VISUAL FUNCTION IN PATIENTS WITH DIABETIC RETINOPATHY

A thesis submitted by

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Author's declaration

Unless otherwise specifically acknowledged, the investigations reported in this thesis are entirely my own work.

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Abstract

The screening efficiency of tests of visual acuity, colour vision, contrast sensitivity and central visual field in screening for Diabetic retinopathy (DR) was assessed (STUDY 1). ROC curve analysis and Bayesian test predictive values revealed the Composite Pseudoisochromatic Plate (Comp PIC) test of colour vision comprising 8 red-green Ishihara plates and 7 tritan plates, to be the most efficient test of all tests evaluated. For the screening of DR the test was 0.51 sensitive and 0.83 specific; whilst when used for screening of DR and/or other ocular complications the figures were 0.64 and 0.83, respectively. The performance of the other tests, when evaluated on their own, was unsatisfactory. When evaluated as a test battery the 3-test battery comprising the Comp PIC, Vistech VCTS 6000 and Amsler grid gave poorer results for the screening of DR alone (sensitivity=0.41 & specificity=0.83) when compared to the results obtained for the screening of DR and/or complications (sensitivity=0.72 & specificity=0.71).

In STUDY 2, tests of colour vision, contrast sensitivity and visual field were assessed for their ability to grade the severity of visual dysfunction in patients with 3 clinically-defined grades of DR. Two tests were identified as being most appropriate for the purpose: the same Composite plates described earlier and the Standard Pseudoisochromatic Plates Part 2; the former was able to distinguish "significant DR" from mild DR while the latter was able to distinguish "referrable DR" (ie. proliferative DR needing laser treatment) from mild and moderate DR. These two tests were also least affected by age and VA of the patients.

Two studies were carried out to investigate the effects of laser panretinal photocoagulation treatment for DR on the following visual functions: Visual acuity, colour vision, contrast sensitivity and visual field. In STUDY 3 the comparative effects on visual function of three treatment modalities for proliferative DR (Argon 488/514nm; DYE-577nm; DYE-595nm) were investigated. Transient central field deterioration was noted for all three treatment modalities; this corresponded to the areas lasered. A mild and transient effect on colour vision was observed with the Argon 488/514nm which manifested as an increase in the blue-yellow partial scores on the Farnsworth-Munsell 100-Hue test. Overall there were not any clinically significant differences in the effects on the visual functions amongst the 3 treatment modalities tested. In STUDY 4, a visual function assessment was made on patients with extensive Argon laser panretinal photocoagulation (range 4,100 to 10,402). Patients were found to have a higher prevalence of tritan colour vision defects and some inner (zones 10 degrees inwards) visual fields losses when compared to a group with untreated proliferative DR. Relationships between visual function deficits and the amount/intensity of treatment were found to be unexpected; this included negative relationships for colour vision & contrast sensitivity defects.

List of abbreviations

ANOVA	- Analysis of variance
Arg	- Argon treated eyes
Chi-Sq	- Chi-square test
Crit	- Criterion
CSF	- Contrast sensitivity function
BDR	- Backround diabetic retinopathy
BY	- Blue-yellow
Comp PIC	- Composite Pseudoisochromatic Plates
CS	- Contrast sensitivity
D15(5/4)	- Panel D15 Saturated (5/4)
D15(5/2)	- Panel D15 Desaturated (5/2)
dFb	- Degrees of freedom for between-groups variability
dFe	- Degrees of freedom for within-groups error variance
dFt	- Total degrees of freedom
DR	- Diabetic retinopathy
DR+C	- Diabetic retinopathy with other complications
DRS	- Diabetic Retinopathy Study
DMac	- Diabetic maculopathy
ETDRS	- Early Treatment Diabetic Retinopathy Study
F	- Female
FFA	- Fundus Fluorescein Angiography
FM 100-H	- Farnsworth-Munsell 100-Hue
GLM	- General Linear Models
IRMA	- Intraretinal microvascular abnormality
LTA	- Lanthony Tritan Album
M	- Male
MBPS	- Mean number of burns per session
MIBS	- Mean interval between sessions (months)
MS	- Mean square
ND	- Neutral density
No DR	- No diabetic retinopathy
No DR+C	- No diabetic retinopathy but with complications
NS	- Not significant
p	- Probability value
p(D/F)	- Predictive value of a positive test result
PDR	- Proliferative diabetic retinopathy
PIC	- Pseudoisochromatic
PL	- Plate
p(N/P)	- Predictive value of a negative test result
PDR	- Proliferative diabetic retinopathy
PRP	- Panretinal photocoagulation
RG	- Red-green
ROC	- Receiver Operator Characteristics
S	- Short wavelength sensitive
sd	- Standard deviation
SE, SEM	- Standard error of the mean
Sp/f	- Spatial frequency
SPP1	- Standard Pseudoisochromatic Plates Part 1
SPP2	- Standard Pseudoisochromatic Plates Part 2
SS	- Sum of squares
SSb	- Sum of squares for "between the groups effect"
SSe	- Sum of squares for "within the groups effect"
Sq	- Square-root
T	- Tritan
TALT	- Time interval after last treatment (months)
TES	- Total error score
TF	- Total field
TotPRP	- Total number of Argon PRP burns
TPE	- Total plate error
TSS	- Total sum of squares

List of abbreviations/contd

TypeDR	- Type of diabetic retinopathy at start of treatment
VA	- Visual acuity
VCTS 6000	- Vistech Contrast Sensitivity System 6000
VFA I	- Friedmann Visual Field Analyser Mark 1
XL	- Extensively lasered group
YrsDM	- Years of diabetes
Z	- Zone
577	- 577nm treated eyes
595	- 595nm treated eyes

CHAPTER 1

Introduction

1.1 A REVIEW OF DIABETIC RETINOPATHY AND ITS EFFECTS ON VISUAL FUNCTION

1.1.1 The Disease

Diabetic retinopathy (DR) is the collective name for the retinal and vascular complications of Diabetes mellitus. DR consists of a spectrum of conditions. However, for clinical purposes DR may be divided into 4 main groups (Aiello et al.1981; Murphy,1982): background retinopathy, preproliferative retinopathy, and proliferative retinopathy. Maculopathy is classified separately, irrespective of the stage of retinopathy. More sophisticated methods of classification are also available (DRS Res.Gp.1981; Klein et.al.1984a). A review of the clinical manifestation of the disease is given by Ariffin et al.(1992).

Based on diabetic clinic populations, at least 23% of all diabetic patients will show some manifestation of DR (Donovan,1978). 8% of all diabetics (10% of those with type II DM) will have some form of DR at the time of diagnosis (Soler et al.1969). The incidence of DR is closely related to the duration of the disease since it is a complication of long-standing diabetes. The total incidence of DR is 5% per year while that of sight-threatening DR is 1.2% per year (Foulds et al.1983). 25% of all diabetics will eventually get DR (Hill et al.1987).

Photocoagulation is the only clinically proven successful mode of therapy for DR. Sources of light available for photocoagulation are mainly of two types: Light coagulators (Xenon) and Lasers. Lasers have gained more popularity over Xenon Arc photocoagulators because of the ease of application and wide margin of safety afforded (Hamilton et al.1983). Being essentially monochromatic light sources, lasers are practically capable of producing selected wavelengths, depending on the source.

The Argon laser which has its wavelengths at 488nm and

514nm is the most commonly utilised source in the treatment of DR. Of late the Dye and Diode lasers have become popular; the Dye laser is a variable-wavelength (360 to 960nm) laser whilst the Diode is a long-wavelength (810nm) laser (L'Esperance,1985a,1985b; Brancato et al.1986; Brancato & Pratesi,1987; Brancato,1988; McHugh et al.1989; Balles & Puliafito,1990; Balles et al.1990). The use of longer-wavelength lasers has theoretical advantages (L'Esperance,1985a,1985b) although therapeutically their efficacy is no different (Schulenberg et al.1979; Brancato & Bandello,1987).

In the main, photocoagulation is used for the treatment of proliferative DR and diabetic maculopathy (DMac). In proliferative DR, the midperipheral retinal tissues are photocoagulated by a Xenon arc or a laser source to induce regression of new vessels employing a technique called panretinal photocoagulation (PRP). Clinical trials (DRS Res.Gp.1981; British Multicentre Study Gp.1984) have demonstrated conclusively that PRP with either modality (Argon or Xenon) preserved visual acuity better than no treatment. "Focal" photocoagulation treatment with either modality (Xenon or Argon) of DMac is most effective in selected cases (Whitelocke et al.1979) where 50% of blindness could be prevented (British Multicentre Study Gp.1983; ETDRS Res.Gp.1985).

1.1.2 The Effects on Visual Function

1.1.2a Visual acuity (VA)

Association with macular involvement

DR on its own is often associated with relatively good VA (Beetham,1963; McLeod et al.1988). However, when VA can be compromised in DR and the normal causes are: macular oedema, traction on the macula by proliferative processes of PDR, haemorrhage or hard exudate formation near the macula and macular ischaemia. These conditions constitute diabetic maculopathy. Bresnick et al.(1985), found VA loss to correlate more significantly with macular oedema than with overall DR; the correlation being more significant for fluorescein leakage in the macula than for capillary non-perfusion in the macula. VA was noted to correlate well with findings of fluorescein fundus angiography (FFA) at the macular region (Cambie,1980; Hori et al.1988). Interestingly Suzuki & Kogure (1987) argue that VA alone is not sufficient for detecting diabetic macular oedema in its early stages. Valone et al.(1981) reported a correlation between advanced degrees of hard exudation and and poor visual prognosis but found subtle loss in VA more difficult to explain, suggesting macular oedema as a cause.

A large proportion of patients with DR will also have lens opacities (Ariffin et al.1992) which would also contribute to the fall in VA in those with or without macular problems.

In relation to grades of DR

Patients with no DR or early BDR suffer no loss of VA. However, those with early maculopathy may experience reduced or variable VA (Blach,1983). Since DR is a patchy disorder (Shimizu et al.1981), patients afflicted are asymptomatic as long as retinal damage is confined to the area outside the macula. Patients with severe preproliferative DR or florid DR will often have reduced VAs in the region of 6/18 to 6/24 (Kohner & Hamilton,1987). Since the prevalence of macular oedema is also high in

these patients, this could contribute to the fall in VA.

It is a common experience to find patients with PDR to have clinically 'normal' VA and thus appear asymptomatic, until the time when vitreous haemorrhage occurs before VA becomes severely affected (Kohner,1991). However, patients with PDR may experience VA loss, the severity of which is influenced by the position and severity of the areas of neovascularisation (Birch et al.1980). In fact, a good correlation was found by Price et al.(1972) to exist between extensive PDR and reduced VA while isolated flat areas of PDR had little effect on vision. Once VA deteriorates the decline will be relentless in most cases (Cambie,1980) unless appropriate laser therapy is given. Severe loss of VA also occurs in the advanced stages of PDR when the macula gets wrinkled or when there is traction on it.

Clinical aspects of VA screening in diabetics

Cockburn (1987) found no significant differences in the corrected VA distributions of 100 consecutive diabetics and 100 randomly selected non-diabetics. He attributed this to selection bias, suggesting that his optometric sample differed from the population of diabetics which present themselves at diabetic outpatients' clinics.

The prime objective of VA measurements in diabetic patients is to detect any changes that accompany or preclude sight threatening DR (maculopathy and/or PDR) (Ariffin et al.1992). Unfortunately VA decrement due to DR occurs less frequently in old people as they have other reasons for loss of VA such as lens opacities or age-related maculopathy. VA has been repeatedly alleged to be an insensitive test for detecting the majority of patients with DR without maculopathy (Birch et al.1980; Foulds & McClure,1980; Bresnick,1989). VA measurements have also been said to be misleading in indicating the progress of DR in an individual patient (L'Esperance & James,1981). It appears that the role of VA in diabetic screening may therefore be limited. Nevertheless, as the prevalence of

age-related ocular disorders (eg cataract) is likely to be increased in diabetics with retinal involvement (Corcoran et.al.1985), the finding of a fall in corrected VA in these patients might not necessarily be a futile one. This avenue has been explored by Corcoran et al.(1985) who found that with a VA cut-off of 6/12 they were able to detect 72% of diabetics with "clinically discernible eye disease" whilst failing 10% of diabetics with normal fundi. Impaired VA is always a warning of eye disease and when the clinician is searching for subtle fundus changes, especially for maculopathy, any assistance is important.

Birch et al.(1980) stated that VA was not a helpful measure for grading the severity of DR, calling for the employment of more specific techniques. Corcoran et al.(1985), on the other hand, found that with the pinhole test, a fail criterion of 6/12 detected 93% of patients with maculopathy while failing 34% of diabetics with normal fundi. They, considering patients, calculated the predictive value of a positive test result to be 0.22 and that of a negative test result was 0.99. They concluded that a normal VA (defined as 6/12 or better) provides reasonable assurance that maculopathy is not present, which they considered to be a useful clinical pointer as maculopathy is amenable to treatment in its early stages. It would have been better if Corcoran et.al.(1985) had considered more than one cut-off criterion by carrying out an ROC analysis to identify the optimal VA cut-off criteria. This would have meant that a better trade off between the number of false positives and false negatives would have been attained.

1.1.2b Colour vision

General features of defect

The frequency of diagnosed colour vision defects in diabetics depends upon the selection of diabetics examined and the colour vision test used. In general about 30% to 70% of adult diabetic populations have been reported to have colour vision defects (Kinnear et al.1972; Lombrail et al.1984; Bresnick et al.1985; Silverman et al.1990).

The colour vision defect in DR has been described as an acquired type III defect (Cox,1960; Verriest,1963) with the following features: loss of hue discrimination with a blue-yellow (tritan-like) axis, abnormal colour matching using blue-yellow and blue-green anomaloscope equations, and colour confusions associated with tritan-like defects. The colour vision defect varies from a slight loss of hue discrimination to a mild, medium or strong type III (tritan) defect (Birch et al.1980). The severity of the colour vision defect can be related to the duration of diabetes (Caird et al.1969; Utku & Atmacia,1992) although this could not be generalised to all diabetics (Begg & Lakowski,1980; Roy et al.1986).

Some authors state that the colour defect starts as a disorder of the blue-yellow component of colour vision, but includes the red-green system as retinopathy worsens (Lakowski et al.1972/73; Vola et al.1982; Bresnick,1987; Suzuki & Kogure,1987).

A subclinical disorder ?

It is now well established that diabetics, even those without apparent DR, are more likely to have abnormal colour vision than are non-diabetics matched for age (Kinnear,1965; Lakowski et.al.1972/73), especially in those older than 30, even before any observable change in VA (Kinnear et al.1972; Begg & Lakowski,1980). Scase et al.(1990) and Hardy et al.(1992) are quite categorical that diabetics with normal fundi may have abnormal tritan vision.

Kinnear et al.(1972) suggested that diabetic colour vision deterioration may be an accelerated version of senile colour vision deterioration. They found that approximately 2/3 of diabetics without DR but with tritan defects could be expected to develop DR within 5 years. Studies which utilised mainly clinical colour vision tests have indicated that colour vision defect exists in eyes with mild DR and without retinopathy (Kinnear et al.1972; Lakowski et al.1972/73; Roy et al.1986; Scase et al.1987; Arden et al.1988a; Trick et al.1988; Hardy et al.1992) although some, however, disagree (Bronte-Stewart et al.1970; Howes et al.1982; Roy et al.1984; Spafford & Lovasik,1986; Birch et al.1987). Two recent studies have also provided conflicting evidence with regards to the matter: Greenstein et al.(1990) could not find any evidence of colour losses in patients with normal FFA, while Hardy et al.(1992) demonstrated colour vision losses in those without any biomicroscopic or angiographic evidence of oedema.

Birch et al.(1987) hypothesised that the acquired colour defect occurs together with DR rather than preceed it, a view endorsed by Bronte-Stewart et al.(1984), Roy et al.(1984), Spafford & Lovasik (1986), Arden et al.(1988a), Gunduz et al.(1988a) and Tregear et.al.(1993). However, as will be noted later, the use of more advanced laboratory tests has not confirmed this hypothesis. Whether those without DR but with colour defects will eventually develop DR is controversial (Bronte-Stewart et al.1984) and can only be resolved by a longitudinal study. One such study (Aspinall et al.1983) found poor yellow-blue discrimination on the anomaloscope to be the best single predictor of the development of DR over a 7-year period, of a number of factors examined.

Relation to severity of DR

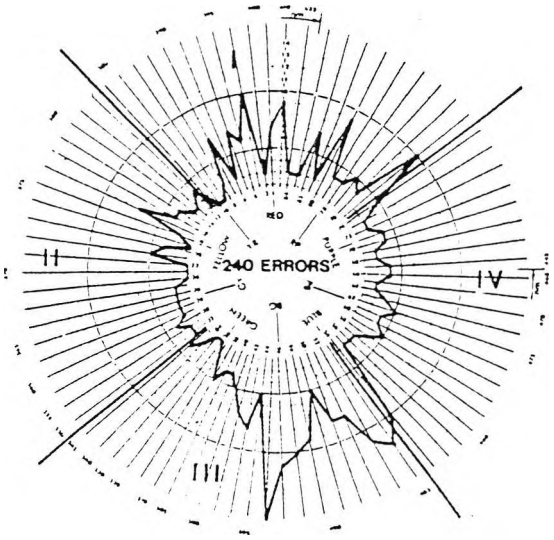
In the early stages of DR there is a slight type III defect accompanied by a slight overall reduction in hue discrimination (Birch et al.1980); hue discrimination gets worse as the retinopathy progresses. Extensive peripheral lesions in PDR seem to cause a loss of general hue

discrimination, which is presumably mainly in the tritan mode (Birch-Cox,1978) whereas direct insult to the macular results in definite tritan defect. The patient can even be tritanopic in cases of PDR and maculopathy (Birch,1988). In others, the overall hue discrimination becomes so poor that the patient becomes a monochromat.

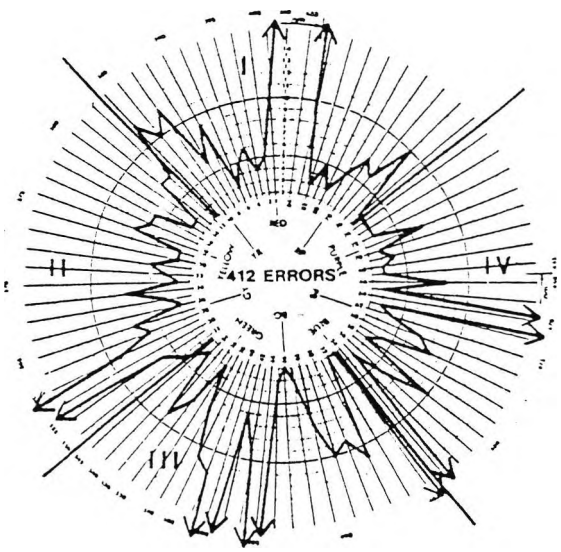
The correlation between colour vision deficit and severity of DR at the background stage has been reported to be poor, possibly due to the varying manifestations of the disease at this stage (Moloney & Drury,1982). Higgins et al.(1989) measured spectral saturation discrimination in diabetics with normal VA having different grades of DR. Although diabetics without DR showed normal saturation discrimination functions, in those with DR, there was little correlation between losses in saturation discrimination and the degree of DR.

Cambie (1980) reported a colour vision defect of the "blue axis" to be present in eyes with ischaemic or avascular zones, even in the presence of good VA. A correlation between the extent of zones of non-perfusion and the severity of the colour defect was found. Cambie (1980) argued that it was logical for the perception of blue to be affected in conjunction with severe peripheral retinal lesions alterations.

The colour defect is also more pronounced in eyes with macular oedema (Birch et al.1980; Cambie,1980; Bresnick et al.1985). Bresnick et al.(1985) found the magnitude of the acquired tritan defect in diabetics with DR to correlate significantly and to a similar extent with both the severity of overall DR and the severity of macular oedema and of hard exudate formation. Quadrant analysis of the FM 100-H test (as explained in 2.2) showed a predominance of a tritan axis in the scores. It was shown that as DR progressed from nonproliferative to proliferative, the severity of the colour defect increased. Of particular importance, was the development of macular oedema since the most profound deficit in hue discrimination on the FM 100-H

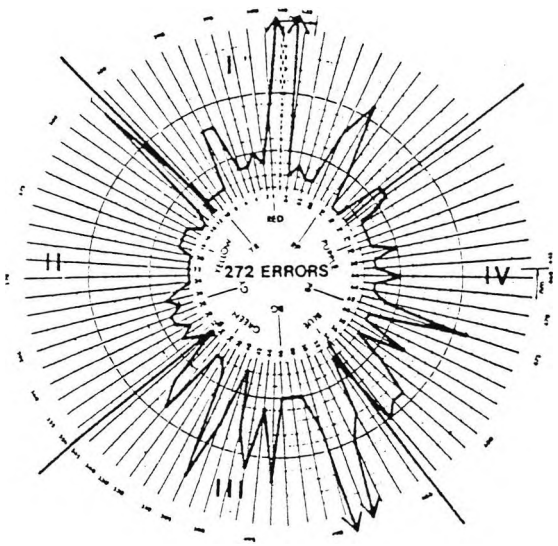


Nonproliferative DR without macular oedema (TES= 240/Axis=Tritan)

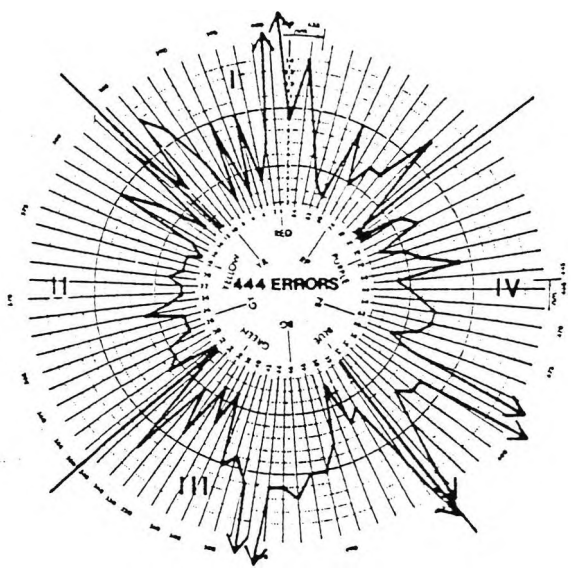


Nonproliferative DR with macular oedema (TES=412/Axis=Tritan)

Fig 1.1 Score sheets from FM 100-H test (after Bresnick et al.,1985)



Proliferative DR without macular oedema (TES=272/Axis=Tritan)



Proliferative DR with macular oedema (TES=444/Axis=Tritan)

Fig 1.1/Contd

test occurred in patients with macular oedema, regardless of the presence of PDR (fig 1.1). Begg & Lakowski (1980) also noted losses in colour vision in cases with foveal oedema in both young and old diabetics. The development of red-green impairment can also mark the development of exudative maculopathy (Green et al.1985).

Macular non-perfusion or ischaemia lateral to it was found to be associated with a gross loss of hue discrimination (with clinical tests) while colorimetric investigations revealed a tritanopic defect with intact red-green colour mechanisms (Birch et al.1980). In cases of maculopathy, in the presence of a marked tritan defect, VA may be only slightly reduced but metamorphopsia (on the Amsler grid) is readily detectable. The FM 100-H error score also becomes very large and the diagnostic pattern is difficult to interpret (Birch,1989). The most severe colour vision losses were observed in patients showing a combination of macular ischaemia and oedema (Begg & Lakowski,1980).

Involvement of the red-green system

Birch & Dain (1987) applied a computational technique called "the averaging method" on the FM 100-H plots of patients with proliferative DR (PDR), in order to confirm the presence of tritan axes amidst these complex polar plots. This revolutionary technique of extended analysis enabled the authors to reveal the tritan defect when visual inspection was equivocal; in most cases the defect resembled a congenital tritan defect. PDR patients with very high error scores and no discernible axis by inspection were shown by the analysis to have characteristics similar to typical rod monochromats. A hierarchy of colour deficiency in DR which leads to complete colour blindness, in the presence of moderately reduced VA was shown by Dain & Birch (1987).

Bresnick et al.(1987) applied the Kitahara scoring technique (Kitahara,1984) and found the mean axis of the FM 100-H plots to shift from a tritan axis (5.9 degrees) in eyes with nonproliferative DR toward deutan-like or

scotopic axis (19.9 degrees) in eyes with PDR. The axis shift was postulated to represent progressive involvement of medium-wavelength sensitive and long-wavelength sensitive cone mechanisms, or even optic nerve involvement as the more severe levels of DR develop. It has been reported that diabetics may develop overt optic atrophy which results in an acquired red-green defect which is distinguishable from the functional disturbance due to retinal disease (Foulds & McClure,1980).

A few reports support earlier involvement of both the red-green and blue-yellow systems (Green et al.1985; Trick,1988; Trick et al.1988). Trick et al.(1988) warned that their results neither confirmed nor disputed the proposition that the blue-yellow channel is selectively sensitive to diabetes-induced damage. Their results may simply indicate that the FM 100-H test is relatively insensitive to this early damage. Birch (1988) suggests that the red-green involvement is a manifestation of poor hue discrimination rather than a specific acquired red-green defect. Trick (1988) concluded that there is no evidence of a selective blue-yellow loss in diabetics; this was however, challenged by Atchison et al.(1991a).

Spectral sensitivity studies

Recent studies using spectral sensitivity measurements ie. studies of the increment threshold to blue light against a yellow or white background have furnished increasing amounts of evidence to validate the existence of the "preretinopathy" visual disorder (Adams et al.1980; Zwas et al.1980; Adams,1982; Adams et al.1982; Zisman & Adams,1982; Adams et al.1987a; Greenstein et al.1989a; Greenstein et al.1990). For instance Greenstein et. al.(1990) measured short wavelength (S) against Middle wavelength (M) cone sensitivity loss and found 70% of early diabetics have up to 1.2 log units loss of S cone response and no loss of M cone response. These studies have thus indicated that the short wavelength (S) pathway is selectively compromised early in diabetes, compared to other pathways resulting in a loss of sensitivity to blue light and tritan-like colour

defects. The selective depression is presumably secondary to changes in the retina such as vascular damage and hypoxia as a result of prolonged elevation in blood glucose. Additionally, short term, induced hypoxia also produces similar S-cone deficits (Schneck et al.1991).

The loss of S-cone sensitivity begins in patients with very early DR, or even in the absence of ophthalmoscopically detectable DR and also prior to VA changes or defects detected with standard clinical colour vision tests (Adams,1982; Adams et al.1982; Zisman & Adams,1982; Adams et al.1987a). The degree of S-cone loss increases with the severity of DR (Adams et al.1987a; Greenstein et al.1989b; Greeinstein et al.1990) and in the presence of macular oedema (Adams et al.1987b).

Influence of "metabolic" and "vascular" factors

Both metabolic (blood sugar regulation) and retinal vascular factors have been implicated in the pathogenesis of colour vision defects in DR (Bresnick et al.1985; Bresnick,1986). Diabetes-related metabolic dysfunction in the retina particularly contributes to the colour defect in the very early stages of the disease. Recent evidence also indicates that the colour vision loss occurring before the onset of DR may not have a vascular aetiology (Hardy et al.1992). Scase et al.(1990), although reported that colour vision losses occur before any angiographic changes, hence implying the involvement of other factors presumably metabolic, however, did not rule out vascular changes *per se* as the cause.

However, when obvious vascular changes i.e. leakage and non-perfusion become evident, it is possible that both the metabolic and vascular changes combine to cause the colour defect. Selective damage to the post-receptor pathways has also been suggested (King-Smith et al.1984; Applegate et al.1987).

A number of studies have indicated that colour vision is affected by metabolic control (Adams et al.1982; Muntoni et

al.1982; Zisman & Adams,1982) while others have not found such a correlation (Lakowski et al.1972/73; Trick et al.1988; Scase et al.1987); thus often causing the lack of a meaningful correlation between visual function test results in general and the severity of DR.

Prompted by the unclear correlation between overall metabolic control and colour vision defects in diabetics, Volbretch et al.(1989) examined the functional relationship between visual (spectral) sensitivity and metabolic control. They found diabetics that displayed a significant decrease in S-cone sensitivity during both hyperglycaemic and hypoglycaemic episodes. Schneck et al.(1991) also found that the fluctuations in blood glucose that diabetics exhibit over hours and days can significantly affect S-cone sensitivity; however, other colour discrimination tasks (e.g. FM 100-H and D15 tests) might not be affected.

Normal colour vision

Despite all that has been said about the type of colour vision defects existing in patients with DR, there are occasional patients with extensive PDR who have normal or nearly normal colour vision (Moloney & Drury,1982; Roy et al.1984). The colour defect may also improve when the underlying pathology undergoes remission (Lovasik & Kothe,1987).

Clinical studies of colour vision testing in diabetics

Birch et al.(1980) defined three purposes of colour vision testing of diabetics: 1) To detect patients with BDR in the early stages, 2) To monitor the progress of DR and 3) To assess the effects of treatment. Having found colour vision tests to be effective in demonstrating the deterioration in macular blood supply, Birch et al.(1980) suggested tritan PIC plates and the panel D15 (saturated & desaturated) to be used as a first measure. Monitoring the progress of DR and assessing the effects of treatment require a more extensive test battery; a wider range of PIC plates and the FM 100-H test are suggested while colorimetric tests, are also desirable. Since diabetics are expected to show a

reduction in blue-green discrimination, this fact should be exploited fully in designing or selecting the appropriate tests.

Using different PIC plate tests, Lagerlof (1984) found the detection rates of his battery of colour vision tests in 112 diabetics to range from 3% to 61%. Very few "mixed" defects (red-green & tritan), and no sole acquired red-green defects were found. The Ishihara plates showed very poor sensitivity for acquired defects. The presence (or absence) of DR was not mentioned in the sample. Nevertheless, the contention that PIC plates are unsuitable for use in acquired colour vision defects is no longer valid nowadays with the availability of new "tritan" plates (e.g. Standard PIC II, Lanthony Tritan Album etc).

A set of PIC plates including a combination of red-green Ishihara and "Birch's tritan plates" was used by Birch et al.(1987) together with the Lanthony D15 (8/2) test (Lanthony,1978). The test battery was found to identify 50% of eyes with severe background DR whose retinal condition required monitoring. It also identified all patients who required laser treatment. Birch et al.(1987) also described the screening usefulness of the modified TNO tritan test in a study involving 24 diabetics. The TNO test is a spectral test of blue perception (Van Norren & Went,1981) and it was modified by having the luminance of the blue test field on continuous adjustment rather than on discrete steps as in the prototype version.

The use of a combination of PIC plates designed to detect both red-green and tritan defects in diabetics was again explored by Birch et al.(1991) in a similarly designed double-masked study. The test combination have been reported to detect an average of 52.5% of eyes with DR whilst giving an average of 14% of false positives; an overwhelming majority being detected by the "tritan series" alone. The tritan plates were also more effective in detecting eyes with more severe forms of DR; this included all patients with significant DR who required monitoring

and those who needed immediate laser treatment. Patients with minimal DR who were not detected did not require regular supervision. The 8 red-green plates from the Ishihara test used in combination with the tritan plates were found to be failed by 15 eyes (42.9%) with DR, mainly by those with more severe DR and no false positives were generated (Birch et al.1987). Birch et al.(1991) remarked that additional failure on these plates (in addition to failing the tritan plates) indicated the presence of severe DR with macular involvement.

The PIC series used by Birch et al.(1987) and Birch et al.(1991) also contained the single demonstration plate from the Standard PIC plates I (SPP1) (see chapter 2). This particular tritan plate detected 25.7% of eyes with DR (Birch et al.1987). In a later evaluation (Birch & Ariffin,1990), it was found that this plate, in combination with plate 5 from the Lanthony Tritan Album (LTA plate 5), detected 20% of eyes with DR while also failing 5% of those without DR. The single LTA plate 5 was quoted to detect about 25% of eyes with DR, generating 5% false positives.

The single SPP1 plate was shown by Birch et al.(1987) to detect the more severe forms of DR. LTA plate 5 was shown by Birch et al.(1988) and Birch et al.(1991) to be failed by patients with severe DR having concurrent macular involvement, and by those with a combination of DR and media opacities. In a study on diabetic children with no DR or mild DR, Mantyjarvi et al.(1988) were not able to find any colour defects using the LTA (full version). Mantyjarvi (1989a) tested 66 diabetics who had been treated with laser and found the LTA to detect colour defects in only 25 (38%) of the patients. Out of this 25, only 9 patients failed plate 5 exclusively. Some of those who passed were confirmed to have a tritan defect on the FM 100-H test.

The combination of PIC plates used by Birch et al.(1987) were shown by Ariffin (1990) to be as effective as the Standard PIC plates II for identifying diabetics with proliferative DR.

The Standard PIC II (see chapter 2) was used by Mantyjarvi (1987a) to identify diabetics who could not read colour-dependent blood glucose tests. These plates were found to detect 62% of diabetics who already had laser treatment. These patients presumably had more severe retinal conditions as a result of advancing DR and/or as a result of laser treatment. It has been shown that patients undergoing laser treatment are made tritan (to be elaborated later). In later study Mantyjarvi et al.(1988) found the plates to be ineffective in detecting colour vision defects in diabetic children with little or no DR.

Using the Fletcher-Hamblin Simplified Colour Vision Test (SCVT) on 204 diabetics, Allwood & Tyler (1988) also found red-green, tritan and mixed colour vision defectives within the sample. A further development of the SCVT called the DS8 test was described by Fletcher (1991); tested on 87 diabetics with 3 grades of DR and on 69 controls by Maxwell (1989), females with any type of DR showed "mixed" defects often and up to 40% in the 30 to 60 age group while for male diabetics with any grade of DR showed "mixed" defects ranging from 40% to 90%.

The panel D15 test has also been suggested for screening of colour defects in diabetics (Lovasik & Kothe,1987). The original version (5/4) (see chapter 2) was found to be too insensitive for detecting DR (Mantyjarvi et al.1988). Birch et al.(1987) used the Lanthony's D15 (8/2) for the purpose of screening for DR and reported some very encouraging results. All eyes without DR passed the test while 26 eyes with severe DR, 21 failed the test. The fail criterion was, however, not made clear in the report. Furthermore, the small number of "normal" patients had also boosted the reported specificity of the test.

Benson & Farber (1988) examined the screening efficiency of the test on a heterogeneous sample of 175 diabetics. They detected 73% of patients with DR while generating 41% of false positives. They concluded that the test's poor specificity and positive predictive value prevents its

promotion as a good screening test for DR. The high value (value=8) of the test caps presents a difficulty tc elderly patients, contributing to the poor specificity of the test. Mantyjarvi et al.(1988) found the test to be performed better by older children and that it was also not sensitive enough for detecting mild DR.

The desaturated version (5/2) has also been evaluated (Adams & Haegerstrom-Portnoy,1987). In two preliminary reports (Birch et al.1988; Birch,1989) it was reported that the D15(5/2) was highly efficient in detecting DR and that the errors made increased with increasing DR severity. The test was found to be 80% efficient as a screening test for DR, generating 15% of false positives consisting mainly of elderly patients (Birch,1989). The test was also reported to be effective in distingushing slight acquired colour defects which accompanied the onset of significant DR. However, this optimism waned as it was later found, in a more comprehensive evaluation (Birch et al.1991) that the test gave too many false positives as it was poorly understood by elderly patients.

Bresnick et al.(1984a & 1984b) found the D15 (5/2) performed under dim illumination identified 85% of patients with high urinary glucose. 35% of those who performed the urinary tests correctly also failed the D15(5/2) test. As the D15(5/2) was also found to correlate with the FM 100-H test, Bresnick et al.(1985) further suggested that the test be used in place of the FM 100-H for the screening of diabetics with PDR.

Birch (1989) also reported that a graded series of D15 tests comprising the 5/4, 5/2 and 8/2 versions offer an alternative test strategy which is both quick and effective. Having found the type and number of errors made by diabetics in the three D15 tests to be related to the FM 100-H test pattern and error score, a grading system was proposed for use in grading the severity of the colour defect in DR.

The FM 100-H test has been suggested as a useful screening test for PDR by Bresnick et al.(1984b). From the data of Bresnick et al.(1984b) and Green et al.(1985) the detection rate of the FM 100-H test for detecting PDR has been calculated as 54% and 55%, respectively. Suzuki & Kogure (1987) reported that the test was effective for detecting macular oedema in the early stages. Despite the good correlation between abnormal hue discrimination and the severity of DR (and lesions of DR), the FM 100-H test was not regarded as a good screening test for DR by Roy et al.(1984), Roy et al.(1986) and Green et al.(1985).

Maione et al.(1984) observed in "preretinopathic" diabetics that with more aggressive diabetic therapy, the prevalence of errors in the FM 100-H test shifted from boxes 2 & 3 (blue region) to boxes 1 & 4. Thus by identifying such regional deterioration, they claimed that they had demonstrated the value of the FM 100-H test in predicting the risk of DR.

Adams et al.(1987a) described a simple forced-choice clinical test called the Berkeley Colour Threshold (BCT) Test which isolated blue cone function much along the lines described by Stiles. The test is able to bypass media and pupil effects in isolating the blue cone response. Using the test, blue cone sensitivity losses were shown to be related to the severity of DR in 60 diabetics. When the test was evaluated against the FM 100-H test and the D15(8/2), it was found to be a more powerful functional measure of DR than the other two (Witkin et al.1986). The test was able to predict both the level of macular oedema and DR.

Using a new computer graphics-colour TV system (Arden et al.1988b), Gunduz et al.(1988a) found an increased tritan threshold in 23 out of 25 patients with BDR in whom FM 100-H scores were below 50 and no demonstrable tritan axes. Greenstein et al.(1990) argued for increment threshold testing at two or more levels of adaptation to be used as a sensitive method for detecting early DR. Scase et al.(1987)

used short duration flashes test stimuli on diabetics with and without DR. Diabetics without DR were found to have increased thresholds along the tritan axis with reduced flash duration. They concluded, in agreement with Gunduz et al.(1988b), that measures of hue discrimination with short duration flashes detect losses in colour not found using the FM 100-H test and may predict later, more marked, losses in colour vision.

Birch et al.(1991) argued that the potential accuracy of screening for acquired type III (tritan) colour vision defects is affected by the age profile of the patients being examined. False positive results have been quoted to occur due to age-related physiological changes in the eye-media, such as increased density of the crystalline lens which may occur at a younger age in diabetics. In fact lenses of young type I diabetics age or "yellow" at an accelerated rate, similar to that of normals over the age of 60 years (Lutze & Bresnick,1991). Additional confounding factors found in the elderly diabetic eye are: Increased macular pigmentation (Bone & Sparrock,1971; Bornstein,1977) and senile miosis (Pinckers,1980). Physiological progressive yellowing of the lens with age, and light scatter in the ageing lens also play a part (Said & Weale,1959; Verriest,1963; Ruddock,1965a & 1965b).

It is evident from the foregoing discussion that many tests using Munsell colours have been done to detect DR; the results however, have been unsatisfactory. In conclusion it would appear that there is no test with a sufficient sensitivity and specificity, that there is no broad measure of agreement among various authors although tritan abnormalities are most frequent.

1.1.2c Contrast Sensitivity (CS)

General features of defect

Diabetes has been reliably reported to affect CS (Arundale,1978; Arden,1978b; Foulds & McClure,1980; Zisman et al.1981; Ghafour et al.1982; Yamazaki et al.1982;

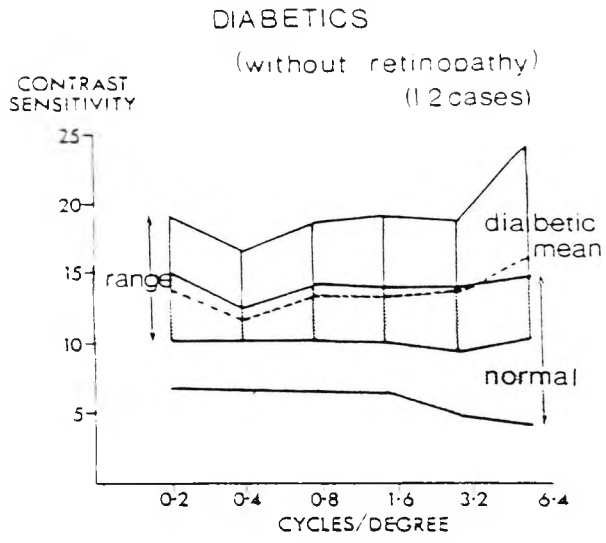


Fig 1.2 Arden grating test results: Patients without DR.

An overall depression of CS at all spatial frequencies tested is apparent (after Foulds & McClure)

Hyvarinen et al.1983; Della-Sala et al.1985; Kawasaki et al.1986; Sokol et al.1985; Marmor,1986). In diabetics with DR, CS is often abnormal even in the presence of normal VA.

A few authors have reported loss of CS in the absence of DR (Foulds & McClure,1980; Ghafour et al.1982; Moloney & Drury,1982; Hirsch & Puklin,1983; Della-Sala et al.1985; Sokol et al.1985; Elliot et al.1988; Trick et al.1988), while others (Arden,1978b; Regan & Neima,1984; Khosla et al.1991), do not share this view. Fig i.2 shows the results of Foulds & McClure (1980) using the Arden gratings.

Khosla et al.(1991) have suggested that studies which demonstrated losses in CS amongst patients without DR could have inadvertently mixed patients up. Those with early maculopathy could have been grouped into those with BDR and similarly, those with early DR into the group without DR.

CS is reduced in diabetic maculopathy and so is VA (Arden,1983). There have been reports suggesting that mild maculopathy can be detected with CS tests when VA is still normal (Arden,1978b; Wolkstein et al.1980; Ghafour et al.1982; Howes et al.1982; Khosla et al.1991). This is expected in view of the patchy nature of the disease.

Relation to severity of DR

CS dysfunction generally parallels an increase in DR severity (Yamazaki et al.1982; Hyvarinen et al.1983; Regan & Neima,1984; Kawasaki et al.1986) but with increasing variability in the results (Ghafour et al.1982). Howes et al.(1982) found loss of CS over all spatial frequencies which are related to both the severity of DR and cataracts. Some investigators, however, disagree (Moloney & Drury,1982; Hirsch & Puklin,1983; Collier et al.1985; Elliot et al.1988). The reason for a poor correlation between CS impairment and DR features is because the retinopathy is often very localised (Della-Sala et al.1985). Thus, depending on how wide an area covered by the test being utilised, different results could be obtained.

Arden (1978b) concluded that CS is only abnormal when DR has progressed to the point where VA has deteriorated significantly. However, there was also a proportion with definite DR who had normal CS. Consequently, the value of CS as a screening tool is thought to be doubtful. Another unexplicable finding was the similarity in DR severity in patients with good VA whether or not they had abnormal CS. Arden (1978b) and Arden (1979) also tested diabetics with mild DR and found that the proportion of patients with early DR and poor CS was greater than originally thought. The detection of early DR in asymptomatic patients was then thought to be feasible. However, the exact proportion of diabetics with minimal DR and losses in CS is unknown. It is perhaps not sufficiently high to warrant the use of CS as a screening test for every diabetic. The following were noted as having CS deficits: 60% of diabetics with normal VA and DR, and 100% of patients with VA less than 6/12. Arden (1979) in agreement with Zisman et al.(1981) consider that in routine use, CS testing should be useful for detecting a number of asymptomatic patients with mild DR whose fundi are difficult to detect in routine funduscopy.

Spatial frequencies involved

Using the Arden gratings, Ghafour et al.(1982) showed that diabetics had CS deficits at all spatial frequencies tested when compared to normals. Diabetics without DR had significantly lower CS at the high spatial frequencies (3.2 & 6.4 c/degree). CS was also significantly lower in patients with BDR than in those without DR. They, in agreement with Moloney & Drury (1982) have suggested that the Arden gratings are a poor screening tool for DR due to the large variances in the test scores.

Moloney & Drury (1982) assessed 66 well controlled type I diabetics with normal VA and found abnormal Arden grating scores (scores > 82) in 70 (53%) eyes. Increased score was apparent on all plates. The mean grating score and the prevalence of abnormal scores were similar in patients with and without DR. The mean scores were also not correlated with age or duration of diabetes.

Skalka & Helms (1983) reported CS measurements using both a TV monitor (sine wave gratings) and the Arden gratings on 42 juvenile onset diabetics with 6/6 or better VA. They found a significantly increased incidence of abnormal CS, especially at low spatial frequencies (0.8 and 3.2 c/degree) in well-regulated juvenile onset diabetics with disease of short duration who were free of DR.

It is clear that the early results of Arden (1978b) were encouraging, but they were essentially subjective. The point about the work of Skalka & Helms (1983) was that they took a tightly controlled group, with the same sort of diabetes, and did proper psychophysical measures and hence showed that there was a real loss of CS. However, the use of CS tests for screening is quite another matter.

It is not generally agreed as to which spatial frequencies are more prone to the effects of DR (Virsu et al.1981), as also evident from the the preceeding discussion. A few have shown that the higher spatial frequencies are more vulnerable (Sjostrand & Frisen,1977; Arundale,1978; Ghafour et al.1982). Sokol et al.(1985) showed that in type II diabetics, the higher spatial frequencies become first affected; but as DR becomes more severe, all spatial frequencies eventually become involved. In these patients, who are often elderly, the increased prevalence of cataract and other degenerative changes results in a wider range of CS deficits; showing how difficult it is to make precise statements about the role of CS testing in such conditions (Arden,1988).

All types of maculopathy cause a marked loss in mid to high spatial frequency although high frequency loss is expected to be most marked in the oedematous type (Swann & Lovie-Kitchin,1990). Diabetic maculopathy can affect CS over a range of spatial frequencies without changes in VA (Mittl et al.1989). There is an indication that significant deficits in CS are evident only for the mid-range spatial frequencies (Burde et al.1986; Trick et al.1988) while Howes et al.(1982) reported involvement of low and medium

spatial frequencies in BDR. In a review paper, Arden (1988) stated that the CS of patients with BDR is normal, but low frequency losses may occur with BDR even though VA is normal.

Clinical studies on CS testing of diabetics

TV generated sine-wave gratings were employed by Howes et al.(1982) on 55 diabetics having DR, macular disease and cataract of differing severities. Their results suggest that CS testing may be a practical screening device for early diabetic macular involvement or cataract. Loss of CS over all spatial frequencies was related to the severity of both DR and cataract. Cataract, however, had a more pronounced effect on CS than DR. BDR depressed CS particularly at the low to medium spatial frequencies which was more pronounced with macular involvement.

Hyvarinen et al.(1983) found normal or slightly depressed CS in patients with early BDR in comparison with normals. Patients with more severe DR or those with PDR who had had laser treatment had the worst CS. Interestingly, hypoglycaemia was found to cause a reversible decrease in CS.

Regan & Neima (1984) examined the CS of 15 diabetics using low-contrast letter charts and compared their findings with those obtained with TV-based sine wave gratings. Their finding was that low-contrast letter charts can detect visual loss that is not detected by the standard VA test. Of 9 patients with VA of less than 6/7.5, 4 showed losses (at low spatial frequencies) on the gratings and 6 had abnormal results on the letter charts. They also showed correlation between CS deficits and results of fluorescein angiography. The point about this work is that the losses in VA were not detected on a standard chart; there is no evidence that CS is "magic" and somehow tests a different visual function. The work by Sokol et al.(1985) is the only one that gets near to establishing this.

Using TV-based apparatus, Sokol et al.(1985) found high

the Vistech VCTS 6500 chart by Trick et al.(1988). Significant CS reductions were observed in 24.3% of the diabetics with no DR and 45% of those with DR. An overall reduction in CS was evident for both groups, but the largest and the most frequently significant abnormalities were detected with mid-spatial frequency gratings (6 & 12 c/degree). No statistically significant correlation between CS and glycosylated haemoglobin was found. There was a significant negative correlation between CS at 6 c/degree and the duration of diabetes. No evidence of any difference in CS was found between type I and type II patients.

Khosla et al.(1991) also used the Cambridge Low CS Charts to evaluate the CS of 22 diabetics with 6/6 VA. They found that CS was significantly lower in diabetic eyes with DR compared to normals eyes or eyes of diabetics without DR. All patients were screened with fluorescein angiography. Their results substantiate the notion that CS deterioration in diabetes is secondary to the occurrence of DR and does not occur prior to it. They also failed to reveal any loss of CS in those without DR in type II patients. As a test for screening patients with DR, the Cambridge Low CS Chart had a sensitivity of 50%. For screening of BDR, the test was 88% specific with an agreement rate of 82% of the clinical diagnosis based on ophthalmoscopy/angiography. The authors felt that CS evaluation may have a role in screening patients for DR in primary care facilities.

CS to sinusoidal gratings of low, medium and high spatial frequencies (0.8, 3 and 10 c/degree) was measured in 16 diabetics with diabetic maculopathy by Mittl et al.(1989) using a modified forced-choice procedure which was relatively bias-free. Significant CS losses were noted at all 3 spatial frequencies for diabetics in comparison to age-matched controls. The losses even occurred in cases where VA was near normal.

Yamazaki et al.(1982) measured the CS at 2 c/degree of 27 diabetics suffering from different grades of DR by means of visually evoked cortical potentials (VECP) with

checkerboard patterns. They showed that both VECP and psychophysical contrast thresholds were significantly higher in diabetics than in normals, even when no DR was present. In those with DR, there was a significant difference in the results between patients with mild DR and those with severe DR. Besides DR, the authors stated that the decrease in CS could also be the result of diabetes affecting the cerebral cortex and the optic nerve. The VECP measure, however, is a suprathreshold measure and is susceptible to modification by optic neuropathy, which occurs in DR.

Some concluding remarks

In summary great variability in CS results have hitherto been noted due to the age range of the population investigated and the likelihood of intercurrent conditions simultaneously affecting the CS. This (variability) reduces the value of the CS test in separating the population into groups with no DR, mild BDR and those with severe DR needing treatment. Arden (1983) argues that the problem faced with printed CS tests was the large inter-individual variation and hopes to improve the usefulness of such tests by serially testing the same individuals. Arden (1983) adds that there are no large longitudinal studies that have examined whether in each individual the gratings scores increase at the stage of DR where treatment is warranted. This, according to Arden (1983) is important because the reproducibility and reliability of CS measurements with printed gratings is much greater for repeated tests in one individual (Weatherhead,1980: Vaegan & Halliday,1982) than across a whole population.

1.1.2d Visual fields

General features of defect

Early reports by Livingston (1943) and King et al.(1963), while not specifying the field instruments used, suggested the presence of central field scotomata in diabetic eyes with no DR and the persistence of such defects in eyes with exudative DR even after the resolution of exudates. A more

recent report by Bresnick (1989). also not mentioning the instrument employed, suggested that field defects in DR are normally expected to be of a focal nature, corresponding to the localised lesions present. Trick et al.(1990), using the Humphrey Field Analyser state that field defects can often be detected in diabetics with most moderate DR, with greater frequency in type II patients. Furthermore it has been suggested by Werner (1991) that often a generalised loss of sensitivity with scattered scotomata is found in DR, that does not seem to fit any specific anatomic pattern.

Ironically, visual fields as determined by Goldmann perimetry have been reported to be usually within normal limits in diabetics (Benson et al.1988), even in those with PDR (Frank,1975).

Variations in reported frequency of defects

There is a variation in the reported frequency of field defects in DR; part of the difference is attributed to variations in the extent of DR evident in the patients as well as the different field instruments used. Roth (1969) detected scotomata in 100% of diabetics with visible DR whereas Wiznia et al.(1971) found significant field defects in 54% of the patients with nonproliferative DR. These early studies used manual and basic instrumentations which meant that the reported presence of scotomata be questionable; if the patient had maculopathy how was fixation maintained on such unsophisticated apparatus ? Jagger & Hamilton (1984) reported that visual fields examined with the Topcon perimeter and the Friedmann Visual Field Analyser showed reduction in visual field of up to 20% in patients with PDR. They unfortunately did not mention how the calculations were made in deriving those figures. Trick et al.(1990) noted field defects in 47.4% of patients with mild background DR (BDR).

Areas of visual field affected

As is found with FFA, the earliest defects have been

reported to be located in the mid-periphery (Greite et al.1981). In the early stages of DR these losses have been reported to be located between 15 to 45 degrees from the macula (Federman & Lloyd,1984; Sabry et al.1987) which then become more advanced in the later stages of DR as the retinal hypoxia increased. An overall drop in sensitivity has been found with static perimetry among diabetics with BDR (Foulds & McClure,1980). Trick et al.(1990), on the other hand, noted that field defects in BDR tended to be localised in the superior quadrants i.e. between 20 to 30 degrees eccentricity. Obviously differences between reports are largely due to different instruments employed although this would not be expected to alter the position of the defects in the field.

It is common clinical experience that PDR and large haemmorhages cause significant field losses (Wiznia et al.1971) although it is doubtful if a field test can be done after a vitreous haemorrhage. Most of the scotomata in DR are generally small, except in PDR where they may be expected to be large and located distal to the area of neovascularisation (Bek,1990a: description of work to be elaborated later). Scotomata which are not related to any fundus pathology have also been found in PDR at 30 degrees eccentricity.

A subclinical disorder ?

Relative and absolute field defects in DR may occur in areas with no apparent abnormality (Bek & Lund-Andersen,1990; Bek,1991). Caird et al.(1969) pointed out the possibility that small visual field defects unassociated with visible DR may precede observable fundus changes. Trick et al.(1990) showed such defects to be more prevalent in type II diabetics: however, they remarked that it was unclear whether such defects represented a preretinopathic stage related to focal areas with neovascular abnormalities or localised regions of defective circulation. In either case the fact that early vascular abnormalities such as microaneurysms may disappear could afterall mean that the preretinopathy stage was not

preretinopathic at all.

Roth (1969) used the Roth Scotometer and found central field defects in all diabetic eyes with DR. However, about 50% of patients without DR also had field defects. Roth (1969) suggested that the scotomata in eyes without DR represented preretinopathy which were also associated with microangiopathy. Later studies which employed more advanced instrumentation (Sabry et al.1987 -using the Friedmann Field Analyser Mk II; Trick et al.1990- using the Humphrey Automated perimeter) have largely confirmed the existence of field defects in diabetics before the development of clinically detectable DR.

Bloom et al.(1972) recorded the presence of transient scotomata in patients with no visible DR. In those with DR, they found that the scotomata did not necessarily occur at sites of ophthalmoscopically visible retinal lesions. Recently, the notion of field defects in diabetes occurring very closely in relation to microangiopathy has been challenged (Foulds & McClure,1980; Bek & Lund-Andersen,1990; Bek,1990b; Bek,1991). Foulds & McClure (1980) found the majority of patients with DR showed no recognisable defect in visual field (includes static perimetry), even when a significant degree of capillary non-perfusion was revealed on fluorescein angiography.

Trick et al.(1992) argue that there is adequate supporting the presence of field defects in diabetics with little or no DR. This conclusion is further supported by a recent study by Bek (1991) who found no relationship between the localised scotomata and vascular occlusion in diabetics with PDR. In the opinion of Trick et al.(1992), the issue is resolved; field defects can be present and are detectable with appropriate techniques. Effort should now be directed at establishing the relationship, if any, between these visual field defects and retinal microvacular abnormalities or pathologic mechanisms associated with diabetes. It would even be more useful, academically at least, to be able to correlate this finding with

Greenstein et al.(1990) for example, who found no changes in M-wave cones even though the S-wave cones had gone.

Relationship with fundus morphology

Studies have shown that field defects in DR relate to the sites of overall and macular angiographic abnormalities (Bell & Feldon,1984; Bek,1991). Field defects also correlate with retinal vascular compromise as evident from vitreous fluorophotometry in type II diabetics (Trick et al.1990) but not in type I patients (Shields & Trick,1989). Studies either using manual techniques (Roth,1969; Williams et al.1970; Hasunuma et al.1983) or computerised perimetry (Gandolfo et al.1983; Federman & Lloyd,1984; Yabuki et al.1987) have recorded field defects which correspond specifically to retinal oedema and capillary non-perfusion. Some (Bek & Lund-Andersen,1990b; Bek,1991) have not found consistent relationships between capillary non-perfusion/leakage and field defects. The field defects in areas of non-perfusion are supported by histological evidence (Bresnick et al.1975); these are attributed to retinal ischaemia at the level of the terminal arteriole and capillary network (Bek,1991). The occasional finding of non-perfused retinal areas with normal sensitivity (Foulds & McClure,1980; Bek,1991) still remains to be explained.

Williams et al.(1970) found isolated absolute scotomata in areas corresponding to cotton-wool spots; they suggested that the deficit was caused by damaged retinal neurones rather than nerve fibre bundle defects. The field defects did not resolve despite the disappearance of the lesions, suggesting that they were permanent functional deficits. It could however be argued that the scotomata were not caused by the cotton wool spots afterall. Since cotton wool spots are about 300 microns in diameter, so the corresponding area of field loss would be rather small and hardly able to plotted by perimetry.

Temme et al.(1980) made a detailed investigation of both the static and kinetic visual fields of a patient with very early DR. There was a consistent constriction of isopters

in the area of anomalous vascular bed. Static perimetric findings also showed a marked decrease in sensitivity in the same area. However, in the area with microaneurysms no orderly alteration in sensitivity was noted.

Bell & Feldon (1984) correlated static perimetric findings with wide-angle fluorescein angiography in 11 patients with non-proliferative DR. They found overall visual fields to correlate linearly with capillary perfusion. Relative scotomata were found in areas of capillary non-perfusion. Scotomata were also found in central field areas which had normal perfusion. The authors postulated the involvement of local metabolic factors in causing the field loss apart from capillary drop-out.

Federman & Lloyd (1984) performed perimetry on 90 patients with DR using the Octopus perimeter. Their data showed a consistent relationship between localised threshold sensitivity depression and perfusion abnormalities in asymptomatic patients with early DR. They also found direct correlation between the extent of the field defects and the presence of PDR. Mild field losses were noted in patients with BDR whereas moderate and advanced losses were found in both patients with BDR and those with PDR. The midperiphery was shown to be at greatest risk of developing early field losses where a ring scotoma is seen at 20 to 45 degrees from the fovea. The whole field (up to 60 degrees) eventually becomes involved, with the peripheral region being the worst affected.

Studying on 90 diabetics with different grades of DR Bresnick et al.(1985) found field loss to correlate more significantly with overall DR than with macular oedema. This implied that field abnormalities reflected disease more in the peripheral retina than in the central area.

Sabry et al.(1987) made threshold measurements on the Friedmann Visual Field Analyser II on 20 type I diabetics with no signs of DR. All eyes showed reductions in field sensitivity especially in the area 15 to 20 degrees from

the fixation point. Those with angiographic changes were significantly worse than those without angiographic changes. Patients with no angiographic changes showed significant reductions in sensitivity in the overall 30-degree field when compared to normals. A correlation between retinal light sensitivity and duration of diabetes was demonstrated.

The results of Trick et al.(1990) agreed with other reports that visual field defects are often evident in diabetics before the development of advanced DR. Field defects were noted in 26.3% of diabetics, including 15.8% of those with no or little DR. This reduction occurred primarily in type II diabetics, especially in those with mild BDR (72.3%) where the defects were mainly found to be located in the superior quadrants (between 20 and 30 degrees of eccentricity) which corresponded to areas of vascular compromise. Foveal thresholds were not found to be increased in all the diabetics in comparison to normal controls.

Bek & Lund-Andersen (1990) examined for the presence of field defects in areas of hard exudates in the fundi of 20 type I diabetics using the Humphrey Field Analyser. They noted an absence of abnormality where abnormality was expected. There was a poor topographical correlation between scotomata and barrier leakage. Contrary to Gandolfo et al.(1983) they remarked that hard exudates often but not consistently caused scotomata, even when present in conglomerates. In other words late hyperfluorescence can be observed in areas where there is no loss of sensitivity. It seemed that breakdown of the blood-retinal barrier is an earlier event than disturbance of neurosensory function.

Bek (1990a) examined the visual fields of patients with PDR with the Humphrey Field Analyser. In the majority of eyes an absolute scotoma was found at a location distal to the point of neovascularisation. In these eyes, the scotomatous areas often corresponded to areas of non-perfusion although in some the scotomata did not correspond to any pathology.

It was hypothesised that non-perfused areas in the retina liberate angiogenic factors which exert a vasoproliferative effect on vessels that lie upstream from the actual point of non-perfusion. As the neovascularised areas were found to have normal sensitivity it was thought that the presence of unimpaired retinal tissue is necessary for angiogenesis to occur. However, the author could not prove that the scotoma was caused by non-perfusion (and the subsequent development of new vessels). The localised nature of the scotomata was thought by Bek to indicate damage to cells located in layers supplied by the retinal vascular system. The nerve fibers were not thought to be damaged as no arcuate scotoma was noted to extend from the lesions. However, the nerve fibre could still be affected in the absence of arcuate scotoma because if the scotoma is very small, the lesion will encompass only a few cells or optic nerve fibres thus not manifesting in an arcuate fashion.

Bek & Lund-Andersen (1991) examined the light sensitivity of areas of cotton-wool spots in 14 patients with the Humphrey Field Analyser. For all the patients, the cotton-wool spots were found to be associated with localised non-arcuate scotomata. A year later the cotton-wool spots and the corresponding scotomata persisted, except in 2 out of 4 cases where the cotton-wool spots resolved but the scotomata persisted. The authors postulated that the function of nerve fibres traversing the lesions in these two eyes is probably preserved and that scotomata are not always entirely due to opacity of the lesion blocking light from reaching the photoreceptors, but probably are also due to structural injury to some part of the retina.

Bek (1991) studied 13 patients who had localised scotomata in the central fields which could not be ascribed to visible lesions of diabetic maculopathy. In about 62% of cases perimetric findings corresponded to focal retinal non-perfusion in the macular area. The finding of normal fields in the non-perfused macular area lying adjacent to a patent vessel traversing across was because the retinal tissue in this area receives nutrition by direct diffusion

from the vessel. Generally, all the scotomata which corresponded to non-perfusion areas had localised non arcuate appearances, signifying retained integrity of nerve fibers traversing these zones. Bek (1991) concluded that factors other than retinal vascular occlusion are probably operational in causing injury to sensory cells in diabetic maculopathy.

Apart from studies described above which have investigated the correlation between field defects and the extent of capillary non-perfusion, very few (Wiznia et al.1971; Greite et al.1981; Hasunuma et al.1983; Federman & Lloyd, 1984; Bresnick et al.1985; Hamada,1988) have specifically addressed the relation of field defects to the overall severity of DR. The prevalence of field defects in different grades of DR is largely dependent on the apparatus used although it has been stated that automated techniques may be no more sensitive than Goldmann perimetry in detecting such defects (Trick et al.1990).

Description of specific types of defect by various authors

Wiznia et al.(1971) found in eyes with both BDR and PDR arcuate defects similar to those found in glaucoma. However, in the severe stages of DR generalised depression of the isopters can be seen and relative scotomata can be found in the presence of macular oedema. No field defects were found in the 3 diabetics with no DR.

Five types of defects were described in DR by Szymanska (1981): 1)generalised depression, 2)depression of the curve peak near the centre of the fovea, 3)small scotomata in the perifoveolar area, 4)defects within the extramacular area and 5)defects near the blind spot. It was postulated that the field defects found in latent diabetics represented functional disorders preceding the clinical manifestation of diabetes.

Examination with the Octopus perimeter on 67 diabetics with different grades of DR by Greite et al.(1981) revealed field changes in the form of flecked, partially confluent

relative scotomata which correlated with areas of capillary non-perfusion. They found evidence of field losses in diabetics with very mild DR. The mid-peripheral loss which was evident in the early stages of DR became more pronounced with increasing DR severity, especially in the PDR stage.

Hasunuma et al.(1983) attempted to correlate automated perimetric findings with panoramic fluorescein angiographic findings (Shimizu et al.1981) on 57 patients with DR. They noted that the contours of each isopter corresponded to the outline of the non-perfused areas. Contrary to Greite et al.(1981) and Yabuki et al.(1987), these areas were found to retain light perception to the largest target (V4e). As their fluorescein angiography technique was a "panoramic" one, the authors cast doubt on the findings by others of the presence of field defects prior to retinal vascular changes. The authors were not certain of the fate of the visual function of the non-perfused areas in the long run.

Gandolfo et al.(1983) provided a comprehensive description of the types of field defects produced by different lesions in DR. Absolute defects only occur in PDR and when there is a concentration of lesions in the same area. Haemorrhages do not generate absolute defects. Hard exudates cause defects, also relative scotomata, only when they are grouped together. Exudative maculopathy produces a plateau in central sensitivity. Cystoid macular oedema produces a depression in the central static profile which rapidly progresses into a deep scotoma. The fall in field sensitivity is dramatic at the border between normal and ischaemic territories.

As regards the above attempts by authors to categorise field defects in DR, they are perhaps misguided. DR is very various in its early manifestations, and as an ischaemic retina might well produce localised losses of sensitivity. The pattern would change from individual to individual. Indeed the FFA and ophthalmoscopic changes are not fixed, but change with time in the same eye.

Effect of altering blood glucose levels

Two studies investigated the effects of reduction in the levels of blood glucose on the visual fields: Mosier & Deshmukh (1990) noted decreased field sensitivity (which was more marked in the temporal meridians) during a period of induced hypoglycaemia. The authors proposed that retinal sensitivity was depressed via one of two mechanisms: 1) retinal hypoxia and 2) "toxic" effects on retinal cells due to reduced blood glucose.

On the other hand, intensive supervision of conventional diabetic therapy (which ensured conditions of normoglycaemia), did not appear to be associated with significant deterioration in the visual fields over a period of 3 years (DR Study Group St. Thomas',1987).

Clinical application: Proposals

Bresnick (1987) suggested that perimetry may offer a non-invasive alternative to FFA for evaluating both the posterior and the midperipheral fundus in diabetics. Threshold visual field is useful as an alternative procedure for patients in whom fluorescein angiography is contraindicated (Szymanska,1981; Hasunuma et al.1983; Sabry et al.1987; Hamada,1988). Federman & Lloyd (1984) suggested automated perimetry as an excellent screening test for DR, particularly by concentrating on the area 20 to 45 degrees from the fovea. Bresnick (1989) have also suggested more widespread use of computerised perimetry in the follow-up of diabetics with DR; as a non-invasive tool, perimetry may be prove to be worthwhile especially in the early stages.

Perimetry may also be useful in documenting the presence and extent of paracentral scotomata because these areas may be shown by fluorescein angiography to correspond to areas of capillary non-perfusion (Bresnick,1989), despite contrary evidence by other workers cited previously. A thorough field examination in diabetics is perhaps of little value, apart from the need to be aware of field disturbances caused by DR. Assessing the central 20-degree

fields is particularly useful for detecting DR in general. It has been suggested that central field screening is more useful especially for detecting maculopathy which requires treatment (Ariffin et al.1992).

Some investigators (Birch et al.1980; Birch & Ariffin,1990; Birch et al.1991; Adams & Haegerstrom-Portnoy,1987; Wall & May,1987; Wall et al.1990) have suggested the Amsler grid for detecting patients with DR. Patients with maculopathy have reduced or variable VA and may report metamorphopsia on the Amsler grid (Birch et al.1980). Metamorphopsia will be more apparent than scotomata on the Amsler grid (Birch et al.1980; Wall & Sadun,1986) in these patients. Since macular oedema can occur in diabetics without visible BDR (Klein et al.1984b), this ability of the Amsler grid is useful. Birch & Ariffin (1990) reported the standard Amsler grid to detect 14% of "eyes" with DR while generating 2% false positives. Failure on the grid therefore reinforces the need to refer patients.

Failure on the Amsler grid can be related to the presence of severe DR, which includes the presence of maculopathy (Birch et al.1991). The Amsler grid was reported to detect 23% of "eyes" with DR while giving 2% of false positives. Unfortunately the results were contaminated by the inclusion of patients who have had laser photocoagulation treatment; the true detection ability of the Amsler grid for patients with "strictly DR" could have been overestimated. The authors recommended the use of the Amsler grid to indicate diabetic macular involvement; in addition it may also detect age related macular changes. In any case, failure on the Amsler grid in addition to failure on colour vision tests reinforces the need for urgent referral.

It has also been established that some patients with ophthalmoscopically visible macular lesions do not report visual defects on the standard Amsler grid (Wall & May,1987). The standard Amsler grid has been said to be more effective for detecting metamorphopsia than relative

scotomata (Wall & Sadun,1986; Wall et al.1990). The use of the "threshold" Amsler grid has been explored (Sadun & Lessell,1985; Wall & Sadun,1986; Wall & May,1987; Wall et al.1990). In DR relative scotomata are more prevalent than metamorphopsia (Werner,1991), although they (scotomata & metamorphopsia) often occur together; the threshold Amsler grid has been suggested as a more sensitive test for use in diabetics (Wall & May,1987) as it detects scotomata more readily than metamorphopsia.

The sensitivity of Amsler grid testing for visual loss in diabetics without BDR improves with the use of the threshold Amsler grid (Wall et al.1990). Testing 22 "eyes" (of 12 diabetics) without BDR they found the threshold grid to detect the largest number of scotomata and the largest total area of scotomata when compared to the 3 other Amsler grids (standard white, bright red and fine red). It was not reported, however, if eyes tested positive subsequently needed laser therapy. This is vital, as they might have just turned out to be "false positives".

1.1.2e Multiple Visual Dysfunction

Relationship between colour vision, contrast sensitivity & visual field defects

In a study of 3 visual functions in diabetic eyes with very early DR, Ariffin & Birch (1989) observed 78% had abnormal colour vision, 50% had contrast sensitivity defects while only 20% had visual field abnormalities. The results showed that approximately 50% of eyes with early DR had combined losses in at least 2 visual functions. The excess prevalence of colour vision defects suggests that of the three visual functions, the colour function seems to be the first affected in the early stages of DR. This is then followed by contrast sensitivity and visual fields. Static fields were obtained on the Friedmann Visual Field Analyser; arguably, a more sensitive apparatus could have revealed more field defects.

The relationship between colour vision and visual fields in diabetics with severe degrees of DR has been explored. Szymanska (1981) reported the occurrence of field defects even in eyes with normal colour vision and VA. Birch et al.(1980) showed that loss of equatorial or fields caused a general loss of hue discrimination together with a mild type III defect. The observation that large field defects are associated with tritan defects has suggested that the peripheral retina is intimately involved in the perception of small colour differences. In addition, the central blue mechanism is also found to be vulnerable to the loss of peripheral visual field. It must be noted that such observations refer to visual dysfunctions as revealed by "clinical" tests. It is possible for the "colour dysfunction" to be detected well before the appearance of field defects with more advanced instrumentation.

In fact, the rather poor correlation between colour vision dysfunction and specific field defects in diabetics was elegantly demonstrated by Silverman et al.(1990) recently. No relationship was found between the relative spatial distribution of visual field damage and the relative hue discrimination deficit in DR; a preponderance of relative tritan defect was present in nearly all eyes with DR, without regard to the spatial distribution of visual field defect. The authors asserted the colour defect in DR is not determined by the spatial distribution of central field damage. This is not surprising as the damage in DR is not always necessarily at the post-receptor level. Difficulties with blue-yellow vision as determined with pigment-based colour vision tests are known to be caused by both prereceptor (Lutze & Bresnick,1991) and receptor factors (Zisman & Adams,1982). According to Bresnick et al.(1985), in DR VA points to disturbances in the central macula while colour vision defect reflects disease in both the central macula and the peripheral retina. Visual field abnormalities, on the other hand, seem to reflect disease more in the peripheral retina.

Prevalence of multiple defects

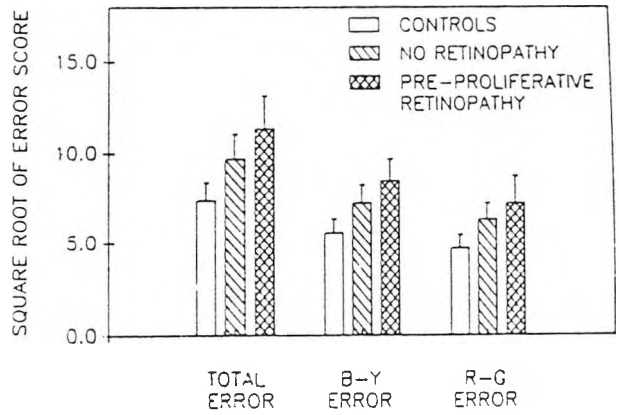
Moloney & Drury (1982) showed patients with no DR to have more colour vision abnormalities (60%) than contrast sensitivity abnormalities (44%). Hue and contrast discrimination correlated with each other, implying sharing of a common aetiology.

Burde et al.(1986) examined the relationship between colour vision and contrast sensitivity in diabetics and found colour vision abnormalities to be more frequent than contrast sensitivity abnormalities. 50% of those with no DR and 75% of those with BDR had colour vision defects. Contrast sensitivity defects were noted in 38% of patients in each of the group without DR and with BDR.

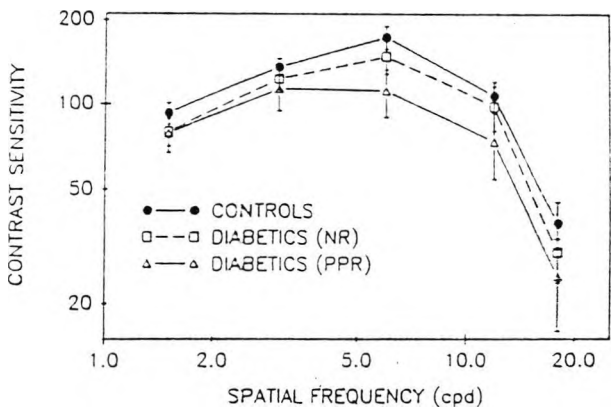
Fig 1.3 shows the results obtained by Trick et al.(1988) in examining both colour vision (with the FM 100-H test) and contrast sensitivity (with the Vistech VCTS 6500) in a mixed group of patients with types I and II diabetes. Trick et al.(1988) found some evidence of visual dysfunction in 37.8% of diabetics with no DR and 60% of those with background DR. Contrary to the findings of Burde et al.(1986), contrast sensitivity was abnormal more frequently than colour vision in this heterogenous group of diabetics. 18.9% of diabetics with no DR and 25% of those with background DR had abnormal colour vision whereas 24.3% of those without DR and 45% of those with BDR had abnormal contrast sensitivity. Only 5.4% of those without DR and 10% of those with background DR had abnormalities in both visual functions.

1.1.2f Scope for clinical research

The foregoing review has detailed the various effects of DR on visual functions. Whilst a great number of visual tests have been described, the exploration of the ability of easily available and familiar clinical tests (of the appropriate visual function) for identifying diabetics with DR (& other significant ocular pathology) has not been emphasized. There is a scope for a rigorous identification



Mean colour vision results. The square-root of the TES and the red-green and blue-yellow partial error scores are shown.



Mean contrast sensitivity (VCTS 6500) results

Fig 1.3 Mean colour vision and contrast sensitivity results for diabetic patients and age-matched controls. The error bars represent the 95% confidence interval (after Trick et al., 1988).

of such tests for two purposes: as a screening tool and as a monitoring tool for DR. Consideration also needs to be given of the real benefit of such "other tests" ancillary to the normal clinical routine ie. fundal examination in this respect.

As a screening tool such tests would aid personnels in a physician's clinic to screen out diabetic patients who are at risk of having ocular involvement(s). As a monitoring tool, such tests will aid clinicians in primary eye care practice in deciding to refer diabetic patients for ophthalmological intervention by way of supplementing the clinician with more clinical information in addition to information obtained with routine ophthalmoscopy. In either case there is no additional great cost to be involved if simple, rapid and portable tests are selected.

1.1.3 Visual Function after Photocoagulation treatment for Proliferative Diabetic Retinopathy

The extramacular application of PRP should not theoretically cause any effects on central visual function by way of direct macular injury. The effects on the peripheral fields are rather expected and have been extensively documented (DRS Res.Gp.1981; Hamilton et al.1981). However, despite the extramacular target, the Argon laser (488/514nm) has also been shown to cause a deterioration in some central visual functions. These changes may be either transient or long-term, depending on the various laser parameters.

1.1.3a Visual acuity

Various authors have reported that between 3 to 25% of patients will experience a fall in VA following PRP (Zweng et al.1974; DRS Res.Gp.1976; Crick et al.1978; Liang & Goldberg,1980; Lavergne & Ramioul-Gougnard,1980; Zetterstrom,1980; DRS Res.Gp.1981; Hamilton et al.1981; L'Esperance & James,1981; Plumb et al.1982; Little,1983; Ghafour et al.1984; McDonald & Schatz,1985a & 1985b; Blakenship,1988; Kleiner et al.1988; Theodossiadis et al.1990; Seiberth & Alexandridis,1991). The fall in VA can vary from very mild to very severe and can be either transient or long-lasting.

The fall in VA following PRP can be caused by exudative macular detachments (Doft & Blakenship,1982) or macular oedema (Meyers,1980; McDonald & Schatz,1985a & 1985b), although sometimes no obvious cause could be found (Kleiner et al.1988). No significant difference in the effects on VA was noted by Plumb et al.(1982) when they compared between Argon laser and Xenon arc PRP. However, Xenon arc PRP has been found by others to be more likely to cause an initial small loss of VA than the Argon laser (Crick et al.1978; DRS Res.Gp.1981; Hamilton et al.1981). Cambie (1980), however, associates the fall in VA with an increase in macular ischaemia following PRP, VA is not affected if only

the avascular zones are being treated. Interestingly, there have also been reports of no significant changes in VA after PRP (Kitagawa et al.1983; Schulenberg et al.1979) either with the Argon or Krypton laser.

1.1.3b Colour vision

Argon (488/514nm) PRP treatment of PDR has been found to accentuate the acquired type III (tritan) colour vision defect in diabetics (Birch-Cox,1978; Cambie,1980; Lavergne & Ramioul-Gougnard,1980; Birch & Hamilton,1981; Birch,1987). Some, however, have failed to find any significant changes in colour vision (Crick et al.1978; Cambie,1980; Ghafour et al.1984; Mantyjarvi,1989b). The exact mechanism for the deterioration of colour vision towards the tritan mode is not fully understood; some suggestions point to temporary or permanent central blue receptor damage caused by light scatter within the ocular media during treatment (Kuwabara,1970; Sperling & Harwerth,1972). On the contrary, Moreland (1980) suggested that photocoagulation may lead to a change in spectral transmission of the media rather than cause a spectral change in sensitivity of the cones.

Birch-Cox (1978) monitored the colour vision of 7 diabetics with PDR treated with Argon (488/514nm) and Xenon over a period of 12 months. It was found that in both the Argon laser and Xenon treated eyes, no blue mechanism could be detected after treatment and that all the colour vision tests showed a reduction in hue discrimination and an increase in the severity of the type III colour vision defect. However, slight improvements in hue discrimination ability was noted with time, and failure of the FM100-H test score to improve usually indicated the need for further treatment. The author suggested that the effect of PRP was to accelerate a change in colour vision which would have taken place as a consequence of the retinopathy if left untreated.

Crick et al.(1978) compared the effects on colour vision

between the Xenon arc and the Argon laser in 15 diabetics. There were no significant changes either in error scores or axis found using the FM 100-H test between Argon and Xenon treated eyes; almost equal numbers deteriorated, improved or were unchanged after treatment with both modalities. The authors also reported that in a few eyes there was an improvement in colour vision afterwards.

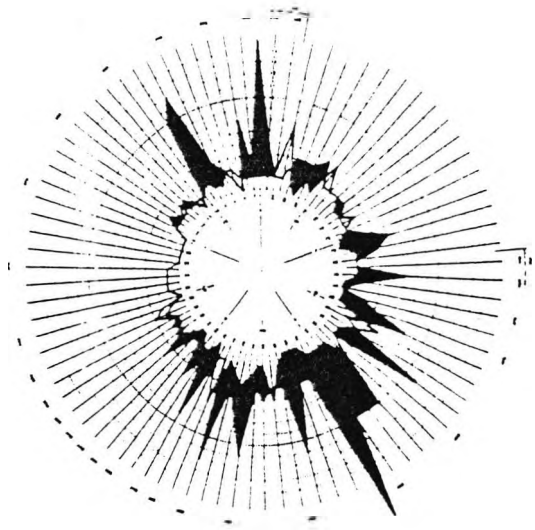
Moreland (1980) tested 48 diabetics using a "tritan" equation on an anomaloscope developed by the author (Moreland & Kerr,1978). The mean match of all diabetics who had received photocoagulation (Argon 11 eyes; Xenon 6 eyes; Both 1 eye) required more blue than those who had not, for both 2-degree and 11-degree fields. However this was only to the extent of the result being "tritan-like" rather than a tritanopic dichromasy since the tests used by Birch-Cox (1978) were not sensitive enough to distinguish between dichromasy and severe anomalous trichromasy. No variations of matching range with the number of burns were observed. The means of the difference in matching range between the 11-degree and 2-degree fields for diabetics without treatment and those with treatment were found to be practically identical; this according to Moreland (1980) was contrary to the claim by Birch-Cox (1978) that photocoagulation accelerates the process which would take place as a natural consequence of DR if left untreated. Although in general the foveal region (2-degree) was found to be much more affected in all diabetics than for the 11-degree field, some eyes (which had photocoagulation) performed better on the 11-degree field. This was attributed to non-uniformity of treatment which meant that some parts of the retina were treated more intensely than other portions.

Lavergne & Ramioul-Gougnard (1980) concluded that although there are "acceptable" deteriorations in colour vision following PRP, there is also the possibility that the change is due to the progress of retinopathy rather than to the treatment.

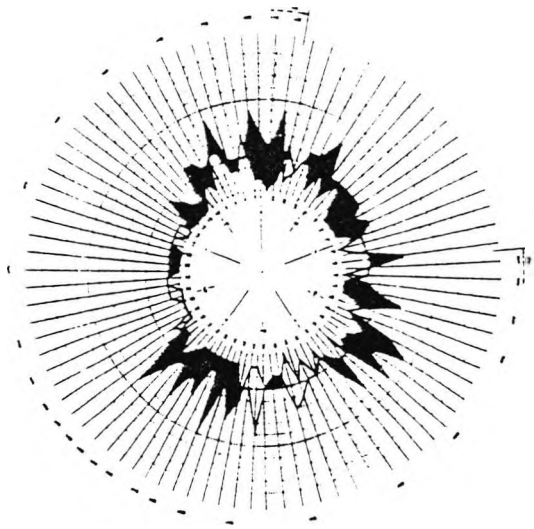
Cambie (1980) stated that if only avascular and ischaemic zones are treated, or if photocoagulation is loosely scattered in the midperiphery, then colour vision remains unchanged. Only with more extensive treatment (such as with PRP) or treatment which leads to macular oedema will a loss of blue discrimination be apparent. In those with normal colour vision before treatment, a tritan defect only occurs if multiple closely-placed laser burns are given. On the other hand in cases where the diffuse leakage in the midperipheral retina disappears after treatment, the tritan defect is found to improve although VA remains unchanged. It is also possible to find a progressive deterioration of the tritan defect (without any change in VA) which is not related to the effects of the laser treatment; such deterioration correlates with an increase in midperipheral retina non-perfusion instead. If more than one treatment session is given, a tritan defect is more likely to result even in eyes with normal VA due to further destruction of remaining viable blue receptors of the peripheral retina or to permanent damage of the blue receptors by the intense light.

So tritan colour vision can get better or get worse after treatment, and the amount of the treatment, where it is placed, and the success of treatment are all variables.

Birch & Hamilton (1981) examined the colour vision of 21 diabetics with VAs of 6/12 or better undergoing PRP treatment with the Argon (488/514nm) and the Xenon arc. Both treatment modalities were found to increase the severity of the type III colour defect and to reduce hue discrimination ability yet further; no significant differences were noted between Argon-treated and Xenon-treated eyes. All eyes were tritanopic after treatment and did not recover during the 12-month follow-up (fig 1.4). Some fluctuations in the FM 100-H test error scores were found but the final score after 12 months was generally in excess of the original value. Although not statistically proven, the authors remarked that the appearance of a tritan axis was usually more marked in the Argon-treated



ARGON laser: Before treatment the TES was 100 (inner line). After PRP the TES increased to 259 (dark line). The dark area represents the difference between the two scores.



XENON arc: Before treatment the TES was 113 (inner line). After PRP the TES increased to 231 (dark line). The dark area represents the difference between the two scores.

Fig 1.4 FM 100-H test before and after panretinal photocoagulation (after Birch & Hamilton, 1981).

than in the Xenon-treated eyes, but the overall hue discrimination loss was greater in the latter.

Birch (1987) attributed the previously observed permanent tritan change in patients undergoing PRP to the number of burns and treatment style. Reporting on different groups of patients, she observed that long-duration burns (0.5s) produce permanent tritanopia and reduced hue discrimination whilst short-duration burns (0.05 to 0.08s) produce an initial loss of blue vision with poor overall hue discrimination which recovers over a few weeks. The wavelength of the laser light was also found to be important. Longer wavelengths (filtered Argon and Krypton) caused less disruption to the colour vision mechanism (ie on tritan colour tests), purpotedly adding support to the hypothesis that the cause of the colour vision changes is the short-wavelength stray light that is present during PRP. Unfortunately whether these results have any evidential value is open to criticms, as unfortunately, very short wavelengths (such as 0.05 to 0.08s) is not frequently employed by retinal surgeons for various reasons. A realistic burn duration in current practice is circa 0.1s. Krypton is also no longer the laser of choice in current day practice.

The colour vision of 60 diabetics who had undergone photocoagulation treatment was studied by Mantyjarvi (1989b). Five patients had previously been treated with Argon (488/514nm) PRP alone while 55 patients had also received macular treatment in addition to PRP. The number of PRP burns in these patients ranged from 200 to 3174 and the time after last treatment averaged at 29 months. Thirty (60%) had a colour vision defect and 24 (of the 30) were diagnosed as having a tritan defect. The author also observed no significant differences between patients with normal colour vision and those with defective colour vision in their VAs, number of laser burns, duration of diabetes and their ages. This was largely due to the heterogeneity of the study sample where not all patients had been treated with PRP alone.

1.1.3c Contrast sensitivity (CS)

A deterioration in the CS function following Argon (488/514nm) laser PRP has been noted in both the low spatial frequency and the high spatial frequency regions (Bodis-Wollner,1983; Ghafour et al.1984; Higgins et al.1986; Cavallerano & Aiello,1990; Miller,1992). The effect is mainly concentrated in the foveal region and has been described as temporary. CS studies (cited by Bodis-Wollner (1983)) performed on diabetics before and after laser PRP demonstrated that foveal CS (5-degree field) can be uniformly decreased.

Ghafour et al.(1984) measured the CS of diabetics using the Arden gratings before and after Argon laser PRP. Patients only showed a significant increase in plate 3 (0.4 c/degree) scores 20 minutes after PRP; 24 hours post-treatment, there was no significant change in the CS when compared to the pretreatment value (fig 1.5). It was concluded that PRP with less than 1000 Argon burns only leads to a transitory deterioration of CS.

Higgins et al.(1986) used a computer-controlled test system to monitor changes in the CS in 2 patients undergoing Argon PRP treatment. Three eyes did not develop any macular oedema (hence had no changes in VA) and yet showed temporary losses in high spatial frequency CS following closely-spaced PRP treatment.

Russell et al.(1987), however, questioned the true effects of PRP treatment on CS function. The authors tested 5 diabetics who had undergone PRP with a VA of 6/12 or better under conditions of rapid adaptation. With one exception, each diabetic showed losses in CS when rapid adaptation was required. However, their results also indicated that PRP introduced no additional visual disability for a particular patient thus suggesting that the disease, rather than the treatment that was causing the deficit. It was concluded that PRP does not necessarily worsen the CS of a diabetic.

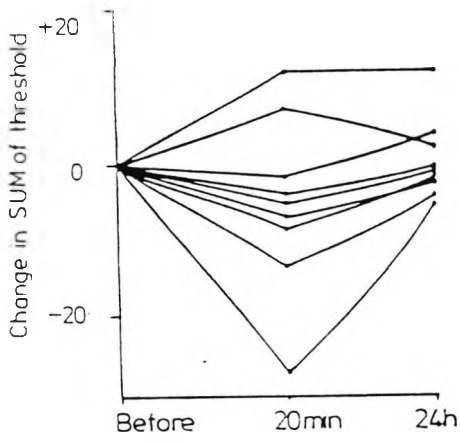


Fig 1.5 Changes in sum of contrast thresholds from Arden grating test of 9 patients undergoing laser PRP treatment for proliferative DR. Deterioration of contrast threshold is shown as a negative factor (after Ghafour et al., 1984).

1.1.3d Visual fields

It is to be expected that patients will suffer a loss of the visual fields following photocoagulation treatment for PDR. In fact at least 14% of the retinal area is destroyed in patients who undergo a successful Xenon arc photocoagulation (Taylor,1970). Riaskoff (1972) was the first to demonstrate the types of field defects using multiple isopter testing. Two types of defects were described: 1)circumscribed defects which correspond to the laser burns and 2)more extensive defects which are due to nerve fibre damage or occlusion of peripheral retinal arteries.

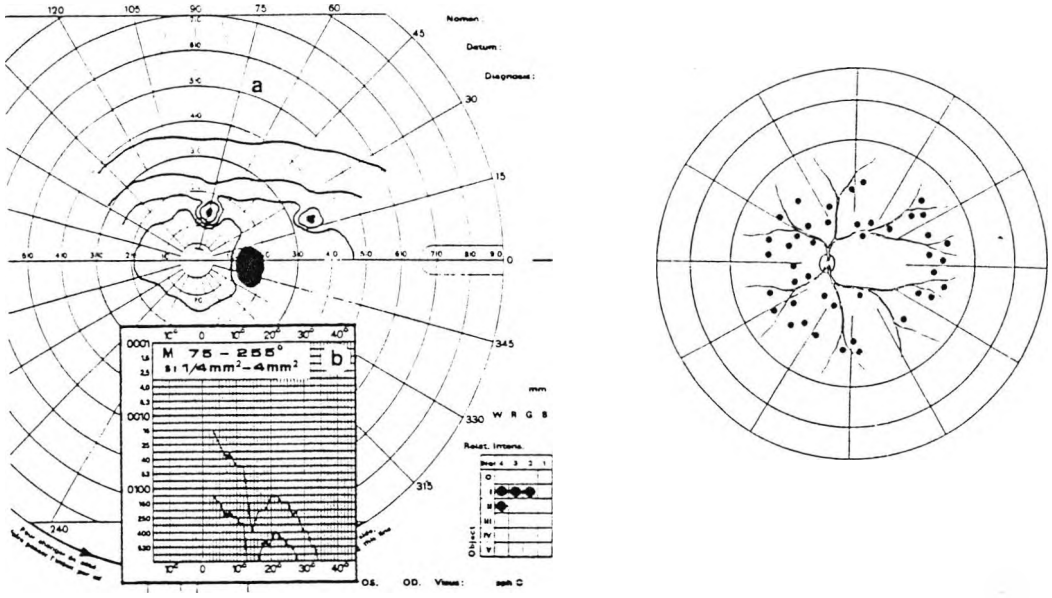
Some of the early treatments were also undertaken with coagulation burns placed reasonably isolated from each other; they were reported to produce well circumscribed (although numerous) lesions which were often unrecognisable (Zetterstrom,1972; Zetterstrom & Gjotterberg,1973). These visual fields were obtained with large and bright test objects; hence the apparent minimal visual field constriction noted, giving rise to the common misconception that Argon laser PRP has minimal effects on the visual field (Benson et al.1988). The same procedural error was also the reason why nerve fibre damage was previously not regarded as a complication of photocoagulation treatment.
Some of the early studies also demonstrated severe effects on the visual fields following photocoagulation treatment for PDR; severe nerve fiber bundle defects were found in some patients while in others, severe constrictions of all isopters were noted (Little,1973; Frank,1975). These reports have included patients who had received focal treatment on the disc in addition to PRP thus explaining the severe nature of the field defects effects. Even avoiding the optic disc, PRP can still cause nerve fibre bundle defects and general constriction (Benson et al.1988). However, nerve fibre damage is not so frequent after the first photocoagulation session (Little,1976).

Repeated treatment over previously photocoagulated areas

increases the risk of nerve fibre layer defect (Apple et al.1973; Zweng et al.1974), particularly if given near the disc (Little,1976). Treatment of preretinal haemorrhage can also result in similar field defect (Frank,1975; Little,1976). If an area had been photocoagulated before, a second burn may coagulate and interrupt the nerve fibre layers irrespective of the wavelength used (Benson et al.1988). This is because with repeated treatment, the retina becomes thin as a result of the loss of photoreceptors (Patz,1972; Apple et al.1973) and hence the nerve fibre layer comes into close proximity with the retinal pigment epithelium where most of the heat energy from the laser beam is deposited. Therefore patients who receive repeated treatment would be expected to have more severe visual field loss. In addition, closely spaced photocoagulation burns and burns which are too intense may also give rise to nerve fibre damage (Little,1973).

Earlier when Xenon arc arc was the only source of treatment, significant constriction of the visual field was noted. With the advent of the Argon laser, the field defects are much less severe but still recordable (Foulds & McClure,1980; Lavergne & Ramioul-Gougnard,1980). Peripheral field constriction due to PRP was shown to be more marked in Xenon-treated than in Argon-treated eyes (Crick et al.1978; DRS Res.Gp.1981; Hamilton et al.1981). In 1976, the DRS group reported that one year post treatment with the Xenon arc, 44 % had field scores in the range of 240-500 degrees; only 6 % of Argon-treated eyes had scores in this range (DRS Res.Gp.1976). As laser burns in general do not damage the nerve fibre layer the scotomata produced tend to be limited to the areas treated (although this strictly applies only to "first time" burns with short-duration Argon beam). Xenon arc and strong Argon laser burns do in fact cause full thickness retinal necrosis (Wallow & Davies,1979; Doft & Blakenship,1982) although Zetterstrom (1980) noted only minor scotomata in 18 of 40 eyes treated with the Xenon arc.

