，即为合适位置，这时屏幕上相邻两个刺激点与眼之间的夹角跟视野度数约成1:1的关系。[2]

2. 确定刺激点出现位置的方法

刺激点在屏幕上出现的位置及分布的情况，对于视野检查结果的可靠性和检查速度有很大的影响。在APPLE Ⅱ的显示器上一共有40×24＝960个位置可以出现刺激点。我们在软件设计时采用了几种方法来确定刺激点在屏幕上的位置（即坐标）。一种是由计算机随机地选择刺激点的坐标，这时刺激点是均匀分布的。这种方法适合在普查时用。但是在临床应用中，往往需要对指定的部位进行集中检查，这就要求刺激点集中出现在指定部位中心的附近。所以WHA系统还采用了另一种方法确定刺激点的坐标，可以灵活、迅速地对指定部位进行集中检查。即预先造好一个图形表（共有960个刺激点的坐标）存放在计算机内存中，每点占用2个字节，前一个字节为刺激点的X坐标，后一个字节为Y坐标。

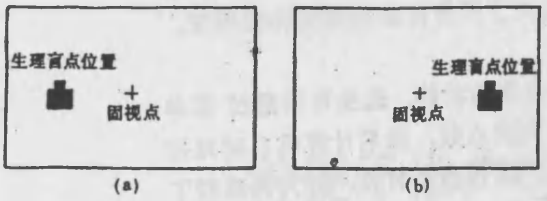

图1　定距专用画面

(注：(a)检查左眼时使用，(b)检查右眼时使用)

图形表一共占用1920个字节的内存。整个图形呈圆形，其中在中心10°范围内，密集分布着350个点（其中有些点的坐标是重复的），另外在11°—46°范围内，平均每度分布16个点。图形表在内存中是以离圆心的半径大小顺序排列的，半径小的点放在前面，半径大的点排在后面。设每次检查时产生N个刺激点，则总是由计算机在图形表的前$4N$个点中随机地选择刺激点的坐标。这样既保证了刺激点坐标的随机性，又能保证刺激点出现在指定中心的附近。图形表中刺激点坐标的分布概率见表1。

表1　图形表中刺激点的分布概率

刺激点数	取点范围	0°—5°	6°—10°	11°—15°	16°—20°
10	40	40/1			
30	120	120/1			
70	280	150/0.536	130/0.464		
100	400	150/0.375	200/0.500	40/0.100	5/0.013
240	960	150/0.156	200/0.208	114/0.119	46/0.048

注1：表中数据，例如150/0.536中，150为图形表中落在5°以内的刺激点数，0.536为刺激点在该区段出现的概率。
注2：该表数据是当图形中心在屏幕中心时（即X座标为20，Y座标为12)测得的。

由全概率定理可以得知，当欲刺激点数N＜30时，尽管计算机是在图形表的前120个点(或更少）中随机地选择30个点（或更少），而这些点出现在指定部位中心5°范围内的概率为1，即为一必然事件，刺激点100％地出现在中心5°范围内；当N＝100时，刺激点出现在指定中心10°范围内的概率为0.875，而在10°范围以外亦有少量刺激点出现。图形表之所以采用这种概率分布，为的是既能用较少的刺激点对已知的视野暗点进行定量检查，提高检查速度和灵活性，又能防止患者在检查时间稍长时习惯地转动眼睛去追踪集中出现刺激点的地方。

在一般的电脑视野计中，多采用Heijl方法，定期在生理盲点位置出现刺激点，如果患者回答看见了，就认为患者的眼已转动，随即发出警告[3]。但本系统在通过移动固视点来扩大

检查范围时，生理盲点的位置可能落在屏幕之外，故不能直接应用Heijl方法。因此WHA系统采用了定期闪动固视点的方法，要求患者按键作为回答，否则就发出声响警报，提醒患者注意固视点，并记录警告次数，供医生参考。这样就大大提高了视野检查的精度和可信度。

3. 自编程序检查方式

为了使操作尽量简便，在WHA系统中设计了自编检查程序的功能。医生可以通过菜单式提问，一次输入几个（不多于20个）欲检查部位的坐标、刺激点数，然后计算机自动地按照程序完成视野检查。这种方法能充分发挥医生的临床经验，缩短检查时间，并大大减轻了医生的操作负担。