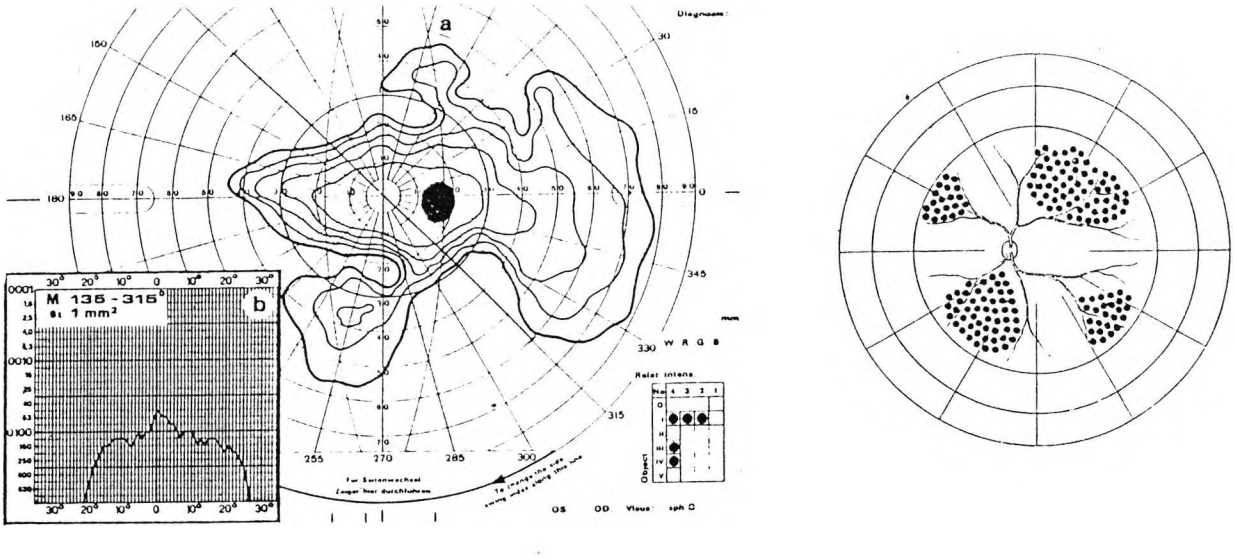
Frank (1975) examined the visual fields of 24 patients who



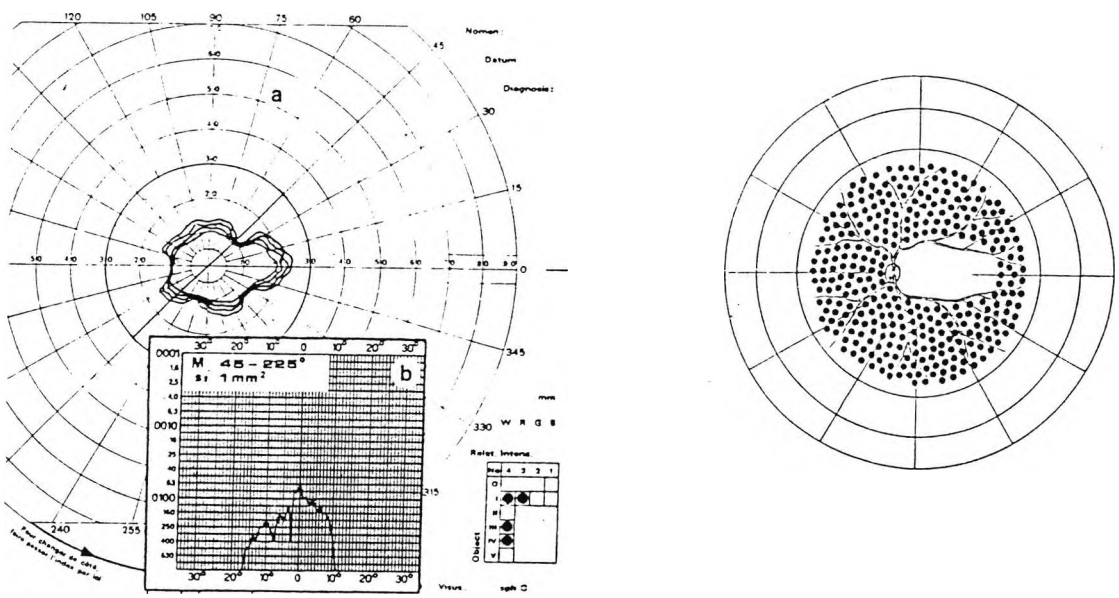
Circumscribed defects produced by isolated photocoagulation spots

Defects produced by confluent photocoagulation spots

Fig 1.6 Visual field changes after photocoagulation treatment for DR; treatment pattern is illustrated (after Zingirian et al., 1977).



Typical irregular visual field after extensive photocoagulation



Concentric contraction of visual field after PRP

Fig 1.6/contd

underwent Argon laser therapy (PRP and disc treatment amounting to a mean of 1544 burns) with the Goldmann perimeter. Changes in the visual fields were divided into 4 groups: 1)mild to moderate constriction of all isopters-these patients mainly received PRP only, 2)Discrete scotomata in addition to (1), these patients had more extensive vascular anomalies prior to treatment, 3)nerve fibre bundle defects-these patients had received prior Xenon treatment and the subsequent Argon treatment was delivered over previously photocoagulated areas in a PRP mode, and 4)severe constriction to all isopters (to all but the largest and brightest test objects)-the most severely affected had also had prior Xenon treatment, but the number of subsequent Argon laser burns was not greater in these patients than in others. None of patients in the 4 groups suffered loss of VA of more than 2 lines.

Zingirian et al.(1977) studied the visual fields of 28 eyes which had received photocoagulation treatment with the Xenon arc using both kinetic and static perimetric methods. They described two types of defects (fig 1.6) which depended on the photocoagulation method employed: 1)circumscribed defects corresponding to the treated area which may have an absolute central nucleus and normal periphery, and 2)absolute defects which extend to the periphery; the peripheral retina (the treated area and a portion of the untreated area) become irreversibly non-functional. Isolated or confluent burns give rise to the first type of defect whereas extensive treatment with multiple closely-spaced spots (including PRP) produces the second type of defect, signifying a damage in the nerve fibre layer. These results concur with the later report by Cambie (1980).

Fifteen diabetics with PDR having VAs of 6/12 or better were randomly treated by either Xenon arc or Argon laser PRP and their visual fields were assessed before and after treatment by Crick et al.(1978). With the Goldmann I4 isopter, all the Xenon fields but only half of the Argon fields experienced a reduction. However, with the III4

isopter, significantly more Xenon fields were reduced compared to the Argon ones. Fields of both treatment modalities recovered eventually, in agreement with Hamilton et al.(1976). There was also a reduction of the central fields as measured on the Friedmann Visual Field Analyser, but the two treatment modalities were not statistically different. In addition, the authors also demonstrated decreases in the macular thresholds in both treatment groups, similarly not significantly different from each other.

Schulenberg et al.(1979) confirmed the assertion that longer-wavelength laser burns cause less damage to the inner retinal layers (including the nerve fibre layer) than do Argon burns, in a comparative study on 12 eyes. The authors, however, found that the difference in the amount of field loss between Krypton (647nm) and Argon (488/514nm) to be only a few degrees. The visual fields remained unchanged for the V4 target; changes were only recorded for the I4 & I2 targets. Ten weeks post treatment, both groups (Krypton-treated & Argon-treated) showed some recovery of their visual fields, though it was more pronounced in the Krypton-treated group.

Cambie (1980) stated that field defects produced by isolated burns are detectable only by static perimetry. However,if only the avascular zones are photocoagulated no field changes should occur with the Argon laser. This could explain the lack of significant field loss following Argon PRP to areas located in regions of poor perfusion, as recorded by Bell & Feldon (1984). Also no field changes occur if widely-spaced burns are applied; it is only after PRP with closely-placed burns that the visual fields become narrowed upon testing with kinetic perimetry. Cambie (1980) concluded that visual field changes from photocoagulation are minimal. Changes are only expected in cases of confluent, intense and repeated PRP.

The Diabetic Retinopathy Study found that, using the relatively large Goldmann IV4e target, only 5% of eyes had

constriction of the visual field to less than 45 degrees per meridian following Argon PRP (DRS Res.Gp.1981). No patients had constriction to less than 30 degrees per meridian. With the I4e target an average constriction of 50% in visual field score is seen (Schulenberg et al.1979; Cambie,1980; Doft & Blakenship,1982) which correlates well with the subjective complaints of many patients (Benson et al.1988).

With the Goldmann perimeter, Hamilton et al.(1981) studied pre and post operative visual field loss in 21 diabetics who were randomly assigned to Xenon arc and Argon laser PRP. They found the induced loss of visual fields in patients treated with the Xenon arc and the Argon laser to be 16.8% and 6.2%, respectively at 1 month after treatment. One year post-treatment, the Xenon arc group still experienced 16.9% field loss while the Argon group only had 4.6% field loss.

Zalusky et al.(1987) reported that field losses from PRP may only involve areas outside the 12-degree field. Two techniques were compared: a "scattered" technique and a "cluster" technique. Both techniques were reported to lead to a loss of retinal sensitivity in the central and peripheral visual fields, sparing the central 12-degrees. Although the mean number of burns was greater in the cluster technique (scattered: 1678; cluster: 2189), there was no significant difference in the field loss between the two techniques.

Blakenship (1988) randomly assigned 50 eyes to receive Argon PRP treatment with either the central or peripheral pattern mode. Six months after treatment, using the Goldmann I4e target he noted mean visual field constrictions of 39% and 29% for the two treatment modes, respectively. The mean field contriction with the IV4e target was 12% for the central mode and 7% for the peripheral mode.

Theodossiadis et al.(1990) also explored the effects of two

different modes of Argon laser PRP delivery in 53 eyes, using computerised perimetry of the central 30-degree field. 26 eyes were assigned to a PRP pattern which was more "central" while 27 eyes were treated with a PRP pattern which was more "peripheral". Visual field deterioration was noted in the central 30-degree field with both modes of PRP, with a more pronounced deterioration with the more central mode. An improvement in the central 15-degree field sensitivity was found with the more peripheral mode.

Seiberth & Alexandridis (1991) employed static perimetry to investigate the effects of the "intensity" of PRP burns on the central 30-degree field in 24 eyes of 12 diabetics. One eye was treated with "moderate" burns (av=300mW) and the fellow eye was treated with "intense" burns (av=600mW). The spot size was kept identical for the two treatment modes, since Seiberth et al.(1987) showed previously that persistent visual field scotomata occurred more frequently in eyes treated with small-spot burns (compared to large spots). One year after treatment, visual field loss was more prevalent in eyes treated with intense burns although the difference between the two treatment mode was not apparent a few days after treatment.

In summary, PRP with the widely-used Argon (488/514nm) laser can cause both central and peripheral field losses with minimal changes in VA and often with subsequent recovery. Defects may range from insignificant mild circumscribed scotomata to the presence of absolute scotomata within the 30-degree field and nerve fibre bundle defects. Varying degrees of field defects have been described to result and this is attributable to the "aggressiveness" of the treatment delivered. Heavy, longer-duration burns with profiles affecting the nerve fibre layer or ganglion cells produce extensive field loss (Jagger & Hamilton,1984).

1.1.3e Scope for clinical research

Although much is known about the effects of Argon PRP on the visual function of diabetics, no work has hitherto been done to investigate the effects on colour vision, contrast sensitivity and visual fields of longer wavelength lasers. This is particularly relevant as longer wavelengths have recently been introduced as more suitable (on theoretical grounds) sources of PRP treatment for PDR.

Finally, the current clinical practice of continually applying PRP to eyes which do not "respond" to the initial doses has never considered the eventual effects on the visual function. Some ophthalmologists query the state of visual function in this special group of patients who seemingly have retained "good vision" despite the constant bombardment of laser spots onto their retinae.

1.2 THE PRESENT STUDY : AIMS AND ORGANISATION

1.2.1 Studies undertaken & Objectives

STUDY 1: Screening of Diabetic Retinopathy using Clinical tests of Visual Function.

To assess the screening efficiency of clinical tests of visual function (colour vision, contrast sensitivity and central visual fields) in screening for diabetic retinopathy amongst diabetics.

STUDY 2: Grading of Visual Dysfunction in Diabetic Retinopathy using Clinical Tests of Visual Function.

To determine whether such clinical tests (in Study 1 above) could be used to grade the visual dysfunction in patients with different clinical grades of diabetic retinopathy.

STUDY 3: Evaluating the effects of Therapeutic DYE Laser Photocoagulation Treatment for Diabetic Retinopathy on Visual Function.

To compare the effects of therapeutic panretinal photocoagulation treatment using longer wavelengths (DYE 577 and DYE 595 nm) with the standard wavelength (ARGON 488/514 nm) on the visual function (colour vision, contrast sensitivity and central visual fields) of patients with proliferative diabetic retinopathy.

STUDY 4: Assessment of Visual Function in patients with Extensive Argon Laser Photocoagulation Treatment.

To assess the visual function (as above in 3) in patients who had undergone extensive ARGON laser photocoagulation treatment for diabetic retinopathy.

Table 1.1 sets out a summary of the 4 studies carried out.

STUDY	VENUE	NO. OF PATIENTS
1. Screening of Diabetic Retinopathy using Clinical Tests of Visual Function	Middlesex & Whittington Hospitals	**463**
2. Grading of Visual Dysfunction in Diabetic Retinopathy using Clinical Tests of Visual Function	University College & Moorfields Eye Hospitals	87
3. Evaluating the effects of Therapeutic DYE Laser Photocoagulation Treatment for Diabetic Retinopathy on Visual Function	Moorfields Eye Hospital	26
4. Assessment of Visual Function in patients with Extensive ARGON Laser Photocoagulation treatment	Moorfields Eye Hospital	24

Table 1.1 Studies undertaken

CHAPTER 2

Instrumentation for Clinical Testing

2.1. Visual acuity

Four standard Snellen charts were used in the study: 2 internally illuminated charts (at Middlesex and Moorfields Eye Hospitals) and 1 externally illuminated chart (at Whittington Hospital). All charts consisted of Snellen letters from 6/5 to 6/60. The steps in the visual acuity scale were 6/5, 6/6, 6/9, 6/12, 6/18, 6/24, 6/36, and 6/60. The number of letters on each line corresponded with the line number i.e. 6/60 being the first line had one letter while the 6/5 line being the eighth line, had 8 letters.

The luminance of the internally illuminated charts was measured to be between 120 and 550cd/sq.m (500cd/sq.m at Middlesex Hospital, 120cd/sq.m at University College Hospital and 550cd/sq.m at Moorfields). The luminance of the surround was between 350 and 450cd/sq.m at Middlesex Hospital, between 100 to 120cd/sq.m at University College Hospital and between 450 and 550cd/sq.m at Moorfields.

The illumination on the externally illuminated chart at the Whittington Hospital measured 1700 lux. The room illumination was between 1590 and 1620 lux on all points between the patient and the chart. These test conditions complied with British Standards for measuring visual acuity (British Standard,1968) i.e. illumination of not less than 480 lux or luminance of not less than 120cd/sq.m.

All charts were viewed from an effective distance of 6m by the use of a mirror. The best-corrected monocular visual acuity was measured, which was obtained with the patient's habitual correction (and the use of a pinhole if necessary). The right eye was measured first in those who had both eyes eligible for the study. The patient was encouraged to continue to try reading smaller lines, guessing if necessary. The level of acuity assigned was the smallest line with which 50% of the letters could be identified by the patient. A transformation of the Snellen notation to Log minimum angle of resolution (MAR) was performed for the purpose of analysis to convert the VA

data to an interval scale for parametric analysis (Bailey & Lovie,1976; Westheimer,1979; Holladay & Prager,1991). The conversion to the logarithmic scale shown in table 2.1.

2.2 Colour vision

A battery of colour vision tests was used comprising pseudoisochromatic plates and panel arrangement tests. Different tests were used on the premise that each test measures a unique aspect of colour vision (Aspinall,1974a). Combinations of red-green and tritan plates were used (Birch,1978) since colorimetric studies in acquired disease have shown that one colour mechanism is never affected without some involvement of the other two (Marre,1972).

1) Composite Pseudoisochromatic Plates (Comp PIC)

A composite selection of 16 plates for detecting red-green and tritan colour vision defects was used, comprising the following plates:

RED-GREEN plates

Eight plates from the *Ishihara 36-plate edition* series (Ishihara,1962). Spectrophotometric and colorimetric data on the Ishihara plates have been undertaken (Lakowski,1965; Lakowski,1966).

Plate 1 is the demonstration plate in the original series; it contains the numeral 12.

Plates 2,3 and 4 which, in the original series are plates 2,6 and 7, respectively. These are "screening" plates which carry confusion digits; numbers 8,5, and 3 on these plates are seen as 3,2, and 5, respectively by red-green defectives. People with severe acquired red-green defects and acquired tritan type III do not see either the "normal" or the "confusion" numerals (Birch,1988).

Plates 5 and 6, which are plates 10 and 14 in the original

Snellen VA	Logarithm of the minimum angle of resolution (LogMAR)
6/5	-0.08
6/6	0
6/9	0.18
6/12	0.30
6/18	0.48
6/24	0.60
6/36	0.78

Table 2.1 Snellen visual acuity (VA) scored to a log scale

(after Westheimer, 1979)

Plate 1

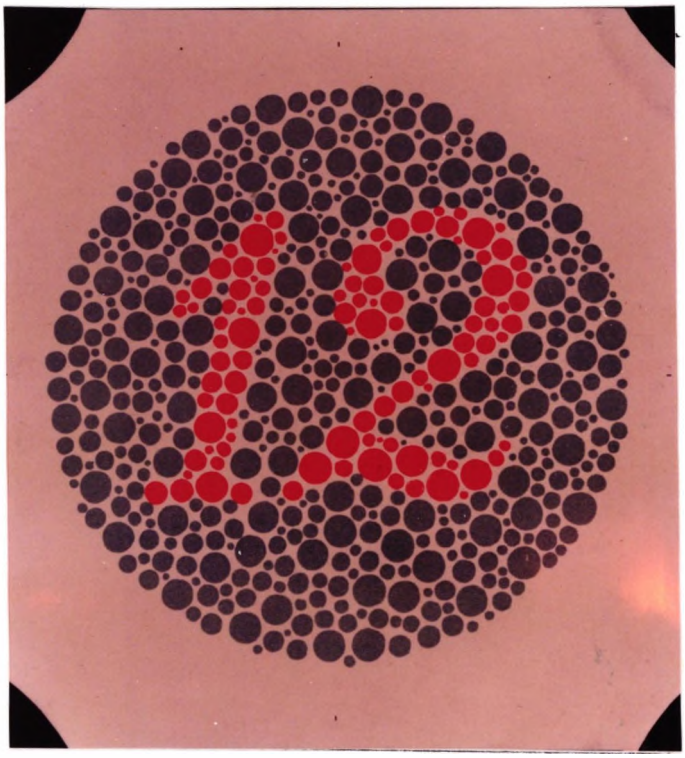


Plate 2

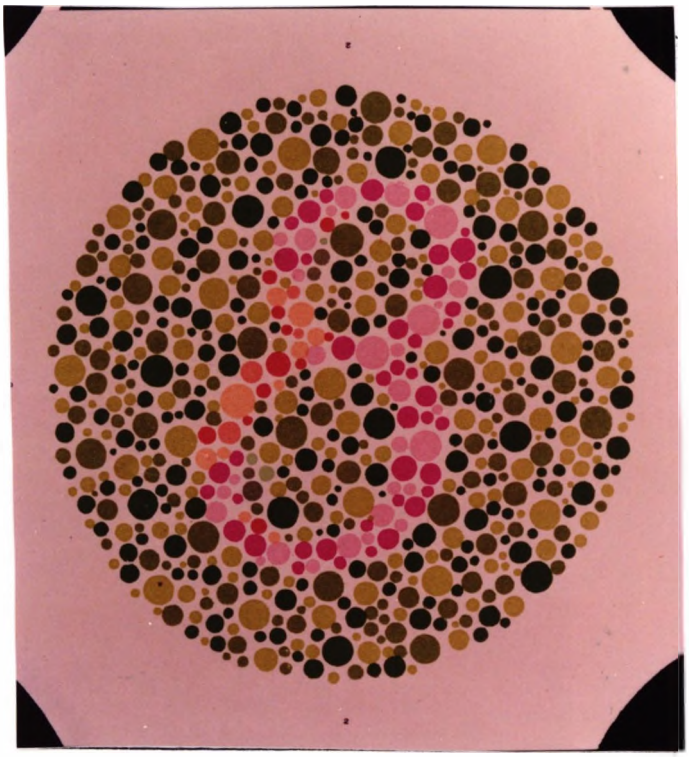


Fig 2.1 Comp PIC: Red-green plates from the Ishihara series

Plate 3

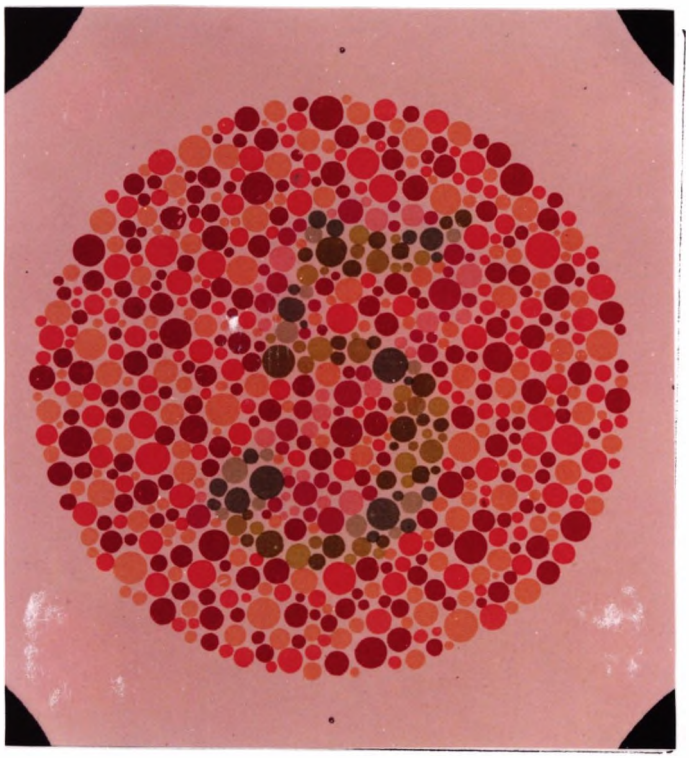


Plate 4

Fig 2.1/Contd

Plate 5

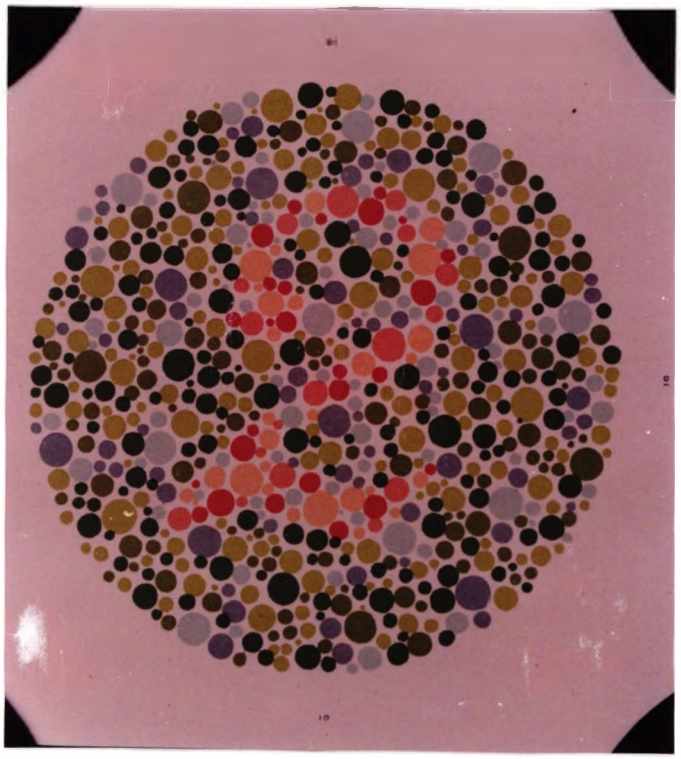


Plate 6

Fig 2.1/Contd

Plate 7

Plate 8

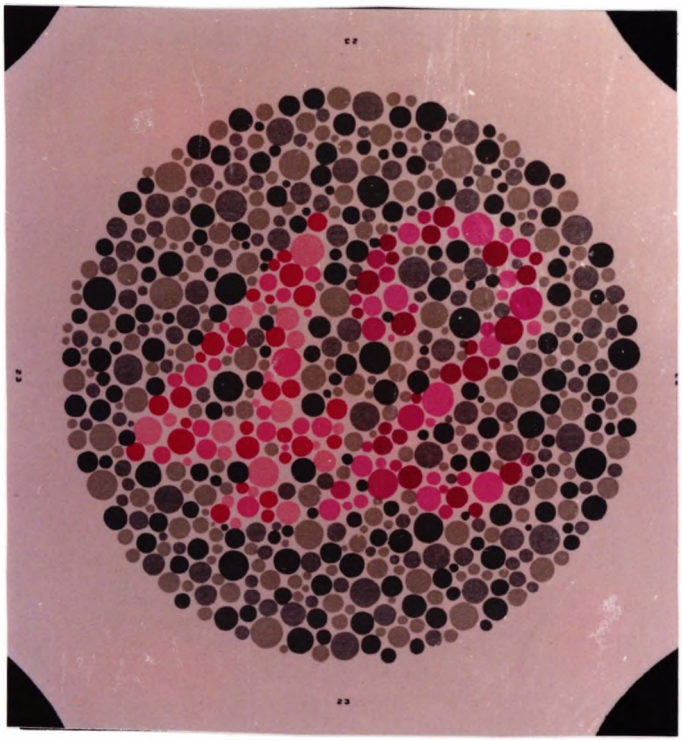


Fig 2.1/Contd

Plate 9

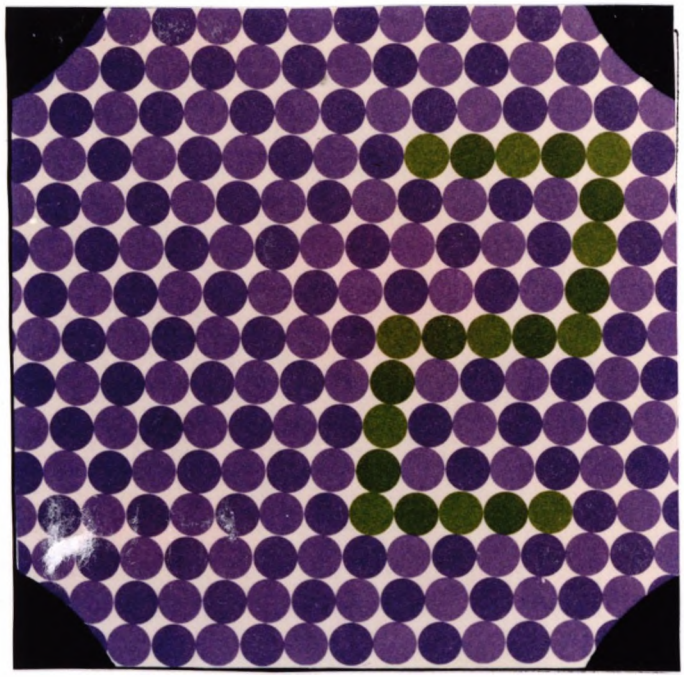


Fig 2.2 Comp PIC: Tritan plate from the SPP1 series (demontration plate).

series. These "screening" plates are of the vanishing design; the numerals 2 and 5 are not be visible to red-green defectives.

Plates 7 and 8, which are plates 22 and 23 in the original series. These are "classification" plates used to differentiate between protan and deutan patients. Two numerals are displayed: one a pure red, the other a purple-red, both on a neutral background. A protan or deutan will not see both numerals on these two plates. The protan patient will have difficulty with the first numeral on each plate (red numerals 2 and 4) whilst the deutan patient, with the second numeral (purple numerals 6 and 2). Patients with very severe acquired tritan type III defects do not see both numerals on these plates (Birch,1986).

Fig 2.1 shows the 8 red-green plates in the Comp PIC series (not to original size).

TRITAN plates

Plate 9, which is the demonstration plate from the *Standard Pseudoisochromatic Plate Test Part I (SPP1)* series (Ichikawa et al.1978). This plate has been shown to be useful for detecting both acquired and congenital tritan defects (Ichikawa et al.1978; Birch & Hamon,1984; Mantyjarvi,1987b; Honson & Dain,1988). It contains a regular matrix of similarly-sized dots making up the numeral 2 (in a digital configuration). The stroke width of the numeral equals the diameter of a dot, that is, 8mm. Two hues are employed for the figure and two for the background. The hues forming the figure and the background are those which a tritan defective confuses and they are of varying saturations and values. The luminance contrast between the figure and the background according to Honson & Dain (1988) is within acceptable limits ie. the maximum differenve in reflectance between the figure and its background is 2.1%. The chromatic locations of the colours used for the figure and background on this plate are given in appendix 2A. Spectrophotometric and colorimetric data

for the complete SPP1 test are available (Chioran & Sheedy,1983). Fig 2.2 shows plate 9 of the Comp PIC series.

Plates 10,11,12,13,14,15 and 16. which are 7 of the plates in the series of *'Experimental Tritan plates"* screen-printed by J.Birch of the City University for the detection of acquired tritan defects (Birch-Cox,1976; Birch,1978). These plates consist of pairs of colours which are intended to be confused by people with tritan defects. The pairs of colours were selected to lie on the tritan isochromatic lines and they were derived from colour matching experiments. The saturation and value of each hue are kept constant. The luminance contrast between the figure and background is also kept constant within 5%.

Two designs are available: The random-dot matrix design which contains a symbol and the regular-dot matrix design which contains a numeral. In the random-dot design the symbol is contained in an area of 4.5cm sq. either on the right or the left hand side. The stroke width of the symbol is 5mm and the format is composed of dots ranging in diameter from 1 to 5mm. The regular-dot design consists of a regular matrix of dots in which a numeral is concealed. The numeral is contained in a rectangle of 4 by 5.5cm. Only dots with diameters of 4 and 2mm are used and the stroke width of the numeral is 1cm.

Fig 2.3 shows the 7 experimental tritan plates of the Comp PIC series. Plates 10,12,13,14 and 16 are the "screening" plates having very small colour differences (low threshold) between the figure and the background. Plates 10 and 16 are of the regular-dot design while plates 12,13 and 14 are of the random-dot design. Plates 11 and 15 are the "classification" plates which have larger colour differences between the figure and the background. Both are of the random-dot design.

These plates have been evaluated (Verriest & Caluwaerts,1978). The C.I.E. colour coordinates of these plates are given in appendix 2B. Acquired tritan colour

Plate 10

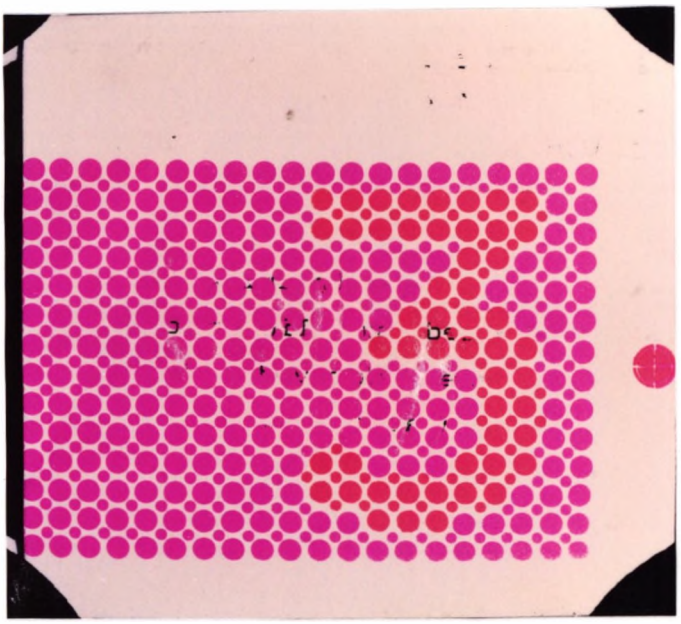


Plate 11

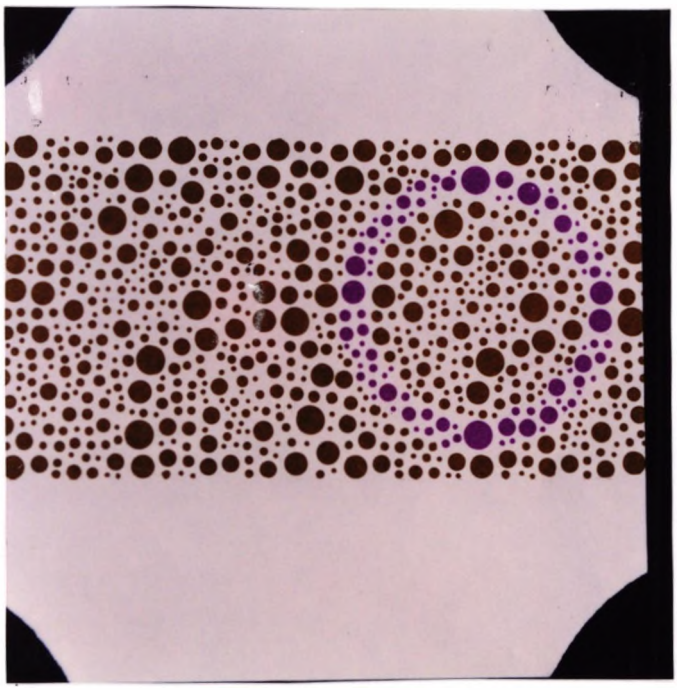


Fig 2.3 Comp PIC: Tritan plates from the Birch Experimental Tritan series.

Plate 12

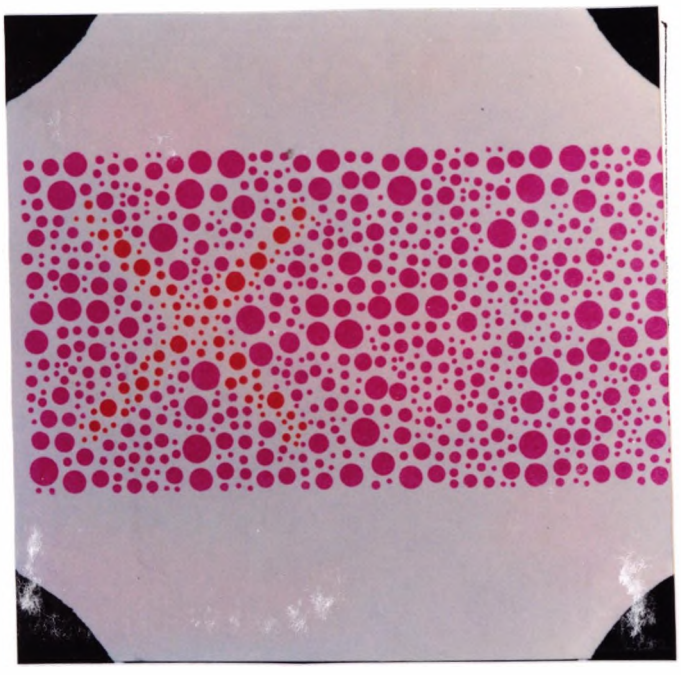


Plate 13

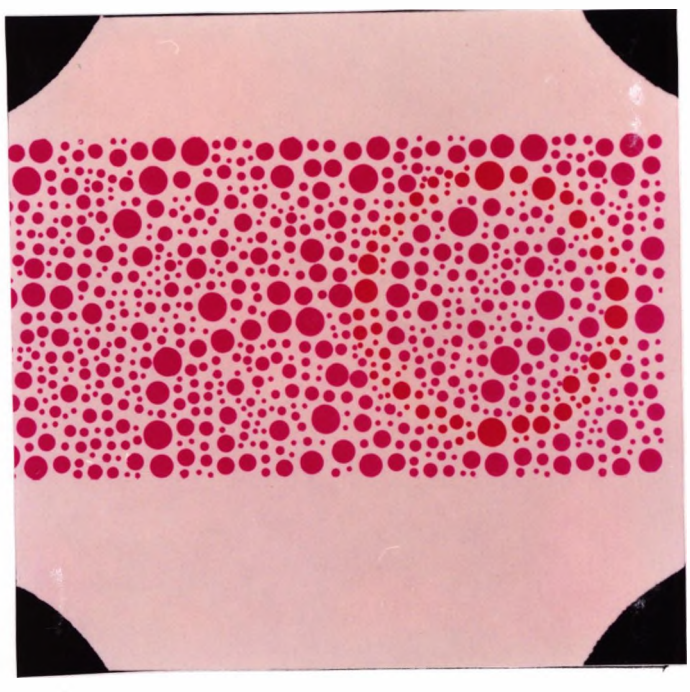


Fig 2.3/Contd

Plate 14

Plate 15

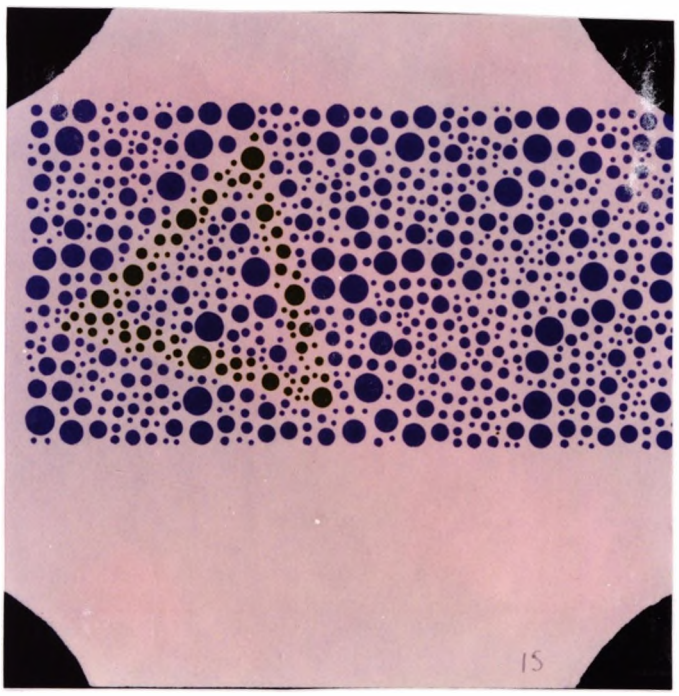


Fig 2.3/Contd

Plate 16

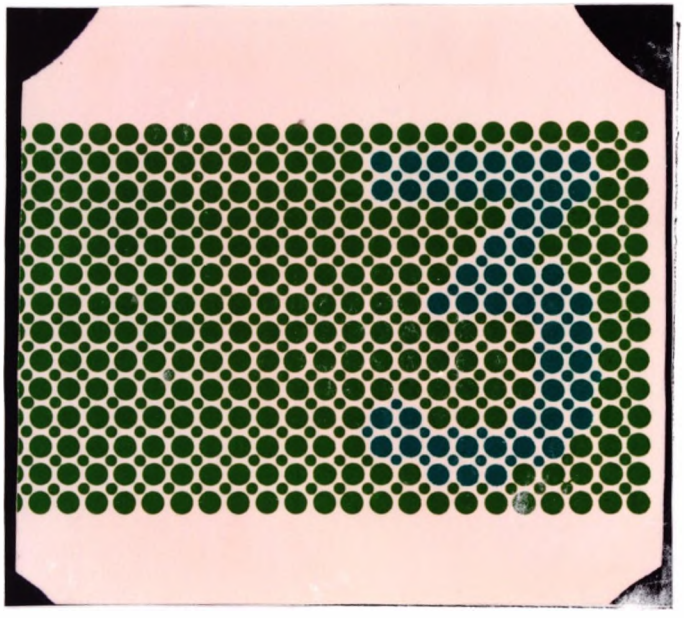


Fig 2.3/Contd

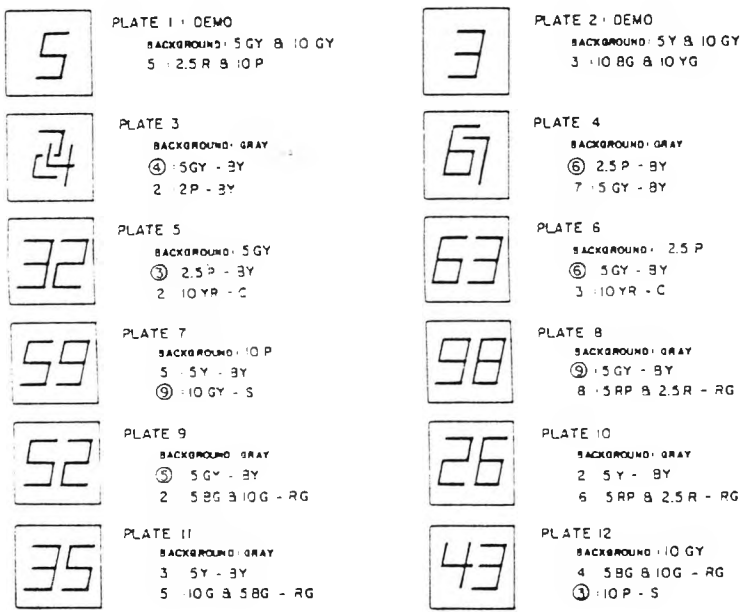


Fig 2.4 Schematic representation of the SPP2 plates. The figure/background colours are specified by the Munsell colours and are based on the prototype version. Letters adjacent to the figure's Munsell colours indicate whether the digit tests for blue-yellow (BY), red-green (RG), or scotopic (S) colour defects or severe as a comparison (C) for visibility judgements. Circled numbers are the figures on each test plate that should appear as the more distinct of the two figures (after Hovis et al., 1990)

defectives are not expected to see the numerals/symbols contained in these plates. As the names screening and diagnostic imply, they vary in their ability. The screening plates are meant to be the more sensitive ones. Errors on the "classification" plates indicate the presence of a severe defect (Birch,1986).

2) The Standard Pseudoisochromatic Plates Part 2 (SPP2)

The SPP2 plates were designed for the detection and diagnosis of acquired colour vision defects (Ichikawa et al.1983). The test incorporates plates for detecting both red-green and tritan defects and consists of 12 plates in total. The first two are demonstration plates while the remaining 10 are "classification" plates. Except for the two demonstration plates, two "digital" numerals (left and right) in a regular dot format are displayed in each plate. Altogether 20 numerals are used: 11 are for the detection of tritan defects, 5 for the detection of red-green defects, 2 for the detection of rod monochromatism, and 2 for non-specific colour defects. The test numerals are referred to as "vanishing", because patients with a colour vision defect will be unable to discriminate the digit from the background.

Fig 2.4 shows a schematic for each plate, the type of defect when a patient fails to report a numeral and the approximate Munsell colours of the figures and the backgrounds. The SPP2 plates have been evaluated by several authors (Tanabe et al.1984; Pinckers et al.1985; Ichikawa et al.1987; Mantyjarvi,1987a). The SPP2 test was described by Marre et al.(1991) as an excellent clinical colour test for the examination of acquired defects. Age-related normative data for the SPP2 test obtained from an independent analysis on a large sample of normal subjects is provided by Hovis et al.(1990). Lakowski et al.(1989) have provided objective data of the SPP2 test from colorimetric measurements.

3) The Lanthony Tritan Album (LTA)

The LTA (Lanthony,1985) is a form of PIC plate test for the diagnosis and evaluation (quantitative & qualitative) of tritan colour vision defect which makes use of the principle of confusion between violets and greys (Lanthony,1987). The album consists of 6 plates which are numbered 0 to 5. Each plate contains a diamond shape made of regular-sized grey dots (Munsell values about 4,5 and 6) on a black background. A group of coloured dots making a small square is located in one of the corners of the grey diamond. The grey dots of the diamond therefore form the background upon which the coloured square is located in one of its corners.

Plate 0 is the demonstration plate; it contains an orange coloured square of dot (2.5R) located at the top corner of the diamond. The rest of the plates (1 to 5) contain a violet square of dots (10PB) of decreasing saturation (10,8,6,4,2) in one of the corners of the diamond. Fig 2.5 shows plate 5 of the LTA.

All plate tests (Comp PIC, SPP2 & LTA) were viewed by the patient from a distance of 35-40cm under the level of illuminance available at the different venues of the study (see patients & procedures sections of chapters 3, 4, 5 & 6). The walls of the examination rooms at each venue were pastel coloured. Examination was carried out monocularly with the patient using an appropriate correction. For the Comp PIC and the SPP2, the patient was asked to report the number(s)/symbol which he saw on each plate. A time limit of 4-5s was imposed on the patients. Patients were not allowed to manipulate the test. Numbers/symbols that were not seen by the patient were marked as errors. Slight topographical misinterpretations (such as 6 interpreted as 8) were not regarded as errors.

For the purpose of analysis, performance on the Comp PIC plates was designated as the number of plate errors made (Long et al.1985); which was in three categories: total plate errors, red-green plate errors and tritan plate errors. Failure to read a numeral on plates containing two

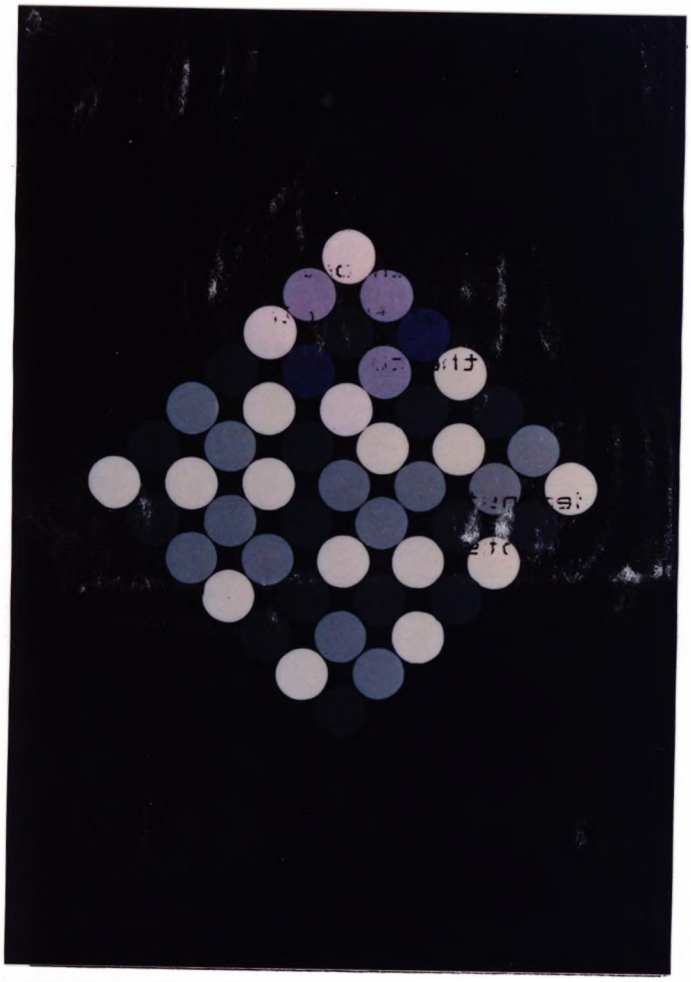


Fig 2.5 Plate 5 of the LTA

numerals (plates 7 & 8) constituted an error on that particular plate.

For the SPP2 test, failure to see the individual red-green and tritan numerals (see fig 2.4) constituted as an error. Performance was therefore designated as total errors, red-green errors and tritan errors.

For the LTA the patient was required to indicate the position of the "coloured square of dots" (right, left, top or bottom) within the larger grey square. In study 1 (see table 2.4) only plate 5 was used; failure to indicate the position of the coloured square of dots constitued as a failure on the test. In the rest of the studies (2 to 4), a score was given to the patient; the score being the plate number of the last correctly read plate. Thus if all the plates were correctly read the score is 5.

4) Panel D15 saturated test (5/4)
5) Panel D15 desaturated test (5/2)

Each of the two panel D15 tests uses 15 evenly spaced Munsell hues mounted on movable numbered discs of effective diameter about 12mm, which make up an incomplete colour circle thus representing the colour gamut. There is also an additional "pilot" disc of blue paper (Munsell 10B 5/6). The discs are set in plastic caps which subtend 1.5 degrees at 0.50m. The movable caps are numbered on the back according to the ideal colour circle.

The hue specifications in the Munsell system of colours (Fletcher & Voke,1985) are as follows: Pilot (10B 5/6),1 (5B), 2 (10BG), 3 (5BG), 4 (10G), 5 (5G), 6 (10GY), 7 (5GY), 8 (5Y), 9 (10YR), 10 (2.5YR), 11 (7.5R), 12 (2.5R), 13 (5RP), 14 (10P), 15 (5P)

Although the test was originally designed for separating individuals with significant congenital colour vision defect from colour normals (thus the alternative name "dichotomous test"), the test has been described as a

useful test of acquired colour vision defects (Francois & Verriest,1961; Cole,1964; Collin,1966).

The desaturated panel D15 differs from the standard (saturated) version in that each of the coloured cap has a Munsell chroma notation two less than the standard aturated) D15 i.e. each cap of the desaturated version has value 5 and chroma 2. Recent reports (Adams & Rodic,1982; Birch et al.1987; Birch,1989) have indicated the usefulness of the panel D15 (5/2) for the study of acquired colour vision defects. A recent report by Dain & Adams (1990) gives an analytical comparison between the two D15s (5/4 vs 5/2) in the assessment of congenital colour vision defects. Figure 2.6a shows the two D15 tests used.

Having been taken out of the box, the 15 caps were first mixed up randomly. Viewing monocularly from a distance of 40cm, with an appropriate correction and under the level of illuminance available at the different venues of the study (see patients & procedures sections of chapters 3, 4, 5 & 6), the patient was required to find a cap (colour) which looked nearest in colour to the pilot cap from the randomly mixed 15 caps and to place it next in the box; the procedure was then repeated until the caps formed a colour sequence. The patient was allowed as long as was necessary to complete the test.

When completed and after having been reviewed by the patient (in case of further changes), the box was closed and turned over. On opening it the numbered bases of the caps were recorded on a scoring diagram provided with the test. The order of the caps was plotted directly on the diagram that shows correct cap positions extending in a circle from the pilot cap; a line connecting the caps in the order arranged by the patient was drawn.

A quantitative score of the patient's performance was also computed according to the method suggested by Bresnick et al.(1984a): The pilot cap was considered as zero and a notional cap of 16 was created at the right end of the cap

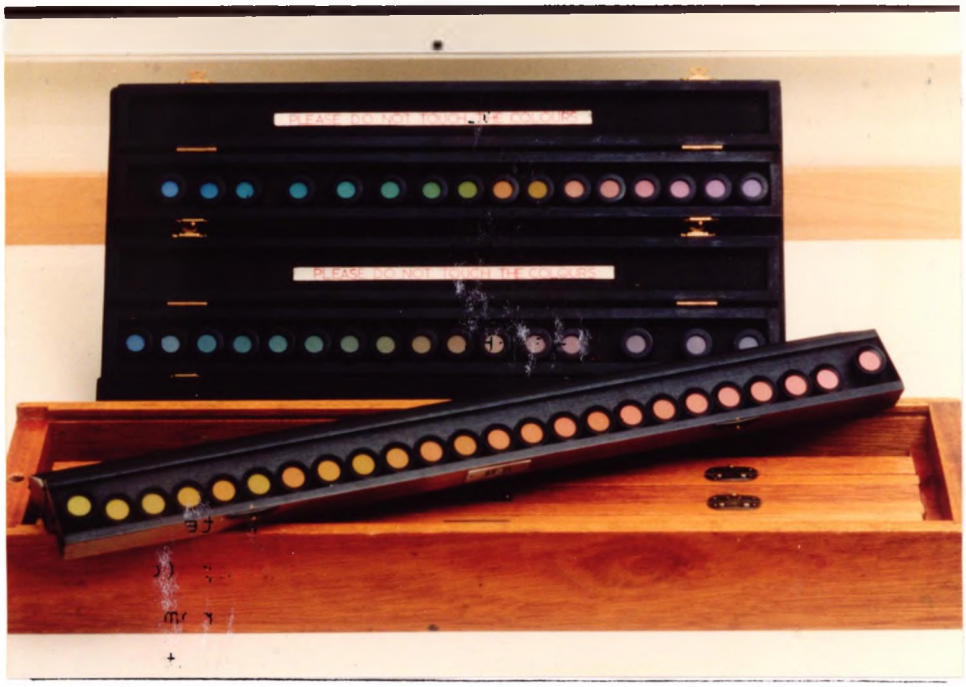
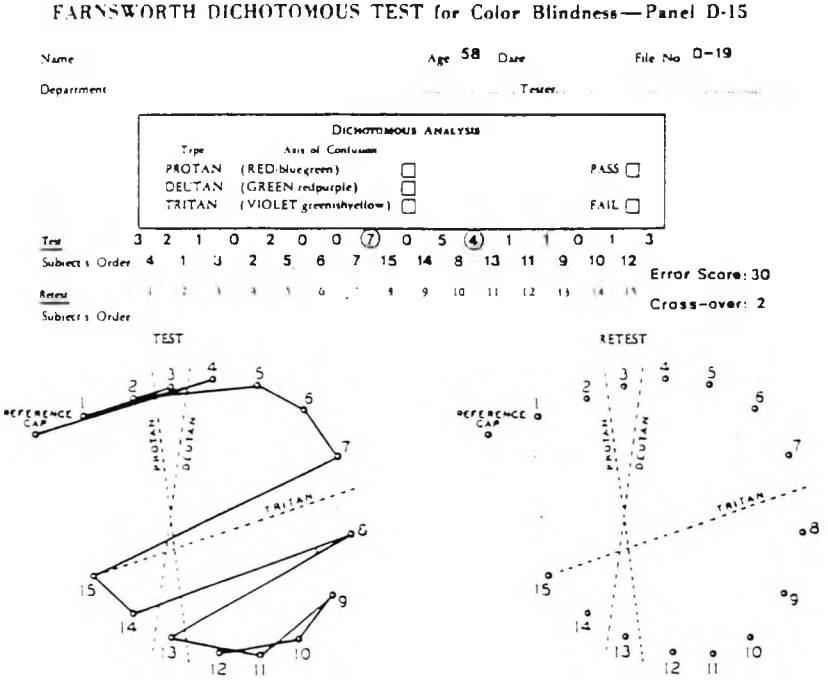


Fig 2.6a Colour vision arrangement tests: Top panel is the saturated version and the lower panel is the desaturated (5/2) version.

Below the two panel D15s is the FM 100-H test. Only one of the four boxes of the FM 100-H test is shown.



Desaturated Farnsworth D15 test in a 58 year-old male diabetic patient with proliferative diabetic retinopathy and macular edema. The cap sequence is indicated by connecting the numbers with lines in the order that the patient placed the caps. The score obtained is 30 and "diagnostic crossings" resulted in two tritan axes.

Fig 2.6b Example of method used to compute the D15 test results (after Bresnick et al.1984a).

arrangement. A score for each cap (cap score) was determined based on its relative position with respect to its neighbours; the total score was thus calculated by subtracting one from each cap score and summing the results. In addition, the number of "axes" (i.e. diagnostic crossings) was also computed for each performance; an axis was defined to be present when a cap score has a value of 4 or greater. For the end positions, only the pilot cap was used to compute the axes; the notional cap was not considered. See fig 2.6b for an example of how the total score and the number of axes are computed. The orientation (by visual inspection) of these axes identified the specific type of defect. Axes were classified (on visual inspection) into one of two: red-green or tritan, depending on their orientation relative to the pre-marked axis locations for the 3 types of defects.

6) Farnsworth-Munsell 100-Hue test (FM 100-H)

The FM 100-H test comprises a set of hues from the Munsell range with a fixed chroma and value, which are mounted in bakelite caps with an aperture of 1.25cm diameter. The colours form an ellipse in C.I.E. xy colour space with approximately equal steps in hue from one cap to its neighbour. The FM 100-H test examines hue discrimination ability and is the clinical equivalent of the colorimetric wavelength discrimination curve (Farnsworth,1943). The colour differences between adjacent caps are small; measurements by Lakowski (1966) showed these to vary between 0.6 to 5.7 NBS units.

The 85 caps are presented in 4 separate boxes, breaking the hue circle into 4 quadrants. Each of the four boxes has two reference (pilot) caps fixed, one at each end of the box and 21 movable caps. Each cap subtends an angle of about 2 degrees when viewed at a test distance of 40cm. The caps are numbered on the back according to the ideal colour order of the hue circle. The contents of the 4 boxes are as follows:

Box 1 caps 85-21 (Pink, through orange, to yellow)
Box 2 caps 22-42 (Yellow to blue-green)
Box 3 caps 43-63 (Blue-green to blue-purple)
Box 4 caps 64-84 (Blue to reddish purples, to pink)

Fig 2.6a shows the FM 100-H test. The FM 100-H test has gained recognition as a sensitive tool for the evaluation of acquired colour vision defects (Verriest,1963; Birch,1985) i.e. in demonstrating specific colour vision defects, combined forms or poor overall hue discrimination (Birch & Dain,1987). The degree of the defect can be estimated from the error score and error pattern. The graphical representation of the results illustrates an axis of confusion which is indicative of the type of defect. Reeves et al.(1989) delineated two major functions of the FM 100 - H test in the examination of acquired colour vision defects: 1)to detect a pathology and 2)to make decisions about a patient's management.

Commencing with box 1, the caps were taken out of the box and mixed up randomly. Viewing monocularly from a distance of 40cm, with an appropriate correction and under the level of illuminance available at the different venues of the study (see patients & procedures sections of chapters 3, 4, 5 & 6), the patient was required to rearrange the coloured caps, between the two reference pilot caps, to form a colour series. An unlimited viewing time was allowed. Having finished the task, the patient was allowed to review the initial colour sequence and to correct any errors. This was repeated for boxes 2,3 and 4. The final arrangement for all 4 boxes was then recorded on the recording sheet provided, using the number on the reverse side of each cap. An error score was calculated for each colour (cap) by obtaining the sum of the numerical differences between the adjacent caps. This was also represented on a radial line, designated for that colour, in a polar diagram. A total error score was then calculated, which was the sum of the individual "cap scores", in each of which the normal score of 2 was not counted. The square root of the total error score was also computed as it was shown to be statistically

Age	Tritan Axis	Red-green Axis
20 to 29	+2.3	-3.3
30 to 39	+2.8	-2.8
40 to 49	+3.5	-2.1
50 to 59	+4.1	-1.5

Table 2.2 Estimate of a significant axis on the FM 100-H test

To calculate an axis take SqBY scores and subtract the SgRG scores. Positive scores exceeding the values in the tritan column indicate a tritan axis; negative scores exceeding the values in the red-green column indicate a red-green axis (after Smith et.al.1985).

more informative (Kinnear,1970; Aspinall,1974b). The total error scores were categorised as normal or abnormal using the age norms of Verriest et al.(1982) i.e. abnormal when exceeded 95th percentile for patient's age for monocular testing without prior binocular testing.

Quadrant analysis as described by Smith et al.(1985) was performed on the raw scores to evaluate the tendency towards a particular axis of dyschromatopsia. Total error scores were partitioned into blue-yellow (caps 1-12, 34-54, 76-84) and red-green (caps 13-33, 55-75) partial scores. A relative axis was determined by subtracting the square root of the red-green partial score from the square root of the blue-yellow partial score; the value obtained was compared against an age-related norm provided (table 2.2) in order to specify the presence (and type) of axis present. A positive value corresponds to a relative blue-yellow (tritan) axis while a negative value denotes a relative red-green axis.

A statistical evaluation of the significance of the retest score by Chisholm (1969) showed that it was not influenced by patient age; however, higher initial scores increased the variance in retesting. Reeves et al.(1989) have provided normative data for assessing the clinical significance at the 95% confidence level of a change in FM100-H test total error scores on successive visits.

2.3 Contrast sensitivity

Two clinical contrast sensitivity tests (available at the time of the study) were used, with different designs and different methods of administration being employed.

1. Arden gratings

The Arden gratings were designed by Professor Arden at the Institute of Ophthalmology in London as an ingenious series of 6 photographically-printed (by offset litho) test plates in the form of plasticised sheets. Each plate consists of

uniform sinusoidally modulated bar gratings of a particular spatial frequency with contrast increasing gradually on a logarithmic scale from nil at the top of each plate to well above normal threshold at the bottom (Arden & Jacobson,1978). The test plates are contained in a neutral grey holder (with a matte surface of roughly the same albedo to the test pattern) measuring 44 by 35cm, which stands up like an easel in front of the patient.

Of the 6 test plates, the first plate is a demonstration plate; the next four plates are numbered 2 to 5 while the last plate carries plates 6 and 7 on the same sheet (in two halves). The bar gratings are printed on the plates at 6 different spatial frequencies; when used at 57cm, the bars subtend 0.2, 0.4, 0.8, 1.6, 3.2 and 6.4 c/degree from plates 2 to 7. Each plate measures 30.5 by 28cm and subtends approximately 28 degrees at the eye.

Each plate has 20 scale divisions, on the basis of which an arbitrary score ranging from 1 to 20 is derived. At the scale mark of 12 the contrast is nominally 2.8%. As the contrast on each plate increases in a logarithmic fashion by 0.088 log units (1.22 contrast sensitivity units) per division (per cm), the range of contrast on each plate extends over approximately 24 contrast sensitivity units from top to bottom. Fig 2.7 shows the Arden gratings.

Prior to testing, the demonstration plate was removed completely from the holder and the patient was shown the full extent of the dark and light bars on the plate; the patient was made to understand that the bars appear to fade toward the top of the plate. The patient was instructed to observe the junction of the matte surface of the holder and the plate while viewing monocularly from a distance of 57cm, with an appropriate correction in place and under the level of illuminance available at the different venues of the study (see patients & procedures sections of chapters 3, 4, 5 & 6),

Each plate was then gradually withdrawn from the holder at

Fig 2.7 The Arden gratings (only the demonstration plate is shown in full).

an angle parallel to the face plane so that the contrast of the grating increased as the plate was withdrawn, until the patient could discern the "start" of the gratings. The scale division showing in the gap between two scale lines when the patient first reported seeing the bars was read off at the edge of the plate as the score for that particular plate. Each plate was withdrawn successively and the six scores finally obtained were summed up to give the total score. If the patient could not recognise the gratings by 20 on the scale, a score of 25 was listed. Abnormality on the test was defined according to Arden's normal criteria viz 1)total score of exceeding 81 and/or 2)plate score exceeding 16.

Skalka (1980) noted a significant increase in test scores on all test plates of the Arden gratings with increasing age despite such effects being reported as negligible in Arden's original series of patients (Arden & Jacobson,1978). However, no such age-related age norms have been established for general clinical use. The evaluation by Reeves et al.(1988) showed the Arden gratings to have considerable inter-tester variance but good reliability, in agreement with Woo & Prentice (1983) who found the test to be a statistically reliable tool with small test-retest variation.

2) Vistech VCTS System 6000 (VCTS 6000)

The VCTS 6000 allows a relatively simple measure of contrast sensitivity. It is both quick and simple to use as standard vision charts. The test takes the form of a chart measuring 13 by 18cm consisting of 5 rows of photographically produced circular "patches" of sine wave gratings at carefully calibrated levels of contrast (Ginsburg,1984). Each row (A to E) has 9 patches of the same spatial frequency, which when viewed from 18 ins, are as follows: A)1.5 c/degree, B)3 c/degree, C)6 c/degree, D)12 c/degree and E)18 c/degree, with each patch subtending an angle of 1.43 degrees at the eye.

Gratings of decreasing contrast levels in steps of approximately 0.1 log units are found in each row; the range of contrast on patches along a particular row is from well above the normal visual threshold (patch 1) to zero contrast (patch 9). The test gratings are randomly arranged in one of three orientations: vertical, left and right, the angle of tilt being +/- 15 degrees from vertical.
Fig 2.8 shows the VCTS 6000 test together with the evaluation form provided. A key is provided (for the examiner) which gives the correct orientation of gratings in all the patches and also the contrast sensitivity values for each patch. A light meter (Sekonic) is provided to ensure that the chart luminance is within recommended limits (30 to 70ft.L i.e. 103 to 240cd/sq.m). The recommended "green area" on the meter dial was measured by Tracey (1989) to correspond to a luminance range of 40 to 100ft.L i.e. 137 to 343cd/sq.m.

The contrast sensitivity of the majority of the normal population between the ages of 10 and 70 (N=300) lies in the shaded area on the evaluation form (Ginsburg et al.1984; VCTS Application Manual,1985)(fig 2.8) which forms the normal range expected when the chart is used according to the instructions specified.

The VCTS 6000 was supported in a well-designed holder which held the chart at a constant distance of 45.6cm (18 ins) from the patient's eye. Viewing the chart monocularly with an appropriate correction in place and under a level of illuminance which complied with the specified level (measured using the light meter provided), the patient was required to report whether or not gratings were visible, and if visible at what orientation, for each patch along each of the 5 rows of different spatial frequencies. Observations started with the highest contrast gratings and progressed along the row until the contrast was so low that the patient was unable to see the gratings. One of four responses was sought i.e. vertical, right, left or blank; the patient being encouraged to guess when difficulty arose at the patch with the least contrast level. Thus the test

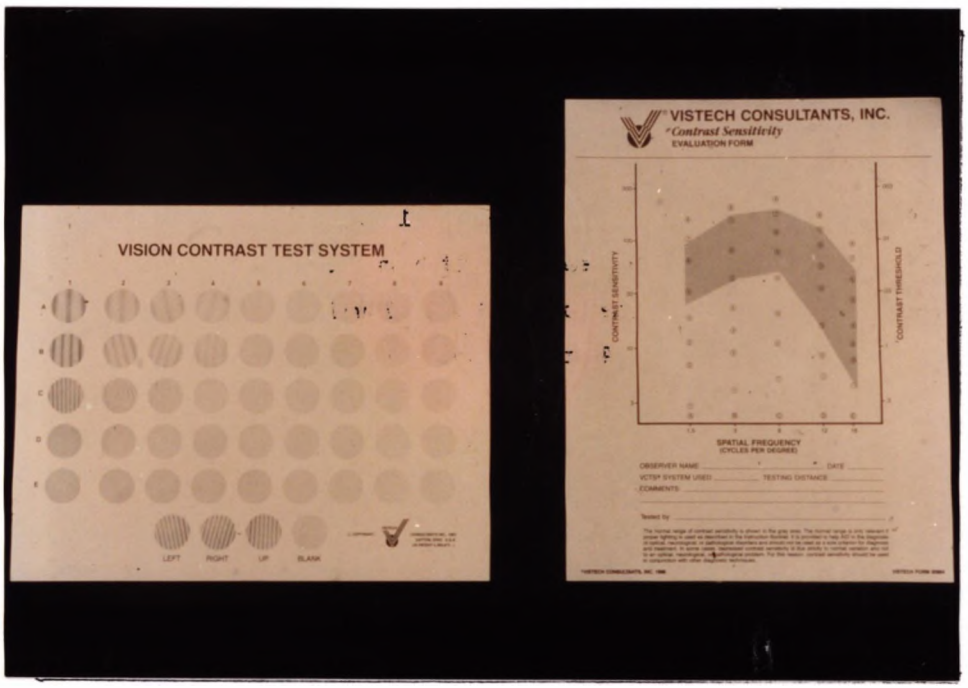


Fig 2.8 The VCTS 6000 and its evaluation form.

method was essentially 4-alternative forced-choice The highest numbered patch (lowest contrast patch) that was correctly identified in each row was taken as the patient's contrast sensitivity for that spatial frequency.

The results for each spatial frequency were thus obtained as scores i.e. 0 to 8 (Teahan,1989; Wallace & Patel,1990) which were plotted directly on the evaluation form. The contrast sensitivity curve for the patient was drawn by connecting the points. The contrast sensitivity curve drawn for a patient was compared to this "normal" population curve; abnormality was defined as a curve which lay out of the normal range. A "global score" was also computed for each performance by summing up the individual spatial frequency scores (Edwards & Brown,1987).

Various authors have mixed views regarding the VCTS 6000 (Woo & Bohnsack,1986; Edwards & Brown,1987; Ginsburg,1987; Reeves & Hill,1987; Hill et al.1989; Wood et al.1989; Elliot & Whitaker,1992a & 1992b). The chart's limited precision has been one of the main criticisms directed at the test i.e. the step-by-step changes in contrast between neighbouring discs may not be fine enough to resolve any genuine differences between averages. Test-retest reliability of the test has been reported to be low as a result of only one trial possible at each contrast (Rubin,1988). However, on the positive side, it is an easily and rapidly applied clinical test and for this reason at least, it should be regarded primarily as a clinical tool and not a research tool. It has also been shown to be adequate for repeated measures in clinical studies (Woo & Bohnsack,1986; Kennedy & Dunlap,1990). Deviations from the normative curves have also been found to be highly useful indications of a pathologic disorder (Steinberg,1987).

2.4 Visual fields

The quantitative and qualitative measures of the central visual fields were obtained with two types of field apparatus:

1) Friedmann Visual Field Analyser Mark I (VFA I)

The VFA I is a compact multiple-pattern screening instrument designed for testing the central 25-degree visual fields at 33cm. It consists of a hemispherical fibreglass moulding with a front plate at the front end employing its own external illumination device (providing 10 Lux) in the form of a ring illuminator (Friedmann,1966; Bedwell,1967; Bedwell,1978).

Groups of 2,3 or 4 stimuli (employing a total of 15 stimulus patterns) are presented on a black matte screen of diameter 40cm when apertures in the fixed front plate and a rotating plate coincide. The rotating plate is movable with a lever device; rotating it enables the 15 stimulus positions to be displayed in turn. The positions of the stimuli and the groups of stimuli which are presented simultaneously are shown in fig 2.9.

The patient views the stimuli which come from the diffuser through the illuminating apertures, the apertures having been illuminated for a brief period (0.33s) by the illuminating system consisting of a Xenon flash tube and an integrating hemisphere. The light from the Xenon tube that enters the rear of the bowl is attenuated by easily controlled neutral density (ND) filters. Two ND filter wheels are provided which allow control of target luminance: 0 to 0.8 ND in 0.2 steps and 0 to 4.0 in 1.0 steps, which when used in combination provide 0 to 4.8 ND values in 0.2 steps.

Seated at the instrument with the appropriate correction in place, the patient was required to report the number of "spots" seen each time the stimuli were flashed. The right

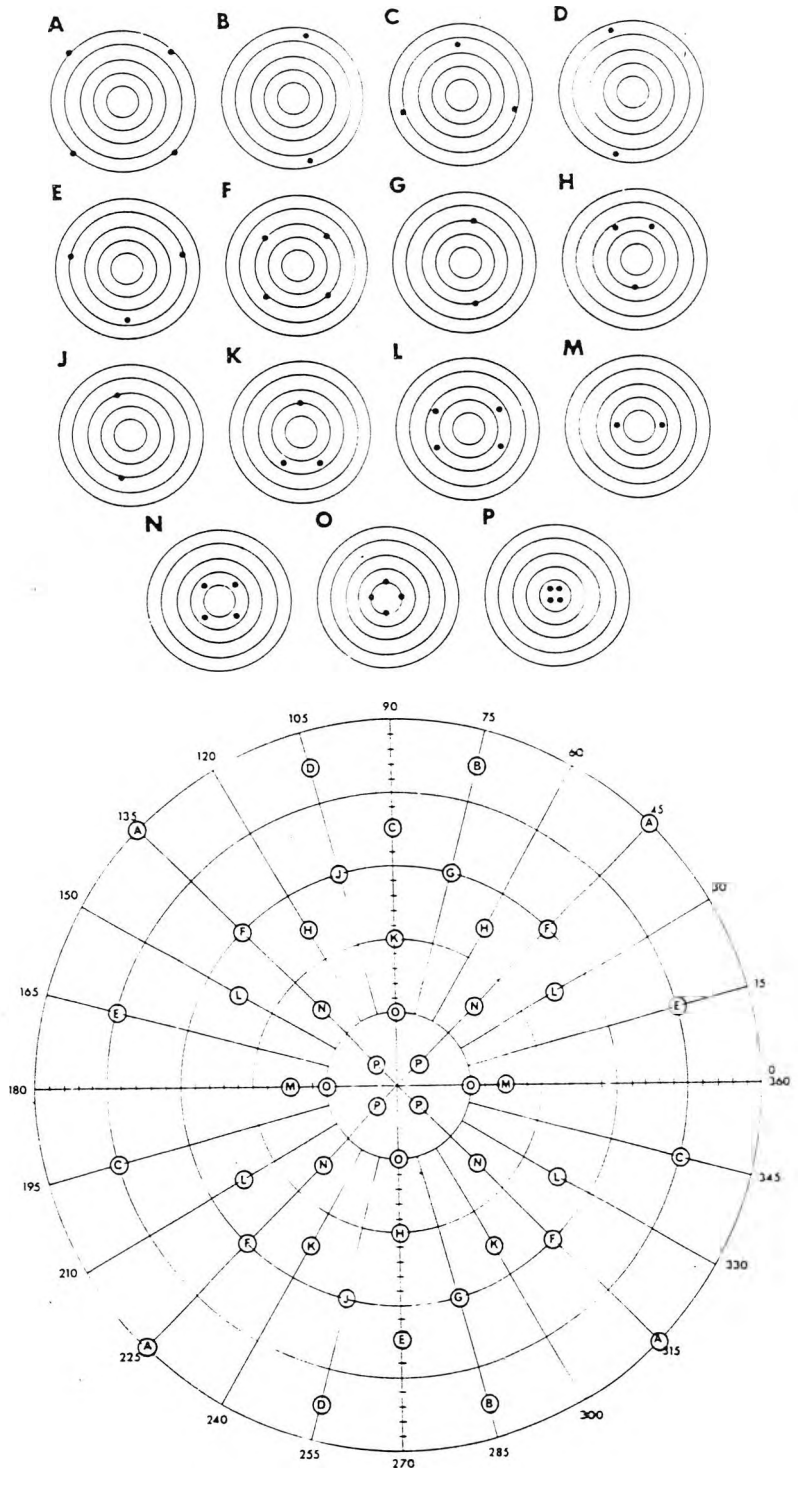


Fig 2.9 Positions of the stimuli on the VFA I.

eye was examined first in the case of patients having both eyes in the study. The visibility threshold for each of the 46 stimuli (Greve,1971; Greve,1973; Gazzard & Thomas,1975; McClure,1988) of the test was obtained, beginning with the most central pattern P and progresing to the most peripheral pattern A.

Each pattern was examined in turn from below threshold by asking the patient to report the number of "spots" seen each time a group of stimuli was presented. The stimuli for each pattern were presented three times at a particular setting and those detected twice out of the three exposures were marked with the particular filter setting as the threshold value. The stimulus intensity was increased in 0.2 steps and the procedure was repeated until all the stimuli of the 15 patterns were recorded as seen at their threshold filter settings. The macular threshold was finally obtained by presenting the central stimulus (after removing the white fixation target and placing the lever between A and B) in the same manner as for the peripheral stimuli.

Threshold values for all 46 peripheral stimuli and the central stimuli were recorded on the composite field sheet provided. Field scores were computed for each composite performance (modified after Crick,1975). Each threshold filter setting was assigned a "numerical score" starting with a score of 0 for an absolute defect (not seen at filter setting 0), 1 for just seen at filter setting 0.0, 2 for 0.2, 3 for 0.4 and so on. The total field score (excluding the macular threshold) was calculated by:

$$\text{Total field score} = \frac{xi + xii + xiii + xiv + \ldots\ldots + xn}{46} * 10$$

where xi, xii, xiii, xiv,....xn are the numerical scores of the stimuli.

A pilot investigation revealed a very large difference in sequential threshold measurements for pattern A (varying by

as much as 1.4 log units) agreeing with what Henson et al.(1984) noted in their evaluation of the Mark II version of the instrument. Thus pattern A was excluded in the investigation proper; the total field score was therefore calculated using only 42 stimuli.

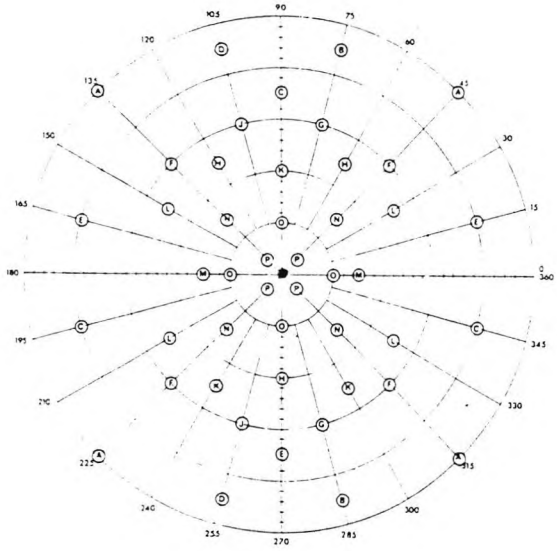
Zonal scores (modified after Sabry et al.(1987)) were also computed (for the 5 zones as shown in fig 2.10) along the same lines as for the total field; the computation, however, depended on the number of stimuli contained within each of the 5 zones.

Total field scores were designated as normal or abnormal on the basis of the age-norms established by the designer (Friedmann,1966). Although these have been suggested by some (Gutteridge,1983; Pitman,1983) to result in underdiagnosis of field defects, they have also been shown to provide a readily available set of guidelines for rapid clinical use (Greve & Wijnans,1972/73; Bynke & Nordenfelt,1974). For the purposes of analysis (in the present study) cut-off total field scores were employed in the decisions of normal/abnormal as shown in table 2.3.

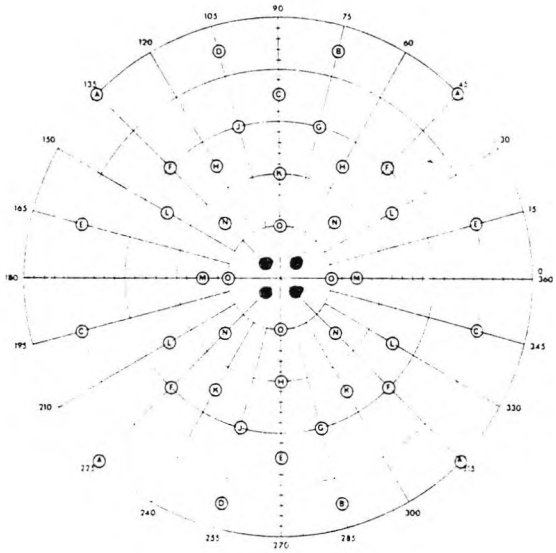
Test-retest investigation for the total field score was carried out as part of the present study to assess the reproducibility of the field measures (field scores) as derived by the method described above. 55 normal patients with a mean age of 34.2 years (sd 10.9; range 23 to 63) were examined twice, having the repeated test performed within 3 weeks of the first test. The test-retest results are illustrated on a scatter-plot (fig 2.11). Two measures of repeatability were obtained:

i) Correlation coefficient

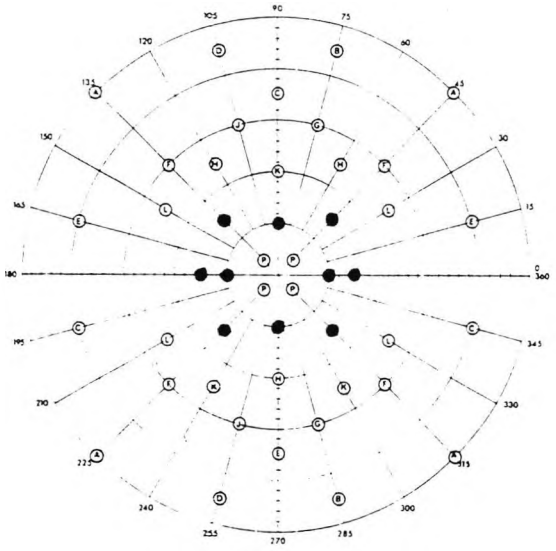
The plot (fig 2.11) illustrates a good correlation between the two sets of results ($r=0.82$, $p=0.0001$).



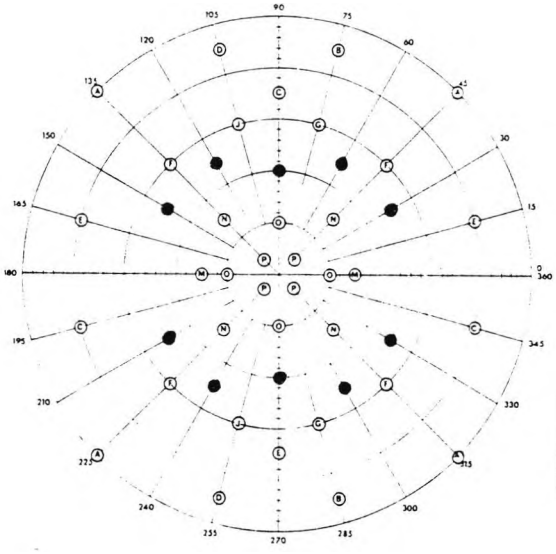
Macular zone



Zone 1

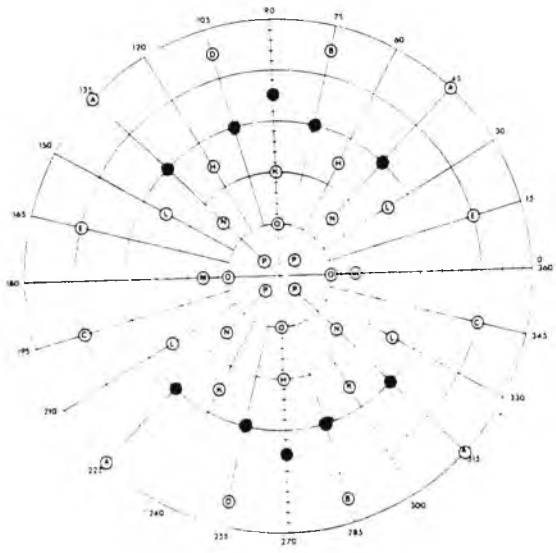


Zone 2

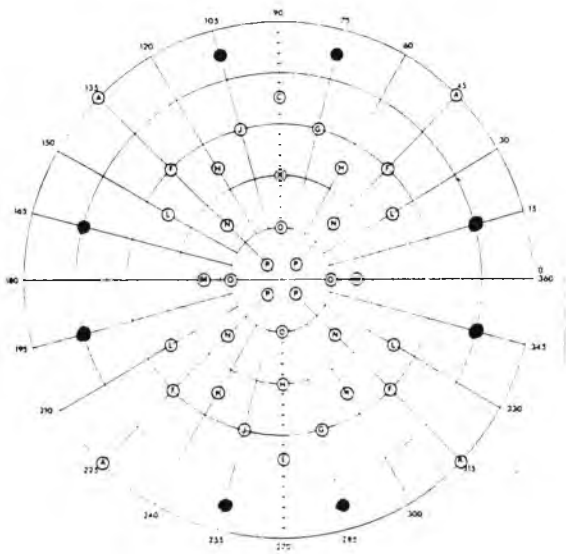


Zone 3

Fig 2.10 Zonal analysis: VFA I.



Zone 4



Zone 5

Fig 2.10/Contd

Age	Normal filter setting recommended	Abnormal filter setting (i.e -0.4) recommended	Minimum field score for normal
< = 40	2.0	1.6	100
41-50	1.8	1.4	90
51-60	1.6	1.2	80
61-70	1.4	1.0	70
71-80	1.2	0.8	60

Table 2.3 Criteria for defining abnormality on the VFA I

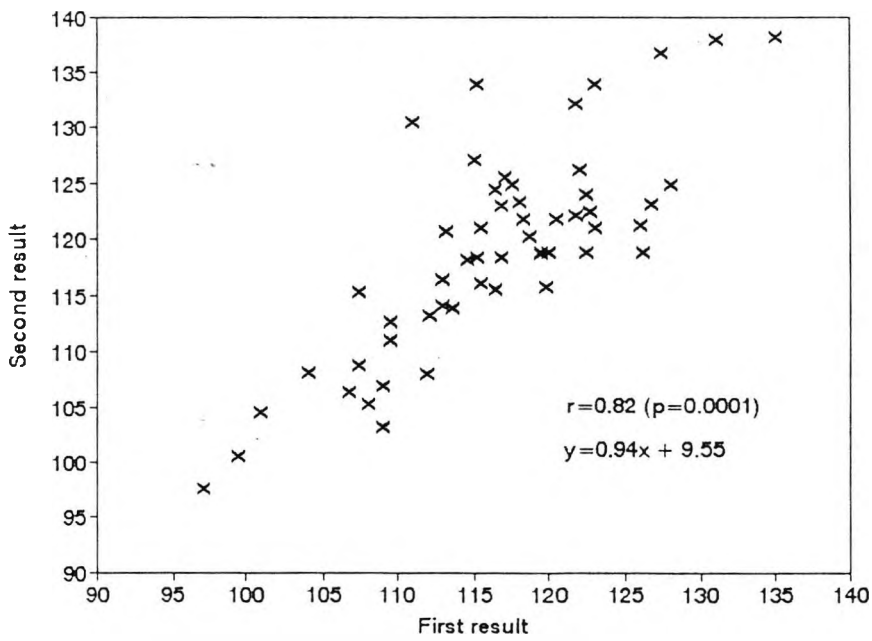


Fig 2.11 Scatterplot showing results of total field scores for test-retest on 55 eyes

ii) Dispersion

The mean of the differences between the two sets of results was 2.5 with a sd of 5.4. The small mean and sd reflect good repeatability (note that 100% repeatability would be reflected by mean and sd values of zero).

In view of the statistics performed in i) and ii) above, test-retest variability of threshold measurements on the VFA I was not expected to be significant.

2) Amsler grid (Amsler,1953)

Only chart No. 1 of the seven charts available was used in the present study. This chart, referred to as the "standard grid", is normally the only chart required and is considered to be sufficient in many cases (Grosvenor,1982). It consists of a black grid on a white background (reversed version) with a central fixation point. It has an overall size of 10 by 10cm and each square of the grid is 5mm in each direction. The entire grid subtends an angle of 20 degrees when viewed from 30cm, thus each square subtends as angle of 1 degree. The entire grid image corresponds to an area of the retina that is 10 degrees in radius from the fovea. The Amsler grid is said to be excellent for detecting metamorpopsia but not sensitive for scotoma detection (Wall & Sadun,1986).

With the patient wearing an appropriate correction, the Amsler grid was held at about 30cm from the patient under the level of illuminance available at respective study venues (see patients and procedures of chapters 3,4,5 & 6); with care taken to ensure an even intensity. The patient was instructed to stare at the fixation spot in the middle of the grid and simultaneously to report the appearance of the network of the whole grid. Failure was recorded when the patient reported areas of defect on the grid, be it distortion, disruption or missing areas.

2.5 Tests used and respective studies

Not all the tests described above were used in every study; tests involved in each study are listed in table 2.4.

2.6 Methods of analysis of test results: Statistical tests employed.

The statistical tests employed in the analysis of data for the 4 studies are as follows (Kirkwood,1988; Portney & Watkins,1993; SAS Version 5 User's Guide,1985):

Unpaired t-test
Paired t-test
Chi-Square test
One-way analysis of variance (ANOVA)
Pearson product-moment correlation
Linear regression
Multivariate analysis using the *General Linear Models (GLM)* which included *multiple regression*

In the main, the analysis of the results of visual tests involved comparison of mean results between different groups of patients to determine if they were significantly different from each other.

The *unpaired t-test* was used when the mean results of two independent groups of subjects were compared. The *unpaired t-test* is based on the assumptions that scores from the two sample of patients represented an underlying normal distribution, that patients have been randomly selected and assigned to groups, and that the variances of the two groups are relatively equal. The t-ratio is calculated and a probability value which indicates if the difference between the two means is due to chance.

In essence the t formula measures the size of the difference between the means of two samples and converts this into a standard measure of deviation. A large value of t signifies a marked difference between the sample means

STUDY	TESTS EMPLOYED										
	VISUAL ACUITY	COLOUR VISION						CONTRAST SENSITIVITY		VISUAL FIELDS	
	* PH test	Comp PIC	SPP2	LTA	D15(5/4)	D15(5/2)	FM 100 H	Arden gratings	VCTS 6000	VFA I	Amsler grid
1	+	+ a		+ b		+ c		+ d	+ e		+
2	+	+ a	+	+	+	+	+	+	+	+	+
3	+	+	+	+	+	+	+	+	+	+	+
4	+	+ a	+	+	+	+	+	+	+	+	+

+ =Test was used

* PH =Pinhole was used when applicable

a =Excluding plate #16

b =Only plate 5 was used

c,d =Used on 171 patients only (at Middlesex Hospital)

e =Used on 305 patients only (at Whittington Hospital)

Table 2.4 Clinical tests used in the present study

Note: Not all the tests described earlier were used in every study. The tests involved in each study are listed in table 2.4.

to indicate if significant changes have occurred.

The one-way *analysis of variance (ANOVA)* was carried out when three or more independent group means were compared. The ANOVA is a general formal method of comparing different models for a set of data. It is a logical extension of the t-test; its employment is always accompanied later by an adjunct multiple comparison procedure (the Scheffe's test in this Thesis), used to control the type I error rate in allowing valid interpretations of several comparisons.

In performing ANOVA, a continuous response variable known as dependent variable is measured under experimental conditions identified by classification variables, known as independent variables. The variation in the response is explained as being due to effects in the classification, with random error accounting for the remaining variation. The null hypothesis for the one-way ANOVA is that no significant differences exist between the means of all the groups involved (independent variable) whilst the alternate hypothesis proposed states that at least two means would differ. When the alternative hypothesis is accepted, a separate test (the Scheffe's test in this Thesis) is done to determine exactly where the significant differences lie. In the case that the null hypothesis is accepted no further analysis is carried out.

The following is a detailed example of how the one-way ANOVA is carried out:

Consider the mean results for a visual test on three different groups of patients with different clinical characteristics, each group having 5 patients. The total number of patients in the study is 15 (N=15). The independent variable, patient group, has three levels (k=3). This is formally, a one-way multilevel design. The dependent variable is the result of the visual test. The data for this example is given below:

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Group 1		Group 2		Group 3	
X1	$X2^2$	X1	$X2^2$	X1	$X2^2$
9	81	8	64	6	36
15	225	17	289	7	49
12	144	10	100	5	25
16	256	9	81	8	64
13	169	11	121	4	16

Table 2.5 One-way ANOVA for independent samples: Visual test result (X) in different patient groups.

The aim of the analysis here is to determine if the means of groups 1, 2 and 3 (respectively, 13,11 and 6) are significantly different from each other. Suppose it is assumed that there is no underlying difference between the three groups so that only random variation causes the mean results on the test to differ from a single common value, which can be estimated to be the observed overall mean. The grand mean for all the 15 results is 10. A measure of lack of fit can be expressed as total sum of squares about the overall mean. The sum of squares for the total sample ie. the square of the deviations of each individual test result from the grand mean (TSS) is calculated as follows:

$$TSS = (9-10)^2 + \ldots\ldots + (8-10)^2 + \ldots\ldots + (4-10)^2$$
$$= 220$$

This total sum of squares reflects the total variability that exists within this set of data; some of the this total variability are attributed to a "between the groups effect" and the rest to "within the groups effect". The ANOVA partitions the total variance into these two components. The "between the groups effect" reflects the spread of

group means around the grand mean; the larger this effect, the greater the separation between groups. On the other hand, the "within the groups effect" reflects the spread of results within each group. The sum of squares for "within the groups effect" (SSe) is calculated as follows:

$$SSe = (9-13)^2 + \ldots + (8-11)^2 + \ldots + (4-6)^2$$
$$= 90$$

The sum of squares for the "between the groups effect" (SSb) is simply calculated by subtracting SSe from TSS ie.

$$SSb = TSS - SSe$$
$$= 220-90 \text{ ie. } 130$$

The concepts of between-groups and within-groups variability are then used to define a statistical ratio or a variance estimate, called the mean square. The mean square (MS) represents the average lack of fit per observation. The sums of squares are converted to the mean square by dividing each sum of squares by its respective degrees of freedom. The total degrees of freedom (dFt) within a set of data will always be one less than the total number of observations. Since in the example above the total number of patients is 15, it follows that dFt=14. The number of degrees of freedom associated with the between-groups variability (dFb) is one less than the number of groups, in the case above dFb=2. The number of degrees of freedom for the within-groups error variance (dFe) is equal to the total number of observations minus the total number of groups; for the above example dFe=15-3 ie. 12.

The mean squares for the between and within groups variance components for the above example are calculated as follows:

Mean square for between-group variance, MSb = SSb/dFb
ie. 130/2 = 65

Mean square within-group variance, MSe = SSe/dFe
ie. 90/12 = 7.5

The two mean squares above are then used to calculate the F statistic, as a ratio of the two values:

F = MSb/MSe
= 65/7.5
= 8.67

The larger the F-ratio, the greater the difference between the group means relative to the variability within the groups. In other words when no group effect exists, the total variance in the sample is due to error, therefore MSe is equal to or larger tha MSb yielding an F-ratio of 1.0 or less. However, when there is a significant difference between the group means, the between-groups variance is large resulting in an F-ratio of greater than 1. For the above example, the calculated F-ratio (8.67) is then compared with a critical value to determine its significance by referring to the critical F table. With dFb=2 and dFe=12, reference to tables of critical value of F for alpha = 0.05 gives a value of 3.89. Large F-ratios are evidence against equality of group means. Hence the whole one-way analysis of variance to determine if the mean values of groups 1,2 and 3 were significantly different is written conventionally as ANOVA F(2,12)=3.89 at 0.05. It means that comparison between this critical value to the calculated value of 8.67 shows the calculated value to be greater, thus conferring statistical significance at the 0.05 level. This means that there is less than 5% chance that the observed differences within the overall set of means are due to chance alone. Note that if the F-ratio is smaller than the critical value, no further analysis is undertaken as it means that no significant differences exist among the three means.

The results of dividing the sum of squares into components corresponding to different sources is presented formally in the ANOVA table below:

Source of variance	dF	SS	MS	F	p
Between groups	2	130	65	8.67	<0.05
Error	12	90	7.5		
Total	14	220			

Table 2.6 Summary table for a one-way ANOVA for data from table 2.5

A significant F-ratio does not, however, indicate that each group is different from all other groups; it only shows that there is a significant difference between at least two of the means. A post-hoc test needs to be done at this stage to determine exactly where the significant difference is and a multiple comparison test called the *Scheffe's comparison test* is carried out for the purpose of deciding which means are significantly different from each other. This particular test is a conservative test which provides a strong protection against type I error, but it also makes the procedure much less powerful than other post-hoc tests.

The minimum significant difference for the Scheffe's comparison test is given by:

Sqrt (k-1)F * Sqrt (2MSe/n), where k is the total number of means, F is the critical value for the specified dFb and dFe and n is the total number of observations in each group. For the example above where k=3 and F (critical)=3.89, the minimum significant difference is calculated as follows:

Sqrt ((3-1)(3.89)) * Sqrt (2(7.5)/5) = 4.83

Thus all differences between means must exceed this value to be significant. The table below details the comparison between group means and the associated differences between the means. As denoted by asterisks, the table shows that this exercise results in two significant comparisons. The means of groups A and C are significantly different, and so are the means of groups C and B. The means of groups A and B are not significantly different from each other at the 5% level.

Minimum significant difference by Scheffe's comparison test			
Group	A (13)	B (11)	C(6)
A (13)	-	2	7*
B (11)		-	5*

Number in parentheses represent means

Table 2.7 Significant differences for Scheffe's test

Often there were situations when mean values were not meaningful and the data was non-quatitative. The *chi-square test* was used for the comparison of groups in which patients' performance on a visual test had been classified into discrete, qualitatively different categories such as pass or fail. In such cases the proportions of patients with a particular attribute needed to be compared across different groups, and the data consisted of frequency counts of the number of times a particular attribute occurred. The observations were then frequency counts of the number of patients coming within each category. It was also possible to have more than two attributes such as "became better" or "stayed the same" and "became worse" and more than two groups for eg. after treatment with 3 different types of lasers. The test was used to determine

whether groups of patients differ in terms of the proportion of patients falling into one category rather than the others.

The chi-square test is essentially a non-parametric technique which provides a method of analysing the numbers of patients falling into given categories (with particular attributes) to see if the distribution of observed frequencies are significantly different from each other. The approach used in the chi-square test is to compute the frequencies that would have occurred if the groups being compared were identical with respect to the proportion of patients who had a particular attribute (called the expected frequencies). The chi-sq value is then calculated on the basis of the difference between the expected frequencies and the observed frequencies. The statistical tables will indicate the probability that a difference as large or larger than that represented by chi-sq could have occurred by chance. A related procedure, called the *Fisher exact probability test*, was alternatively used (ie. automatically computed by SAS version 5) when sample sizes were very small.

Correlation analysis between test results and patient variables were also undertaken to explore significant associations between these variables. The most commonly used measure of correlation in the present Thesis is the *Pearson product-moment correlation*, a parametric measure which is appropriate for measuring the degree of linear association between two numerical variables (such as between logMAR and age), where the x (age) and y (logMAR) are continuous variables with underlying normal distributions on the interval or ratio scale.

The association is measured by the correlation coefficient, r, which is always a number between -1 and +1 and equals zero if the variables are not associated. The value of r is positive if the two variables tend to be high or low together; the larger its value the closer the association. Conversely, the value of r is negative if high values of

one variable tend to go with low values of the other variable, and vice versa. A t-test is then used to test whether r is significantly different from zero ie. whether the observation correlation coefficient could simply be due to chance. The significance of the correlation is a function of both the size of the correlation coefficient and the sample size.

Closely related to the measure of closeness of an association is the *linear regression*, which gives the equation of the straight line that best describes how the dependent variable (y) increases (or decreases) with an increase in the independent (x) variable. The equation of the regression line takes the form y=a+bx, where a is the intercept, and b is the slope of the line. The values for a and b are calculated so as to minimise the sum of squared vertical distances of the points from the line, a method called the least squares fit. The slope b is the regression coefficient, and it has the same sign as the r value. With no correlation b equals zero, a situation orresponding to a horizontal regression line at a height equivalent to mean of y. As with the previously desribed correlation analysis, a t-test is subsequently used to test whether b differs significantly from zero.

Situations frequently arosed when the dependency of a variable (eg a test result) on several independent variables needed to be evaluated. The joint influence of the variables, taking account of possible correlations among them was investigated using *multivariate analysis* using the *General Linear Models (GLM)* procedure on the SAS Version 5 that included techniques which are similar to multiple regression. This was undertaken via the "main effects" model where the main effects were determined using the multi-way ANOVA procedure without considering any interaction effects. An example would be to determine the dependence of VA on variables such as age of patients and patient grouping.

In such a procedure available in the GLM, the CLASS

statement is used to specify the categorical variable (group) whereas "age" is categorised as a continuous variable. Sum of squares is calculated for the whole model (SSb) and for the error factor (SSe); the SSb is then broken down into component sum of squares for each effect (variable) in the model. Thus in the above example the SSb due to the regression of VA on variables "age" and "group" comprises the sum of squares explained by "age" plus the extra sum of squares due to "group" after allowing for "age". The analysis will show the significant effects of "age" and/or "group" even when one or the other is taken into account via the calculated F-ratios. Large F-ratios indicate more significance and these are identified by the respective p-values. Since the order of breaking down the combined SS into separate separate SS does not give the same component SS (because these variables are themselves correlated), there is a need for the calculation of two SS namely Type I SS and Type III SS.

Type I SS is known as the sequential sum of squares and correspond to a partitioning of SS due to the individual coefficients as they are sequentially added to the model in the order given in the MODEL statement. In the example above "age" precedes "group", so the SS due to "age" does not consider the effects of "group". The SS due to "group" is over and above that contributed by "age".

Type III SS is the adjusted sum of squares; these SS are the contribution of each coefficient over and above that provided by all other coefficients in the model. In the above example, the type III SS for "age" is not necessarily the same as the type I SS because the type III SS is calculated after adjusting for the contribution of "group" in the model. For the variable "group" on the other hand, there is no difference in the two sum of squares because in both cases the contribution of "age" is considered since "group" is the last variable specified in the MODEL statement. The p-value for the type III SS of each variable is taken to indicate their significant contribution to the variation of the dependent variable (VA in the above

example).

Finally using the same GLM procedure *multiple regression* was carried out with all the independent variables (the effects) assigned as continuous variables ie. by removing the CLASS statement. Similar calculations of types I and III SS are done in the first part of the analysis. In addition the analysis also gives the partial regression coefficients for each of the independent variables included in the model (and an intercept value for the regression), together with their associated p-values. A regression equation thus results.

It is often desirable to include discrete/categorical as well as continuous independent variables in a multiple regression analysis. Some of these discrete variables may even have non-linear relationships with the dependent variable. The most versatile method is to define the variable into distinct subgroups and include it as a factor with a level corresponding to each subgroup (ie. by introducing a series of dummy variables). The relationship with the dependent variable will then be based on a comparison of the means of the dependent variable in each subgroup and would make no assumption about the exact form of relationship with the dependent variable. This results in an analysis which forces such variables to be considered linear. Thus as a result of this rather artificial analytical technique, in the presence of categorical variables only the direction of the regression coefficients (ie whether + or -) is given attention to for the purpose of determining the direction of association between the dependent variable and the independent variables (those which are identified as significant main effects on account of the magnitude of their respective F-ratios, as described previously).

CHAPTER 3

Study 1 Screening of Diabetic Retinopathy using Clinical Tests of Visual Function

3.1 INTRODUCTION

This chapter examines the use of clinical visual function tests for the screening of DR in a diabetic population. A battery of tests involving different visual functions i.e. visual acuity, colour vision, contrast sensitivity and central visual fields was used. The screening efficiency of each test and of different test batteries were evaluated using standard analysis of sensitivity and specificity ertz,1978). See appendix 3A for derivation of terms.

The Bayesian approach to decision making (Lusted,1971) was also employed following the suggestions by Aspinall and Hill (Aspinall & Hill,1983,1984a,1984b). With Bayes's theorem, the clinician can calculate the posterior prabability of a condition/disease by knowing the following (Sox et al.1989):

a. The prior probability of the disease/condition
b. The probability of a test result conditional upon the patient's having the disease/condition
c. The probability of the test result conditional upon the patient's not having the disease

In essence, when applying a clinical test, the probable presence of an abnormality when a patient failed the test (p(D/F)) and the probable absence of an abnormality when a patient passed the test (p(N/P)) were stated. See appendix 3B for derivation of terms. Clinical tests were regarded as means of making decisions in a state of uncertainty. Hill (1987a) further suggests that in order to state these two probabilities satisfactorily, two appropriately chosen cut-off fail criteria are needed rather than just the conventional single criterion; any performance between these two criteria represents uncertainty in either decision for normal or abnormal. This method of "double cut-off criteria" of Hill (1987a) was also employed in the analysis of the results.

Pinhole visual acuity (VA) test

Despite its relative inefficiency, VA measurement is still the simplest test for many clinicians to administer, and yields some useful information. The assessment of an individual's VA provides the single best index of his functional vision (Michaels,1985). The first section of this chapter examines the clinical utility of the pinhole test in screening a diabetic out-patient population for DR.

Colour vision tests

Simple tests of colour vision have been suggested as useful screening tools for use in a diabetic outpatients' clinic (Birch et al.1980; Birch et al.1987; Birch et al.1991). The selection of tests for screening diabetic patients for DR depends on the time available and the skill of the examiner. Amongst the clinical tests available, pseudoisochromatic (PIC) plates and arrangement tests are the most commonly used. PIC plate tests can be performed rapidly and are easily understood by patients in all age groups and from all social backgrounds. Arrangement tests, on the other hand, are more sophisticated and require a little more skill, but are also preferred screening tests.

The second section of this chapter examines the clinical utility of colour vision tests in screening diabetic patients for DR. A battery of colour vision tests, consisting of a selection of PIC plates designed for the detection of red-green and tritan colour vision defects, and the panel D15 Desaturated (5/2) test.

Contrast sensitivity (CS) tests

The use of CS tests as screening tools is somewhat controversial (Legge & Rubin,1986; Reeves & Hill,1987; Rubin,1988). However, there is likely to be a case for using CS measurements to screen diabetics (Cavarellano & Aiello,1990) as such patients have been reliably reported to have reduced CS. The simplicity of printed gratings

suggests that they could be used in a screening situation.

The third section of this chapter examines the clinical utility of two clinical CS tests (the Arden gratings and the Vistech VCTS 6000) in screening diabetic patients for DR.

Central visual field test

The visual fields of patients with diabetes and in particular those with DR have been well documented. To screen for DR and monitor a diabetic patient's progress, the Amsler grid can be used in conjunction with VA, colour vision and CS (Adams & Haegerstrom-Portnoy,1987; Birch et al.1980; Cavallerano & Aiello,1990)

About 9% of diabetics have macular oedema (Klein et.al.1984b); this may be demonstrated with the Amsler grid (Birch et al.1991). Screening the central fields should prove useful for detecting diabetics with macular problems which escape detection with the conventional VA test. The fourth section of this chapter examines the clinical utility of the Amsler grid in screening diabetic patients for DR.

Combination of test information

The tests described above vary in their ability to isolate individuals with DR. The final section of this chapter examines the clinical utility of the tests when used in a battery.

3.2 PATIENTS and PROCEDURES

Patients attending diabetic outpatients' clinics at the Middlesex and Whittington Hospitals in London were examined. Although these patients did not represent a random selection of diabetics at large, nevertheless they were selected at random while waiting to be seen by a diabetic physician for medical review.

463 patients (878 eyes) were seen, ranging in age from 16 to 85 years (mean 56.1 sd 15.2 years). There were 269 males and 194 females. The duration of diabetes in these patients ranged from 1 to 67 years (mean 11.1 sd 10.7 years). 239 patients were taking insulin, the rest were on a diet or tablets for the management of their diabetes. The age distribution of these patients is shown in fig 3.1.

Pinhole VA measurement using a 1mm diameter pinhole was made at 6 meters with the patient wearing his habitual correction. Two charts were used at the two venues; test conditions complied with British Standard for measuring VA (British Standard,1968).

Colour vision was examined with 3 clinical tests. All patients completed tests 1 and 2, and 163 patients (at Middlesex Hospital only) completed test 3. The tests were:

1) Comp PIC (excluding plate 16)
2) LTA plate 5
3) D15 (5/2)

CS measurements were made with two clinical tests. 163 patients (at Middlesex Hospital) completed the Arden gratings and 300 (at Whittington Hospital) completed the VCTS 6000. All 463 patients were examined with the Amsler grid.

The level of illuminance was 350 Lux at Middlesex Hospital and 550 Lux at Whittington Hospital. Illumination was provided by fluorescent tubes (Osram 65/80w,8000K) supplemented by natural daylight from a north facing window. The examination rooms at both venues had pastel coloured walls which had minimal reflections and were similar in size. Patients were appropriately corrected for the test distance.

SEE CHAPTER 2 FOR DETAILS OF THE TESTS USED

Visual function tests were performed by the author.

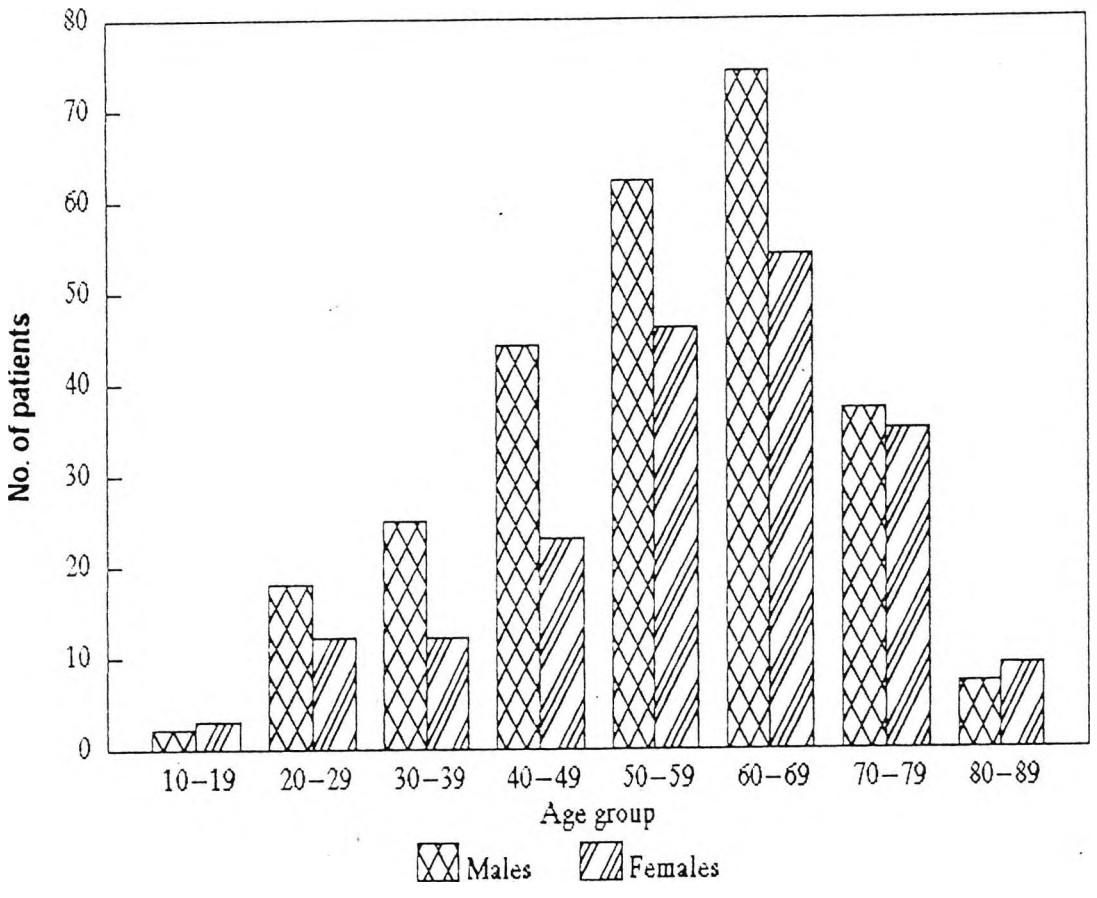


Fig 3.1 Age distribution of patients in Study 1 (N=463)

Patients who had obvious language difficulties, mobility problems, or visual acuity of less than 6/12 were excluded. Direct ophthalmoscopy was subsequently performed independently by the physician after the patient's pupil had been dilated with tropicamide 1%. The state of the fundus was categorised as having no visible DR and with visible DR. Other presenting ocular complications (cataracts, glaucoma, macular degeneration, laser therapy etc) were also noted during the physical examination by the physician. The study was thus a double-masked investigation, in this context meaning the author did not have any knowledge of the physician's results at the time of examination and neither did the physician any knowledge of the author's results.

Patients examined were divided into 4 diagnostic groups (profiles are shown in table 3.1):

1. No Diabetic Retinopathy
2. No Diabetic Retinopathy but with other complications
3. With Diabetic Retinopathy only
4. With DR and other complications

Group 3 (with DR) was sub-divided into 4 categories: Minimal DR (41 patients), Moderate DR (40 patients), Proliferative DR (8 patients) and Maculopathy (7 patients). Minimal DR represented a stage characterised by the presence of isolated and dispersed early vascular lesions such as a few microaneurysms and/or small hard exudates in the retinal periphery or at the posterior pole. Moderate DR was defined as a stage that included the presence of more extensive microaneurysms, confluents of hard exudates and dot/blot haemorrhages. Also included were the presence of deep haemorrhages, soft exudates, venous beeding and intra-retinal microvascular abnormalities short of frank neovascularisation.

Table 3.2 shows the complications which were found in the 116 patients of groups 2 and 4.

Only results from the first examined eye are included in the present analysis because of the high correlation between the two eyes of an individual (Ray & O'Day,1985). Results are expressed as means and sd values. The data was analysed on the IBM mainframe using the SAS statistical package (SAS Software Version 5 edition). Statistical tests carried out included one-way ANOVA (followed by Scheffe's test), student's t-test, Chi-Square test and multivariate analysis (using the GLM procedure). In all the statistical tests a probability (p value) of less than 0.05 was taken as being significant.

In the multivariate analysis using the GLM procedure LogMAR VA was assigned as the dependent variable in the determination of significant contributors of VA performance. Independent variables included in the model were: Venue, diagnostic group, age, duration of diabetes and insulin therapy. The same model was used in the determination of other tests performances, but with LogMAR VA added as one of the independent variables. Venue, diagnostic group, insulin therapy were assigned as categorical variables whereas age, duration of diabetes (and LogMAR VA) were assigned as continuous variables. Having identified the significant contributors of a particular test's performance, the direction of effect of each contributor was determined by the sign of the regression coefficients which were obtained subsequently by multiple regression.

Test characteristics-Sensitivity, specificity and the predictive values of a test (and test battery) result were calculated over a range of cut-offs. The accuracy of each test of visual function (and test battery) was compared by use of Receiver Operating Characteristic (ROC) curves, in which sensitivity was plotted against (1-Specificity).

Profile	Group			
	1 No DR	2 No DR+C	3 DR	4 DR+C
No	251	70	96	46
Mean age	53.6 sd 14.7	65.2 sd 13.8	54.0 sd 15.5	60.3 sd 13.2
Mean duration of diabetes	7.6 sd 8.3	12.4 sd 12.6	15.9 sd 10.4	17.9 sd 12.1
No. on Insulin	135 (54%)	20 (29%)	60 (62%)	24 (52%)

DR=Diabetic Retinopathy; C=Complications

Table 3.1 Patient profile for Study 1

Complications	No.
Cataract	42
Laser treatment for Diabetic Retinopathy	27
Glaucoma	8
Aphakia	5
Drusen with age-related maculopathy	6
Congenital Colour Vision Deficiency	6
Parietal ischaemia/stroke	5
Hypertensive Retinopathy	5
Cataract and age-related maculopathy	4
Intraocular lens	3
Multiple Sclerosis	1
Glaucoma and cataract	2
Cataract and congenital Colour Vision Deficiency	1
Graves Ophthalmopathy	1
Total	116

Table 3.2 Other ocular complications present in patients examined

3.3 RESULTS

3.3.1 Test performance

3.3.1a Visual acuity (VA)

Table 3.3 shows the mean VA of the four groups (total number of patients = 463). Significant differences were found across the four groups of patients (ANOVA $F(3,459)=20.32$, $p<0.05$). Significance of differences between groups is summarised in table 3.4. Patients with complications (groups 2 or 4) had significantly lower VA than those without complications (groups 1 or 3), Patients with DR but no complications (group 3) were not statistically different from patients free of visible pathology (group 1). There was no significant difference in VA between those with complications (i.e. group 2 vs group 4) and there was also no significant difference between those with DR (group 3) and those without DR (group 1). A sub-analysis showed no significant differences in the mean VAs between the different categories of DR (within group 3), although this could be due to the small number of patients in the groups with proliferative DR and maculopathy.

Multivariate analysis revealed age ($F=52.0$), "diagnostic group" ($F=10.2$) and insulin therapy ($F=10.4$) as significant determinants of the level of VA. There was a low but significant correlation between VA and Age for all the patients in the sample ($r=0.34$, $p<0.05$). Duration of diabetes and venue were not found to have any significant influence on VA.

The results of an extended analysis on patients with *type I diabetics* only (N=204) are shown in table 3.3a. Comparison between the mean VA of patients with DR only (group 3) and those without DR (group 1) showed no statistically significant difference by Scheffe's test although across the 4 groups ANOVA showed marginally significant differences between the mean VAs ($F(3,200)=4.15$, $p=0.0068$).

The numbers in parentheses show the results obtained with 10 patients from the group with DR and complications (group 4) relocated to group 3. The mean VAs of patients from groups 1 and 2 were still statistically not significantly different although across the 4 groups ANOVA showed significant differences between the mean VAs ($F(3,200)=5.38$, $p=0.0014$).

3.3.1b Colour Vision

1. Comp PIC

Table 3.5 shows the mean results obtained by the 4 groups of patients for 3 measures of performance on this test (total number of patients = 463). There was a significant difference in the mean total number of plate errors among the 4 groups of patients (ANOVA, $F(3,459)=53.45, p<0.05$). Table 3.6 summarises the significance of differences between groups. Patients with DR and complications (group 4) made significantly more errors than the other 3 groups. Patients with DR (group 3) and those without DR but with complications (group 2) were not significantly different, but both groups had significantly more errors than those without DR (group 1). Although both diabetes and DR affect colour vision the relative change in red-green to tritan errors from the No DR (group 1) to the DR alone (group 3) is indicative of an additional impairment to the blue-yellow system as DR sets in. The results also show that the presence of DR or other complications increases the tendency towards an error (any error) on the Comp PIC.

Figures 3.2, 3.3, 3.4 and 3.5 show the number of patients in each diagnostic group failing the individual plates. Fig 3.2 shows that plates 5,6 and 8 from the Ishihara series were likely to be failed by normal patients (group 1). For the other groups (figs 3.3,3.4 and 3.5) all the Ishihara plates were equally likely to be failed, with plates 6,7 and 8 being the most likely ones. Tritan plates 12,13 and 14 were the most frequently failed ones in all patient groups, although the the proportion of patients from each

Group	Mean VA (LogMAR)
1. No DR	0.01 sd 0.11
2. No DR+C	0.11 sd 0.13
3. DR	0.04 sd 0.13
4. DR+C	0.11 sd 0.14

DR=Diabetic retinopathy; C=Complications

Table 3.3 Mean VA per patient

	No DR+C	DR	DR+C
No DR	p<0.05	NS	p<0.05
No DR+C		p<0.05	NS
DR			p<0.05

DR=Diabetic Retinopathy; C=Complications

Table 3.4 Significance of differences in mean VAs between groups

Group	Mean VA (LogMAR)
1. No DR (n=101)	0.03 sd 0.13
2. No DR+C (n=20)	0.10 sd 0.15
3. DR (n=59)	0.02 sd 0.13 (0.03 sd 0.13)+
4. DR+C (n=24)	0.10 sd 0.10 (0.14 sd 0.12)+

DR=Diabetic retinopathy; C=Complications

Table 3.3a Mean VA per patient *for type I patients only N=204*

+ VA in parentheses represent the mean results of patients in groups 3 & 4 after ten patients who had been lasered before were relocated from group 4 to group 3

Group	Total	Red-green	Tritan
1. No DR	0.3 sd 0.9	0.02 sd 0.20	0.3 sd 0.8
2. No DR+C	2.4 sd 2.6	0.5 sd 1.6	1.9 sd 2.1
3. DR	1.8 sd 2.6	0.2 sd 1.0	1.6 sd 2.1
4. DR+C	3.7 sd 3.3	0.6 sd 1.6	3.2 sd 2.4
NORMALS#	0.03 sd 0.16	0	0.05 sd 0.23

DR=Diabetic retinopathy; C=Complications

Normal results were obtained on 37 clinically normal subjects (VA range: 6/5-6/12, Age range: 26-77) under the same conditions.

Table 3.5 Mean number of Comp PIC plate errors per patient

Group	Total	Red-green	Tritan
1. No DR (n=101)	0.2 sd 0.7	0.03 sd 0.22	0.2 sd 0.65
2. No DR+C (n=20)	2.3 sd 1.8	0.3 sd 1.1	2.1 sd 1.8
3. DR (n=59)	1.7 sd 2.6	0.2 sd 0.9 (0.2 sd 0.8)	1.5 sd 2.0 (2.0 sd 2.3)+
4. DR+C (n=24)	3.1 sd 2.6	0.3 sd 0.8 (0.4 sd 0.9)	2.8 sd 2.3 (2.6 sd 2.4)+

DR=Diabetic retinopathy; C=Complications

Table 3.5a Mean number of Comp PIC plate errors per patient *for type I patients only N=204*

+ Numbers in parentheses represent the mean results of patients in groups 3 & 4 after ten patients who had been lasered before were relocated from group 4 to group 3

	No DR+C	DR	DR+C
No DR	p<0.05	p<0.05	p<0.05
No DR+C		NS	p<0.05
DR			p<0.05

DR=Diabetic Retinopathy; C=Complications

Table 3.6 Significance of differences in mean errors between groups: Comp PIC total plate errors

	No DR+C	DR	DR+C
No DR	p<0.05	NS	p<0.05
No DR+C		NS	p<0.05
DR			p<0.05

DR=Diabetic Retinopathy; C=Complications

Table 3.7 Significance of differences in mean errors between groups: Comp PIC red-green plate errors

	No DR+C	DR	DR+C
No DR	p<0.05	p<0.05	p<0.05
No DR+C		NS	p<0.05
DR			p<0.05

DR=Diabetic Retinopathy; C=Complications

Table 3.8 Significance of differences in mean errors between groups: Comp PIC tritan plate errors

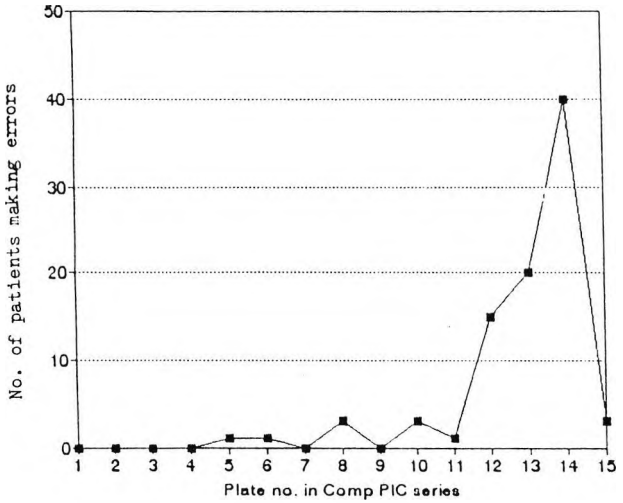


Fig 3.2 Errors made on Comp PIC: No DR group (n=251)

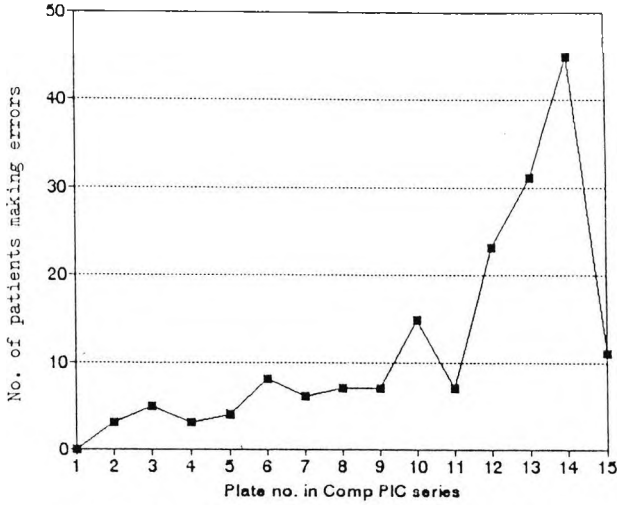


Fig 3.3 Errors made on Comp PIC: No DR+C group (n=70)

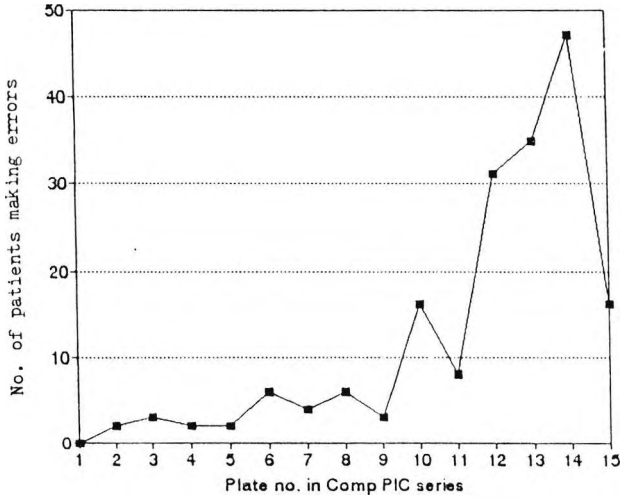


Fig 3.4 Errors made on Comp PIC: DR group (n=96)

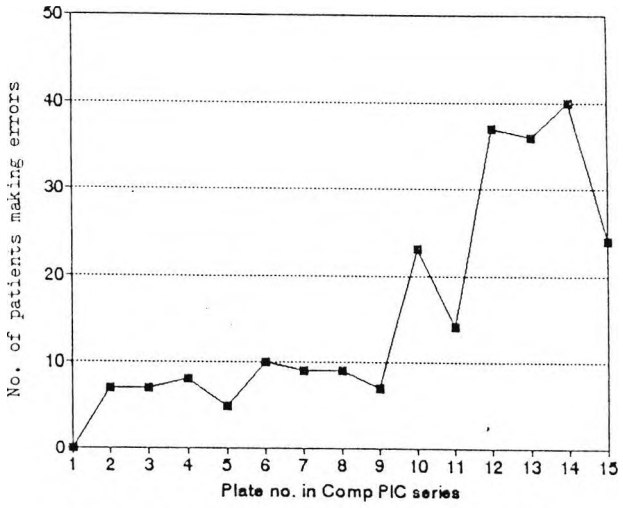


Fig 3.5 Errors made on Comp PIC: DR+C group. (n=46)

group failing these plates were different. Plate 10 seemed to be mainly failed by patients with some sort of ocular complication (groups 2,3 and 4). It was not failed significantly by patients without DR or complication (group 1).

In fig 3.6 Venn diagrams show the number of patients in each group making different types of errors on the Comp PIC. There were very few patients who made sole red-green plate errors. These were: 1 from the group without DR (group 1), 3 from the group without DR with complications (group 2) and none from the other two groups (groups 3 and 4). The 3 patients from group 2 were those with congenital colour vision deficiency (ie. out of 7 who had congenital colour vision deficiency in this group- see table 3.2). It can be seen that most patients made tritan plate errors and there was a tendency for patients to make errors on both red-green and tritan plates in patients with a complication, be it DR or otherwise.

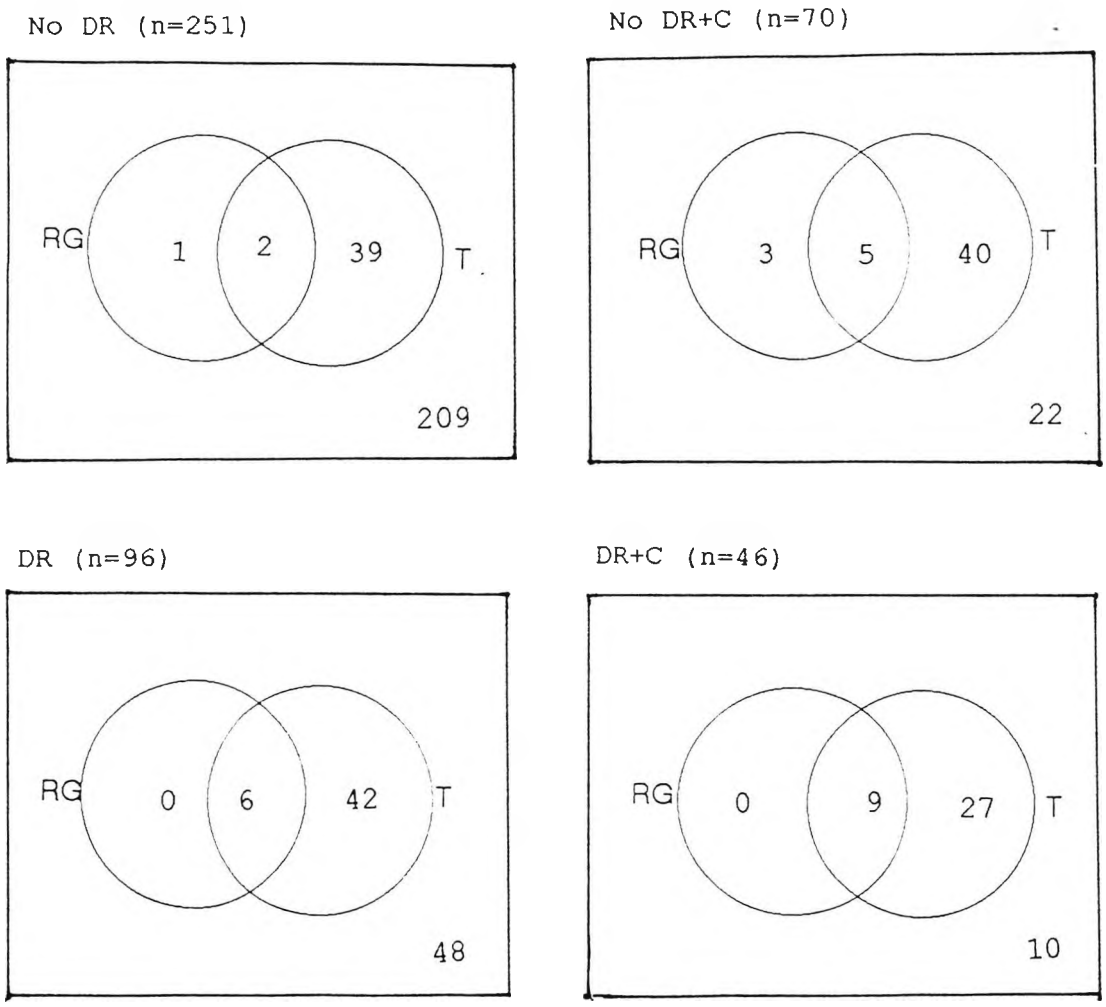
Significant differences were found in the mean number of red-green (Ishihara) plate errors across the 4 groups of patients (ANOVA, $F(3.459)=15.20, p<0.05$). Table 3.7 summarises the significance of the differences between the groups. Patients with DR and complications (group 4) had significantly more errors than the rest of the patients. Patients without DR but with complications (group 2) made significantly more errors than patients without DR (group 1), but did not differ significantly from those with DR (group 3). The mean red-green plate errors of patients with DR (group 3) was, however, not significantly different from those without DR (group 1). The results show that the presence of a complication other than DR contributes to red-green plate errors. This is expected in those with a congenital colour vision deficiency; however, those with DR and other complications are also more prone to making errors on these plates.

There was a significant difference in the number of tritan plate errors made by the 4 groups of patients (ANOVA

$F(3,459)=64.94, p<0.05$). Significance of differences between groups in the mean number of errors is shown in table 3.8. The pattern of significance resembles that of total plate errors. Patients with DR and complications (group 4) made significantly more errors than did the rest of the patients. Patients without DR (group 1) made significantly fewer errors than those with DR or those without DR with complications (groups 2 and 3). There was no statistically significant difference in the number of errors between those with DR (group 3) and those without DR but with complications (group 2). Both the presence of DR and other complications contribute to the observed increased in the number of tritan plate errors.

The results of an extended analysis on patients with *type I diabetics* only (N=204) are shown in table 3.5a. ANOVA showed a statistically significant difference across the 4 groups in the mean total number of plate errors ($F(3,200)=22.9$, $p<0.05$) and number of tritan plate errors ($F(3,200)=26.1$, $p<0.05$). No significant differences were found in the mean number of red-green plate errors (ANOVA, $F(3,200)=1.76$, $p>0.05$). As with the previous analysis on all the patients (main analysis of both types I and II patients mixed together) the mean total number of plate errors and the mean number of tritan plate errors of patients with DR only (group 3) was significantly more than those of patients without DR (group 1). The non significance of results between the same two groups in the total number of red-green plate errors was also shown earlier in the main analysis where both types I and II patients were mixed together.

The numbers in parentheses show the results obtained with 10 patients from the group with DR and complications (group 4) relocated to group 3. As above, statistically significant differences were only found between groups 1 and 3 in the mean total number of plate errors (ANOVA, $F(3,200)=19.0$, $p<0.05$) and number of tritan plate errors (ANOVA, $F(3,200)=20.9$, $p<0.05$).



RG=Red-green plate errors
T =Tritan plate errors

Fig 3.6 Venn diagrams demonstrating the number of patients making RG and T on the Comp PIC

2. LTA plate 5

Table 3.9 shows the number (%) of patients failing this plate in the 4 groups of patients (total number of patients = 463). The rates of failure in the groups were significantly different (Chi-Sq=56.02,dF=3,p<0.05). A significantly greater number of patients with DR and complications (group 4) failed this test compared to all the other groups. Although the number of patients with DR (group 3) and those without DR but with complications (group 2) failing the test were not significantly different, both groups had significantly more patients failing than those without DR (group 1).

The results of an extended analysis on patients with *type I diabetics* only (N=204) are shown in table 3.9a. As with the previous analysis on all the patients (main analysis of both types I and II patients mixed together) the number (proportion) of patients with DR only (group 3) who failed the plate was significantly more than the proportion of patients without DR (group 1) (Chi-Sq=28.2,dF=3,p<0.05).

The numbers in parentheses show the results obtained with 10 patients from the group with DR and complications (group 4) relocated to group 3. As above, the proportion of patients in group 3 failing the plate was significantly more than the proportion of patients in group 1 who failed it (Chi-Sq=17.8,dF=3,p<0.05).

3. D15 (5/2)

Table 3.10 shows the mean results obtained by the 4 groups of patients for 3 measures of performance on this test. The total number of patients were only 163 in this case ie. only those patients at Middlesex Hospital. Significant differences occurred in the scores obtained by the 4 groups (ANOVA, F(3,159)=6.82,p<0.05). Table 3.11 summarises the significance of the differences in the scores between groups. Patients with DR and complications (group 4) had a significantly higher mean score than patients with no DR

(group 1); their scores were, however, not significantly different from those without DR but with complications (group 2) and those with DR alone (group 3). Patients without DR but with complications (group 2) had a significantly higher mean score than those without DR (group 1) but were not significantly different from those with DR (group 3) and those with DR and complications (group 4). Patients with DR (group 3) were also not significantly different from all the other groups in their mean scores, indicating that the presence of DR did not seem to have much influence on the error scores. Other ocular complications, when present, tended to make the scores higher (worse).

In fig 3.7 Venn diagrams show the different diagnostic axes made. There were very few patients who had solely red-green axes: 1 from the group without DR (group 1), 1 from the group without DR with complications (group 2) and 3 from the other two groups (groups 3 and 4). The 1 patient from group 2 was a patient with congenital colour vision deficiency. Very few also had mixed axes, most patients who had an axis tended to have tritan axes.

ANOVA showed only a marginal difference in the mean number of red-green axes obtained by the 4 groups of patients ($F(3,159)=3.39, p<0.05$); post-hoc Scheffe's test failed to reveal any significant differences between individual groups.

Significant differences were found between the 4 groups in the mean number of tritan axes (table 3.12) (ANOVA $F(3,159)=14.76, p<0.05$). Patients with DR and complications (group 4) had significantly more tritan axes when compared to the other groups. Patients with no DR (group 1), patients without DR but with complications (group 2) and patients with DR (group 3) had mean numbers of tritan axes which were not significantly different. A meaningful number of tritan axes was present only in patients with severe pathology i.e. when both DR and complications were present.

Group	No. (%) failing
1. No DR	11 (4.4%)
2. No DR+C	16 (22.9%)
3. DR	13 (13.5%)
4. DR+C	19 (41.3%)
NORMALS#	0 (0%)

DR=Diabetic retinopathy; C=Complications

Normal results were obtained on 37 clinically normal subjects range: 6/5-6/12. Age range: 26-77) under the same conditions.

Table 3.9 Number (%) of patients failing LTA plate 5

Group	No. (%) failing
1. No DR (n=101)	3 (3%)
2. No DR+C (n=20)	6 (30%)
3. DR (n=59)	7 (11.9%) (13/18.8%)+
4. DR+C (n=24)	9 (37.5%) (3/21%)+

DR=Diabetic retinopathy; C=Complications

Table 3.9a Number (%) of patients failing LTA plate 5 *for type I patients only N=204*

+ Numbers in parentheses represent the results of patients in groups 3 & 4 after ten patients who had been lasered before were relocated from group 4 to group 3

Group	Score	No of red-green axis	No of tritan axis
1. No DR (n=70)	8.2 sd 8.3	0.0 sd 0.2	0.3 sd 0.6
2. No DR+C (n=29)	19.7 sd 21.8	0.7 sd 1.9	0.8 sd 0.9
3. DR (n=45)	10.9 sd 11.4	0.2 sd 0.9	0.4 sd 0.7
4. DR+C (n=19)	20.1 sd 20.3	0.3 sd 1.4	1.7 sd 1.9
NORMALS#	5.6 sd 6.6	0	0.2 sd 0.6

DR=Diabetic retinopathy; C=Complications

Normal results were obtained on 37 clinically normal subjects (VA range: 6/5-6/12, Age range: 26-77) under the same conditions.

Table 3.10 Mean D15(5/2) results per patient

Group	Score	No of red-green axis	No of tritan axis
1. No DR (n=35)	4.7 sd 5.3	0	0.1 sd 0.3
2. No DR+C (n=11)	19.1 sd 23.6	0.6 sd 2.1	0.6 sd 0.9
3. DR (n=33)	10.6 sd 12.7 (11.6 sd 12.6)+	0.2 sd 1.1 (0.2 sd 0.9)+	0.3 sd 0.8 (0.5 sd 1.1)+
4. DR+C (n=13)	13.1 sd 11.9 (9.4 sd 11.5)+	0 (0)+	1.1 sd 1.5 (0.6 sd 0.9)+

DR=Diabetic retinopathy; C=Complications

Table 3.10a Mean D15(5/2) results per patient *for type I patients only N=92 who were examined at Middlesex Hospital*

+ Numbers in parentheses represent the mean results of patients in groups 3 & 4 after six patients who had been lasered before were relocated from group 4 to group 3

	No DR+C	DR	DR+C
No DR	p<0.05	NS	p<0.05
No DR+C		NS	NS
DR			P<0.05

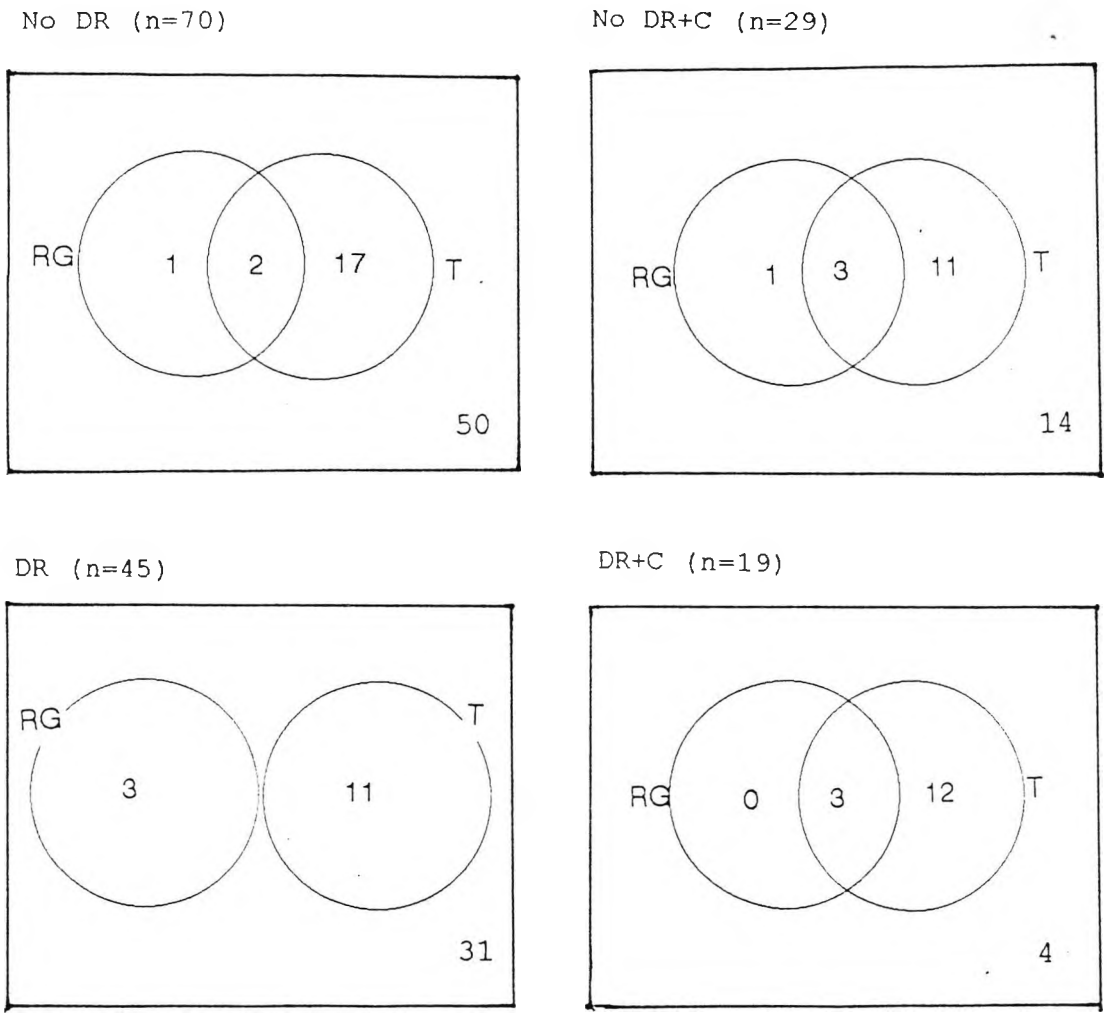
DR=Diabetic Retinopathy; C=Complications

Table 3.11 Significance of differences in mean scores between groups: D15(5/2)

	No DR+C	DR	DR+C
No DR	NS	NS	p<0.05
No DR+C		NS	p<0.05
DR			p<0.05

DR=Diabetic Retinopathy; C=Complications

Table 3.12 Significance of differences between groups: Number of D15(5/2) tritan axes



RG=Red-green axes
T =Tritan axes

Fig 3.7 Venn diagrams demonstrating the number of patients showing RG and T on the D15(5/2)

(Patients at Middlesex Hospital only, n=163)

The results of an extended analysis on patients with *type I diabetics* only (N=92 ie. patients at Middlesex Hospital) are shown in table 3.10a. ANOVA showed a statistically significant difference across the 4 groups in the mean score ($F(3,88)=4.4$, $p<0.05$) and number of tritan axis ($F(3,88)=4.7$, $p<0.05$). No significant differences were found in the mean number of red-green axis (ANOVA, $F(3,88)=1.4$, $p>0.05$). As with the previous main analysis of both types I and II patients mixed together, none of these test measures were significantly different between the No DR group (group 1) and the DR alone group (group 3).

The numbers in parentheses show the results obtained with six patients from the group with DR and complications (group 4) relocated to group 3. As above, statistically significant differences were not found between groups 1 and 3 in all of the test measures of the D15(5/2) test, although across the four groups ANOVA showed significant differences in the mean scores of the four groups of patients ($F(3,88)=4.3$, $p>0.05$).

Table 3.13 summarises the correlations between the colour vision test results and patient variables. "Diagnostic group" correlated with all of the test results except the number of red-green axes on the D15(5/2). Age correlated with the tritan plate errors on the Comp PIC. Venue correlated with tritan plate errors (Comp PIC) and LTA plate 5. Insulin therapy affected the performance of D15(5/2), being significant determinants of both the score and the number of tritan axes, but not the red-green axes. VA correlated with all the test results.

3.3.1c Contrast sensitivity

1. Arden gratings

Table 3.14 shows the mean results of the 4 groups of patients. The total number of patients were only 163 in this case ie. only those patients at Middlesex Hospital. There was a significant difference in the total scores

among the 4 groups of patients (ANOVA, $F(3,159)=4.80, p<0.05$). Table 3.15 summarises the significance of differences between the 4 groups.

Significance in the differences between total mean scores was only found between patients without DR but with complications (group 2) and those without DR (group 1). There was a large spread in the results thus obscuring any other differences between the patient groups. The presence of DR alone was not associated with any significant increase in the mean total scores. On the other hand the presence of other complications, with or without DR, contributed to the increase in scores.

The results of an extended analysis on patients with *type I diabetics* only (N=92 ie. patients at Middlesex Hospital) are shown in table 3.14a. ANOVA showed no statistically significant difference across the 4 groups in the mean total score ($F(3,88)=1.6$, $p>0.05$). As with the previous main analysis of both types I and II patients mixed together, the mean total scores of the No DR group (group 1) and the DR alone group (group 3) were not significantly different.

The numbers in parentheses show the results obtained with six patients from the group with DR and complications (group 4) relocated to group 3. As above, statistically no significant differences were not found between groups 1 and 3 in the mean total scores ($F(3,88)=1.6$, $p>0.05$).

Appendix 3C shows the mean score for each plate of the Arden gratings for the 4 groups of patients. Significant differences existed (ANOVA $F(3,159)=5.74, p<0.05$) between the 4 groups in the scores obtained for plates 3,4 and 5 (ANOVA $F(3,159)=5.74$, 5.31, 6.30; $p<0.05$ for plates 2,3 and 4 respectively). Only marginally significant differences were found in the scores of plates 2,6 and 7 (Appendices 3D,3E and 3F).

Multivariate analysis revealed age and VA to be

Test	Patient variable					
	Venue	Diagnostic Group	Age	Duration of diabetes	Insulin therapy	VA
Comp PIC						
TPE	7.5	30.5	3.6	-	-	25.5
RGE error	-	5.2	-	-	-	4.5
T error	6.9	32.0	7.9	-	-	25.6
LTA plate 5	12.1	9.2	-	-	-	17.5
D15(5/2)						
Score	NA	4.8	-	-	4.5	6.5
RG axis	NA	-	-	-	-	5.1
T axis	NA	11.5	-	-	6.0	5.9

NA=Not applicable; -=NS; TPE=Total plate error; RG=Red-green; T=Tritan

Table 3.13 F-values for significant correlations between colour vision test results and patient variables

Group	Mean total score
1. No DR (n=70)	80.7 sd 17.0
2. No DR+C (n=29)	92.6 sd 18.5
3. DR (n=45)	81.3 sd 18.4
4. DR+C (n=19)	93.6 sd 16.2
NORMALS#	73.9 sd 7.3

DR=Diabetic retinopathy; C=Complications

Normal results were obtained on 37 clinically normal subjects (VA range: 6/5-6/12, Age range: 26-77) under the same conditions.

Table 3.14 Mean total score per patient: Arden gratings

Group	Mean total score
1. No DR (n=35)	76.6 sd 17.1
2. No DR+C (n=11)	90.2 sd 23.7
3. DR (n=33)	79.6 sd 19.4 (79.6 sd 18.3)+
4. DR-C (n=13)	82.6 sd 16.9 (85.0 sd 22.6)+

DR=Diabetic retinopathy: C=Complications

Table 3.14a Mean total score per patient: Arden gratings *for type I patients only N=92 who were examined at Middlesex Hospital*

+ Numbers in parentheses represent the mean results of patients in groups 3 & 4 after six patients who had been lasered before were relocated from group 4 to group 3

	No DR+C	DR	DR+C
No DR	p<0.05	NS	NS
No DR+C		NS	NS
DR			NS

DR=Diabetic Retinopathy; C=Complications

Table 3.15 Significance of differences in mean total scores between groups: Arden gratings

Test	Patient variable				
	Diagnostic Group	Age	Duration of diabetes	Insulin therapy	VA
Arden gratings score					
Total	-	4.8	-	-	4.1
PL 2	-	4.2	-	-	-
PL 3	3.9	-	-	-	-
PL 4	2.9	-	-	-	-
PL 5	-	-	-	4.7	-
PL 6	-	-	-	-	17.9
PL 7	-	-	-	3.9	18.9
VCTS 6000 score					
Global	5.4	51.2	-	-	94.1
Sp/f A	6.9	11.9	-	-	27.3
Sp/f B	-	41.5	-	-	52.9
Sp/f C	3.9	33.3	-	-	58.9
Sp/f D	3.9	46.2	-	-	71.4
Sp/f E	3.7	31.4	-	-	62.4

-=NS; PL2-PL7=Plates 2 to 7; Sp/f A-Sp/f E=Spatial frequencies A to E

Table 3.16 F-values for significant correlations between contrast sensitivity test results and patient variables

significantly correlated with the total score on the Arden gratings (table 3.16). The age factor was reflected mainly in the performance on plate 2 whereas the VA factor in plates 6 and 7.

2. VCTS 6000

Table 3.17 shows the mean global scores of the 4 groups of patients. The total number of patients were 300 in this case ie. those patients seen at Whittington Hospital. ANOVA revealed statistically significant differences across the 4 groups of patients ($F(3,296)=26.34, p<0.05$). Table 3.18 summarises the significance of differences between groups. Patients with DR alone (group 3) had global scores which were significantly worse (lower) than those without DR (group 1) but were not significantly different from those without DR but with complications (group 2). Patients with DR and complications (group 4) were significantly worse than those with DR alone (group 3) but were not significantly different from those without DR but with complications (group 2).

The results of an extended analysis on patients with *type I diabetics* only (N=112 ie. patients at Whittington Hospital) are shown in table 3.17a. ANOVA showed statistically significant difference across the 4 groups in the mean global score ($F(3,108)=8.9$, $p<0.05$). Unlike the main analysis of both types I and II patients mixed together where the mean global score of the No DR group (group 1) was significantly more than the DR alone group (group 3), the two mean scores were now not significantly different from each other although there were significant differences across the 4 groups (ANOVA, $F(3,108)=8.9, p<0.05$).

Relocating four patients from the group with DR and complications (group 4) to group 3 did not make any difference (numbers in parentheses); the two groups were still not significantly different from each other in their mean global scores even though ANOVA showed significantly different scores across the 4 groups ($F(3,108)=8.0, p<0.05$).

Appendix 3G shows the mean score for each spatial frequency of the VCTS 6000 test. Significant differences existed among the 4 groups. All spatial frequencies recorded significant differences in the scores between patients without DR and those with DR alone. The presence of complications alone tended to make the scores lower. The degradation of CS (on this test) by such complications, however, are not necessarily always more than that caused by DR. See appendices 3H to 3L.

Multivariate analysis revealed "diagnostic group", age and VA to be correlated with the global score on the VCTS 6000 (table 3.16). This also applied to all spatial frequencies, apart from spatial frequency B, where "diagnostic group" did not seem to affect its performance.

3.3.1d Visual field

Table 3.19 compares the number (%) of failures in the 4 groups of patients (total number of patients = 463). The proportions of failures among the 4 groups of patients were significantly different (Chi-Sq=63.68,dF=3,$p<0.05$). Table 3.20 summarises the significance of differences between the 4 groups in the percentages of failures.

A significantly greater number of patients with DR and complications (group 4) failed the test compared to all other groups. The number of patients with DR (group 3) failing the test was significantly different from those without DR (group 1) but was not significantly different from those without DR but with complications (group 2). The number of patients without DR but with complications (group 2) failing were not significantly different from those without DR (group 1).

The presence of other complications contributed significantly to failure on the test. More patients with DR (group 3) failed the test, but the number of failures was not significantly different from those without DR but with complications (group 2).

Group	Mean global score
1. No DR (n=181)	22.7 sd 4.7
2. No DR+C (n=41)	16.9 sd 5.27
3. DR (n=51)	19.6 sd 5.1
4. DR+C (n=27)	16.2 sd 5.5
NORMALS#	28.0 sd 4.4

DR=Diabetic retinopathy; C=Complications

Normal results were obtained on 37 clinically normal subjects (VA range: 6/5-6/12, Age range: 26-77) under the same conditions.

Table 3.17 Mean global score per patient: VCTS 6000

	No DR+C	DR	DR+C
No DR	p<0.05	p<0.05	p<0.05
No DR+C		NS	NS
DR			p<0.05

DR=Diabetic Retinopathy; C=Complications

Table 3.18 Significance of differences in mean global scores between groups: VCTS 6000

Group	Mean global score
1. No DR (n=66)	22.7 sd 5.2
2. No DR+C (n=9)	17.4 sd 6.2
3. DR (n=26)	20.8 sd 5.5 (20.2 sd 5.4)+
4. DR+C (n=19)	14.8 sd 3.5 (14.0 sd 4.1)+

Table 3.17a Mean global score per patient: VCTS 6000 *for type I patients only N=112 who were examined at Whittington Hospital*

+ Numbers in parentheses represent the mean results of patients in groups 3 & 4 after four patients who had been lasered before were relocated from group 4 to group 3

Group	No. (%) failing
1. No DR	4 (1.6%)
2. No DR+C	5 (7.1%)
3. DR	9 (9.4%)
4. DR+C	16 (34.8%)
NORMALS#	0 (0%)

DR=Diabetic retinopathy; C=Complications

Normal results were obtained on 37 clinically normal subjects (VA range: 6/5-6/12, Age range: 26-77) under the same conditions.

Table 3.19 Number (%) of patients failing the Amsler grid

	No DR+C	DR	DR+C
No DR	NS	p<0.05	p<0.05
No DR+C		NS	p<0.05
DR			p<0.05

DR=Diabetic Retinopathy; C=Complications

Table 3.20 Significance of differences in frequency of failing between groups: Amsler grid

Group	No. (%) failing
1. No DR (n=101)	1 (1%)
2. No DR+C (n=20)	1 (5%)
3. DR (n=59)	6 (10.2%) (13/18.8%)+
4. DR+C (n=24)	9 (37.5%) (2/14.3%)+

DR=Diabetic retinopathy; C=Complications

Table 3.19a Number (%) of patients failing the Amsler grid *for type I patients only N=204*

+ Numbers in parentheses represent the results of patients in groups 3 & 4 after ten patients who had been lasered before were relocated from group 4 to group 3

Multivariate analysis revealed failure on the test to correlate significantly with "diagnostic group" (F=17.1) only but not with venue, age, duration of diabetes, insulin therapy and VA.

The results of an extended analysis on patients with *type I diabetics* only (N=204) are shown in table 3.9a. As with the previous analysis on all the patients (main analysis of both types I and II patients mixed together) the number (proportion) of patients with DR only (group 3) who failed the grid was significantly more than the proportion of patients without DR (group 1) (Chi-Sq=34.4,dF=3,p<0.05).

The numbers in parentheses show the results obtained with 10 patients from the group with DR and complications (group 4) relocated to group 3. As above, the proportion of patients in group 3 failing the grid was significantly more than the proportion of patients in group 1 who failed it (Chi-Sq=18.0,dF=3,p<0.05).

3.3.2 Analysis of screening efficiency

The screening efficiency of all the tests in screening for DR was *primarily* analysed in the following section. However, since patients also presented with other ocular complications in addition to DR, the screening efficiency of all the tests was also analysed in their ability to discriminate between the group without DR (group 1) and the rest of the patients (all other groups combined). In the following discussion, the two situations will be constantly referred to.

Note that screening must be for a purpose and it is plausible that a population of diabetics could be screened for the presence of DR, and therefore it is of interest to analyse group 1 against group 3 ie. referred to as the first situation. Group I versus "the rest", as in the second situation is an attempt to define those with poor results (from various causes) from those who are free from DR. In the real world, group 2 is an awkward complication,

especially since the inclusions include congenital colour vision defects, drusen, cataract etc. The value of a screening test which deposits a large number of different patients in someone else's waiting room, when often they will only have trivial complaints can be argued. However, similar analyses have been undertaken by other authors eg. Corcoran et al.(1985) and Yap et al.(1985).

In determining the two cut-off criteria as suggested by Hill (1987a), often a range of maximum values of p(N/P) and p(D/F) was available. The maximum p(N/P) stated for each test was that associated with the "least possible" fail criterion. The maximum p(D/F) selected was that associated with "the most stringent" fail criterion possible. The prior probability of DR was taken as 0.30 (Aspinall & Hill,1983).

3.3.2a Visual acuity (VA)

Fig 3.8 shows the VA distribution in the four groups of patients (total number of patients = 463). In the first situation 119 normals (47%) had a VA of 6/5 vs 36 patients with DR (37%). Table 3.21 shows the screening parameters in the first situation and fig 3.9 is the associated ROC curve. The minimum rate of misclassification between false positives and false negatives was achieved with a VA cut-off of 6/5 which gave a sensitivity of 0.63 and a specificity of 0.47. The associated p(N/P) and p(D/F) values were 0.75 and 0.34, respectively. The highest value of p(N/P) obtained was 0.75, i.e. for a VA cut-off of 6/5. The highest value of p(D/F) obtained was 0.52 i.e. with a VA cut-off of 6/9. These two cut-off criteria represent the maximum confidence limits for decisions of normal given a pass and decisions of DR given a fail, respectively. Note that the sample of patients here was not a totally unbiased one because the exclusion procedure eliminated those with VAs of less than 6/12. Thus any estimate of sensitivity and specificity based on VA<6/9 has to be taken with caution.

Table 3.21a shows the screening figures which were

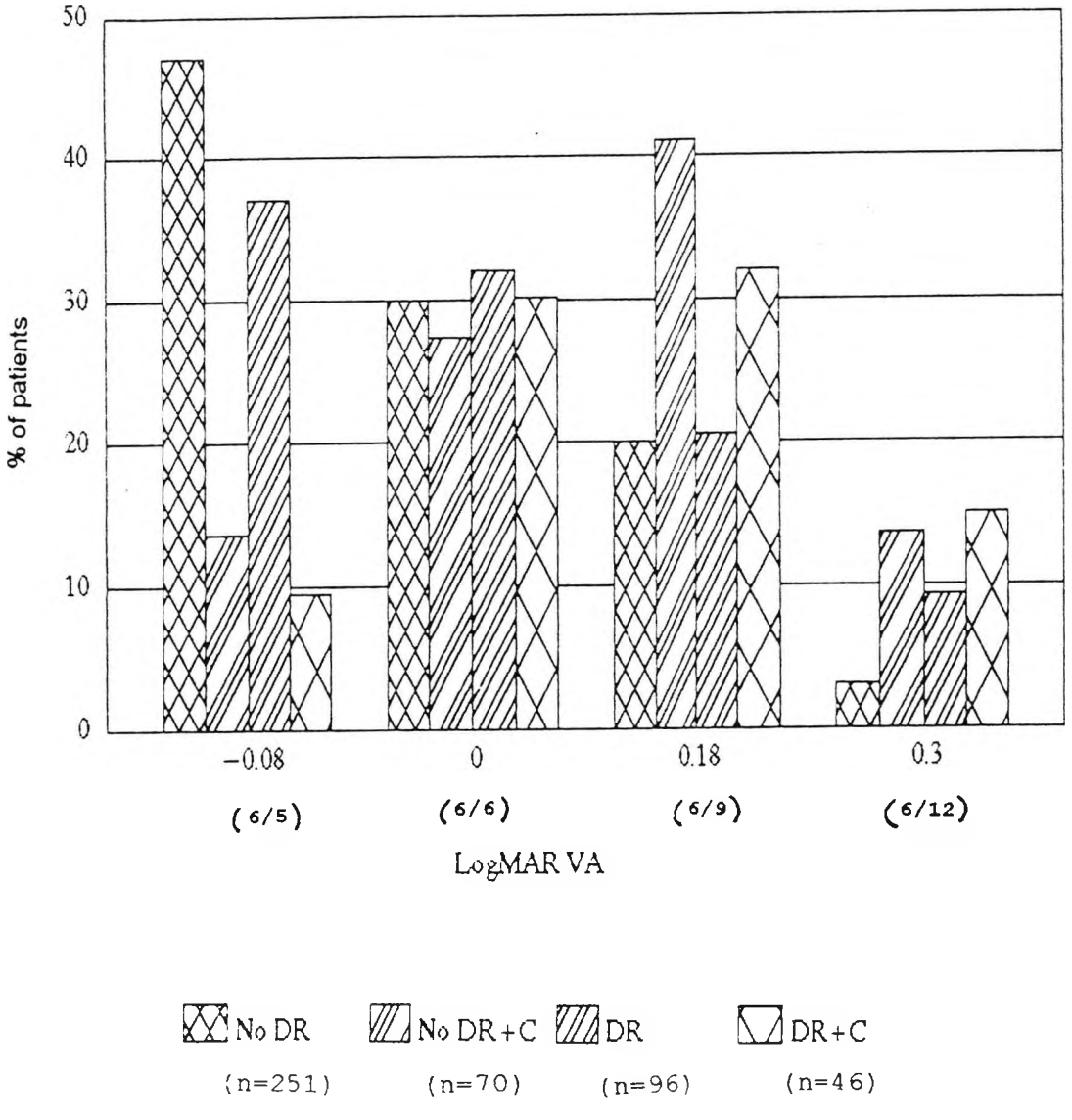


Fig 3.8 Comparison of VA in different groups

Fail Crit	Sensitivity	Specificity	p(N/P)	p(D/F)	False +	False -
<6/5	0.63	0.47	0.75	0.34	0.53	0.37
<6/6	0.31	0.77	0.72	0.37	0.23	0.69
<6/9	0.10	0.96	0.71	0.52	0.04	0.90

Crit=Criterion

p(N/P) is probability that the disease is absent given a pass

p(D/F) is probability that the disease is present given a fail

False + = False positives False - = False negatives

See appendices 3A & 3B for explanation of terms

Table 3.21 Screening parameters for different pass/fail criteria: VA for discriminating between patients without DR and those with DR

Fail Crit	Sensitivity	Specificity	p(N/P)	p(D/F)
<6/5	0.59 (0.61)	0.47	0.73 (0.74)	0.32 (0.33)
<6/6	0.25 (0.26)	0.68	0.68 (0.68)	0.25 (0.26)
<6/9	0.08 (0.09)	0.95	0.71 (0.71)	0.41 (0.44)

Explanation of terms as per table 3.21

Table 3.21a Screening parameters for different pass/fail criteria: VA for discriminating between patients without DR from those with DR among *type I patients only N=170*

+ Numbers in parentheses represent the screening figures after ten patients who had been lasered before were relocated from group 4 to group 3

Fail Crit	Sensitivity	Specificity	p(N/P)	p(D/F)	False +	False -
<6/5	0.77	0.47	0.70	0.56	0.53	0.23
<6/6	0.47	0.77	0.62	0.64	0.23	0.53
<6/9	0.17	0.96	0.57	0.81	0.04	0.83

Explanation of terms as per table 3.21

Table 3.22 Screening parameters for different pass/fail criteria: VA for discriminating between patients without DR and the "rest of the patients".

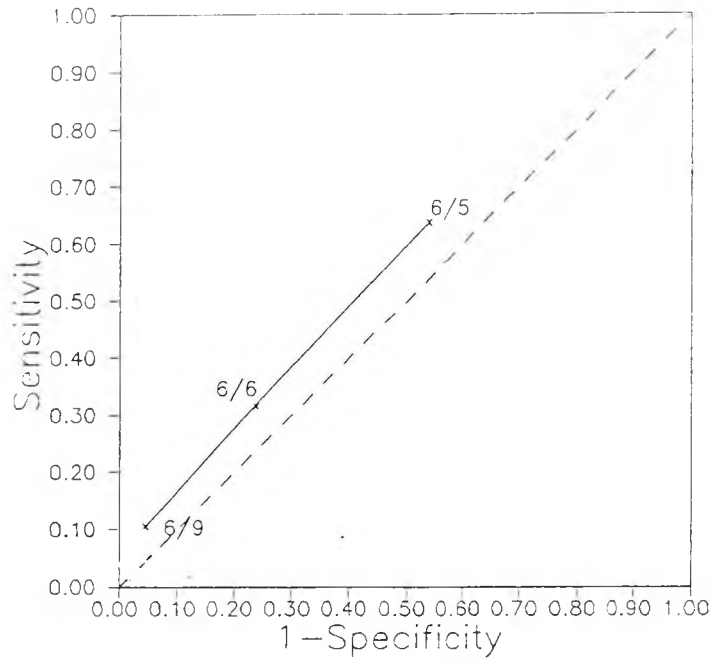


Fig 3.9 ROC curve: VA for discriminating between patients without DR and those with DR

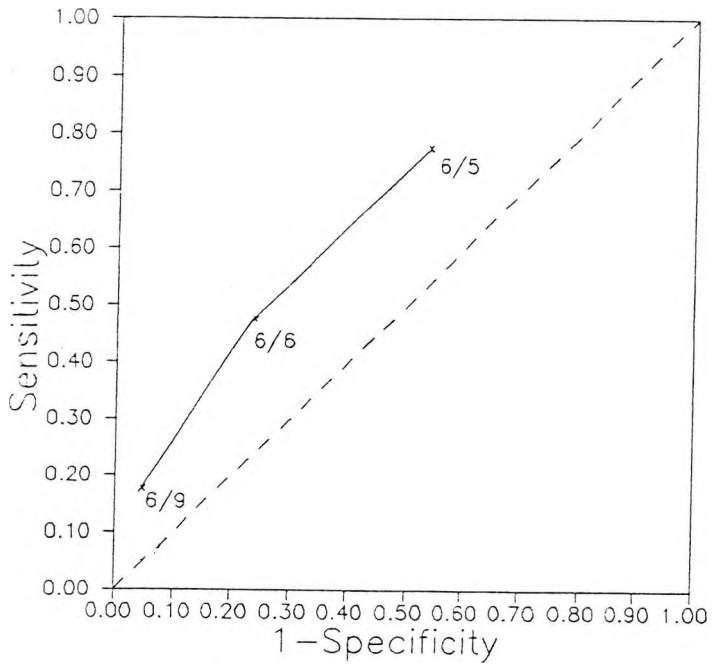


Fig 3.10 ROC curve: VA for discriminating between patients without DR and the rest of the patients

calculated for patients with *type I diabetes* only (101 from group 1 and 69 from group 3). Generally, the sensitivity of the test is less in this subanalysis and the specificity is about the same. The minimum rate of misclassification between false positives and false negatives was also achieved (as with the analysis of both types I and II patients mixed together) with a VA cut-off of 6/5, which gave a lower sensitivity of 0.59 and a specificity of 0.47. Numbers in parentheses are figures recalculated after ten patients from group 4 who had been lasered before were relocated to group 3; the same trend was noted and a slightly higher sensitivity resulted generally. Analysis of type I patients only also revealed slightly lower values of predictive values as evident in table 3.21a.

In the second situation 119 diabetics without DR (47%) had a VA of 6/5 vs 51 patients with DR and/or other complications (24.1%). Table 3.22 shows the screening parameters in the second situation. The ROC curve in fig 3.10 shows that the minimum rate of misclassification between false positives and false negatives was achieved with a VA cut-off of 6/5 which gave a sensitivity of 0.77 and a specificity of 0.47. The associated p(N/P) and p(D/F) values were 0.70 and 0.56, respectively. The highest value of p(N/P) was 0.70 i.e. with a VA cut-off of 6/5 and the highest p(D/F) value was 0.81 obtainable with a VA cut-off of 6/9. These two cut-off criteria represent the maximum confidence limits for decisions of normal given a pass and diseased given a fail, respectively.

3.3.2b Colour vision

1. Comp PIC

In evaluating the screening utility of these plates (taken as a series), performance was designated as "total number of plate errors" made. Figures 3.11,3.12,3.13 and 3.14 show the distributions of total plate errors in the 4 groups of patients (total number of patients = 463).

In the first situation 83% of patients without DR (group 1) made no errors at all (17% of patients made at least one error). For the group with DR and no other complications (group 3), 49.5% of patients did not make any errors at all (50.5% made at least one error). Table 3.23 shows the screening parameters in the first situation with the associated ROC curve shown in fig 3.15. The optimal fail criterion which minimised the rate of misclassification between false positives and false negatives was "at least one plate error". This gave a sensitivity of 0.51 and a specificity of 0.83. The associated values of p(N/P) and p(D/F) were 0.80 and 0.56, respectively.

The highest value of p(N/P) obtained was achieved with a fail criterion of "at least one plate error". The highest value of p(D/F) obtained was achieved with a fail criterion of "six plate errors or more".

Table 3.23a shows the screening figures which were calculated for patients with *type I diabetes* only (101 from group 1 and 69 from group 3). Generally, the sensitivity of the test is less in this subanalysis and the specificity is slightly increased. The optimal fail criterion which minimised the rate of misclassification between false positives and false negatives was also "at least one plate error" (as in the case of analysis of both types I and II patients mixed together). This gave a slightly lower sensitivity of 0.49 and a specificity of 0.88. Numbers in parentheses are figures recalculated after ten patients from group 4 who had been lasered before were relocated to group 3; the same trend was noted and a slightly higher sensitivity resulted generally. Analysis of type I patients only also revealed almost similar negative predictive values but higher positive predictive values as evident in table 3.23a.

In the second situation 83% of patients without DR (group 1) made no errors at all (17% of patients made at least one error). For the rest of the patients (groups 2,3 and 4 combined), 36.3% of patients did not make any errors at all

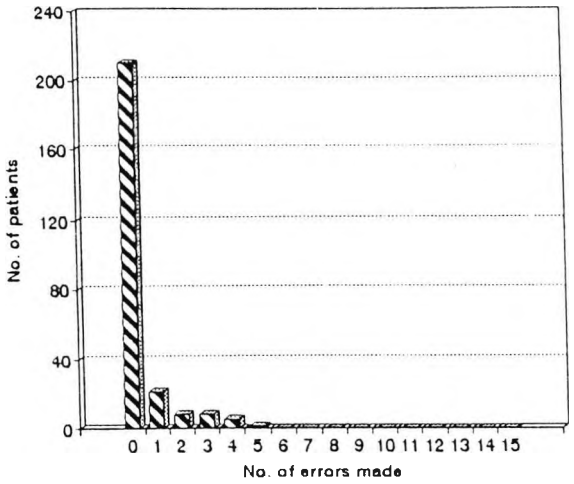


Fig 3.11 Comp PIC performance: No DR group (n=251)

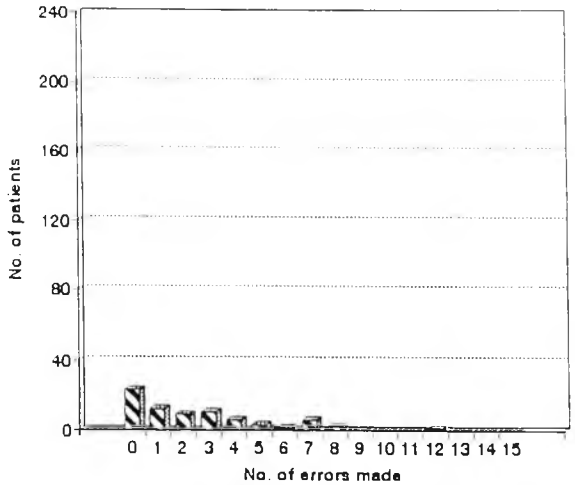


Fig 3.12 Comp PIC performance: No DR+C group (n=70)

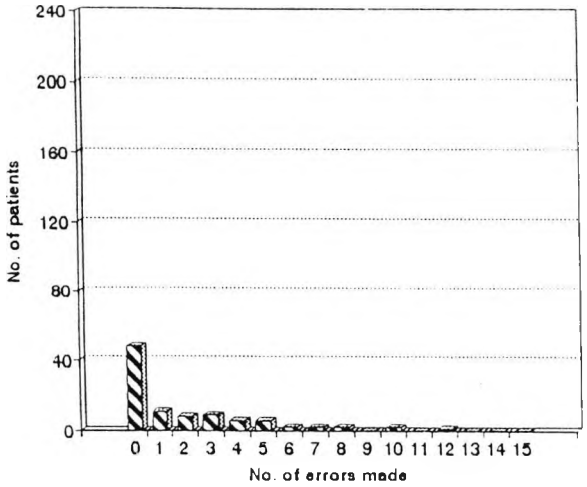


Fig 3.13 Comp PIC performance: DR group (n=96)

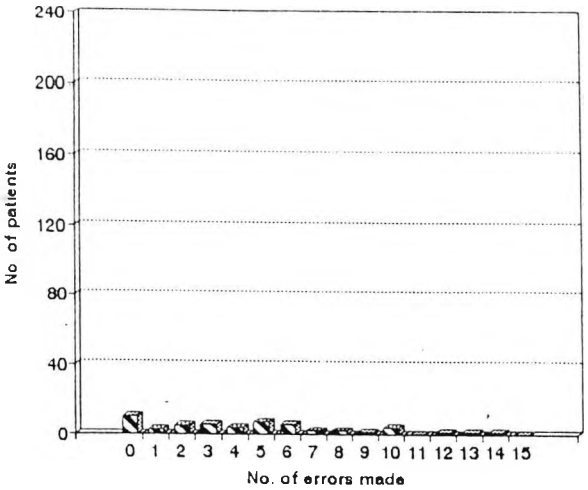


Fig 3.14 Comp PIC performance: DR+C group (n=46)

Fail Crit	Sensitivity	Specificity	p(N/P)	p(D/F)	False +	False -
>=1	0.51	0.83	0.80	0.56	0.17	0.49
>=2	0.38	0.91	0.77	0.70	0.07	0.62
>=3	0.30	0.94	0.76	0.72	0.05	0.70
>=4	0.21	0.98	0.74	0.82	0.02	0.79
>=5	0.14	0.99	0.73	0.94	0.01	0.86
>=6	0.08	1.00	0.72	1.00	0.00	0.92

Crit=Criterion

p(N/P) is probability that the disease is absent given a pass

p(D/F) is probability that the disease is present given a fail

False + = False positives False - = False negatives

See appendices 3A & 3B for explanation of terms

Table 3.23 Screening parameters for different pass/fail criteria: Comp PIC for discriminating between patients without DR and those with DR (Fail criterion defined as total number of plates failed).

Fail Crit	Sensitivity	Specificity	p(N/P)	p(D/F)
>=1	0.49 (0.54)	0.88	0.80 (0.82)	0.64 (0.66)
>=2	0.36 (0.41)	0.94	0.77 (0.79)	0.72 (0.75)
>=3	0.27 (0.33)	0.97	0.76 (0.77)	0.79 (0.83)
>=4	0.23 (0.26)	0.98	0.75 (0.76)	0.83 (0.85)

Explanation of terms as per table 3.23

Table 3.23a Screening parameters for different pass/fail criteria: Comp PIC for discriminating between patients without DR from those with DR among *type I patients only N=170*

+ Numbers in parentheses represent the screening figures after ten patients who had been lasered before were relocated from group 4 to group 3

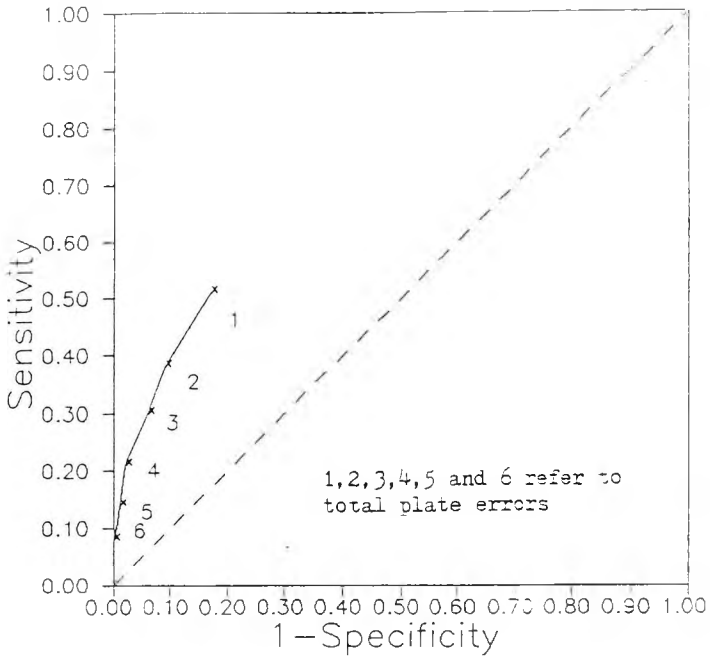


Fig 3.15 ROC curve: Comp PIC for discriminating between patients without DR and those with DR

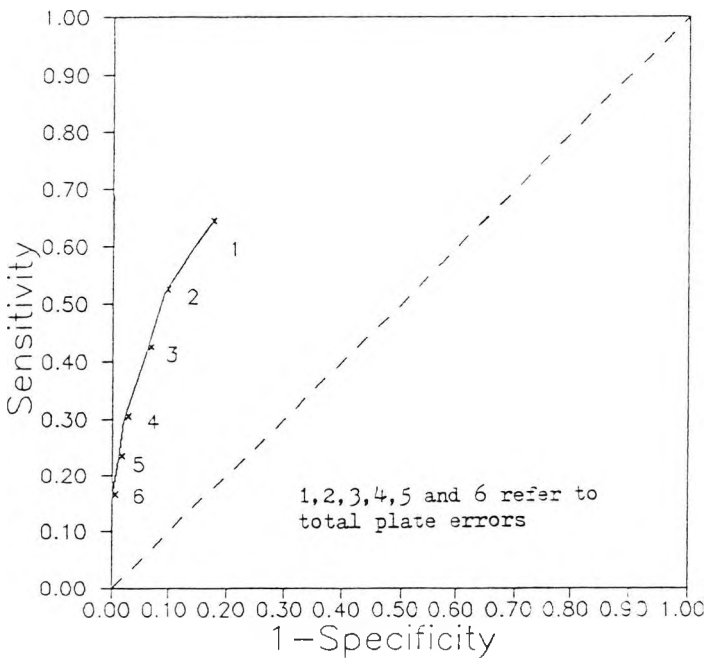


Fig 3.16 ROC curve: Comp PIC for discriminating between patients without DR and the rest of the patients

Fail Crit	Sensitivity	Specificity	p(N/P)	p(D/F)	False +	False -
>=1	0.64	0.83	0.73	0.81	0.17	0.36
>=2	0.52	0.91	0.68	0.84	0.07	0.48
>=3	0.42	0.94	0.65	0.87	0.05	0.58
>=4	0.30	0.98	0.61	0.92	0.02	0.70
>=5	0.23	0.99	0.60	0.98	0.01	0.77
>=6	0.16	1.00	0.58	1.00	0.00	0.84

Explanation of terms as per table 3.23

Table 3.24 Screening parameters for different pass/fail criteria: Comp PIC for discriminating between patients without DR and the "rest of the patients" (Fail criterion defined as total number of plates failed).

Sensitivity	Specificity	p(N/P)	p(D/F)	False +	False -
0.13	0.95	0.72	0.53	0.05	0.87

p(N/P) is probability that the disease is absent given a pass
p(D/F) is probability that the disease is present given a fail
False + = False positives False - = False negatives
See appendices 3A & 3B for explanation of terms

Table 3.25 Screening parameters of LTA plate 5 for discriminating between patients without DR and those with DR.

Sensitivity	Specificity	p(N/P)	p(D/F)
0.12	0.97	0.72	0.63
(0.19)		(0.74)	(0.73)

Explanation of terms as per table 3.25

Table 3.25a Screening parameters of LTA plate 5 discriminating between patients without DR from those with DR among *type I patients only N=170*

+ Numbers in parentheses represent the screening figures after ten patients who had been lasered before were relocated from group 4 to group 3

Sensitivity	Specificity	p(N/P)	p(D/F)	False +	False -
0.24	0.95	0.59	0.81	0.05	0.76

Explanation of terms as per table 3.25

Table 3.26 Screening parameters of LTA plate 5 for discriminating between patients without DR and the "rest of the patients".

(63.7% made at least one error). Table 3.24 shows the screening parameters associated with the use of these plates in the second situation with the associated ROC curve shown in fig 3.16. The optimal fail criterion which minimised the rate of misclassification between false positives and false negatives was also "at least one plate error". This gave a sensitivity of 0.64 and a specificity of 0.83. The associated values of p(N/P) and p(D/F) were 0.73 and 0.81, respectively. The highest value of p(N/P) obtained was achieved with a fail criterion of "at least one plate error". The highest value of p(D/F) obtained was achieved with a fail criterion of "six plate errors or more".

2. LTA plate 5

Table 3.25 shows the screening parameters of this single plate in the first situation (total number of patients = 463).

With the test having only one fixed criterion, the test had a sensitivity of 0.13 and a specificity of 0.95. Fig 3.17 is the ROC curve depicting the performance of the test. The associated predictive values of the test were p(N/P)=0.72 and p(D/F)=0.53. Table 3.25a shows the screening figures which were calculated for patients with *type I diabetes* only (101 from group 1 and 69 from group 3). The sensitivity of the test now (0.12) was similar to when the analysis was done with both types I and II patients mixed together. A slightly better specificity resulted ie. 0.97. Numbers in parentheses are figures recalculated after ten patients from group 4 who had been lasered before were relocated to group 3; a slightly higher sensitivity resulted ie. 0.19. Analysis of type I patients only also revealed almost a similar negative predictive value, but a slightly higher positive predictive value (0.63 compared to 0.53 previously) as evident in table 3.25a.

Table 3.26 shows the screening parameters in the second situation. Here, the test had a sensitivity of 0.24 and a

specificity of 0.95. Fig 3.18 is the ROC curve depicting the performance of the test in the second situation. The associated predictive values of the test were p(N/P)=0.59 and p(D/F)=0.81.

3. D15 (5/2)

In evaluating the screening utility of the D15 (5/2) test, performance was designated as the "score" obtained. Figs 3.19, 3.20, 3.21 and 3.22 show the distributions of scores for the 4 groups of patients (total number of patients = 163 only).

In the first situation 31% of patients without DR (group 1) made minor errors (defined as a single cap inversion i.e. a score of 2) or no errors at all. For the group with DR and no other complications (group 3), 30.4% of patients fell into this same category. Table 3.27 shows the screening parameters of the test in the first situation with the associated ROC curve shown in fig 3.23. The optimal fail criterion which minimised the rate of misclassification between false positives and false negatives was "a score of greater than 14". This gave a sensitivity of 0.28 and a specificity of 0.82. The associated values of p(N/P) and p(D/F) were 0.73 and 0.40, respectively. The highest value of p(N/P) obtained was achieved with a fail criterion of "a score greater than 14". The highest value of p(D/F) was achieved with a fail criterion of "a score greater than 44".

Table 3.27a shows the screening figures which were calculated for patients with *type I diabetes* only (35 from group 1 and 33 from group 3). The sensitivity of the test now is generally lower compared to the analysis where both types I and II patients were mixed together; the specificity was however generally slightly better. The optimal fail criterion which minimised the rate of misclassification between false positives and false negatives was different from that obtained in the case of analysis of both types I and II patients mixed together;

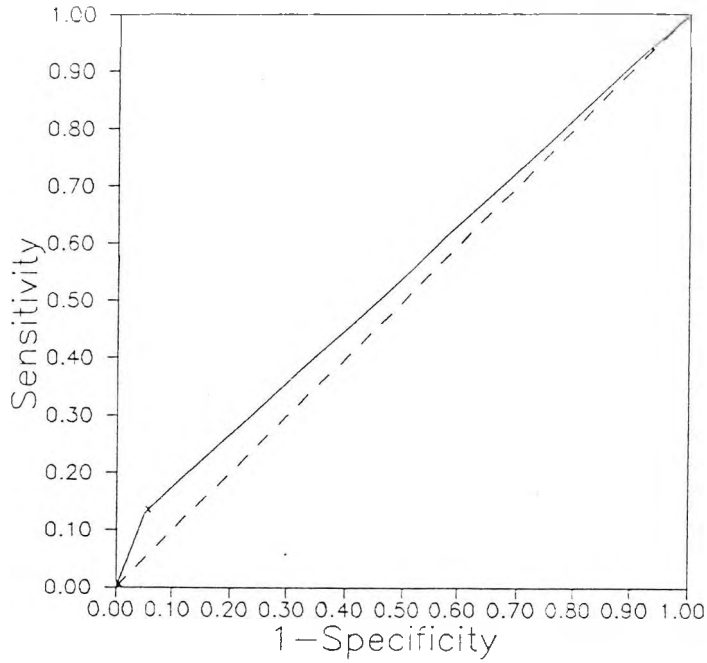


Fig 3.17 ROC curve: LTA plate 5 for discriminating between patients without DR and those with DR

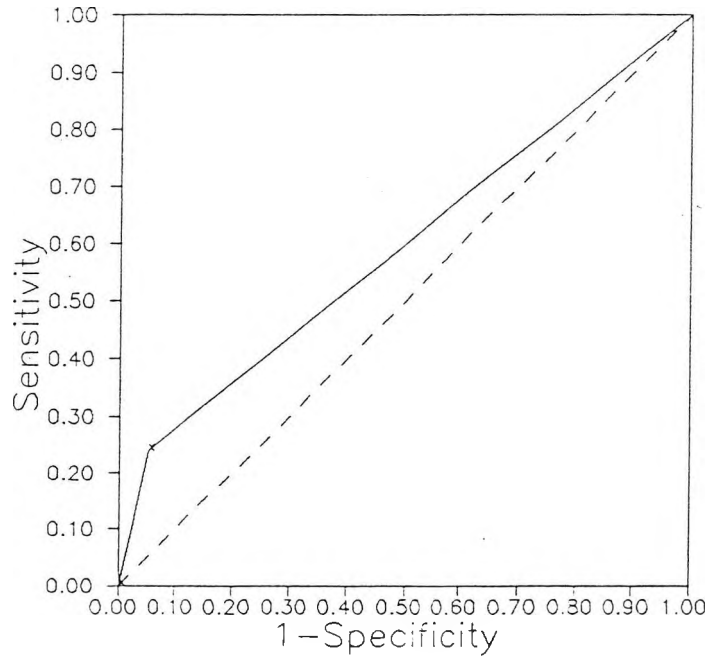


Fig 3.18 ROC curve: LTA plate 5 for discriminating between patients without DR and the rest of the patients

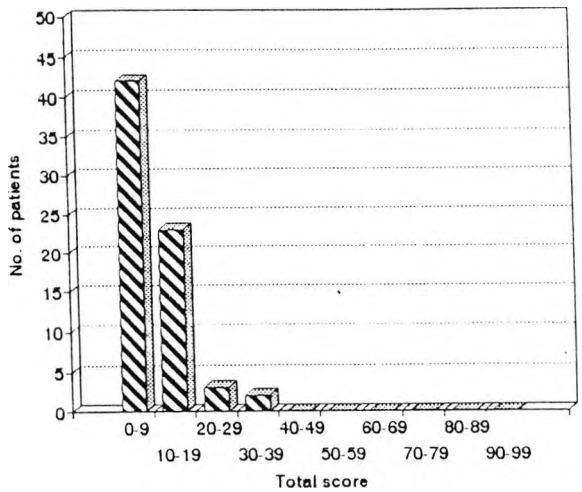


Fig 3.19 D15(5/2) performance: No DR group (n=70)

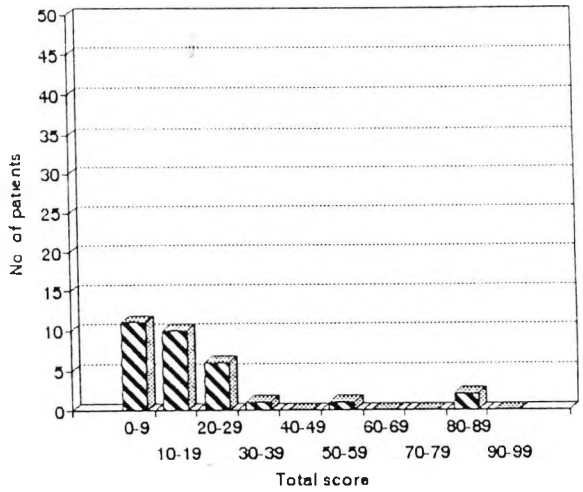


Fig 3.20 D15(5/2) performance: No DR+C group (n=29)

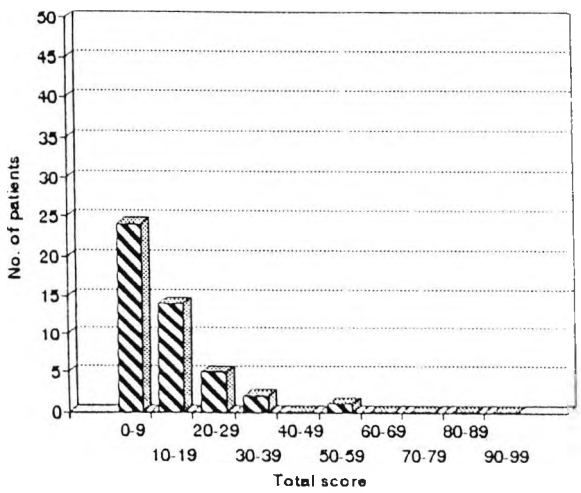


Fig 3.21 D15(5/2) performance: DR group (n=45)

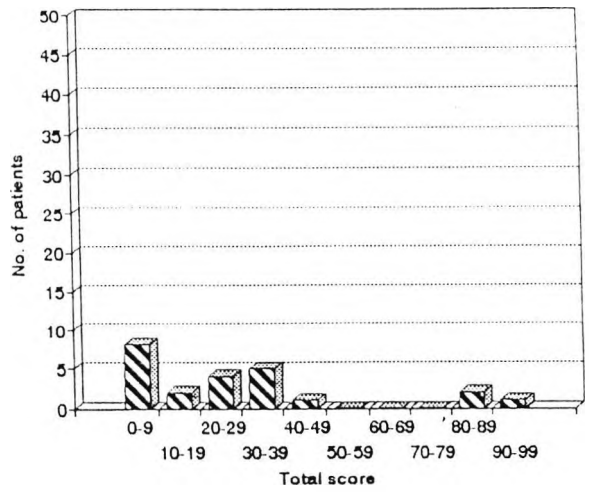


Fig 3.22 D15(5/2) performance: DR+C group (n=19)

Fail Crit	Sensitivity	Specificity	p(N P)	p(D/F)	False +	False -
>2	0.70	0.31	0.71	0.30	0.69	0.30
>4	0.63	0.42	0.73	0.32	0.58	0.37
>9	0.48	0.59	0.73	0.33	0.41	0.52
>14	0.28	0.82	0.73	0.40	0.18	0.72
>19	0.17	0.92	0.72	0.48	0.08	0.83
>24	0.11	0.96	0.72	0.54	0.04	0.89
>29	0.07	0.96	0.71	0.43	0.04	0.93
>34	0.02	0.97	0.70	0.22	0.03	0.98
>39	0.02	0.99	0.70	0.46	0.01	0.98
>44	0.02	1.00	0.70	1.00	0.00	0.98

Crit=Criterion

p(N/P) is probability that the disease is absent given a pass

p(D/F) is probability that the disease is present given a fail

False – = False positives False - = False negatives

See appendices 3A & 3B for explanation of terms

Table 3.27 Screening parameters for different pass/fail criteria: D15(5/2) for discriminating between patients without DR and those with DR (Fail criterion defined as score obtained).