4. 多点检查方式

我们还设计了一种多点检查方法，主要用于青光眼的普查。其方法是当被检查者固视屏幕中心时，在屏幕的不同位置（这些位置为青光眼视野改变出现几率最大的位置[4]）同时出现每次数目不等的刺激点。被检查者只需通过按N次键表示看见了N个刺激点即可。如果N小于出现的刺激点数时，计算机会自动查出没看见的点，并在其附近作更仔细的检查，直到得出结果为止。用这种方法检查一只眼只需要2—3分钟。

5. 扩大检查范围

由于受到显示器的限制，当固视点在屏幕中心时，只能对中心视野的20°×12°的矩形范围进行检查，满足不了临床的需要。如果用缩短检查距离来扩大检查范围，则因为离显示器太近，患者感到不适。由于平面视野计在30°的中心视野范围内与球形视野计相比，其误差可以忽略不计[2]，因此WHA系统用软件移动固视点位置的方法扩大检查范围。例如固视点下移，上方检查范围可从12°扩大到24°；同理，通过几次移动固视点，可以把检查范围由原来的约20°×10°扩大到30°×24°。而80%以上的视野病理改变在此范围内有暗点或缺损[1,5]，所以本系统基本上能满足临床的需要。

6. 对照检查与资料库

在临床应用中，经常需要在与上次检查时相同的位置上进行定量对照检查。因此WHA系统可以把患者以前做过的检查结果从磁盘上调入计算机，计算机就会按与原来相同的刺激点位置进行对照检查。

为了便于复查，在WHA系统中建立了一个资料库。可以把检查结果加以编号并存入资料库，保存在磁盘上，随时可以调入计算机重新在屏幕上显示出来。也可以通过打印机得到硬拷贝，供医生分析视野用。此外还能对资料库进行顺序检索和一些简单的库维护。

WHA电脑视野计在湖南省人民医院眼科及别的一些医院投入了临床试用。临床应用表明WHA系统有如下特点。

1）造价便宜，便于推广。

2）操作方便。

3）检查时间缩短，视野暗点检出率明显提高。对既有WHA视野报告，又有Goldmann视野报告或Humphery电脑视野报告的32只眼进行统计表明，WHA视野计发现暗点或视野缺损与Goldmann视野计对照符合率为92%，与Humphery视野计对照符合率是98%。

4）对操作人员熟练程度的依赖性减少。

5）修改、扩充方便。90%以上的软件是用BASIC语言编写。

参 考 文 献

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软 件 交 流

绘图程序编辑软件 **编号：88-0213**

本软件包括适用于SPL-400型绘图仪的EDSPL.COM，适用于DXY-101的EDXY1.COM，适用于DXY-800的EDXY8.COM以及适用于PLOT-1型绘图仪的EDPLT.COM。以上四种软件允许用户在直接编辑绘图程序时出现错误。软件对错误的处理方法有两种，即清除错误提示再输入和清除错误不提示。这一特点允许用户在编程时进行屏幕注释。软件由著名的ED.COM改编而成，除具有ED.COM的全部功能外，还增加了换行检测及行清除、行建立测试功能以及修改插入错误前置提示等功能。软件语言为8080汇编语言。软件占用内存实际为256字节，另有256字节备用。软件可在CP/M2.0以上版本环境下运行。该软件很容易改编为其他数控装置的程序代码编辑专用软件。

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BASIC-CAD数据采集及交换程序 **编号：88-0214**

计算机高级语言BASIC与AutoCAD各有所长。为用其所长，常常碰到BASIC与CAD互换数据的问题。由高级语言形成的数据，以·SCR文件的形式，很容易地为CAD所接受；用CAD采集的数据却不能直接为高级语言所使用。本程序所解决的问题是：将由CAD采集的数据格式自动转换成为高级语言所识别的数据格式。其中，CAD数据的采集可用键盘、数字化仪或鼠标器作为采集工具。本程序是针对地质制图中剖面图与平面图的转换问题而设计编写的。根据用户的具体要求作少量变动后，可用于工程地质、矿井地质、地震等剖面图数据向平面图转换的问题。数据整理、数据组合、数值计算三个功能模块用BASIC编写；CAD操作模块使用LISP语言。共占约2000字节。需要的软件环境是：PC-DOS2.0及其以上的版本、BASIC、编译BASIC、CC-DOS2.0及其以上版本、Auto CAD2.17b及其以上版本；硬件环境为：IBM PC/XT，IBM PC/AT机及其兼容机，可选用数字化仪及具备相同功能的设备、绘图仪等。

本程序以源程序和目标程序两种方式提供给用户。也可用能够计算三维图形的程序进行交换。

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