Fail Crit	Sensitivity	Specificity	p(N/P)	p(D/F)
> 2	0.64 (0.67)	0.31	0.77 (0.78)	0.36 (0.37)
> 4	0.58 (0.61)	0.55	0.79 (0.80)	0.42 (0.43)
> 9	0.39 (0.44)	0.77	0.75 (0.76)	0.42 (0.45)
>14	0.27 (0.33)	0.91	0.74 (0.76)	0.56 (0.61)
>19	0.18 (0.21)	1.00	0.74 (0.75)	1.00 (1.00)

Explanation of terms as per table 3.27

Table 3.27a Screening parameters for different pass/fail criteria: D15(5/2) for discriminating between patients without DR from those with DR among *type I patients only* N=99

+ Numbers in parentheses represent the screening figures after six patients who had been lasered before were relocated from group 4 to group 3

Fail Crit	Sensitivity	Specificity	p(N/P)	p(D/F)	False +	False -
>2	0.79	0.31	0.51	0.62	0.69	0.21
>4	0.74	0.42	0.54	0.64	0.58	0.26
>9	0.57	0.59	0.49	0.66	0.41	0.43
>14	0.43	0.82	0.50	0.77	0.18	0.57
>19	0.31	0.92	0.49	0.84	0.08	0.69
>24	0.22	0.96	0.47	0.88	0.04	0.78
>29	0.16	0.96	0.45	0.84	0.04	0.84
>34	0.08	0.97	0.43	0.80	0.03	0.92
>39	0.08	0.99	0.43	0.89	0.01	0.92
>44	0.08	1.00	0.44	1.00	0.00	0.92

Explanation of terms as per table 3.27

Table 3.28 Screening parameters for different pass/fail criteria: D15(5/2) for discriminating between patients without DR and the 'rest of the patients' (Fail criterion defined as score obtained).

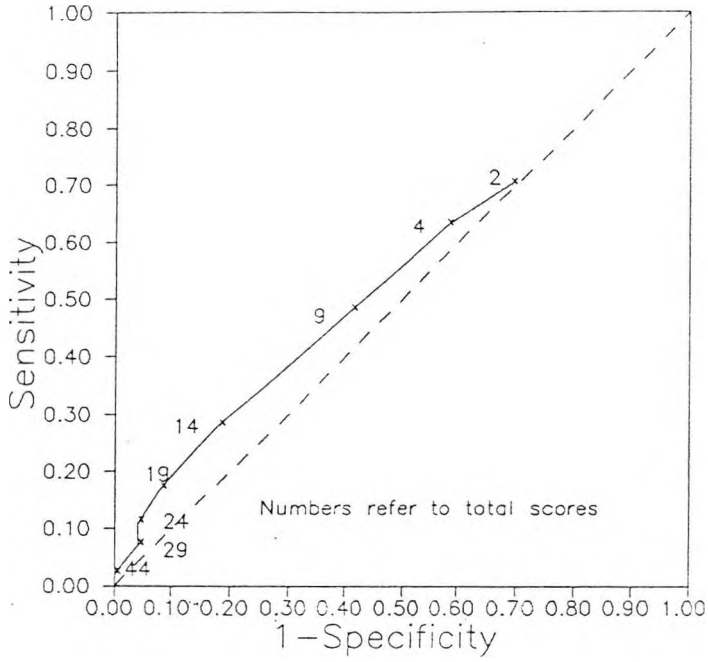


Fig 3.23 ROC curve: D15(5/2) for discriminating between patients without DR and those with DR

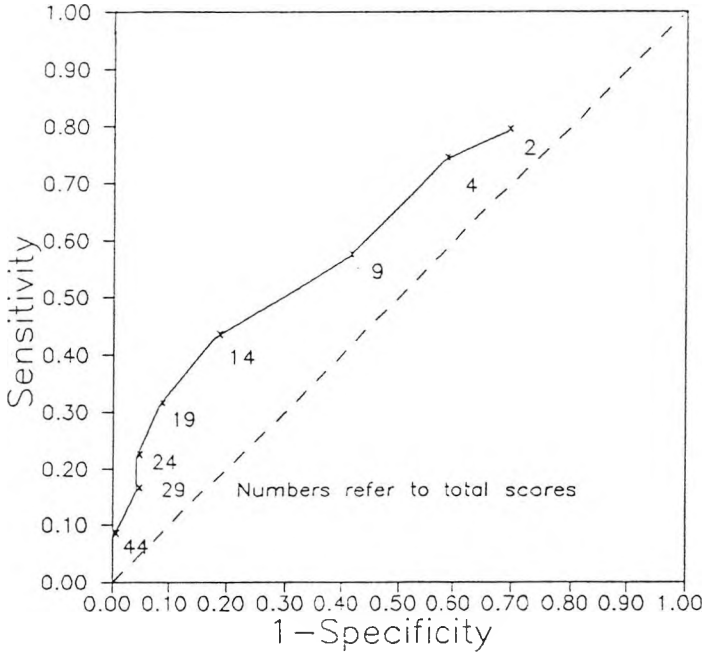


Fig 3.24 ROC curve: D15(5/2) for discriminating between patients without DR and the rest of the patients

the criterion now was "a score of greater than 4". This gave a higher sensitivity of 0.58 and a specificity of 0.66. Numbers in parentheses are figures recalculated after six patients from group 4 who had been lasered before were relocated to group 3; this improved the sensitivity slightly. Analysis of type I patients only also revealed higher predictive values as evident in table 3.27a.

In the second situation 31% of patients without DR or complications (group 1) made minor errors (defined as a single cap inversion i.e. a score of 2) or no errors at all. For the rest of the patients (groups 2,3 and 4), 21% of patients fell into this same category. Table 3.28 shows the screening parameters in the second situation with the associated ROC curve shown in fig 3.24. The optimal fail criterion identified from the ROC curve which minimised the rate of misclassification between false positives and false negatives was "a score of greater than 14". This gave a sensitivity of 0.43 and a specificity of 0.82. The associated values of p(N/P) and p(D/F) were 0.50 and 0.77, respectively. The highest value of p(N/P) obtained was achieved with a fail criterion of "a score greater than 4". The highest value of p(D/F) obtained was achieved with a fail criterion of "a score greater than 44".

3.3.2c Contrast sensitivity (CS)

1. Arden gratings

Figs 3.25,3.26,3.27 and 3.28 show the distributions of total scores on the Arden gratings for the 4 groups of patients (total number of patients = 163 only). In the first situation 51% of patients without DR (group 1) had total scores which exceeded 82 (Arden's criterion for normal) vs 53% of patients with DR alone (group 3).

Fig 3.29 is the ROC curve in the first situation. The curve straddles the line of indecision. No cut-off criterion could be chosen to minimise the rate of misclassification between false positives and false negatives. The fact that

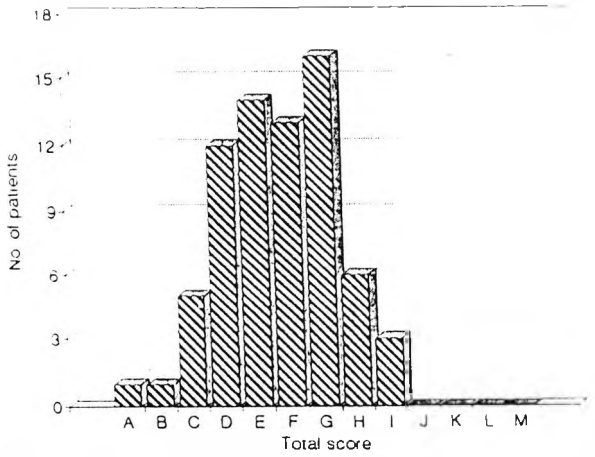
some data points fall below the indecision line is a function of sampling variance. Appendix 3M shows the screening parameters for the Arden gratings for this first purpose. Appendix 3Ma shows the screening figures which were calculated for patients with *type I diabetes* only (35 from group 1 and 33 from group 3). The specificity is slightly increased compared to the previous mixed analysis although the sensitivity was better for some cut-offs (in the lower range of total scores) whereas not for other cut-offs in the higher range of scores. As with the analysis of data where types I & II patients were mixed together, no cut-off criterion could be chosen to minimise the rate of misclassification between false positives and false negatives. Numbers in parentheses are figures recalculated after six patients from group 4 who had been lasered before were relocated to group 3; the same trend of indecision was noted as before.

The analysis for the second situation revealed 67% of patients in groups 2,3 and 4 combined with scores exceeding 82. Fig 3.30 is the associated ROC curve. Although the points on the curve do not exactly lie on the indecision line, they are scattered almost parallel to it. No single cut-off criterion could be chosen to minimise the rate of misclassification between false positives and false negatives. Appendix 3N shows the screening parameters for the Arden gratings calculated for this second situation.

2. VCTS 6000

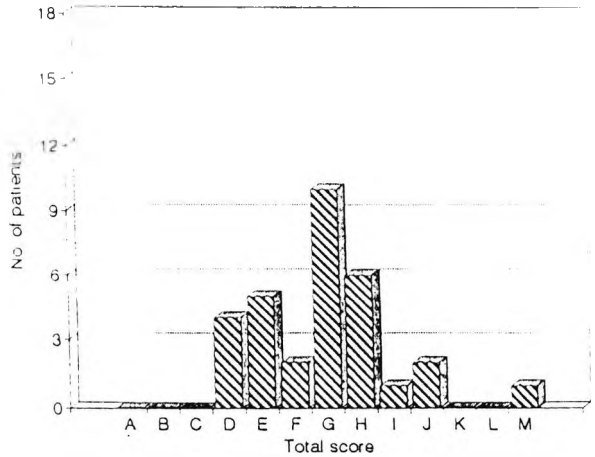
Figs 3.31,3.32,3.33 and 3.34 show the distributions of the global scores on the VCTS 6000 for the 4 groups of patients (total number of patients = 300 only).

In the first situation 24% of patients without DR (group 1) and 45% of those with DR (group 3) had global scores of less than 20. Table 3.29 shows the screening parameters for the VCTS 6000 in the first screening situation with the associated ROC curve in fig 3.35. The optimal fail criterion which minimised the rate of misclassification



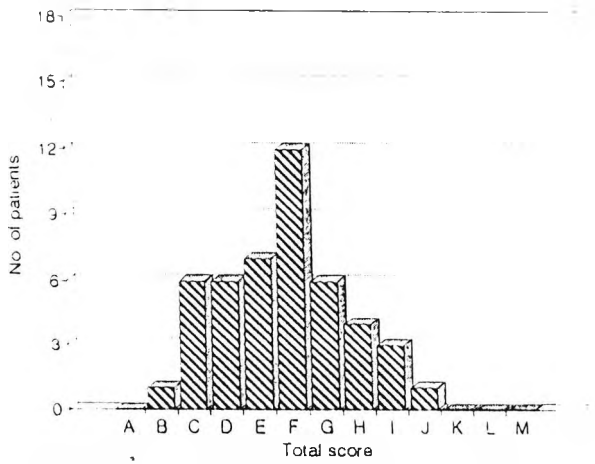
A = < 40 B = < 50; C = < 60; D = < 70; E = < 80; F = < 90; G = < 100; H = < 110 I = < 120 J = < 130 K = < 140; L = < 150; M = < 160

Fig 3.25 Arden gratings performance: No DR group (n=70)



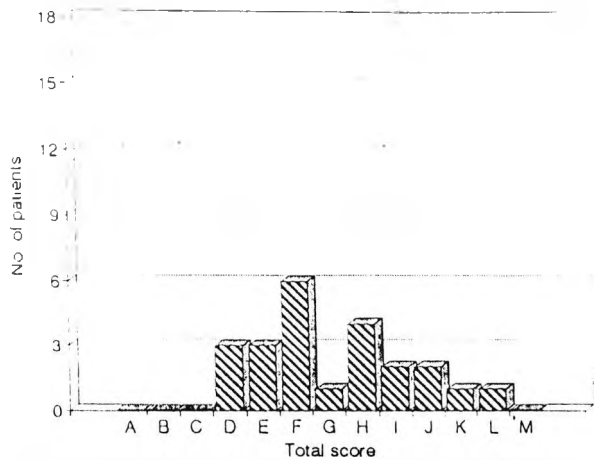
A = < 40; B = < 50; C = < 60; D = < 70; E = < 80; F = < 90; G = < 100; H = < 110; I = < 120; J = < 130; K = < 140; L = < 150; M = < 160

Fig 3.26 Arden gratings performance: No DR+C (n=29)



A = < 40 B = < 50; C = < 60; D = < 70; E = < 80, F = < 90; G = < 100; H = < 110; I = < 120 J = < 130. K = < 140; L = < 150; M = < 160

Fig 3.27 Arden gratings performance: DR group (n=45)



A = < 40; B = < 50; C = < 60; D = < 70; E = < 80; F = < 90; G = < 100, H = < 110; I = < 120; J = < 130; K = < 140; L = < 150; M = < 160

Fig 3.28 Arden gratings performance: DR+C group (n=19)

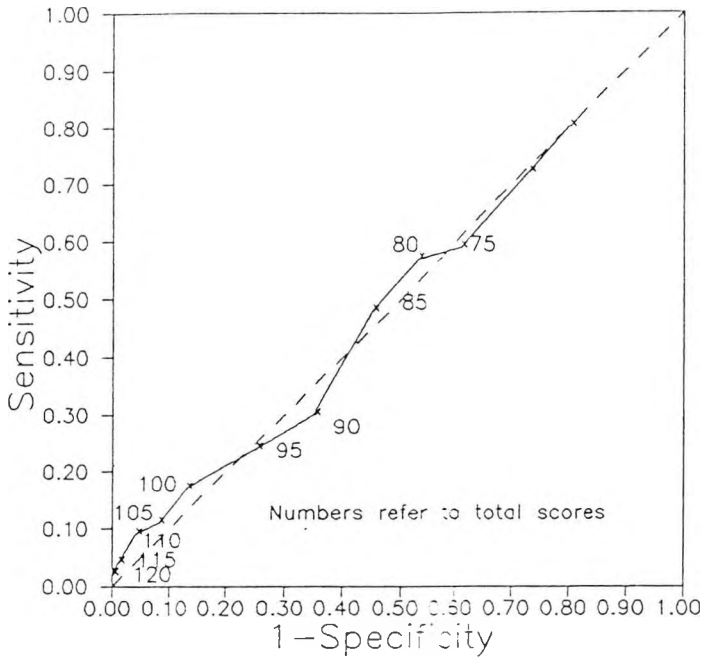


Fig 3.29 ROC curve: Arden gratings for discriminating between patients without DR and those with DR

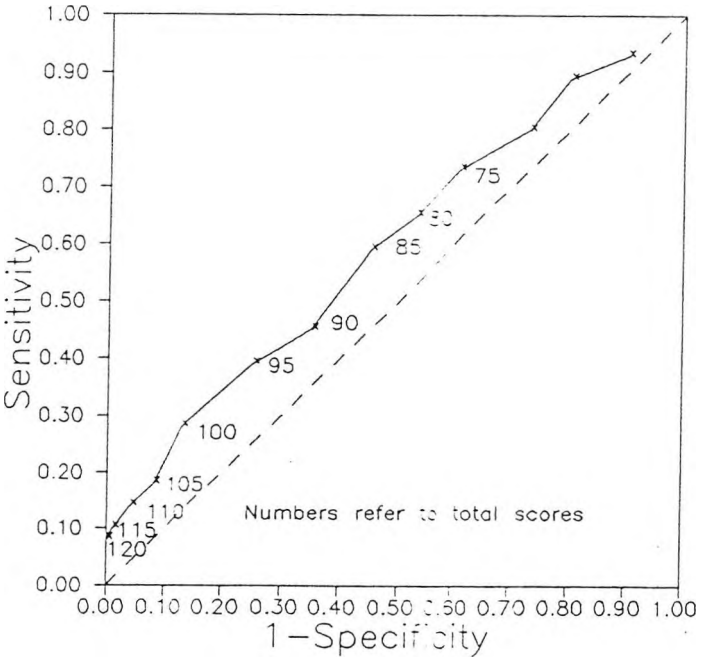


Fig 3.30 ROC curve: Arden gratings for discriminating between patients without DR and the rest of the patients

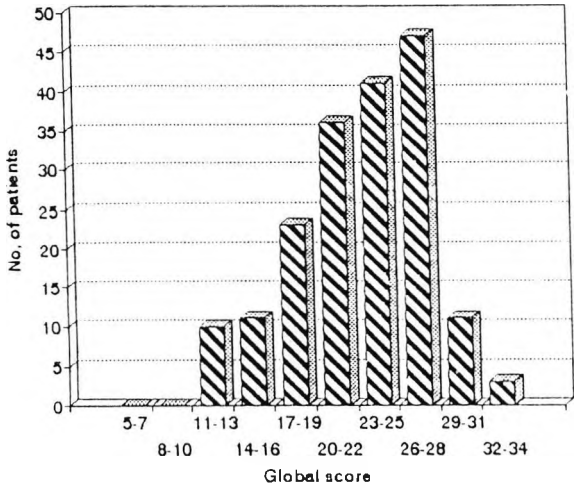


Fig 3.31 VCTS 6000 performance: No DR group (n=181)

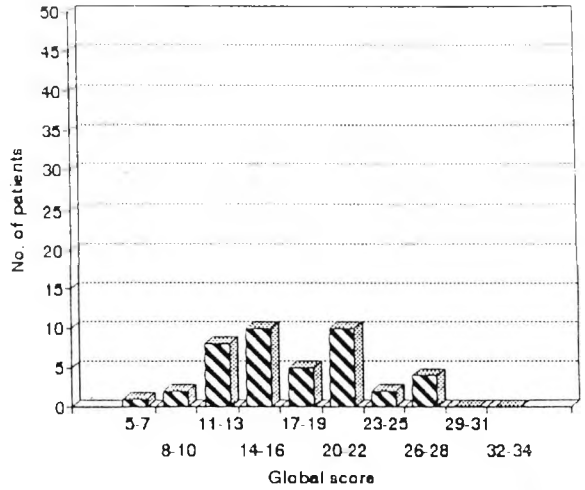


Fig 3.32 VCTS 6000 performance: No DR+C group (n=41)

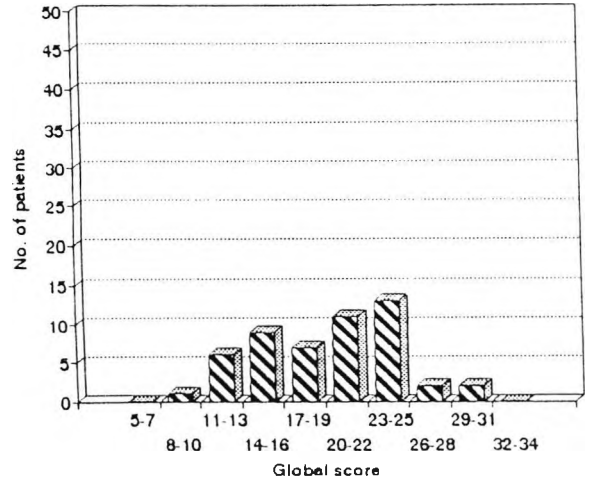


Fig 3.33 VCTS 6000 performance: DR group (n=51)

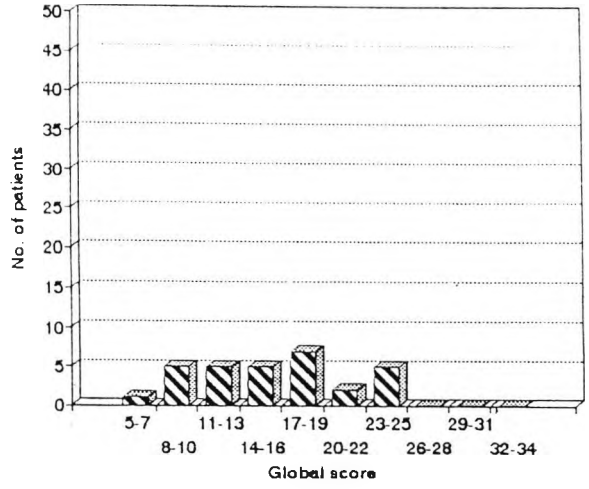


Fig 3.34 VCTS 6000 performance: DR+C group (n=27)

Fail crit	Sensitivity	Specificity	p(N/P)	p(D/F)	False +	False -
<=31	1.00	0.02	1.00	0.30	0.98	0.00
<=28	0.96	0.08	0.82	0.31	0.92	0.04
<=25	0.92	0.34	0.91	0.37	0.66	0.08
<=22	0.67	0.56	0.80	0.39	0.44	0.33
<=19	0.45	0.76	0.76	0.45	0.24	0.55
<=16	0.31	0.88	0.75	0.53	0.12	0.69
<=13	0.14	0.95	0.72	0.54	0.05	0.86
<=10	0.02	1.00	0.70	1.00	0.00	0.98

Crit=Criterion

p(N/P) is probability that the disease is absent given a pass

p(D/F) is probability that the disease is present given a fail

False + = False positives False - = False negatives

See appendices 3A & 3B for explanation of terms

Table 3.29 Screening parameters for different pass/fail criteria: VCTS 6000 for discriminating between patients without DR and those with DR (Fail criterion defined as global score obtained).

Fail Crit	Sensitivity	Specificity	p(N/P)	p(D/F)
<=31	1.00	0.02	1.00	0.30
	(1.00)		(1.00)	(0.30)
>=28	0.92	0.12	0.78	0.31
	(0.93)		(0.80)	(0.31)
>=25	0.85	0.33	0.84	0.35
	(0.87)		(0.86)	(0.36)
>=22	0.54	0.58	0.75	0.35
	(0.60)		(0.77)	(0.38)
>=19	0.38	0.73	0.73	0.38
	(0.47)		(0.76)	(0.43)
>=16	0.23	0.85	0.72	0.40
	(0.27)		(0.73)	(0.44)
>=13	0.12	0.94	0.71	0.46
	(0.10)		(0.71)	(0.42)
>=10	0.04	1.00	0.71	1.00
	(0.03)		(0.71)	(1.00)

Explanation of terms as per table 3.29

Table 3.29a Screening parameters for different pass/fail criteria: VCTS 6000 for discriminating between patients without DR from those with DR among *type I patients only* N=92

+ Numbers in parentheses represent the screening figures after four patients who had been lasered before were relocated from group 4 to group 3.

Fail crit	Sensitivity	Specificity	p(N/P)	p(D/F)	False +	False -
<=31	1.00	0.02	1.00	0.41	0.98	0.00
<=28	0.98	0.08	0.88	0.42	0.92	0.02
<=25	0.92	0.34	0.88	0.49	0.66	0.08
<=22	0.77	0.56	0.78	0.54	0.44	0.23
<=19	0.59	0.76	0.73	0.62	0.24	0.41
<=16	0.43	0.88	0.70	0.72	0.12	0.57
<=13	0.24	0.95	0.65	0.74	0.05	0.76
<=10	0.08	1.00	0.62	1.00	0.00	0.92

Explanation of terms as per table 3.29

Table 3.30 Screening parameters for different pass/fail criteria: VCTS 6000 for discriminating between patients without DR and the 'rest of the patients' (Fail criterion defined as global score obtained).

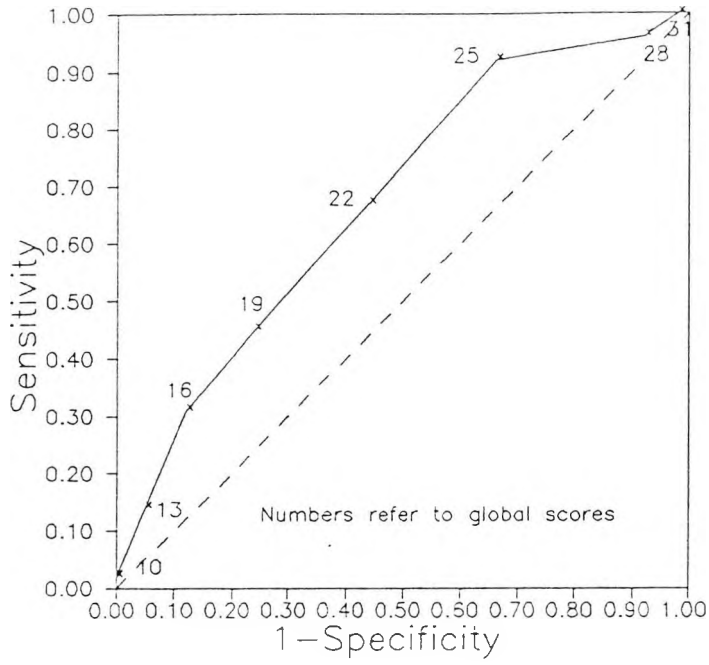


Fig 3.35 ROC curve: VCTS 6000 for discriminating between patients without DR and those with DR

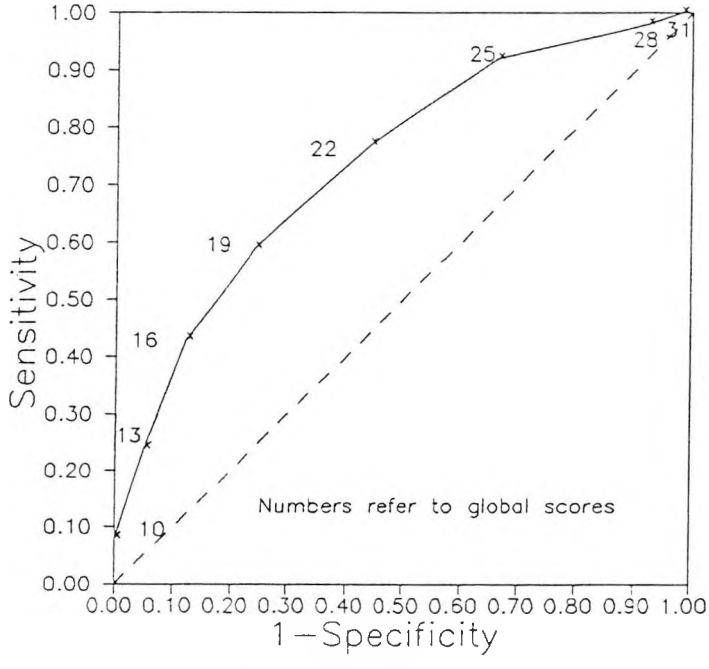


Fig 3.36 ROC curve: VCTS 6000 for discriminating between patients without DR and the rest of the patients

between false positives and false negatives was "a global score less than or equal to 25". This gave a sensitivity of 0.92 and a specificity of 0.34. The p(N/P) and p(D/F) values associated with this fail criterion were 0.91 and 0.37, respectively. The highest p(N/P) obtained was achieved with a fail criterion of "a global score less than or equal to 31". The highest p(D/F) obtained was achieved with a fail criterion of "a global score less than or equal to 10".

Table 3.29a shows the screening figures which were calculated for patients with *type I diabetes* only (66 from group 1 and 26 from group 3). In general the sensitivity of the test was found to be lower whereas the specificity was essentially the same compared to the previous analysis. The optimal fail criterion which minimised the rate of misclassification between false positives and false negatives was the same as that obtained in the previous case of analysis where types I and II patients were grouped together ie. "a global score less than or equal to 25". This gave a lower sensitivity of 0.85 and a specificity of 0.33. Numbers in parentheses are figures recalculated after six patients from group 4 who had been lasered before were relocated to group 3; a slightly higher sensitivity resulted generally. Analysis of type I patients only also revealed lower predictive values as evident in table 3.29a.

In the second situation 24% of patients without DR (group 1) and 58.5% of those in the other groups (2,3 and 4 combined) had global scores less than 20. Table 3.30 shows the screening parameters in the second situation with the associated ROC curve in fig 3.36. The optimal fail criterion which minimised the rate of misclassification between false positives and false negatives was "a global score less than or equal to 19". This gave a sensitivity of 0.59 and a specificity of 0.76. The p(N/P) and p(D/F) values associated with this fail criterion were 0.73 and 0.62, respectively. The highest p(N/P) obtained was achieved with a fail criterion of "a global score less than or equal to 31". The highest p(D/F) obtained was achieved

with a fail criterion of "a global score less than or equal to 10".

3.3.2d Visual field

The following analyses were completed for all the patients ie. 463. Table 3.31 shows the screening parameters for the Amsler grid in the first situation. The test had a sensitivity of 0.10 and a high specificity of 0.98 with associated p(N/P) of 0.72 and p(D/F) of 0.68. These two values represent 72% and 68% confidence limits for decisions of normal (given a pass) and DR (given a fail) respectively. Fig 3.37 is the ROC curve constructed from the data.

Table 3.31a shows the screening figures which were calculated for patients with *type I diabetes* only (101 from group 1 and 69 from group 3). The sensitivity of the test now (0.10) was similar to when the analysis was done with both types I and II patients mixed together; the same specificity also resulted ie. 0.99. Numbers in parentheses are figures recalculated after ten patients from group 4 who had been lasered before were relocated to group 3; a slightly higher sensitivity resulted ie. 0.19. Analysis of type I patients only also revealed almost a similar negative predictive value, but a slightly higher positive predictive value (0.81) as evident in table 3.31a.

Table 3.32 shows the screening parameters for the Amsler grid in the second situation. Here, the sensitivity of the test improved to 0.15 and the specificity was 0.98. The p(N/P) was 0.57 and the p(D/F) was 0.87 representing 57% and 87% confidence limits for decisions of normal (given a pass) and disease (given a fail), respectively. Fig 3.38 is the associated ROC curve.

Sensitivity	Specificity	p(N/P)	p(D/F)	False +	False -
0.10	0.98	0.72	0.68	0.02	0.90

p(N/P) is probability that the disease is absent given a pass
p(D/F) is probability that the disease is present given a fail
False + = False positives False - = False negatives
See appendices 3A & 3B for explanation of terms

Table 3.31 Screening parameters of the Amsler grid for discriminating between patients without DR and those with DR

Sensitivity	Specificity	p(N/P)	p(D/F)
0.10	0.99	0.72	0.81
(0.19)		(0.74)	(0.89)

Explanation of terms as per table 3.31

Table 3.31a Screening parameters of the Amsler grid for discriminating between patients without DR from those with DR among *type I patients only N=170*

+ Numbers in parentheses represent the screening figures after ten patients who had been lasered before were relocated from group 4 to group 3

Sensitivity	Specificity	p(N/P)	p(D/F)	False +	False -
0.15	0.98	0.57	0.87	0.02	0.85

Explanation of terms as per table 3.29

Table 3.32 Screening parameters of the Amsler grid for discriminating between patients without DR and the "rest of the patients".

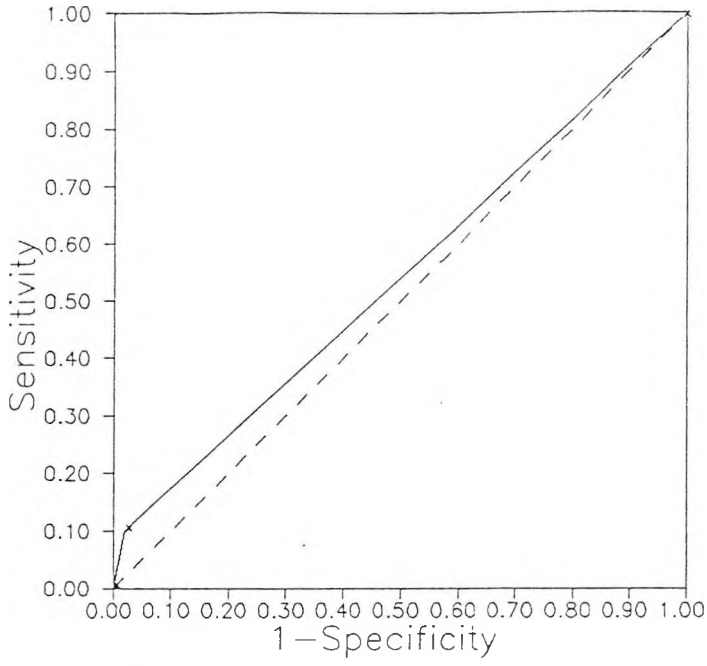


Fig 3.37 ROC curve: Amsler grid for discriminating between patients without DR and those with DR

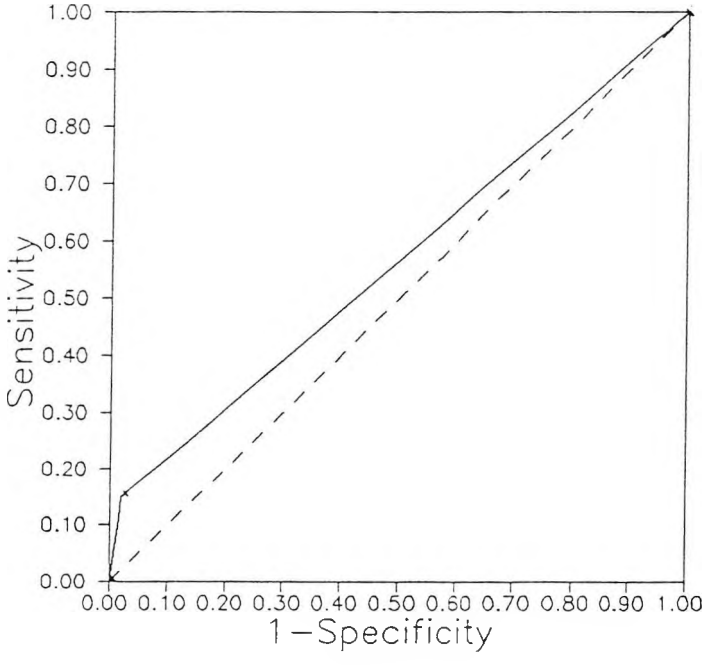


Fig 3.38 ROC curve: Amsler grid for discriminating between patients without DR and the rest of the patients

3.3.3 Combined test information

3.3.3a Test battery performance

2-test battery

From the preceding *analysis on all patients in the study (463 patients)*, two tests (Comp PIC and Amsler grid) emerged as the most useful ones. They were selected to form the 2-test battery. Venn diagrams in fig 3.39 show the number of patients in the 4 groups failing each test/test combination of the 2-test battery. As the fail criteria for both tests (derived from the ROC curves in 3.3.2) were the same for the screening of DR alone and for the screening of DR and/or other complications, the following analysis applies to both situations. To reiterate, the fail criteria for the two tests in the 2-test battery are:

Comp PIC : "at least one plate error"
Amsler grid : "any reported areas of defect on the grid"

Table 3.33 shows the mean number of tests failed by the 4 groups of patients with this 2-test battery. ANOVA revealed significant differences in the mean number of tests failed by the 4 groups of patients ($F(3,459)=60.56$, $p<0.05$). Table 3.34 summarises the significance of the differences. Significant differences occurred between all groups except between patients without DR but with complications (group 2) and those with DR alone (group 3). The mean number of tests failed was significantly greater in patients with DR and other ocular complications (group 4) compared to all other groups. Both patients with DR (group 3) and those without DR but with complications (group 2) had significantly greater mean test errors than patients without DR (group 1), but were not significantly different from each other. A similar analysis on patients with *type I diabetes* only (fig 3.39a) by using the t-test ($t=-5.7$, $p<0.05$) revealed that the mean number of tests failed by patients in group 3 (DR alone, n=59) ie. 0.6 sd 0.7 was significantly more than the mean number of tests failed by patients in group 1 (No DR.n=101) ie. only 0.1 sd 0.4.

Relocating ten patients who had received laser treatment from group 4 to group 3 also revealed the same trend of statistical significance ($t=-7.1$, $p<0.05$).

3-test battery

From the *analysis on the 300 patients seen at Whittington Hospital only*, three tests (Comp PIC, Amsler grid and VCTS 6000) were identified as the most efficient ones, and they were selected to form the 3-test battery. Since the fail criterion for each test (derived from the ROC curves in 3.3.2) was different for the screening of DR alone and for the screening of DR and/or other complications, separate analyses were required for the two situations.

For the screening of DR alone, Venn diagrams in fig 3.40 shows the number of patients in the 2 groups of patients failing each test/test combination of the 3-test battery. The respective fail criteria for the tests involved are:

Comp PIC : "at least one plate error"
VCTS 6000 : "a global score less than or equal to 25"
Amsler grid : "any reported areas of defect on the grid"

The mean number of tests failed by patients with DR (group 3) was 1.4 while that of patients without DR (group 1) was 1.1 (significant by t-test, $p<0.05$). A similar analysis on patients with *type I diabetes* only (fig 3.40a) by using the t-test ($t=-3.0$, $p<0.05$) revealed that the mean number of tests failed by patients in group 3 (DR alone, n=26) ie. 1.2 sd 0.7 was significantly more than the mean number of tests failed by patients in group 1 (No DR, n=66) ie. 0.8 sd 0.7. Relocating four patients who had received laser treatment from group 4 to group 3 also revealed the same trend ($t=-3.9$, $p<0.05$).

For the screening of DR and/or other complications, Venn diagrams in fig 3.41 shows the number of patients in the 4 groups failing each test/test combination of the 3-test battery. The respective fail criteria for the tests involved are:

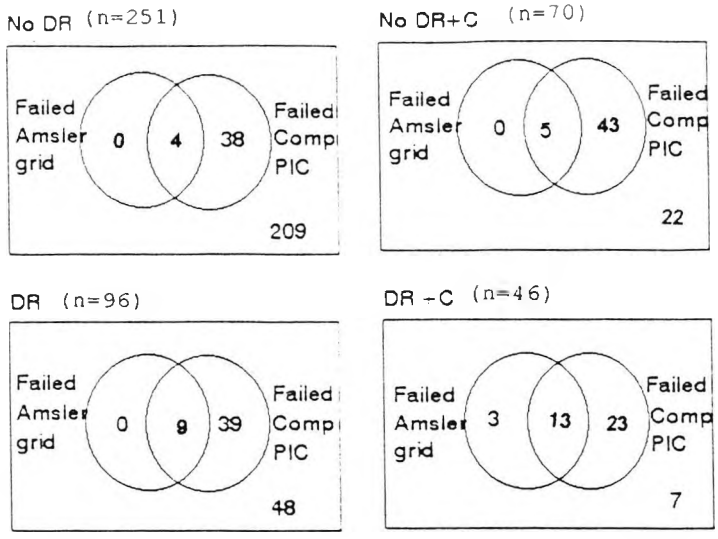


Fig 3.39 The 2-test battery: Number of failures on each test/test combination

Group	Mean number of tests failed
1. No DR	0.2 sd 0.4
2. No DR+C	0.8 sd 0.6
3. DR	0.6 sd 0.7
4. DR+C	1.2 sd 0.6

DR=Diabetic Retinopathy; C=Complications

Table 3.33 Mean number of tests failed per patient: 2-test battery

	No DR+C	DR	DR+C
No DR	$p<0.05$	$p<0.05$	$p<0.05$
No DR+C		NS	$p<0.05$
DR			$p<0.05$

DR=Diabetic Retinopathy; C=Complications

Table 3.34 Significance of difference in the mean number of tests failed between groups: 2-test battery

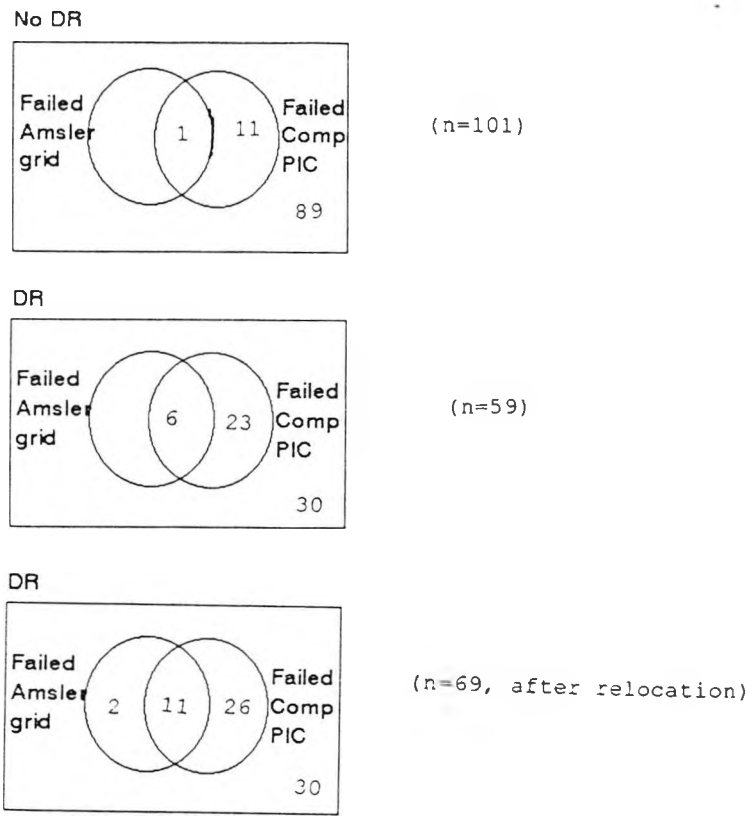


Fig 3.39a The 2-test battery: Number of failures on each test/test combination

(Patients with type I diabetes only)

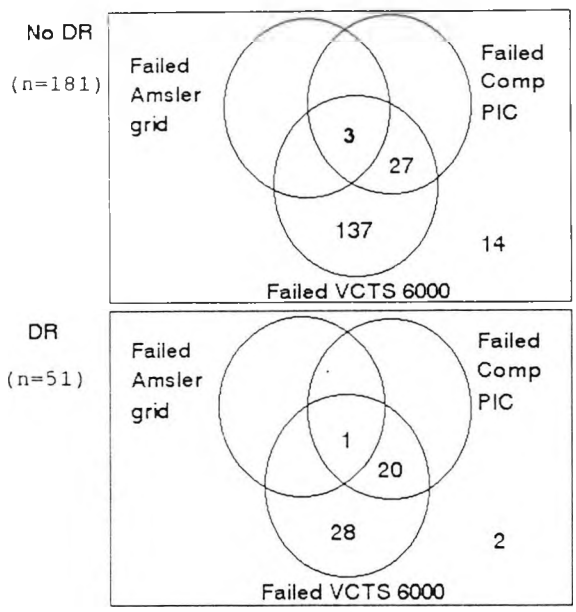


Fig 3.40 The 3-test battery for screening of DR alone: Number of failures on each test/test combination

(Patients at Whittington Hospital only)

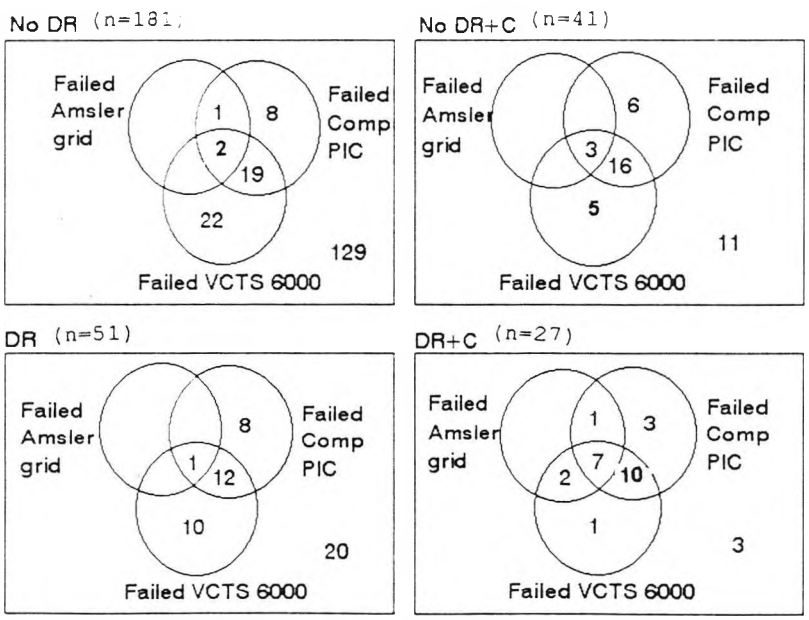


Fig 3.41 The 3-test battery for screening of DR and/or other complications: Number of failures on each test/test combination

(Patients at Whittington Hospital only)

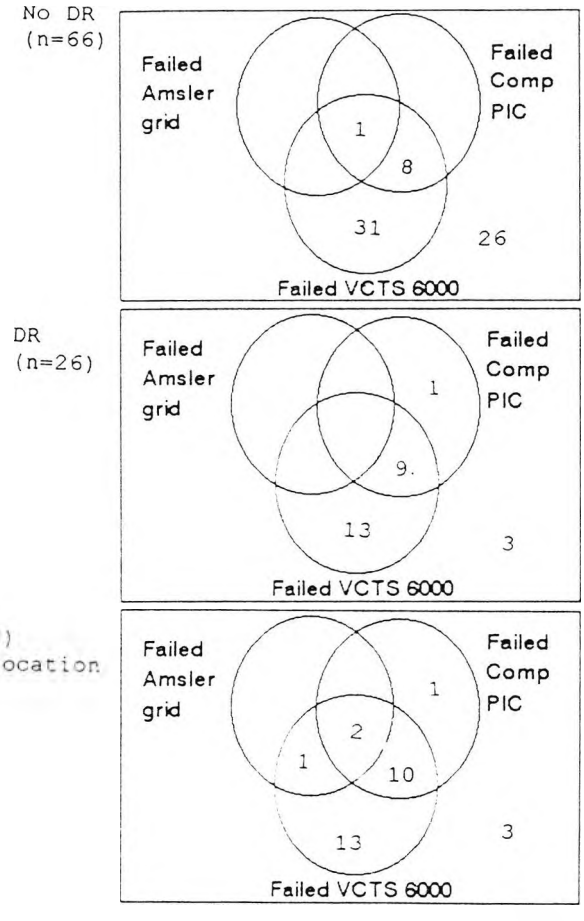


Fig 3.40a The 3-test battery for screening of DR alone: Number of failures on each test/test combination

(Patients with type I diabetes only)

Comp PIC : "at least one plate error"
VCTS 6000 : "a global score less than or equal to 19"
Amsler grid : "any reported areas of defect on the grid"

Table 3.35 shows the mean number of tests failed by the 4 groups of patients. There was a significant difference in the mean number of tests failed (ANOVA, $F(3,296)=35.51, p<0.05$). Table 3.36 summarises the significance of the differences. Significant differences occurred between all groups except between patients without DR but with complications (group 2) and those with DR alone (group 3). The mean number of tests failed was greatest in those who had DR and other complications (group 4). Patients with DR (group 3) and those without DR but with complications (group 2) had significantly greater mean test errors than patients without DR (group 1), but were not significantly different from each other.

3.3.3b Screening efficiency of test battery

1) 2-test battery: Analysis on 463 patients

When the 2-test battery was used to discriminate between patients without DR (group 1) and those with DR alone (group 3), about 83% of patients in group 1 and about 50% of patients in group 3 passed both tests. Only 2% of patients without DR failed both tests vs about 10% of patients with DR. Therefore the results show that while most patients without DR can see the colour plates, about half the eyes with DR can also see them. Table 3.37 shows the screening parameters for the 2-test battery in this screening situation, using two defined fail criteria and each test having the following fail criteria:

Comp PIC : "at least one plate error"
Amsler grid : "any reported areas of defect on the grid"

The highest value of p(N/P) was 0.80, achieved with a fail criterion of "failed any test". The highest value of p(D/F) was 0.68 , which was achieved with a fail criterion of

"failed two tests". Fig 3.42 is the corresponding ROC curve for the test battery. The optimal fail criterion which minimised the rate of misclassification between false positives and false negatives was "failed any test" which gave a sensitivity of 0.51 and a specificity of 0.83.

A similar analysis on patients with *type I diabetes* only (refer to fig 3.39a) shows that in general the sensitivity of the test battery was found to be slightly lower for the criterion "failed any test" but was essentially the same for the criterion "failed two tests"; whereas the specificity was slightly higher for both criteria, compared to the previous analysis. The optimal fail criterion which minimised the rate of misclassification between false positives and false negatives was the same as that obtained in the previous case of analysis (where types I and II patients were grouped together) ie. "failed any test". This gave a slightly lower sensitivity of 0.49 and a slightly higher specificity of 0.88 with associated p(N/P) and p(D/F) values of 0.80 and 0.64, respectively. Relocating ten patients who had been lasered from group 4 to group 3 raised the sensitivity to 0.57 and gave higher values of p(N/P) ie. 0.83 and p(D/F) ie. 0.67. Analysis of type I patients only also revealed slightly higher positive predictive values and similar negative predictive values, as evident in table 3.37a.

When the 2-test battery was used to discriminate between patients without DR (group 1) and the rest of the patients (groups 2,3 and 4 combined), as before about 83% of patients in group 1 passed both tests and so did 36% of those in the other groups. The fail criteria for each test in the battery are similar to the analysis in the first situation. It can be seen that only about 2% of patients without DR failed both tests while the figure for the rest of the patients was about 13%. Table 3.38 shows the screening parameters for the 2-test battery in this second screening situation, using two defined fail criteria. The highest value of p(N/P) was 0.73, achieved with a fail criterion of "failed any test". The highest value of p(D/F)

Group	Mean number of tests failed
1. No DR	0.4 sd 0.8
2. No DR+C	1.3 sd 0.9
3. DR	0.9 sd 0.8
4. DR+C	1.9 sd 0.9

DR=Diabetic Retinopathy; C=Complications

Table 3.35 Mean number of tests failed per patient: 3-test battery for screening of DR and/or other complications

	No DR+C	DR	DR+C
No DR	$p<0.05$	$p<0.05$	$p<0.05$
No DR+C		NS	$p<0.05$
DR			$p<0.05$

DR=Diabetic Retinopathy; C=Complications

Table 3.36 Significance of differences in the mean number of tests failed between groups: 3-test battery for screening of DR and/or other complications

Fail crit.	Sensitivity	Specificity	p(N/P)	p(D/F)	False +	False -
Any test	0.51	0.83	0.80	0.56	0.17	0.49
Two tests	0.10	0.98	0.72	0.68	0.02	0.90

See appendices 3A & 3B for explanation of terms

Table 3.37 Screening parameters of the 2-test battery: Screening for DR alone

Fail Crit	Sensitivity	Specificity	p(N/P)	p(D/F)
Any test	0.49	0.88	0.80	0.64
	(0.57)		(0.83)	(0.67)
Two tests	0.10	0.99	0.72	0.81
	(0.16)		(0.73)	(0.87)

See appendices 3A & 3B for explanation of terms

Table 3.37a Screening parameters of the 2-test battery: *Screening for DR alone among type I patients only (total number of patients = 170)*

+ Numbers in parentheses represent the screening figures after ten patients who had been lasered before were relocated from group 4 to group 3

Fail crit.	Sensitivity	Specificity	p(N/P)	p(D/F)	False +	False -
Any test	0.65	0.83	0.73	0.77	0.17	0.35
Two tests	0.14	0.98	0.56	0.86	0.02	0.86

See appendices 3A & 3B for explanation of terms

Table 3.38 Screening parameters of the 2-test battery: Screening for DR and/or other complications.

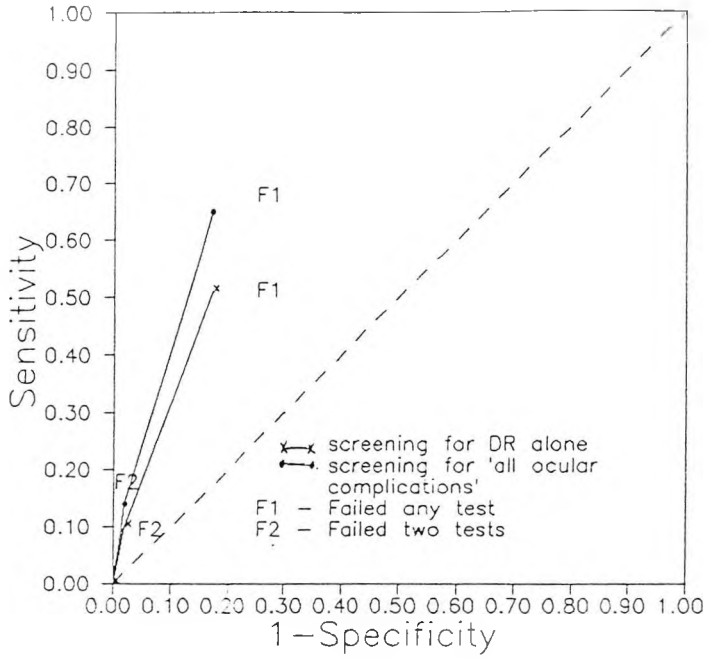


Fig 3.42 ROC curve: 2-test battery

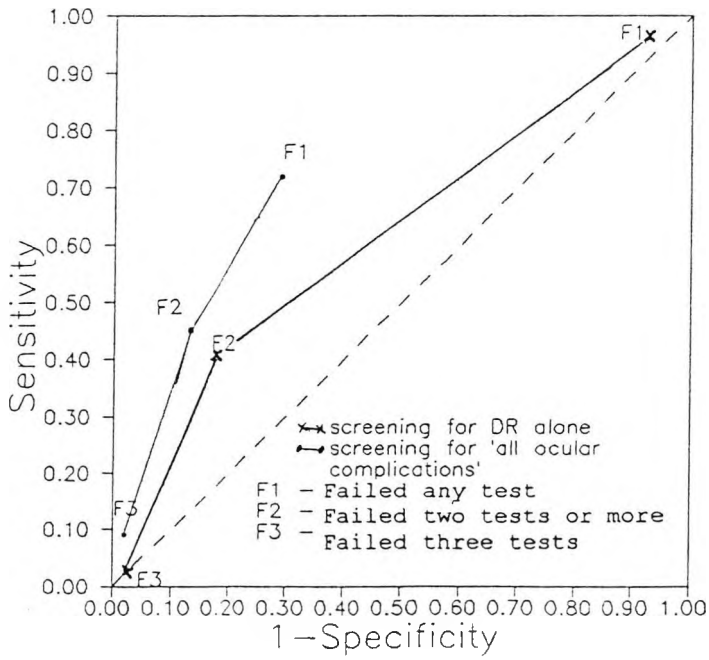


Fig 3.43 ROC curve: 3-test battery

was 0.86 which was achieved with a fail criterion of "failed two tests".

Fig 3.42 also shows the ROC curve of the test battery in the second situation. The optimal fail criterion which minimised the rate of misclassification between false positives and false negatives was "failed any test". This gave a sensitivity of 0.65 and a specificity of 0.83.

2) 3-test battery: Analysis on 300 patients only

When used for discriminating between patients without DR (group 1) and those with DR alone (group 3), 7.7% of patients in group 1 and 3.9% of patients in group 3 passed all three tests. Similar percentages of patients without DR and with DR failed all three tests ie. about 2%. Note therefore that if three tests were used, then apparently most patients could not pass all three tests (93% of all 300 tested), indicating that the number of false positives was outrageously high if failure was to be defined as "failed any test" since most patients tested had no DR. The main reason for this being, that most would be failing the VCTS 6000 at that particular fail criterion which was derived before hand (see below). Table 3.39 shows the screening parameters for the 3-test battery in this situation using three defined fail criteria with each test having the following fail criteria:

Comp PIC : "at least one plate error"
VCTS 6000 : "a global score less than or equal to 25"
Amsler grid : "any reported areas of defect on the grid"

The highest value of p(N/P) was 0.82, achieved with a fail criterion of "failed any test". The highest value of p(D/F) was 0.51 which was achieved with the fail criterion "failed two tests or more".

Fig 3.43 is the corresponding ROC curve for the test battery. The optimal fail criterion which minimised the rate of misclassification between false positives and false

negatives was "failed two tests or more". This gave a sensitivity of 0.41 and a specificity of 0.77.

A similar analysis on patients with *type I diabetes* only (refer to fig 3.40a) shows that in general the sensitivity of the test battery was found to be lower whereas the specificity was slightly higher compared to the previous analysis. The optimal fail criterion which minimised the rate of misclassification between false positives and false negatives was the same as that obtained in the previous case of analysis where types I and II patients were grouped together ie. "failed two tests or more". This gave a slightly a lower sensitivity of 0.35 and a higher specificity of 0.86 with associated p(N/P) and p(D/F) values of 0.76 and 0.52, respectively. Relocating ten patients who had been lasered from group 4 to group 3 raised the sensitivity to 0.43 and also gave higher values of p(N/P) ie. 0.52 and p(D/F) ie. 0.57. Analysis of type I patients only also revealed slightly higher positive predictive values and almost similar negative predictive values (especially at less stringent cut-off criteria), as evident in table 3.39a.

When used for discriminating between patients without DR (group 1) and the rest of the patients (groups 2,3 and 4 combined), 71.2% of patients in group 1 passed all three tests and so did 28.6% of those in the other groups. Only 1.1% of patients without DR failed all three tests while 9.2% of the rest of the patients did. Table 3.40 shows the screening parameters for the 3-test battery in the second situation. The highest value of p(N/P) was 0.79, achieved with a fail criterion of "failed any test". The highest value of p(D/F) was 0.78 , which was achieved with a fail criterion of "failed all three tests".

Fig 3.43 also shows the ROC curve of the 3-test battery in the second situation with each test having the following fail criteria:

Comp PIC : "at least one plate error"

Fail Crit.	Sensitivity	Specificity	p(N/P)	p(D/F)	False +	False -
Any test	0.96	0.08	0.82	0.31	0.92	0.04
Two tests	0.41	0.83	0.77	0.51	0.17	0.59
Three tests	0.02	0.98	0.70	0.30	0.02	0.98

Crit=Criterion

See appendices 3A & 3B for explanation of terms

Table 3.39 Screening parameters of the 3-test battery: Screening for DR alone

Fail Crit	Sensitivity	Specificity	p(N/P)	p(D/F)
Any test	0.88 (0.90)	0.39	0.88 (0.90)	0.38 (0.39)
Two tests	0.35 (0.43)	0.86	0.76 (0.78)	0.52 (0.57)
Three tests	0.00 (0.07)	0.98	0.70 (0.71)	0.00 (0.60)

See appendices 3A & 3B for explanation of terms

Table 3.39a Screening parameters of the 3-test battery: *Screening for DR alone among type I patients seen at Whittington Hospital only (total number of patients = 92)*

+ Numbers in parentheses represent the screening figures after four patients who had been lasered before were relocated from group 4 to group 3

Fail Crit.	Sensitivity	Specificity	p(N/P)	p(D/F)	False +	False -
Any test	0.72	0.71	0.79	0.63	0.29	0.28
Two tests	0.45	0.87	0.70	0.71	0.13	0.55
Three tests	0.09	0.98	0.62	0.78	0.02	0.91

Explanation of terms as per table 3.39

Table 3.40 Screening parameters of the 3-test battery: Screening for DR and/or other complications

VCTS 6000 : "a global score less than or equal to 19"
Amsler grid : "any reported areas of defect on the grid"

The optimal fail criterion which minimised the rate of misclassification between false positives and false negatives was "failed any test". This gave a sensitivity of 0.72 and a specificity of 0.71. Note that the fail criterion for the VCTS 6000 was different in this situation compared to the first situation; hence this explains the rather large difference in the sensitivity/specificity values of the test battery obtained in the latter situation.

Appendix 30 is the computer print-out showing the results of all patients examined.

3.4 DISCUSSION

The present study showed that on the basis of ROC analysis the Comp PIC was the best test (of all the tests evaluated) for screening of DR in a group of mixed type I and II diabetic patients (sensitivity=0.51; specificity=0.83; p(N/P)=0.80 and p(D/F)=0.56). Combining different visual function tests such as the VCTS 6000 and Amsler grid in a battery did not reveal any significant improvement over the sole use of the Comp PIC test. In fact with the VCTS 6000 in the test battery, too many false positives resulted even when the fail criterion used for the VCTS 6000 was the one that was found to be optimal (within the circumstances) for discriminating between patients without DR and those with DR. In such a battery it was also noted that patients who failed the Amsler grid would have also failed the Comp PIC but not vice-versa.

The following discussion of findings pertains to results which were obtained from a group of patients which comprised a mixture of types I and II diabetics. Thus the comments that follow must only be taken to apply to a heterogenous group of diabetics, and not to a single group of type I or type II patients. A separate subanalysis of

type I patients only was undertaken and the results have been detailed in the results section of the chapter; these will be discussed at the end.

3.4.1 Visual acuity (VA)

The major finding of this section of the study is that the optimum fail criterion for the VA pinhole test for determining normality in diabetics is 6/5. Although this fails 53% of patients without DR, it detects 77% of patients with significant ocular pathology and gives a probability of not having DR of 0.70 given a pass result. VA of less than 6/9 is found to yield a probability of having significant pathology of 0.81 given a fail result, although it detects only 17% of such patients (while failing only 4% of those without DR). It must be borne in mind that the screening requirements of this study removed patients with VA lower than 6/12; if there had not been such an exclusion, and if galucoma and/or cataract were more common than DR, the sensitivity might have been reduced if the VA limitation were to have been relaxed.

The results also indicate that within diabetics in the present study sample, VA is worst in those with ocular complications and that DR *per se* is not shown to be a determinant of poor VA. There was no significant difference in the mean VA between the group without DR (group 1) and the group with DR (group 3). The presence of other complications such as glaucoma, age-related maculopathy, cataracts, previous laser therapy etc in diabetics as a whole seems to be a major factor in causing a decrement in VA, irrespective of the presence of DR. This is further illustrated by the insignificant difference between the mean VAs of the groups without DR with complications and the group with DR plus complications (groups 3 and 4). However had the sample included more patients with severe DR, it would have been possible to demonstrate the major visual impairments that result from severe changes of DR such as proliferative DR and maculopathy, as are normally stated in the literature.

Age is found to be significantly correlated to LogMAR VA. The fall in VA with age found (0.03 LogMAR units per decade) is in reasonable agreement with Weale's findings (Weale,1982). The present study is consistent with those of Klein et al.(1984a) and Jerneld & Algvere (1987) regarding the effect of age and insulin therapy on VA in diabetics. The present data does not show the effects of diabetes duration and DR, as noted by Jerneld & Algvere (1987). This may be due to differences in the sizes of the samples; the present study had relatively small numbers. The present findings emphasise that the effects of DR and duration of diabetes are much less significant than the effects of age and complications. Pooling of results from the two venues does not seem to have any effect on the VA performance indicating how robust VA measurements are with respect to lighting levels.

According to Jerneld & Algvere (1987) the major cause of severely impaired vision in insulin-taking patients is DR whereas in the non insulin-taking patient the major causes are cataracts and age-related maculopathy. The lack of a DR effect on VA in the present study does not contradict this finding. DR has been associated with relatively good VA; Beetham (1963) reported that 50% of those with proliferative DR had "fairly good" vision. McLeod et al.(1988) found only 3% of his sample had a corrected VA of less than 6/24 which was attributable to DR. In the present study, cases with severely impaired VA have been excluded in the selection of patients for entry into the study.

The results of the present study confirm that VA deficit in diabetics within the study sample (of mixed types I & II patients) is mostly caused by other complications other than DR such as cataract and age-related maculopathy. This is evident from the low mean VA demonstrated by the group with complications (groups 2 and 4); these groups also had an older mean age and a higher proportion of non insulin-taking patients. A sub-analysis on patients with type I diabetes only was also undertaken, and this is discussed later. An increased incidence of cataract, age-related

maculopathy, DR and glaucoma are generally all associated with advancing age (Leibowitz et al.1980).

The VA test is found to be an inefficient clinical test for the screening of DR only. The ROC curve for this test gives a sensitivity of 0.63 and a specificity of 0.47 using a 6/5 cut-off (note that as explained earlier, if there had been no VA exclusion criterion the same figures would not have been obtained). However, considerations of double cut-off criteria as advocated by Hill (1987a) reveal VAs of 6/5 and 6/9 as appropriate cut-offs. The former (6/5), minimises false negative errors for decisions of p(N/P) and the latter (6/9) minimises false positive errors for decisions of p(D/F). Using a cut-off VA of 6/5 the probability of being free from DR is 0.75 having passed the test. Alternatively, using a VA cut-off of less than 6/9, the probability of a patient having DR is 0.52, having failed the test. A patient with a VA that falls between 6/5 and 6/9 presents to the examiner an uncertainty in making a decision of either DR or no DR.

The present study shows that the screening efficiency of the VA test is slightly better in the second situation i.e. when the test is used to discriminate between those without DR (group 1) and the rest of the patients (groups 2,3,4 combined). A VA of 6/5 is identified to be the optimum operating criterion. This gives a sensitivity of 0.77 and a specificity of 0.47. There is a slight fall in the value of p(N/P) relative to the first situation, but this is made good by an increase in p(D/F) ie. more confidence in having an ocular complication given a failure on the test. Consideration of double cut-off criteria reveals 6/5 and 6/9 as satisfactory cut-offs. A cut-off VA of 6/5 gives the probability of being normal as 0.70, having passed the test. On the other hand, a VA of less than 6/9 gives the probability of a patient having DR and/or other complications as 0.81.

Corcoran et al.(1985) suggested that using a VA cut-off of 6/12 the pinhole VA test was useful in detecting 72% of

diabetic patients with "clinically discernible eye disease". Although Corcoran et al.(1985) did not use the same exclusion criteria, their results are in close agreement with the results of the present study, where a cut-off of 6/5 gives a sensitivity of 0.77 in detecting all patients with ocular complications, DR or otherwise. The results of the present study suggest that a VA of less than 6/9 with the pinhole in diabetics is an important signal. It warns the clinician of the probable presence of pathology which could be related to diabetes.

The pinhole VA test also proves to be a highly specific test at the 6/9 cut-off level, with a specificity of 0.96. The use of a "pinhole" in a general screening situation has been shown to reduce the number of false positives by half (Loewenstein et al.1985). The present study confirms its utility.

3.4.2 Colour vision

As remarked before, the results indicated that the colour vision tests investigated in the present study were generally not discriminatory for the purpose of detecting DR within a heterogenous population of diabetics. However, amongst the tests evaluated this section of the study has identified the Comp PIC as the best colour vision test for discriminating patients with DR from those without DR. This is evident from the comparison of ROC curves. The ROC curves for the D15(5/2) and LTA plate 5 show that these two tests are comparable. The relatively good Bayesian probabilities on passing the test (p(N/P)) and on failing it (p(D/F)) add to the good screening utility of the Comp PIC.

Table 3.41 compares the screening parameters of each test using fail criteria derived from the respective ROC curves. The Comp PIC plates afford the best detection rate (51%) and this is followed by the D15(5/2) (43%) and LTA plate 5 (13%). More confidence is attached to the normality of a patient when he passes the Comp PIC (p=0.80) than with the

other two tests. The probability of a patient having DR when he fails a particular test is low for the 3 tests individually; the best is by the Comp PIC (p=0.56), the second by LTA plate 5 (p=0.53) and the third, by the D15(5/2) (p=0.40).

When the three tests are compared in their use for screening for any ocular complication in diabetics (table 3.42), there is a general increase in the values of p(D/F) for all the tests (using fail criteria derived from ROC curves for the second purpose). There is also an associated decrease in the values of p(N/P) for all tests (compared to table 3.44). For decisions of normal having passed the test, the Comp PIC plates afford the best confidence level (p=0.73) among the three tests. For decisions of abnormal (having failed the test) the Comp PIC and LTA plate 5 are comparable in their confidence limits (p=0.81). The D15(5/2) test provides the worst probability for such decisions (p=0.77).

For both screening purposes, the D15(5/2) and LTA plate 5 are comparable in their ROC performance. However, the D15(5/2) test has better sensitivity. Since the prevalence of DR and/or other complications in this survey is higher than that of DR alone, a test with a higher sensitivity (albeit lower p(D/F)) is desirable. Hence, for the second purpose at least, the D15(5/2) may be taken as the better test of the two because of its higher sensitivity.

Two cut-off criteria could be set for the Comp PIC in order to maximise both probabilities p(N/P) and p(D/F). The first criterion is "at least one plate error" and the second is "5 or more plate errors". The former represents a 92% confidence limit for decisions of normal and the latter represents a 94% confidence limit for decisions of DR. Similarly, in screening for "any ocular complications" the same criteria would give an 85% chance of being normal (no DR and/or other complications) and a 98% chance of having an abnormality.

Test	Sensitivity	Specificity	p(N/P)	p(D/F)
Comp PIC	0.51	0.83	0.80	0.56
LTA plate 5	0.13	0.95	0.72	0.53
D15(5/2)	0.28	0.82	0.73	0.40

See appendices 3A & 3B for explanation of terms

Table 3.41 Screening parameters of all the colour vision tests (using optimum fail criteria): Screening for DR alone

Test	Sensitivity	Specificity	p(N/P)	p(D/F)
Comp PIC	0.64	0.83	0.73	0.81
LTA plate 5	0.24	0.95	0.59	0.81
D15(5/2)	0.43	0.82	0.50	0.77

Explanation of terms as per table 3.41

Table 3.42 Screening parameters of all the colour vision tests (using optimum fail criteria): Screening for DR and/or other complications

With LTA plate 5, only one criterion is possible, hence similar manipulation cannot be done. With the D15(5/2) test. for screening of DR alone, the confidence limits afforded by the test are very low in both decisions for normal and DR. If the fail criterion is set at "a score greater than 2", there is only a 71% chance of the patient being normal having passed the test. In order to get a satisfactory confidence limit for the decision of DR when a patient fails the test, the fail criterion has to be set very high i.e. "a score greater than 44".

In screening for "any ocular complications", the confidence limits for decisions of normal afforded by the D15(5/2) test are not found to be satisfactory. At best, a fail criterion set at "a score greater than 14" will only give a 50% chance of being normal (having passed). On the other hand, relatively good confidence limits are possible for the decision of disease; a fail criterion set at "a score greater than 39" gives an 89% chance of having some sort of ocular complication, having failed the test.

The Comp PIC compare very favourably with the the FM 100-H test in the screening of DR i.e. about 55% (Bresnick et al.1984b; Green et al.1985). Additionally, the Comp PIC prove to be more specific, failing only 17% of those without DR. The FM 100-H test was quoted to fail 32% of diabetics without DR (Green et al.1985).

It is shown in the present study that better discrimination is achieved with all the tests when they are used for screening diabetics with DR and/or other complications. The ROC curves still single out the Comp PIC as the best when compared to the other two tests. In essence, the results from the three colour vision tests confirm the association of poor colour vision and DR, but the results also show that the presence of "ocular complications" adds significantly to the severity of colour vision defect in these patients. The presence of a tritan defect in ocular diseases such as found in this sample (cataracts, age-related maculopathy, glaucoma etc) is well documented

(Krastel & Moreland,1991).

Results from the multivariate analysis confirm the contribution of age on the results of the tritan plates in the Comp PIC series. Although this was not apparent on the other tests used, the association between age and tritan defect is well established (Ruddock,1965a & 1965b; Pinckers,1980). The acquired red-green defect in the sample is not found to have any association with age, implying minimal influence of age on such acquired defects. Other factors identified as significant determinants of the colour vision test results are: insulin therapy and VA. VA within the range studied (6/5 to 6/12) is significantly associated with all the test results, thus agreeing with Birch (1988) of the importance of VA in the testing for acquired colour vision defects. Insulin therapy is negatively correlated with both the scores and the number of tritan axes the D15(5/2) test ie. better colour vision with insulin therapy. This is in contrast with Trick et al.(1988) but in agreement with Begg & Lakowski (1980). No information on the actual blood glucose levels was available at the time of testing; even if it is assumed that patients taking insulin had poor metabolic control, the large degree of variation in each patient's blood glucose quite possibly had obscured any meaningful relationship between insulin therapy and the D15(5/2) results (Schneck et al.1991). The results of a sub-analysis carried out on patients with type I diabetes only will be discussed later.

As the results of the Comp PIC and LTA plate 5 were pooled from the two venues, the influence of venue found on the results, is discussed in chapter 7.

The finding of acquired colour vision defects in patients with no visible fundus lesions (false positives) could also indicate the presence of "subclinical DR". Acquired colour vision defects in diabetics have been noted in early DR and in patients without ophthalmoscopically visible DR (see 1.1.2b). Whether these false positives will eventually

develop DR is controversial, and can only be answered by a longitudinal study.

3.4.2a Comp PIC

The same "tritan" plates in the Comp PIC series have been reported to detect 50% of "eyes" with DR and 15% of "eyes" without DR (Birch & Ariffin,1990). Results of the present study show 48.5% of patients with DR failed these plates with 16.6% false positives. Although these results are not too inconsistent with those of Birch & Ariffin (1990), considering the better approach taken in the present study, the present results give a more realistic picture of the performance of these plates. The present study confirms the preliminary observations by Birch et al.(1987) and Birch & Ariffin (1990) of the usefulness of these tritan plates for detecting severe forms of DR. The present study found that these plates detected 11 of 41 patients with minimal DR, 24 of 40 patients with moderate DR, 6 of 8 patients with proliferative DR and 7 of 7 patients with maculopathy. Figs 3.2 & 3.4 show plates 10, 12,13 and 14 to be the most useful ones.

The Comp PIC series also contained a few of the "best-identified" Ishihara plates (Birch,1974). Plates 6,7 and 8 appear to be the most useful ones, plates 2,3,4 are less useful while plate 5 is not very useful (figs 3.2 & 3.4). Birch et al.(1987) stated that these Ishihara plates were failed mainly by eyes with more severe DR. In the present study, only 7 patients (7.2%) failed them, a low detection rate compared to the figure (42.9%) by Birch et al.(1987). The consideration of "eyes" rather than "patients" and the small number of patients in the sample of Birch et al.(1987) could explain this large discrepancy. Only one patient without DR (of 251) in the present study failed them while 3 out of 7 with DR who failed them had either severe DR or maculopathy. This confirms that the plates are failed mainly by those with severe DR.

Red-green plate errors (on the Comp PIC) occurred

significantly more in the group without DR but with complications (group 2) than in the group without DR (group 1). This was expected, as those who failed only the red-green plates are those with congenital colour-vision defects. There is no significant difference in the red-green plate errors between those with DR and those without DR. This shows the relative unimportance of red-green defects in distinguishing between patients with DR from those without DR. In fact, no patient with DR alone made sole red-green plate errors.

The usefulness of red-green plates for detecting DR as suggested by Birch (1988) cannot be justified here. Fig 3.6 shows that none of the patients with DR alone or with other complications (groups 3 and 4) failed these plates solely. Those who did fail, failed the tritan plates concomitantly. Had the red-green plates not been used, no information would have been lost. The only possible use for these red-green plates is in indicating the severity of the condition. Out of the 15 patients (in groups 3 and 4) who failed both red-green and tritan plates, 6 had previously received laser photocoagulation treatment, 4 had maculopathy or proliferative DR and 5 had minimal or moderate DR.

The presence of sole acquired red-green defects in diabetics is very unlikely (Lagerlof,1984). In the present study "mixed defects" are generally found in patients with more severe degrees of DR and in those who have had laser photocoagulation treatment. The finding of the present study of a trend toward red-green defect (in addition to the tritan defect) in patients who have had laser photocoagulation treatment is contrary to reports by Birch-Cox (1978) and Birch & Hamilton (1981) who demonstrated an increase in the severity of the tritan defect. The present results concur with Mantyyjarvi (1987a), who also found similar "mixed" red-green and tritan defects in her sample of patients who had received laser photocoagulation treatment. Nevertheless, it could be the further activity of the retinopathy that was causing the involvement of the

red-green system (Cambie,1980; Lavergne & Ramioul-Gougnard,1980) in the present sample. Interestingly, a small number of patients with less severe DR manifested red-green defects on the Comp PIC. This supports the observation that patients with even mild degrees of DR may have equal changes to both the red-green and blue-yellow channels (Spafford & Lovasik,1986; Trick,1988; Trick et al.1988).

In the present study only 3 patients with DR alone failed the single SPP1 plate used (plate 9). These 3 had either moderate DR or maculopathy. Those with DR and complications who failed it (n=7) were mainly those who had been treated with laser photocoagulation for DR (n=5). Thus patients who have had laser treatment for DR are likely to fail the plate, indirectly implying the plate's ability to detect severe forms of DR (Birch et al.1987). Results of the present study also show that this plate was not failed by "normal" patients (group 1). However, it was also failed by a few with cataract (4 patients) and glaucoma (2 patients) even without any DR.

3.4.2b LTA plate 5

The small detection rate (13.4% for DR) by LTA plate 5 is not too different with results reported previously. Birch & Ariffin (1990) and Birch et al.(1991) reported that the detection rate of "eyes" with DR with this plate (including eyes which had received laser treatment) was between 20 to 25%. However, in their data, when eyes which had been lasered are removed, the detection rate is only 15%.

Of the 13 with DR who failed this plate, 6 had proliferative DR and/or maculopathy. The plate also detected 10 patients with cataracts out of 16 without DR but (with other complications) who failed it. Furthermore, the plate detected 14 patients who had received laser treatment out of the 19 with DR and complications who failed it. These findings support the claim by Birch et al.(1987) and Birch et al.(1991) that the LTA is only

failed by patients with severe DR with macular involvement, and by those having DR with media opacities. One more condition could be added i.e. patients who have had laser treatment. The same conclusion as that of the present study was reached by Mantyjarvi et al.(1988) and Mantyjarvi (1989a) with regards the sensitivity of the test in picking up only severe DR, and those with complications However, some may still be undetected. The present study also recorded 12 (4.8%) of patients without DR failing this plate, agreeing with Birch et al.(1991) and Birch & Ariffin (1990) who stated that about 5% of "eyes" without DR failed it.

3.4.2c D15(5/2)

The D15(5/2) failed to show any significant differences in the number of red-green axes across the four groups of patients. Despite the presence of congenital colour vision defect (n=6) in the group without DR but with complications (group 2), the D15(5/2) was not sensitive enough to show any statistically significant differences. This was despite the claim of increased in the sensitivity of the test by Dain & Adams (1990).

The results of the D15(5/2) showed none with "mixed axes" in the DR group (group 3). There was 1 patient with "mixed axes" in the group with DR and complications (group 4); this patient had received laser treatment for DR before.

Allowing for minor errors (scores of less than or equal to 4), the test detected 63% of patients with DR and 58% of those without DR. These results do not concur with those of Bresnick et al.(1984b) who found the test to be useful. The older mean age of patients in the present could explain the discrepancy. The present results, however, agree with Birch et al.(1991) that the test gives too many false positives in diabetic patients. Even if the fail criterion was made very low ie. by failing only those who exhibited an axis, the test only detects 2 patients with proliferative DR or maculopathy (out of 7 in the group with DR ie. 3 with

maculopathy and 4 with proliferative DR). This illustrates that the test is not even "severity-specific".

In summary, the present study has demonstrated that a proper selection of PIC plates (comprising red-green and tritan plates) can be used as an effective clinical tool for the screening of patients with DR or other ocular pathology related to diabetes.

3.4.3 Contrast sensitivity (CS)

The present study has identified the VCTS 6000, of the two CS tests, as having better measures of test performance. For the sole screening of DR, the ROC curve for the VCTS 6000 is seen to be superior. The detection rate of DR by the VCTS 6000 is 92% with a false positive rate of 66%, using the optimum ROC-derived fail criterion. With this fail criterion (global score less than or equal to 25) there is more confidence attached to a pass result (p=0.91) than to a fail result (p=0.37).

The fail criterion which gives a 100% confidence level for decision of DR (having failed) is "a global score of 10 or less" which generates a sensitivity of only 0.02. However, if a slightly higher sensitivity is desired for decisions of DR, another fail criterion can be chosen; the next best (" a global score of 13 or less") has a sensitivity of 0.14 but will only generate a 54% confidence level for decision of DR, having failed the test. Whatever the two chosen criteria (for maximising the values of p(N/P) and p(D/F), any performance falling between them will represent uncertainty in either decision for normal or DR.

Performance of each test improves when used for detecting "related ocular complications" in diabetics. This is evident from the improved ROC curves of both tests. The VCTS 6000, especially, improves markedly. Although the detection rate for the VCTS 6000 decreases in this situation compared to previously (0.59 vs 0.92), nevertheless, the rate of false positive misclassification

is very much reduced. The specificity of the VCTS 6000 now improves to 0.76 (compared to 0.34 previously). There is a general increase in the values of p(D/F), with an associated decrease in the values of p(N/P) (table 3.30). There is therefore more confidence in a diabetic patient having some sort of ocular complication given that he fails the test (than just having DR alone).

Taking an 88% confidence limit for decisions of normal (having passed the VCTS 6000), a fail criterion can be chosen as "a global score of 28 or less" with a low 8% rate of false negatives. On the other hand, the fail criterion which gives a 100% confidence level for decision of abnormal (having failed the test), is "a global score of 10 or less". The sensitivity is only 0.08 with this fail criterion. If a slightly higher sensitivity is desired for decisions of abnormal, another fail criterion has to be chosen. The next best (global score of 13 or less) only generates a 74% confidence level but with a slightly improved sensitivity rate of 0.24. Whatever the two chosen criteria are for maximising values of p(N/P) and p(D/F), any performance falling between them will represent uncertainty in either decision for normal or abnormal.

Strictly it would appear to be inappropriate to compare the two tests (VCTS 6000 vs Arden gratings) whose data were obtained on two different populations (Henson & Dix,1984). This is no doubt a weakness of the study as a result of various constraints. Despite this, the VCTS 6000 is obviously superior to the Arden gratings.

3.4.3a Arden gratings

In general, the results of the present study support the view that the Arden gratings are not useful as a screening tool for DR (Ghafour et al.1982; Moloney & Drury,1982). Furthermore, although the presence of an ocular complication (besides DR) elevates the score, it does not necessarily make the score significantly worse than in the presence of DR alone. Even in the presence of both DR and

other complications, the scores are not always consistently worse than in the presence of ocular complications alone.

The present study did not find DR *per se* to have a significant influence on the scores; no significant differences were found in the scores of the individual plates between those with DR and those without DR (appendix 3D). This finding disagrees with Ghafour et al.(1982); the difference between the present results and those of Ghafour et al.(1982) could be due to the older mean age of the patients in the present study.

The total score on the Arden gratings is found to be significantly affected by age and VA rather than "diagnostic group". This explains the poor discriminatory ability of the Arden gratings. Arden (1978a) reported that "...in the age range 11 to 70 there was no influence of age..". Skalka (1980), on the other hand, noted a significant increase in test scores with increasing age irrespective of spatial frequency. Sokol et al. (1980) stated that a high percentage of false positives occur in older normals; they suggested that caution be exercised when testing patients older than 50 years old. In the present study the dependence on age was particularly reflected in the performance on plate 2. VA affects the performance of Arden plates with high spatial frequency (plates 6 and 7). The relationship between CS and VA is widely noted (Marmor,1986; Marmor & Gawande,1988). Uncorrected refractive blur has been reported to adversely affect the scores on plates 6 and 7 (Minassian et al.1978). The only plates whose visibility are not affected by refractive error are plates 2, 3 and possibly 4 (Marmor,1986). Hence the high incidence of false positives reported previously (Sokol et al.1980; Weatherhead,1980) with the Arden gratings was largely attributed to uncorrected ametropia by Yap et al.(1985). Patients in the present study were appropriately corrected for the test, therefore negating the influence of uncorrected ametropia.

Only plates 3 and 4 are affected by "diagnostic group".

Plates 5 and 7 are found to be affected by insulin therapy, where a negative relationship is noted. These results agree with Sokol et al.(1985) who found that patients with non-insulin dependent diabetes tended to have poor CS irrespective of the presence of DR. The results of patients with type I diabetes only are discussed in at the end of this discussion section.

The literature is equivocal about the ability of the Arden gratings to detect ocular abnormalities. Moloney & Drury (1982) detected 45.3% of patients with DR, using a score that exceeded 82 as the fail criterion. The present study (using such similar criterion) recorded 53%; however, they recorded 58.2% false positives while the present study only had 51% false positives. The finding of false positives could indicate the presence of "subclinical DR" no doubt, since CS deficits have been noted in early DR and in patients without ophthalmoscopically visible DR (Ghafour et al.1982; Skalka & Helms,1983; Hirsch & Puklin,1983).

On the positive side again, using the fail criterion of "score exceeding 82", Yap et al.(1985) detected 92.7% of "eyes" with any ocular abnormality while generating only 10% false positives. With similar fail criterion, the present study only detected 67% of patients with any diabetes-related ocular abnormality with 51% false positives. The optimistically high detection rate by Yap et al.(1985) could be due to their study design. Apart from their calculations being based on "eyes", patients were also not randomly selected and the study was not masked.

The screening utility of the Arden gratings has recently been seriously questioned by Reeves et al.(1988), who concluded that the test is largely unreliable as a consequence of its high misclassification rate. This is contrary to the evaluation by Woo & Prentice (1983) who found the test to be a statistically reliable tool for establishing an index of CS. The results of the present study agree with the rigorous evaluation by Reeves et al.(1988) that the Arden gratings produce many false

negatives and false positives, irrespective of whether they are used to screen for DR alone or for screening of any ocular complications in diabetics.

3.4.3b VCTS 6000

With the VCTS 6000, the better discriminatory ability could be explained by the fact that the test in general correlates well with "diagnostic group" (table 3.16). All spatial frequencies (apart from the middle spatial frequency B) are similarly affected by 3 factors: diagnostic group, age and VA. The age dependence of this test has been reported by Scialfa et al.(1988). Similarly, the VA dependence of the test has been demonstrated (Rubin,1988; Scialfa et al.1988). "Diagnostic group" does not feature as a significant determinant of the performance on spatial frequency B, while age and VA do (table 3.26). It seems that this particular spatial frequency has very little use for detecting DR and/or other complications in a diabetic patient.

There appears to have been no major evaluation of the VCTS 6000 for its screening efficiency in detecting DR apart from the study by Farber & Lotshaw (1986) which suggested that the test was useful for the screening of DR. However, other studies have produced discouraging results (Reeves & Hill,1987; Hill et al.1989; Wood et al.1989). Harper et al.(1990) concluded that the VCTS tests (both distance and near versions) had poor sensitivity and specificity irrespective of the cut-off criterion chosen. The near version (System 6000) which was used in the present study has been found to compare well with the distance version (System 6500) by Woo & Bohnsack (1986). The results of the present study clearly indicate that for the purpose of screening for ocular complications in diabetic patients, the VCTS 6000 gives clinically useful results.

3.4.4 Visual field

The Amsler grid is demonstrated in the present study as a

test with high specificity. For the screening of DR alone, although the sensitivity is only 0.1, the rate of false positives is a low 2%. When the test is used to screen for any ocular complication, the sensitivity increases slightly to 0.15. The improvement in the performance of the test is, however, minimal in this second situation, as can be seen from the ROC curves (figs 3.37 & 3.38).

For the screening of DR alone, the confidence attached to a pass or a fail result is not too different; a slightly higher confidence level (72%) is attached to a pass result than to a fail result (68%). In screening for any ocular complication, the Amsler grid gives a high predictive value for a positive test result (87%) as a consequence of the high specificity of the test. There is an increase in the value of p(D/F) but with an associated decrease in the value of p(N/P) in this second situation, p(N/P) being 0.57.

The present study generated a similar percentage of false positives (2%) as those found by Birch et al.(1991), but only found the test to detect 10% of patients with DR. The high detection rate recorded by Birch et al.(1991) i.e. 23% was because they considered "eyes" rather than patients, and more importantly, because they included patients with laser photocoagulation treatment into the group with DR. The actual detection rate by Birch et al.(1991) recalculated is only 8%. Adams & Haegerstrom-Portnoy (1987) pointed out that the Amsler grid is not necessarily failed by patients with DR although it is a macular function test. Thus, the low detection rate of the Amsler grid in detecting DR is acceptable.

Birch et al.(1980) noted that the Amsler grid detected all "eyes" with maculopathy in their small series of 5 eyes. In the present study only 2 (out of 7) patients with maculopathy failed the test. Therefore, the present results show that macular lesions may be demonstrated using Amsler grid, but some cases may still escape detection. In fact, it is well established that some patients with

ophthalmoscopically visible macular lesions do not report visual defects on the standard Amsler grid (Wall & May,1987).

Birch et al.(1991) stated that failure on the test indicates the presence of severe DR, particularly maculopathy; the present results indicate that failure is more related to the presence of DR with other complications rather than to the sole presence of maculopathy. The results also show that a high proportion of patients who have had laser photocoagulation treatment failed the Amsler grid ie. 11 of 17 (with DR and complications who failed) had been lasered before.

Performance with the Amsler grid is significantly determined by "diagnostic group". Duration of diabetes, age, insulin therapy and VA have no significant influence. The present study found DR to have a significant influence on the results of the Amsler grid. The presence of other complications (in the absence of DR) has no significant influence on the results of the Amsler compared to those without DR. However, despite the higher percentage of patients with DR alone failing the test, compared to those without DR but with complications, the difference did not reach statistical significance. Nevertheless, the presence of DR with an ocular complication is very likely to result in a failure on the Amsler grid. Birch et al.(1991) assert that (in addition to diabetic maculopathy) the Amsler grid is useful for detecting age-related maculopathy; the present study confirms this. Also the different venues involved did not have any significant influence on the results.

The non-significant effect of VA on the Amsler grid performance is not surprising considering that both tests evaluate different extent of central vision. The non-dependence of the test on VA could be useful in that the test could be used to pick up defects in maculopathy patients with relatively good VA as suggested by Birch et al.(1980). The total number of patients with maculopathy in

the present study is too small (n=7) in order to examine this point in detail. Looking at individual patients it is seen that only those with maculopathy with reduced VA (2 patients) failed the test. Of the 5 maculopathy patients who passed, 4 had 6/6 or better.

The finding of false positives could indicate the presence of "subclinical DR". Field defects on the Amsler grid have been noted in patients without ophthalmoscopically visible DR (Wall et al.1990). Macular oedema can also occur in diabetics without the usual lesions of DR such as microaneurysms, exudates and haemorrhages. Thus, since direct ophthalmoscopy was the sole criterion for the diagnosis of DR in the present study, some cases of macular oedema may have not have been noted; hence making the sensitivity of the Amsler grid artificially low. Macular oedema which occurs in diabetics in the absence of DR is known to progress, causing visual field defects (Klein et al.1984b). Furthermore, Amsler (1949 & 1953) suggested that patients with abnormalities with Amsler grid testing in association with a normal ophthalmoscopic examination may progress to ophthalmoscopically visible lesions.

The present study found the sensitivity of the Amsler grid to be low; not surprising a fact as patients with obvious macular abnormalities have been shown to test negative (Wall & May,1987). Wall et al.(1990) suggested that the sensitivity of the Amsler grid testing for visual loss in diabetics could be improved by decreasing the intensity of the grid (through cross-polarising filters). Nevertheless, the present results indicate that for the purpose of screening for ocular complications in diabetic patients, the conventional Amsler grid is still a useful supplementary test. Birch et al.(1980 & 1991) recommend its inclusion in a battery of visual tests to be used in a diabetic clinic; failure on the grid is implied to indicate macular involvement. However, this needs to substantiated before any firm recommendation could be made. Nevertheless, its high specificity and the high confidence level which can be attached to a positive test result should present no

barrier to its inclusion in such a test battery.

3.4.5 The test battery

As explained in 3.3.3 in view of the way the data was collected, two test batteries were considered.

Data collected on all the patients (N=463) allowed a *2-test battery* comprising the Comp PIC and the Amsler grid to be formulated. The respective fail criterion for each test was:

Comp PIC : "at least one plate error"
Amsler grid: "any reported areas of defect on the grid"

A *3-test battery* comprising the tests: Comp PIC, Amsler grid and VCTS 6000 was also formulated and analysed from the data collected on only 300 patients at Whittington Hospital. These were the only patients who completed the three tests of colour vision, contrast sensitivity and central visual field.

The 2-test battery

With the 2-test battery, in screening for DR alone, the optimal fail criterion derived from the ROC curve gives a sensitivity of 0.51 and a specificity of 0.83. These figures, together with their associated predictive values, are similar to those of the Comp PIC alone (table 3.43). There does not appear to be any added advantage in using the test battery. Similar screening efficiency is well achieved with the use of the Comp PIC alone. In fact, there is more confidence in a patient being normal having passed the Comp PIC than the 2-test battery.

When the 2-test battery is used for screening DR and/or other complications, it gives a sensitivity of 0.65 and a specificity of 0.83. These figures are also similar to those of Comp PIC alone (table 3.44), but the probabilities of a patient having an ocular complication having failed the 2-test battery and the patient being normal having

passed the test battery are inferior to those values afforded by the Comp PIC. This reinforces the statement earlier that the test battery gives no added advantage. In fact, the test battery provides slightly lower confidence levels to a pass or a fail result in the screening of ocular complications in diabetes.

The 3-test battery

With the 3-test battery, in screening for DR alone, the optimal criterion generates a sensitivity of 0.41 and a specificity of 0.83 (table 3.43). Of the tests/test combinations shown in the table, the 2-test battery and the Comp PIC are the better ones in terms of screening efficiency, with both having the same screening efficiency. Similar to what has been noted before there does not appear to be any added advantage in having the VCTS 6000 test in the test battery for the purpose of screening for DR alone. The Comp PIC on its own does the job well enough in the circumstances.

Although the screening efficiency of a test battery (either 2-test or 3-test) for screening of DR alone is similar to that of the Comp PIC, further analysis shows that it is possible to formulate a test battery with good screening properties for the screening of "ocular complications" in diabetes. For this purpose, the 3-test battery proves to be a very efficient test battery (sensitivity=0.72; specificity=0.71) (table 3.44). The better screening efficiency derived here owes to the more efficient fail criterion of the VCTS 6000 in this second siituation. Previously in screening for DR only its fail criterion was "a global score less than or equal to 25"; but now the optimum fail criterion has changed to a less stringent one ie. "a global score less than or equal to 19".

Considering that the prevalence of all complications is higher than that of DR alone, the higher sensitivity afforded by the 3-test battery when compared to the Comp PIC makes it the better test of the two. This is despite the lower confidence levels which are attached to the

Test/ Battery	Sensitivity	Specificity	p(N/P)	p(D/F)	False +	False -
2-test	0.51	0.83	0.80	0.56	0.17	0.49
3-test	0.41	0.83	0.77	0.51	0.17	0.59
Comp PIC	0.51	0.83	0.80	0.56	0.17	0.49
Amsler grid	0.10	0.98	0.72	0.68	0.02	0.90
VCTS 6000	0.92	0.34	0.91	0.37	0.66	0.08

See appendices 3A & 3B for explanation of terms

Table 3.43 Comparison of screening parameters: Screening for DR alone

Test/ Battery	Sensitivity	Specificity	p(N/P)	p(D/F)	False +	False -
2-test	0.65	0.83	0.73	0.77	0.17	0.35
3-test	0.72	0.71	0.79	0.63	0.29	0.28
Comp PIC	0.64	0.83	0.73	0.81	0.17	0.36
Amsler grid	0.15	0.98	0.57	0.87	0.02	0.85
VCTS 6000	0.59	0.76	0.73	0.62	0.24	0.41

Explanation of terms as per table 3.43

Table 3.44 Comparison of screening parameters: Screening for DR and/or other complications

results of the 3-test battery.

For both screening purposes, there are significant differences in the mean number of tests failed among patients, with both test batteries. Patients with DR alone (group 3) fail significantly more tests, on average, than those without DR (group 1). The mean number of tests failed by patients in groups 2,3,4 combined is also significantly more than that of patients without DR (group 1). However, the mean number of tests failed is not found to be related to the sole presence of DR; it is also found to be elevated in patients without DR but with complications.

The rationale for using a test battery is for testing of different aspects of the visual system which are affected by the disease in question. The advantage of a test battery is the increased in sensitivity achieved (Safran,1987); the present analysis shows that a sensitivity of 0.72 is achieved for the screening of all complications with a 3-test battery. The set-back, however, is the reduction in test specificity; the specificity being only 0.71. However, when this specificity figure is not much of a drawback when compared to those of the 3 respective tests (Comp PIC=0.83, Amsler grid=0.98 and VCTS 6000=0.76). It is also acceptable when compared to specificity values obtained by others who have done sensitivity/specificity analysis of combinations of visual tests (Heron et al.1990).

The specificity of a test battery is statistically reduced when different tests are multiplied (Safran,1987). Hill (1987b) argued that a test battery does not necessarily represent a poorly specific tool, however, the tests making up the test battery would have to be carefully chosen and the fail criterion for each constituent test chosen has to be appropriately derived. The analysis presented in this section fulfills these two conditions. It is shown in the present study that three tests of visual function (colour vision, central fields and contrast sensitivity) which are appropriately chosen, give the resultant test battery excellent screening utility for the screening of DR and/or

other ocular complications in diabetes.

Sub-analysis of patients with type I diabetes only (N=204)

The above major discussion is concerned with the analysis of results of all the patients involved in the study ie. a mixed group of patients with types I and II diabetes (N=463). A sub-analysis of patients with type I diabetes only (N=204) was also undertaken to determine whether the statistical evaluation is altered. The following summarise the results of the separate statistical evaluation carried out on patients with type I diabetes only:

1. The same pattern of significance (as was found in the previous mixed analysis) was noted for all the tests (with the exception of one) as regards to the difference in tests scores between patients without DR (group 1) and those with DR alone (group 3).

The only difference was for the VCTS 6000 where it was found that the test now (within type I patients only) was not able to show significant differences in test scores between group 1 and group 3 patients as it was able to in the previous analysis.

2. The specificity of the tests was found to be generally increased except for the VA and VCTS 6000 tests where it was found to be unaltered.

3. The sensitivity of the tests was found to be generally decreased except for the LTA plate 5 and Amsler grid where it was found to be unaltered.

4. The AGT remained as an indecisive test as was revealed in the main mixed analysis.

5. The positive predictive value of the tests was generally found to be increased for the following tests: Comp PIC, LTA plate 5, D15(5/2) and Amsler grid.

Whereas for the VA and VCTS 6000, the positive predictive value was decreased.

6. Relocation of patients who had received laser photocoagulation treatment from group 4 (DR with complications) to group 3 (DR alone) resulted in the increase in sensitivity for all the tests.

7. The optimal cut-off criterion (from the ROC curve) was the same in this analysis (but with obviously different absolute sensitivity/specificity values) as was found in the previous mixed analysis for all the tests except for the D15(5/2) whereby it was also noted that the test had a generally better screening performance when used on type I patients only.

CHAPTER 4

Study 2 Grading of Visual Dysfunction in Diabetic Retinopathy using Clinical Tests of Visual Function

4.1 INTRODUCTION

The ophthalmoscopic examination of a diabetic with DR often presents a challenge to the clinician. Often it is clinically difficult to decide if the retinal changes present warrant referral. The additional use of clinical visual function tests for aiding the decision-making process is examined in this chapter.

The severity of visual dysfunction in relation to different stages of DR has been the topic of many investigations (see 1.1.2) where various visual functions have been studied. Many of the previous studies have investigated the utility of visual function tests for determining visual dysfunction in the very early stages of DR. Some have addressed the correlation between visual dysfunction and DR severity, but none, has assessed the ability of clinical tests of visual function for differentiating between grades of DR, in particular the ability to differentiate between the following categories of patients: 1)those requiring acknowledgement of the condition, 2)those requiring frequent examinations and 3)those requiring referral to an ophthalmologist.

The present study was undertaken using different clinical tests of 3 visual functions (colour vision, contrast sensitivity and visual field) on patients with 3 clinically defined grades of DR. The aim was to ascertain whether the tests showed gradations in visual dysfunction with increasing severity of DR, i.e. their ability to differentiate between the 3 grades of DR. Individual test performance was examined in order to identify those tests which could be used to aid in the subsequent management of the patient. Of late some groups of optometrists and ophthalmologists in certain areas of the United Kingdom have been engaged in some form of "shared scheme" in providing care to patients with ocular manifestations of diabetes (Hunter,1993). It is hoped that useful visual function tests (as to be investigated in the present study) could be used by optometrists in deciding the referral of a

patient with DR to the ophthalmologist. However, it is to be noted that such "tests" (if identified) should only be strictly used as *supplementary aids*; the main definitive criterion for any referral must always be careful fundus examination. At this juncture it cannot be overemphasised that an Optometrist has a statutory duty to report any evidence of DR to a medical practitioner, without any necessity to wait for a visual dysfunction to appear first.

4.2. PATIENTS and PROCEDURES

Diabetic patients attending University College and Moorfields Eye Hospitals for their routine check-ups were recruited for the study. Only those with visual acuity of 6/12 or better (with present correction and/or pinhole) were selected. None had received laser treatment to the retina before. Patients with known neurological or other eye diseases were excluded in order to eliminate conditions which themselves might affect the test results (such as glaucoma, cataract, optic neuritis, age-related macular degeneration, hypertensive retinopathy, etc). Patients with congenital colour vision deficiency or amblyopia were also excluded.

Ocular examination was performed by an ophthalmologist, which included indirect ophthalmoscopy and fundus biomicroscopic examinations. On the basis of such procedures patients were divided into the following grades:

I. MINIMAL DIABETIC RETINOPATHY: A stage characterised by the presence of isolated and dispersed early vascular lesions such as a few microaneurysms and/or small hard exudates in the retinal periphery or at the posterior pole without any macular involvement (fig 4.1).

II. MODERATELY SEVERE DIABETIC RETINOPATHY: Characteristics of this stage included the presence of more extensive microaneurysms, confluents of hard exudates and dot/blot haemorrhages which were scattered in the retina. It also included the presence of severe capillary non-perfusion

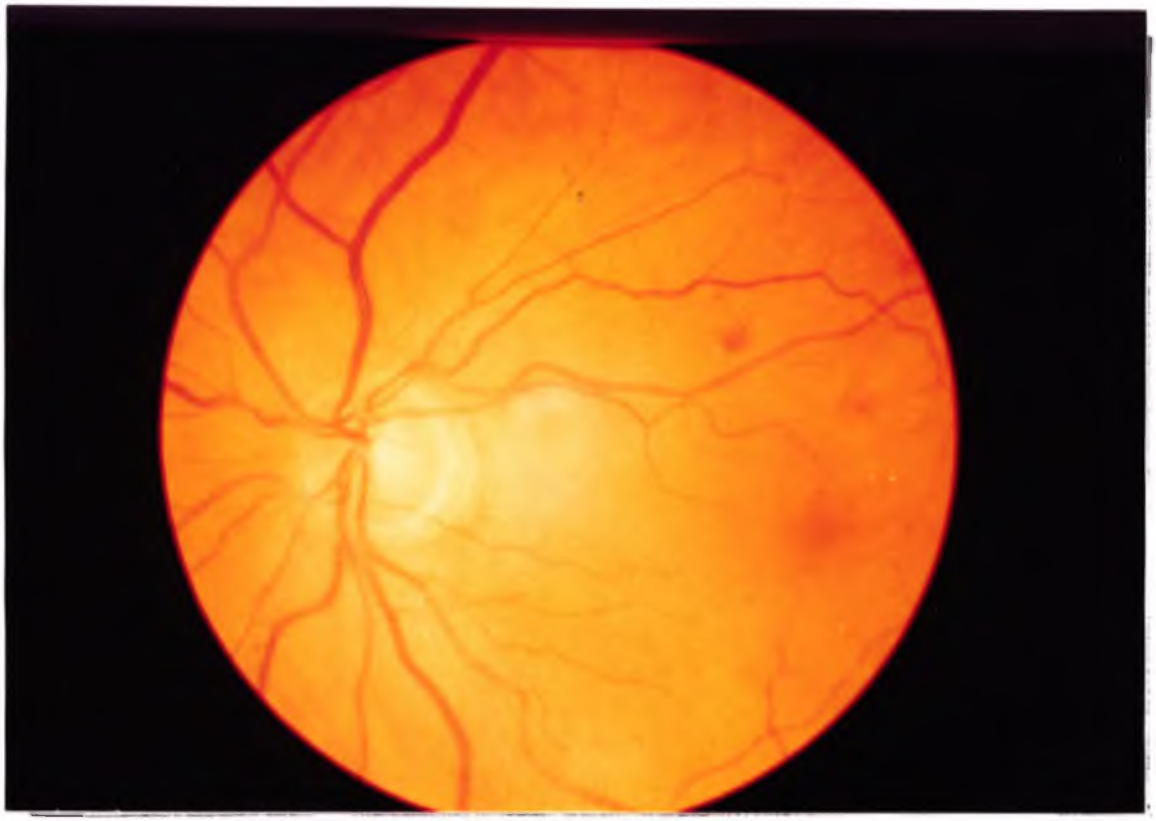


Fig 4.1 Minimal DR (grade I).

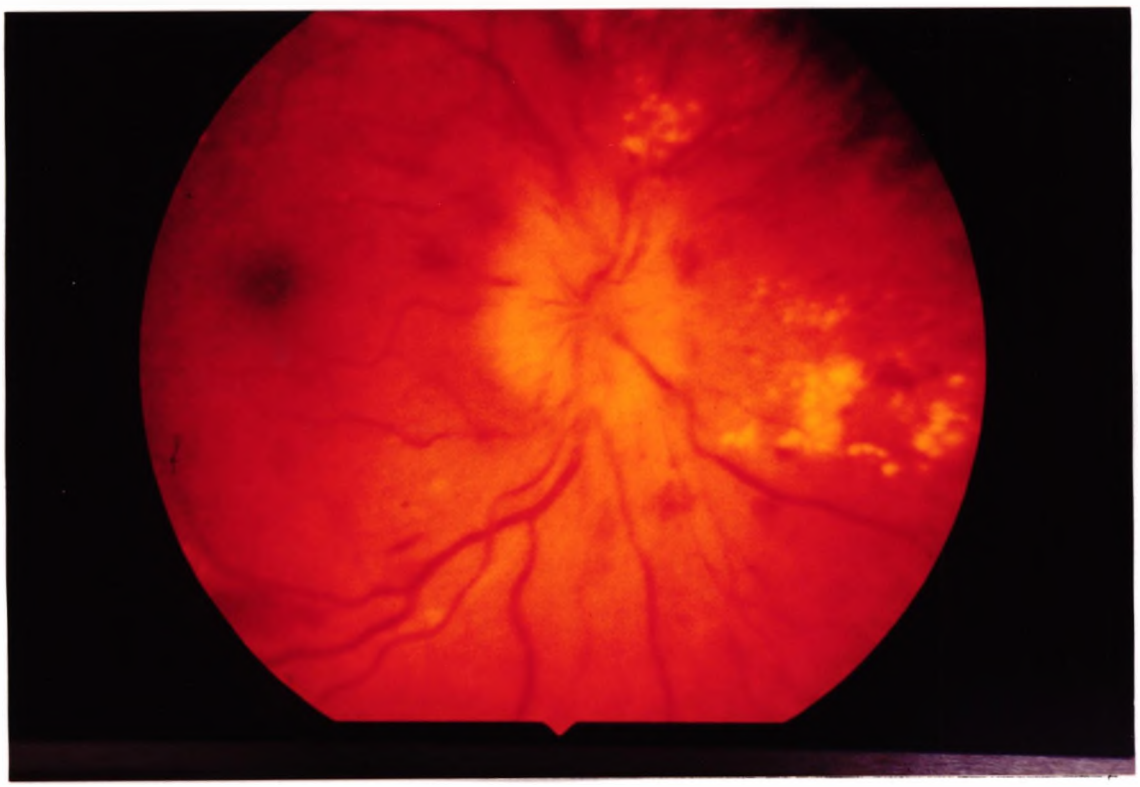


Fig 4.2 Moderately severe DR (grade II).

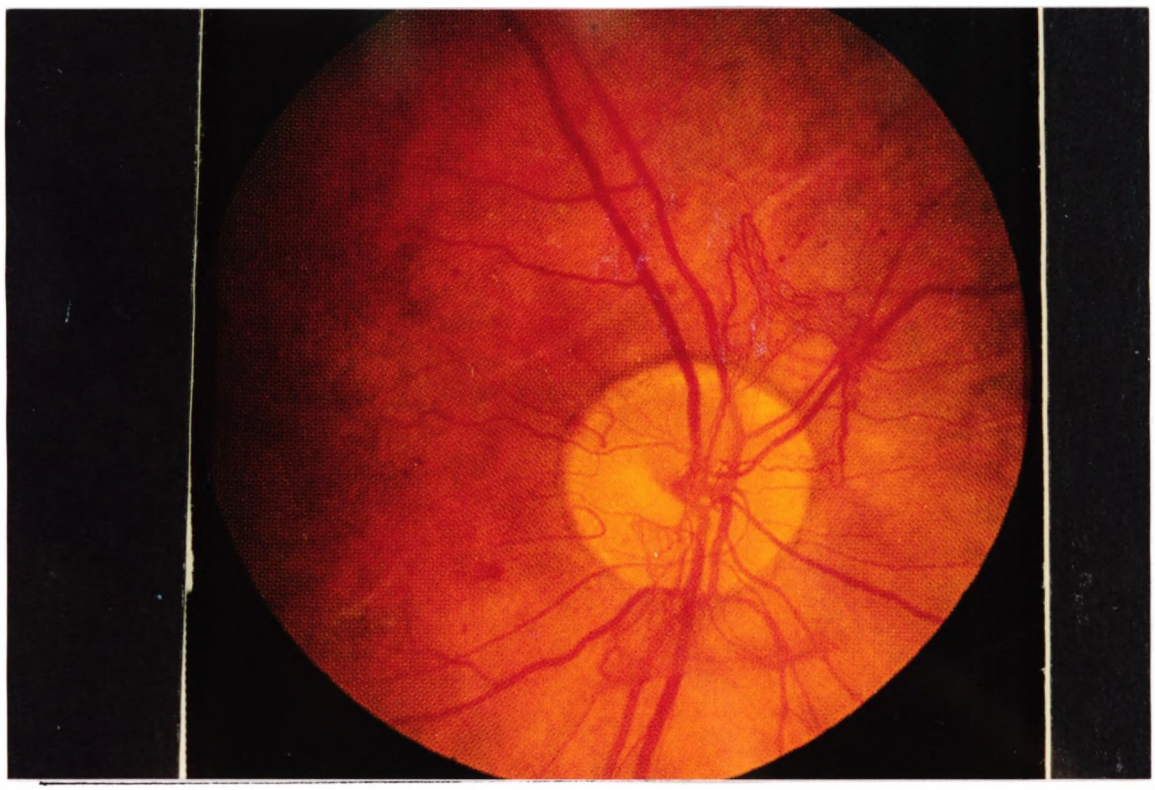


Fig 4.3 Proliferative DR (grade III)

signified by deep haemorrhages, soft exudates, venous beading and intra-retinal microvascular abnormalities (IRMA). The macula is occasionally minimally involved (fig 4.2).

III. PROLIFERATIVE DIABETIC RETINOPATHY: A stage characterised by the presence of preretinal new blood vessels at the disc or elsewhere, confirmed by fluorescein angiography (fig 4.3).

Grade I were those who required future observations. Grade II although including a wide range of conditions, were those who required frequent follow-ups because of the evidence of extensive ischaemic retinal changes and would thus be considered as targets for laser panretinal photocoagulation. Grade III was a well-defined group which included patients who required referral to an ophthalmologist for laser photocoagulation treatment of proliferative DR.

87 patients were selected; their ages ranged from 19 to 75 years with a mean of 48.7 sd 15.7 years. 56 male patients and 31 females were examined. 59 were on insulin and 28 were on diet or tablets for the management of diabetes. The duration of diabetes ranged from 1 to 42 years with a mean of 14.7 sd 9.6 years. Table 4.1 shows the number of patients in each grade and their clinical profiles. There was no significant difference in the ages of patients between the 3 grades of DR (ANOVA $F(2,84)=0.06$, $p>0.05$).

COLOUR VISION was examined with 6 clinical tests:

1) Comp PIC (excluding plate # 16)
2) SPP2
3) LTA
4) D15(5/4)
5) D15(5/2)
6) FM 100-H

CONTRAST SENSITIVITY measurements were made with 2 clinical tests: 1) Arden gratings and 2) VCTS 6000

VISUAL FIELDS were evaluated with 2 clinical tests:
1) VFA I and 2) Amsler grid

SEE CHAPTER 2 FOR DETAILS OF THE TESTS USED

All tests were administered monocularly for near vision under an illuminance of 550 Lux at University College Hospital and 1000 Lux at Moorfields Eye Hospital. Illumination was provided by fluorescent tubes (Osram 65/80w, 8000K). Patients were appropriately optically corrected for the test distance. The examination room had pastel coloured walls which had minimal reflections.All visual function tests were carried out by the author.

Only results from the first examined eye are included in the present analysis. Results are expressed as means and sd values. The data was analysed on the IBM mainframe computer using the SAS statistical package (SAS Software Version 5 edition). Statististical analyses carried out included one-way ANOVA (followed by Scheffe's test), Chi-Square test and multivariate analysis (using the GLM procedure). In all the statistical tests a probability (p value) of less than 0.05 was taken as being significant.

In the multivariate analysis using GLM procedure each test was assigned as the dependent variable in the determination of its significant contributors. Independent variables included in the model were were: Venue, "diagnostic grade", age, duration of diabetes, insulin therapy and LogMAR VA. Venue, "diagnostic grade" and insulin therapy were assigned as categorical variables while age, duration of diabetes and LogMAR VA were assigned as continuous variables. Having identified the significant contributors of a particular test's performance, the direction of effect of each contributor was determined by the sign of the regression coefficients which were obtained subsequently by multiple regression.

A sub-analysis of patients with *type I diabetes only* was also undertaken to determine whether this alters the

Profile	Grade of DR		
	I	II	III
Number	29 20M / 7F	24 13M / 11F	34 12M / 13F
Age Range Mean	 20-70 49.3 sd 15.4	 22-74 48.9 sd 14.6	 19-75 47.9 sd17.2
No (%) on Insulin	 22(75.9)	 16(66.7)	 21 (61.8)
VA Range Mean (LogMAR)	6/5-6/9 -0.02 sd 0.08	6/5-6/12 0.09 sd 0.13	6/5-6/12 0.12 sd 0.14

Table 4.1 Clinical profiles of patients with different grades of Diabetic Retinopathy (DR)

statistical evaluation of the earlier main analysis done on the group consisting of types I and II diabetic patients mixed together. The group of patients with type I diabetes only consisted of 59 patients ie. 22 with grade I (mean age=45.0 sd 14.6), 16 with grade II (mean age=44.3 sd 14.7) and 21 with grade III (mean age=40.4 sd 17.3). The ages of patients among the three grades were not significantly different (ANOVA $F(2,56)=0.52, p>0.05$).

4.3 RESULTS

4.3.1 Test performance

4.3.1a Colour vision

1. Comp PIC

Figure 4.4 shows the mean number of total plate errors made by the patients. Significance of differences between grades is indicated in the figure (ANOVA, $F(2,84)=13.94$, $p<0.05$). Significantly more mean total plate errors were made by patients with grades II and III in comparison to those with grade I. No significant difference was found between grades II and III. Sub-analysis of the results obtained by patients with *type I diabetes only (N=59)* revealed similar trends of significance ie. the mean total plate errors were made by patients with grades II (mean=3.12 sd 2.82) and III (mean=4.14 sd 3.78) were significantly more than those with grade I (mean=0.77 sd 1.26). No significant difference was found between grades II and III (ANOVA $F(2,56)=8.13, p<0.05$).

Table 4.2 shows the mean number of red-green and tritan plate errors made by all patients (N=87). Significant differences were noted only in the mean number of tritan errors made (ANOVA, $F(2,84)=16.85$, $p<0.05$). Significantly more tritan plate errors were made by patients with grades II and III in comparison to those with grade I. No significant difference was found between grades II and III. No significant differences were found between the 3 grades

in the mean number of red-green plate errors (ANOVA $F(2,84)=3.05$, $p>0.05$).

Normal results obtained on 37 clinically normal subjects (age range 26-77) with VA ranging from 6/5 to 6/12 under similar conditions were as follows:

Mean total plate errors = 0.03 sd 0.16
Mean red-green errors = 0
Mean tritan plate errors = 0.05 sd 0.23

2. SPP2

Figure 4.5 shows the mean number of total errors made by the patients. Significance of differences is indicated (ANOVA, $F(2,84)=15.92$, $p<0.05$). Significantly more mean total errors were made by patients with grade III in comparison with those with grades I and II. No significant difference was found between grades I and II. Sub-analysis of the results obtained by patients with *type I diabetes only (N=59)* revealed a different trend of significance (ANOVA $F(2,56)=9.97, p<0.05$). Only the mean total plate errors made by patients with grades III (mean=6.09 sd 4.40) was significantly more than those with grade I (mean=1.63 sd 1.36); no significant difference was found between grades II (mean=4.0 sd 3.4) and III.

Table 4.3 shows the mean number of red-green and tritan errors made by all patients (N=87). The trend of significance (for mean total errors) applied to both red-green (ANOVA $F(2,84)=13.22$, $p<0.05$) and tritan errors (ANOVA $F(2,84)=14.91$, $p<0.05$).

Normal results obtained on 20 clinically normal subjects (age range 24-69) with VA ranging from 6/5 to 6/12 under similar conditions were as follows:

Mean total plate errors = 1.10 sd 0.31
Mean red-green errors = 0.05 sd 0.22
Mean tritan plate errors = 1.05 sd 0.22

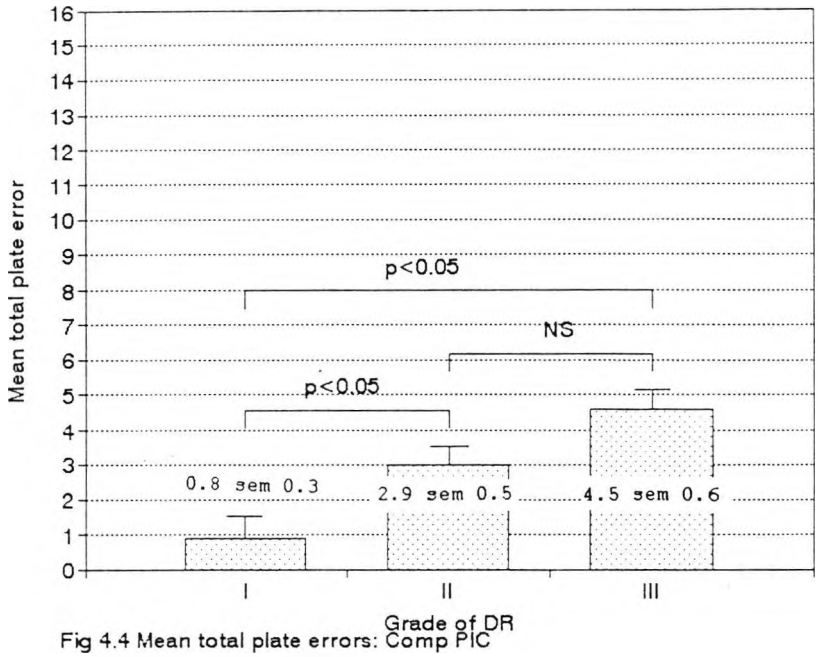


Fig 4.4 Mean total plate errors: Comp PIC
The error bars represent SEM

Grade of DR	Mean plate errors	
	Red -green	Tritan
I	0.1 sd 0.6	0.7 sd 1.6
II	0.3 sd 0.8	2.6 sd 2.2
III	0.9 sd 1.7	3.7 sd 2.3

Table 4.2 Mean number of plate errors per patient: Comp PIC

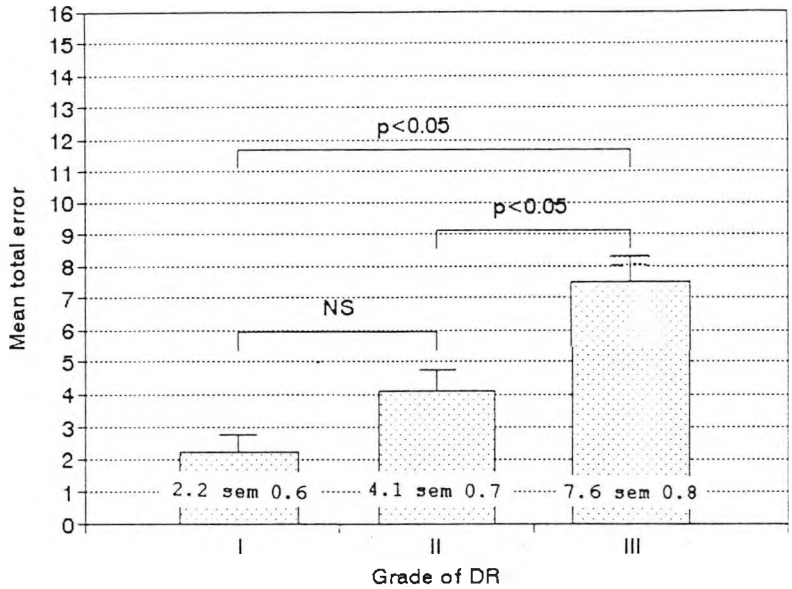


Fig 4.5 Mean total errors: SPP2
The error bars represent SEM

Grade of DR	Mean errors	
	Red-green	Tritan
I	0.5 sd 1.2	1.8 sd 2.1
II	0.9 sd 1.2	3.1 sd 2.4
III	2.2 sd 1.7	5.4 sd 3.2

Table 4.3 Mean number of errors per patient: SPP2

3. LTA

The mean scores obtained by the patients are shown in table 4.4; only marginal differences were found in the scores (ANOVA, $F(2,84)=3.36$, $p=0.05$). Sub-analysis of the results obtained by patients with *type I diabetes only (N=59)* revealed a similar trend ie. no significant differences were found across the 3 groups of patients (ANOVA $F(2,56)=2.14, p>0.05$). The mean scores of the 3 groups of type I patients were 4.90 sd 0.29 (grade I), 4.68 sd 1.01 (grade II) and 4.14 sd 1.85 (grade III).

Normal results obtained on 25 clinically normal subjects (age range 26-77) with VA ranging from 6/5 to 6/12 under similar conditions revealed no failures at all (all with a score of 5).

4. D15(5/4)

Figure 4.6 shows the mean scores obtained by the patients. Differences between grades are indicated (ANOVA $F(2,84)=4.21$, $p<0.05$). No significant differences were found in the mean scores between grades II and III and between grades I and II. Only patients with grade III had significantly more mean scores than those with grade I. Sub-analysis of the results obtained by patients with *type I diabetes only (N=59)* revealed a different trend ie. no significant differences were found across the 3 groups of patients (ANOVA $F(2,56)=2.28, p>0.05$). The mean scores of the 3 groups of type I patients were 1.45 sd 3.91 (grade I), 5.37 sd 7.57 (grade II) and 9.04 sd 17.89 (grade III).

Table 4.5 shows the mean number of red-green and tritan axes obtained by all patients (N=87) with the 3 grades of DR on the D15(5/4). No significant differences were found in the mean number of red-green axes between patients with the 3 grades (ANOVA $F(2,84)=0.91$, $p>0.05$).

The mean number of tritan axes were, however, significantly different among the three groups of patients (ANOVA

$F(2,84)=3.58, p<0.05$). No significant differences were found between patients with grades III and II and between those with grades II and I. Only those with grade III had significantly more mean number of tritan axes than patients with grade I.

Normal results obtained on 25 clinically normal subjects (age range 26-77) with VA ranging from 6/5 to 6/12 under similar conditions were as follows:

Mean score = 3.0 sd 7.93
Mean no. of red-green axes = 0
Mean no. of tritan axes = 0.14 sd 0.37

5. D15(5/2)

Figure 4.7 shows the mean scores of patients with the 3 grades of DR. Differences between grades are indicated (ANOVA $F(2,84)=3.84$, $p<0.05$). No significant differences were found in the mean scores between patients with grades III and II and between those with grades II and I. Only patients with grade III had significantly more mean scores than those with grade I. Sub-analysis of the results obtained by patients with *type I diabetes only (N=59)* revealed a different trend ie. no significant differences were found across the 3 groups of patients (ANOVA $F(2,56)=2.07, p>0.05$). The mean scores of the 3 groups of type I patients were 5.54 sd 7.99 (grade I), 9.31 sd 9.93 (grade II) and 11.61 sd 11.48 (grade III).

Table 4.6 shows the mean number of red-green and tritan axes obtained by all patients (N=87). No significant differences were found in the mean number of red-green axes (ANOVA $F(2,84)=0.85$ $p>0.05$) and tritan axes (ANOVA $F(2,84)=1.86$, $p>0.05$) between patients.

Normal results obtained on 37 clinically normal subjects (age range 26-77) with VA ranging from 6/5 to 6/12 under similar conditions were as follows:

Grade of DR	Score
I	4.8 sd 0.9
II	4.7 sd 0.9
III	3.9 sd 1.8

Table 4.4 Mean LTA score per patient

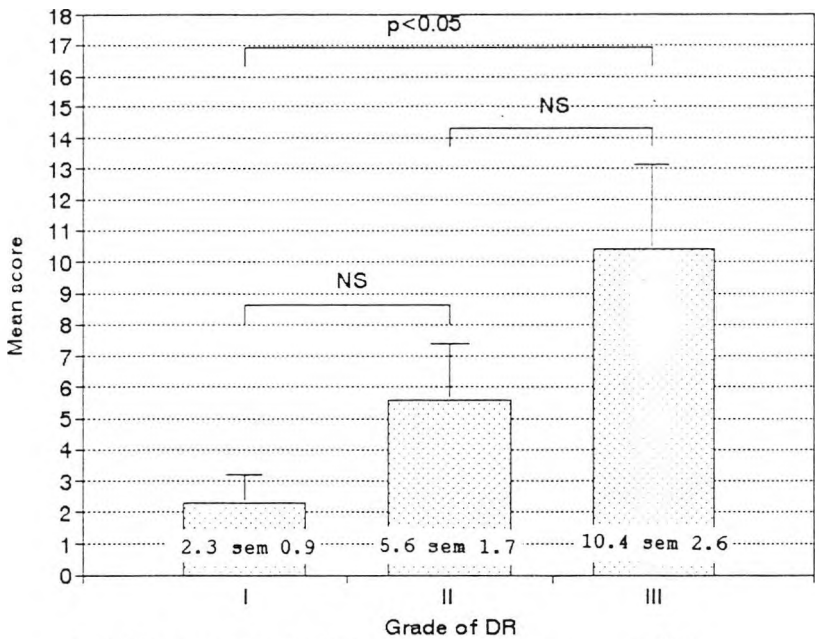


Fig 4.6 Mean scores: D15(5/4). The error bars represent SEM

Grade of DR	Mean no. of axes	
	Red-green	Tritan
I	0.0 sd 0.0	0.1 sd 0.3
II	0.1 sd 0.4	0.2 sd 0.4
III	0.3 sd 1.4	0.4 sd 0.8

Table 4.5 Mean number of axes per patient: D15(5/4)

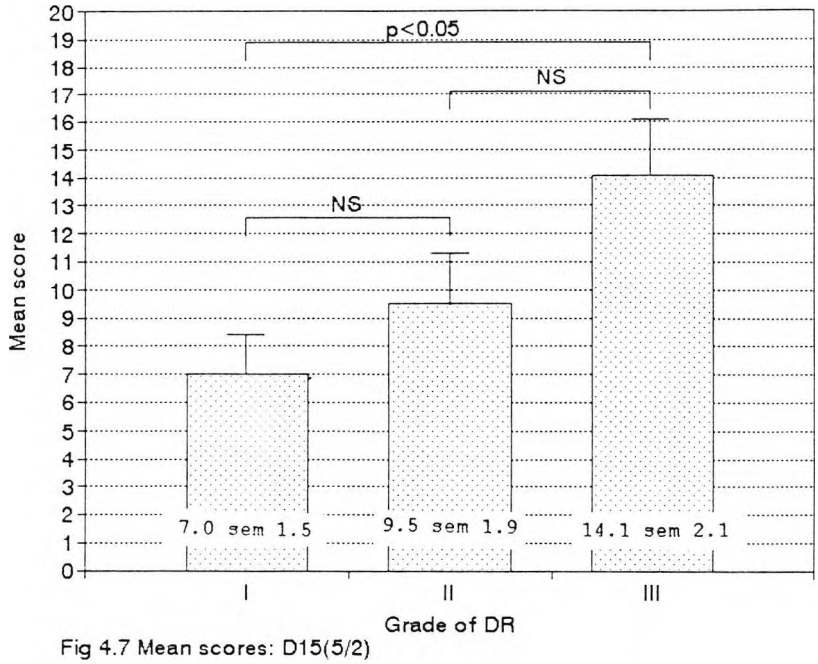


Fig 4.7 Mean scores: D15(5/2)
The error bars represent SEM

Grade of DR	Mean no. of axes	
	Red-green	Tritan
I	0.0 sd 0.2	0.2 sd 0.8
II	0.0 sd 0.0	0.6 sd 1.1
III	0.1 sd 0.4	0.8 sd 1.4

Table 4.6 Mean number of axes per patient: D15(5/2)

Mean score = 5.62 sd 6.60
Mean no. of red-green axes = 0
Mean no. of tritan axes = 0.24 sd 0.60

6. FM 100-H

Figure 4.8 shows the mean square-root of the total error scores (SqTES) obtained by the patients. Differences between grades are indicated (ANOVA $F(2,84)=4.21$, $p<0.05$). No significant differences were found in the mean sqTES between those with grades III and II and between those with grades II and I. Only patients with grade III had significantly more mean SqTES than those with grade I. This trend of significance across the three groups also applied to the square-roots of red-green and blue yellow scores (table 4.7).

Sub-analysis of the results obtained by patients with *type I diabetes only (N=59)* revealed similar trends of significance (ANOVA $F(2,56)=6.42$, $p<0.05$) ie. the mean SqTES of patients with grade III (14.70 sd 5.98) was significantly more than that of patients with grade I (mean=9.88 sd 2.65). No significant differences were found in the mean sqTES between those with grades III and II (mean=12.43 sd 3.86) and between those with grades II and I. Exactly the same trend of significance was also observed for the square-roots of red-green and blue yellow scores of these type I patients.

Table 4.8 shows the mean differences between square-roots of red-green and blue-yellow scores (SqBY-SqRG) obtained by all patients (N=87). No significant differences were found between the 3 grades (ANOVA $F(2,84)=0.91$, $p>0.05$). The same trend of no significant differences (ANOVA $F(2,56)=0.001$, $p>0.05$) was also observed among the 3 groups of type I patients only with regard to the differences between square-roots of red-green and blue-yellow scores (SqBY-SqRG).

Normal results obtained on 10 clinically normal subjects

(age range 26-62) with VA ranging from 6/5 to 6/12 under similar conditions were as follows:

Mean SqTES = 7.75 sd 2.74
Mean SqRG = 4.86 sd 1.58
Mean SqBY = 5.12 sd 2.84
Mean SqBY-SqRG = 0.25 sd 1.70

4.3.1b Contrast sensitivity

1. Arden gratings

Figure 4.9 shows the mean total scores obtained by the patients. No significant differences were found in the mean total scores between the 3 groups of patients (ANOVA $F(2,84)=3.09$, $p>0.05$). Sub-analysis of the results obtained by patients with *type I diabetes only (N=59)* revealed the same trend of no significant differences across the 3 groups of patients (ANOVA $F(2,56)=2.63$, $p>0.05$). The mean total scores of the 3 groups of type I patients were 73.6 sd 8.5 (grade I), 78.8 sd 15.5 (grade II) and 81.4 sd 9.8 (grade III).

Table 4.9 shows the mean scores obtained for each plate of the test by all patients (N=87). No significant differences were found in the mean scores of plates 2 to 4 between the 3 grades. Significant differences were, however, found between grades III and I for plates 6 (ANOVA $F(2,84)=4.01$, $p<0.05$) and 7 (ANOVA $F(2,84)=3.86$, $p<0.05$).

Normal results obtained on 14 clinically normal subjects (age range 26-66) with VA ranging from 6/5 to 6/12 under similar conditions were as follows:

Mean total score = 73.9 sd 7.3 (<78)*
Mean score for plates
2 = 13.1 sd 1.6 (11.5)*
3 = 11.9 sd 1.6 (10.0)*
4 = 12.8 sd 1.5 (11.5)*
5 = 12.1 sd 1.6 (11.5)*
6 = 12.3 sd 1.8 (10.0)*

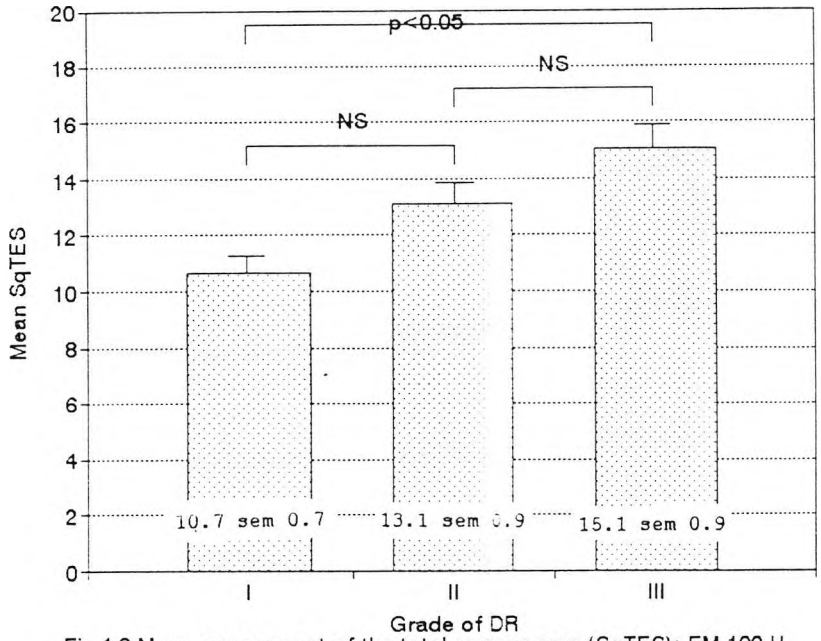


Fig 4.8 Mean square-root of the total error scores (SqTES): FM 100-H
The error bars represent SEM

Grade of DR	SqRG score	SqBY score
I	6.8 sd 2.4	8.0 sd 2.7
II	8.5 sd 2.8	9.8 sd 3.2
III	9.7 sd 3.4	11.3 sd 4.0

SqRG = Square-root of red-green
SqBY = Square-root of blue-yellow

Table 4.7 Mean square-roots of red-green and blue-yellow scores per patient: FM 100-H

Grade of DR	Mean difference
I	1.2 sd 1.4
II	1.3 sd 1.6
III	1.6 sd 1.6

Table 4.8 Mean difference between square-roots of red-green and blue-yellow scores per patient: FM 100-H

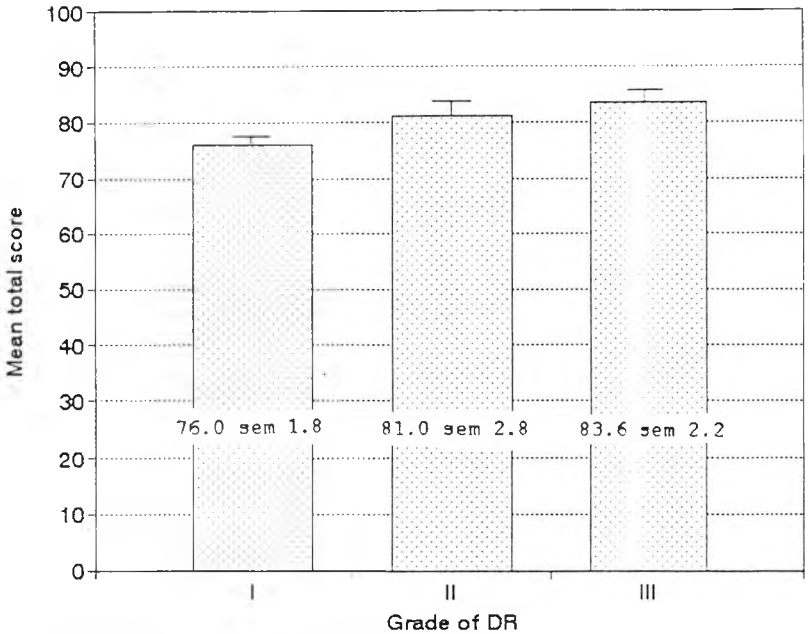


Fig 4.9 Mean total scores: Arden gratings

Grade of DR	Mean score for plate					
	2	3	4	5	6	7
I	13.0 sd 2.2	11.8 sd 1.8	12.6 sd 1.9	12.2 sd 2.4	13.1 sd 2.4	13.3 sd 3.6
II	12.8 sd 2.2	11.4 sd 2.5	13.3 sd 2.8	12.8 sd 2.8	14.6 sd 3.4	16.2 sd 5.7
III	12.9 sd 2.7	12.0 sd 1.6	13.4 sd 2.0	13.7 sd 3.3	15.2 sd 3.2	16.4 sd 4.7

Table 4.9 Mean score for each plate per patient: Arden gratings

7 = 11.6 sd 1.8 (9.0)*

* Numbers in parentheses are the original normal results given by Arden & Jacobson (1978).

2. VCTS 6000

Figure 4.10 shows the mean global scores obtained by the patients. Table 4.10 shows the mean scores of each spatial frequency obtained. Significant differences in the mean global scores were only found between grades III and I (ANOVA $F(2,84)=4.07$, $p<0.05$). The same was also true for spatial frequencies A, C and D. However, no significant differences were found in the mean scores for spatial frequencies B and E between the 3 grades.

Sub-analysis of the results obtained by patients with *type I diabetes only (N=59)* revealed a different trend ie. no significant differences were found across the 3 groups of patients (ANOVA $F(2,56)=0.64, p>0.05$) in the mean global scores. The mean global scores of the 3 groups of type I patients were 21.7 sd 5.4 (grade I), 20.3 sd 5.1 (grade II) and 20.0 sd 5.6 (grade III).

Normal results obtained on 34 clinically normal subjects (age range 26-66) with VA ranging from 6/5 to 6/12 under similar conditions were as follows:

Mean global score = 28.0 sd 4.4

Mean score for spatial frequency

A = 5.5 sd 0.6

B = 6.0 sd 0.7

C = 5.9 sd 1.1

D = 5.5 sd 1.5

E = 5.1 sd 1.67

4.3.1c Visual field

1. VFA I

Figure 4.11 shows the mean total field scores for each grade of DR. Significance of differences is indicated (ANOVA, $F(2,84)=6.26, p<0.05$). Table 4.11 shows the mean scores for each zone of the central fields (zones 1 to 5 and the macular area) for each grade of DR.

Patients with grades II and III each had significantly lower mean total field scores compared to those with grade I, but between them they were not significantly different from one another. This pattern of significance also applied to zone 5 (between 15-25 degrees) (ANOVA, $F(2,84)=5.65, p<0.05$). No significant differences were found between the 3 grades in the mean macular scores (ANOVA, $F(2,84)=0.63, p>0.05$). For other zones (zones 1 to 4), patients with grade III had significantly lower mean scores than those with grade I. However, the mean scores were not significantly different between grades I and II and between grades II and III.

Sub-analysis of the results obtained by patients with *type I diabetes only (N=59)* revealed a different trend ie. although marginally significant differences were found across the 3 groups of patients in the mean total field scores (ANOVA $F(2,56)=3.9, p=0.025$), no two groups were significantly different at the 0.05 level when the Scheffe's test was applied *post-hoc*. The mean total field scores of the 3 groups of type I patients were 104.7 sd 12.0 (grade I), 93.6 sd 13.9 (grade II) and 95.0 sd 14.9 (grade III). However as with the earlier analysis of patients type I and II diabetes mixed together, the mean macular scores of patients with type I only were also not significantly different from each other (ANOVA $F(2,56)=1.3, p>0.05$).

Normal results obtained on 33 clinically normal subjects (age range 23-63) with VA ranging from 6/5 to 6/12 were as

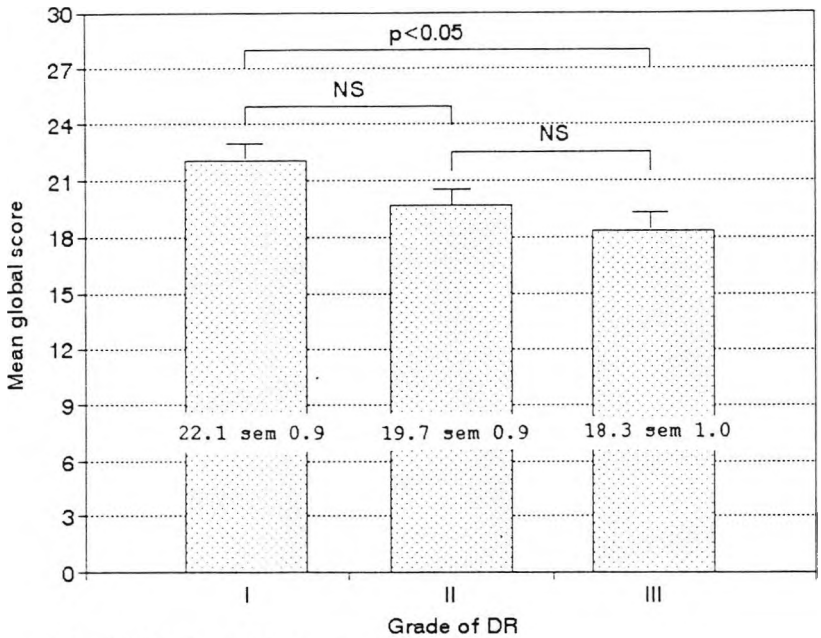


Fig 4.10 Mean global scores: VCTS 6000
The error bars represent SEM

Grade of DR	Mean score for spatial frequency				
	A	B	C	D	E
I	5.1 sd 0.6	5.6 sd 0.7	4.7 sd 1.1	3.9 sd 1.4	2.8 sd 1.8
II	4.8 sd 0.7	5.1 sd 0.8	4.3 sd 1.0	3.3 sd 1.4	2.3 sd 1.9
III	4.6 sd 0.9	5.1 sd 0.9	3.7 sd 1.3	2.9 sd 1.6	2.1 sd 1.9

Table 4.10 Mean score for each spatial frequency per patient: VCTS 6000

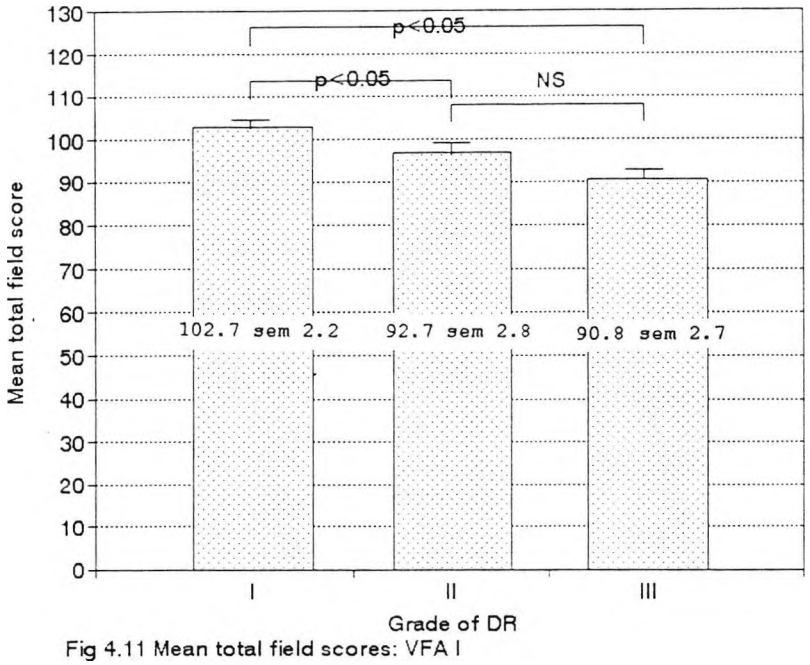


Fig 4.11 Mean total field scores: VFA I
The error bars represent SEM

Grade of DR	Mean score for zone					Mean macular score
	1	2	3	4	5	
I	105.3 sd 12.9	107.1 sd 12.4	101.4 sd 11.6	97.7 sd 12.5	103.7 sd 13.8	123.5 sd 15.9
II	94.8 sd 14.0	98.8 sd 11.9	93.0 sd 14.1	87.8 sd 15.5	89.6 sd 19.5	119.2 sd 14.4
III	90.4 sd 19.8	94.8 sd 15.2	90.2 sd 16.1	87.7 sd 16.4	90.7 sd 19.2	119.1 sd 19.1

Table 4.11 Mean field scores per patient: VFA I zonal scores

Grade of DR	No failing (%)
I	3 (10.3)
II	6 (25)
III	11 (32.4)

Table 4.12 Number of patients in each grade of DR failing the Amsler grid

follows:

Mean total field score = 115.1 sd 8.0
Mean score for zones

Macular	=	135.2 sd 8.7
1	=	118.8 sd 8.0
2	=	116.1 sd 7.4
3	=	112.5 sd 8.9
4	=	112.8 sd 9.4
5	=	118.4 sd 9.1

2. Amsler grid

The percentage of patients failing the grid in each grade of DR is shown (table 4.12). No significant differences were found in the percentages of patients failing the Amsler grid between the 3 groups (Chi-Sq=4.39,dF=2,p>0.05). However, sub-analysis of the results obtained by patients with *type I diabetes only (N=59)* revealed a different trend ie. there were marginally significant differences in the percentages of patients failing the Amsler grid between the 3 groups (Chi-Sq=5.87,dF=2,p<0.05). The percentages of patients failing were: 4.5% (grade I), 18.8% (grade II) and 33.3% (grade III).

Normal results obtained on 25 clinically normal subjects (age range 26-77) with VA ranging from 6/5 to 6/12 under similar conditions revealed no failures at all.

4.3.1d Factors affecting test performance

The results from the multivariate analyses performed on each test are set out in table 4.13. All the tests, with the exception of the Amsler grid and VCTS 6000, are significantly correlated with "diagnostic grade". Insulin therapy was significant correlated with the following tests: SPP2, D15(5/2), VCTS 6000 and VFA I. As patients in this main analysis comprised those with types I and II diabetes grouped together the effect of "insulin" or type

of diabetes *per se* is discussed separately at the end of the discussion. Venue was not found to be significantly associated with any of the tests, and neither was duration of diabetes.

Inclusion of two additional independent variables (age & VA) gave the results set out in table 4.14. Age and/or VA appeared to be significantly correlated with all the tests. Only two tests (Comp PIC and SPP2) correlated with "diagnostic grade" despite the appearance of age and VA as significant correlates; comparing tables 4.13 and 4.14 the significance of "diagnostic grade" disappeared in the other six tests (LTA, D15(5/4), D15(5/2), FM 100-H, Arden gratings and VFA I). The Arden gratings also appeared to be significantly correlated with other factors as well ie. venue and duration of diabetes. The disappearance of "diagnostic grade" as a significant correlate with the appearance of age and VA as substitutes imply that the information contained in the tests (apart from the Comp PIC and SPP2) are not really helpful in determining dignostic grade. Venue only appeared to be correlated with the Arden gratings.

Appendix 4A is the computer print-out showing the results on all the tests of all patients in the study.

4.4 DISCUSSION

The present study shows that for a mixed clinical population of patients with type I and II diabetes the Comp PIC and SPP2, each separately, provided satisfactory differentiation between the 3 grades of DR.

The Comp PIC was able to differentiate between patients with "significant DR" i.e. grades II & III from those with minimal DR (grade I). However, the Comp PIC was not able to separate between patients requiring referral to an ophthalmologist (grade III patients) from those who only required close follow-ups (grade II patients). Fig 4.12 shows individual patient results demonstrating clear

Test	Patient variable			
	Venue	Diagnostic grade	Duration of diabetes	Insulin therapy
Comp PIC	-	7.4	-	-
SPP2	-	8.7	-	7.3
LTA	-	3.0	-	-
D15(5/4)	-	3.1	-	-
D15(5/2)	-	4.0	-	3.9
FM 100-H	-	3.7	-	-
Arden gratings	-	4.7	-	-
VCTS 6000	-	-	-	5.3
VFA I	NA	5.3	-	5.4
Amsler grid	-	-	-	-

All indicated F-values are for $p<0.05$; -=NS; NA=Not applicable

Table 4.13 F-values for significant correlations between visual function test results and patient variables

Test	Patient variable					
	Venue	Diagnostic Grade	Duration of diabetes	Insulin therapy	VA	Age
Comp PIC	-	5.8	-	-	5.2	13.0
SPP2	-	7.5	-	-	6.0	12.3
LTA	-	-	-	-	6.0	7.6
D15(5/4)	-	-	-	-	10.0	10.9
D15(5/2)	-	-	-	-	10.8	15.9
FM 100-H	-	-	-	-	18.4	8.2
Arden gratings	4.5	-	3.9	-	23.4	7.1
VCTS 6000	-	-	-	-	3.90	27.1
VFA I	NA	-	-	-	22.4	22.9
Amsler grid	-	-	-	-	7.9	7.9

All indicated F-values are for $p<0.05$; -=NS; NA=Not applicable

Table 4.14 F-values for significant correlations between visual function test results and patient variables (including age and VA)

Note
The "insulin therapy" factor is included in both tables because the analyses were performed on a mixed group of type I and II patients.

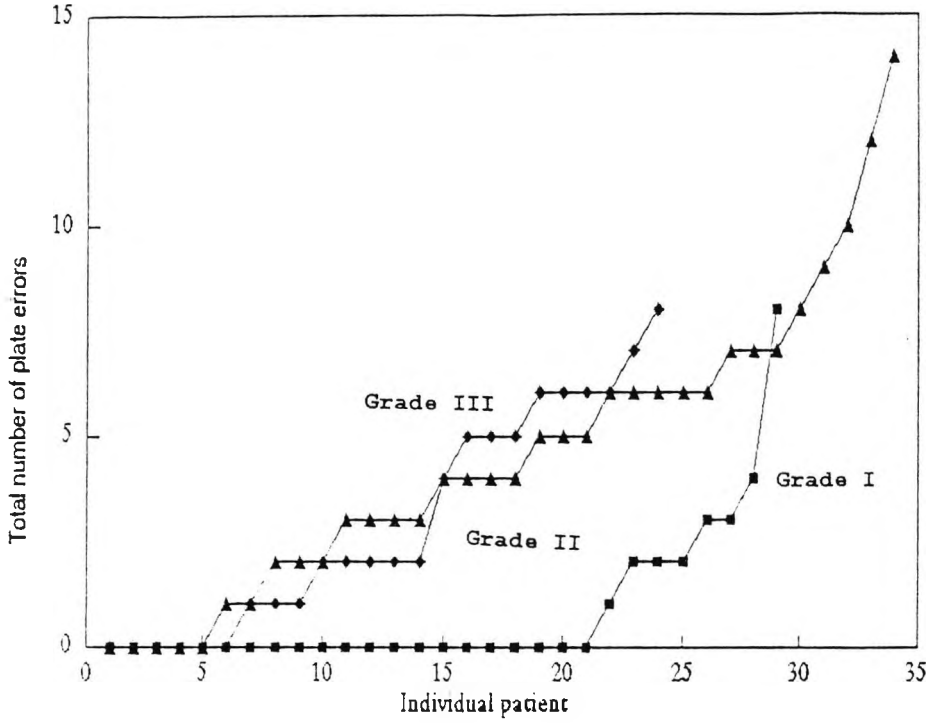


Fig 4.12 Individual Comp PIC results

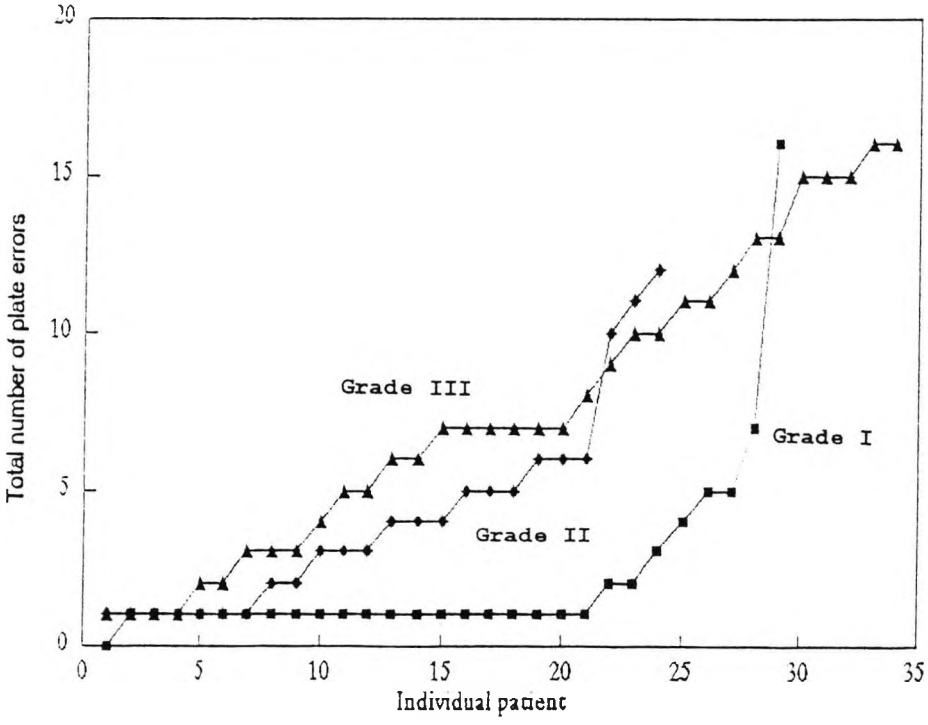


Fig 4.13 Individual SPP2 results

distinction between grade I and grades II & III combined. The SPP2, on the other hand, was able to separate those requiring referral (grade III patients) from those requiring close follow-ups and those with mild DR (grades II & I). The SPP2 was less successful in differentiating between patients with minimal DR (grade I) from those requiring close follow-ups (grade II). Fig 4.13 shows individual patient results demonstrating less overlap between grades II and III.

The following tests: D15(5/4), D15(5/2), FM 100-H, and VCTS 6000 were only able to separate patients who required referral (grade III patients) from those with minimal DR (grade I). They failed to show significant differences in their performance between patients who required referral (grade III) from those who required close follow-ups (grade II) and between patients with minimal DR (grade I) from those who required close follow-ups (grade II). The LTA only managed to show marginally significant differences in the scores between the 3 grades of DR while the Arden gratings and Amsler grid did not show any significant differences in performance between the 3 groups of patients.

VA and age affect the performance of all the tests (table 4.14). However despite the influence of VA and age, "diagnostic grade" was still significantly correlated with the Comp PIC and SPP2 (when VA and age were factored into the analysis), whereas for the other tests the significance of "diagnostic grade" vanished as revealed by table 4.14. Thus even though the ages of the patients selected for the study were not significantly different across the 3 grades, age still showed a powerful influence on the test results. The same goes with VA where despite the selection of patients with VA of 6/12 or better the effect of VA was significant in the results of the tests. The decline of visual function as a function of VA and age is well documented (Atchison,1987; Birch,1988; Marmor & Gawande,1988; Werner et al.1990). The shifting of significance from "diagnostic grade" to age and VA can be

taken to mean that these other tests (i.e. not including Comp PIC and SPP2) are not really helpful in determining the grade of severity of DR.

Some tests (SPP2, D15(5/2), VCTS 6000 and VFA I) also initially showed dependence on insulin therapy . Dependence of visual function on insulin status has been noted in the literature (Sokol et al.1985; Trick et al.1988; Trick et al.1990). The present results suggest that non insulin-taking patients had poorer visual function than those who were on insulin. However, it was later found that the insulin factor was also substituted largely by the age and VA factors. The analysis of results from patients with type I diabetes only is discussed at the end of this discussion section.

ANOVA also revealed the performance of the VFA I to be similar to that of the Comp PIC. However, in contrast to the Comp PIC, the VFA I results were too dependent on the age and VA of the patients as shown in table 4.14. It is also interesting to note that the VCTS 6000 was not found to correlate with "diagnostic grade" at all, even in the absence of age and VA in the analysis (table 4.13).

There might have been some overlap in the grouping of patients since they were arbitrarily divided into 3 grades, especially between grades I & II. Grade II patients comprised a wide range of patients categorised as "moderate DR". This factor could have caused the insignificant differences in test results between grades. It was hoped that the overlap of patients was minimal as the diagnosis of patients was carefully done by ophthalmologists (at Moorfields and University College Hospitals) who were experienced diabetic eye specialists. Grade III patients were a well defined group consisting of patients with proliferative DR who required referral to ophthalmologists for laser treatment. However, the chances of these patients having minimal macular involvement could not be totally discounted. It is well documented that the visual function in patients with frank maculopathy is very poor (Bresnick

et al.1985), in fact poorer than in patients with PDR without maculopathy. Nevertheless even if there had been a few patients with maculopathy in the group with grade III, they would still form a group which needed referral on the grounds of having proliferative DR since the overriding diagnostic criterion here was the presence of neovascularisation.

In the present study, with the SPP2, LTA, D15(5/2) and FM 100-H, the predominance of a tritan defect could not be shown in any of the grades of DR. The present results do show that both the red-green and blue-yellow components of the defect increase in severity with increasing retinopathy severity. However,the fact that there were no significant differences in the differences between the square-roots of red-green and blue-yellow scores on the FM 100-H (table 4.8) between the 3 grades of DR, imply that both red-green and blue-yellow errors increase at the same rate with increasing severity of DR. The present results are in agreement with those of Trick et al.(1988) and imply that the proportion of patients with poor overall hue discrimination is the same at each level of DR. However, the finding of no evidence of a selective blue-yellow loss (by the present study and by Trick et al.(1988)) should be viewed cautiously as it is to some extent dependent on the method of analysis employed. Atchison et al.(1991a) has recently taken issue with Trick (1988) arguing that consideration of the polarity of arrangements (in the colour difference vector analysis) in comparing the confusion angles was not made, hence missing the blue-yellow component of the defect. Also since the FM 100-H scores in normals get selectively worse with age, so in older diabetics axes could not be precisely determined especially so with the panel D15(5/2).

Only the results obtained with the Comp PIC and the D15(5/4) showed significant increases in the number of tritan errors made by patients with increasing severity of DR. These two tests did not show any significant increase in the errors of their red-green components. The red-green

plates included in the Comp PIC series were selected Ishihara plates; these might not have been sensitive enough to detect the acquired red-green defects. As for the D15(5/4), it was shown to be insensitive to acquired red-green colour vision defects; its ability for grading acquired colour vision has been earlier demonstrated by Birch (1989) to be inferior to the (5/2) version.

The present contrast sensitivity results obtained with the Arden gratings confirm the involvement of high spatial frequencies in DR as noted by Ghafour et al.(1982). However, there were no significant differences in the total Arden scores between the 3 grades; thus the gradual involvement of all spatial frequencies as noted by Sokol et al. (1985) was not demonstrable in the present study. The Arden gratings were also found to be the least robust of all the tests evaluated with regards to the level of illumination since "venue" was significantly correlated with the test results (see chapter 7 for further discussion). As for the VCTS 6000, significant differences were noted in CS between grades I and III over a wider range of spatial frequencies. This agrees with the results of Trick et al.(1988) who used a similar testing system (distance version). However, the present study found the VCTS 6000 to be largely dependent on age and VA rather than anything else.

The results of the present study showed that significant differences in fields sensitivity between the 3 grades of DR occurred in the midperipheral areas of between 15-25 degrees from the macula. This rather more "central" location of defects agrees with the findings of Sabry et al.(1987), athough is at a slight variance with those of Bell & Feldon (1984) and of Federman & Lloyd (1984), who stated that defects are located more "peripherally" than 15-25 degrees, in this midperipheral zone. The difference in results are possibly due to differences in the instruments employed. The present results, however, could not confirm or deny the possible presence of field defects outside of the areas tested on the VFA I. The results of

the present study also concurr with those of Trick et al.(1990) as regards to the non-involvement of macular thresholds in patients with DR.

The failure of the Amsler grid to show significant differences between grades was probably due to the small number of patients with severe macular involvement in the group with grade III. And if such was the case, the Amsler grid is shown to be ineffective in detecting patients with proliferative DR although it is expected that such patients would have detectable (with the Amsler grid) retinal oedema (Birch et al.1980). The Amsler grid was also revealed to be largely dependent on the VA of the patients rather than anything else. The low sensitivity of the Amsler grid in a screening situation was already shown in chapter 3.

In conclusion, the present study found the SPP2 plates and the Comp PIC plates to be excellent tests for grading the severity of DR in patients with "good VA" (between 6/5 and 6/12). The choice between the two tests depends on the clinician's priority: For the purpose of picking up patients "strictly" for referral, the SPP2 plates would be the ideal choice. Alternatively, if patients with "significant DR" are targeted, then the Comp PIC plates would serve the purpose better.

Sub-analysis of patients with type I diabetes only (N=59)

The above major discussion concerns the analysis of all the patients involved in the study ie. a mixed group of patients with types I and II diabetes (N=87). A sub-analysis of patients with type I diabetes only (N=59) was also undertaken to determine whether the statistical evaluation is altered. The following summarise the results of this additional analysis:

1. Both the Comp PIC and FM 100-H tests maintained the trend of significance which was evident in the earlier analysis of patients mixed together.

The Comp PIC test was able to seperate patients with "mild DR" (grade I) from those with "significant DR" (grades II & III) among patients with type I diabetes only. This applied to both the total plate errors and tritan plate errors.

The FM 100-H test, on the other hand, as in the earlier analysis of patients mixed together was only able to differentiate between patients with grade I and III, but not between grade I and II or between grade II and III. This pattern applied to both the total error scores and partial scores of red-green and blue-yellow components.

2) Both the LTA and Arden gratings maintained the non-significant differences between the results of all three groups of patients, as was evident in the earlier mixed analysis.

3) For the following tests: SPP2, both D15s, VCTS 6000 and VFA I, the analysis on type I patients only revealed no significant differences between the results of all three groups of patients, unlike in the earlier mixed analysis where some significant differences were then obtained.

4) The Amsler grid, when used on type I patients only managed to show some significant differences between the three grades of DR, unlike in the earlier mixed analysis.

CHAPTER 5

Study 3 Evaluating the Effects of Therapeutic DYE Laser Photocoagulation Treatment for Diabetic Retinopathy on Visual Function

5.1 INTRODUCTION

Argon blue-green lasers (488/514 nm) have been used most commonly in panretinal photocoagulation (PRP) treatment of proliferative diabetic retinopathy (PDR). Their efficacy in arresting the progress of retinopathy has been conclusively established (DRS Res.Gp.1981; British Multicentre Study Gp.1984). As the aim of PRP in proloferative DR is to effect regression of retinal new blood vessels via the heating effects on the retinal pigment epithelium, the wavelength of the laser light used is an important parameter because its absorption by the retinal pigment epithelium is dependent on its wavelength(s).

The dominant wavelengths of the Argon laser are in the blue-green (488/514 nm). Of late, there has been an increasing awareness of the potential phototoxic hazards of short wavelength lasers both for the operator and for the patient (Berninger et al.1989; Gunduz & Arden,1989; Arden et al.1991; Canning et al.1991b). Blue wavelengths, in particular, are said to be damaging to the retinal receptors (Ham & Mueller,1976; Ham et al.1980). Xanthophyll, the pigment found in the macular area, also absorbs some light at 488 nm (Marshall et al.1975); this is thought to contribute to the macular phototoxicity effects (Geeraets & Berry,1968).

PRP would indeed be expected to influence the central visual function because of the possibility of "stray light" impinging on the macular region as a result of laser light being delivered into the eye in relatively large, albeit therapeutic doses. It has been shown that Argon laser (488/514 nm) PRP causes a deterioration in visual function; these changes may be either transient or long-term, depending on various laser parameters (see 1.1.3).

Ophthalmic Dye lasers are now available which are capable of producing wavelengths between 360 and 960 nm, with peak energy output approximating 0.5 to 1w in the range from 560 to 640nm (L'Esperance,1985a & 1985b). There are theoretical

advantages in choosing wavelengths between green and red for PRP, in particular yellow and orange (Trempe et al.1982; Mainster,1986) although therapeutically the wavelength of the photocoagulator may not be a crucial determinant (Bressler,1993). Yellow light (577nm) is useful as it is absorbed well by oxyhaemoglobin; orange light (595nm) on the other hand, is also well absorbed by oxyhaemoglobin while penetrating hazy ocular media better and also scatters less. More important, both wavelengths (577 and 595nm) are theoretically less phototoxic to the macula and are also poorly absorbed by xanthophyll. The use of these wavelengths should therefore be expected to produce less effects on central visual function. The retinal pigment epithelium is the primary site for the absorption of light energy for the above-mentioned wavelengths when used for PRP treatment (Lachenmayr et al.1984; Marshall et al.1984; Borges et al.1987).

The aim of the present study was to compare, by a battery of visual function tests, the effects on central visual function of comparable amounts of PRP with the standard Argon laser (488/514nm) and with two other wavelengths of the Dye laser (577nm and 595nm).

5.2 PATIENTS and PROCEDURES

Patients attending Moorfields Eye Hospital with untreated proliferative diabetic retinopathy were recruited for this prospective randomised trial. Patients selected were those who had proliferative DR either with disc new vessels or with new vessels elsewhere, as assessed by fundus biomicroscopy and fluorescein angiography. Figure 4.3a in chapter 4 illustrates an example of an eye which fulfilled the entry criteria. They had a visual acuity of 6/12 or better, clear media, and no clinically significant macular oedema as defined by the Early Treatment Diabetic Retinopathy Study Research Group (ETDRS Res.Gp.1985). The exclusion criteria were:

1. Presence of optic nerve or other macular disorders (e.g.

glaucoma, optic neuritis, age-related maculopathy etc).
2. History of previous photocoagulation treatment.
3. Presence of congenital colour vision deficiency or amblyopia.

A total of 26 patients (36 eyes) were selected. There were 16 males and 10 females. The ages of the patients ranged from 19 to 75 years with a mean of 48.0 (sd 18.0) years. The mean duration of diabetes in these patients was 14.9 (sd 9.4) years with a range from 1 to 37 years. 17 were on insulin while 9 were on diet or tablets for the management of diabetes. Eight eyes had a visual acuity of 6/5, 8 had 6/6, 14 had 6/9 and 6 had 6/12. Table 5.1 shows the profiles of all patients in the study.

At entry eyes were randomised for treatment with one of three wavelengths: Argon Blue-green (488/514nm), Dye Yellow (577nm) or Dye Orange (595nm). Where both eyes of the same patient were enrolled, one was treated with Argon (488/514nm), and the other was randomly assigned to Dye (577nm) or Dye (595nm). All treatments were carried out on the Coherent Argon/Dye laser Model 920.

Fifteen eyes fell in the Argon treated group, 11 in the Dye-577nm treated group and 10 in the Dye-595nm treated group. Eleven eyes had disc new vessels only, 17 had new vessels elsewhere only while 8 had new vessels at both locations (table 5.2).

Prior to treatment each patient had a full ophthalmic assessment which included slit lamp fundus biomicroscopy and binocular indirect ophthalmoscopy. All patients had fluorescein angiography and fundus colour photography prior to laser treatment. The patients were treated through a maximally dilated pupil with either a Rodenstock lens or in the case where only partial treatment could be obtained, a Goldmann 3-mirror lens. The patients were usually treated in a single treatment session with topical anaesthesia. 2000 burns were applied to each eye, of spot size 200 microns and duration 0.1s. In those eyes in which treatment

was completed with a 3-mirror lens, the spot size was increased to 500 microns. The power was adjusted to produce just noticeable blanching of the retinal pigment epithelium. No additional laser treatment was given during the 3 months needed to complete the study. Follow-up fluorescein angiography was undertaken at the end of the study period (3 months) to assess macular perfusion and confirm regression of the new vessels.

All patients were examined with a battery of visual function tests before PRP treatment and then one week, one month and three months after treatment. Patients also received fundal examinations at these visits.

VISUAL ACUITY was measured with a standard distant Snellen chart.

COLOUR VISION was examined with 6 clinical tests:

1) Comp PIC
2) SPP2
3) LTA
4) D15 (5/4)
5) D15 (5/2)
6) FM 100-H

CONTRAST SENSITIVITY was measured with 2 clinical tests:

1) Arden gratings (Plates 2 & 3 were categorised as low spatial frequency plates while plates 4 & 5 and 6 & 7 were classified as mid and high spatial frequency plates respectively).

2) VCTS 6000 (Spatial frequencies A & B were classified as low, spatial frequency C was classified as mid while frequencies D & E as high).

VISUAL FIELDS were evaluated with 2 clinical tests:

1) VFA I and 2) Amsler grid

SEE CHAPTER 2 FOR DETAILS OF THE TESTS USED

Number	Mean age	Mean years of diabetes	No. on Insulin	Mean VA (LogMAR)
26 10 bilateral 16 unilateral (36 eyes)	48.0 sd 18.0	14.9 sd 9.4	17	0.10 sd 0.14

Table 5.1 Patient profile for study 3

Group	Type of new vessels			Total No.
	Disc	Elsewhere	Both	
Argon treated	1	9	5	15
Dye-577 treated	4	4	3	11
Dye-595 treated	6	4	0	10

Table 5.2 Number of eyes with new vessels: At entry to the trial

All tests (apart from VA and VFA I) were administered monocularly for near vision under a level of illuminance of 1000 Lux with the patient appropriately corrected. The examination room had pastel coloured walls which had minimal reflections. For VA measurements, patients were tested with the appropriate distance correction with pinhole if necessary. For measurements on the VFA Mk I, the examination was done under the illumination provided by the instrument with patients appropriately corrected. All tests of visual function were administered by the author.

Analysis of data

Results of the visual tests are expressed as means and sd values. The changes in the results of each visual function test (with respect to pre-treatment values) were compared for the three treatment groups, at each follow-up visit. Analysis of results was carried out on the IBM mainframe computer using the SAS statistical package (SAS Version 5 edition). Statistical tests utilised included paired t-test and one-way ANOVA (followed by Scheffe's test). In all the statistical tests a probability value (p value) of less than 0.05 was taken as being significant.

5.3 RESULTS

5.3.1 Changes in "New Vessel" status

Table 5.3 shows the presence of new vessels in the 3 groups randomised to treatments with Argon, Dye-577nm and Dye-595nm at the 3 post treatment follow-up visits. At the end of the study period new vessels were still present in 4 (27%) of the Argon treated eyes, 4 (40%) of the Dye-577nm treated eyes and in 3 (30%) of the Dye-595nm treated eyes.

5.3.2 Changes in Visual Acuity (VA)

Table 5.4 shows the mean VA (LogMAR) for the 3 groups during all visits. Table 5.4a details the mean changes for these groups over the follow up period, with the

statistical analyses undertaken. Between-group analysis (ANOVA) did not show any significant differences between the 3 groups of eyes in the VA changes undergone at each follow-up visit.

5.3.3 Changes in Colour Vision

1. Comp PIC

Table 5.5 shows the mean number of plate errors for the 3 groups during all visits. Table 5.5a details the mean changes for these groups over the follow up period, with the statistical analyses undertaken. Between group analysis (ANOVA) did not show any significant differences between the 3 groups of eyes in the changes in the number of plate errors made at all follow-up visits.

3. SPP2

Table 5.6 shows the mean number of plate errors for the 3 groups during all visits. Table 5.6a details the mean changes for these groups over the follow up period, with the statistical analyses undertaken. Between-group analysis (ANOVA) did not show any significant differences between the 3 groups of eyes in the changes in the number of errors made at all follow-up visits.

3. LTA

Table 5.7 shows the mean LTA scores for the 3 groups during all visits. Table 5.7a details the mean changes for these groups over the follow up period, with the statistical analyses undertaken. Between-group analysis (ANOVA) showed no significant differences between the 3 groups in the changes in LTA scores at all visits post treatment.

4. D15 (5/4)

Table 5.8 shows the mean results for the D15(5/4) test for the 3 groups during all visits. Table 5.8a details the mean

Time	No with disc new vessels			No with new vessel elsewhere			No with both types of vessels		
	Arg	577	595	Arg	577	595	Arg	577	595
1-wk	3	7	6	8	4	4	2	0	0
1-mo	3	3	4	6	3	2	0	0	0
3-mos	2	3	2	2	1	1	0	0	0

Arg=Argon treated group; 577=Dye-577nm treated group; 595=Dye-595nm treated group;
Pre=Pre-treatment; 1 wk=one week post treatment; 1-mo=One month post treatment;
3-mos=3 months post treatment

Table 5.3 Number of eyes with new vessels: At post treatment visits

Group	Pre	1-wk	1-mo	3 mos
Arg	0.07 sd 0.13	0.07 sd 0.13	0.09 sd 0.19	0.12 sd 0.14
577	0.11 sd 0.13	0.15 sd 0.16	0.17 sd 0.17	0.19 sd 0.21
595	0.12 sd 0.16	0.13 sd 0.18	0.16 sd 0.18	0.15 sd 0.15

Arg=Argon treated group; 577=Dye-577nm treated group; 595=Dye-595nm treated group;
Pre=Pre-treatment; 1 wk=one week post treatment; 1-mo=One month post treatment;
3-mos=3 months post treatment

Table 5.4 Mean VA (LogMAR) at all visits

ARGON TREATED EYES				577nm TREATED EYES				595nm TREATED EYES				ANOVA
TIME	NO	MEAN CHANGE	SEM	TIME	NO	MEAN CHANGE	SEM	TIME	NO	MEAN CHANGE	SEM	
1 week	15	0	0.02	1 week	11	0.04	0.03	1 week	10	0.01	0.05	F(2,33)=0.48, NS
1 month	15	0.02	0.02	1 month	11	0.05	0.03	1 month	10	0.04	0.05	F(2,33)=0.32, NS
3 months	15	0.05	0.02	3 months	11	0.08	0.04	3 months	10	0.03	0.04	F(2,33)=0.64, NS

Table 5.4a Comparison of mean changes in VA (LogMAR) for ARGON TREATED EYES, 577nm TREATED EYES and 595nm TREATED EYES at 3 follow-up times post treatment

Group	Pre	1-wk	1-mo	3-mos
Total plate errors				
Arg	5.5 sd 4.6	5.3 sd 4.2	4.5 sd 3.5	4.6 sd 4.3
577	5.1 sd 3.9	4.9 sd 4.1	4.8 sd 3.5	5.3 sd 4.6
595	5.1 sd 4.4	5.2 sd 4.3	4.5 sd 3.6	4.4 sd 3.4
Red-green plate errors				
Arg	1.0 sd 2.1	0.8 sd 1.7	0.3 sd 0.8	0.8 sd 1.9
577	1.0 sd 1.3	1.1 sd 2.1	0.6 sd 1.2	1.0 sd 2.1
595	1.1 sd 1.6	1.3 sd 2.2	0.7 sd 1.1	0.7 sd 1.1
Tritan plate errors				
Arg	4.5 sd 3.0	4.5 sd 3.0	4.2 sd 2.9	3.8 sd 2.9
577	4.1 sd 3.0	3.8 sd 2.5	4.3 sd 2.8	4.3 sd 3.1
595	3.1 sd 2.9	3.2 sd 2.9	3.5 sd 3.3	3.4 sd 2.6

Arg=Argon treated group; 577=Dye-577nm treated group; 595=Dye-595nm treated group; Pre=Pretreatment; 1-wk=One week post treatment; 1-mo=One month post treatment; 3-mos=Three months post treatment

Table 5.5 Mean results for the Comp PIC at all visits

Total plate errors												
ARGON TREATED EYES				577nm TREATED EYES				595nm TREATED EYES				ANOVA
TIME	NO	MEAN CHANGE	SE	TIME	NO	MEAN CHANGE	SE	TIME	NO	MEAN CHANGE	SE	
1 week	15	-0.20	0.34	1 week	11	-0.18	0.63	1 week	10	0.10	0.72	F(2,33) =0.09, NS
1 month	15	-0.93	0.41	1 month	11	-0.27	0.66	1 month	10	-0.60	0.40	F(2,33) =0.47, NS
3 months	15	-0.87	0.29	3 months	11	0.18	0.75	3 months	10	-0.70	0.52	F(2,33) =0.47, NS

Red green plate errors												
ARGON TREATED EYES				577nm TREATED EYES				595nm TREATED EYES				ANOVA
TIME	NO	MEAN CHANGE	SE	TIME	NO	MEAN CHANGE	SE	TIME	NO	MEAN CHANGE	SE	
1 week	15	-0.20	0.30	1 week	11	0.09	0.41	1 week	10	0.20	0.53	F(2,33) =0.29, NS
1 month	15	-0.67	0.36	1 month	11	-0.45	0.34	1 month	10	-0.40	0.31	F(2,33) =0.17, NS
3 months	15	-0.20	0.17	3 months	11	0	0.45	3 months	10	-0.40	0.34	F(2,33) =0.36, NS

Tritan plate errors												
ARGON TREATED EYES				577nm TREATED EYES				595nm TREATED EYES				ANOVA
TIME	NO	MEAN CHANGE	SE	TIME	NO	MEAN CHANGE	SE	TIME	NO	MEAN CHANGE	SE	
1 week	15	0	0.20	1 week	11	-0.27	0.38	1 week	10	0.10	0.86	F(2,33) =0.15, NS
1 month	15	-0.27	0.25	1 month	11	0.18	0.55	1 month	10	0.40	0.79	F(2,33) =0.47, NS
3 months	15	-0.67	0.23	3 months	11	0.18	0.50	3 months	10	0.30	0.56	F(2,33) =1.78, NS

Table 5.5a Comparison of mean changes in errors on the Comp PIC for ARGON TREATED EYES, 577nm TREATED EYES and 595nm

Group	Pre	1-wk	1-mo	3-mos
Total errors				
Arg	7.7 sd 5.8	7.5 sd 5.9	8.1 sd 5.8	8.1 sd 5.8
577	7.9 sd 5.9	8.6 sd 5.8	8.8 sd 5.5	8.6 sd 5.6
595	8.0 sd 5.3	7.9 sd 6.2	7.6 sd 5.7	7.1 sd 5.0
Red-green errors				
Arg	2.2 sd 2.1	2.1 sd 1.9	2.4 sd 1.9	2.5 sd 2.0
577	2.4 sd 2.0	2.7 sd 2.2	2.9 sd 1.8	2.4 sd 2.0
595	2.7 sd 1.9	2.4 sd 2.1	2.6 sd 2.2	2.6 sd 1.9
Tritan errors				
Arg	5.2 sd 3.7	5.4 sd 4.1	5.7 sd 3.9	5.7 sd 3.9
577	5.6 sd 4.0	5.9 sd 3.7	5.9 sd 3.8	6.2 sd 3.7
595	5.3 sd 3.5	5.5 sd 4.2	5.0 sd 3.6	4.5 sd 3.2

Arg=Argon treated group; 577=Dye-577nm treated group; 595=Dye-595nm treated group; Pre=Pretreatment; 1-wk=One week post treatment; 1-mo=One month post treatment; 3-mos=Three months post treatment

Table 5.6 Mean results for the SPP2 at all visits

Total errors												
ARGON TREATED EYES				577nm TREATED EYES				595nm TREATED EYES				ANOVA
TIME	NO	MEAN CHANGE	SE	TIME	NO	MEAN CHANGE	SE	TIME	NO	MEAN CHANGE	SE	
1 week	15	0.13	0.49	1 week	11	0.73	0.66	1 week	10	0.10	0.91	F(2,33)=0.52, NS
1 month	15	0.47	0.43	1 month	11	0.91	1.08	1 month	10	-0.40	0.70	F(2,33)=0.72, NS
3 months	15	0.47	0.65	3 months	11	0.64	1.11	3 months	10	-0.90	0.71	F(2,33)=0.92, NS

Red-green errors												
ARGON TREATED EYES				577nm TREATED EYES				595nm TREATED EYES				ANOVA
TIME	NO	MEAN CHANGE	SE	TIME	NO	MEAN CHANGE	SE	TIME	NO	MEAN CHANGE	SE	
1 week	15	0.07	0.28	1 week	11	0.36	0.28	1 week	10	-0.30	0.40	F(2,33)=1.01, NS
1 month	15	0.20	0.24	1 month	11	0.55	0.43	1 month	10	-0.10	0.28	F(2,33)=0.90, NS
3 months	15	0.27	0.33	3 months	11	0.00	0.50	3 months	10	-0.10	0.18	F(2,33)=0.28, NS

Tritan errors												
ARGON TREATED EYES				577nm TREATED EYES				595nm TREATED EYES				ANOVA
TIME	NO	MEAN CHANGE	SE	TIME	NO	MEAN CHANGE	SE	TIME	NO	MEAN CHANGE	SE	
1 week	15	0.20	0.37	1 week	11	0.36	0.47	1 week	10	0.20	0.55	F(2,33)=0.04, NS
1 month	15	0.53	0.24	1 month	11	0.36	0.80	1 month	10	-0.30	0.52	F(2,33)=0.68, NS
3 months	15	0.47	0.35	3 months	11	0.64	0.72	3 months	10	-0.80	0.611	F(2,33)=1.87, NS

Table 5.6a Comparison of mean changes in errors on the SPP2 for ARGON TREATED EYES, 577nm TREATED EYES and 595nm TREATED EYES at 3 follow-up times post treatment

Group	Pre	1-wk	1 mo	3 mos
Arg	3.5	3.7	3.6	4.0
	sd 2.1	sd 1.9	sd 1.9	sd 1.5
577	4.0	3.8	3.9	3.6
	sd 1.7	sd 1.9	sd 1.6	sd 2.1
595	4.0	4.2	4.1	4.2
	sd 2.1	sd 1.8	sd 1.7	sd 1.8

Arg=Argon treated group; 577=Dye 577nm treated group; 595=Dye 595nm treated group; Pre=Pretreatment; 1-wk=One week post treatment; 1 mo=One month post treatment; 3 mos=Three months post treatment

Table 5.7 Mean LTA scores at all visits

ARGON TREATED EYES				577nm TREATED EYES				595nm TREATED EYES				ANOVA
TIME	NO	MEAN CHANGE	SE	TIME	NO	MEAN CHANGE	SE	TIME	NO	MEAN CHANGE	SE	
1 week	15	0.13	0.22	1 week	11	-0.18	0.18	1 week	10	0.20	0.20	F(2,33)=0.52, NS
1 month	15	0.07	0.18	1 month	11	-0.10	0.10	1 month	10	0.10	0.23	F(2,33)=0.72, NS
3 months	15	0.47	0.38	3 months	11	-0.36	0.34	3 months	10	0.20	0.20	F(2,33)=0.92, NS

Table 5.7a Comparison of mean changes in LTA scores for ARGON TREATED EYES, 577nm TREATED EYES and 595nm TREATED EYES at 3 follow-up times post treatment

Group	Pre	1-wk	1-mo	3-mos
	Scores			
Arg	10.3 sd 11.9	10.5 sd 12.3	9.9 sd 12.6	9.1 sd 10.7
577	5.3 sd 7.1	7.3 sd 8.9	5.8 sd 5.4	4.9 sd 7.3
595	8.4 sd 13.7	8.0 sd 10.8	4.8 sd 6.4	7.4 sd 9.3
	No. of red-green axes			
Arg	0.1 sd 0.3	0.1 sd 0.3	0.0 sd 0.0	0.1 sd 0.3
577	0.0 sd 0.0	0.0 sd 0.0	0.0 sd 0.0	0.0 sd 0.0
595	0.0 sd 0.0	0.0 sd 0.0	0.0 sd 0.0	0.1 sd 0.3
	No. of tritan axes			
Arg	0.7 sd 1.0	0.6 sd 0.9	0.7 sd 1.4	0.5 sd 1.1
577	0.3 sd 0.9	0.6 sd 1.0	0.2 sd 0.4	0.2 sd 0.6
595	0.5 sd 1.1	0.7 sd 1.3	0.3 sd 0.7	0.4 sd 0.7

Arg=Argon treated group; 577=Dye-577nm treated group; 595=Dye-595nm treated group; Pre=Pretreatment; 1-wk=One week post treatment; 1-mo=One month post treatment; 3-mos=Three months post treatment

Table 5.8 Mean results for the D15(5/4) test at all visits

Scores												
ARGON TREATED EYES				577nm TREATED EYES				595nm TREATED EYES				ANOVA
TIME	NO	MEAN CHANGE	SE	TIME	NO	MEAN CHANGE	SE	TIME	NO	MEAN CHANGE	SE	
1 week	15	0.27	1.17	1 week	11	2.0	1.18	1 week	10	-0.40	2.21	F(2,33)=0.62, NS
1 month	15	-0.40	1.71	1 month	11	0.55	1.35	1 month	10	-3.60	2.56	F(2,33)=1.16, NS
3 months	15	-1.20	1.53	3 months	11	-0.36	1.00	3 months	10	-1.00	2.50	F(2,33)=0.07, NS

No. of red-green axes												
ARGON TREATED EYES				577nm TREATED EYES				595nm TREATED EYES				ANOVA
TIME	NO	MEAN CHANGE	SE	TIME	NO	MEAN CHANGE	SE	TIME	NO	MEAN CHANGE	SE	
1 week	15	0.00	0.00	1 week	11	0.00	0.00	1 week	10	0.00	0.00	
1 month	15	-0.07	0.07	1 month	11	0.00	0.00	1 month	10	0.00	0.00	F(2,33)=0.69, NS
3 months	15	0.00	0.00	3 months	11	0.00	0.00	3 months	10	0.10	0.10	F(2,33)=1.32, NS

No. of tritan axes												
ARGON TREATED EYES				577nm TREATED EYES				595nm TREATED EYES				ANOVA
TIME	NO	MEAN CHANGE	SE	TIME	NO	MEAN CHANGE	SE	TIME	NO	MEAN CHANGE	SE	
1 week	15	-0.13	0.09	1 week	11	0.27	0.19	1 week	10	0.20	0.13	F(2,33)=2.71, NS
1 month	15	-0.07	0.18	1 month	11	-0.10	0.21	1 month	10	-0.20	0.20	F(2,33)=0.12, NS
3 months	15	0.20	0.14	3 months	11	-0.10	0.09	3 months	10	-0.10	0.23	F(2,33)=0.16, NS

Table 5.8a Comparison of mean changes in D15(5/4) results for ARGON TREATED EYES, 577nm TREATED EYES and 595nm TREATED EYES at 3 follow-up times post treatment

changes in the results of the test for the 3 groups over the follow up period, with the statistical analyses undertaken. There were no significant differences in the changes in the scores and in the number of red-green and tritan axes between the 3 groups of eyes at all follow-up visits.

5. D15 (5/2)

Table 5.9 shows the mean results for the D15(5/2) test for the 3 groups during all visits. Table 5.9a details the mean changes in the results of the test for the 3 groups over the follow up period, with the statistical analyses undertaken. Between-group analysis (ANOVA) showed significant differences between the 3 groups of eyes in the number of red-green axes at the 3-month visit (ANOVA, $F(2,33)=4.43$, $p<0.05$). There was a significant increase in the number of red-green axes for the Dye-577 treated group at the 3-month follow-up (paired t-test, $t=2.39$, $p<0.05$).

6. FM 100-H

Table 5.10 shows the mean results for the FM 100-H for the 3 groups during all visits. Table 5.10a details the mean changes in the parameters of the test for the 3 groups over the follow up period, with the statistical analyses undertaken. Between-group analysis (ANOVA) showed marginally significant differences between the 3 groups of eyes in the changes in the SqBY scores at the 1-month follow up (ANOVA, $F(2,33)=3.48$, $p=0.04$). There was a significant increase in the SqBY scores for the Argon treated group at 1-month post treatment (paired t-test, $t=2.38$, $p<0.05$).

The significant increase in the scores in the blue-yellow scores (as discussed above), however, was not enough to cause a significant change in the axis of the FM 100-H towards the tritan mode. This was reflected in the insignificant change in the differences between the SqRG scores and SqBY scores for the 3 groups (table 5.10a). Figs

5.1-5.3 show the changes in the axes of the 3 groups through-out the study period; no significant differences can be seen in the changes between the groups over the follow-up period.

5.3.4 Changes in Contrast Sensitivity

1. Arden gratings

Table 5.11 shows the mean results for the Arden gratings for the 3 groups during all visits. Table 5.11a details the mean changes in the results of the test for the groups over the follow up period, with the statistical analyses undertaken. Between-group analysis (ANOVA) showed no significant differences in the changes in any of the Arden gratings results across the 3 groups of eyes.

2. VCTS 6000

Table 5.12 shows the mean results for the VCTS 6000 test for the 3 groups during all visits. Table 5.12a details the mean changes in the results of the test for the groups over the follow up period, with the statistical analyses undertaken. ANOVA failed to show any significant differences in the changes in any of the results of the VCTS 6000 at all post treatment visits.

5.3.5 Changes in Visual Fields

1. VFA I

Table 5.13 shows the mean results of the VFA I for the 3 groups during all visits. Table 5.13a details the mean changes in the results of the test for the groups over the follow up period, with the statistical analyses undertaken.

One week after treatment within-group analysis showed significant decreases ($p<0.05$) in the total field scores for all the 3 groups (paired t-test, $t=-2.84, -4.08, -2.80$ for Argon, 577 & 595, respectively). All three groups also

Group	Pre	1-wk	1-mo	3-mos
	Scores			
Arg	16.0 sd 15.8	14.8 sd 14.5	14.7 sd 15.6	12.4 sd 12.3
577	11.8 sd 12.6	15.7 sd 11.9	16.7 sd 14.9	15.3 sd 12.7
595	9.6 sd 10.4	12.0 sd 12.2	11.6 sd 14.4	10.8 sd 16.9
	No. of red-green axes			
Arg	0.1 sd 0.3	0.0 sd 0.0	0.1 sd 0.3	0.0 sd 0.0
577	0.0 sd 0.0	0.1 sd 0.3	0.2 sd 0.4	0.4 sd 0.5
595	0.1 sd 0.3	0.1 sd 0.3	0.1 sd 0.3	0.2 sd 0.6
	No. of tritan axes			
Arg	1.2 sd 1.9	1.2 sd 1.7	1.0 sd 1.4	1.0 sd 1.6
577	0.6 sd 1.5	1.0 sd 1.3	1.0 sd 1.2	0.9 sd 1.1
595	0.4 sd 0.7	0.8 sd 1.0	1.1 sd 2.0	0.7 sd 1.3

Arg=Argon treated group; 577=Dye-577nm treated group; 595=Dye-595nm treated group; Pre=Pretreatment; 1-wk=One week post treatment; 1-mo=One month post treatment; 3-mos=Three months post treatment

Table 5.9 Mean results for the D15(5/2) test at all visits

Scores												
ARGON TREATED EYES				577nm TREATED EYES				595nm TREATED EYES				ANOVA
TIME	NO	MEAN CHANGE	SE	TIME	NO	MEAN CHANGE	SE	TIME	NO	MEAN CHANGE	SE	
1 week	15	-1.20	1.29	1 week	11	3.91	2.66	1 week	10	2.40	2.22	F(2,33)=1.89, NS
1 month	15	-1.33	1.87	1 month	11	4.91	3.68	1 month	10	2.00	3.22	F(2,33)=1.31, NS
3 months	15	-3.60	1.33	3 months	11	3.45	2.26	3 months	10	1.20	3.20	F(2,33)=3.03, NS

No. of red-green axes												
ARGON TREATED EYES				577nm TREATED EYES				595nm TREATED EYES				ANOVA
TIME	NO	MEAN CHANGE	SE	TIME	NO	MEAN CHANGE	SE	TIME	NO	MEAN CHANGE	SE	
1 week	15	-0.07	0.07	1 week	11	0.10	0.10	1 week	10	0.00	0.00	F(2,33)=1.41, NS
1 month	15	0.00	0.10	1 month	11	0.18	0.12	1 month	10	0.00	0.00	F(2,33)=1.15, NS
3 months	15	-0.07	0.07	3 months	11	0.36	0.15	3 months	10	0.10	0.10	F(2,33)=4.43, p<0.05

No. of tritan axes												
ARGON TREATED EYES				577nm TREATED EYES				595nm TREATED EYES				ANOVA
TIME	NO	MEAN CHANGE	SE	TIME	NO	MEAN CHANGE	SE	TIME	NO	MEAN CHANGE	SE	
1 week	15	0.00	0.22	1 week	11	0.45	0.31	1 week	10	0.40	0.22	F(2,33)=1.07, NS
1 month	15	-0.20	0.26	1 month	11	0.45	0.37	1 month	10	0.70	0.47	F(2,33)=1.85, NS
3 months	15	-0.20	0.26	3 months	11	0.36	0.34	3 months	10	0.30	0.30	F(2,33)=1.18, NS

Table 5.9a Comparison of mean changes in D15(5/2) results for ARGON TREATED EYES, 577nm TREATED EYES and 595nm TREATED EYES at 3 follow-up times post treatment

Group	Pre	1-wk	1-mo	3-mos
	SqTES			
Arg	14.1 sd 5.7	14.9 sd 6.0	15.5 sd 5.2	14.4 sd 5.3
577	15.2 sd 4.9	15.5 sd 4.2	14.9 sd 4.6	14.5 sd 4.9
595	13.9 sd 4.6	13.7 sd 5.3	13.4 sd 5.6	13.0 sd 5.3
	SqRG			
Arg	9.1 sd 3.7	9.6 sd 3.8	10.2 sd 3.3	9.2 sd 3.4
577	10.1 sd 3.2	9.7 sd 2.5	9.6 sd 3.7	9.7 sd 3.3
595	8.9 sd 2.9	9 sd 3.3	8.7 sd 4.2	8.6 sd 3.6
	SqBY			
Arg	10.6 sd 4.4	11.2 sd 5.1	11.5 sd 4.2	10.9 sd 4.1
577	11.2 sd 3.8	11.9 sd 3.6	11.0 sd 3.2	10.6 sd 3.8
595	10.5 sd 3.7	10.2 sd 4.2	9.9 sd 3.8	9.5 sd 3.9
	SqBY-SqRG			
Arg	1.4 sd 1.4	1.6 sd 2.4	1.4 sd 1.7	1.7 sd 1.2
577	1.1 sd 1.7	2.2 sd 2.5	1.4 sd 2.5	1.5 sd 1.5
595	1.6 sd 1.8	1.2 sd 1.9	1.2 sd 2.1	1.6 sd 1.1

Arg=Argon treated group; 577=Dye-577nm treated group; 595=Dye-595nm treated group; Pre=Pretreatment; 1-wk=One week post treatment; 1-mo=One month post treatment; 3-mos=Three months post treatment; SqTES=Square-root of the total error scores; SqRG=Square-root of red-green scores; SqBY=Square-root of blue-yellow scores

Table 5.10 Mean results for the FM 100-H at all visits

SqTES												
ARGON TREATED EYES				577nm TREATED EYES				595nm TREATED EYES				ANOVA
TIME	NO	MEAN CHANGE	SE	TIME	NO	MEAN CHANGE	SE	TIME	NO	MEAN CHANGE	SE	
1 week	15	0.83	0.53	1 week	11	0.24	0.83	1 week	10	-0.14	0.56	F(2,33)=0.61, NS
1 month	15	1.39	0.58	1 month	11	-0.37	0.73	1 month	10	-0.51	0.69	F(2,33)=2.82, NS
3 months	15	0.28	0.66	3 months	11	-0.71	0.79	3 months	10	-0.83	0.73	F(2,33)=0.77, NS

SqRG												
ARGON TREATED EYES				577nm TREATED EYES				595nm TREATED EYES				ANOVA
TIME	NO	MEAN CHANGE	SE	TIME	NO	MEAN CHANGE	SE	TIME	NO	MEAN CHANGE	SE	
1 week	15	0.42	0.45	1 week	11	-0.43	0.49	1 week	10	0.16	0.46	F(2,33)=0.87, NS
1 month	15	1.00	0.45	1 month	11	-0.46	0.70	1 month	10	-0.17	0.70	F(2,33)=1.83, NS
3 months	15	0.08	0.46	3 months	11	-0.44	0.61	3 months	10	-0.23	0.50	F(2,33)=0.27, NS

SqBY												
ARGON TREATED EYES				577nm TREATED EYES				595nm TREATED EYES				ANOVA
TIME	NO	MEAN CHANGE	SE	TIME	NO	MEAN CHANGE	SE	TIME	NO	MEAN CHANGE	SE	
1 week	15	0.60	0.45	1 week	11	0.68	0.79	1 week	10	-0.27	0.43	F(2,33)=0.76, NS
1 month	15	0.92	0.38	1 month	11	-0.15	0.52	1 month	10	-0.61	0.38	F(2,33)=3.48, p<0.05
3 months	15	0.32	0.52	3 months	11	-0.55	0.58	3 months	10	-0.92	0.65	F(2,33)=1.28, NS

SqBY-SqRG												
ARGON TREATED EYES				577nm TREATED EYES				595nm TREATED EYES				ANOVA
TIME	NO	MEAN CHANGE	SE	TIME	NO	MEAN CHANGE	SE	TIME	NO	MEAN CHANGE	SE	
1 week	15	0.18	0.45	1 week	11	1.06	0.80	1 week	10	-0.43	0.40	F(2,33)=1.53, NS
1 month	15	-0.08	0.20	1 month	11	0.32	0.68	1 month	10	-0.44	0.55	F(2,33)=0.56, NS
3 months	15	0.27	0.33	3 months	11	0.40	0.54	3 months	10	0.004	0.45	F(2,33)=0.19, NS

SqTES=Square-root of total error scores; SqRG=Square-root of red-green scores; SqBY=Square-root of blue-yellow scores

Table 5.10a Comparison of mean changes in FM 100-H results for ARGON TREATED EYES, 577nm TREATED EYES and 595nm TREATED EYES at 3 follow-up times post treatment

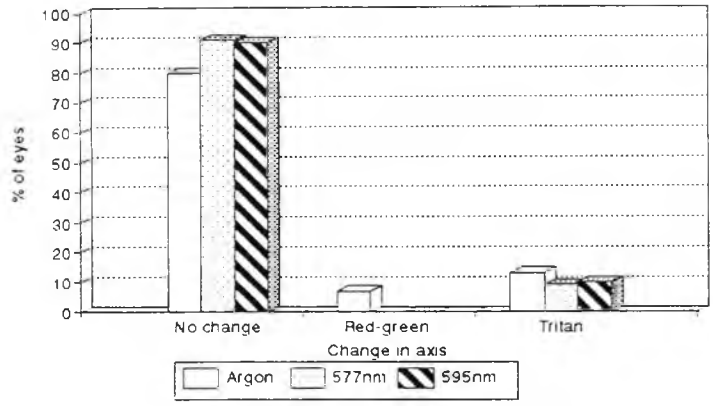


Fig 5.1 Change in axis on the FM 100-H: 1 week post-treatment

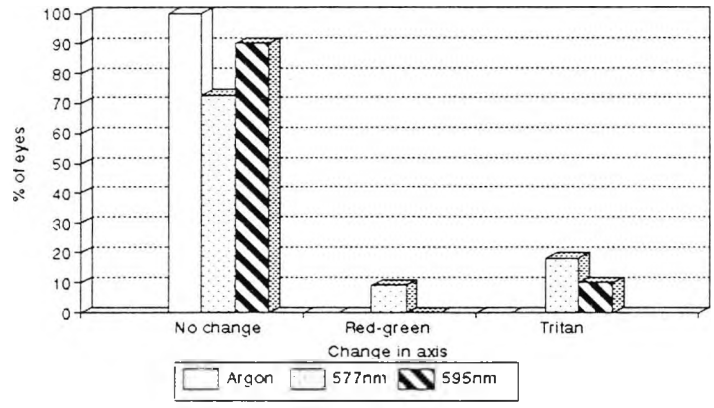


Fig 5.2 Change in axis on the FM 100-H: 1 month post treatment

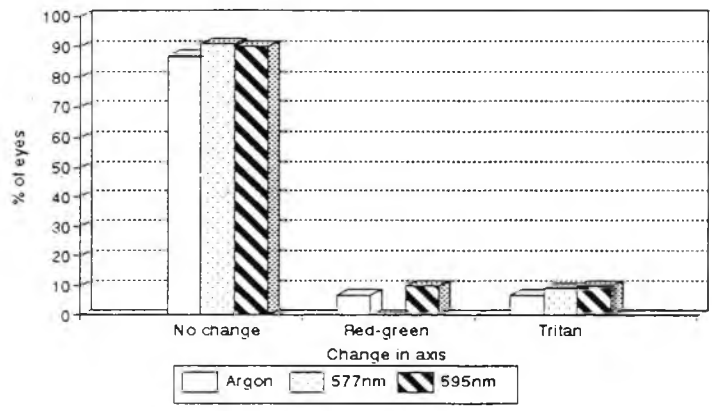


Fig 5.3 Change in axis on the FM 100-H: 3 months post-treatment

Group	Pre	1-wk	1-mo	3-mos
	Total scores			
Arg	82.1 sd 13.1	76.7 sd 13.9	78.3 sd 11.2	80 sd 10.3
577	85.5 sd 12.2	78.4 sd 16.7	79.1 sd 15.6	79.9 sd 14.9
595	80.4 sd 6.5	81.7 sd 11.2	80.7 sd 8.3	80.1 sd 11.2
Low spatial frequency scores				
Arg	24.3 sd 2.8	23.2. sd 3.5	23.9 sd 3.1	24.5 sd 4.1
577	25.6 sd 4.7	23.6 sd 4.9	23.4 sd 5.3	23.5 sd 3.7
595	23.6 sd 2.2	23.5 sd 2.6	24.5 sd 1.7	22.9 sd 2.6
Mid spatial frequency scores				
Arg	26.9 sd 5.5	24.3 sd 4.7	24.0 sd 4.0	25.3 sd 2.9
577	27.3 sd 5.2	25.3 sd 5.1	24.2 sd 4.7	25.1 sd 3.4
595	25.3 sd 3.1	25.7 sd 3.8	26.8 sd 2.9	26.0 sd 2.9
High spatial frequency scores				
Arg	30.9 sd 7.2	29.2 sd 7.2	29.4 sd 5.6	30.3 sd 6.5
577	34.2 sd 8.6	31.6 sd 7.6	31.6 sd8.9	31.5 sd 9.7
595	31.5 sd 6.06	32.5 sd 7.7	29.4 sd 5.2	31.2 sd 7.2

Arg=Argon treated group; 577=Dye-577nm treated group; 595=Dye-595nm treated group; Pre=Pretreatment; 1-wk=One week post treatment; 1-mo=One month post treatment; 3-mos=Three months post treatment;

Table 5.11 Mean results for the Arden gratings at all visits

Total scores												
ARGON TREATED EYES				577nm TREATED EYES				595nm TREATED EYES				ANOVA
TIME	NO	MEAN CHANGE	SE	TIME	NO	MEAN CHANGE	SE	TIME	NO	MEAN CHANGE	SE	
1 week	15	-5.47	2.77	1 week	11	-6.82	4.68	1 week	10	1.30	2.32	F(2,33) = 1.46, NS
1 month	15	-3.87	3.06	1 month	11	-6.36	3.97	1 month	10	0.30	1.79	F(2,33) = 0.98, NS
3 months	15	-2.13	3.29	3 months	11	-5.55	4.11	3 months	10	-0.30	2.27	F(2,33) = 0.54, NS

Low spatial frequency scores												
ARGON TREATED EYES				577nm TREATED EYES				595nm TREATED EYES				ANOVA
TIME	NO	MEAN CHANGE	SE	TIME	NO	MEAN CHANGE	SE	TIME	NO	MEAN CHANGE	SE	
1 week	15	-1.07	0.89	1 week	11	-2.00	1.89	1 week	10	-0.10	0.97	F(2,33) = 0.48, NS
1 month	15	-0.40	0.51	1 month	11	-2.27	1.84	1 month	10	0.90	0.99	F(2,33) = 1.73, NS
3 months	15	0.20	0.92	3 months	11	-2.18	1.61	3 months	10	-0.70	0.65	F(2,33) = 1.19, NS

Mid spatial frequency scores												
ARGON TREATED EYES				577nm TREATED EYES				595nm TREATED EYES				ANOVA
TIME	NO	MEAN CHANGE	SE	TIME	NO	MEAN CHANGE	SE	TIME	NO	MEAN CHANGE	SE	
1 week	15	-2.67	1.14	1 week	11	-2.00	1.18	1 week	10	0.40	1.21	F(2,33) = 1.73, NS
1 month	15	-1.93	1.19	1 month	11	-3.09	1.33	1 month	10	1.50	1.49	F(2,33) = 2.86, NS
3 months	15	-1.67	1.46	3 months	11	-2.18	0.91	3 months	10	0.70	1.45	F(2,33) = 1.13, NS

High spatial frequency scores												
ARGON TREATED EYES				577nm TREATED EYES				595nm TREATED EYES				ANOVA
TIME	NO	MEAN CHANGE	SE	TIME	NO	MEAN CHANGE	SE	TIME	NO	MEAN CHANGE	SE	
1 week	15	-1.73	1.29	1 week	11	-2.55	2.36	1 week	10	1.00	1.05	F(2,33) = 1.13, NS
1 month	15	-1.53	2.07	1 month	11	-2.64	1.74	1 month	10	-2.10	1.05	F(2,33) = 0.10, NS
3 months	15	-0.67	1.92	3 months	11	-2.73	2.50	3 months	10	-0.30	0.99	F(2,33) = 0.40, NS

Table 5.11a Comparison of mean changes in Arden gratings results for ARGON TREATED EYES, 577nm TREATED EYES and 595nm TREATED EYES at 3 follow-up times post treatment

Group	Pre	1-wk	1-mo	3-mos
	Global scores			
Arg	17.7 sd 5.9	17.1 sd 5.5	17.9 sd 5.5	18.9 sd 5.4
577	17.2 sd 7.7	15.5 sd 5.8	17.5 sd 7.4	15.9 sd 5.9
595	19.9 sd 5.6	17.2 sd 4.9	19.9 sd 5.2	20.4 sd 5.7
	Low spatial frequency scores			
Arg	9.3 sd 1.5	9.1. sd 1.7	9.1 sd 1.6	9.8 sd 1.4
577	9.1 sd 2.7	9.1 sd 1.8	9.1 sd 2.1	8.9 sd 1.5
595	10 sd 1.4	9 sd 1.4	9.8 sd 1.5	9.6 sd 1.1
	Mid spatial frequency scores			
Arg	3.7 sd 1.3	3.5 sd 1.3	3.9 sd 1.2	4.1 sd 1.1
577	3.6 sd 1.9	3 sd 1.3	3.6 sd 1.4	3.3 sd 1.6
595	4 sd 1.2	3.8 sd 1.1	4.2 sd 1.0	4.1 sd 1.1
	High spatial frequency scores			
Arg	3.4 sd 3.1	4.5 sd 2.9	4.2 sd 2.7	5 sd 3.5
577	2.6 sd 2.5	2.5 sd 1.9	2.6 sd 1.9	3.7 sd 3.3
595	4.9 sd 2.9	4.4 sd 3.5	5.9 sd 3.1	6.5 sd 3.5

Arg=Argon treated group; 577=Dye-577nm treated group; 595=Dye-595nm treated group; Pre=Pretreatment; 1-wk=One week post treatment; 1-mo=One month post treatment; 3-mos=Three months post treatment;

Table 5.12 Mean results for the VCTS 6000 at all visits

Global scores												
ARGON TREATED EYES				577nm TREATED EYES				595nm TREATED EYES				ANOVA
TIME	NO	MEAN CHANGE	SE	TIME	NO	MEAN CHANGE	SE	TIME	NO	MEAN CHANGE	SE	
1 week	15	-0.53	0.45	1 week	11	-1.73	0.45	1 week	10	-2.70	0.97	F(2,33)=1.22, NS
1 month	15	0.20	0.79	1 month	11	0.27	0.79	1 month	10	0.00	1.17	F(2,33)=0.02, NS
3 months	15	1.27	0.76	3 months	11	-1.27	0.76	3 months	10	0.50	0.92	F(2,33)=1.41, NS

Low spatial frequency scores												
ARGON TREATED EYES				577nm TREATED EYES				595nm TREATED EYES				ANOVA
TIME	NO	MEAN CHANGE	SE	TIME	NO	MEAN CHANGE	SE	TIME	NO	MEAN CHANGE	SE	
1 week	15	-0.20	0.17	1 week	11	0.00	0.70	1 week	10	-1.00	0.39	F(2,33)=1.31, NS
1 month	15	-0.20	0.33	1 month	11	0.00	0.69	1 month	10	-0.20	0.47	F(2,33)=0.05, NS
3 months	15	0.53	0.27	3 months	11	-0.18	0.71	3 months	10	-0.40	0.31	F(2,33)=1.27, NS

Mid spatial frequency scores												
ARGON TREATED EYES				577nm TREATED EYES				595nm TREATED EYES				ANOVA
TIME	NO	MEAN CHANGE	SE	TIME	NO	MEAN CHANGE	SE	TIME	NO	MEAN CHANGE	SE	
1 week	15	-0.13	0.26	1 week	11	-0.64	0.39	1 week	10	-0.20	0.33	F(2,33)=0.73, NS
1 month	15	0.27	0.23	1 month	11	-0.10	0.28	1 month	10	0.20	0.39	F(2,33)=0.43, NS
3 months	15	0.47	0.17	3 months	11	-0.36	0.43	3 months	10	0.10	0.23	F(2,33)=2.32, NS

High spatial frequency scores												
ARGON TREATED EYES				577nm TREATED EYES				595nm TREATED EYES				ANOVA
TIME	NO	MEAN CHANGE	SE	TIME	NO	MEAN CHANGE	SE	TIME	NO	MEAN CHANGE	SE	
1 week	15	1.13	0.84	1 week	11	-0.18	0.96	1 week	10	-0.50	1.06	F(2,33)=0.91, NS
1 month	15	0.80	0.95	1 month	11	-0.10	0.96	1 month	10	1.00	0.76	F(2,33)=0.36, NS
3 months	15	1.60	1.03	3 months	11	1.09	1.21	3 months	10	1.60	0.67	F(2,33)=0.08, NS

Table 5.12a Comparison of mean changes in VCTS 6000 results for ARGON TREATED EYES, 577nm TREATED EYES and 595nm TREATED EYES at 3 follow-up times post treatment

Group	Pre	1-wk	1-mo	3-mos
	Total field scores			
Arg	99.5 sd 17.4	82.8 sd 15.2	86.2 sd 17.4	91.8 sd 15.5
577	91.3 sd 17.6	81.6 sd 21.5	83.4 sd 21.0	89.1 sd 18.7
595	98.2 sd 11.3	89.4 sd 17.9	96.2 sd11.8	101.8 sd 11.1
	Macular zone scores			
Arg	116.0 sd 22.9	114.0 sd 22.9	115.3 sd 22.9	120.0 sd 22.0
577	116.4 sd 26.6	106.4 sd 35.3	105.6 sd 35.1	109.1 sd 31.5
595	124.0 sd 18.9	119.0 sd 22.8	130.0 sd 20.0	132.0 sd 16.9
	Zone 1 scores			
Arg	92.0 sd 19.9	86.6 sd 22.1	89.3 sd 23.3	94.2 sd 24.8
577	89.6 sd 25.2	87.9 sd 25.6	86.8 sd 24.1	92.7 sd 23.9
595	93.0 sd 22.9	91.0 sd 20.3	96.3 sd 16.9	101.0 sd 14.5
	Zone 2 scores			
Arg	93.7 sd 16.0	94.0 sd 14.0	95.3 sd 17.6	100.5 sd 15.3
577	96.5 sd 18.1	93.4 sd 19.6	94.3 sd 20.1	97.3 sd 17.4
595	101.3 sd 12.7	95.9 sd 15.6	102.7 sd 12.6	107.6 sd 9.7
	Zone 3 scores			
Arg	88.4 sd 18.2	86.9 sd 15.6	88.7 sd 17.4	94.3 sd 13.8
577	90.4 sd 16.2	94.8 sd 18.7	86.6 sd 18.2	90.6 sd 18.6
595	98.3 sd 12.9	93.3 sd 16.6	97.7 sd 11.9	101.5 sd 13.2
	Zone 4 scores			
Arg	87.7 sd 18.5	75.9 sd 18.3	80.3 sd 18.9	86.2 sd 16.2
577	88.6 sd 17.9	76.2 sd 27.5	77.2 sd 24.4	84.1 sd 20.7
595	96.1 sd 9.7	84.6 sd 21.5	90.3 sd 14.0	98.9 sd 12.5
	Zone 5 scores			
Arg	91.9 sd 19.8	70.2 sd 21.4	79.4 sd 20.7	83.7 sd 18.2
577	89.5 sd 21.6	69.0 sd 31.3	71.9 sd 28.3	81.6 sd 22.9
595	99.4 sd 14.8	81.9 sd 24.8	95.5 sd 15.2	98.7 sd 14.0

Arg=Argon treated group; 577=Dye-577nm treated group;
595=Dye-595nm treated group; Pre=Pretreatment;
1-wk=One week post treatment; 1-mo=One month post
treatment; 3-mos=Three months post treatment;

Table 5.13 Mean results for the VFA I at all visits

Total field scores												
ARGON TREATED EYES				577nm TREATED EYES				595nm TREATED EYES				ANOVA
TIME	NO	MEAN CHANGE	SE	TIME	NO	MEAN CHANGE	SE	TIME	NO	MEAN CHANGE	SE	
1 week	15	-7.68	2.70	1 week	11	-9.65	2.37	1 week	10	-8.74	3.12	F(2,33)=0.14, NS
1 month	15	-4.30	3.61	1 month	11	-7.86	2.57	1 month	10	-1.97	1.96	F(2,33)=0.81, NS
3 months	15	1.32	3.61	3 months	11	2.17	3.30	3 months	10	3.58	2.84	F(2,33)=0.63, NS

Macular zone scores												
ARGON TREATED EYES				577nm TREATED EYES				595nm TREATED EYES				ANOVA
TIME	NO	MEAN CHANGE	SE	TIME	NO	MEAN CHANGE	SE	TIME	NO	MEAN CHANGE	SE	
1 week	15	-2.00	3.12	1 week	11	-10.00	4.05	1 week	10	-5.00	3.07	F(2,33)=1.43, NS
1 month	15	-0.67	3.45	1 month	11	-10.73	6.83	1 month	10	6.00	3.71	F(2,33)=2.80, NS
3 months	15	4.00	4.12	3 months	11	-7.27	7.27	3 months	10	8.00	3.27	F(2,33)=2.17, NS

Zone 1 scores												
ARGON TREATED EYES				577nm TREATED EYES				595nm TREATED EYES				ANOVA
TIME	NO	MEAN CHANGE	SE	TIME	NO	MEAN CHANGE	SE	TIME	NO	MEAN CHANGE	SE	
1 week	15	-5.41	2.52	1 week	11	-1.68	3.01	1 week	10	-2.00	4.64	F(2,33)=0.44, NS
1 month	15	-2.67	2.82	1 month	11	-2.82	4.00	1 month	10	3.25	3.75	F(2,33)=0.71, NS
3 months	15	2.17	4.37	3 months	11	3.09	5.01	3 months	10	8.00	5.01	F(2,33)=0.40, NS

Zone 2 scores												
ARGON TREATED EYES				577nm TREATED EYES				595nm TREATED EYES				ANOVA
TIME	NO	MEAN CHANGE	SE	TIME	NO	MEAN CHANGE	SE	TIME	NO	MEAN CHANGE	SE	
1 week	15	0.33	1.88	1 week	11	-3.10	1.47	1 week	10	-5.40	1.60	F(2,33)=2.83, NS
1 month	15	1.67	3.47	1 month	11	-2.18	2.35	1 month	10	1.40	2.29	F(2,33)=0.49, NS
3 months	15	6.80	3.36	3 months	11	0.82	3.97	3 months	10	6.30	2.83	F(2,33)=0.88, NS

Table 5.13a Comparison of mean changes in VFA I results for ARGON TREATED EYES, 577nm TREATED EYES and 595nm TREATED EYES at 3 follow-up times post treatment

Zone 3 scores												
ARGON TREATED EYES				577nm TREATED EYES				595nm TREATED EYES				ANOVA
TIME	NO	MEAN CHANGE	SE	TIME	NO	MEAN CHANGE	SE	TIME	NO	MEAN CHANGE	SE	
1 week	15	-1.50	1.99	1 week	11	-5.55	2.11	1 week	10	-5.00	2.23	F(2,33)=1.19, NS
1 month	15	0.33	3.36	1 month	11	-3.82	3.13	1 month	10	-0.60	2.13	F(2,33)=0.49, NS
3 months	15	5.87	3.87	3 months	11	0.18	3.57	3 months	10	3.20	3.05	F(2,33)=0.63, NS

Zone 4 scores												
ARGON TREATED EYES				577nm TREATED EYES				595nm TREATED EYES				ANOVA
TIME	NO	MEAN CHANGE	SE	TIME	NO	MEAN CHANGE	SE	TIME	NO	MEAN CHANGE	SE	
1 week	15	-11.70	4.22	1 week	11	-12.36	4.92	1 week	10	-11.50	4.80	F(2,33)=0.01, NS
1 month	15	-7.40	4.18	1 month	11	-11.36	3.49	1 month	10	-5.80	2.78	F(2,33)=0.51, NS
3 months	15	-1.47	3.94	3 months	11	-4.45	3.04	3 months	10	2.80	3.28	F(2,33)=0.88, NS

Zone 5 scores												
ARGON TREATED EYES				577nm TREATED EYES				595nm TREATED EYES				ANOVA
TIME	NO	MEAN CHANGE	SE	TIME	NO	MEAN CHANGE	SE	TIME	NO	MEAN CHANGE	SE	
1 week	15	-21.71	5.37	1 week	11	-20.45	5.24	1 week	10	-17.44	5.58	F(2,33)=0.15, NS
1 month	15	-12.53	4.78	1 month	11	-17.50	3.88	1 month	10	-5.87	2.82	F(2,33)=1.63, NS
3 months	15	-8.25	4.82	3 months	11	-7.84	4.47	3 months	10	-0.74	3.37	F(2,33)=0.79, NS

Table 5.13a/Contd

ARGON TREATED			577nm TREATED			595nm TREATED		
Time	Normal	Defective	Time	Normal	Defective	Time	Normal	Defective
Pre	12	3	Pre	10	1	Pre	4	6
Post 1-week	11	4	Post 1-week	7	4	Post 1-week	4	6
Post 1-month	12	3	Post 1-month	7	4	Post 1-month	4	6
Post 3 months	10	5	Post 3 months	6	5	Post 3 months	4	6

Pre=Before treatment; Defective=includes all positive responses (metamorphopsia and/or scotoma)

Table 5.14 Amsler grid results of ARGON TREATED EYES, 577nm TREATED EYES and 595nm TREATED EYES at pre and post treatment times

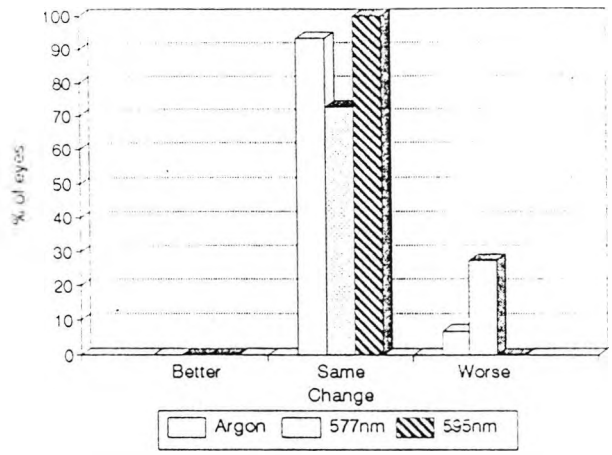


Fig 5.4 Change in Amsler grid results: 1 week post-treatment

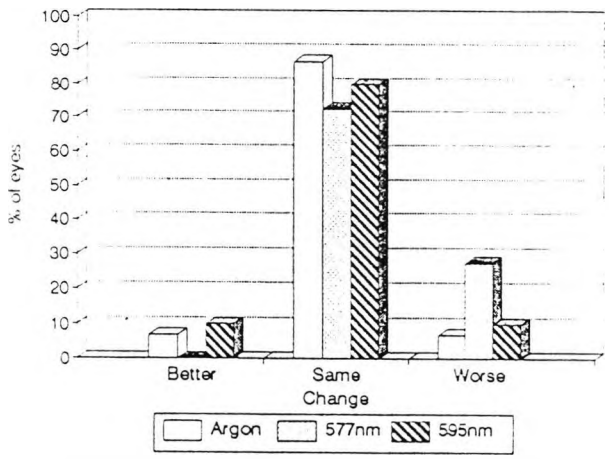


Fig 5.5 Change in Amsler grid results: 1 month post-treatment

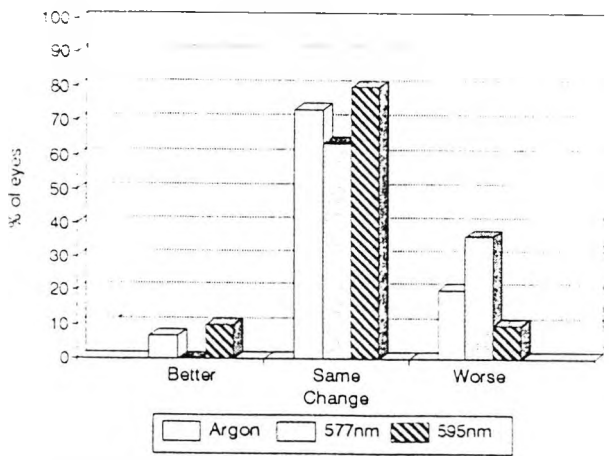


Fig 5.6 Change in Amsler grid results: 3 months post-treatment

showed significant decreases ($p<0.05$) in the scores of zones 4 (paired t-test, $t=-2.77, -2.51, -2.40$ for Argon, 577 & 595, respectively) and 5 (paired t-test, $t=-4.04, -3.90, -3.13$ for Argon, 577 & 595, respectively) one week post treatment. Between-group analysis, however, failed to show any significant differences ($p>0.05$) in the changes undergone by the 3 groups (ANOVA $F(2,33)=0.14$, 0.01, 0.15 for total field score, zone 4 and zone 5, respectively) implying that all 3 groups underwent similar deterioration in the central fields, particularly in the outer 15-degree regions, immediately after treatment irrespective of the wavelength used. At one month and 3 months post treatment, between-group differences in the field changes were not statistically significant anymore by ANOVA and paired t-test.

ANOVA failed to show any significant differences between the 3 groups in the changes in the other zones of the test (1,2, and 3) at all follow-up visits.

2. Amsler grid

Table 5.14 also shows the Amsler grid results in the 3 groups at each visit. Inspection of the table reveals that the majority of eyes treated with Argon and Dye-595nm did not undergo any changes while there was an indication of a slight increase (4 eyes) in the number of failures on the Amsler for the Dye-577nm treated group at the end of the study period.

Figures 5.4-5.5 show no significant differences in the changes in the Amsler grid results between the 3 groups through-out the follow-up period.

Appendix 5A is the computer print-out showing the results on the tests for all the patients in the study through-out the study period.

5.4 DISCUSSION

The concern about macular phototoxicity effects from Argon blue-green lasers (488/514nm) has resulted in a change in the practice by ophthalmologists at Moorfields Eye Hospital where they have now abandoned the use of the 488nm component in delivering PRP to diabetic patients. The findings of this study provide evidence that such phototoxicity effects (to the patient) are very mild with current practice of PRP delivery.

The Argon (488/514nm) laser has been found in the present study to produce a marginal increase in the blue-yellow (tritan) scores on the FM 100-H when compared to the other two longer wavelengths (577 and 595nm). This transient differential effect on the tritan region of colour vision confirms previous studies on the effects of Argon (488/514nm) on the colour vision of patients undergoing PRP for PDR (Birch-Cox,1978; Cambie,1980; Lavergne & Ramioul-Gougnard,1980; Birch & Hamilton,1981; Birch,1987).

The present study demonstrated a novel finding i.e. a much milder tritan effect, such that the obvious change in the axis towards the tritan mode could not be demonstrated. The change in the style of treatment could account for this; treatment given in the present study much reflected the current state-of-the art in PRP delivery. The number of burns given were restricted to only 2000, the burns were strictly applied to the areas outside the major arcades of the central vessels, the intensity of burns used was kept to the minimum possible and the duration of burns were short (0.1s). Cambie (1980) had noted that PRP given in a "loosely-scattered" fashion did not cause any changes in colour vision. In addition, patients in the present study were followed for only 3 months after only one session of treatment. The effects thus documented could not possibly reflect the actual colour vision changes undergone by diabetic patients; as in normal clinical practice additional treatment is often required over the ensuing period of time (Aylward et al.1989).

What the study has attempted to define is the short term effects of laser PRP with different wavelengths on macular function. In this way "confounding effects", such as different number of burns and different follow-up periods of patients, were avoided. The final visual effect thus produced would be that due to the laser alone. Previous studies (as quoted above) have not been able to segregate such "confounding effects" from those of the laser alone. The slight, but significant increase in the number of red-green axis on the D15(5/2) for patients treated with Dye-577nm in a way provides an indication of the subsequent involvement of the red-green system in patients with residual new vessels; for only 60% of eyes in this group had experienced regression of new vessels at the end of the study period (table 5.2). This original observation should not be confused with changes in colour vision that are attributable to the progression of retinopathy (rather than to the laser treatment *per se*) which have been discussed (Cambie,1980; Lavergne & Ramioul-Gougnard,1980).

The transient effects on the central fields recorded on the VFA I for all wavelengths used, in particular on the outer zones (zones 4 & 5), show that the light sensitivity of areas which were directly affected by the lasers were depressed, regardless of the wavelength used. The effects did not involve the inner areas (macular zone & zones 1 to 3), although (theoretically) shorter wavelengths (Argon 488/514nm) were supposed to scatter more within the eye media (Schepens,1983), and hence should have caused some inner-zone field defects. Nevertheless, the Argon laser employed did not prove to be affecting the central fields any more than the longer wavelengths.

The results of the present study confirm the effect of stray light on the macula during PRP (Birch-Cox,1978) that causes the deterioration in colour vision. The stray light from the Argon laser affected the tritan scores as expected, whilst the same laser did not cause any measurable changes in the inner-zone fields; the absence of such effects is an evidence for the indirect effects of

peripheral retinal lasering on the colour vision mechanism. The outer-zone fields were, as expected, directly affected by all the wavelengths employed. However, it was only after one month that the effect on the blue-yellow (tritan) scores became apparent; this could have been due to variation in the scores or could have meant that effects on the colour system was more of a "delayed" nature compared to the more "acute", direct fields effect. Nevertheless, at 3 months post treatment both effects have resolved, pointing to the transient nature of the effect; agreeing with previous reports (Birch,1987; Seiberth et al.1987; Canning et al.1991a).

Further evidence of central visual function effects from the stray light indirectly impinging on the macula could not be demonstrated by changes in the contrast sensitivity function and the Amsler grid results in the present study. The transient effects on contrast sensitivity reported (Bodis-Wollner,1983) could have very well tied up with the effects on colour vision observed. Such an acute effect was shown by Bodis-Wollner (1983) using laboratory-based CRT devices. However, since the effect of the stray light on colour vision is very small, it is not surprising such similar effect on the contrast sensitivity function was not demonstrable with the relatively gross clinical contrast sensitivity tests used in the present study (Arden gratings & VCTS 6000). In accord with Ghafour et al.(1984) the results of the clinical contrast tests showed considerable variations; any systematic effect that intense illumination might have was evidently more subtle than could be detected with the limited number of patients in the study. Furthermore, Mantyjarvi (1989b) had noted that some visual functions are so "robust" that they do not change at all as a result of laser PRP.

Canning et al.(1991b) showed convincingly that a mild dose of Argon (488/514nm) caused significant reduction in the tritan axis sensitivity of patients undergoing laser treatment for peripheral retinal holes using a colour contrast sensitivity apparatus devised by Arden (Arden et

al.1988a & 1988b). Such an exaggerated effect is not possible to be noted in patients with clinically available colour vision tests because of the imprecision of clinical tests. This is particularly true in diabetic patients, who normally manifest coarse colour vision defects (Gunduz & Arden,1989). The results of the present study show how poor and variable macular function is even in a group of diabetics with PDR selected for their good pretreatment visual acuity (i.e. 6/12 or better). In general the standard deviation of the baseline tests was large, and the values themselves were worse than those in non-diabetic patients. The diabetic eye is a poor model for the assessment of the subtle clinical side effects of lasers (Canning et al.1991a).

Histological studies have demonstrated that PRP treatment in the midperipheral retina with Argon (488/514nm), Argon green (514nm), Dye-577nm, Dye-590nm ,and Krypton (647nm) gave indistinguishable full-thickness retinal involvement (Smiddy et al.1984; Johnson et al.1987; Brooks et al.1989). Lighter PRP burns might spare the ganglion cell layer with the longer Dye wavelengths (Smiddy et al.1988). From these earlier works it seems that the 3 wavelengths that are being examined in the present study (Argon-488/514nm, Dye-577nm and Dye-595nm) do not differ much in their extent of destruction of the retinal layers. It is unlikely therefore that the amount of peripheral destruction by each wavelength would produce any differential effects on central visual functions. In fact this has been confirmed by the present results which showed that the outer fields were similarly affected by all 3 wavelengths.

Recent evidence also shows the possibility of short-wavelength light transmission via Henle's fibers to the central fovea, thus increasing the fovea's risk of photochemical damage (Mainster,1988). However, if it had been the act of peripheral burning (and consequently the induction of a "defect" via internal light transmission) that was causing the observed colour defect, then all 3 wavelengths would have also been expected to have given

rise to similar effects on other visual functions such as contrast sensitivity since the depth of burns were similar for all 3 wavelengths. But the effect was only evident for colour vision thus discounting the peripheral burning factor as a possible cause of the colour vision defect induced.

It has been shown that the Xenon arc, with wavelengths ranging from 350 to 1100nm produced similar tritan effects as those produced by Argon (488/514nm) (Birch-Cox,1978; Birch & Hamilton,1981). Thus, the contribution of peripheral damage (by laser light) to the induction of central damage to visual function (in this case colour vision) is weak. The most likely explanation for the effects on the blue-yellow scores by the Argon laser is the "splash over" or "light scatter" effect. Thus the only possible advantage of longer wavelengths is their theoretical relative intoxicity to the macular cones owing to their reduced "light scatter" effect in comparison with shorter wavelengths such as Argon (488/514nm). The blue cones, being the most vulnerable of all the cone systems in the retina (Mollon,1982) are particularly susceptible to the "light scatter" effect from Argon (488/514nm) light which is mainly targeted at the peripheral retina during PRP treatment. The fear of greater absorption of the Argon (488/514nm) by xanthophyll is also irrelevant with respect to PRP treatment, as laser light is only directed towards the midperiphery. In fact recent works have pointed out to the fact that the macular pigment confers a "protective" role to the macula rather than a "destructive" one (Haegerstrom-Portnoy,1985).

In conclusion, whilst acknowledging the limits imposed by the small number of patients having regression of new vessels over the follow-up period, the present study shows in an original and convincing manner that indirect macular effects from current practice of PRP for PDR (*in a mixed group of patients with types I & II diabetes*) tend to be of a very mild and transient nature. The differential effect on the blue-yellow system by the Argon (488/514nm)

was also statistically demonstrated, although not clinically important since obvious tritan defects were not produced by the treatment style given in the study; let alone permanent tritanopia. The more gross effects on colour vision could, nevertheless, be produced with much higher and repeated doses of long-duration doses of laser. There is some evidence from a small-scale study that PRP with smaller number (between 1627 & 2957) of short-duration (0.05-0.08s) burns produces transient acquired tritan defects (Birch,1987). Despite the fact that long wavelength lasers are less phototoxic to the macula and also scatter less within the eyeball (thus should be expected to produce less of a "light scatter" effect), the results of the present study do not show any clinically significant differential effects between the 3 wavelengths evaluated. The results of the present study could not support suggestions that filtering to remove the short wavelength (488nm) reduces the severity of the acquired tritan defects (Birch,1987), since the magnitude of the effect is too small. This lack of significance in the results should not, however, be taken as evidence that short wavelength lasers are as safe as longer wavelength ones. There is gathering proof (Berninger et al.1989; Gunduz & Arden,1989; Canning et al.1991a) in favour of longer wavelengths, and it seems that more ophthalmologists have avoided the Argon (488/514nm) laser in the light of these recent works.

CHAPTER 6

Study 4 Assessment of Visual Function in patients with Extensive Photocoagulation Treatment

6.1 INTRODUCTION

Studies on the efficacy of panretinal photocoagulation (PRP) treatment for proliferative diabetic retinopathy (PDR) by the Diabetic Retinopathy Study (DRS) Research Group showed that a single session of PRP reduced the incidence of severe visual loss (DRS Res.Gp.1981). The group, however, did not address the question of whether additional PRP was beneficial in those who did not respond to the initial dose of PRP.

Various authors have reported on this special group of patients who require PRP dosages in excess of the "standard" dose (Singerman & Weaver,1981; Little,1985; Vine,1985; Aylward et al.1989). Doft & Blakenship (1984) have coined the term "non-responders" to describe those who do not show any regression of retinopathy risk factors within a period of 3 weeks after the initial treatment. It has been shown in experimental animals that in such cases the new vessels continue to grow after PRP toward the adjacent non-photocoagulated (hypoxic) territory (Pournaras et al.1989). This indicates that PRP should be applied to the whole ischaemic/hypoxic territory in order to effect vessel regression and inhibit further neovascularisation. It is logical and indeed, clinically, it is a widespread practice to apply further PRP until regression of new vessels occurs. The application of more extensive PRP is said to reduce the risk of severe visual loss further than that achieved by the DRS Research Group, although Doft & Blakenship (1984) found no evidence that such therapeutic approaches are of proven benefit.

Aylward et al.(1989) found that 89% of eyes in their "non-responder" series of patients had a visual acuity of 6/18 or better, hence remarking that despite having received large amounts of PRP (range 5136 to 11,513 burns) their patients managed to maintain excellent functional vision. They, however, concluded with a cautionary note that those patients were very unlikely to have normal visual fields or colour vision.

In the present innovative study advantage was taken of the availability of such patients at Moorfields Eye Hospital to study in some detail the state of visual function in these patients. This was a cross-sectional observation of the colour vision, contrast sensitivity and visual fields of patients who had received ARGON laser PRP in excess of 4,000 burns, who at the time of examination had VA of 6/12 or better and whose retinopathy status were regarded as static. There have not been any previous studies on the visual function of patients who had undergone extensive amount of ARGON PRP for PDR. Most studies have been on those with lesser amounts of PRP. Furthermore, these studies have been concerned with patients who were still largely undergoing treatment (e.g. Cambie,1980; Birch & Hamilton,1981) and not those whose retinopathy have been described as "stable". Hence, as will be developed through this chapter and emphasised at its end, the present study broke new ground and achieved significant new knowledge; this has distinct benefits for clinicians and patients.

6.2 PATIENTS and PROCEDURES

Patients who had received extensive photocoagulation treatment for PDR were recruited for this study which was carried out at Moorfields Eye Hospital. The records of all patients attending a particular clinic session were reviewed beforehand and the records of those who satisfied the entry criteria were identified. The entry criteria were:

1. Have had ARGON laser photocoagulation treatment of more than 4000 burns. Fig 6.1 shows an example of an eye which satisfied the criterion.
2. Have had the last photocoagulation treatment at least three months before and no further photocoagulation pending.
3. Had not received Xenon Arc/Krypton laser photocoagulation or focal treatment to the macula.
4. No optic nerve or other macular disorders (e.g. glaucoma, optic neuritis, age-related maculopathy etc).

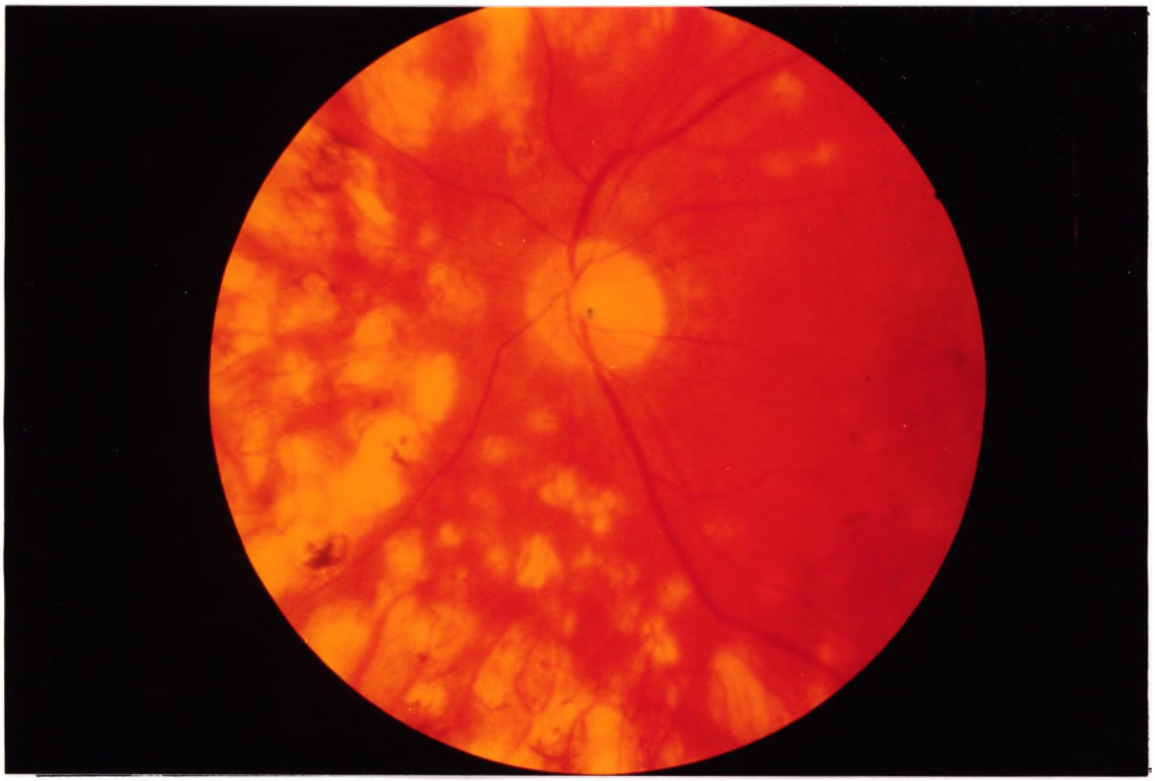


Fig 6.1 Fundus of an eye with extensive Argon laser PRP (case SMR, TotPRP=5909).

Number	Mean age (years)	Mean duration of diabetes (years)	No. on insulin	Mean VA (LogMAR)
24	39.9 sd 12.9	26.5 sd 11.6	22	0.12 sd 0.12

Table 6.1 Patient profile for Study 4

5. Had clear media.
6. No known congenital colour vision defects or amblyopia.

On the clinic day those who were earlier identified were asked to participate in the study. Only those with visual acuity of 6/12 or better (with habitual correction and/or pinhole) were finally admitted to the study. A total of 24 patients (9 males & 15 females) aged 22-65 yrs (mean 39.9 sd 12.9) were selected. The mean duration of diabetes was 26.5 years (sd 11.6) (range 9-49 years). 22 were on insulin while 2 were on diet or oral management. 3 patients had a visual acuity of 6/5, 5 had 6/6, 14 had 6/9 and 2 had 6/12. Table 6.1 displays the profiles of all patients selected for the study.

After informed consent was obtained, patients were examined with a battery of visual function tests comprising the following:

COLOUR VISION was examined with 6 clinical tests:
1) Comp PIC (excluding plate #16)
2) SPP2
3) LTA
4) D15 (5/4)
5) D15 (5/2)
6) FM 100-H

CONTRAST SENSITIVITY was measured with 2 clinical tests:
1) Arden gratings and 2) VCTS 6000

VISUAL FIELD was evaluated with 2 clinical tests:
1) VFA I and 2) Amsler grid

SEE CHAPTER 2 FOR DETAILS OF THE TESTS USED.

All tests (apart from VFA I) were administered monocularly for near vision under a standard illuminance of 1000 lux with the patient appropriately corrected. The examination room had pastel coloured walls which had minimal reflections. For the VFA I, examinations were done under

the illumination provided by the instrument, with the patient appropriately corrected. All tests of visual function were performed by the author.

After completing the test battery, patients underwent a full ophthalmic assessment which included slit lamp fundus biomicroscopy and binocular indirect ophthalmoscopy. Fundus photographs were also taken of some selected patients. Other pertinent information extracted from the notes included: VA at the start of laser treatment, indication for laser treatment (location of new vessels), details regarding delivery of laser treatment including total number of burns, number of treatment sessions and duration of treatment.

Analysis of data

Only results from the first examined eye are included in the present analysis. Results of visual function tests are expressed as means and sd values. Results of the FM 100-H, the VCTS 6000 and the VFA I were also classified as normal or abnormal, based on published age-norms of each test (see Chapter 2). The data obtained was analysed using the SAS statistical package (SAS Software Version 5 edition). Statistical tests carried out included t-test, Chi-Square test and Multivariate analysis (using the GLM procedure). In all statistical tests a probability value (p value) of less than 0.05 was taken as being significant.

In the multivariate analysis using the GLM procedure each test was assigned as the dependent variable in the determination of its significant contributors. Independent variables included in the model were: Age, duration of diabetes, type of DR at the start of treatment, total PRP, mean number of burns per session, mean interval between sessions, time after last treatment and LogMAR VA. Type of DR at the start of treatment was assigned as a categorical variable while the rest were assigned as continuous variables. Having identified the significant contributors of a particular test's performance, the direction of effect

Patient	Total no. of PRP burns	No. of sessions	Mean no. of burns per session	Duration of treatment (months)	Mean interval between sessions (months)	Time lapse after last treatment (months)	Visual acuity at start	Final visual acuity
IHL	12242	19	644	20	1.1	3	6/9	6/9
AOR	10402	14	743	28	2.0	3	6/6	6/5
CBL	10127	12	844	21	1.8	71	6/5	6/9
SKR	9703	12	809	29	2.4	18	6/9	6/9
JLL	8669	11	788	47	4.3	33	6/5	6/6
ABR	8382	24	349	96	4.0	53	6/5	6/9
MPR	8170	15	545	34	2.3	14	6/6	6/12
RLR	7844	12	654	86	7.2	3	6/6	6/9
PTL	7833	10	783	54	5.4	14	6/9	6/9
THR	7659	10	766	17	1.7	46	6/5	6/5
LWR	7541	10	754	47	4.7	24	6/5	6/9
LDR	7212	9	801	35	3.9	16	6/36	6/9
LPL	7097	8	887	10	1.3	65	6/9	6/6
JTR	6894	10	689	36	3.6	3	6/9	6/12
JSL	6817	6	1136	21	3.5	13	6/5	6/6
GDR	6716	8	840	15	1.9	3	6/9	6/9
HCR	6162	13	474	24	1.9	56	CF	6/5
LDL	5909	6	985	50	8.3	5	6/24	6/9
SMR	5909	8	739	6	0.8	36	6/9	6/9
JIL	5445	11	495	15	1.4	29	6/9	6/9
ENL	5000	7	714	77	11.0	41	6/6	6/6
PDR	4891	7	699	40	5.7	19	6/9	6/9
EGL	4868	5	1106	55	11.0	22	6/9	6/9
TBR	4100	2	2050	9	4.5	27	6/5	6/6

Table 6.2 Data on treatment and visual acuity

of each contributor was determined by the sign of the regression coefficients which were generated subsequently by multiple regression.

6.3 RESULTS

6.3.1 Treatment data

In all cases treatment was delivered by an ARGON (488/514nm) laser through a Goldmann 3-mirror or a Rodenstock panfunduscopic contact lens. Spot size was 500 microns when using the Goldmann and 200 microns when using the Rodenstock contact lens. The duration of burns recorded in the notes ranged between 0.1 to 0.2s. The power levels recorded were those which were required to give slight blanching of the retinal pigment epithelium whilst delivering the laser treatment. The end point of treatment was complete regression of new vessels, or complete regression of new vessels with gliosis, or residual fine, flat new vessels with fibrosis which remained static. All 24 patients satisfied at least one of these end-point criteria and hence were considered to be stable at the time of examination.

Data on the number of burns, number of treatment sessions, duration of treatment, time after last treatment and visual acuity at the start of treatment is shown in table 6.2. The mean total number of burns for the 24 patients was 7316.3 (sd 1967.3), range 4100 to 12.242. The mean number of treatment sessions for each patient was 9.96, range 2 to 23, and the mean duration of treatment was 36.3 months, range 9 to 96. The mean of the mean interval between sessions was calculated to be 4 months (sd 2.9). The mean of the mean number of laser burns per session was calculated to be 803.9 (sd 320.9). The mean time after the last treatment session was 25.7 months, range from 3 to 71 months.

Fig 6.2 is a scattergram showing the VAs before and after treatment of the patients in the study. Within this group

of patients selected for their good VA (6/12 or better), 9 patients (37.5%) had VAs lower than the pretreatment values, 5 patients (20.8%) had better VAs whilst 10 patients (41.7%) ended with no change in VA after treatment.

6.3.2 Test results in comparison with an untreated group

Twenty five patients with proliferative DR (PDR) without any macular involvement (from chapter 4 of this Thesis) who had been tested with the same battery of tests were compared with the present group of patients. The mean age of patients in the "PDR" group, (47.2 sd 17.8 yrs) was not significantly different from that of the "extensively lasered" (XL) group (t-test, $t=-1.6$, $p>0.05$). The mean duration of diabetes in the PDR group, (15.6 sd 9.4yrs) was significantly less than that of the XL group (t-test, $t=3.6$, $p<0.05$). The mean VA of the two groups was not significantly different i.e. 0.12 vs 0.09 for the XL and PDR groups respectively (t-test, $t=0.9$, $p>0.05$).

6.3.2a Colour vision

Table 6.3 shows the mean results of the colour vision tests for the two groups. Significant differences in the mean values between the two groups are indicated (t-test). Significant differences between the two groups were only noted in the LTA scores and in the difference between the square roots of the blue-yellow and red-green scores on the FM 100-H test. This indicates a higher prevalence of tritan defects in the XL group than in the PDR group.

Fig 6.3 shows the percentages of patients showing diagnostic axes on the FM 100-H test for the two groups of patients. Patients in the XL group can be seen to possess more tritan axes than those in the PDR group (although for most patients in both groups, no significantly identifiable axes could be demonstrated), confirming the statement above regarding the excess prevalence of tritan axis in the XL group, relative to the PDR group.

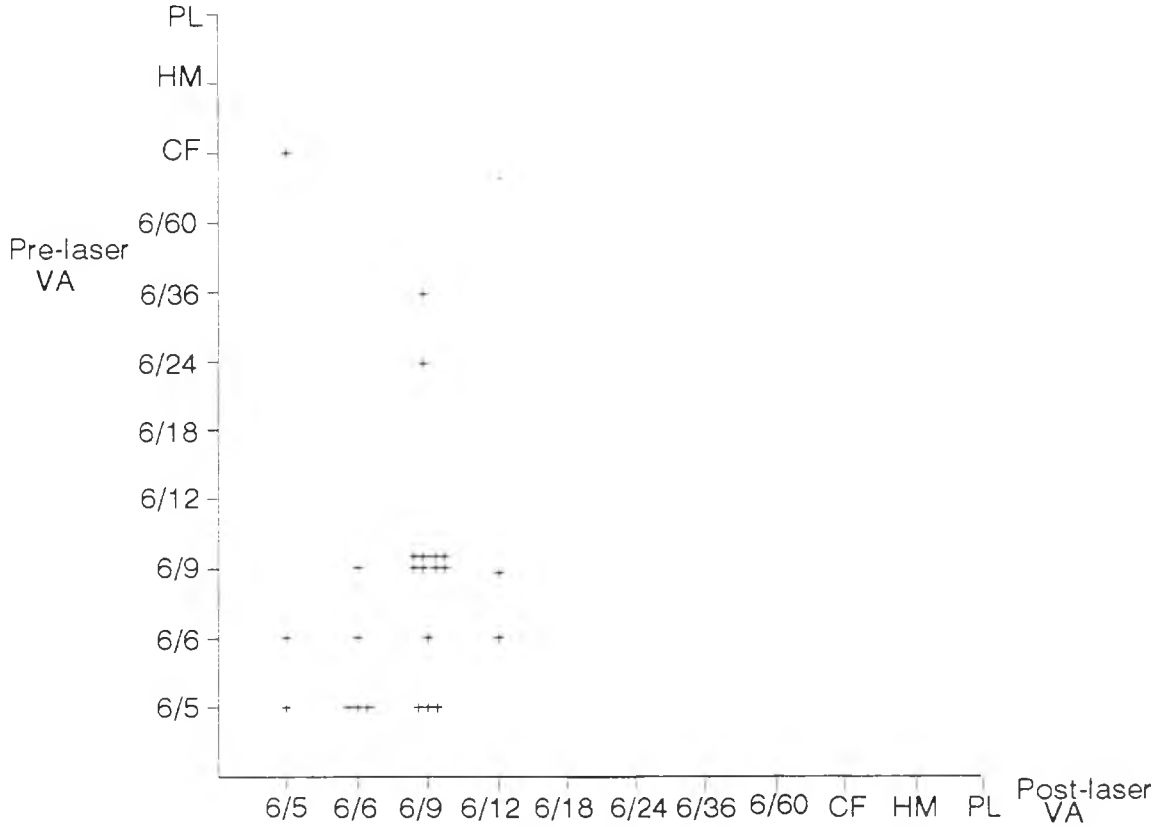
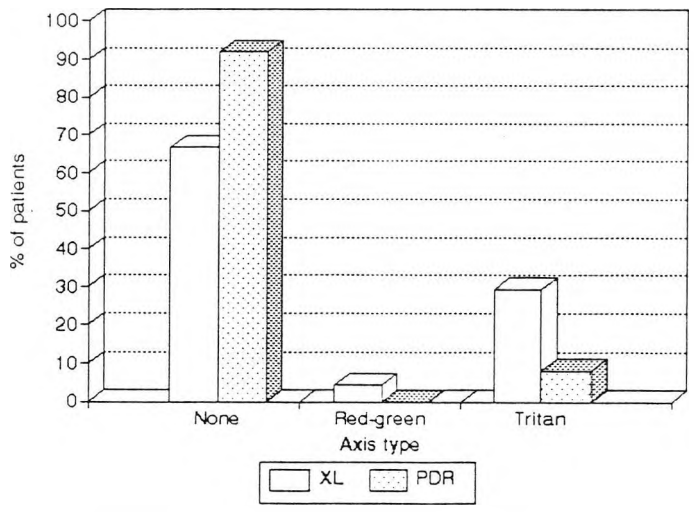


Fig 6.2 Scattergram showing visual acuities before & after ARGON PRP

Test results	Group		t-test	
	XL	PDR		
Comp PIC				
TPE	5.5 (sd 3.8)	4.4 (sd 3.6)	t=1.0	NS
RG errors	1.3 (sd 2.1)	0.8 (sd 1.7)	t=0.8	NS
Tritan errors	4.3 (sd 2.2)	3.7 (sd 2.4)	t=0.9	NS
SPP2				
Total errors	8.1 (sd 4.7)	7.2 (sd 4.9)	t=0.7	NS
RG errors	2.6 (sd 1.8)	2.1 (sd 1.8)	t=1.1	NS
Tritan errors	5.5 (sd 3.3)	5.1 (sd 3.3)	t=0.4	NS
LTA	1.5 (sd 1.6)	3.9 (sd 2.0)	t=-4.6	p<0.05
D15(5/4)				
Score	5.5 (sd 7.1)	8.2 (sd 10.0)	t=-1.1	NS
RG axis	0.0	0.04 (sd 0.20)	t=-0.9	NS
T axis	0.3 (sd 0.7)	0.5 (sd 0.9)	t=-0.8	NS
D15(5/2)				
Score	15.5 (sd 13.3)	13.8 (sd 12.8)	t=0.4	NS
RG axis	0.08 (sd 0.41)	0.04 (sd 0.20)	t=0.5	NS
T axis	0.9 (sd 1.4)	0.8 (sd 1.5)	t=0.1	NS
FM 100-H				
SqTES	14.4 (sd 4.2)	14.4 (sd 4.7)	t=0.04	NS
SqRG	8.8 (sd 3.1)	9.3 (sd 3.1)	t=-0.5	NS
SqBY	11.1 (sd 3.1)	10.8 (sd 3.7)	t=0.4	NS
SqBY-SqRG	2.4 (sd 1.4)	1.5 (sd 1.5)	t=2.0	p<0.05

TPE=Total plate errors; RG=Red-green; T=Tritan; SqTES=Square root of total error scores; SqRG=Square-root of red-green scores; SqBY=Square-root of blue-yellow scores; XL=Extensively lasered group; PDR=Proliferative DR group

Table 6 3 Mean colour vision test results for groups XL and PDR



XL=Extensively lasered group; PDR=Proliferative DR group

Fig 6 3 Presence of diagnostic axes in XL and PDR groups

Multivariate analysis revealed that this preponderance of tritan axis in the XL group did not depend on any other confounding factors (age, insulin therapy, duration of diabetes or VA). The "grouping" of the patient was the main determinant (F=5.92) of the tritan defect.

6.3.2b Contrast sensitivity

Table 6.4 shows the mean results of the two contrast sensitivity tests for the two groups. Significant differences in the mean values between the two groups are indicated (t-test). No significant differences were found in any of the contrast sensitivity test results between the two groups.

6.3.2c Visual field

1. VFA I

The mean field values on the VFA I of groups XL and PDR are shown in table 6.5. Significant differences in the mean values between the two groups are indicated (t-test). Statistically significant differences between the two groups were found in the following scores: total field, zones 3,4 and 5.

Multivariate analysis revealed that the poorer visual fields in the XL group, relative to the PDR group, depended on 2 factors i.e. the "grouping" of the patient (F=20.5,13.5,21.1,39.1 for total field, zones 4,5 & 6 respectively, all $p<0.05$) and VA (F=11.9,8.1,9.4,6.9 for total field, zones 4,5 & 6 respectively, all $p<0.05$). Age, insulin therapy and duration of diabetes did not feature as significant determinants of the visual field.

2. Amsler grid

Fifteen (62.5%) of the patients in the XL group showed a positive response on the Amsler grid compared to 7 (28%) from the PDR group. This difference was statistically

significant (Chi-Sq=5.89,dF=1,p<0.05).

Appendix 6A is the master table showing the results of all the visual function tests on all the patients (including those in the "control" group with PDR).

6.3.3 Multiple visual dysfunction

Fig 6.4 shows the percentage of patients in the two groups (XL & PDR) having abnormal visual functions. Abnormality in each function was defined as an abnormal result on the FM 100-H (colour vision), the VCTS 6000 (contrast sensitivity) and the VFA I (visual field) according to criteria explained in chapter 2. It can be seen that within the XL group there was a high percentage of patients with abnormalities in the 3 visual functions.

Between-group (XL vs PDR) analysis of fig 6.6 showed significantly more patients with colour vision defects in the XL (20(83.3%)) group than in the PDR (13(52%)) group (Chi-Sq=5.47,dF=1,p<0.05). There were also significantly more patients with visual field defects in the XL group compared to the PDR group i.e. 20(83.3%) vs 9(36%) (Chi-Sq=11.36,dF=1,p<0.05). No significant differences were noted in the proportion of patients with contrast sensitivity defects between the two groups (Chi-Sq=0.50,dF=1,p>0.05).

Fig 6.5 is a Venn diagram showing the overlap in the visual dysfunction of the XL group. Most patients (62.5%; n=15) had abnormalities in all 3 functions simultaneously. Equal numbers of patients (3) had combined abnormalities in colour vision & visual field and contrast sensitivity & visual field. Only one patient with normal contrast sensitivity was abnormal in both colour vision and visual field. There was also only one patient who had a sole colour vision or visual field defect. No patient had a contrast sensitivity defect alone. Therefore it can be seen that most patients (92%) had combined losses, with a majority having abnormalities in all 3 functions.

Test results	Group				t-test	
	XL		PDR			
Arden gratings						
Total score	79.3	(sd 14.8)	82.1	(sd 11.3)	t=-0.8	NS
Plate 2	12.0	(sd 2.9)	12.8	(sd 2.3)	t=-0.9	NS
Plate 3	11.2	(sd 2.5)	11.8	(sd 1.5)	t=-1.0	NS
Plate 4	12.6	(sd 2.6)	13.1	(sd 1.7)	t=-0.8	NS
Plate 5	12.7	(sd 2.8)	13.6	(sd 3.4)	t=-0.9	NS
Plate 6	14.6	(sd 3.5)	14.8	(sd 2.8)	t=-0.3	NS
Plate 7	16.2	(sd 4.1)	16.1	(sd 4.3)	t=0.0	NS
VCTS 6000						
Global score	18.1	(sd 4.8)	19.0	(sd 6.1)	t=-0.6	NS
Sp/f A	4.4	(sd 0.8)	4.6	(sd 1.0)	t=-0.9	NS
Sp/f B	4.9	(sd 0.7)	5.2	(sd 1.0)	t=-1.0	NS
Sp/f C	4.0	(sd 1.0)	3.9	(sd 1.3)	t=0.5	NS
Sp/f D	2.8	(sd 1.6)	3.0	(sd 1.7)	t=-0.4	NS
Sp/f E	1.9	(sd 1.8)	2.3	(sd 2.0)	t=-0.7	NS

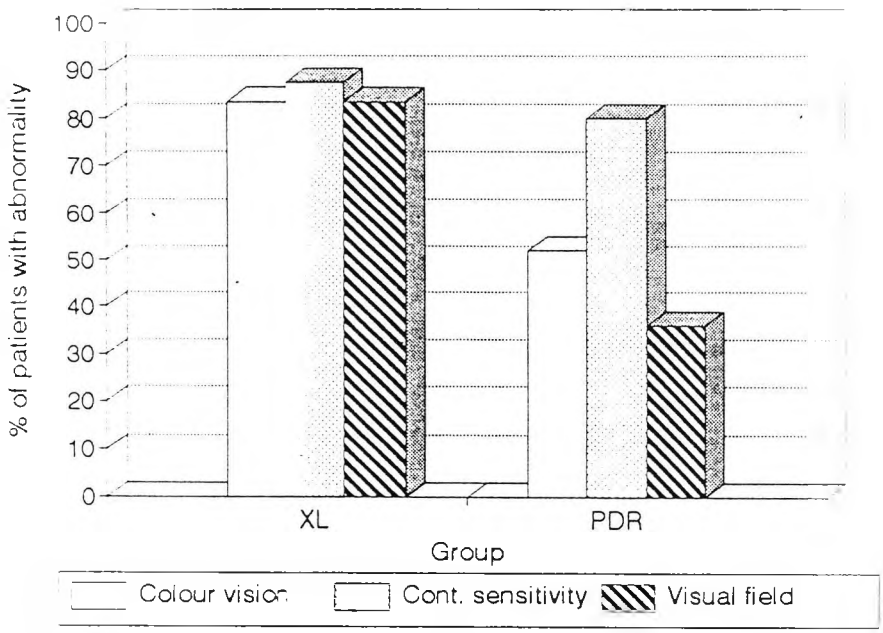
Plate 2 - Plate 7=Scores for plates 2 to 7; Sp/f A - Sp/f E=Scores for spatial frequencies A to E; XL=Extensively lasered group; PDR=Proliferative DR group.

Table 6.4 Mean contrast sensitivity results for groups XL and PDR

Test results	Group				t-test	
	XL		PDR			
TF score	68.8	(sd 17.3)	92.0	(sd 16.3)	t=-4.8	p<0.05
Macular Zone	116.7	(sd 13.4)	119.2	(sd 20.2)	t=-0.5	NS
Zone 1	85.6	(sd 16.9)	91.1	(sd 20.7)	t=-1.0	NS
Zone 2	90.3	(sd 13.2)	96.4	(sd 15.6)	t=-1.5	NS
Zone 3	70.5	(sd 19.8)	91.1	(sd 17.1)	t=-3.9	p<0.05
Zone 4	59.5	(sd 22.4)	88.8	(sd 16.8)	t=-5.2	p<0.05
Zone 5	43.1	(sd 27.4)	91.9	(sd 19.9)	t=-7.2	p<0.05

TF=Total field; XL=Extensively lasered group; PDR=Proliferative DR group

Table 6.5 Mean field scores on the VFA I for groups XL and PDR



XL = Extensively lasered group; PDR = Proliferative DR group

Fig 6.4 Proportion of patients with abnormal visual functions in the XL and PDR groups

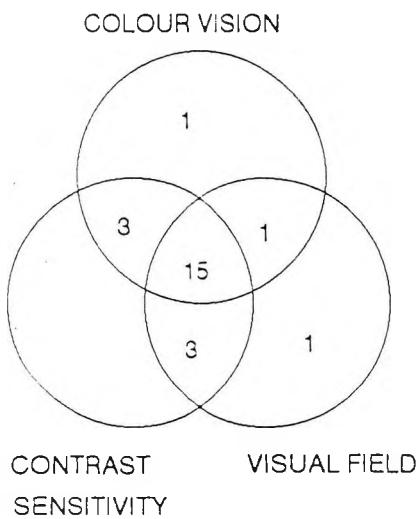


Fig 6.5 Number of patients with different combinations of visual dysfunctions

6.3.4 Relationship between visual function and patient/treatment variables

The results of multivariate analysis on all the visual function test results are shown in table 6.6. Significant correlations between visual function test results and patient/treatment variables are noted by their respective F-values. The following comments are made in reference to table 6.6 where the directions of association were determined by the sign of the regression coefficients, as explained on page 298.

Of the patient-related variables, duration of diabetes seemed to have a major effect; paradoxically, diabetes duration related negatively to errors on the tritan plates of the Comp PIC, number of tritan axes on the D15 (5/4) and mid spatial frequency contrast sensitivity scores on the VCTS 6000. Age (at examination) also affected some colour vision test variables, both in the red-green and tritan regions; age related negatively to errors on the red-green plates of the Comp PIC, errors on the LTA and number of red-green axes on the D15(5/2). However, on the contrary, age related positively to the number of tritan axes on the D15(5/2).

Of the treatment related variables, the mean number of burns per session (MBPS) and the total number of burns (TotPRP) emerged as significant determinants of many colour vision and contrast sensitivity test variables. MBPS in particular affected performance on the red-green and tritan PIC plates of the Comp PIC, both the red-green and blue-yellow scores on the FM 100-H test and the low and high spatial frequency scores on the VCTS 6000. For all these variables, MBPS unexpectedly related negatively i.e. decreasing values of MBPS were associated with poorer performance on the test variables (table 6.7). TotPRP affected both the red-green and tritan plates of the Comp PIC but only the tritan plates of the SPP2 test. TotPRP also affected the mid and high spatial frequency scores of the VCTS 6000. In these cases, the relationship was

unexpectedly an inverse one i.e. increasing TotPRP was associated with better visual performance (table 6.8). In inspecting tables 6.7 and 6.8 note that two variables can have a low correlation but a strong relationship ie. the relationship could be quadratic.

Other treatment related variables seemed to be of lesser importance, although increased mean interval between treatment sessions (MIBS) was associated with increases in LTA scores and the number of red-green axes on the D15(5/2) but a decrease in the number of tritan axes on the same test. The time after the last treatment session (TALT) also affected the D15(5/2) such that an increase in TALT was associated with less number of tritan axes.

Poorer VA was associated with increases in tritan errors on the Comp PIC, poorer high spatial frequency contrast sensitivity scores on the VCTS 6000 and poorer field scores (particularly the macular zone and zone 2). The Arden grating scores were not found to be significantly related to any of the variables tested in the model.

6.4 DISCUSSION

Two major aspects of visual dysfunction in diabetics have been highlighted in the present study. First, the results show that there is an excess prevalence of tritan defects among patients who have received extensive amount of ARGON laser PRP. This is "expected", as distinct from the second aspect which is novel. That is, it is shown that despite the expected decline in visual function with increasing amount or intensity of PRP, the relationship seems unclear, although the converse has been unexpectedly demonstrated in the case of colour vision and contrast sensitivity.

6.4.1 The Visual dysfunction

The finding that most of these patients had tritan colour vision defects was rather expected. Previous studies showed that ARGON laser PRP accentuates the tritan colour defect

Visual function test	Patient/Treatment variables							
	Age	YrsDM	TypeDR	TotPRP	MBPS	MIBS	TALT	VA
Comp PIC								
TPE	-	6.6 b	-	9.9 b	20.2 b	-	-	-
RG error	8.3 b	-	-	7.4 b	11.6 b	-	-	-
Tritan error	-	20.1 b	-	19.5 b	50.1 b	-	-	6.1 b
SPP2								
Total error	-	-	-	4.9 b	10.1 b	-	-	-
RG error	-	-	-	-	4.4 b	-	-	-
Tritan error	-	4.9 b	-	5.6 b	10.8 b	-	-	-
LTA	5.3 b	4.8 b	-	-	13.4 b	4.3 a	-	-
D15(5/4)								
Score	-	-	-	-	4.5 b	-	-	-
RG axis	-	-	-	-	-	-	-	-
T axis	-	5.0 b	-	-	6.0 b	-	-	-
D15(5/2)								
Score	-	-	-	-	-	-	9.3 b	-
RG axis	4.4 b	-	-	-	-	9.5 a	-	-
T axis	12.7 a	-	-	-	-	6.1 b	9.6 b	-
FM 100-H								
SqTES	-	-	-	-	10.1 b	-	-	-
SqRG	-	-	3.7 a	-	14.7 b	-	-	-
SqBY	-	-	-	-	8.4 b	-	-	-
SqBY-SqRG	-	-	-	-	-	-	-	-
Arden gratings								
Total	-	-	-	-	-	-	-	-
PL2	-	-	-	-	-	-	-	-
PL3	-	-	-	-	-	-	-	-
PL4	-	-	-	-	-	-	-	-
PL5	-	-	-	-	-	-	-	-
PL6	-	-	-	-	-	-	-	-
PL7	-	-	-	-	-	-	-	-
VCTS 6000								
Global	-	-	-	5.7 a	12.2 a	-	-	7.2 b
SpA	-	-	-	-	4.8 a	-	-	-
SpB	-	-	-	-	-	-	-	-
SpC	-	4.8 a	-	6.4 a	-	-	-	-
SpD	-	-	-	-	10.4 a	-	-	6.9 b
SpE	-	-	-	5.2 a	-	-	-	14.0 b
VFA I								
TF	-	-	-	-	-	-	-	4.5 b
Macular	-	-	-	-	-	-	-	8.4 b
Z1	-	-	-	-	-	-	-	-
Z2	-	-	-	-	-	-	-	5.3 b
Z3	-	-	-	-	-	-	-	-
Z4	-	-	-	-	-	-	-	-
Z5	-	-	-	-	-	-	-	-

All indicated F-values are for $p<0.05$; -=NS ; a=positive correlation; b=negative correlation

TPE=Total plate errors; RG=Red-green; T=Tritan; SqTES=Square-root of total error scores; SqRG=Square-root of red-green scores; SqBY=Square-root of blue-yellow scores; PL2 to PL7=Scores on plates 2 to 7; Global=Global score; SpA to SpE=Scores of spatial frequencies A to E; TF=Total field score; Macular=Macular zone score; Z1 to Z5=Scores of zones 1 to 5; YrsDM=Years of diabetes; TypeDR=Type of DR at start of treatment; TotPRP=Total number of PRP burns; MBPS=Mean number of burns per session; TALT=Time interval after last treatment (months); VA=LogMAR

Table 6.6 F-values for significant correlations between visual function test results and patient/treatment variables

Patient	MBPS	Comp PIC		FM 100-H		VCTS 6000	
		RGE	BYE	SqRG	SqBY	SPA	SPD
ABR	349	0	2	4.58	6.78	6	3
HCR	474	3	7	11.00	14.53	4	2
JIL	495	4	7	11.05	11.66	2	1
MPR	545	6	5	11.58	13.49	4	1
IHL	644	2	4	9.27	12.21	5	2
RLR	654	0	2	9.75	8.12	4	2
JTR	689	0	6	12.57	15.10	4	1
PDR	699	0	1	4.80	6.00	5	2
ENL	714	1	4	13.53	14.56	5	3
SMR	739	6	7	10.10	14.28	5	2
AOR	743	0	6	8.54	10.68	5	6
LWR	754	1	3	10.58	13.56	4	2
THR	766	0	6	7.00	9.75	4	4
PTL	783	0	5	5.48	8.54	4	3
JLL	788	0	7	8.49	14.21	4	3
LDR	801	0	2	9.22	9.80	4	2
SKR	809	0	3	9.06	11.70	5	3
GDR	840	1	7	11.09	14.35	5	2
CBL	844	0	1	7.68	9.43	4	4
LPL	887	0	4	8.77	10.95	5	3
LDL	985	6	7	12.88	14.46	4	4
EGL	1106	0	3	5.48	7.87	4	1
JSL	1136	0	4	8.31	11.53	4	4
TBR	2050	0	0	0.00	3.87	6	8

MBPS=Mean number of burns per session; RGE=Number of red-green plate errors; BYE=Number of tritan plate errors; SqRG=Square-root of red-green scores; SqBY=Square-root of blue-yellow scores; SPA=Score for spatial frequency A; SPD=Score for spatial frequency D

Table 6.7 MBPS (in increasing order) in relation to colour vision and contrast sensitivity test results

Patient	TotPRP	Comp PIC		VCTS 6000	
		RGE	BYE	SPC	SPE
TBR	4100	0	0	7	8
EGL	4868	0	3	3	1
PDR	4891	0	1	0	1
ENL	5000	1	4	4	4
JIL	5445	4	7	2	0
SMR	5909	6	7	4	0
LDL	5909	6	7	4	1
HCR	6162	3	7	3	2
GDR	6716	1	7	4	0
JSL	6817	0	4	4	3
JTR	6894	0	6	3	0
GDR	7097	1	7	4	0
LDR	7212	0	2	4	1
LWR	7541	1	3	4	5
THR	7659	0	6	5	0
PTL	7833	0	5	4	0
RLR	7844	0	2	3	0
MPR	8170	6	5	3	1
ABR	8382	0	2	5	2
JLL	8669	0	7	5	3
SKR	9703	0	3	4	1
CBL	10127	0	1	4	3
AOR	10402	0	6	5	6
IHL	12242	2	4	5	0

TotPRP=Total number of ARGON PRP burns; RGE=Number of red-green plate errors; BYE=Number of tritan plate errors; SPC=Score for spatial frequency C; SPE=Score for spatial frequency E

Table 6.8 TotPRP (in increasing order) in relation to colour vision and contrast sensitivity test results

in diabetic patients, at least transiently (Birch-Cox,1978; Cambie,1980; Birch & Hamilton,1981; Birch,1987). In fact, in chapter 5 of this thesis, a study conducted to compare the short term effects on visual function of different wavelengths of the Dye laser showed that the blue-green (488/514nm) wavelength produces a very mild deterioration in colour vision in the blue-yellow region of the colour spectrum. It is only logical to assume that repeated bombardment of the retina will produce a cumulative effect and will have added to the mild transient effect in order to produce the observed (prolonged) tritan defect.

In chapter 5 the observed effect on colour vision was partly attributed to the "light scatter" effect of laser light onto the macula. In the present study the finding of defects encroaching onto the inner zones of the central visual field, together with the presence of tritan colour vision defects serve to consolidate this postulation. Extensive lasering of the peripheral retina with ARGON laser has not only affected the outer zones of the 30-degree visual field (zones 4 & 5) confirming the results of chapter 5, but has now shown some impinging effects on the inner zone as well (zone 3). This support for the earlier observation (of chapter 5) again, emphasises the original finding of the study presented in this chapter.

There is also the possibility that destruction of the peripheral receptors may contribute to the central deficit. This is inferred from the observation by Trezona (1970) that some rods have intimate connections with the central blue cones, hence when disrupted will effect changes in colour vision (Birch-Cox,1978). However, this could not be unequivocally said before, as in chapter 5. From the calculations of Vine (1985), the maximum number of contiguous but non-overlapping 500 micron ARGON burns that may be applied to the retina is approximately 5500. One of the reasons why there were patients in the present study with more than this amount of ARGON burns is because these people had received overlapping burns (Aylward et al.1989). Thus in the majority (79.2%) of patients in the present

series (i.e. those with overlapping burns), the peripheral retina can be assumed to be thinned as a result of extensive lasering. The resulting tritan defects could be explained by this fact alone. Nevertheless, with the concurrent finding of inner central field defects, the role of the "light scatter" effect (as mentioned earlier) in causing central visual function deficit is not only confirmed but also strengthened, in the present study.

Only a few isolated reports could be found in the literature pertaining to the visual function in patients with extensive amount of laser (Birch,1987; Mantyjarvi,1989b), although the number of burns does not match the burns received by patients in the present study. The induced tritan defect was reported to persist even one year after the treatment, particularly when treatment was carried out using long duration burns (0.5s) (Birch,1987). However, it not clear if the patients were already "stable" when they were examined for their colour vision one year after the treatment. The observed colour vision defect could be due to active retinopathy (Cambie,1980; Lavergne & Ramioul-Gougnard,1980) if the patients had not achieved the stable phase at the time. Moreover, it has been shown before that those who did not recover from the induced tritan defect were those who needed more treatment (Birch-Cox,1978). The present study, however, comprised patients whose retinopathy status was stable and thus confirms that laser-induced tritan effects can be permanent. Whilst Birch (1987) has shown that long duration ARGON burns produce permanent tritan defects (even tritanopia!), the results of the present study show that extensive and repeated lasering even with relatively short duration burns (0.1 to 0.2s) can also produce permanent tritan defects.

It must be pointed out that the statements made above are inferred from the comparison made in the visual functions of the XL group and those of the untreated PDR group. It is assumed that the pretreatment visual functions in the XL group were similar to the PDR group. It could be argued that the poor colour vision/central fields of the XL

patients are due to extraneous causes other than the treatment factor. These two groups were comparable in their ages; the only difference was the length of time they had been diabetic. Obviously, patients in the XL group had significantly longer durations of diabetes (26.5 vs 15.6 yrs). However, considerations of all variables in the multivariate analysis (section 6.3.2) showed duration of diabetes to be an insignificant contributor to the observed variation in the colour vision and visual field results. The "grouping" of the patient i.e. XL or PDR, was the main determinant.

It could also be argued that these patients were a special "breed" who required such an extensive amount of PRP, and thus had extensive amounts of retinal ischaemia (Vine,1985) which could have contributed to the retinal dysfunctions. The PDR group, which was used as the "control" group, might have contained patients with lesser amount of retinal ischaemia thus representing a group which did not need such extensive PRP. This is a weakness of the study; being cross-sectional in nature this was inevitable. The ideal way would be to examine the patients before and after treatment. However, in order to assemble patients with such extensive amount of PRP it would have taken a lot longer time than was available for the study. It is fully realised that the evidence for the existence of a causal association is inconclusive without satisfying other and more stringent confirmatory criteria in studies such as the present one, which are cross-sectional and retrospective in design (Marshall,1990). However, since the two groups were matched as closely as practical, it is reasonable to conclude that multiple sessions of ARGON PRP had caused the dysfunctions noted. Two mechanisms are possible: A) Further destruction of the remaining viable "blue receptors" in the peripheral retina or B) Permanent damage to the central blue receptors indirectly by intense scattered light (Kuwabara,1970; Sperling & Harwerth,1972).

No significant differences were noted in most of the other visual function tests. It is possible that recovery had

taken place in some of these visual functions.

6.4.2 Visual dysfunction vs treatment variables

As the effects of PRP on visual function are thought to be cumulative (Jagger & Hamilton,1984; Birch,1987), it is reasonable to expect a progressive decline in visual function with increasing amount/intensity of PRP. Despite this, some of the results obtained have proved to be the opposite. An increase in total number of PRP burns (TotPRP) is shown to correlate with better colour vision (-ve correlation) and contrast sensitivity (+ve correlation), for instance. Mantyjarvi (1989b) showed that there was no significant difference in the mean number of PRP burns between patients who had colour vision defects and those who did not, implying that TotPRP burns had little, if any, contribution to the observed colour vision defect.

Perhaps a more accurate reflection of the "aggressiveness" of treatment is the "mean number of burns per session" (MBPS); this factor too has an unexpected relationship with colour vision and contrast sensitivity. In fact MBPS has a stronger relationship with colour vision and contrast sensitivity (table 6.6), inversely that is.

It seems that both regions (red-green & tritan) of the colour spectrum are similarly related to the two above-mentioned treatment variables (TotPRP & MBPS). The same applies to the contrast sensitivity function, with all spatial frequencies being similarly related to TotPRP and MBPS. The reason for the unexpected relationships between visual function test results and treatment variables is open to speculation. Some postulations can be offered to explain this. Perhaps, treating large areas of ischaemia has given the eye better visual function by getting rid of all of the "sick areas" of the retina (Meyer-Schwickerath & Schott,1968). Increasing duration of diabetes is also shown to result in better scores on some tritan tests (table 6.6). Such a paradoxical relationship (with colour vision scores) has been reported by Malone et al.(1984). In such

cases, it could be that with increasing duration the eye has finally reached the "burnt-out" stage (Kanski,1984) and is doing some good to the visual function. Alternatively, a short duration of diabetes meant a more rapid progression of the resulting DR, and hence could explain for the poorer visual function in those with shorter durations. Lastly, perhaps the incremental technique as suggested by Rogell (1983) had been carried out on these patients, which had subsequently minimised the side effects.

Although the analysis revealed some unexpected relationships, particularly between colour vision/contrast sensitivity and TotPRP/MBPS, some relationships are easier to explain. For example, time after the last treatment (TALT) is shown to determine the outcome of the D15(5/2) where (as expected) the longer the time interval, the better is the colour vision. Another treatment variable i.e. mean interval between treatment sessions (MIBS), is shown to have a mixed effect. Increasing MIBS correlates with better scores on the LTA test and decreasing number of tritan axis on the D15(5/2) tritan axis, but increasing number of red-green axis on the same test. The visual fields measured on the VFA I only showed a relationship with the VA of the patients. VA, as expected, is also related to the high spatial frequency scores on the VCTS 6000.

It seems that these relationships are not simple linear ones as shown by an example in fig 6.6, hence explaining the poor linear correlation observed in spite of good association revealed by the analysis. In this figure, although the SqTES on the FM 100-H is revealed by the multivariate analysis to be negatively associated with the MBPS, the relationship does not seem to be linear. In fact, this applies to most of the other relationships between visual function test results and treatment variables that were investigated.

In summary, despite the observed tritan and "encroaching" field defects, the differences in visual function between

the XL and PDR groups are slight. This could be due to some drastic recovery of the visual system from the previously described "light scatter" effects. Also, despite the extensive thinning of the peripheral retina, the deficit in visual function is not as great (inferred from the insignificant differences between the mean values of most of the visual function test results) as expected. This could be that the observed tritan defect/contrast sensitivity deficit is largely due to the macular "light scatter" effects rather than to peripheral retinal thinning. Indeed the visual system is able to (at least partially) recover from these effects.

A pleasant observation made in the study is the non-dependence of some visual function deficits (colour vision & contrast sensitivity) on the amount/intensity of PRP. Moreland (1980) reported some similar results, where no correlation was found between the Anomaloscope matching range and the number of laser burns. This finding of the present study is a fresh piece of evidence to dispell the oft-heard, ill-founded fears about unnecessarily inducing central visual dysfunction with extensive amount of lasering. The present study not only agrees with Aylward et al.(1989) that despite large amounts of PRP, some patients have managed to maintain excellent VA but also adds another useful piece of information. That is, in those who presented with good VA, central visual functions have also been reasonably maintained.

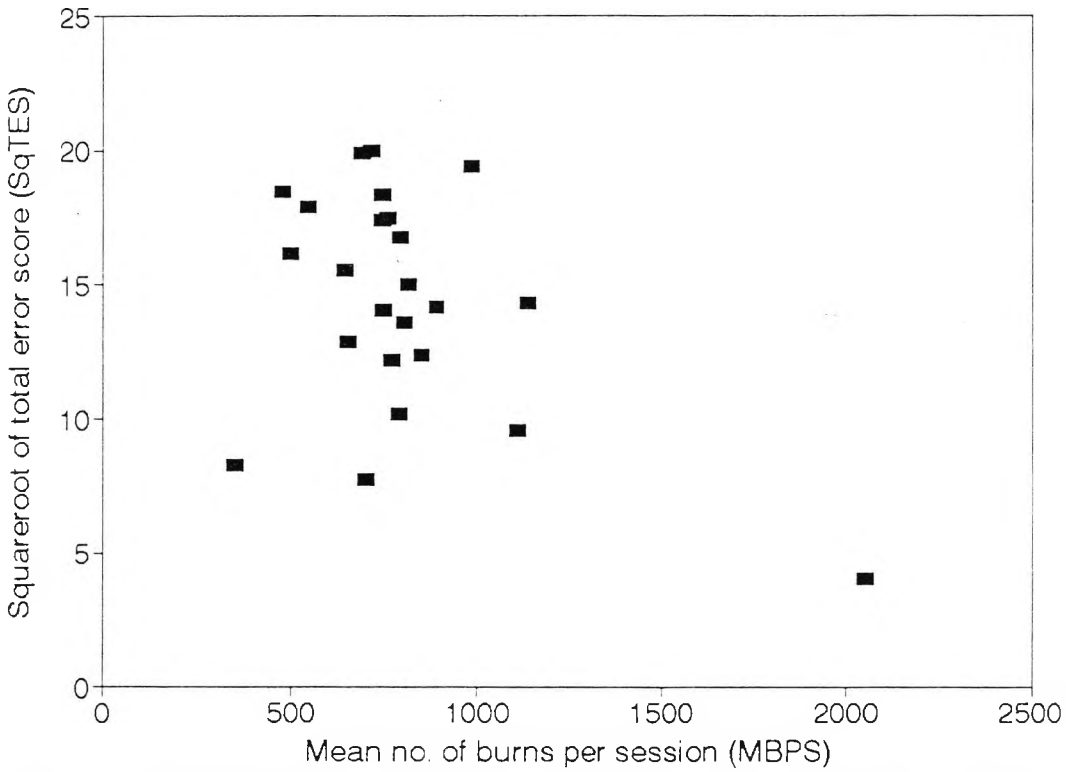


Fig 6.6 Scattergram showing the relationship between SqTES and MBPS of Argon PRP treatment

CHAPTER 7

General Discussion and Conclusions

7.1 Introduction

This Thesis selects and explores certain aspects of visual function in relation to the screening and monitoring of diabetic retinopathy (DR) in a heterogenous group of patients having types I and II diabetes.

The first part of the research evaluated the screening efficiency of clinical tests (of visual acuity, colour vision, contrast sensitivity & central fields) in the screening of DR in diabetic patients. The clinical tests were also evaluated for their ability to show gradations in visual dysfunction as a function of the severity of DR. This objective was prompted by the relative insensitivity (purportedly) of the conventional Snellen acuity test, both for detecting DR and for monitoring the condition. The research thus selected clinical tests of visual function which can be used by personnels involved in the care of diabetics, particularly those who screen for sight-threatening DR and also by those who monitor the disease. Positive guidance emerges from the studies presented in chapters 3 & 4 of the thesis.

The effects of laser photocoagulation treatment of varying types and doses on the same visual functions (colour vision, contrast sensitivity and visual fields) are demonstrated and evaluated in the second half of the thesis with specific implications for clinicians. This part of the thesis was prompted by the need to accumulate information on the effects of therapeutic intervention on visual function under 3 different circumstances: 1)when long-wavelengths were used and 2)when the amount of treatment exceeded the conventional dose. Treatment by lasers has therefore influenced the studies presented in chapters 5 & 6 of the thesis; this part of the thesis makes informed comments, with certain conclusions, about laser effects.

Experience during this investigation, while involving only some of the visual function tests considered in the extensive survey of the literature (chapter 1), has

prompted some definite guidelines. In the opinion of the present author there is a distinct need for a protocol of strategic visual function testing to be applied in appropriate situations and ways. Since the needs of patients and the facilities and instruments available differ and time factors do not always permit "ideal" procedures, practical alternatives have been considered in the studies carried out.

The 4 studies presented clarify the issues as never before, presenting data on an unusual range of patients. The diversities inherent in the groupings, backgrounds and treatments of patients have had to be overcome, which has been possible to a considerable extent. The following comments are offered to round up the studies carried out, each of which has been dealt with elaborately in their respective chapters.

7.2 Detecting Diabetic Retinopathy using Clinical tests of Visual Function

The values of fluorescein angiography, fundus angiography and careful ophthalmoscopy through a dilated pupil in detecting DR are well known (Ivanisevik & Stanic,1990; Yamana et al.1983; Moss et al.1985). There is, however, an urgent need to find simple cost-effective screening methods to discover treatable eye disease and that do not need to be performed by ophthalmologists (Tindall et al.1990). Reports on subjective tests of visual function for detecting DR have produced results encouraging enough to recommend the inclusion of some of these tests for routine clinical use (see 1.1.2). Some of these previous studies have explored the use of visual function tests in screening situations, but few, have evaluated this aspect (screening application) in a rigorous manner. It has become clear that for the primary eye care practitioner, simple non-invasive tests of visual function will provide additional tools, complementary to conventional ophthalmoscopy, to aid in the detection of DR and perhaps other diabetes related significant ocular pathology.

The above issue is tackled in chapter 3 of the Thesis where the screening utility of a few tests of visual function (visual acuity, colour vision, contrast sensitivity and central visual fields) was examined using techniques which have arisen from analysis used in Signal Detection Theory (McNichol,1972). Based on the recommendations by Aspinall & Hill (1983,1984a,1984b) and Hill (1987a), the Bayesian approach (Lusted,1971) to decision making was also employed in the analyses of these tests.

Whilst the primary objective of chapter 3 was to evaluate the screening efficiency of visual tests in the screening of DR alone, it was found in general that the screening efficiency of the tests evaluated was better when they were used for the detection of DR and/or other ocular complications which the patients presented with. The following points are the main findings which have emerged from the study:

1) While the pinhole test is not sufficiently sensitive to pick out all diabetics with ocular pathology, clinically, fail criteria could be set which optimise its value. Using 6/5 and 6/9 as the limits, satisfactory values of p(N/P)(ie. 0.70) and p(D/F)(ie. 0.81) for the two limits respectively, were obtained for the screening of DR and/or other ocular pathology. Values for the screening of DR alone are 0.75 and 0.52 for p(N/P) and p(D/F), respectively.

2) An composite selection of PIC plates comprising 8 Ishihara plates and 7 tritan plates (one SPP1 plate & 6 "Birch" plates) was found to be an effective screening tool for the identification of diabetics with DR and/or other ocular pathology. Using a fail criterion of "at least one plate error", the Comp PIC was found to be 0.64 sensitive and 0.83 specific with associated p(N/P) and p(D/F) values of 0.73 and 0.81, respectively. For the screening of DR alone the same fail criterion affords the plates 0.51 sensitivity and 0.83 specificity with p(N/P) of 0.80 and p(D/F) of 0.56. On the basis of these results the Comp PIC

are thus recommended for use in clinics to assist in the identification of diabetics requiring an ophthalmological assessment. The D15(5/2) was found to be the least efficient among the colour vision tests evaluated.

3) Of the two contrast sensitivity tests evaluated, the VCTS 6000 was found to be the better test for detecting DR and/or other ocular pathology in diabetics. Using a fail criterion of "a global score less than or equal to 19" the test gave a sensitivity of 0.59 and a specificity of 0.76, with corresponding values of 0.73 and 0.62 for p(N/P) and p(D/F), respectively. For the screening of DR alone the fail criterion "a global score less than or equal to 25" affords the test 0.92sensitivityand 0.34 specificitywith p(N/P) of 0.91 and p(D/F) of 0.37.

4) Using any report of abnormality as the fail criterion, the Amsler grid was found to be very specific (=0.98), with a p(D/F) value of 0.87 for detecting DR and/or other ocular pathology. For the screening of DR alone the test has a p(D/F) of 0.68.

5) Using test batteries comprising the best tests identified from individual test analyses, it was found that the test batteries (2 or 3 tests) provided little gain in screening efficiency when used for the screening of DR alone when compared to the use of the Comp PIC. However, in the screening of diabetes and/or ocular pathology, the test battery comprising Comp PIC, VCTS 6000 and Amsler grid was found to give excellent screening results i.e. sensitivity=0.72, specificity=0.71, p(N/P)=0.79 and p(D/F)=0.63.

From the results obtained, a selection of PIC plates comprising a few Ishihara plates and some novel tritan plates may be used in conjunction with the VCTS 6000 and the Amsler grid to assist the practitioner in identifying diabetic patients with DR and/or ocular pathology with VA of 6/12 or better. Fig 7.1 shows actual results obtained by patients in each of the 4 groups examined. A sensitive test

Group 1: No DR

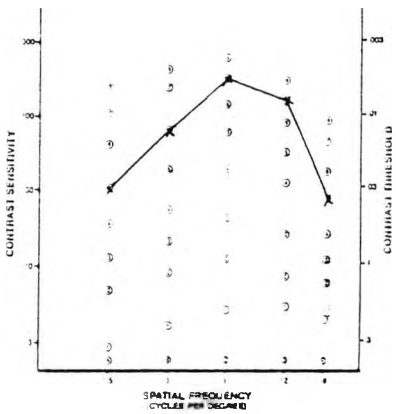
PH , male, aet 42, 18 years of diabetes, Insulin therapy, VA=6/5

1) Comp PIC plate # (0 plate errors)

1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
12	8	5	3	2	5	26	42	2	3	0	X	0	□	△

2)VCTS 6000

3)Amsler grid: NAD



Global score = 30

Group 2: No DR but with complications

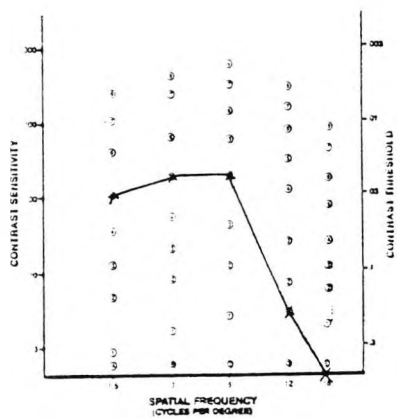
DR , female, aet 56, 46years of diabetes, Insulin therapy, Cataracts, VA=6/9

1) Comp PIC plate # (1 plate error; tritan error)

1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
12	8	5	3	2	5	26	42	2	3	0	X	0	□	△

2)VCTS 6000

3)Amsler grid: NAD



Global score = 15

Fig 7.1 Actual results of 4 patients, one from each group

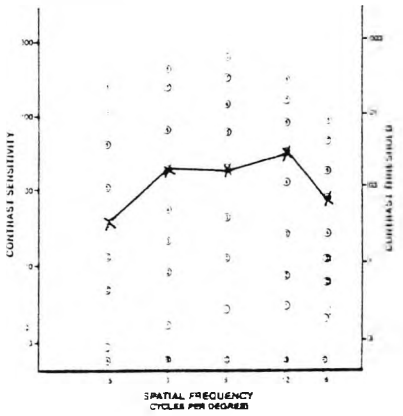
Group 3: With DR

KA, male, aet 42, 10 years of diabetes, Insulin therapy, Moderate DR, VA=6/6

1) Comp PIC plate # (3 plate errors; all tritan errors)

1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
12	8	5	3	2	5	26	42	2	3	0	X	0	□	△

2)VCTS 6000



3)Amsler grid: NAD

Global score = 23

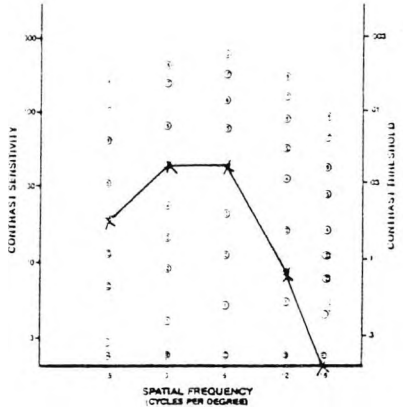
Group 4: With DR and complications

EP, male, aet 56, 17years of diabetes, Diet therapy, Moderate DR & Cataracts, VA=6/9

1) Comp PIC plate # (5 plate errors: 2 red-green & 3 tritan)

1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
12	8	5	3	2	5	26	42	2	3	0	X	0	□	△

2)VCTS 6000



3)Amsler grid: Failed

Global score = 15

Fig 7.1 (contd)

other complications among diabetics.

The results involving multiple comparisons of the various tests and test batteries must, however, be taken in context. First, with regards to the different venues involved. In chapter 3 where the work was carried out at 2 venues with different illumination levels (see 3.2), results from the two venues were pooled together in the analysis of the following tests: Pinhole VA, Comp PIC, LTA plate 5 and Amsler grid. However "venue" only influenced the results of Comp PIC and LTA plate 5; and even then, although the "venue" factor was significant in the performance of these two tests, nevertheless, "diagnostic group" still maintained its significance as can be seen from multivariate analysis. The influence of different lighting conditions on VA measurements is well realised (Riggs,1965). The charts used at both venues complied with standards laid down in British Standard (1968), and furthermore, the pinhole used (1mm diameter) complied with the requirement as suggested by Bennett & Rabbetts (1990). As a result of these precautionary measures, VA emerged as a very robust test in as far as differences in illuminance levels were concerned, as evident from the non-significance of "venue" on its performance.

As for colour vision, although both venues had levels of illuminance in excess of 100 Lux, which is the upper limit recommended by Bowman & Cole (1980) for avoiding the induction of tritan defect. And despite there being less importance in the quality of illumination in the examination of acquired colour vision defects as suggested by Adams & Haegerstrom-Portnoy (1987), it is evident that colour vision, as a test of visual function is sensitive to changes in illuminance levels as shown by the present results.

Secondly, the problem of comparing tests (and test batteries) whose analyses were derived from different populations deserves some comments. Strictly, measures of sensitivity and specificity can be compared with each other

is needed obviously, but high sensitivity will compromise the chances of being defective having failed the test ie. resulting in a low p(D/F) but a high p(N/P). On the other hand whilst it is desirable to have a test with high specificity in order to maximise the chances of being diseased having failed the test ie. to achieve a high p(D/F), being too specific will compromise the sensitivity and might not be appropriate forconditions/diseasesof high prevalence because of the resulting low p(N/P). A balance had to be struck and in doing so the suggestion by Hill (1987a) to consider double criteria for each test was constantly adhered to.

It is realised that contrast sensitivity testing with the VCTS 6000 device has recently come under question (Wood et al.1989; Harper et al.1990). Nevertheless, Elliot & Whitaker (1992a & 1992b) have provided some justifications for the use of this test in primary eye care, that is, with proper interpretation with regards to normal values and the effects of age (Elliot & Whitaker,1990a). There is an overwhelming evidence that the VCTS chart is the most commonly used clinical contrast sensitivity chart at the moment (Mantyjarvi et al.1989; Koch & Liu,1990; Nordmann et al.1991). Even two recent optometric and ophthalmologic texts (Patorgis,1991; Chang,1992) still endorse the VCTS chart for contrast sensitivity assessment despite all the criticisms.

Thus although when used on its own the VCTS 6000 provides little useful information, the results of chapter 3 show that when used in a test battery (with Comp PIC and the Amsler grid) the VCTS 6000 does provide some useful additional clinical information for the screening of DR and/or diabetes related ocular pathology. The 3-test battery gives the following screening figures: sensitivity=0.72, specificity=0.71, p(N/P)=0.79 and p(D/F)=0.63. The relatively higher sensitivity obtained compared to the 2-test battery and the other single tests, is useful for picking up conditions of relatively high prevalence (Wood et al.1992), such as cases of DR and/or

other complications among diabetics.

The results involving multiple comparisons of the various tests and test batteries must, however, be taken in context. First, with regards to the different venues involved. In chapter 3 where the work was carried out at 2 venues with different illumination levels (see 3.2), results from the two venues were pooled together in the analysis of the following tests: Pinhole VA, Comp PIC, LTA plate 5 and Amsler grid. However "venue" only influenced the results of Comp PIC and LTA plate 5; and even then, although the "venue" factor was significant in the performance of these two tests, nevertheless, "diagnostic group" still maintained its significance as can be seen from multivariate analysis. The influence of different lighting conditions on VA measurements is well realised (Riggs,1965). The charts used at both venues complied with standards laid down in British Standard (1968), and furthermore, the pinhole used (1mm diameter) complied with the requirement as suggested by Bennett & Rabbetts (1990). As a result of these precautionary measures, VA emerged as a very robust test in as far as differences in illuminance levels were concerned, as evident from the non-significance of "venue" on its performance.

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Secondly, the problem of comparing tests (and test batteries) whose analyses were derived from different populations deserves some comments. Strictly, measures of sensitivity and specificity can be compared with each other

only when they are derived from the same population groups (Henson & Dix,1984). Despite this, because of the constraints of the study it was not possible to collect data of all tests on all the patients. Therefore, the comparisons made in chapter 3 between the following tests should be interpreted with caution i.e. Arden gratings vs VCTS 6000 and VCTS 6000 vs D15(5/2), since the Arden gratings and D15(5/2) results were obtained from the Middlesex population and the VCTS 6000 results from the Whittington patients. On the other hand the screening efficiencies of the Pinhole VA, Comp PIC, LTA plate 5 and Amsler grid were calculated from data pooled from the two venues making comparisons between these tests justified. The results of the comparison between the two test batteries will also need careful interpretation. The 2-test battery (Comp PIC & Amsler grid) had data from both venues whilst the 3-test battery (Comp PIC, Amsler grid & VCTS 6000) had data from the Whittington Hospital only. It is perhaps inconclusive to state that the VCTS 6000 in combination with the Comp PIC and Amsler grid provided the best combination (as said earlier). The relative "success" of the VCTS 6000 in combination with the Comp PIC and Amsler grid might be a little optimistic; one would have to be guarded against such optimism considering the manner the calculations were made. Hence having made the above comments and after removing the 3-test battery from the analysis, it would seem that the Comp PIC is the only test with an acceptable level of screening efficiency for the purpose of screening for DR with or without other ocular complications in diabetics. This confirms earlier suggestions by Birch et al.(1987); Birch et al.(1988); Birch & Ariffin (1990) and Birch et al.(1991).

Previous studies differ from the present investigation mainly in the way the data is analysed. In the main, previous studies have only addressed patients with DR alone thus assuming that other complications (retinal or optic nerve) have been excluded in the physical examination of the eye. Since some complications are easier than others to detect, it was felt that any screening analysis of clinical

influence of age and VA, thus reinforcing the clinical usefulness of the two tests. In clinical use, on its own the Comp PIC is expected to be able to sort out patients with "significant DR" from those with minimal DR; 2 plate errors or more will indicate significant DR (72.4% of such patients were detected). Whilst with the SPP2, the test will be useful for sorting out grade III (referrable) DR from the rest; 6 errors or more will indicate grade III DR (67.7% of such patients were detected). Obviously using both tests <u>together</u> will provide the clinician with more information.

It is pertinent to emphasise here that consideration of both plate tests did not take into account of the different levels of "difficulty" of the component plates in each series. Clinical application is only made on account of number of plate errors made, irrespective of "which" plates. This was felt to be justifiable based on previous works by leading authorities in colour vision research (Hill & Aspinall,1982; Long et al.1985; Somerfield et al.1989). This does not mean that the importance attached to individual plate performance has been ignored; it only means that a simpler method has been undertaken in lieu of a more complex analytical approach such as that involving information theory as suggested by Chauhan & Block (1986). Nevertheless, with respect to the Comp PIC at least, the different levels of performance afforded by different plates in the series ("grading" vs "screening" plates; see chapter 2) have been examined, albeit qualitatively in chapter 3 (figures 3.2 through 3.5) in their ability to detect DR and/or other complications.

Other tests evaluated in chapter 4 were not found to be . They were too dependent on age and VA. One particular test, the VFA I, had a similar degree of performance as the Comp PIC in separating out patients with grade I and those with grades II & III but unfortunately, was found to be significantly correlated with age and VA more than to "diagnostic grade" of DR. Others (D15(5/4), D15(5/2), FM 100-H) managed to show some significance in

crystalline lens which may occur at a younger age in diabetics. It is also unavoidable that a proportion of patients actually having the disease is missed in such endeavour. The reason accounting for such false findings is described by Reeves (1989) as two-fold: Firstly, whatever measure one chooses to define a disease, a result that is normal for one person may be abnormal for another and secondly, there is always a certain degree of error associated with any measurement, estimates of human sensory performance e.g. colour vision etc are particularly susceptible to this kind of error.

In chapter 3 the confirmation of the presence of "DR" was made by diabetic physicians adequately trained in ophthalmoscopy. A study (Sussman et al.1982) performed to determine the accuracy of diabetologists in the USA showed that this group had a serious error rate; nevertheless adequately trained physicians have been shown to be as effective as ophthalmologists in identifying DR (Barrie et al.1981). Hence it was felt justifiable and practical to employ such physicians for the purposes of the study in chapter 3, especially when the procedure (ophthalmoscopy) was carried out on patients with dilated pupils. Furthermore, Barrie et al.(1981) showed that there was no increase in the yield of clinically important retinopathy by subjecting patients to procedures more extensive than ophthalmoscopy.

Chapter 4 evaluated the usefulness of clinical visual tests for the purpose of monitoring of DR in patients already diagnosed with the disease. The results indicate that among the tests evaluated, the two colour vision test plates (Comp PIC & SPP2) proved to be the best tests to show satisfactory grades of visual dysfunction among diabetic patients with the 3 grades of DR considered. The Comp PIC showed significantly worse results in grades II & III compared to grade I and the SPP2 showed significantly worse results in grade III compared to grades I & II. In addition, these two tests also proved to be significantly correlated with "diagnostic grade of DR" despite the

influence of age and VA, thus reinforcing the clinical usefulness of the two tests. In clinical use, on its own the Comp PIC is expected to be able to sort out patients with "significant DR" from those with minimal DR; 2 plate errors or more will indicate significant DR (72.4% of such patients were detected). Whilst with the SPP2, the test will be useful for sorting out grade III (referrable) DR from the rest; 6 errors or more will indicate grade III DR (67.7% of such patients were detected). Obviously using both tests <u>together</u> will provide the clinician with more information.

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Other tests evaluated in chapter 4 were not found to be satisfactory. They were too dependent on age and VA. One particular test, the VFA I, had a similar degree of performance as the Comp PIC in separating out patients with grade I and those with grades II & III but unfortunately, was found to be significantly correlated with age and VA more than to "diagnostic grade" of DR. Others (D15(5/4), D15(5/2), FM 100-H) managed to show some significance in

the test results but were only confirmatory in the separation of those with grades I and III. They failed to provide finer discrimination between grades I and II and similarly between grades II and III. This poor correlation between visual function and the severity of DR at the background stage has been noted (Moloney & Drury,1982; Higgins et al.1989; Greeinstein et al.1990) and it has been attributed to the heterogeneous nature of the disease (DR) at this particular stage, thus causing the increased scatter in the results

On the basis of results presented in chapter 4 it is recommended that for the purpose of monitoring DR (in those diabetic patients whom a diagnosis of DR had already been made) the Comp PIC and the SPP2 tests be used. The tests will aid the clinician in deciding on the severity of the retinal involvement (diabetic retinopathy), in conjunction with ophthalmoscopic examination, before embarking on making a referral to the ophthalmologist. Hence the objective set out for chapter 4 has been fulfilled.

As noted earlier, evaluation of test performance in both chapters 3 and 4 revealed the existence of other factors which influence (albeit partially) the performance of the individual tests besides the desired effect (the desired effects being presence of "DR and/or other ocular complications" in chapter 3 and "grades of DR" in chapter 4). The most notable of these "extraneous" factors are "VA", "age" and to a lesser extent "insulin therapy". Hence besides the "disease" in question, the age of the patient is of paramount importance in determining test performance. The same goes with VA, which is hardly surprising since the tests evaluated are mainly macular tests. It is ironic that despite various assertions (Birch et al.1980; L'Esperance & James,1981) of the VA test being insensitive to the early changes of DR and also, to changes at the proliferative stage, VA is not altogether a useless test. Duration of diabetes was not found to be a significant factor in performance of the tests evaluated apart from the Arden gratings.

7.3 The Effects of Laser Photocoagulation treatment for Diabetic Retinopathy on Visual Function

The first chapter that dealt with the laser issue (chapter 5) gave findings which emphasise the fact that despite the theoretical advantages in longer wavelength lasers, wavelength *per se* has not been shown to be an exclusively important determinant of central visual function immediately following PRP treatment. This conclusion applies to a) PRP given in doses of 2000 burns (0.1s & spot size 200/500 microns), b) the wavelengths evaluated i.e. Argon 488/514nm, 577nm and 595 nm and c) a follow-up period of 3 months following treatment only. This negative finding may be explained by the comparatively few numbers in the study or the relatively good visual function in the patients selected prior to laser PRP. Alternatively the transmission and absorption characteristics of the wavelengths used in the study might not be sufficiently different so as to achieve clinical relevance.

The major effects noted (albeit minor) were those on the colour vision function and the visual fields. The results in chapter 5 confirm the deleterious effects on colour vision of the Argon laser (488/514nm), in agreement with previous investigators (see 1.1.3). However, the effect (increase in the blue-yellow scores) was very marginal in comparison to the longer wavelengths tested (577nm & 595nm) so that the actual "induction" of a specific tritan defect could not be conclusively stated. Furthermore, the transient nature of the effect adds to its clinical insignificance. The non-involvement of the contrast sensitivity function further supports the very mild and clinically insignificant effects on colour vision produced by Argon (488/514nm) relative to the other two wavelengths (577 & 595nm).

The was an immediate loss of sensitivity in the part of the visual fields post treatment which corresponded with the bombarded areas; this was expected as a result of direct trauma. Likewise, the effects were also transient in

Kitchin,1992). In practice, however, with discerning interpretation, the clinician is forced to use the available tests; to some extent the present study tried to elucidate the likelihood of these tests being satisfactory guides.

It must be pointed that the clinical tests evaluated can never substitute a comprehensive ocular examination; at best, clinical visual tests can only complement the physical ocular examination in the identification of diabetics with DR or in the determination of the severity of DR. This is despite visual dysfunction (especially acquired colour vision) being related to onset of DR and to its features. The results of chapters 3 & 4 indicate that clinically, in individual cases, the relationship between visual dysfunction and DR did not help much in predicting DR. On a positive note, however, the colour vision test plates were slightly better in predicting the severity of DR in patients already diagnosed with DR. These tests could very well be used as supplementary tests in clinics of those provide primary ocular care to diabetics.

Further work should be aimed at rigorous evaluation of other means of detecting DR. Ideally the work not only needs to be undertaken at one venue but also on the same patients so that the comparative evaluation of tests can be properly carried out. As for the choice of tests to be evaluated, other tests of visual function abound, in particular some of the more recent tests like the Berkerley Colour Test (Adams et al.1987a), the Pelli-Robson contrast sensitivity test (Pelli et al.1988) which has had very favorable reviews of late (Elliot & Hurst,1990; Elliot et al.1990; Reeves,1991) and the threshold Amsler grid (Wall & Sadun,1986; Wall & May,1987; Wall et al.1990). Emphasis should still be in the more "clinical" tests, with the practising clinician in mind. Additionally, other more elaborate means (often involving expensive instrumentation) such as the non-mydriatic fundus cameras, automated perimeters could also be evaluated in a rigorous manner for both their "screening" and "grading" of DR abilities.

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The first chapter that dealt with the laser issue (chapter 5) gave findings which emphasise the fact that despite the theoretical advantages in longer wavelength lasers, wavelength *per se* has not been shown to be an exclusively important determinant of central visual function immediately following PRP treatment. This conclusion applies to a) PRP given in doses of 2000 burns (0.1s & spot size 200/500 microns), b) the wavelengths evaluated i.e. Argon 488/514nm, 577nm and 595 nm and c) a follow-up period of 3 months following treatment only. This negative finding may be explained by the comparatively few numbers in the study or the relatively good visual function in the patients selected prior to laser PRP. Alternatively the transmission and absorption characteristics of the wavelengths used in the study might not be sufficiently different so as to achieve clinical relevance.

The major effects noted (albeit minor) were those on the colour vision function and the visual fields. The results in chapter 5 confirm the deleterious effects on colour vision of the Argon laser (488/514nm), in agreement with previous investigators (see 1.1.3). However, the effect (increase in the blue-yellow scores) was very marginal in comparison to the longer wavelengths tested (577nm & 595nm) so that the actual "induction" of a specific tritan defect could not be conclusively stated. Furthermore, the transient nature of the effect adds to its clinical insignificance. The non-involvement of the contrast sensitivity function further supports the very mild and clinically insignificant effects on colour vision produced by Argon (488/514nm) relative to the other two wavelengths (577 & 595nm).

The was an immediate loss of sensitivity in the part of the visual fields post treatment which corresponded with the bombarded areas; this was expected as a result of direct trauma. Likewise, the effects were also transient in

nature. Interestingly, the depression in field sensitivity of the outer 30-degree field was not significantly different between the 3 wavelengths tested. This shows the non-importance of wavelength, as a parameter in determining the visual fields effects of PRP treatment. Hence, the objective set out for chapter 5 has been fulfilled.

Strict adherence to both the amount of PRP given and the follow-up time of 3 months was the original approach of the study carried out in chapter 5. This was essential in order to avoid "confounding factors" in delineating the true effects of laser PRP. Previous studies in the literature have often been flawed by the non-standardisation of the dose of laser given and the variable follow-up times afforded to patients involved. In the present study this effect was evident in those eyes which still had "unregressed" new vessels at the end of the trial; which manifested as an increase in the red-green defect on the D15 test.

Further research should be directed at elucidating the effects of more extensive doses of PRP, on a larger group of patients using standard follow-up times as already done. Comparison of only two wavelengths should be undertaken i.e. the standard control (Argon green nowadays) versus a longer wavelength (either DYE-577nm or the more recently introduced DIODE-810nm). A longer follow-up period should be attempted in order to delineate the long term effects; hence all the more reason why the numbers need to be large in order to maintain sufficient numbers for realistic statistical evaluation having excluded those which will need additional treatment and/or focal macular treatment. Extensively lasered patients (with the Argon laser) examined in chapter 6 were an interesting group of patients. The report presented is perhaps the only piece of literature which details the visual function in such category of patients. These patients (N=24), selected on the basis of having had more than 4000 Argon laser burns and for having good VA (6/12 at least), were subjected to a series of visual tests. Surprisingly, the results when

compared to those of a group (N=25) with PDR, showed very slight differences implying that the visual functions tested were well preserved in these patients despite the ordeal that they have undergone. Chapter 6 sheds some light on the aftermath of extensive PRP treatment for persistent PDR, representing the first evaluation ever undertaken of the visual functions in such patients.

The only two functions which showed some depression relative to the group with PDR were colour vision and visual fields. Although there was no significant difference in the SqTES on the FM 100-H test between the two groups, both mean values of SqTES were abnormal (14.14 for both groups), thus confirming these patients showed poor overall hue discrimination with the FM 100-H test, as is normally noted in acquired tritanopes (Marre,1973; Birch,1989). The extensively lasered group exhibited more tritan defects and their visual fields were reduced, not only in the areas which were directly bombarded by the laser, but also in the inner areas which were not directly involved. These results have confirmed the fear of macular phototoxicity following PRP treatment for PDR with the Argon 488/514 nm; the primary cause for this has also been demonstrated as being due to the "splash over" or "light scatter" effect from the peripheral bombardment taking place during PRP treatment. The blue content of the Argon laser (488nm) has been singled out as the cause of the colour deficit noted (Birch,1987). It is said to be scattered more in the eye-media and thus is more likely to affect the already vulnerable blue cones and cause the observed colour vision effect (Sperling & Harwerth,1972). However, as noted in chapter 5, in order for the effects to be clinically significant, the amount of lasering would have to be far in excess of 2000 burns i.e. the lasering would have to have taken place "extensively".

Despite the expected decline in visual function with increasing amount/intensity of PRP, the results in chapter 6 show that this relationship is very unclear, apart from the unexpected finding of an inverse relationship in some

of the variables tested. That is, more extensive treatment was found to be associated with better colour vision and contrast sensitivity. This "inverse relationship" is an original feature arising from the data presented in chapter 6. It must be admitted that such inverse relationships (or no relationships at all for some other variables e.g. between fields and number of burns) should be viewed with caution, particularly if the amount of "laser overlapping" differed in this group of patients. Such a gross factor (ie degree of burn overlapping) was not possible to be determined in the patients examined, even had fundus photographs been available. It could also be argued that in patients with longer duration of burns (>0.5s), different relationships could have been obtained.

It is hoped that this data will furnish some new clinical evidence to some ophthalmologists who have been uneasy about subjecting their patients to large amounts of PRP. The results could assist ophthalmologists in weighing the risk-to-benefit ratio of such a venture. In the main, it has been shown that at least, recovery from the expected adverse visual side-effects is possible in these patients. Secondly, the amount of PRP applied (number of burns) bears very little relationship with the level of visual dysfunction suffered. With the two major findings, the objective set out for chapter 6 has been fulfilled.

Further research should be directed at establising the effects of large amounts of lasering ideally in a longitudinal controlled study involving larger numbers of patients. With more patients it would be possible to have a larger and a more complete range of laser parameters such as the total number of burns or the mean number of burns per session, in order to better define the relationship between these parameters and visual function.

As noted in 7.1, recently-introduced techniques of colour vision test analyses (Kitahara,1984; Allan,1985; Dain & Birch,1987; Vingrys & King-Smith,1988) were not undertaken in chapters 5 and 6. However, these recent quantitative

scoring techniques are not the perfect solution to all analyses of colour vision arrangement tests. For example, Atchison et al.(1991b) recently showed that the colour difference vector method of Vingrys & King-Smith (1988) provided similar diagnostic rates with the "visual inspection" method in cases of congenital colour vision defects, although the technique (vector method) was suggested to be useful in clinical trials and in monitoring changes of colour vision over time. Hence, in the studies presented in this thesis it was thought that such techniques would not have provided additional insight into the matter and that sufficient "sophistication" had been achieved with the more basic clinical type of analyses undertaken (ie. for colour vision and other tests alike), in order for the results to be readily applied to the clinical situation.

A large variety of patients has been involved and thanks are due to these as to the clinical and scientific professionals who have been involved over a very long period. Statistical evaluation of the type of data which has been gathered presents inevitable difficulties, which have been reduced as the result of specialist advice. The conclusions of this research are offered in the firm belief that a sound series of indications for clinical use has emerged, not a final step but a major step in what must always be regarded as a continuous if slow progress.

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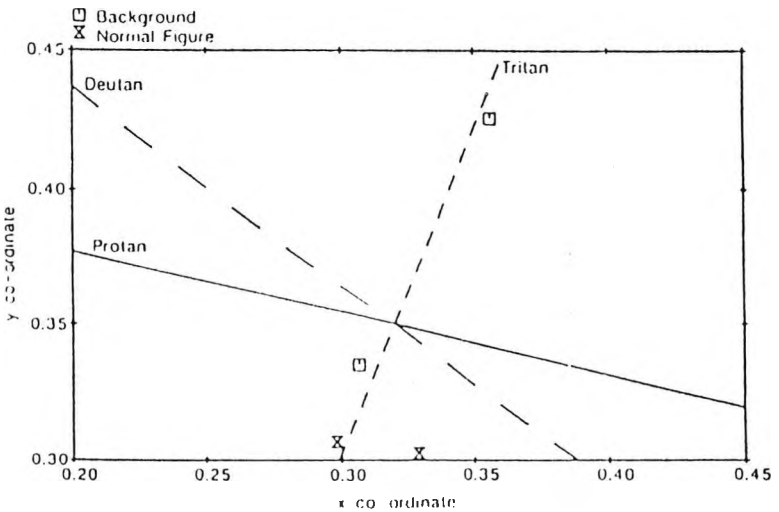
APPENDICES

Appendix 2A Chromaticities of the colours of plate 9 (demonstration plate from the SPP1 series) (after Honson & Dain, 1988)



Appendix 2B Colour coordinates of the Comp PIC tritan plates (Birch Experimental Tritan series)

PLATE NO.	MUNSELL VALUES (Pantone inks)	PYE UNICAM B				MUNSELL				Y UNICAM	
		Background		Figure		Background		Figure		Background	Figure
		x	y	x	y	x	y	x	y		
10	**Background** 5RP 7/10 (224)	0.380	0.255	0.500	0.338	0.371	0.288	0.447	0.341	33.06	33.56
	Figure 3 7.5R 7/10 (171)										
11	**Background** 7.5Y 5/8 (111)	0.414	0.438	0.314	0.261	0.480	0.395	0.327	0.248	33.82	32.61
	Symbol O 10P 5/8 (257)										
12	**Background** 7.5RP 6/10 (204)	0.407	0.217	0.480	0.391	0.396	0.287	0.490	0.380	30.75	37.64
	Symbol X 2.5YR 6/10 (144)										
13	**Background** 10RP 5/12 (RR)	0.445	0.266	0.505	0.336	0.402	0.252	0.548	0.365	21.41	21.74
	Symbol O 10R 5/12 (179)										
14	**Background** 2.5YR 6/10 (144)	0.480	0.391	0.407	0.217	0.490	0.380	0.396	0.287	37.64	30.75
	Symbol □ 7.5RP 6/10 (204)										
15	**Background** 10BP 5/8 (271)	0.263	0.238	0.378	0.441	0.257	0.225	0.408	0.507	26.35	29.49
	Symbol △ 2.5GY 5/8 (384)										
16	**Background** 10GY 5/10 (362)	0.307	0.432	0.222	0.366	0.303	0.523	0.197	0.321	26.42	28.25
	Figure 3 2.5BG 5/10 (334)										

(Courtesy of J. Birch)

Appendix 3A Measures of test performance: Sensitivity, Specificity and Receiver Operator Characteristic (ROC) curve.

Statistical principles for assessing diagnostic tests can be represented in their simplest form by a 2 X 2 decision matrix in which the test results can be logically related to the clinical outcome. If,

D indicates the presence of a disease;

N indicates the absence of a disease;

F indicates a positive result of a screening test and

P indicates a negative result of a screening test,

the decision matrix will be represented as follows:

Disease	Screening test result	
	Positive (F)	Negative (P)
Present (D)	a	b
Absent (N)	c	d

The following definitions are derived:

1) **SENSITIVITY=p(F/D)**

i.e. the conditional probability of a positive test result (F) given that the patient has the disease (D)

=a/a+b

2) **SPECIFICITY=p(P/N)**

i.e. the conditional probability of a negative test result (P) given that the patient does not have the disease (N)

=d/c+d

3) **FALSE POSITIVE RATE,** which is the rate of incorrect test indication of the disease

=c/c+d (i.e. 1-SPECIFICITY)

4) **FALSE NEGATIVE RATE,** which is the rate of incorrect test indications of no disease

=b/a+b (i.e. 1-SENSITIVITY)

Appendix 3A/contd Receiver Operator Characteristics (ROC) curve

An ROC curve is simply a plot of test sensitivity against test specificity. Specificity is either plotted on a reverse scale or the derivative (1-specificity) is plotted in the usual manner on the x-axis (Mertz 1978).

Fig 1 (after Aspinall & Hill, 1984c) shows the ROC curves for two hypothetical tests A and B; these curves having been derived from the frequency distributions depicted in fig 2 (after Aspinall & Hill, 1984c). For each test, the ROC curve is a means of providing two separate measures for discrimination problems: first, an index of discrimination (dA, dB) and the other, the decision point selected as criterion score (Tc1 or Tc2). Points along A in fig 1 represent different test score values which can be used in the test as criteria or cut-off points (eg Tc1 & Tc2). The relative positions of points Tc1 and Tc2 and their effects on the false positive and the false negative error rates are illustrated in fig 2.

The dotted diagonal line is the indecision line i.e. an ROC curve for a test which could not discriminate between the two populations (e.g. normal & diseased). When the test scores provide greater separation between the two populations (dB>dA) the corresponding ROC curve for test B is nearer the upper area of the graph. Test B is therefore a better screening test than test A in fig 1.

Several measures of diagnostic quality can be derived from ROC curves; one useful measure in screening situations is the optimum operating criterion. The optimum criterion is the point on the ROC which is farthest from the indecision line; it gives the minimum number of total misclassifications. The ROC curve thus allows the visualisation of the trade-off between sensitivity and specificity for various test cut-off criteria and hence provides information regarding the consequences of implementing particular cut-off criteria for referral.

Fig 1

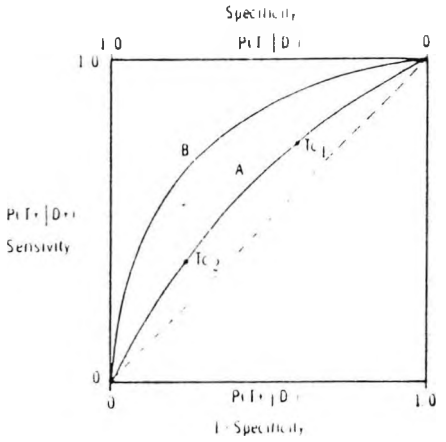
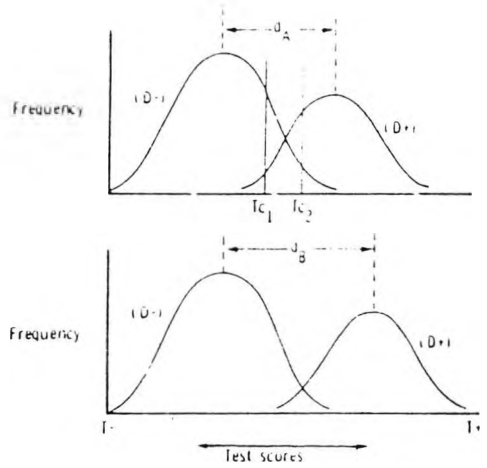


Fig 2



(after Aspinall & Hill, 1984c)

Appendix 3B Bayes' Theorem: Predictive value of a test

By combining measures of sensitivity and specificity with a prior knowledge of the frequency of the disease in the population being examined, two probabilities (of particular interest to the clinician facing a diagnosis decision) may be derived a diagnostic decision) may be derived (Lusted, 1971):

1) PREDICTIVE VALUE OF A POSITIVE TEST RESULT (p(D/F)),
which is the conditional probability that the patient has the disease, given a fail test result.

$$p(D/F) = \frac{p(D).p(F/D)}{p(D).p(F/D) + p(N).p(F/N)}$$

where
p(D) is the prior probability of disease D
p(F/D) is the test sensitivity
p(N) is the prior probability of no disease i.e. 1-p(D)
p(F/N) is 1-specificity

2) PREDICTIVE VALUE OF A NEGATIVE TEST RESULT (p(N/P)),
which is the conditional probability that the patient does not have the the disease, given a pass test result.

$$p(N/P) = \frac{p(N).p(P/N)}{p(N).p(P/N) + p(D).p(P/D)}$$

where
p(D) is the prior probability of disease D
p(P/N) is the test specificity
p(N) is the prior probability of no disease i.e. 1-p(D)
p(P/D) is 1-sensitivity

When the prior probability of the disease in question is not known, the following formulae (Daubs, 1972) are used to calculate the two predictive values:

$$p(D/F) = \frac{n(D,F)}{n(F)} \quad \text{and} \quad p(N/P) = \frac{n(N,P)}{n(P)}$$

where
n(D,F) is the number of patients with the disease who fail
n(N,P) is the number of normals who pass
n(F) is the total number of patients who fail
n(P) is the total number of patients who pass

Appendix 3C Mean score per patient for each plate: Arden gratings

Group	Mean score					
	PL2	PL3	PL4	PL5	PL6	PL7
1. No DR	13.1 sd 2.5	11.1 sd 2.5	12.6 sd 2.7	12.7 sd 3.2	14.7 sd 4.1	16.9 sd 6.0
2. No DR+C	14.3 sd 3.1	12.9 sd 3.4	14.5 sd 3.3	15.6 sd 4.2	16.8 sd 4.9	19.7 sd 5.5
3. DR	12.8 sd 2.8	11.5 sd 2.7	13.0 sd 3.4	12.9 sd 3.6	14.8 sd 3.7	16.5 sd 5.8
4. DR+C	14.6 sd 3.1	13.5 sd 3.5	15.3 sd 4.3	15.1 sd 4.3	16.9 sd 4.8	19.6 sd 6.2

DR=Diabetic Retinopathy; C=Complications

PL2 to PL7=Scores on plates 2 to 7

Appendix 3D Significance of differences in mean scores between groups: Arden gratings plate 3

	No DR+C	DR	DR+C
No DR	p<0.05	NS	p<0.05
No DR+C		NS	NS
DR			NS

DR=Diabetic Retinopathy; C=Complications

Appendix 3E Significance of differences in mean scores between groups: Arden gratings plate 4

	No DR+C	DR	DR+C
No DR	NS	NS	p<0.05
No DR+C		NS	NS
DR			NS

DR=Diabetic Retinopathy; C=Complications

Appendix 3F Significance of differences in mean scores between groups: Arden gratings plate 5

	No DR+C	DR	DR+C
No DR	p<0.05	NS	NS
No DR+C		p<0.05	NS
DR			NS

DR=Diabetic Retinopathy; C=Complications

Appendix 3G Mean score per patient for each spatial frequency: VCTS 6000

Group	Mean score				
	A (1.5 c/d)	B (3 c/d)	C (6 c/d)	D (12 c/d)	E (18 c/d)
1. No DR	5.0 sd 0.5	5.6 sd 0.7	4.6 sd 1.0	4.1 sd 1.5	3.3 sd 1.9
2. No DR+C	4.6 sd 0.7	4.9 sd 0.9	3.7 sd 1.1	2.5 sd 1.5	1.4 sd 1.7
3. DR	4.7 sd 0.6	5.3 sd 0.9	3.9 sd 1.0	3.2 sd 1.6	2.5 sd 1.8
4. DR+C	4.1 sd 0.8	4.7 sd 0.9	3.4 sd 1.4	2.2 sd 1.6	1.3 sd 1.5

DR=Diabetic Retinopathy; C=Complications

Appendix 3H Significance of differences in mean scores between groups: VCTS 6000 spatial frequency A (1.5 c/d)

	No DR+C	DR	DR+C
No DR	p<0.05	p<0.05	p<0.05
No DR+C		NS	p<0.05
DR			p<0.05

DR=Diabetic Retinopathy; C=Complications

Appendix 3I Significance of differences in mean scores between groups: VCTS 6000 spatial frequency B (3 c/d)

	No DR+C	DR	DR+C
No DR	p<0.05	p<0.05	p<0.05
No DR+C		NS	NS
DR			p<0.05

DR=Diabetic Retinopathy; C=Complications

Appendix 3J Significance of differences in mean scores between groups: VCTS 6000 spatial frequency C (6 c/d)

	No DR+C	DR	DR+C
No DR	$p<0.05$	$p<0.05$	$p<0.05$
No DR+C		NS	NS
DR			NS

DR=Diabetic Retinopathy; C=Complications

Appendix 3K Significance of differences in mean scores between groups: VCTS 6000 spatial frequency D (12 c/d)

	No DR+C	DR	DR+C
No DR	$p<0.05$	$p<0.05$	$p<0.05$
No DR+C		NS	NS
DR			$p<0.05$

DR=Diabetic Retinopathy; C=Complications

Appendix 3L Significance of differences in mean scores between groups: VCTS 6000 spatial frequency E (18 c/d)

	No DR+C	DR	DR+C
No DR	$p<0.05$	$p<0.05$	$p<0.05$
No DR+C		$p<0.05$	NS
DR			NS

DR=Diabetic Retinopathy; C=Complications

Appendix 3M Screening parameters for different pass/fail criteria: Arden gratings for discriminating between patients without DR and those with DR (Fail criterion defined as total score obtained).

Fail Crit	Sensitivity	Specificity	p(N/P)	p(D/F)	False +	False -
>=65	0.80	0.20	0.70	0.30	0.80	0.20
>=70	0.72	0.27	0.69	0.30	0.73	0.28
>=75	0.59	0.39	0.69	0.28	0.66	0.41
>=80	0.57	0.47	0.72	0.32	0.53	0.43
>=85	0.48	0.55	0.71	0.31	0.45	0.52
>=90	0.30	0.65	0.68	0.27	0.35	0.70
>=95	0.24	0.75	0.70	0.29	0.25	0.76
>=100	0.17	0.87	0.71	0.36	0.13	0.83
>=105	0.11	0.92	0.71	0.37	0.08	0.89
>=110	0.09	0.96	0.71	0.49	0.04	0.91
>=115	0.04	0.99	0.71	0.63	0.01	0.96
>=120	0.02	1.00	0.70	1.00	0.00	0.98

Crit=Criterion

p(N/P) is probability that the disease is absent given a pass

p(D/F) is probability that the disease is present given a fail

False + = False positives False - = False negatives

See appendices 3A & 3B for explanation of terms

Appendix 3N Screening parameters for different pass/fail criteria: Arden gratings for discriminating between patients without DR and the 'rest of the patients' (Fail criterion defined as total score obtained).

Fail Crit	Sensitivity	Specificity	p(N/P)	p(D/F)	False +	False -
>=60	0.93	0.10	0.50	0.59	0.90	0.07
>=65	0.89	0.20	0.56	0.61	0.80	0.11
>=70	0.80	0.27	0.49	0.61	0.73	0.20
>=75	0.73	0.39	0.47	0.61	0.61	0.27
>=80	0.65	0.47	0.49	0.63	0.53	0.35
>=85	0.59	0.55	0.49	0.65	0.45	0.41
>=90	0.45	0.65	0.46	0.64	0.35	0.55
>=95	0.39	0.75	0.46	0.68	0.25	0.61
>=100	0.28	0.87	0.46	0.76	0.13	0.72
>=105	0.18	0.92	0.44	0.75	0.08	0.82
>=110	0.14	0.96	0.44	0.82	0.04	0.86
>=115	0.10	0.99	0.44	0.91	0.01	0.90
>=120	0.08	1.00	1.00	1.00	0.00	0.92

Explanation of terms as per appendix 3M

Appendix 3Ma Screening parameters for different pass/fail criteria: Arden gratings for discriminating between patients without DR and those with DR among *type I patients only N=68* (Fail criterion defined as total score obtained).

Fail Crit	Sensitivity	Specificity	p(N/P)	p(D/F)
>=65	0.73	0.20	0.63	0.28
	(0.77)		(0.67)	(0.29)
>=70	0.67	0.31	0.69	0.29
	(0.69)		(0.70)	(0.30)
>=75	0.52	0.43	0.68	0.28
	(0.56)		(0.70)	(0.30)
>=80	0.52	0.63	0.74	0.36
	(0.51)		(0.74)	(0.35)
>=85	0.48	0.69	0.76	0.40
	(0.46)		(0.75)	(0.39)
>=90	0.30	0.74	0.71	0.33
	(0.26)		(0.70)	(0.30)
>=95	0.24	0.80	0.71	0.34
	(0.28)		(0.72)	(0.38)
>=100	0.18	0.97	0.73	0.72
	(0.15)		(0.73)	(0.68)
>=105	0.09	1.00	0.72	1.00
	(0.15)		(0.73)	(1.00)

Explanation of terms as per appendix 3M

+ Numbers in parentheses represent the screening figures after six patients who had been lasered before were relocated from group 4 to group 3

Appendix 3O Results master table: Chapter 3

Key

VEN=Venue; 1-Middlesex Hospital, 2-Whittington Hospital
GP=Group; 1-No DR, 2-No DR+C, 3-DR, 4-DR+C
YRSDM=Duration of diabetes in years
RX=Therapy for diabetes; 1-Insulin, 0-Others
VA=Visual acuity in LogMAR units
RGE=Number of red-green plate errors on the Comp PIC
BYE=Number of tritan plate errors on the Comp PIC
TPE=Total plate errors on the Comp PIC
LTA5=LTA plate 5 result; 1-pass, 0-fail
D15DS=D15(5/2) score
D15DR=Number of red-green axes on the D15(5/2)
D15DT=Number of tritan axes on the D15(5/2)
PL2=Score for plate 2 on the Arden gratings
PL3=Score for plate 3 on the Arden gratings
PL4=Score for plate 4 on the Arden gratings
PL5=Score for plate 5 on the Arden gratings
PL6=Score for plate 6 on the Arden gratings
PL7=Score for plate 7 on the Arden gratings
AGT=Arden gratings total score
SPA=Score for spatial frequency A on the VCTS 6000
SPB=Score for spatial frequency B on the VCTS 6000
SPC=Score for spatial frequency C on the VCTS 6000
SPD=Score for spatial frequency D on the VCTS 6000
SPE=Score for spatial frequency E on the VCTS 6000
GS=VCTS 6000 global score
AMS=Amsler grid result; 1-pass, 0-fail

OBS	NAME	VEN	GP	AGE	YRSDM	RX	VA	RGE	BYE	TPE	LTAS	D15DS	D15DR	D15DT	PL2	PL3	PL4	PL5	PL6	PL7	AGT	SPA	SPB	SPC	SPD	SPE	GS	AMS
1	DB	1	1	37	7	1	-0.08	0	0	0	1	2	0	0	14	11	12	11	16	25	89	.	.	.	.	.	.	1
2	LR	1	1	33	10	1	-0.08	0	0	0	1	0	0	0	8	8	9	6	9	10	50	.	.	.	.	.	.	1
3	NC	1	1	53	8	0	-0.08	0	0	0	1	8	0	1	13	9	9	10	11	11	63	.	.	.	.	.	.	1
4	HC	1	1	48	1	0	0.00	0	0	0	1	0	0	0	16	12	13	13	14	18	86	.	.	.	.	.	.	1
5	AC	1	1	29	4	1	-0.08	0	0	0	1	0	0	0	10	8	8	8	7	7	48	.	.	.	.	.	.	1
6	EC	1	1	55	13	1	0.18	0	0	0	1	2	0	0	15	14	13	16	17	16	91	.	.	.	.	.	.	1
7	JC	1	1	62	1	0	0.18	0	0	0	1	10	0	0	8	11	8	9	13	11	60	.	.	.	.	.	.	1
8	PC	1	1	61	4	0	-0.08	0	0	0	1	0	0	0	16	14	14	13	10	9	76	.	.	.	.	.	.	1
9	RDB	1	1	74	6	1	0.18	0	0	0	1	16	0	1	13	12	13	13	13	15	79	.	.	.	.	.	.	1
10	LD	1	1	44	3	0	-0.08	0	0	0	1	10	0	0	15	10	16	14	16	17	88	.	.	.	.	.	.	1
11	JE	1	1	65	8	0	-0.08	0	0	0	1	18	0	1	14	12	14	10	15	25	90	.	.	.	.	.	.	1
12	IG	1	1	67	7	0	0.00	0	1	1	1	5	0	0	16	14	18	17	17	25	107	.	.	.	.	.	.	1
13	PG	1	1	38	9	1	-0.08	0	0	0	1	0	0	0	12	10	9	8	12	10	61	.	.	.	.	.	.	1
14	RH	1	1	35	8	1	-0.08	0	0	0	1	0	0	0	14	11	11	13	13	11	73	.	.	.	.	.	.	1
15	JH	1	1	65	38	1	0.00	0	0	0	1	8	0	0	11	11	13	11	10	11	67	.	.	.	.	.	.	1
16	TH	1	1	27	5	1	-0.08	0	0	0	1	2	0	0	12	11	14	12	15	14	78	.	.	.	.	.	.	1
17	WJ	1	1	72	1	0	-0.08	0	0	0	1	16	0	1	13	12	13	17	16	25	96	.	.	.	.	.	.	1
18	MK	1	1	55	31	1	-0.08	0	0	0	1	4	0	0	14	10	11	10	14	13	72	.	.	.	.	.	.	1
19	EK	1	1	73	1	0	0.18	0	0	0	1	6	0	0	17	16	18	16	18	17	102	.	.	.	.	.	.	1
20	CM	1	1	46	36	1	0.00	0	0	0	1	0	0	0	12	11	12	13	14	16	78	.	.	.	.	.	.	1
21	NM	1	1	31	6	1	-0.08	0	0	0	1	0	0	0	13	11	12	11	10	10	67	.	.	.	.	.	.	1
22	OM	1	1	63	11	0	0.18	0	1	1	0	12	0	1	16	13	13	17	18	25	102	.	.	.	.	.	.	1
23	SP	1	1	41	13	0	0.00	0	0	0	1	0	0	0	10	9	12	11	9	13	64	.	.	.	.	.	.	1
24	PPC	1	1	66	21	0	0.48	0	0	0	0	22	0	3	16	16	19	17	17	25	110	.	.	.	.	.	.	0
25	SS	1	1	34	1	1	0.18	0	0	0	1	16	0	1	12	11	9	8	12	25	77	.	.	.	.	.	.	1
26	DS	1	1	56	26	1	0.00	0	4	4	0	10	0	0	15	11	16	18	19	18	97	.	.	.	.	.	.	1
27	SS	1	1	48	8	1	-0.08	0	0	0	1	4	0	0	13	9	11	11	10	13	67	.	.	.	.	.	.	1
28	NS	1	1	68	3	0	0.00	0	0	0	1	10	0	0	13	11	10	11	16	25	86	.	.	.	.	.	.	1
29	RS	1	1	46	4	1	0.18	0	0	0	1	2	0	0	15	13	15	15	16	18	92	.	.	.	.	.	.	1
30	ST	1	1	81	5	0	0.18	0	5	5	1	36	1	3	13	11	12	10	14	14	74	.	.	.	.	.	.	1
31	RU	1	1	58	2	0	-0.08	0	0	0	1	0	0	0	10	8	11	10	10	10	59	.	.	.	.	.	.	1
32	PV	1	1	48	6	0	0.18	0	1	1	1	16	0	1	11	10	10	13	19	25	88	.	.	.	.	.	.	1
33	EW	1	1	56	1	0	0.18	0	0	0	1	10	0	0	14	12	13	12	17	25	93	.	.	.	.	.	.	1
34	DW	1	1	45	13	1	0.00	0	0	0	1	0	0	0	12	11	14	14	15	17	83	.	.	.	.	.	.	1
35	GS	1	1	59	3	0	0.18	0	0	0	1	10	0	0	15	11	15	9	14	16	80	.	.	.	.	.	.	1
36	RS	1	1	54	4	1	-0.08	0	0	0	1	8	0	0	15	12	12	12	14	14	79	.	.	.	.	.	.	1
37	HS	1	1	63	7	1	-0.08	0	1	1	1	12	0	0	12	12	13	15	19	25	96	.	.	.	.	.	.	1
38	RP	1	1	53	18	0	0.00	0	0	0	1	4	0	0	10	10	11	11	10	9	61	.	.	.	.	.	.	1
39	AM	1	1	38	3	0	-0.08	0	0	0	1	4	0	0	11	8	9	8	10	9	55	.	.	.	.	.	.	1
40	WJ	1	1	72	1	0	-0.08	0	0	0	1	20	1	1	11	7	11	10	12	14	65	.	.	.	.	.	.	1
41	CJ	1	1	65	26	1	0.18	0	0	0	1	10	0	0	13	11	12	13	16	16	81	.	.	.	.	.	.	1
42	GE	1	1	63	6	0	0.00	0	0	0	1	8	0	0	12	10	11	10	10	10	63	.	.	.	.	.	.	1
43	LDZ	1	1	44	3	0	-0.08	0	0	0	1	40	1	0	16	9	15	14	15	14	83	.	.	.	.	.	.	1
44	MC	1	1	36	20	1	-0.08	0	0	0	1	4	0	0	12	10	11	11	13	12	69	.	.	.	.	.	.	1
45	EWZ	1	1	56	1	1	0.18	0	0	0	1	12	0	0	14	11	14	13	20	25	97	.	.	.	.	.	.	1
46	SS	1	1	48	8	1	-0.08	0	0	0	1	0	0	0	15	13	16	15	14	15	88	.	.	.	.	.	.	1
47	GZ	1	1	40	4	0	-0.08	0	0	0	1	6	0	0	16	12	11	15	12	18	84	.	.	.	.	.	.	1
48	UR	1	1	64	1	0	0.18	0	0	0	1	8	0	0	15	14	16	16	15	19	95	.	.	.	.	.	.	1
49	HJ	1	1	75	1	0	0.30	0	0	0	0	30	0	3	17	14	16	19	20	20	106	.	.	.	.	.	.	1
50	VA	1	1	48	41	1	0.00	0	2	2	1	2	0	0	13	11	12	18	20	25	99	.	.	.	.	.	.	1
51	RH	1	1	55	13	0	0.00	0	0	0	1	8	0	0	13	10	15	14	15	25	92	.	.	.	.	.	.	1
52	RI	1	1	72	1	1	0.18	0	0	0	1	8	0	0	17	14	16	17	20	25	109	.	.	.	.	.	.	1
53	GN	1	1	27	14	1	-0.08	0	0	0	1	0	0	0	15	10	12	14	16	14	81	.	.	.	.	.	.	1
54	PJ	1	1	26	1	1	-0.08	0	0	0	1	0	0	0	10	11	11	11	17	19	79	.	.	.	.	.	.	1
55	JI	1	1	67	9	0	0.00	0	0	0	1	20	0	1	7	8	9	12	20	20	76	.	.	.	.	.	.	1

OBS	NAME	VEN	GP	AGE	YRSDM	RX	VA	RGE	BYE	TPE	LTA5	D15DS	D15DR	D15DT	PL2	PL3	PL4	PL5	PL6	PL7	AGT	SPA	SPB	SPC	SPD	SPE	GS	AMS
56	DR	1	1	46	1	0	-0.08	0	0	0	1	12	0	0	18	15	16	15	18	20	102	.	.	.	.	.	.	1
57	GP	1	1	37	8	1	-0.08	0	0	0	1	0	0	0	7	5	9	8	11	11	51	.	.	.	.	.	.	1
58	MR	1	1	23	1	1	-0.08	0	0	0	1	0	0	0	10	5	8	9	10	8	50	.	.	.	.	.	.	1
59	RG	1	1	26	2	1	0.30	0	0	0	1	4	0	0	10	8	13	10	12	10	63	.	.	.	.	.	.	1
60	CAZ	1	1	28	3	1	-0.08	0	0	0	1	0	0	0	7	4	5	4	8	6	34	.	.	.	.	.	.	1
61	CF	1	1	73	19	0	0.00	0	1	1	1	4	0	0	15	12	14	13	13	18	85	.	.	.	.	.	.	0
62	MC	1	1	60	5	0	-0.08	0	0	0	1	12	0	1	13	9	11	14	16	16	79	.	.	.	.	.	.	1
63	DB	1	1	73	4	0	0.18	0	3	3	1	8	0	1	16	16	13	15	25	25	110	.	.	.	.	.	.	1
64	ML	1	1	80	11	0	0.00	0	2	2	1	14	0	1	15	13	16	17	16	16	93	.	.	.	.	.	.	1
65	BS	1	1	74	5	0	0.00	0	1	1	1	10	0	0	12	15	14	15	18	25	99	.	.	.	.	.	.	1
66	BW	1	1	53	1	0	0.00	0	1	1	0	14	0	1	15	15	16	19	25	25	115	.	.	.	.	.	.	1
67	WH	1	1	63	10	1	0.30	0	0	0	1	8	0	0	14	13	14	12	18	25	96	.	.	.	.	.	.	1
68	WHZ	1	1	63	10	1	0.30	0	0	0	1	12	0	1	12	12	11	11	14	13	73	.	.	.	.	.	.	1
69	DW	1	1	59	44	1	0.18	0	0	0	1	4	0	0	14	10	10	12	25	25	96	.	.	.	.	.	.	1
70	GA	1	1	23	1	1	-0.08	0	0	0	1	16	0	1	15	14	15	15	4	8	71	.	.	.	.	.	.	1
71	GM	1	1	73	15	0	0.30	0	0	0	1	18	0	1	13	12	15	15	17	20	92	.	.	.	.	.	.	1
72	HB	2	1	61	3	0	-0.08	0	1	1	1	.	.	.	.	.	.	.	.	.	.	5	6	4	2	0	17	1
73	GB	2	1	72	9	0	0.00	0	3	3	0	.	.	.	.	.	.	.	.	.	.	5	5	3	1	0	14	1
74	PB	2	1	49	1	1	0.13	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	6	5	6	3	25	1
75	MC	2	1	61	6	0	0.18	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	5	4	3	3	20	1
76	DC	2	1	28	7	1	0.00	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	6	4	4	1	20	1
77	AD	2	1	22	1	1	-0.08	0	0	0	1	.	.	.	.	.	.	.	.	.	.	4	6	6	6	5	27	1
78	SE	2	1	63	7	1	0.30	0	2	2	0	.	.	.	.	.	.	.	.	.	.	4	4	2	2	1	13	1
79	WF	2	1	43	7	0	-0.08	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	6	4	4	6	25	1
80	JF	2	1	64	20	0	0.00	0	0	0	1	.	.	.	.	.	.	.	.	.	.	6	6	5	3	4	24	1
81	EG	2	1	79	1	1	0.00	0	0	0	1	.	.	.	.	.	.	.	.	.	.	4	5	4	2	0	15	1
82	JH	2	1	66	2	1	0.00	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	6	4	2	0	17	1
83	DK	2	1	22	2	1	-0.08	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	6	6	6	4	27	1
84	AK	2	1	55	11	1	0.00	0	1	1	1	.	.	.	.	.	.	.	.	.	.	5	5	4	4	1	19	1
85	EL	2	1	63	7	0	0.00	0	2	2	0	.	.	.	.	.	.	.	.	.	.	5	6	5	5	4	25	0
86	BM	2	1	52	6	1	0.18	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	6	5	4	4	24	1
87	CM	2	1	27	18	1	0.18	1	0	1	1	.	.	.	.	.	.	.	.	.	.	5	6	6	4	4	25	1
88	JM	2	1	45	1	1	0.00	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	6	6	3	1	21	1
89	BM	2	1	40	17	1	0.00	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	5	4	3	3	20	1
90	JP	2	1	53	12	1	0.00	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	6	5	4	4	24	1
91	RP	2	1	24	4	1	-0.08	0	0	0	1	.	.	.	.	.	.	.	.	.	.	6	6	6	6	4	28	1
92	SR	2	1	38	5	1	0.18	0	0	0	1	.	.	.	.	.	.	.	.	.	.	6	6	4	3	2	21	1
93	RR	2	1	70	21	1	0.18	0	3	3	0	.	.	.	.	.	.	.	.	.	.	4	4	3	1	1	13	1
94	SS	2	1	23	11	1	0.00	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	6	5	3	4	23	1
95	DS	2	1	59	1	0	-0.08	0	0	0	1	.	.	.	.	.	.	.	.	.	.	6	6	6	6	4	28	1
96	RS	2	1	47	5	1	0.18	0	0	0	1	.	.	.	.	.	.	.	.	.	.	6	6	6	3	3	24	1
97	GSZ	2	1	60	4	0	-0.08	0	1	1	1	.	.	.	.	.	.	.	.	.	.	5	5	4	3	1	18	1
98	DB	2	1	21	7	1	-0.08	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	5	5	6	5	26	1
99	VZ	2	1	46	16	1	0.18	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	6	6	3	0	20	1
100	AB	2	1	47	7	0	-0.08	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	6	5	6	5	27	1
101	JB	2	1	33	2	0	-0.08	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	6	5	5	5	26	1
102	RB	2	1	62	16	1	0.18	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	5	4	3	1	18	1
103	FC	2	1	68	13	0	-0.08	0	0	0	1	.	.	.	.	.	.	.	.	.	.	6	6	5	4	3	24	1
104	JC	2	1	66	3	0	0.00	0	0	0	1	.	.	.	.	.	.	.	.	.	.	4	5	4	3	3	19	1
105	TC	2	1	53	17	0	-0.08	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	6	5	5	5	26	1
106	MC	2	1	62	4	0	0.18	0	0	0	1	.	.	.	.	.	.	.	.	.	.	4	4	3	3	3	17	1
107	TC	2	1	30	16	1	-0.08	0	0	0	1	.	.	.	.	.	.	.	.	.	.	6	6	6	6	6	30	1
108	HD	2	1	60	5	0	-0.08	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	6	5	5	5	26	1
109	MD	2	1	59	1	0	0.00	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	6	6	3	1	21	1
110	TDS	2	1	60	11	0	-0.08	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	6	4	3	1	19	1

OBS	NAME	VEN	GP	AGE	YRSDM	RX	VA	RGE	BYE	TPE	LTA5	D15DS	D15DR	D15DT	PL2	PL3	PL4	PL5	PL6	PL7	AGT	SPA	SPB	SPC	SPD	SPE	GS	AMS
166	WB	2	1	65	14	0	-0.08	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	6	5	3	1	20	1
167	MM	2	1	44	1	0	-0.08	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	6	6	5	5	27	1
168	RG	2	1	64	1	0	0.00	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	6	5	3	3	22	1
169	SC	2	1	30	4	1	0.00	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	6	5	6	5	27	1
170	CK	2	1	37	11	1	-0.08	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	6	5	6	6	28	1
171	TH	2	1	52	3	0	-0.08	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	6	5	4	4	24	1
172	AS	2	1	60	7	1	0.00	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	6	5	4	3	23	1
173	SP	2	1	58	9	1	-0.08	0	0	0	1	.	.	.	.	.	.	.	.	.	.	6	6	5	4	4	25	1
174	DP	2	1	68	10	0	0.00	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	5	4	3	3	20	1
175	LS	2	1	61	3	0	-0.08	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	6	5	5	4	25	1
176	NR	2	1	44	22	1	-0.08	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	7	6	7	6	31	1
177	VE	2	1	37	10	0	-0.08	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	6	7	6	6	30	1
178	MC	2	1	45	8	0	0.00	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	7	6	7	5	30	1
179	AC	2	1	26	13	1	0.00	0	0	0	1	.	.	.	.	.	.	.	.	.	.	6	7	6	6	7	32	1
180	CR	2	1	73	2	1	0.00	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	5	4	2	1	17	1
181	SZ	2	1	52	5	1	-0.08	0	0	0	1	.	.	.	.	.	.	.	.	.	.	6	6	5	3	2	22	1
182	JS	2	1	54	1	0	0.00	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	6	5	4	5	25	1
183	RP	2	1	50	5	0	-0.08	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	6	5	6	5	27	1
184	NR	2	1	60	4	0	-0.08	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	5	5	4	2	21	1
185	JB	2	1	53	2	0	0.00	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	6	4	3	2	20	1
186	GS	2	1	53	1	0	-0.08	0	0	0	1	.	.	.	.	.	.	.	.	.	.	6	6	6	6	6	30	1
187	BC	2	1	61	2	0	0.18	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	5	4	3	3	20	1
188	CT	2	1	54	2	0	0.00	0	0	0	1	.	.	.	.	.	.	.	.	.	.	6	6	4	5	5	26	1
189	BB	2	1	48	1	0	-0.08	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	6	5	5	5	26	1
190	ML	2	1	34	29	1	-0.08	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	6	5	5	5	26	1
191	ES	2	1	54	12	0	0.00	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	6	5	6	4	26	1
192	JD	2	1	61	2	1	-0.08	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	6	6	6	6	29	1
193	NS	2	1	51	3	0	-0.08	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	6	5	5	4	25	1
194	FM	2	1	34	11	1	-0.08	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	6	6	5	6	28	1
195	ST	2	1	29	8	1	-0.08	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	6	5	6	6	28	1
196	DE	2	1	66	1	0	0.00	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	6	5	5	5	26	1
197	TM	2	1	65	8	0	0.00	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	6	4	3	3	21	1
198	DR	2	1	57	1	0	0.00	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	6	4	3	1	19	1
199	CP	2	1	58	2	1	0.00	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	6	5	4	3	23	1
200	HR	2	1	43	9	0	-0.08	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	5	3	1	0	14	1
201	PH	2	1	59	9	0	-0.08	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	6	4	4	4	23	1
202	HG	2	1	67	25	0	0.00	0	0	0	1	.	.	.	.	.	.	.	.	.	.	4	4	2	2	0	12	1
203	JB	2	1	40	4	0	0.00	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	6	4	3	2	20	1
204	PA	2	1	70	18	0	0.00	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	6	5	5	5	26	1
205	JI	2	1	29	4	1	0.18	0	0	0	1	.	.	.	.	.	.	.	.	.	.	4	4	3	2	2	15	1
206	RP	2	1	47	10	0	0.18	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	6	4	3	1	19	1
207	MB	2	1	52	4	0	0.00	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	6	4	5	4	24	1
208	AS	2	1	41	1	0	-0.08	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	6	4	3	2	20	1
209	LC	2	1	64	4	0	0.18	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	6	4	5	5	25	1
210	JM	2	1	42	21	1	-0.08	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	6	5	5	5	26	1
211	KW	2	1	84	6	1	0.18	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	4	3	0	0	12	1
212	PJ	2	1	26	9	1	-0.08	0	0	0	1	.	.	.	.	.	.	.	.	.	.	6	7	6	6	6	31	1
213	AM	2	1	38	1	1	-0.08	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	6	5	5	5	26	1
214	PG	2	1	17	1	1	-0.08	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	6	6	7	6	30	1
215	AMZ	2	1	37	1	0	-0.08	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	6	5	6	6	28	1
216	RGZ	2	1	64	1	0	0.00	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	6	5	5	5	26	1
217	CR	2	1	78	2	0	0.00	0	1	1	1	.	.	.	.	.	.	.	.	.	.	5	5	3	1	1	15	1
218	AH	2	1	68	1	1	-0.08	0	1	1	1	.	.	.	.	.	.	.	.	.	.	5	5	4	4	3	21	1
219	CM	2	1	65	15	0	0.00	0	1	1	1	.	.	.	.	.	.	.	.	.	.	5	6	5	5	5	26	1
220	BL	2	1	74	60	0	-0.08	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	5	4	4	4	22	1

OBS	NAME	VEN	GP	AGE	YRSDM	RX	VA	RGE	BYE	TPE	LTA5	D15DS	D15DR	D15DT	PL2	PL3	PL4	PL5	PL6	PL7	AGT	SPA	SPB	SPC	SPD	SPE	GS	AMS
221	SP	2	1	43	16	1	-0.08	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	5	5	4	4	23	1
222	JC	2	1	42	7	1	0.18	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	6	4	5	1	21	1
223	AB	2	1	64	1	1	-0.08	0	0	0	1	.	.	.	.	.	.	.	.	.	.	6	5	4	4	3	22	1
224	JM	2	1	74	14	1	0.18	0	0	0	1	.	.	.	.	.	.	.	.	.	.	4	5	4	3	2	18	1
225	KK	2	1	73	9	0	0.00	0	0	0	1	.	.	.	.	.	.	.	.	.	.	4	5	4	3	3	19	1
226	NC	2	1	78	1	0	0.18	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	6	4	3	1	19	1
227	DS	2	1	48	10	1	0.00	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	6	4	2	1	18	1
228	GC	2	1	61	3	0	0.00	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	6	4	5	3	23	1
229	CC	2	1	55	7	0	0.00	0	4	4	0	.	.	.	.	.	.	.	.	.	.	5	6	4	3	1	19	1
230	DC	2	1	41	11	0	-0.08	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	6	5	5	5	26	1
231	ZG	2	1	61	1	0	0.00	0	3	3	1	.	.	.	.	.	.	.	.	.	.	4	4	2	1	0	11	1
232	GB	2	1	64	5	0	-0.08	0	3	3	1	.	.	.	.	.	.	.	.	.	.	5	5	4	5	4	23	1
233	GL	2	1	60	4	1	0.00	0	2	2	1	.	.	.	.	.	.	.	.	.	.	5	4	3	2	1	15	0
234	AB	2	1	33	2	0	0.18	2	2	4	1	.	.	.	.	.	.	.	.	.	.	4	6	5	5	3	23	1
235	FP	2	1	69	5	1	0.18	2	2	4	1	.	.	.	.	.	.	.	.	.	.	4	4	3	2	1	14	1
236	LH	2	1	62	1	0	-0.08	0	1	1	1	.	.	.	.	.	.	.	.	.	.	5	6	6	5	4	26	1
237	DC	2	1	55	1	0	0.00	0	2	2	1	.	.	.	.	.	.	.	.	.	.	4	6	4	3	4	21	1
238	EC	2	1	62	17	0	-0.08	0	2	2	1	.	.	.	.	.	.	.	.	.	.	4	5	3	3	1	16	1
239	DP	2	1	60	14	1	0.18	0	1	1	1	.	.	.	.	.	.	.	.	.	.	4	4	3	2	0	13	1
240	ET	2	1	69	2	0	-0.08	0	3	3	1	.	.	.	.	.	.	.	.	.	.	5	6	5	6	5	27	1
~~241~~	~~KJ~~	~~2~~	~~1~~	~~75~~	~~1~~	~~0~~	~~0.48~~	~~0~~	~~4~~	~~4~~	~~0~~											~~4~~	~~4~~	~~3~~	~~1~~	~~0~~	~~12~~	~~0~~
242	RJ	2	1	75	1	0	-0.08	0	3	3	0	.	.	.	.	.	.	.	.	.	.	5	5	4	3	1	18	1
243	CS	2	1	51	4	0	-0.08	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	5	4	4	3	21	1
244	MM	2	1	60	20	0	0.00	0	2	2	1	.	.	.	.	.	.	.	.	.	.	5	6	3	2	1	17	1
245	AW	2	1	64	13	0	0.00	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	5	5	4	4	23	1
246	DP	2	1	70	16	0	0.18	0	3	3	1	.	.	.	.	.	.	.	.	.	.	4	4	3	2	0	13	1
247	ES	2	1	70	3	0	0.00	0	0	0	1	.	.	.	.	.	.	.	.	.	.	6	6	6	7	7	32	1
248	VT	2	1	74	7	0	0.00	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	6	4	3	3	21	1
249	AN	2	1	16	1	1	0.18	0	0	0	1	.	.	.	.	.	.	.	.	.	.	6	6	6	5	5	28	1
250	TB	2	1	45	1	0	-0.08	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	6	4	4	3	22	1
251	CJ	2	1	70	8	0	0.00	0	1	1	1	.	.	.	.	.	.	.	.	.	.	4	4	3	2	1	14	1
252	WE	2	1	62	5	0	0.18	0	1	1	0	.	.	.	.	.	.	.	.	.	.	4	4	4	1	0	13	0
253	MM	2	1	66	39	1	0.18	0	0	0	1	.	.	.	.	.	.	.	.	.	.	4	5	4	5	5	23	1
254	LG	2	2	47	1	0	0.18	0	1	1	0	.	.	.	.	.	.	.	.	.	.	5	6	3	2	0	16	0
255	ME	2	2	77	11	1	0.18	0	3	3	1	.	.	.	.	.	.	.	.	.	.	4	5	4	1	1	15	1
~~256~~	~~TOH~~	~~2~~	~~2~~	~~73~~	~~21~~	~~0~~	~~0.48~~	~~0~~	~~0~~	~~0~~	~~1~~											~~5~~	~~5~~	~~4~~	~~0~~	~~5~~	~~21~~	~~1~~
257	PRB	2	2	55	13	0	0.18	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	6	5	3	2	21	1
258	EW	2	2	17	7	1	0.00	0	0	0	1	.	.	.	.	.	.	.	.	.	.	6	7	5	3	1	22	1
259	MS	2	2	33	1	0	0.00	0	0	0	1	.	.	.	.	.	.	.	.	.	.	4	5	4	3	1	17	1
260	DR	2	2	56	46	1	0.30	0	1	1	1	.	.	.	.	.	.	.	.	.	.	5	5	4	1	0	15	1
261	EB	2	2	85	8	1	0.30	0	7	7	1	.	.	.	.	.	.	.	.	.	.	2	2	1	0	0	5	1
262	EM	2	2	76	12	0	0.30	0	0	0	1	.	.	.	.	.	.	.	.	.	.	4	4	2	2	0	12	1
263	MR	2	2	83	10	1	0.18	0	3	3	1	.	.	.	.	.	.	.	.	.	.	4	4	3	2	0	13	1
264	AS	2	2	58	5	0	0.00	0	4	4	1	.	.	.	.	.	.	.	.	.	.	3	3	2	1	0	9	0
265	FP	2	2	48	12	1	0.18	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	6	6	3	0	20	1
266	IM	2	2	74	4	0	0.00	0	3	3	0	.	.	.	.	.	.	.	.	.	.	5	5	4	2	2	18	1
267	AM	2	2	82	1	0	0.18	0	1	1	1	.	.	.	.	.	.	.	.	.	.	4	4	3	2	0	13	0
268	BY	2	2	63	29	0	0.18	0	1	1	1	.	.	.	.	.	.	.	.	.	.	3	3	2	1	0	9	1
269	YP	2	2	82	1	0	0.00	0	2	2	1	.	.	.	.	.	.	.	.	.	.	5	5	3	2	0	15	1
270	CL	2	2	83	7	0	0.30	0	3	3	1	.	.	.	.	.	.	.	.	.	.	5	5	4	1	0	15	1
271	PS	2	2	64	17	0	0.18	0	2	2	1	.	.	.	.	.	.	.	.	.	.	4	4	3	3	0	14	1
272	GA	2	2	77	22	0	0.18	0	0	0	1	.	.	.	.	.	.	.	.	.	.	4	5	3	2	0	14	1
273	EG	2	2	75	22	0	0.18	0	1	1	1	.	.	.	.	.	.	.	.	.	.	4	5	2	1	0	12	1
274	FJ	2	2	77	8	0	0.00	0	1	1	1	.	.	.	.	.	.	.	.	.	.	4	5	3	2	1	15	1
275	CL	2	2	72	1	0	0.18	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	4	3	2	0	14	1

OBS	NAME	VEN	GP	AGE	YRSDM	RX	VA	RGE	BYE	TPE	LTAS	D15DS	D15DR	D15DT	PL2	PL3	PL4	PL5	PL6	PL7	AGT	SPA	SPB	SPC	SPD	SPE	GS	AMS
276	GY	2	2	58	16	0	0.00	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	6	5	6	5	27	1
277	MJ	2	2	58	4	1	0.18	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	6	4	3	2	20	1
278	HD	2	2	81	1	0	0.00	0	1	1	1	.	.	.	.	.	.	.	.	.	.	4	4	3	2	0	13	1
279	CN	2	2	63	1	0	0.30	0	0	0	1	.	.	.	.	.	.	.	.	.	.	4	5	2	0	0	11	1
280	FW	2	2	66	8	0	0.00	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	5	4	2	2	18	1
281	KC	2	2	66	15	0	-0.08	7	1	8	1	.	.	.	.	.	.	.	.	.	.	5	6	5	5	5	26	1
282	WC	2	2	72	1	0	0.00	5	0	5	1	.	.	.	.	.	.	.	.	.	.	5	6	5	4	1	21	1
283	BA	2	2	64	4	0	-0.08	3	1	4	1	.	.	.	.	.	.	.	.	.	.	5	6	4	5	3	23	1
284	AT	2	2	64	3	0	0.00	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	6	5	5	5	26	1
285	JK	2	2	73	16	0	0.18	0	4	4	1	.	.	.	.	.	.	.	.	.	.	4	4	3	1	0	12	1
286	FP	2	2	82	23	0	0.18	0	3	3	0	.	.	.	.	.	.	.	.	.	.	5	5	4	3	1	18	1
287	CP	2	2	73	8	0	0.18	0	3	3	1	.	.	.	.	.	.	.	.	.	.	5	5	4	2	1	17	1
288	VM	2	2	64	1	0	0.18	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	5	4	3	3	20	1
289	ET	2	2	36	2	1	-0.08	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	6	5	6	4	26	1
290	GY	2	2	73	1	0	0.18	0	1	1	1	.	.	.	.	.	.	.	.	.	.	5	5	4	3	3	20	1
291	CE	2	2	68	10	0	0.18	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	5	4	3	3	20	1
292	DS	2	2	64	18	0	0.00	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	5	3	2	0	15	1
293	VH	2	2	75	6	0	0.00	0	1	1	1	.	.	.	.	.	.	.	.	.	.	5	6	5	4	5	25	1
294	AT	2	2	57	25	1	0.00	0	2	2	1	.	.	.	.	.	.	.	.	.	.	5	5	5	3	3	21	1
295	PG	2	2	76	13	0	0.18	0	6	6	0	.	.	.	.	.	.	.	.	.	.	5	4	3	1	0	13	1
296	SS	1	2	47	1	0	-0.08	0	0	0	1	0	0	0	12	11	11	11	11	11	67	.	.	.	.	.	.	1
297	ES	1	2	76	20	1	0.30	0	4	4	0	26	0	3	13	13	15	14	14	17	86	.	.	.	.	.	.	1
298	ES	1	2	72	10	0	0.48	0	2	2	1	18	0	1	17	17	17	25	25	25	126	.	.	.	.	.	.	1
299	PRB	1	2	54	12	0	0.18	0	0	0	1	10	0	0	14	12	14	14	15	25	94	.	.	.	.	.	.	1
300	MP	1	2	78	9	0	0.30	1	1	2	1	8	0	0	9	8	12	15	13	20	77	.	.	.	.	.	.	1
301	EM	1	2	72	8	0	0.00	0	0	0	1	6	0	0	13	13	13	13	16	25	93	.	.	.	.	.	.	1
302	BL	1	2	66	10	0	-0.08	0	2	2	1	6	0	0	15	10	14	11	13	12	75	.	.	.	.	.	.	0
303	NF	1	2	79	20	0	0.18	0	3	3	1	10	0	0	12	14	15	14	16	25	96	.	.	.	.	.	.	1
304	SD	1	2	70	38	1	0.18	0	4	4	0	8	0	0	14	13	16	14	19	25	101	.	.	.	.	.	.	1
305	MB	1	2	57	24	1	-0.08	0	2	2	1	24	0	1	16	15	16	16	15	15	93	.	.	.	.	.	.	1
306	PS	1	2	59	7	0	0.18	7	0	7	1	85	7	1	9	11	11	14	13	13	71	.	.	.	.	.	.	1
307	HS	1	2	75	7	0	0.30	0	7	7	0	18	0	1	16	15	17	17	17	17	99	.	.	.	.	.	.	1
308	ASZ	1	2	75	7	0	0.18	0	7	7	0	28	0	2	14	15	18	20	20	20	107	.	.	.	.	.	.	1
309	LS	1	2	65	11	1	0.00	0	1	1	1	6	0	0	13	12	9	12	15	14	75	.	.	.	.	.	.	1
310	EG	1	2	67	67	1	-0.08	0	1	1	1	18	0	0	15	13	17	17	13	20	95	.	.	.	.	.	.	0
311	AM	1	2	27	5	1	0.00	5	0	5	1	86	7	0	12	10	13	12	10	10	67	.	.	.	.	.	.	1
312	CF	1	2	71	5	0	0.00	0	0	0	1	6	0	0	13	13	14	14	16	25	95	.	.	.	.	.	.	1
313	MD	1	2	77	13	0	0.18	0	7	7	1	16	0	0	16	14	17	16	25	25	113	.	.	.	.	.	.	1
314	RB	1	2	68	7	0	-0.08	0	5	5	0	34	0	3	13	12	15	15	17	25	97	.	.	.	.	.	.	1
315	MA	1	2	54	4	1	0.18	0	2	2	0	6	0	0	15	10	10	11	12	10	68	.	.	.	.	.	.	1
316	FM	1	2	62	23	1	0.30	0	3	3	0	10	0	1	14	11	11	9	9	14	68	.	.	.	.	.	.	1
317	SL	1	2	54	1	0	0.18	0	0	0	0	12	0	1	16	14	17	16	19	25	107	.	.	.	.	.	.	1
318	WR	1	2	63	6	0	0.00	2	6	8	1	20	1	2	19	16	14	18	18	19	104	.	.	.	.	.	.	1
319	HD	1	2	40	24	1	-0.08	0	3	3	0	0	0	0	18	19	17	17	14	15	100	.	.	.	.	.	.	1
320	VP	1	2	47	5	0	0.48	0	1	1	1	12	0	0	13	9	11	15	25	25	98	.	.	.	.	.	.	1
321	HR	1	2	60	58	1	0.18	0	3	3	0	18	0	1	10	7	8	25	14	25	89	.	.	.	.	.	.	1
322	MF	1	2	83	15	0	0.00	0	0	0	1	0	0	0	14	13	13	10	12	14	76	.	.	.	.	.	.	1
323	CF	1	2	53	15	0	0.18	6	6	12	0	58	4	2	17	16	17	20	25	25	120	.	.	.	.	.	.	1
324	BMZ	1	2	56	23	1	-0.08	0	2	2	1	8	0	0	25	25	25	25	25	25	150	.	.	.	.	.	.	1
325	JM	1	2	73	1	0	0.18	0	2	2	1	20	0	2	13	10	16	19	19	20	97	.	.	.	.	.	.	1
326	AS	1	2	64	14	0	0.30	0	4	4	0	24	0	2	14	13	16	13	25	25	106	.	.	.	.	.	.	1
327	CB	1	3	58	5	0	-0.08	0	2	2	1	10	0	1	17	14	16	16	17	25	105	.	.	.	.	.	.	0
328	MB	1	3	42	24	1	-0.08	0	0	0	1	2	0	0	12	9	5	6	13	10	55	.	.	.	.	.	.	1
329	SR	1	3	32	24	1	-0.08	0	0	0	1	0	0	0	6	7	6	10	9	9	47	.	.	.	.	.	.	1
330	MC	1	3	51	11	1	0.00	0	1	1	1	0	0	0	14	14	16	16	16	25	101	.	.	.	.	.	.	1

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OBS	NAME	VEN	GP	AGE	YRSDM	RX	VA	RGE	BYE	TPE	LTAS	D15DS	D15DR	D15DT	PL2	PL3	PL4	PL5	PL6	PL7	AGT	SPA	SPB	SPC	SPD	SPE	GS	AMS
331	CC	1	3	81	27	0	0.18	0	7	7	0	12	0	0	10	12	16	12	19	25	94	.	.	.	.	.	.	1
332	IDS	1	3	59	8	0	0.00	0	1	1	1	10	0	0	12	8	11	12	11	13	67	.	.	.	.	.	.	1
333	JDS	1	3	57	13	1	0.18	4	4	8	1	58	6	0	13	13	12	14	16	17	85	.	.	.	.	.	.	1
334	PF	1	3	52	2	0	-0.00	0	0	0	1	0	0	0	15	14	17	15	13	10	84	.	.	.	.	.	.	1
335	MF	1	3	74	2	0	0.18	1	3	4	1	14	0	1	10	10	13	11	16	20	80	.	.	.	.	.	.	1
336	CG	1	3	45	26	1	-0.08	0	0	0	1	0	0	0	10	11	9	10	11	11	62	.	.	.	.	.	.	1
337	CL	1	3	47	28	1	0.00	0	2	2	1	14	0	1	9	9	10	11	14	14	67	.	.	.	.	.	.	0
338	BL	1	3	55	21	1	-0.08	0	4	4	1	16	0	0	14	13	18	15	18	25	103	.	.	.	.	.	.	0
339	SP	1	3	33	16	1	0.00	0	0	0	1	0	0	0	14	13	16	17	16	17	93	.	.	.	.	.	.	1
340	WR	1	3	51	13	1	0.18	2	6	8	0	12	0	0	15	15	17	17	25	25	114	.	.	.	.	.	.	1
341	AW	1	3	51	17	1	0.00	0	0	0	1	2	0	0	11	9	11	11	14	15	71	.	.	.	.	.	.	1
342	SH	1	3	21	20	1	0.30	0	2	2	1	10	0	0	14	13	15	16	17	25	100	.	.	.	.	.	.	0
343	JB	1	3	36	26	1	-0.08	0	0	0	1	0	0	0	13	11	11	9	10	9	63	.	.	.	.	.	.	1
344	AK	1	3	20	16	1	0.00	0	5	5	1	6	0	0	12	13	14	15	16	17	87	.	.	.	.	.	.	1
345	DB	1	3	46	18	1	-0.08	0	1	1	1	8	0	0	13	11	13	11	13	12	73	.	.	.	.	.	.	1
346	AS	1	3	65	12	0	-0.08	0	2	2	0	4	0	0	18	13	14	13	14	16	88	.	.	.	.	.	.	1
347	AS	1	3	26	19	1	0.48	5	5	10	1	6	0	0	17	17	14	17	19	20	96	.	.	.	.	.	.	0
348	JR	1	3	58	41	1	0.00	0	0	0	1	6	0	0	13	11	15	13	16	17	85	.	.	.	.	.	.	1
349	SP	1	3	41	13	0	0.00	0	0	0	1	13	0	0	12	10	12	11	13	11	69	.	.	.	.	.	.	1
350	CM	1	3	59	16	1	0.00	0	4	4	0	30	0	3	16	13	15	13	14	16	87	.	.	.	.	.	.	1
351	EL	1	3	68	46	1	0.30	5	7	12	0	32	0	3	17	16	17	19	19	25	113	.	.	.	.	.	.	0
352	SV	1	3	41	28	1	0.30	0	0	0	1	18	0	1	12	11	15	15	17	25	95	.	.	.	.	.	.	1
353	DB	1	3	60	26	0	-0.08	0	0	0	1	16	0	1	15	13	13	14	14	15	84	.	.	.	.	.	.	1
354	RL	1	3	38	8	0	0.00	1	6	8	1	20	0	2	16	15	20	20	25	25	121	.	.	.	.	.	.	1
355	WG	1	3	67	57	1	0.30	0	6	6	0	20	0	0	13	13	15	17	18	19	95	.	.	.	.	.	.	0
356	RW	1	3	50	12	1	0.18	1	4	5	1	6	0	0	17	18	19	19	20	25	118	.	.	.	.	.	.	0
357	BN	1	3	30	6	1	-0.08	0	0	0	1	8	0	0	13	14	13	13	17	10	88	.	.	.	.	.	.	1
358	BJZ	1	3	35	25	1	-0.08	0	0	0	1	2	0	0	13	12	12	12	12	13	74	.	.	.	.	.	.	1
359	MG	1	3	35	31	1	-0.08	0	1	1	1	12	0	0	12	11	12	11	12	13	71	.	.	.	.	.	.	1
360	FG	1	3	58	16	1	-0.08	0	5	5	0	26	0	1	11	11	10	20	20	20	92	.	.	.	.	.	.	1
361	GH	1	3	27	18	1	0.18	0	2	2	1	4	0	0	6	6	8	11	11	11	53	.	.	.	.	.	.	1
362	AG	1	3	33	23	1	0.00	0	0	0	1	0	0	0	11	11	11	12	12	12	69	.	.	.	.	.	.	1
363	BG	1	3	24	9	1	0.00	0	0	0	1	6	0	0	11	10	12	9	8	6	56	.	.	.	.	.	.	1
364	MM	1	3	53	24	1	0.00	0	2	2	1	26	1	0	12	10	10	9	10	6	57	.	.	.	.	.	.	1
365	FJ	1	3	44	26	1	0.18	0	0	0	1	2	0	0	8	7	9	7	11	13	55	.	.	.	.	.	.	1
366	WE	1	3	61	13	1	0.18	0	3	3	1	2	0	0	11	5	7	6	16	25	70	.	.	.	.	.	.	1
367	HS	1	3	75	29	1	0.18	0	5	5	0	18	0	1	13	12	18	13	15	15	86	.	.	.	.	.	.	1
368	RA	1	3	42	24	1	0.00	0	1	1	1	0	0	0	13	7	8	6	11	12	57	.	.	.	.	.	.	1
369	JM	1	3	62	2	0	0.18	0	3	3	1	22	1	0	18	12	13	11	15	18	87	.	.	.	.	.	.	0
370	EO	1	3	66	13	0	-0.08	0	0	0	1	0	0	0	13	11	13	12	12	13	74	.	.	.	.	.	.	1
371	MP	1	3	39	1	1	-0.08	0	0	0	1	4	0	0	16	14	15	16	13	10	84	.	.	.	.	.	.	1
372	LS	1	3	64	8	0	0.00	0	1	1	1	18	0	1	10	13	13	14	14	15	79	.	.	.	.	.	.	1
373	SP	2	3	34	17	1	-0.08	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	6	4	4	3	22	1
374	LGH	2	3	22	17	1	-0.08	0	1	1	1	.	.	.	.	.	.	.	.	.	.	5	6	5	4	4	24	1
375	DC	2	3	54	30	1	0.30	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	6	3	2	1	17	1
376	RR	2	3	76	24	0	0.18	0	5	5	0	.	.	.	.	.	.	.	.	.	.	5	4	3	2	1	15	1
377	AA	2	3	54	14	1	0.18	0	4	4	0	.	.	.	.	.	.	.	.	.	.	4	4	3	2	0	13	0
378	MR	2	3	63	7	0	0.00	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	5	3	2	0	15	1
379	EI	2	3	55	20	0	-0.08	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	5	4	5	5	24	1
380	BM	2	3	65	10	0	-0.08	0	0	0	1	.	.	.	.	.	.	.	.	.	.	4	5	4	3	3	19	1
381	HM	2	3	48	6	0	0.00	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	6	4	3	3	21	1
382	GM	2	3	53	30	1	0.00	0	0	0	1	.	.	.	.	.	.	.	.	.	.	4	5	4	3	1	17	1
383	TK	2	3	47	5	0	0.18	0	0	0	1	.	.	.	.	.	.	.	.	.	.	4	5	3	2	0	14	1
384	AU	2	3	40	19	1	0.18	0	0	0	1	.	.	.	.	.	.	.	.	.	.	6	6	3	4	1	20	1
385	HS	2	3	84	6	0	0.18	7	3	10	0	.	.	.	.	.	.	.	.	.	.	3	3	2	1	0	9	1

/Continued

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OBS	NAME	VEN	GP	AGE	YRSDM	RX	VA	RGE	BYE	TPE	LTAS	D15DS	D15DR	D15DT	PL2	PL3	PL4	PL5	PL6	PL7	AGT	SPA	SPB	SPC	SPD	SPE	GS	AMS
386	MI	2	3	54	16	1	-0.08	0	3	3	1	.	.	.	.	.	.	.	.	.	.	5	6	6	4	5	26	1
387	MH	2	3	57	17	1	0.18	0	3	3	1	.	.	.	.	.	.	.	.	.	.	4	5	4	2	1	16	1
388	DC	2	3	75	1	0	0.00	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	6	4	2	2	19	1
389	KP	2	3	67	16	0	0.00	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	6	5	4	4	24	1
390	EA	2	3	65	12	0	-0.08	0	0	0	1	.	.	.	.	.	.	.	.	.	.	4	6	4	5	3	22	1
391	KN	2	3	55	12	1	-0.08	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	6	5	6	6	28	1
392	KA	2	3	42	10	1	0.00	0	3	3	1	.	.	.	.	.	.	.	.	.	.	4	5	4	5	5	23	1
393	AK	2	3	82	30	1	0.00	0	1	1	1	.	.	.	.	.	.	.	.	.	.	4	4	4	3	2	17	1
394	JO	2	3	69	9	1	-0.08	0	0	0	1	.	.	.	.	.	.	.	.	.	.	6	6	5	3	4	24	1
395	CR	2	3	66	11	1	-0.08	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	6	5	5	3	24	1
396	MP	2	3	57	12	0	-0.08	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	5	1	4	5	23	1
397	PC	2	3	75	19	1	0.18	0	2	2	1	.	.	.	.	.	.	.	.	.	.	4	4	4	0	0	12	1
398	AS	2	3	58	6	0	-0.08	0	3	3	1	.	.	.	.	.	.	.	.	.	.	5	6	4	4	3	22	1
399	GZ	2	3	65	3	0	0.00	0	3	3	1	.	.	.	.	.	.	.	.	.	.	4	5	3	2	2	16	1
400	GW	2	3	29	26	1	-0.08	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	6	5	5	3	24	1
401	BT	2	3	62	3	1	-0.08	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	6	6	7	6	30	1
402	SR	2	3	50	10	0	0.30	0	7	7	0	.	.	.	.	.	.	.	.	.	.	4	5	3	2	1	15	1
403	WF	2	3	70	35	1	0.00	0	1	1	1	.	.	.	.	.	.	.	.	.	.	4	4	3	3	1	15	1
404	LN	2	3	60	5	1	0.00	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	4	3	1	1	14	1
405	MG	2	3	54	7	0	0.18	0	4	4	1	.	.	.	.	.	.	.	.	.	.	5	6	5	4	4	24	1
406	KM	2	3	66	4	0	0.00	0	3	3	1	.	.	.	.	.	.	.	.	.	.	5	6	4	4	1	20	1
407	MK	2	3	84	20	0	0.30	0	2	2	1	.	.	.	.	.	.	.	.	.	.	4	4	3	3	1	15	1
408	GC	2	3	66	8	1	0.00	0	0	0	1	.	.	.	.	.	.	.	.	.	.	4	5	3	0	0	12	1
409	CB	2	3	57	22	1	0.00	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	5	4	5	3	22	1
410	RB	2	3	61	12	1	-0.08	0	4	4	1	.	.	.	.	.	.	.	.	.	.	5	5	4	3	5	22	1
411	JB	2	3	55	10	1	-0.08	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	6	4	5	4	24	1
412	RG	2	3	58	5	1	0.00	0	6	6	0	.	.	.	.	.	.	.	.	.	.	4	4	3	0	0	11	1
413	JF	2	3	48	7	0	0.30	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	4	1	2	1	13	1
414	LB	2	3	76	5	0	0.18	0	0	0	1	.	.	.	.	.	.	.	.	.	.	4	5	4	3	3	19	1
415	AN	2	3	32	16	1	0.00	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	6	5	4	4	24	1
416	SB	2	3	60	6	0	-0.08	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	6	4	4	3	22	1
417	AC	2	3	73	15	0	0.18	0	1	1	1	.	.	.	.	.	.	.	.	.	.	5	6	4	3	3	21	1
418	KP	2	3	69	36	1	-0.08	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	6	5	4	3	23	1
419	LR	2	3	78	11	0	0.30	0	5	5	1	.	.	.	.	.	.	.	.	.	.	4	4	3	0	0	11	1
420	DO	2	3	20	14	1	-0.08	0	0	0	1	.	.	.	.	.	.	.	.	.	.	6	7	7	6	5	31	1
421	JO	2	3	39	8	0	0.00	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	5	4	3	3	20	1
422	MB	2	3	70	6	0	-0.08	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	5	4	5	4	23	1
423	DK	2	3	62	8	1	-0.08	0	1	1	1	.	.	.	.	.	.	.	.	.	.	5	6	4	3	0	18	1
424	BR	1	4	42	40	1	0.00	0	3	3	1	0	0	0	12	11	13	13	13	13	75	.	.	.	.	.	.	1
425	WJ	1	4	78	33	1	0.48	4	5	9	0	22	0	1	13	18	20	12	14	25	102	.	.	.	.	.	.	0
426	KM	1	4	68	13	1	0.18	0	0	0	1	6	0	0	18	14	10	8	8	4	62	.	.	.	.	.	.	1
427	SE	1	4	65	17	1	0.00	0	0	0	1	26	0	2	13	10	12	14	18	19	86	.	.	.	.	.	.	1
428	RH	1	4	66	1	1	0.18	0	3	3	0	4	0	0	15	13	16	14	19	25	102	.	.	.	.	.	.	1
429	MG	1	4	74	23	0	0.18	0	4	4	0	30	0	3	15	14	16	16	17	25	103	.	.	.	.	.	.	1
430	CA	1	4	82	30	0	0.30	1	1	2	0	4	0	0	14	11	13	19	19	19	95	.	.	.	.	.	.	0
431	JL	1	4	62	20	0	0.48	7	5	12	0	90	8	1	17	17	18	18	25	25	120	.	.	.	.	.	.	1
432	HT	1	4	57	22	0	0.18	3	7	10	0	34	0	3	19	14	25	25	25	25	133	.	.	.	.	.	.	1
433	MA	1	4	70	14	1	0.30	0	6	6	0	2	0	0	18	16	20	20	25	25	124	.	.	.	.	.	.	1
434	RH	1	4	53	32	1	0.00	0	0	0	1	2	0	0	13	11	14	13	17	18	86	.	.	.	.	.	.	1
435	JF	1	4	46	20	1	0.30	0	3	3	1	26	0	2	6	9	9	12	12	12	60	.	.	.	.	.	.	1
436	JM	2	4	54	41	1	0.18	0	1	1	1	.	.	.	.	.	.	.	.	.	.	4	4	3	1	0	12	1
437	WZ	2	4	58	31	0	0.48	4	4	8	0	.	.	.	.	.	.	.	.	.	.	4	3	3	1	0	11	1
438	ED	2	4	73	14	0	0.18	0	3	3	1	.	.	.	.	.	.	.	.	.	.	5	6	5	4	2	22	1
439	NU	2	4	65	23	1	0.00	0	1	1	1	.	.	.	.	.	.	.	.	.	.	5	5	4	3	2	19	1
440	AM	2	4	79	15	1	0.48	0	4	4	1	.	.	.	.	.	.	.	.	.	.	3	4	1	0	0	8	1

OBS	NAME	VEN	GP	AGE	YRSDM	RX	VA	RGE	BYE	TPE	LTA5	D15DS	D15DR	D15DT	PL2	PL3	PL4	PL5	PL6	PL7	AGT	SPA	SPB	SPC	SPD	SPE	GS	AMS
441	EP	2	4	56	7	0	0.18	2	3	5	1	.	.	.	.	.	.	.	.	.	.	4	5	4	2	0	15	0
442	OB	2	4	85	19	0	0.18	0	7	7	0	.	.	.	.	.	.	.	.	.	.	3	4	1	0	0	8	1
443	SC	2	4	68	10	0	0.30	7	6	13	0	.	.	.	.	.	.	.	.	.	.	2	3	1	0	0	6	1
444	CT	2	4	58	3	0	0.00	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	5	4	5	4	23	1
445	CG	2	4	58	9	0	0.00	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	6	5	4	3	23	1
446	AH	2	4	62	4	0	0.00	0	0	0	1	.	.	.	.	.	.	.	.	.	.	4	6	6	5	4	25	1
447	FI	2	4	54	35	1	0.18	2	4	6	0	.	.	.	.	.	.	.	.	.	.	4	4	3	2	2	15	1
448	NP	2	4	70	30	0	0.30	0	4	4	1	.	.	.	.	.	.	.	.	.	.	4	4	1	0	0	9	1
449	LC	2	4	76	20	0	0.18	0	0	0	0	.	.	.	.	.	.	.	.	.	.	4	5	4	3	2	18	0
450	JD	2	4	82	1	1	0.18	3	4	7	1	.	.	.	.	.	.	.	.	.	.	4	4	3	0	0	11	0
451	NM	2	4	66	3	1	0.00	0	0	0	1	.	.	.	.	.	.	.	.	.	.	4	5	4	3	3	19	1
452	GN	2	4	60	10	0	0.00	0	5	5	1	.	.	.	.	.	.	.	.	.	.	5	6	4	3	3	21	1
453	LV	2	4	61	39	1	0.18	0	2	2	1	.	.	.	.	.	.	.	.	.	.	4	4	3	2	1	14	0
454	RC	2	4	52	5	0	0.00	0	6	6	1	.	.	.	.	.	.	.	.	.	.	6	6	5	1	0	18	1
455	GK	2	4	77	17	1	0.48	5	5	10	1	.	.	.	.	.	.	.	.	.	.	3	5	4	1	0	9	1
456	EA	2	4	69	10	0	0.30	0	3	3	1	.	.	.	.	.	.	.	.	.	.	4	4	3	2	0	13	1
457	HE	1	4	57	19	1	0.18	0	5	5	0	30	0	4	13	11	14	12	13	14	77	.	.	.	.	.	.	0
458	JG	1	4	54	30	1	-0.08	1	2	3	0	16	0	1	14	12	13	13	13	16	81	.	.	.	.	.	.	1
459	MS	1	4	48	1	0	0.00	0	2	2	0	34	0	4	19	25	25	25	25	25	144	.	.	.	.	.	.	1
460	JW	1	4	56	29	1	-0.08	0	0	0	1	8	0	0	14	11	10	11	11	11	68	.	.	.	.	.	.	0
461	BH	1	4	41	25	1	-0.08	0	1	1	1	2	0	0	12	13	13	13	12	13	76	.	.	.	.	.	.	1
462	HS	1	4	39	33	1	0.18	1	7	8	0	16	0	1	14	11	12	10	16	25	88	.	.	.	.	.	.	0
463	KA	1	4	64	34	0	0.00	0	2	2	1	24	0	2	19	18	19	17	19	25	117	.	.	.	.	.	.	1
464	MJ	1	4	70	23	0	0.18	7	7	14	0	86	6	7	17	15	17	18	20	25	112	.	.	.	.	.	.	0
465	FB	1	4	37	16	0	0.18	1	7	8	0	48	0	4	11	11	12	14	16	18	93	.	.	.	.	.	.	0
466	SA	1	4	27	15	1	0.00	0	6	6	0	32	0	4	16	12	13	14	15	19	89	.	.	.	.	.	.	0
467	MA	1	4	60	20	0	0.48	7	3	10	0	88	5	4	14	14	16	16	18	25	103	.	.	.	.	.	.	0
468	BW	2	4	52	34	1	0.00	0	0	0	1	.	.	.	.	.	.	.	.	.	.	5	5	4	3	1	18	0
469	MS	2	4	69	4	1	0.30	0	6	6	0	.	.	.	.	.	.	.	.	.	.	4	6	3	2	0	15	0
470	MD	2	4	41	31	1	0.00	0	5	5	0	.	.	.	.	.	.	.	.	.	.	4	4	4	2	0	14	1
471	AL	2	4	72	11	1	0.00	0	5	5	1	.	.	.	.	.	.	.	.	.	.	5	5	4	2	2	18	0
472	TD	2	4	43	36	1	0.48	3	7	10	0	.	.	.	.	.	.	.	.	.	.	4	4	3	1	1	13	1
473	BK	2	4	33	7	0	-0.08	0	2	2	1	.	.	.	.	.	.	.	.	.	.	4	5	5	5	5	24	1
474	WR	2	4	75	2	0	0.18	0	4	4	0	.	.	.	.	.	.	.	.	.	.	3	4	1	1	0	9	0
475	DP	2	4	45	4	0	-0.08	0	6	6	0	.	.	.	.	.	.	.	.	.	.	5	6	5	5	3	24	0
476	HW	2	4	59	13	0	0.18	0	5	5	1	.	.	.	.	.	.	.	.	.	.	4	5	4	2	2	17	0

Appendix 4A Results master table: Chapter 4

Key

VEN=Venue; 1-Moorfields Eye Hospital, 2-University College Hospital
GP=Group; 1-Grade I, 2-Grade II, 3-Grade III
SEX; 1-Male, 2-Female
YRSDM=Duration of diabetes in years
RX=Therapy for diabetes; 1-Insulin, 0-Others
VA=Visual acuity in LogMAR units
RGE1=Number of red-green plate errors on the Comp PIC
BYE1=Number of tritan plate errors on the Comp PIC
TPE1=Total plate errors on the Comp PIC
RGE2=Number of red-green errors on the SPP2
BYE2=Number of tritan errors on the SPP2
TPE2=Total errors on the SPP2
LTA=LTA score
D15SS=D15(5/4) score
D15SR=Number of red-green axes on the D15(5/4)
D15ST=Number of tritan axes on the D15(5/4)
D15DS=D15(5/2) score
D15DR=Number of red-green axes on the D15(5/2)
D15DT=Number of tritan axes on the D15(5/2)
SQTES=Square-root of the total error score (FM 100-H)
SQBY=Square-root of the blue-yellow score (FM 100-H)
SQRG=Square-root of the red-green score (FM 100-H)
DIFF=SQBY-SQRG
AXIS=Presence of axis on FM 100-H; 1-none, 2-redgreen, 3-tritan
PL2=Score for plate 2 on the Arden gratings
PL3=Score for plate 3 on the Arden gratings
PL4=Score for plate 4 on the Arden gratings
PL5=Score for plate 5 on the Arden gratings
PL6=Score for plate 6 on the Arden gratings
PL7=Score for plate 7 on the Arden gratings
AGT=Arden gratings total score
SPA=Score for spatial frequency A on the VCTS 6000
SPB=Score for spatial frequency B on the VCTS 6000
SPC=Score for spatial frequency C on the VCTS 6000
SPD=Score for spatial frequency D on the VCTS 6000
SPE=Score for spatial frequency E on the VCTS 6000
GS=VCTS 6000 global score
MZ=Score for macular zone on the VFA I
Z1=Score for zone 1 on the VFA I
Z2=Score for zone 2 on the VFA I
Z3=Score for zone 3 on the VFA I
Z4=Score for zone 4 on the VFA I
Z5=Score for zone 5 on the VFA I
TF=Total field score on the VFA I
AMS=Amsler grid result; 1-pass, 0-fail

OBS	NAME	VEN	GP	AGE	SEX	YRSDM	RX	VA	RGE1	RYE1	TPE1	RGE2	RYE2	TPE2	LTA	D15SS	D15SR	D15ST	D15DS	D15DR	D15DT	SQTES
1	ME	1	3	62	1	14	1	0.00	2	6	8	2	5	7	5	6	0	0	6	0	0	14.42
2	KH	2	3	59	1	1	0	0.18	0	2	2	1	2	3	5	16	0	1	18	0	3	15.49
3	AH	1	3	27	2	10	1	0.30	0	2	2	1	5	6	5	4	0	0	8	0	0	14.14
4	GC	1	3	65	1	8	0	0.30	0	4	4	1	5	6	4	22	1	1	28	0	1	20.59
5	AP	1	3	56	2	16	0	0.30	2	5	7	5	11	16	3	2	0	0	20	0	2	17.32
6	AH	1	3	20	2	18	1	0.00	0	1	1	2	3	5	5	0	0	0	2	0	0	8.94
7	JD	1	3	54	2	14	0	0.30	0	6	6	3	10	13	3	16	0	1	14	0	0	20.30
8	JN	1	3	48	1	32	1	0.30	5	5	10	5	8	13	2	80	8	0	36	2	0	29.60
9	PD	1	3	61	1	4	0	0.18	0	3	3	4	7	11	5	2	0	0	2	0	0	12.00
10	AG	1	1	54	1	4	1	-0.08	0	0	0	0	1	1	5	0	0	0	0	0	0	6.93
11	DW	1	1	53	1	2	0	-0.08	0	0	0	0	1	1	5	0	0	0	2	0	0	9.30
12	EK	2	1	70	2	6	0	0.18	0	0	0	1	6	7	5	4	0	0	16	0	0	15.62
13	AE	2	1	67	1	9	0	-0.08	0	0	0	0	1	1	5	0	0	0	4	0	0	6.00
14	TH	2	1	28	1	6	1	-0.08	0	0	0	0	1	1	5	0	0	0	4	0	0	8.00
15	IH	2	1	25	1	10	1	0.00	0	0	0	0	1	1	5	0	0	0	2	0	0	10.58
16	CV	2	1	63	1	2	1	0.00	0	0	0	0	1	1	5	0	0	0	4	0	0	11.31
17	AT	2	1	47	1	1	1	-0.08	0	0	0	0	1	1	5	0	0	0	4	0	0	8.94
18	GF	2	1	50	1	12	1	-0.08	0	0	0	0	1	1	5	10	0	0	8	0	1	10.20
19	AH	1	1	25	1	9	1	-0.08	0	0	0	0	1	1	5	0	0	0	0	0	0	6.32
20	MF	2	1	39	1	1	1	-0.08	0	0	0	0	1	1	5	0	0	0	4	0	0	8.25
21	RA	1	1	42	1	24	1	0.00	0	1	1	0	1	1	5	0	0	0	0	0	0	8.49
22	LB	1	1	68	1	8	0	0.00	0	0	0	0	1	1	5	0	0	0	14	0	0	12.00
23	JC	1	1	48	1	13	1	-0.08	0	2	2	0	2	2	5	0	0	0	4	0	0	8.94
24	HG	1	1	28	2	17	1	0.00	3	0	3	4	1	5	5	0	0	0	0	0	0	13.42
25	IM	1	1	59	1	11	1	0.18	0	2	2	0	1	1	5	0	0	0	10	0	0	15.49
26	IM	1	1	31	2	31	1	0.00	0	0	0	0	1	1	5	0	0	0	2	0	0	12.00

OBS	SQBY	SQRG	DIFF	AXIS	PL2	PL3	PL4	PL5	PL6	PL7	AGT	SPA	SPB	SPC	SPD	SPE	GS	MZ	Z1	Z2	Z3	Z4	Z5	TF	AMS
1	10.91	8.94	1.97	1	15	12	16	15	14	14	86	5	5	4	4	4	22	120	85.0	88	85	78	82.5	83.6	1
2	11.83	9.70	2.13	1	17	13	16	13	16	12	87	4	5	4	3	1	17	110	87.5	93	88	81	87.5	87.4	1
3	9.22	10.68	-1.46	1	10	10	10	11	14	16	71	5	7	5	3	3	23	140	102.5	102	102	99	102.5	101.4	0
4	16.03	12.49	3.54	1	20	16	19	20	20	25	120	4	4	3	2	0	13	120	90.0	88	90	78	77.5	84.3	1
5	12.49	11.75	0.74	1	11	12	12	18	25	25	103	3	4	2	1	0	10	100	60.0	68	67	67	76.5	68.3	0
6	5.74	6.86	-1.12	1	11	11	12	11	11	12	68	5	6	4	3	2	20	150	117.5	116	114	117	125.0	117.6	1
7	15.68	12.65	3.03	1	15	13	12	13	15	12	80	4	4	3	2	0	13	100	75.0	82	85	84	92.5	84.5	0
8	22.11	19.47	2.64	1	11	13	14	13	15	25	91	4	4	1	0	0	9	110	72.5	79	75	68	67.5	72.6	0
9	10.20	6.00	4.20	3	10	14	15	13	16	15	83	5	5	4	3	4	21	120	105.0	97	84	90	72.5	88.3	1
10	5.39	4.24	1.15	1	9	12	13	10	9	7	60	5	6	6	6	5	28	150	125.0	121	117	116	120.0	119.0	1
11	6.71	7.14	-0.43	1	13	11	14	13	14	14	79	6	5	5	3	4	23	130	100.0	100	98	99	111.3	101.4	0
12	11.87	9.64	2.23	1	15	13	13	17	20	17	95	4	4	3	2	0	13	90	95.0	89	84	79	80.0	84.3	1
13	4.90	3.16	1.74	1	14	15	14	12	9	13	77	5	6	4	5	3	23	130	112.5	109	106	95	105.0	104.5	1
14	6.63	4.36	2.27	1	13	11	11	11	12	10	68	5	6	6	6	5	28	140	115.0	126	118	120	125.0	121.4	1
15	7.81	7.14	0.67	1	14	13	14	13	13	10	77	5	6	5	5	4	25	140	122.5	126	118	119	122.5	121.4	1
16	9.80	5.57	4.23	3	15	12	13	12	13	16	81	5	5	3	3	2	18	130	92.5	110	107	108	112.5	107.6	1
17	6.40	6.24	0.16	1	13	14	12	13	12	12	76	5	6	6	5	4	26	120	110.0	110	110	101	111.3	108.1	1
18	8.60	5.39	3.21	1	13	14	13	11	14	14	79	5	6	5	4	3	23	130	112.5	119	110	107	116.3	112.9	1
19	4.47	4.47	0.00	1	12	12	15	12	12	14	77	4	4	3	4	2	17	140	120.0	118	104	100	113.8	109.8	1
20	7.28	3.87	3.41	3	16	14	15	16	13	10	84	5	6	5	4	3	23	110	110.0	91	78	79	77.5	84.3	1
21	6.24	5.74	0.50	1	13	7	8	6	11	12	57	6	6	5	3	1	21	140	120.0	111	106	105	110.0	109.3	1
22	9.06	7.75	1.31	1	14	11	11	10	12	15	73	5	6	5	6	5	27	120	110.0	110	102	99	105.0	104.5	1
23	6.63	5.74	0.89	1	14	10	9	10	14	12	69	4	5	4	3	2	19	120	95.0	93	90	86	90.0	90.2	1
24	9.95	8.88	1.07	1	12	9	11	11	10	12	65	5	6	4	4	4	23	140	112.5	119	116	114	118.8	116.4	1
25	12.08	9.54	2.54	1	13	9	13	14	16	16	81	4	4	3	2	2	15	120	100.0	104	99	94	100.0	99.3	1
26	9.17	7.62	1.55	1	11	10	11	12	12	10	66	5	5	5	5	4	24	130	112.5	110	104	106	111.3	109.0	1

OBS	NAME	VEN	GP	AGE	SEX	YRSDM	RX	VA	RGE1	BYE1	TPE1	RGE2	BYE2	TPE2	LTA	D15SS	D15SR	D15ST	D15DS	D15DR	D15DT	SQIES
27	RM	1	1	53	1	17	1	0.00	0	0	0	0	1	1	5	0	0	0	0	0	0	3.46
28	DD	2	1	20	1	14	1	-0.08	0	0	0	0	1	1	5	0	0	0	2	0	0	10.20
29	MA	2	1	62	2	30	1	0.00	0	0	0	0	2	2	5	2	0	0	22	1	1	13.11
30	SB	2	1	33	2	24	1	-0.08	0	0	0	0	0	0	5	0	0	0	2	0	0	10.58
31	VD	2	1	69	2	8	1	0.00	0	3	3	1	4	5	4	16	0	1	34	0	4	12.33
32	RL	2	1	65	1	30	0	0.18	0	0	0	0	1	1	5	10	0	0	18	0	0	14.00
33	CP	2	1	67	1	5	0	0.00	1	7	8	5	11	16	0	22	0	1	20	0	1	21.73
34	LB	2	1	50	2	42	1	0.00	0	2	2	1	2	3	5	2	0	0	6	0	0	10.95
35	JH	2	1	50	1	7	0	0.00	0	0	0	0	1	1	5	0	0	0	8	0	0	12.33
36	AW	2	1	48	1	26	1	-0.08	0	0	0	0	1	1	5	0	0	0	2	0	0	7.48
37	MW	2	1	49	1	21	1	-0.08	0	0	0	0	1	1	5	0	0	0	4	0	0	9.80
38	HR	2	1	68	1	2	1	0.00	0	4	4	1	3	4	4	2	0	0	8	0	0	10.77
39	ED	1	2	66	1	13	0	-0.08	0	0	0	0	1	1	5	0	0	0	0	0	0	7.75
40	GN	1	2	67	1	30	0	0.00	1	4	5	1	3	4	5	4	0	0	4	0	0	14.00
41	BL	1	2	58	1	21	1	-0.08	0	4	4	1	4	5	5	14	0	0	14	0	1	15.10
42	CP	1	2	51	2	20	1	-0.08	0	0	0	1	2	3	5	0	0	0	2	0	0	13.71
43	JB	2	2	41	2	9	1	0.18	1	5	6	1	3	4	5	0	0	0	4	0	0	9.17
44	AE	2	2	62	1	20	1	-0.08	0	2	2	0	1	1	5	2	0	0	2	0	0	6.00
45	AK	2	2	31	1	31	1	-0.08	0	0	0	0	1	1	5	0	0	0	2	0	0	8.94
46	VS	2	2	24	2	12	1	0.00	0	1	1	0	2	2	5	2	0	0	6	0	0	11.83
47	JB	2	2	32	2	14	1	0.18	0	0	0	0	1	1	5	0	0	0	2	0	0	11.14
48	AM	2	2	22	1	16	1	0.00	0	1	1	0	1	1	5	0	0	0	10	0	0	11.31
49	AK	2	2	74	2	26	1	0.18	0	6	6	2	9	11	1	20	0	1	16	0	2	16.49
50	RK	2	2	47	2	13	0	0.18	0	0	0	0	1	1	5	0	0	0	6	0	0	10.00
51	RW	2	2	53	1	20	1	0.18	0	5	5	0	2	2	4	18	0	1	38	0	4	21.45
52	SA	1	2	40	1	7	0	0.18	0	2	2	3	3	6	4	0	0	0	12	0	1	14.97

OBS	SQBY	SQRG	DIFF	AXIS	PL2	PL3	PL4	PL5	PL6	PL7	AGI	SPA	SPB	SPC	SPD	SPE	GS	MZ	Z1	Z2	Z3	Z4	Z5	IF	AMS
27	2.00	2.83	-0.83	1	11	11	12	11	14	13	72	6	6	4	3	1	20	120	85.0	86	84	88	87.50	86.20	1
28	7.00	7.42	-0.42	1	14	11	13	9	9	10	66	6	7	7	6	5	31	130	110.0	117	102	83	110.00	103.30	0
29	8.83	9.43	-0.60	1	16	11	10	10	13	16	76	5	5	4	2	0	16	110	100.0	100	97	94	93.80	96.70	1
30	7.55	7.42	0.13	1	14	14	15	14	13	12	82	5	6	6	6	6	29	140	110.0	119	108	105	116.30	111.70	1
31	10.34	6.24	4.10	1	12	11	12	12	13	11	71	5	6	5	3	2	21	110	102.5	106	98	97	100.00	100.40	1
32	11.00	8.60	2.40	1	8	12	13	12	14	10	69	5	6	4	2	0	17	100	100.0	103	96	90	90.00	95.50	1
33	16.00	14.07	1.93	1	18	15	16	15	17	20	101	5	6	6	3	2	1	17	90	70.0	82	83	80	86.30	81.40	0
34	7.28	8.12	-0.84	1	11	12	14	17	15	25	94	5	6	5	4	1	21	120	100.0	105	103	91	95.00	98.80	1
35	9.06	8.25	0.81	1	15	13	13	12	13	14	80	5	5	4	4	3	22	110	110.0	108	106	98	101.30	104.00	1
36	5.66	4.80	0.86	1	14	12	14	12	14	12	78	6	6	7	6	6	31	130	110.0	112	111	108	113.80	111.00	1
37	7.62	5.92	1.70	1	11	11	10	12	14	12	70	5	5	4	4	3	21	140	115.0	118	109	102	107.50	109.80	1
38	7.55	7.62	-0.07	1	10	11	13	14	15	16	81	6	5	5	3	0	19	100	77.5	83	77	71	76.30	76.90	1
39	6.00	4.80	1.20	1	13	11	13	12	12	13	74	5	6	5	4	3	23	140	102.5	108	103	105	107.50	105.50	1
40	10.80	8.66	2.14	1	12	12	15	16	13	13	81	5	6	4	3	3	21	110	92.5	96	89	85	93.80	91.00	1
41	12.37	8.25	4.12	3	12	9	13	15	17	16	82	4	5	5	3	0	17	120	95.0	99	87	58	72.50	81.90	1
42	9.33	10.00	-0.67	1	12	8	9	11	12	12	64	4	5	4	4	3	20	130	112.5	121	115	109	112.50	114.30	1
43	6.78	5.92	0.86	1	16	16	17	15	16	14	94	4	4	4	3	4	19	140	100.0	103	110	109	110.00	107.10	1
44	5.29	2.83	2.46	1	11	7	9	11	16	19	73	5	6	5	5	5	26	130	100.0	108	96	94	96.20	98.80	1
45	5.92	6.56	-0.64	1	9	8	10	6	8	9	50	6	6	7	6	6	31	120	105.0	105	109	106	110.00	107.10	1
46	8.43	8.12	0.31	1	14	14	14	12	12	12	78	4	6	4	4	4	22	130	105.0	104	97	88	98.80	97.60	1
47	7.68	8.00	-0.32	1	7	9	11	9	25	25	86	5	5	4	1	1	16	130	97.5	103	90	88	88.80	95.10	1
48	8.06	7.94	0.12	1	12	12	14	13	15	16	82	5	5	5	6	6	27	130	120.0	115	106	100	108.80	108.60	1
49	13.23	9.70	3.53	1	12	12	20	19	17	25	105	5	4	3	2	0	14	90	65.0	74	68	64	81.30	66.90	0
50	9.11	7.28	1.83	1	15	14	15	13	12	14	83	5	6	5	3	1	20	130	102.5	117	109	110	110.00	110.70	1
51	16.82	12.77	4.05	1	16	12	16	13	15	14	86	4	4	4	2	1	15	80	80.0	91	91	83	82.50	86.40	1
52	10.77	10.05	0.72	1	13	11	13	14	14	14	79	5	6	5	5	4	25	120	82.5	90	92	90	100.00	91.70	1

OBS	NAME	VEN	GP	AGE	SEX	YRSDM	RX	VA	RGE1	BYE1	TPE1	RGE2	BYE2	TPE2	LTA	D15SS	D15SR	D15ST	D15DS	D15DR	D15DT	SQIES
53	JM	1	2	40	2	26	1	0.00	0	0	0	0	1	1	5	0	0	0	0	0	0	7.48
54	RK	1	2	62	1	1	0	0.00	0	2	2	1	2	3	5	0	0	0	2	0	0	11.49
55	KM	1	2	59	2	5	0	0.18	0	1	1	1	2	3	4	12	0	1	16	0	1	20.59
56	AH	1	2	27	2	10	1	0.18	3	5	8	1	4	5	5	0	0	0	8	0	0	13.86
57	GC	1	2	64	1	8	0	0.30	0	5	5	1	9	10	4	31	2	1	28	0	3	21.63
58	LD	1	2	54	1	8	1	0.18	0	6	6	1	4	5	5	18	0	1	23	0	1	14.00
59	BH	1	2	40	2	25	1	-0.08	2	5	7	5	7	12	5	6	0	0	12	0	0	16.12
60	SC	1	2	59	2	4	0	0.18	1	5	6	1	5	6	5	2	0	0	10	0	1	15.23
61	GM	1	2	54	1	28	1	0.18	0	2	2	2	4	6	5	6	0	0	8	0	0	12.49
62	RD	1	2	47	1	10	1	0.30	0	2	2	1	3	4	5	0	0	0	2	0	0	9.80
63	DS	1	3	60	1	37	1	0.18	1	6	7	4	11	15	0	8	0	0	22	0	1	17.55
64	JG	1	3	75	1	25	0	0.00	0	6	6	4	7	11	5	6	0	0	12	0	0	14.00
65	JB	1	3	33	2	14	1	0.18	0	1	1	1	1	2	5	0	0	0	4	0	0	10.00
66	SF	1	3	33	1	12	1	-0.08	0	0	0	0	1	1	5	2	0	0	14	0	1	10.95
67	JM	1	3	60	1	10	0	0.18	0	6	6	1	6	7	3	24	0	2	28	0	2	16.49
68	CE	1	3	69	1	3	0	0.18	5	7	12	4	11	15	0	26	1	1	40	0	4	21.82
69	SL	1	3	37	1	11	1	-0.08	0	4	4	3	4	7	5	6	0	0	14	0	0	14.83
70	EG	1	3	72	1	4	1	0.00	7	7	14	5	11	16	0	28	0	2	38	0	4	25.61
71	EM	1	3	59	1	1	0	-0.08	0	5	5	4	6	10	5	4	0	0	8	0	0	10.39
72	HT	1	3	45	2	33	1	0.00	0	0	0	0	1	1	5	0	0	0	0	0	0	6.00
73	GD	1	3	58	1	16	0	0.18	1	6	7	5	10	15	1	32	0	3	42	0	5	13.27
74	AC	1	3	53	1	10	0	0.30	0	5	5	4	8	12	4	6	0	0	4	0	0	14.70
75	SD	1	3	35	2	23	1	0.30	2	7	9	1	6	7	0	20	0	2	34	0	3	23.24
76	AS	1	3	64	1	11	0	-0.08	0	5	5	4	6	10	5	8	0	1	16	1	0	14.00
77	JM	1	3	61	2	2	1	0.18	0	3	3	3	5	8	5	2	0	0	10	0	0	14.83
78	CB	1	3	21	2	21	1	0.18	0	0	0	0	1	1	5	0	0	0	0	0	0	6.00

OBS	SQBY	SQRG	DIFF	AXIS	PL2	PL3	PL4	PL5	PL6	PL7	AGT	SPA	SPB	SPC	SPD	SPE	GS	MZ	Z1	Z2	Z3	Z4	Z5	TF	AMS
53	5.74	4.69	1.05	1	10	10	10	10	11	10	61	6	6	6	5	4	27	120	107.5	105	107	95	96.30	101.70	0
54	8.54	7.42	1.12	1	15	12	14	11	14	14	80	4	4	3	3	3	17	100	87.5	79	78	71	77.50	77.40	0
55	15.13	13.11	2.02	1	15	14	16	15	16	15	91	4	4	3	2	0	13	110	82.5	86	75	64	56.30	72.10	1
56	9.59	9.90	-0.31	1	13	9	10	12	13	15	72	5	5	5	4	2	21	120	67.5	84	83	77	86.25	80.95	0
57	16.43	13.93	2.50	1	12	13	16	16	15	25	97	4	4	3	2	1	14	110	95.0	97	95	93	100.00	96.00	0
58	11.09	8.19	2.90	1	12	10	10	13	15	25	85	5	6	4	2	1	18	110	80.0	91	64	77	43.80	71.20	1
59	10.05	12.49	-2.44	2	14	11	13	10	13	9	70	5	4	4	3	3	19	130	92.5	104	110	102	112.50	105.50	1
60	11.40	10.10	1.30	1	15	12	14	15	18	25	99	5	5	5	2	0	15	120	85.0	86	79	79	76.30	80.70	0
61	9.80	7.62	2.18	1	11	11	12	10	12	9	65	6	5	4	4	0	19	120	102.5	107	97	90	63.80	91.90	1
62	7.42	6.24	1.18	1	15	17	16	15	20	25	108	5	5	3	1	0	14	120	115.0	97	83	69	85.00	86.40	1
63	13.71	10.25	3.46	1	9	9	13	16	18	25	90	4	4	3	2	0	13	110	70.0	79	72	73	78.80	75.00	1
64	10.05	9.70	0.35	1	14	14	12	10	10	11	71	4	5	3	2	0	14	100	72.5	86	76	65	47.50	70.00	1
65	6.71	7.42	-0.71	1	13	10	12	11	15	17	78	4	4	3	2	1	14	110	77.5	79	80	79	91.30	81.40	1
66	9.00	7.07	0.93	1	14	13	14	14	14	15	84	5	6	4	3	3	21	140	90.0	98	94	92	96.30	94.50	1
67	12.73	10.15	2.58	1	15	12	11	9	13	15	75	5	5	4	3	1	18	110	87.5	90	78	78	76.30	81.40	1
68	16.09	14.35	1.74	1	10	11	15	25	25	25	111	3	3	2	0	0	8	90	60.0	69	61	64	75.00	66.20	0
69	10.63	10.30	0.33	1	12	12	12	12	12	12	72	4	5	4	5	4	22	120	80.0	90	85	89	98.80	89.30	0
70	18.97	16.97	2.00	1	14	11	15	13	14	15	82	4	5	3	3	0	15	100	90.0	96	87	92	95.00	92.10	1
71	8.19	6.32	1.87	1	14	14	15	16	16	17	92	5	5	3	3	3	19	110	100.0	99	100	99	101.30	99.80	1
72	4.90	3.46	1.44	1	12	10	13	13	14	13	75	6	6	5	5	5	27	140	120.0	119	107	107	107.50	111.20	1
73	10.91	7.35	3.56	1	12	11	13	15	14	20	85	4	5	3	0	0	12	60	65.0	75	72	74	80.00	74.00	1
74	11.18	9.22	1.96	1	11	12	13	14	15	11	76	4	4	2	0	0	10	120	90.0	76	59	64	65.00	68.30	0
75	17.69	14.70	2.99	3	16	15	17	19	16	25	108	3	4	3	2	0	12	100	70.0	72	66	52	50.00	61.40	0
76	11.18	8.25	2.93	1	9	13	10	10	11	10	63	5	5	4	3	3	20	130	105.0	106	100	105	113.80	105.70	1
77	10.72	10.10	0.62	1	15	11	13	15	15	16	85	4	5	3	2	2	16	120	110.0	101	98	91	87.50	96.20	1
78	3.46	4.90	-1.44	1	13	12	14	11	16	12	78	5	7	7	7	5	31	150	130.0	115	107	96	112.50	109.50	0

OBS	NAME	VEN	GP	AGE	SEX	YRSDM	RX	VA	RGE1	BYE1	TPE1	RGE2	BYE2	TPE2	LTA	D15SS	D15SR	D15ST	D15DS	D15DR	D15DT	SQIES
79	AH	1	3	20	2	18	1	0.00	0	0	0	1	2	3	5	0	0	0	2	0	0	10.39
80	KH	1	3	64	2	25	1	0.18	0	4	4	1	4	5	5	10	0	0	10	0	0	19.90
81	AK	1	3	20	1	16	1	0.18	2	4	6	1	3	4	5	2	0	0	6	0	0	16.49
82	DB	1	3	46	1	27	1	0.00	0	3	3	0	1	1	5	2	0	0	8	0	0	13.11
83	GR	1	3	35	2	23	1	0.00	0	4	4	2	5	7	5	0	0	0	2	0	0	11.66
84	JS	1	3	28	2	18	1	0.30	2	4	6	3	6	9	5	4	0	0	8	0	0	15.75
85	JK	1	3	19	1	11	1	-0.08	0	3	3	0	3	3	5	0	0	0	8	0	0	11.31
86	CF	1	3	49	1	10	0	-0.08	0	0	0	0	2	2	5	0	0	0	4	0	0	12.49
87	GS	1	3	63	1	10	1	0.18	0	2	2	1	6	7	5	16	0	1	12	0	1	14.14

OBS	SQBY	SQRG	DIFF	AXIS	PL2	PL3	PL4	PL5	PL6	PL7	AGT	SPA	SPB	SPC	SPD	SPE	GS	MZ	Z1	Z2	Z3	Z4	Z5	TF	AMS
79	7.87	6.78	1.09	1	10	11	13	10	13	12	69	6	6	4	3	3	22	140	130.0	121	113	110	126.3	118.3	1
80	14.53	13.23	1.30	1	16	13	14	16	16	17	92	5	5	4	3	2	19	120	106.0	100	91	84	78.9	91.7	1
81	13.56	9.17	4.39	3	17	11	9	12	13	15	77	7	7	6	5	3	28	120	100.0	109	104	105	103.8	105.0	1
82	8.83	9.43	-0.60	1	10	11	12	11	13	12	69	5	6	5	4	4	24	130	107.5	107	99	96	103.8	101.9	1
83	9.22	7.14	2.08	1	11	11	14	13	15	14	78	5	5	4	4	4	22	140	70.0	110	118	113	107.5	108.3	0
84	10.95	11.05	-0.10	1	13	10	13	15	15	17	83	4	6	4	3	3	20	120	72.5	108	105	95	95.0	98.3	0
85	8.37	7.28	1.09	1	10	12	14	12	15	19	82	5	6	4	4	6	25	130	75.0	99	107	105	116.3	103.3	1
86	8.72	8.83	-0.11	1	15	11	12	11	17	19	85	5	5	7	6	5	28	150	120.0	119	113	109	108.8	113.3	1
87	11.62	7.87	3.75	1	14	14	15	16	16	18	93	5	5	3	2	0	15	120	80.0	87	86	82	82.5	84.0	1

Appendix 5A Results master table: Chapter 5

Key

GP=Group; 1-Argon-treated, 2-577-treated, 3-595-treated
YRSDM=Duration of diabetes in years
RX=Therapy for diabetes; 1-Insulin, 0-Others
VA=Visual acuity in LogMAR units
VA0-VA3=Visual acuity at visits 0 to 3
RGE1=Number of red-green plate errors on the Comp PIC
RGE10-RGE13=Results for visits 0 to 3
BYE1=Number of tritan plate errors on the Comp PIC
BYE10-BYE13=Results for visits 0 to 3
TPE1=Total plate errors on the Comp PIC
TPE10-TPE13=Results for visits 0 to 3
RGE2=Number of red-green errors on the SPP2
RGE20-RGE23=Results for visits 0 to 3
BYE2=Number of tritan errors on the SPP2
BYE20-BYE23=Results for visits 0 to 3
TPE2=Total errors on the SPP2
TPE20-TPE23=Results for visits 0 to 3
LTA=LTA score
LTA0-LTA3=LTA scores at visits 0 to 3
D15SS=D15(5/4) score
D15SS0-D15SS3=D15(5/4) scores at visits 0 to 3
D15SR=Number of red-green axes on the D15(5/4)
D15SR0-D15SR3=Results for visits 0 to 3
D15ST=Number of tritan axes on the D15(5/4)
D15ST0-D15ST3=Results for visits 0 to 3
D15DS=D15(5/2) score
D15S0-D15S3=D15(5/2) scores at visits 0 to 3
D15DR=Number of red-green axes on the D15(5/2)
D15DR0-D15DR3=Results for visits 0 to 3
D15DT=Number of tritan axes on the D15(5/2)
D15DT0-D15DT3=Results for visits 0 to 3
SQTES=Square-root of the total error score (FM 100-H)
SQTES0-SQTES3=Results for visits 0 to 3
SQRG=Square-root of the red-green score (FM 100-H)
SQRG0-SQRG3=Results for visits 0 to 3
SQBY=Square-root of the blue-yellow score (FM 100-H)
SQBY0-SQBY3=Results for visits 0 to 3
DIFF=SQBY-SQRG
DIFF0-DIFF3=Results for visits 0 to 3
AX=Presence of axis on FM 100-H; 1-none, 2-redgreen, 3-tritan
AX0-AX3=Results for visits 0 to 3
AGT=Arden gratings total score
AGT0-AGT3=Results for visits 0 to 3
LSF=Low spatial frequency plates score on the Arden gratings
LSF0-LSF3=Results for visits 0 to 3
MSF=Mid spatial frequency plates score on the Arden gratings
MSF0-MSF3=Results for visits 0 to 3
HSF=High spatial frequency plates score on the Arden gratings
HSF0-HSF3=Results for visits 0 to 3
GS=VCTS 6000 global score
GS0-GS3=Results for visits 0 to 3
SPAB=Score for spatial frequencies A & B on the VCTS 6000
SPAB0-SPAB3=Results for visits 0 to 3
SPC=Score for spatial frequency C on the VCTS 6000
SPC0-SPC3=Results for visits 0 to 3

Appendix 5A/Contd

SPDE=Score for spatial frequency D & E on the VCTS 6000
SPDE0-SPDE3=Results for visits 0 to 3
TF=Total field score on the VFA I
TF0-TF3=Results for visits 0 to 3
MZ=Score for macular zone on the VFA I
MZ0-MZ3=Results for visits 0 to 3
Z1=Score for zone 1 on the VFA I
Z10-Z13=Results for visits 0 to 3
Z2=Score for zone 2 on the VFA I
Z20-Z23=Results for visits 0 to 3
Z3=Score for zone 3 on the VFA I
Z30-Z33=Results for visits 0 to 3
Z4=Score for zone 4 on the VFA I
Z40-Z43=Results for visits 0 to 3
Z5=Score for zone 5 on the VFA I
Z50-Z53=Results for visits 0 to 3
AMS=Amsler grid result; 1-pass, 0-fail
AMS0-AMS3=Results for visits 0 to 3

note: Visit 0=Pre treatment; visit 1=One week post treatment; visit 2=One month post treatment; visit 3=Three months post treatment

OBS	NAME	GP	AGE	YRSDM	RX	VA0	VA1	VA2	VA3	TPE10	TPE11	TPE12	TPE13	TRGEE10	TRGEE11	TRGEE12	TRGEE13	BYYE10	BYYE11	BYYE12	BYYE13	TPE20	TPE21	TPE22	TPE23	TRGEE20	TRGEE21	TRGEE22	TRGEE23	BYYE20	BYYE21	BYYE22	BYYE23	LTAA0	LTAA1	LTAA2	LTAA3	D15SRK0	D15SRK1	D15SRK2	D15SRK3
1	JBR	1	33	14	1	0.18	0.18	0.18	0.18	1	2	2	1	0	0	0	0	1	2	2	1	2	3	3	5	1	1	1	2	1	2	2	3	5	5	5	5	0	2	2	0	0	0	0	0
2	SFL	1	33	12	1	-0.08	-0.08	-0.08	0.18	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	0	0	0	0	1	1	1	1	5	5	5	5	2	0	0	0	0	0	0	0
3	JML	1	60	10	0	0.18	0.00	0.18	0.30	7	7	6	6	0	0	0	0	7	7	6	6	7	5	7	5	1	2	1	1	6	3	6	4	3	5	2	3	24	18	14	24	0	0	0	0	2
4	CER	1	69	3	0	0.18	0.18	0.30	0.30	13	14	9	11	5	6	1	3	8	8	8	8	16	16	16	16	5	5	5	5	11	11	11	11	0	0	2	2	26	18	12	12	1	1	0	1	1
5	EGR	1	72	4	1	0.00	0.18	0.18	0.00	15	11	11	15	7	3	3	7	8	8	8	8	16	16	16	15	5	5	5	5	11	11	11	10	0	0	0	4	28	28	20	24	0	0	0	0	2
6	EMR	1	59	1	0	-0.08	-0.08	-0.08	-0.08	6	6	3	3	0	1	0	0	6	5	3	3	10	10	9	10	4	2	3	3	6	8	6	7	5	5	5	5	4	4	4	2	0	0	0	0	0
7	HTL	1	45	33	1	-0.08	-0.08	-0.08	-0.08	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	0	0	0	0	1	1	1	1	5	5	5	5	0	0	0	0	0	0	0	0	0
8	GDR	1	58	16	0	0.18	0.18	0.18	0.18	8	7	7	6	1	0	0	0	7	7	7	6	15	15	16	14	5	4	5	3	10	11	11	11	1	3	2	4	32	36	44	24	0	0	0	0	3
9	ACR	1	53	10	0	0.18	0.18	0.30	0.18	5	6	6	5	0	0	0	0	5	6	6	5	12	13	14	15	4	4	4	5	8	9	10	10	4	4	4	4	6	6	6	2	0	0	0	0	0
10	SDR	1	35	23	1	0.30	0.30	0.30	0.30	10	9	9	8	2	2	1	1	8	7	8	7	7	12	12	14	1	4	4	5	6	8	8	9	0	0	0	0	20	24	26	28	0	0	0	0	2
11	ASL	1	64	11	0	-0.08	-0.08	-0.08	-0.08	6	7	5	5	0	0	0	0	6	7	5	5	14	11	11	10	4	3	3	4	6	8	8	6	5	4	4	5	8	20	16	2	0	0	0	0	1
12	JML	1	61	2	1	0.18	0.18	0.18	0.18	4	5	4	5	0	0	0	1	4	5	4	4	8	5	9	10	3	2	3	3	5	3	6	7	5	5	5	3	2	2	4	12	0	0	0	0	0
13	CBL	1	21	16	1	0.00	-0.08	-0.08	0.00	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	0	0	0	0	1	1	1	1	5	5	5	5	0	0	0	0	0	0	0	0	0
14	DBL	1	46	27	1	0.00	0.00	0.00	0.00	4	3	3	3	0	0	0	0	4	3	3	3	2	2	3	2	0	0	1	0	2	2	2	2	5	5	5	5	2	0	0	0	0	0	0	0	0
15	JKR	1	19	11	1	-0.08	0.00	-0.08	0.18	3	2	3	1	0	0	0	0	3	2	3	1	3	2	3	3	0	0	1	1	3	2	2	2	5	4	5	5	0	0	0	0	0	0	0	0	0
16	DSR	2	60	37	1	0.18	0.18	0.18	0.18	8	8	8	7	1	1	1	0	7	7	7	7	15	14	12	12	4	5	5	3	11	9	7	9	0	0	0	0	8	12	8	4	0	0	0	0	0
17	JGR	2	75	25	0	0.00	0.00	0.00	0.00	6	5	6	7	0	0	0	0	6	5	6	7	11	13	12	9	4	5	4	2	7	8	8	7	5	5	5	5	6	2	10	0	0	0	0	0	0
18	JBL	2	33	14	1	0.18	0.30	0.48	0.48	1	3	3	3	0	0	0	0	1	3	3	3	2	8	13	13	1	3	5	5	1	5	8	8	5	5	5	5	0	2	2	2	0	0	0	0	0
19	CFR	2	49	10	0	-0.08	-0.08	-0.08	-0.08	0	0	0	0	0	0	0	0	0	0	0	0	2	1	2	1	0	0	1	0	2	1	1	1	5	5	5	5	0	6	6	0	0	0	0	0	0
20	EML	2	59	1	0	0.18	0.18	0.18	0.00	9	5	6	6	2	1	0	0	7	4	6	6	12	11	13	12	5	4	4	3	7	7	9	9	4	5	4	5	2	2	2	4	0	0	0	0	0

OBS	D15TRT1	D15TRT2	D15TRT3	D15TRT0	D15TRT1	D15TRT2	D15TRT3	D15TRK0	D15TRK1	D15TRK2	D15TRK3	D15TRT0	D15TRT1	D15TRT2	D15TRT3	SQUARE0	SQUARE1	SQUARE2	SQUARE3	SQUARK0	SQUARK1	SQUARK2	SQUARK3	SQUARB0	SQUARB1	SQUARB2	SQUARB3	SQUARY0	SQUARY1	SQUARY2	SQUARY3	D15IF0	D15IF1	D15IF2	D15IF3
1	0	0	0	4	4	4	0	0	0	0	0	0	0	0	0	10.00	12.00	14.00	11.49	7.42	8.98	10.54	7.81	6.71	7.91	9.11	8.31	-0.71	-1.07	-1.43	0.50
2	0	0	0	0	2	2	2	0	0	0	0	0	0	0	0	9.17	11.14	8.72	7.21	5.48	7.81	5.39	4.47	7.35	7.94	6.86	5.48	1.87	0.13	1.47	1.91
3	1	1	3	28	26	38	22	0	0	0	0	2	1	3	3	16.49	18.44	16.37	16.12	10.15	9.06	10.00	10.39	12.73	15.68	12.69	12.00	2.58	6.62	2.69	1.61
4	0	0	0	40	34	34	34	0	0	0	0	4	3	4	4	21.82	23.32	21.07	21.07	14.35	16.16	13.96	13.96	16.09	16.79	15.39	15.39	1.74	0.63	1.43	1.43
5	2	1	1	38	32	46	32	0	0	1	0	4	2	2	2	25.61	26.61	25.22	23.24	16.97	17.00	16.64	14.56	18.97	20.25	18.79	17.94	2.00	3.25	2.15	3.38
6	0	0	0	8	6	6	8	0	0	0	0	0	0	0	0	10.39	13.27	14.14	14.42	6.32	7.94	8.78	9.06	8.19	10.58	10.82	11.18	1.87	2.64	2.04	2.12
7	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	8.49	9.38	9.17	7.75	5.66	5.74	5.83	5.29	6.25	7.42	7.07	5.57	0.59	1.68	1.24	0.28
8	3	5	3	42	42	26	26	0	0	0	0	5	6	2	2	13.27	18.11	18.87	18.65	7.35	10.82	12.04	11.49	10.91	14.14	14.25	14.39	3.56	3.32	2.21	2.90
9	0	0	0	4	12	12	4	0	0	0	0	0	1	1	0	14.70	17.10	19.49	12.17	9.22	10.78	12.33	7.62	11.18	12.99	14.80	9.27	1.96	2.21	2.47	1.65
10	2	2	1	34	30	30	26	0	0	0	0	3	3	3	4	23.24	21.87	21.87	20.49	14.70	13.89	13.89	13.08	17.69	16.74	16.74	15.78	2.99	2.80	2.85	2.70
11	1	1	0	16	10	2	8	1	0	0	0	0	1	0	0	14.00	15.10	14.83	14.00	8.25	9.95	8.19	9.11	11.18	10.91	12.17	10.49	2.93	0.96	3.98	1.38
12	0	0	0	10	20	10	14	0	0	0	0	0	1	0	0	14.83	13.71	14.28	18.00	10.10	8.25	8.83	12.12	10.72	10.77	10.86	13.19	0.62	2.52	2.03	1.07
13	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	5.66	4.00	6.00	5.29	4.47	4.00	5.20	3.32	3.46	0.00	3.00	4.00	-1.01	-4.00	-2.20	0.68
14	0	0	0	8	2	6	8	0	0	0	0	0	0	0	0	13.11	11.83	14.83	12.17	9.43	8.54	10.91	8.60	8.83	8.19	9.90	8.37	-0.80	-0.35	-1.01	0.23
15	0	0	0	8	2	4	2	0	0	0	0	0	0	0	0	11.31	8.72	14.14	14.28	7.28	4.47	9.70	7.48	8.37	7.28	10.00	12.00	3.09	2.81	0.30	4.52
16	1	0	0	22	23	28	20	0	0	0	0	1	1	2	2	17.55	14.28	17.32	14.77	10.25	9.96	9.38	9.75	13.71	10.20	14.35	11.14	3.46	0.30	4.77	1.57
17	0	0	0	12	20	20	20	0	1	0	0	0	1	1	0	14.00	19.49	15.62	13.86	9.70	9.33	7.94	7.21	10.05	16.64	12.81	11.53	0.35	7.31	4.87	4.32
18	0	0	0	2	4	4	4	0	0	0	0	0	0	0	0	12.96	13.86	15.75	15.75	9.59	10.82	12.04	12.04	8.72	9.39	10.05	10.05	-0.87	-1.99	-1.99	1.99
19	0	0	0	4	16	10	8	0	0	0	0	0	1	1	1	12.49	9.80	8.00	7.48	8.83	6.32	4.12	5.39	8.72	7.35	6.78	5.10	-0.11	1.03	2.66	0.29
20	0	0	0	14	12	14	20	0	0	0	1	0	0	0	2	18.00	16.25	16.00	19.18	11.96	10.20	11.36	12.37	13.23	12.37	11.69	14.35	1.27	2.17	-0.27	1.98

OBS	AX0	AX1	AX2	AX3	AGT0	AGT1	AGT2	AGT3	LSF0	LSF1	LSF2	LSF3	MSF0	MSF1	MSF2	MSF3	HSF0	HSF1	HSF2	HSF3	GS0	GS1	GS2	GS3	SPAB0	SPAB1	SPAB2	SPAB3	SSPC0	SSPC1	SSPC2	SSPC3	SPDE0	SPDE1	SPDE2	SPDE3	TF0	TF1	TF2	TF3	MZ
1	0	0	0	0	78	74	72	70	23	21	22	16	23	22	21	23	32	31	29	31	14	13	13	17	8	8	8	9	3	2	2	3	3	3	3	5	81.4	89.7	97.9	95.5	110
2	0	0	0	0	74	77	81	75	23	24	26	25	25	26	27	24	26	27	28	26	20	20	23	24	10	10	10	10	4	4	5	4	6	6	8	10	95.7	91.7	105.2	118.6	140
3	0	2	0	0	75	79	78	87	27	27	24	28	20	21	26	27	28	31	28	32	18	18	15	16	10	10	9	10	4	3	4	4	4	5	2	2	81.4	70.5	80.2	97.1	110
4	0	0	0	0	111	101	73	73	21	25	21	21	40	32	25	25	50	44	27	27	8	7	14	14	6	6	9	9	2	1	3	3	0	0	2	2	66.2	70.0	86.4	86.4	90
5	0	0	0	0	82	58	91	85	25	16	26	23	28	18	25	22	29	24	40	40	15	15	13	18	9	9	7	11	3	3	3	4	3	3	3	3	92.1	66.4	63.6	75.2	100
6	0	0	0	0	92	61	85	74	28	20	28	21	31	18	27	23	33	23	30	30	19	21	19	17	10	10	10	10	3	4	4	4	6	7	5	3	99.6	89.5	91.7	87.1	110
7	0	0	0	0	76	78	79	70	25	26	27	26	25	25	23	23	26	27	27	21	25	22	22	23	11	12	10	10	5	4	5	5	9	6	7	8	114.3	101.2	100.2	107.6	140
8	0	0	0	0	85	87	74	84	23	24	20	23	28	25	20	24	34	38	26	37	12	12	14	11	9	8	10	8	3	3	3	3	0	1	1	0	74.9	72.4	61.0	84.1	80
9	0	0	0	0	76	78	79	82	23	24	25	25	27	27	26	26	26	27	28	31	10	12	12	17	8	7	6	9	2	3	3	4	0	2	3	4	69.3	66.2	64.1	68.6	120
10	2	2	2	0	108	108	108	111	31	30	30	32	36	35	35	34	41	43	43	45	12	12	12	12	7	7	7	7	3	3	3	3	2	2	2	2	61.4	66.0	66.0	70.5	100
11	0	0	0	0	63	67	71	74	22	19	21	24	20	22	20	28	21	26	30	22	20	17	22	18	10	9	10	10	4	4	5	4	6	4	7	4	105.7	95.2	105.7	103.3	130
12	0	0	0	0	85	82	85	85	26	26	25	31	28	27	28	24	31	29	32	30	16	15	13	16	9	9	8	9	3	3	3	4	4	3	2	3	96.2	73.6	86.9	88.8	120
13	0	1	0	0	76	69	68	72	24	22	20	23	24	22	24	25	28	25	24	24	27	23	22	29	10	9	10	11	7	5	5	7	0	9	7	11	115.5	116.7	116.7	117.6	150
14	0	0	0	0	69	66	63	80	21	22	21	27	23	23	21	26	25	21	21	27	24	24	28	26	11	10	10	12	5	5	6	5	8	9	2	9	101.9	92.4	91.4	94.1	130
15	0	2	0	2	82	65	67	78	22	22	22	22	26	21	19	25	34	22	26	31	25	26	26	26	11	12	12	12	4	6	5	5	9	8	9	9	103.3	80.5	75.7	80.5	150
16	0	0	2	0	90	91	84	89	18	21	18	22	29	25	21	25	43	45	45	42	13	13	13	10	8	9	8	8	3	3	3	2	2	1	2	0	75.0	63.8	64.3	60.7	110
17	0	2	2	2	71	53	60	71	28	16	19	21	22	15	17	22	21	22	24	28	14	15	17	18	9	9	10	10	3	3	3	5	2	3	4	3	70.0	44.5	57.9	68.8	100
18	0	0	0	0	80	55	76	75	20	20	21	21	20	20	21	20	40	36	34	34	11	11	9	11	7	7	5	7	1	1	2	1	3	3	2	3	86.0	87.0	98.3	98.0	100
19	0	0	0	0	95	55	63	58	26	17	18	17	23	20	23	23	36	18	22	18	28	30	32	31	10	13	13	12	7	6	7	7	1	1	2	12	113.3	108.1	112.4	115.7	150
20	0	0	0	0	100	89	92	93	33	27	30	28	33	31	33	30	34	31	29	35	13	13	14	12	8	8	8	8	3	3	3	2	2	2	3	2	80.0	71.7	74.0	77.9	100

OBS	MZ1	MZ2	MZ3	Z10	Z11	Z12	Z13	Z20	Z21	Z22	Z23	Z30	Z31	Z32	Z33	Z40	Z41	Z42	Z43	Z50	Z51	Z52	Z53	AMSS01	AMSS12	AMSS23
1	120	120	120	77.5	88.8	100.0	102.5	79	88.5	98	98	80	88.0	96	99	79	89.0	99	93	91.3	94.4	97.5	87.5	1	1	1
2	120	130	150	97.5	82.5	107.5	120.0	101	100.0	111	125	93	95.0	106	115	92	87.0	97	114	96.3	87.5	106.3	120.0	1	1	1
3	120	110	130	87.5	77.5	80.0	110.0	90	89.0	92	107	78	76.0	81	103	78	53.0	76	96	76.3	58.8	70.0	82.5	1	1	1
4	100	110	110	60.0	75.0	62.5	62.5	69	87.0	98	98	61	75.0	90	90	64	65.0	78	78	75.0	46.3	90.0	90.0	0	0	0
5	100	90	90	90.0	80.0	65.0	80.0	96	88.0	76	85	87	71.0	69	72	92	54.0	53	72	95.0	42.5	53.8	68.8	1	1	1
6	110	130	110	100.0	90.0	90.0	80.0	99	97.0	89	87	100	95.0	96	90	99	84.0	87	85	101.3	80.0	96.3	90.0	1	1	1
7	150	130	140	115.0	120.0	115.0	115.0	117	115.0	118	118	114	108.0	108	108	113	96.0	97	103	112.5	72.5	65.0	96.3	1	1	1
8	70	70	100	65.0	45.0	57.5	95.0	75	73.0	57	94	72	75.0	63	95	74	78.0	62	77	80.0	75.0	63.8	61.3	1	1	1
9	110	110	120	90.0	87.5	85.0	82.5	76	81.5	87	83	59	58.0	58	69	64	57.5	51	52	65.0	56.9	48.8	63.8	0	0	1
10	70	70	70	70.0	62.5	62.5	55.0	72	75.0	75	78	66	70.5	71	75	52	62.0	62	72	50.0	55.7	55.7	61.3	0	0	0
11	130	130	140	105.0	100.0	112.5	115.0	106	103.0	113	114	100	95.0	103	103	105	82.0	100	93	113.8	100.0	103.8	97.5	1	1	1
12	120	130	120	110.0	100.0	105.0	100.0	101	93.0	109	103	98	87.0	96	94	91	47.0	65	76	87.5	52.5	66.3	75.0	1	1	1
13	150	150	150	130.0	130.0	132.5	140.0	118	124.0	119	126	112	114.0	116	112	111	108.0	113	111	115.0	115.0	111.3	111.3	1	1	0
14	120	130	130	107.5	100.0	100.0	100.0	107	107.0	102	104	99	99.0	95	98	96	93.0	86	84	103.8	61.3	76.3	86.3	1	1	1
15	120	120	120	75.0	60.0	65.0	55.0	99	89.0	86	87	107	97.0	83	91	105	84.0	78	87	116.3	55.0	86.3	63.8	1	0	1
16	80	90	90	70.0	77.5	60.0	67.5	79	76.0	70	66	72	68.0	68	62	73	54.0	55	56	78.8	48.8	66.3	55.0	1	1	1
17	90	70	80	72.5	65.0	67.5	70.0	86	82.0	77	81	76	58.0	70	76	65	17.0	50	60	47.5	5.0	23.8	55.0	1	1	1
18	100	100	90	72.5	85.0	97.5	97.5	85	90.0	95	95	84	93.0	102	102	86	92.0	98	98	96.3	97.5	98.3	98.8	1	0	0
19	160	150	160	120.0	130.0	120.0	130.0	119	121.0	125	126	113	111.0	111	118	109	107.0	108	105	108.8	78.8	100.0	106.3	1	1	1
20	90	100	90	92.5	85.0	87.5	100.0	97	88.0	94	96	76	72.0	77	74	70	66.0	64	62	70.0	51.3	51.3	68.8	0	0	0

OBS	NAME	LGE	AGE	YRS	DMX	VA0	VA1	VA2	VA3	TPE1	TPE1	TPE1	TPE1	TRG1	KGE1	KGE1	KGE1	KGE1	BYE1	BYE1	BYE1	BYE1	TPE2	TPE2	TPE2	TPE2	TRG2	KGE2	KGE2	KGE2	KGE2	BYE2	BYE2	BYE2	BYE2	LTA0	LTA1	LTA2	LTA3	D15KS0	D15KS1	D15KS2	D15KS3
21	HTK	2	45	33	1	-0.08	-0.08	-0.08	0.00	0	1	0	0	0	0	0	0	0	1	0	0	1	1	1	1	0	0	0	0	1	1	1	1	5	5	5	5	0	0	0	0	0	0	0	0
22	GDL	2	58	16	0	0.18	0.18	0.18	0.30	10	9	7	9	3	2	0	2	7	7	7	7	15	16	15	16	4	5	4	5	11	11	11	11	2	1	2	2	24	28	14	24	0	0	0	0
23	ACL	2	53	10	0	0.30	0.18	0.30	0.60	10	14	11	15	3	7	4	7	7	7	7	8	16	16	15	16	5	5	4	5	11	11	11	11	3	2	3	0	8	16	12	12	0	0	0	0
24	AHL	2	20	18	1	0.00	0.18	0.18	0.18	1	1	4	2	0	0	0	0	1	1	4	2	4	4	3	6	1	1	1	2	3	3	2	4	5	5	5	5	0	0	0	0	0	0	0	0
25	KHL	2	64	25	1	0.18	0.18	0.18	0.18	5	4	1	1	0	0	0	0	5	4	1	1	5	8	7	4	1	2	3	1	4	6	4	3	5	5	5	5	10	12	12	6	0	0	0	0
26	AKR	2	20	16	1	0.18	0.48	0.30	0.30	6	4	7	8	2	1	1	2	4	3	6	6	4	3	4	4	1	0	1	0	3	3	3	4	5	4	4	3	2	0	0	2	0	0	0	0
27	SFR	3	33	12	1	-0.08	0.18	0.18	0.18	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	0	0	0	0	1	1	1	1	5	5	5	5	2	0	0	0	0	0	0	0
28	CEL	3	69	3	0	0.30	0.48	0.48	0.30	12	8	9	11	4	1	1	3	2	8	9	1	16	15	16	16	5	4	5	5	11	11	11	11	0	0	0	2	32	16	18	26	0	0	0	0
29	DFL	3	72	9	1	0.30	0.18	0.30	0.30	8	13	8	7	3	7	2	2	8	3	8	7	15	16	13	11	5	5	5	5	10	11	8	6	5	5	4	5	2	6	6	16	0	0	0	0
30	SLR	3	37	11	1	-0.08	-0.08	0.00	-0.08	5	6	3	5	0	1	0	1	5	6	3	5	7	2	6	8	3	0	2	3	4	2	4	5	5	5	5	5	6	18	2	4	0	0	0	0
31	SDL	3	35	23	1	0.18	0.18	0.18	0.18	11	10	10	6	3	3	3	0	1	0	0	6	10	16	14	10	3	5	5	4	7	11	9	6	0	2	2	0	26	32	14	18	0	0	0	1
32	CBR	3	21	16	1	0.18	0.00	-0.08	0.00	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	0	0	0	0	1	1	1	1	5	5	5	5	0	0	0	0	0	0	0	0
33	AHR	3	20	18	1	0.00	0.18	0.18	0.18	0	1	1	1	0	0	0	0	0	1	1	3	4	2	3	1	1	0	1	2	3	2	2	5	5	5	5	5	0	0	0	0	0	0	0	0
34	HDL	3	61	4	0	0.18	0.00	0.18	0.18	4	5	5	4	0	0	0	0	4	5	5	4	11	10	9	7	4	4	4	3	7	6	5	4	5	5	5	5	2	2	2	4	0	0	0	0
35	GRR	3	35	23	1	-0.08	-0.08	-0.08	-0.08	5	4	4	5	0	0	0	0	5	4	4	5	7	4	3	3	2	1	1	1	5	3	2	2	5	5	5	5	0	0	0	0	0	0	0	0
36	JSL	3	28	18	1	0.30	0.30	0.30	0.30	6	5	5	5	1	1	1	1	6	5	5	5	9	10	11	11	4	4	4	4	5	6	7	7	5	5	5	5	4	6	6	6	0	0	0	0

OBS	D15TQ1	D15TQ2	D15TQ3	D15TQ4	D15QE1	D15QE2	D15QE3	D15QE4	D15RK1	D15RK2	D15RK3	D15RK4	D15BY1	D15BY2	D15BY3	D15BY4	SQTE1	SQTE2	SQTE3	SQTE4	SQRK1	SQRK2	SQRK3	SQRK4	SQBY1	SQBY2	SQBY3	SQBY4	SQLTA0	SQLTA1	SQLTA2	SQLTA3	D15LTA0	D15LTA1	D15LTA2	D15LTA3
21	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	6.00	8.72	6.93	6.93	3.46	5.57	4.36	5.00	4.90	6.32	5.39	4.80	1.44	0.75	1.03					
22	3	3	1	2	44	34	30	36	0	0	0	1	5	4	3	3	22.54	19.49	18.44	18.97	15.23	11.66	11.27	12.65	16.40	15.52	14.39	14.04	1.17	3.86	3.12					
23	0	0	0	0	14	20	36	34	0	0	1	1	0	1	3	2	18.65	19.49	19.39	20.78	12.65	12.33	13.86	14.70	13.45	14.80	13.49	14.56	0.80	2.47	-0.37					
24	0	0	0	0	2	0	2	0	0	0	0	0	0	0	0	0	8.94	11.31	10.39	8.49	6.86	6.86	7.21	6.08	5.74	8.94	7.48	5.92	-1.12	2.08	0.27					
25	0	2	1	0	10	34	40	20	0	0	1	1	0	3	1	0	19.90	20.10	21.07	16.12	13.23	13.64	15.72	11.18	14.53	14.59	13.96	11.58	1.30	0.95	-1.76					
26	0	0	0	0	6	10	0	6	0	0	0	0	0	0	0	0	16.49	17.44	14.56	17.20	9.17	9.54	8.60	9.75	13.56	14.35	11.62	13.93	4.39	4.81	3.02					
27	0	0	0	0	14	4	4	0	0	0	0	0	1	0	0	0	10.95	9.80	10.39	9.38	7.07	6.48	7.07	5.10	8.00	7.14	7.42	7.68	0.93	0.66	0.35					
28	2	2	2	2	32	34	40	54	1	1	1	2	2	3	6	4	19.70	20.40	21.17	21.35	12.57	13.93	14.90	14.49	15.00	14.70	14.70	15.59	2.43	0.77	-0.20					
29	0	0	0	1	2	13	10	8	0	0	0	0	0	1	0	0	15.75	18.00	17.66	15.36	9.06	12.00	12.12	9.90	12.77	13.27	12.69	11.23	3.71	1.27	0.57					
30	0	1	0	0	14	21	6	6	0	0	0	0	0	1	0	0	14.83	14.97	17.32	14.56	10.30	10.10	12.69	10.54	10.63	10.91	11.66	9.95	0.33	0.81	-1.05					
31	3	4	1	1	20	28	28	24	0	0	0	0	1	2	3	1	21.63	21.07	19.08	19.29	13.82	12.57	11.40	12.61	16.40	16.70	15.10	14.42	2.58	4.13	3.70					
32	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	6.00	5.29	4.47	6.32	4.90	4.00	2.65	4.36	3.46	3.46	3.61	4.58	-1.44	-0.54	0.96					
33	0	0	0	0	2	0	0	0	0	0	0	0	0	0	0	0	10.39	9.80	8.00	8.25	6.78	6.93	4.90	5.10	7.87	6.86	6.24	6.40	1.09	-0.07	1.34					
34	0	0	0	0	2	14	26	12	0	0	0	0	0	1	2	2	12.00	14.83	13.27	15.10	6.00	7.81	6.32	8.31	10.20	12.49	11.18	12.37	4.20	4.68	4.86					
35	0	0	0	0	2	2	0	2	0	0	0	0	0	0	0	0	11.66	8.25	7.75	6.32	7.14	5.48	4.00	5.00	9.22	6.16	6.63	3.87	2.08	0.68	2.83					
36	0	0	0	0	8	4	2	2	0	0	0	0	0	0	0	0	15.75	14.83	14.42	14.42	11.05	11.00	10.95	10.95	10.95	10.09	9.22	9.22	-0.10	-0.91	-1.75					

OBS	DIF3	AX0	AX1	AX2	AX3	AGT0	AGT1	AGT2	AGT3	LSF0	LSF1	LSF2	LSF3	MSF0	MSF1	MSF2	MSF3	HSF0	HSF1	HSF2	HSF3	GS0	GS1	GS2	GS3	SPAB0	SPAB1	SPAB2	SPAB3	SPCC0	SPCC1	SPCC2	SPCC3	SPDE0	SPDE1	SPDE2	SPDE3	TF0	IF1	IF2
21	0.20	0	0	0	0	75	76	76	69	22	24	25	24	27	24	24	23	27	28	27	23	27	21	21	18	12	10	10	9	5	4	4	4	0	7	7	5	111.2	92.4	95.7
22	1.39	0	0	0	0	103	81	82	79	31	22	23	22	32	29	26	26	41	30	33	31	9	9	12	11	5	8	9	8	3	1	3	3	1	0	0	0	72.1	57.1	61.2
23	0.14	0	0	0	0	99	99	116	113	25	30	35	31	35	30	31	32	50	39	50	50	7	12	9	13	6	7	7	8	1	3	2	3	0	2	0	2	81.7	71.0	84.3
24	0.16	0	0	0	0	68	86	72	73	22	29	24	24	22	28	24	25	23	29	24	24	20	14	19	18	11	9	11	11	4	3	5	3	5	2	3	4	117.6	109.5	114.6
25	0.40	0	0	1	0	92	91	66	71	29	29	20	24	32	27	20	25	33	35	26	22	19	18	18	17	10	11	9	8	4	3	3	3	5	4	3	6	92.0	90.2	76.0
26	4.18	2	2	2	2	77	89	83	88	28	25	24	24	25	29	26	25	28	35	33	39	28	14	28	16	14	9	10	9	6	3	4	3	8	2	2	4	105.0	102.4	98.8
27	2.58	0	0	0	0	84	82	75	75	27	27	24	25	28	27	24	23	29	28	27	27	21	19	16	22	11	10	9	10	4	4	3	4	6	5	4	7	94.5	95.2	101.2
28	1.10	0	0	0	0	80	86	80	90	20	23	27	23	19	22	29	27	41	41	32	40	12	8	13	13	8	6	8	8	3	2	3	3	1	0	2	2	80.0	47.1	75.0
29	1.33	0	0	0	0	91	105	95	101	26	23	26	26	23	32	31	31	42	50	38	44	12	10	12	10	8	8	8	8	3	2	3	3	1	0	1	0	98.1	81.7	91.2
30	0.59	0	0	0	0	72	69	75	72	24	23	25	22	24	20	26	24	24	26	24	26	22	23	24	25	9	9	10	10	4	5	5	4	9	9	9	10	89.3	85.5	99.3
31	1.81	0	2	2	0	86	90	85	84	24	28	26	26	28	29	27	27	34	33	32	31	16	17	19	17	10	10	10	9	3	4	5	3	3	3	4	4	97.1	86.0	92.6
32	0.22	0	0	0	0	78	68	75	71	25	19	22	23	25	24	28	25	28	25	25	23	31	23	25	26	12	9	11	11	7	5	5	6	2	9	9	9	109.5	101.4	110.0
33	1.30	0	0	0	0	69	78	71	66	21	24	25	18	23	24	23	24	25	30	23	24	22	15	19	21	12	10	10	10	4	4	4	4	4	1	5	7	118.3	110.7	109.5
34	4.06	2	2	2	0	83	80	78	80	24	22	22	22	28	26	25	23	31	32	31	35	21	18	23	22	10	8	10	10	4	3	4	4	7	7	9	8	88.3	83.6	81.2
35	1.13	0	0	0	0	78	72	74	71	22	22	24	20	27	23	24	25	29	27	26	26	22	19	28	28	10	11	13	11	4	5	6	6	8	3	9	11	108.3	107.1	107.7
36	1.73	0	0	0	0	83	87	91	91	23	24	24	24	28	30	31	31	32	33	36	36	29	20	20	20	10	9	9	9	4	4	4	4	6	7	7	7	98.3	96.0	94.5

OBS	TF	MZ0	MZ1	MZ2	MZ3	Z0	Z1	Z2	Z3	Z0	Z1	Z2	Z3	Z0	Z1	Z2	Z3	Z0	Z1	Z2	Z3	Z0	Z1	Z2	Z3	Z0	Z1	Z2	Z3	MM0	MM1	MM2	MM3
21	98.1	140	130	130	140	120.0	120.0	115.0	120.0	119	117	110	116	107	97	99	101	107	78	93	92	107.5	60.0	67.5	68.8	1	1	1	1
22	91.7	60	40	62	100	45.0	40.0	60.0	82.5	64	60	68	99	75	62	77	99	80	55	48	89	82.5	58.8	50.0	61.3	1	1	1	0
23	64.8	120	90	50	60	70.0	75.0	57.5	52.5	87	74	72	78	82	74	70	66	78	74	58	60	85.0	57.5	60.0	58.8	1	0	0	0
24	112.6	150	160	150	150	117.5	105.0	115.0	110.0	116	112	119	112	114	108	111	112	117	105	111	110	125.0	116.3	116.3	118.8	1	1	1	1
25	91.7	130	120	130	120	106.0	105.0	100.0	107.5	100	100	102	100	91	90	66	91	84	84	66	88	78.9	78.8	56.3	78.8	1	1	1	1
26	100.0	120	110	130	120	100.0	80.0	75.0	82.5	109	107	105	101	104	100	101	95	105	106	98	105	103.8	106.3	101.3	107.5	1	0	0	0
27	113.8	140	130	130	150	90.0	95.0	100.0	120.0	98	97	109	120	94	94	102	110	92	91	93	111	96.3	100.0	101.3	111.3	1	1	1	1
28	89.3	90	70	110	120	82.5	60.0	77.5	85.0	77	61	73	93	79	58	75	90	80	33	68	83	83.8	27.5	85.0	93.8	0	0	0	0
29	85.5	100	100	100	100	100.0	90.0	100.0	100.0	98	93	97	97	97	91	91	80	98	68	80	80	98.8	68.8	93.8	77.5	1	1	0	0
30	98.6	120	110	130	140	80.0	82.5	105.0	100.0	90	85	106	99	85	81	97	93	89	88	98	100	98.8	90.0	92.5	102.5	0	0	0	0
31	106.7	120	110	130	130	70.0	65.0	72.5	92.5	99	88	99	110	101	93	100	109	98	88	91	107	102.5	82.5	87.5	106.3	0	0	1	1
32	111.9	150	140	150	150	130.0	115.0	122.5	120.0	115	109	119	113	107	112	112	115	96	88	95	107	112.5	88.8	100.8	100.8	0	0	0	0
33	114.5	140	150	170	140	130.0	117.5	115.0	110.0	121	114	115	119	113	111	108	117	110	109	107	111	126.3	105.0	103.8	112.5	1	1	1	1
34	91.7	120	130	120	120	105.0	110.0	105.0	112.5	97	97	99	106	84	83	83	88	90	82	70	87	72.5	56.3	58.8	73.8	1	1	1	1
35	111.2	140	130	140	150	70.0	100.0	87.5	92.5	110	110	108	117	118	108	110	114	113	106	110	112	107.5	107.5	112.5	108.8	0	0	0	0
36	94.3	120	120	120	120	72.5	75.0	77.5	77.5	108	105	102	102	105	102	99	99	95	93	91	91	95.0	93.2	91.3	91.3	0	0	0	0

Appendix 6A Results master table: Chapter 6

Key

GP=Group; 1-Extensively lasered group, 2-Proliferative DR group
YRSDM=Duration of diabetes in years
RX=Therapy for diabetes; 1-Insulin, 0-Others
VA=Visual acuity in LogMAR units
RGE1=Number of red-green plate errors on the Comp PIC
BYE1=Number of tritan plate errors on the Comp PIC
TPE1=Total plate errors on the Comp PIC
RGE2=Number of red-green errors on the SPP2
BYE2=Number of tritan errors on the SPP2
TPE2=Total errors on the SPP2
LTA=LTA score
D15SS=D15(5/4) score
D15SR=Number of red-green axes on the D15(5/4)
D15ST=Number of tritan axes on the D15(5/4)
D15DS=D15(5/2) score
D15DR=Number of red-green axes on the D15(5/2)
D15DT=Number of tritan axes on the D15(5/2)
SQTES=Square-root of the total error score (FM 100-H)
DX=Diagnosis of the FM 100-H SQTES; 1-Normal, 0-Abnormal
SQBY=Square-root of the blue-yellow score (FM 100-H)
SQRG=Square-root of the red-green score (FM 100-H)
DIFF=SQBY-SQRG
AXIS=Presence of axis on FM 100-H; 1-none, 2-redgreen, 3-tritan
AGT=Arden gratings total score
ARDX=Arden gratings total score diagnosis; 1-Normal, 0-Abnormal
PL2=Score for plate 2 on the Arden gratings
PL3=Score for plate 3 on the Arden gratings
PL4=Score for plate 4 on the Arden gratings
PL5=Score for plate 5 on the Arden gratings
PL6=Score for plate 6 on the Arden gratings
PL7=Score for plate 7 on the Arden gratings
GS=VCTS 6000 global score
VSDX=Diagnosis of VCTS 6000 result; 1-Normal, 0-Abnormal
SPA=Score for spatial frequency A on the VCTS 6000
SPB=Score for spatial frequency B on the VCTS 6000
SPC=Score for spatial frequency C on the VCTS 6000
SPD=Score for spatial frequency D on the VCTS 6000
SPE=Score for spatial frequency E on the VCTS 6000
TF=Total field score on the VFA I
FDX=Diagnosis of VFA I result; 1-Normal, 0-Abnormal
MZ=Score for macular zone on the VFA I
Z1=Score for zone 1 on the VFA I
Z2=Score for zone 2 on the VFA I
Z3=Score for zone 3 on the VFA I
Z4=Score for zone 4 on the VFA I
Z5=Score for zone 5 on the VFA I
AMS=Amsler grid result; 1-pass, 0-fail

OBS	NAME	AGE	GP	YRSDM	RX	VA	TPE1	RGE1	BYE1	TPE2	RGE2	BYE2	LTA	D15SS	D15SR	D15ST	D15DS	D15DR	D15DT	SQTES	DX	SQRG	SQBY
1	ABR	52	1	47	1	0.18	2	0	2	3	1	2	0	0	0	0	2	0	0	8.25	1	4.58	6.78
2	TBR	24	1	13	1	0.00	0	0	0	1	0	1	0	0	0	0	2	0	0	4.00	0	0.00	3.87
3	LDR	45	1	40	1	0.18	2	0	2	5	3	2	0	2	0	0	8	0	0	13.56	1	9.22	9.80
4	PDR	51	1	46	1	0.18	1	0	1	1	0	1	0	0	0	0	2	0	0	7.75	1	4.80	6.00
5	JIL	33	1	29	1	0.18	11	4	7	13	5	8	1	2	0	0	16	0	1	16.12	0	11.05	11.66
6	SKR	25	1	15	1	0.18	3	0	3	2	1	1	4	2	0	0	2	0	0	14.97	0	9.06	11.70
7	LPL	27	1	24	1	0.00	4	0	4	10	4	6	2	2	0	0	6	0	0	14.14	0	8.77	10.95
8	JTR	49	1	26	1	0.30	6	0	6	10	1	9	2	14	0	0	36	0	4	19.90	0	12.57	15.10
9	LWR	42	1	28	1	0.18	4	1	3	8	2	6	1	14	0	0	8	0	0	17.44	0	10.58	13.56
10	CBL	42	1	9	0	0.18	1	0	1	4	1	3	0	4	0	0	2	0	0	12.33	0	7.68	9.43
11	HCR	41	1	30	1	-0.08	10	3	7	15	5	10	5	26	0	2	20	0	1	18.44	0	11.00	14.53
12	GDR	58	1	16	0	0.18	8	1	7	13	3	10	1	18	0	2	46	0	5	18.33	0	11.09	14.35
13	LDL	27	1	16	1	0.18	13	6	7	12	4	8	5	5	0	0	40	2	0	19.39	0	12.88	14.46
14	THR	35	1	24	1	-0.08	6	0	6	10	4	6	0	0	0	0	4	0	0	12.17	0	7.00	9.75
15	IHL	29	1	18	1	0.18	6	2	4	6	3	3	1	2	0	0	22	0	1	15.49	0	9.27	12.21
16	JLL	43	1	31	1	0.00	7	0	7	13	4	9	2	6	0	0	22	0	3	16.73	0	8.49	14.21
17	RLR	61	1	41	1	0.18	2	0	2	8	5	3	0	0	0	0	24	0	1	12.81	0	9.75	8.12
18	ENL	58	1	49	1	0.00	5	1	4	10	3	7	1	16	0	1	17	0	1	20.00	1	13.53	14.56
19	AOR	26	1	16	1	-0.08	6	0	6	6	1	5	4	4	0	0	32	0	2	14.00	0	8.54	10.68
20	MPR	31	1	18	1	0.30	11	6	5	16	5	11	3	10	0	2	12	0	0	17.89	0	11.58	13.49
21	JSL	22	1	13	1	0.00	4	0	4	4	1	3	1	2	0	0	16	0	1	14.28	0	8.31	11.55
22	PTL	44	1	25	1	0.18	5	0	5	7	1	6	2	0	0	0	2	0	0	10.20	0	5.48	8.54
23	EGL	65	1	32	1	0.18	3	0	3	3	1	2	0	0	0	0	4	0	0	9.59	0	5.48	7.87
24	SMR	29	1	29	1	0.18	13	6	7	15	5	10	2	2	0	0	26	0	1	17.89	0	10.10	14.28
25	DS	60	2	37	1	0.18	7	1	6	15	4	11	0	8	0	0	22	0	1	17.55	0	10.25	13.71
26	JG	75	2	25	0	0.00	6	0	6	11	4	7	5	6	0	0	12	0	0	14.00	1	9.70	10.05

OBS	DIFF	AXIS	AGT	ARDX	FL2	FL3	FL4	FL5	FL6	FL7	GS	VSDX	SPA	SPB	SPC	SPD	SPE	TF	FDX	MZ	Z1	Z2	Z3	Z4	Z5	AMS
1	2.20	0	65	0	5	8	10	12	13	17	21	1	6	5	5	3	2	74.0	0	120	80.0	84	79	76	50.0	0
2	3.87	2	64	1	12	9	10	10	11	12	31	1	6	6	7	8	4	100.7	1	140	110.0	105	100	97	96.3	1
3	0.58	0	70	1	10	11	12	12	13	12	16	0	4	5	4	2	1	64.8	0	100	72.5	85	74	48	45.0	1
4	1.20	0	79	1	14	12	14	13	12	14	17	0	5	5	4	2	1	75.7	0	120	85.0	88	87	72	46.3	1
5	0.61	0	121	0	16	17	18	20	25	25	8	0	2	3	2	1	0	56.4	0	90	65.0	63	55	56	46.3	0
6	2.64	2	87	0	14	14	15	13	15	16	18	0	5	5	4	3	1	69.3	0	100	77.5	84	84	60	40.0	0
7	2.18	0	65	1	7	9	9	11	14	15	20	0	5	5	4	3	3	61.2	0	130	90.0	100	61	49	13.8	0
8	2.53	0	91	0	14	14	14	14	17	18	12	0	4	4	3	1	0	53.6	0	110	72.5	86	56	39	18.8	0
9	2.98	0	72	1	10	9	11	14	13	15	18	0	4	4	4	2	4	47.6	0	110	90.0	88	63	13	0.0	1
10	1.75	0	84	0	14	11	15	15	15	14	20	0	4	5	4	4	3	70.0	0	110	100.0	98	62	65	36.3	0
11	3.53	2	67	1	10	7	10	12	14	14	15	0	4	4	3	2	2	64.0	0	120	92.5	94	60	58	25.0	1
12	3.26	0	75	1	13	8	10	14	15	15	17	0	5	6	4	2	0	75.0	0	100	85.0	84	82	63	65.0	1
13	1.58	0	99	0	16	13	13	14	18	25	18	0	4	5	4	4	1	89.3	0	110	92.5	98	95	76	86.3	1
14	2.75	0	72	1	10	12	12	13	12	13	22	0	4	5	4	4	5	105.2	1	140	120.0	121	107	95	88.8	0
15	2.94	2	72	0	7	12	10	7	19	17	17	0	5	5	5	2	0	65.2	0	120	77.5	67	62	75	48.8	0
16	5.72	2	98	0	16	14	16	16	18	18	20	0	4	5	5	3	3	48.6	0	110	45.0	97	44	37	10.0	0
17	-1.63	0	89	0	14	12	14	12	17	20	14	0	4	5	3	2	0	70.2	1	120	87.5	99	70	53	47.5	1
18	1.03	0	75	1	14	12	16	10	11	12	21	0	5	5	4	3	4	68.1	0	140	102.5	94	59	64	35.0	0
19	2.14	0	57	1	11	8	10	10	8	10	28	1	5	6	5	6	6	71.0	0	120	80.0	89	79	52	57.5	1
20	1.91	0	70	1	13	12	10	12	10	13	14	0	4	5	3	1	1	37.9	0	100	87.5	85	30	9	0.0	0
21	3.22	2	65	1	9	8	10	8	15	15	22	0	4	5	5	4	4	87.1	0	120	90.0	102	90	78	75.0	0
22	3.06	0	83	0	14	11	15	13	15	15	16	0	4	5	4	3	0	74.8	0	130	100.0	98	74	73	36.3	0
23	2.39	0	98	0	13	13	15	17	15	25	14	0	4	5	3	1	1	85.5	1	120	100.0	95	88	86	62.5	0
24	4.18	2	85	0	13	12	14	13	15	18	16	0	5	5	4	2	0	36.4	0	120	52.5	63	32	34	3.8	0
25	3.46	0	90	0	9	9	13	16	18	25	13	0	4	4	3	2	0	75.0	0	110	70.0	79	72	73	78.8	1
26	0.35	0	71	1	14	14	12	10	10	11	14	0	4	5	3	2	0	70.0	1	100	72.5	86	76	65	47.5	1

OBS	NAME	AGE	GP	YRSDM	RX	VA	TPE1	RGE1	BYE1	TPE2	RGE2	BYE2	LTA	D15SS	D15SR	D15ST	D15DS	D15DR	D15DT	SQTES	DX	SQRG	SQBY
27	JB	33	2	14	1	0.18	1	0	1	2	1	1	5	0	0	0	4	0	0	10.00	1	7.42	6.71
28	SF	33	2	12	1	-0.08	0	0	0	1	0	1	5	2	0	0	14	0	1	10.95	0	7.07	8.00
29	JM	60	2	10	0	0.18	6	0	6	7	1	6	3	24	0	2	28	0	2	16.49	0	10.15	12.73
30	CE	69	2	3	0	0.18	12	5	7	15	4	11	0	26	0	1	40	0	4	21.82	0	14.35	16.09
31	SL	37	2	11	1	-0.08	4	0	4	7	3	4	5	6	1	0	14	0	0	14.83	0	10.30	10.63
32	EG	72	2	4	1	0.00	14	7	7	16	5	11	0	28	0	2	38	0	4	25.61	0	16.97	18.97
33	EM	59	2	1	0	-0.08	5	0	5	10	4	6	5	4	0	0	8	0	0	10.39	1	6.32	8.19
34	HT	45	2	33	1	0.00	0	0	0	1	0	1	5	0	0	0	0	0	0	6.00	1	3.46	4.90
35	GD	58	2	16	0	0.18	7	1	6	15	5	10	1	32	0	3	42	0	5	13.27	1	7.35	10.91
36	AC	53	2	10	0	0.30	5	0	5	12	4	8	4	6	0	0	4	0	0	14.70	0	9.22	11.18
37	SD	35	2	23	1	0.30	9	2	7	7	1	6	0	20	0	2	34	0	3	23.24	0	14.70	17.69
38	AS	64	2	11	0	-0.08	5	0	5	10	4	6	5	8	0	1	16	1	0	14.00	1	8.25	11.18
39	JM	61	2	2	1	0.18	3	0	3	8	3	5	5	2	0	0	10	0	0	14.83	1	10.10	10.72
40	CB	21	2	21	1	0.10	0	0	0	1	0	1	5	0	0	0	0	0	0	6.00	1	4.90	3.46
41	AH	20	2	18	1	0.00	0	0	0	3	1	2	5	0	0	0	2	0	0	10.39	1	6.78	7.87
42	KH	64	2	25	1	0.18	4	0	4	5	1	4	5	10	0	0	10	0	0	19.90	0	13.23	14.56
43	AK	20	2	16	1	0.18	6	2	4	4	1	3	5	2	0	0	6	0	0	16.49	0	9.17	13.56
44	DB	46	2	27	1	0.00	3	0	3	1	0	1	5	2	0	0	8	0	0	13.11	0	9.43	8.83
45	GR	35	2	23	1	0.00	4	0	4	7	2	5	5	0	0	0	2	0	0	11.66	0	7.14	9.22
46	JS	28	2	18	1	0.30	6	2	4	9	3	6	5	4	0	0	8	0	0	15.75	0	11.05	10.95
47	JK	19	2	11	1	-0.08	3	0	3	3	0	3	5	0	0	0	8	0	0	11.31	1	7.28	8.37
48	CP	49	2	10	0	-0.08	0	0	0	2	0	2	5	0	0	0	4	0	0	12.49	1	8.83	8.72
49	GS	63	2	10	1	0.18	2	0	2	7	1	6	5	16	0	1	12	0	1	14.14	1	7.87	11.62

OBS	DIFF	AXIS	AGT	ARDX	PL2	PL3	PL4	PL5	PL6	PL7	GS	VSDX	SPA	SPB	SPC	SPD	SPE	TF	FDX	MZ	Z1	Z2	Z3	Z4	Z5	AMS
27	-0.71	0	78	0	13	10	12	11	15	17	14	0	4	4	3	2	1	81.4	0	110	77.5	79	80	79	91.3	1
28	0.93	0	84	0	14	13	14	14	14	15	21	0	5	6	4	3	3	94.5	0	140	90.0	98	94	92	96.3	1
29	2.58	0	75	1	15	12	11	9	13	15	18	0	5	5	4	3	1	81.4	1	110	87.5	90	78	78	76.3	1
30	1.74	0	111	0	10	11	15	25	25	25	8	0	3	3	2	0	0	66.2	0	90	60.0	69	61	64	75.0	0
31	0.33	0	72	1	12	12	12	12	12	12	22	0	4	5	4	5	4	89.3	0	120	80.0	90	85	89	98.8	0
32	2.00	0	82	1	14	11	15	13	14	15	15	0	4	5	3	3	0	92.1	1	100	90.0	96	87	92	95.0	1
33	1.87	0	92	0	14	14	15	16	16	17	19	0	5	5	3	3	3	99.8	1	110	100.0	99	100	99	101.3	1
34	1.44	0	75	1	12	10	13	13	14	13	27	1	6	6	5	5	5	111.2	1	140	120.0	119	107	107	107.5	1
35	3.56	0	85	0	12	11	13	15	14	20	12	0	4	5	3	0	0	74.0	0	60	65.0	75	72	74	80.0	1
36	1.96	0	76	1	11	12	13	14	15	11	10	0	4	4	2	0	0	68.3	0	120	90.0	76	59	64	65.0	0
37	2.99	2	108	0	16	15	17	19	16	25	12	0	3	4	3	2	0	61.4	0	100	70.0	72	66	52	50.0	0
38	2.93	0	63	1	9	13	10	10	11	10	20	0	5	5	4	3	3	105.7	1	130	105.0	106	100	105	113.3	1
39	0.62	0	85	0	15	11	13	15	15	16	16	0	4	5	3	2	2	96.2	1	120	110.0	101	98	91	87.5	1
40	-1.44	0	78	1	13	12	14	11	16	12	31	1	5	7	7	7	5	109.5	1	150	130.0	115	107	96	112.5	0
41	1.09	0	69	1	10	11	13	10	13	12	22	0	6	6	4	3	3	118.3	1	140	130.0	121	113	110	126.3	1
42	1.30	0	92	0	16	13	14	16	16	17	19	0	5	5	4	3	2	91.7	1	120	106.0	100	91	84	78.9	1
43	4.39	2	77	0	17	11	9	12	13	15	28	1	7	7	6	5	3	105.0	1	120	100.0	109	104	105	105.8	1
44	-0.60	0	69	1	10	11	12	11	13	12	24	1	5	6	5	4	4	101.9	1	130	107.5	107	99	96	103.8	1
45	2.08	0	78	1	11	11	14	13	15	14	22	0	5	5	4	4	4	108.3	1	140	70.0	110	118	113	107.5	0
46	-0.10	0	83	0	13	10	13	15	15	17	20	0	4	6	4	3	3	98.3	0	120	72.5	108	105	95	95.0	0
47	1.09	0	82	0	10	12	14	12	15	19	25	0	5	6	4	4	6	103.3	1	130	75.0	99	107	105	116.3	1
48	-0.11	0	85	0	15	11	12	11	17	19	28	1	5	5	7	6	5	113.3	1	150	120.0	119	113	109	108.8	1
49	3.75	0	93	0	14	14	15	16	16	18	15	0	5	5	3	2	0	84.0	1	120	80.0	87	86	82	82.5	1