Eye movements, search and perception of visual field defects in glaucoma

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Abbreviations

Acute Angle Closure Glaucoma (AAG)

Attention-Deficit Hyperactivity Disorder (ADHD)

Best Eye Mean Deviation (BEMD)

Bivariate Contour Ellipse (BCE)

Bivariate Contour Ellipse Area (BCEA)

Early Treatment Diabetic Retinopathy Study (ETDRS)

Heidelberg Retina Tomograph (HRT)

Humphrey Field Analyser (HFA)

Integrated Visual Field (IVF)

Intraocular pressure (IOP)

Mean Deviation (MD)

Normal tension glaucoma (NTG)

Ocular Hypertension (OHT)

Preferred Retinal Locus (PRL)

Primary Open angle glaucoma (POAG)

Quality of life (QoL)

Retinal Ganglion Cells (RGC)

Standard Automated Perimetry (SAP)

Visual Field (VF)

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I would finally like to thank my parents, family and Fiona for their dedication and support throughout my studies.

Declaration

The work contained in this thesis was completed by the candidate, Nicholas David Smith. It has not been submitted for any other degrees, either now or in the past. Where work contained within it has been previously published, this has been stated in the text. All sources of information have been acknowledged and references have been given. The University Librarian of City University London is permitted to allow the thesis to be copied in whole or in part without further reference to the author. This permission covers only single copies made for study purposes, subject to normal conditions of acknowledgement.

In chapters 3, 4, 5 and 7 all the work was collected by Nicholas D. Smith with aid from Fiona C. Glen and Robyn Burton under the supervision of David P. Crabb, David F. Garway-Heath and Gary S. Rubin. All data analysis, study design, application design and development were conducted by Nicholas D. Smith.

The data used in Chapter 6 were collected by Franziska G. Rauscher and Catharine M. Chisholm under the supervision of John L. Barbur and David F. Edgar. Data analysis was performed by Nicholas D. Smith under the supervision of David P. Crabb, David F. Garway-Heath and Gary S. Rubin.

Papers and presentations

The work in chapters 3 and 4 formed a published paper in *Ophthalmic and Physiological Optics* (Smith et al., 2011), although the data in this chapter has been expanded to a larger subset of participants (60 rather than 40). This increase was to allow further analysis in chapter 4, when investigating eye movements in these search tasks, and therefore to keep consistency between chapters for comparison. The work described in chapter 5 has been accepted for publication in *Seeing and Perceiving*.

Chapters 3, 4 and 5 results have been presented in part at the following conferences:

- Association for Research in Vision and Ophthalmology (ARVO) Meeting, Fort Lauderdale on April 27 -1 May 2008 (poster)
- British Congress of Optometry and Vision Science (BCOVS), Brighton, March 8-9 2009 (oral presentation)
- UK and Eire Glaucoma Society (UKEGS) Meeting, Dublin, 2009 (oral presentation)
- Royal College of Ophthalmologists (RCO) Annual meeting, Birmingham, May 21, 2009 (invited oral presentation)
- European Association for Eye and Vision Research (EVER), Portoroz, 30 September - 4 October 2010 (invited oral presentation)
- European Conference of Eye Movements (ECEM), Marseille, 21-25 August 2011 (invited oral presentation)

The research in Chapter 6 is based upon the paper in *PlosOne* (Crabb et al., 2010). This has been presented in various forms at the following conferences:

- Association for Research in Vision and Ophthalmology Meeting, Fort Lauderdale on April 27 -1 May 2007 (oral presentation)
- European Conference of Eye Movements, Potsdam, 20-23 August 2007 (oral presentation)

The work in chapter 7 formed an oral presentation at the Association for Research in Vision and Ophthalmology Meeting (ARVO), Fort Lauderdale on May 1- May 5, 2011.

Abstract

Glaucoma is a progressive disease of the optic nerve that can result in irreversible loss of visual function and impairment in everyday visual tasks. The experimental studies described in this thesis primarily aim to investigate the performance of people with glaucoma on search and other visual tasks whilst simultaneously monitoring eye movements, making comparison with age-related visually healthy people. In an experiment focussing on visual search, a patient group (n=30) took significantly longer on average to find a target in images of everyday scenes than controls (n=30). Furthermore, comparison of eye movements made by the participants during this task revealed there was a statistically significant reduction (6%) in saccade rate in the patients compared to the controls, and that saccade-rate correlated with performance. Similar differences in eye movements were observed when the same groups passively viewed a selection of images in a slide-show. A bivariate contour ellipse (BCE) analysis revealed that, on average, patients viewed smaller regions of the images compared to the controls. Eye movement differences between patients and controls were also examined in a different cohort of people with glaucoma (n=14) and visually healthy controls (n=22) whilst they watched a selection of *Hazard Perception Test* driving films. Saccade rate of the patients was found to increase by 9%, though results from the BCE analysis suggested the average size of viewing area was similar in both groups. Finally, a novel interview-based study of 50 people with glaucoma provides evidence that patients do not perceive their visual field defect as a black 'tunnel' effect, or as 'black patches', but more like blurred regions: this finding may, for example, impact on how glaucomatous visual field loss is depicted in patient information about the condition. In conclusion, the results from this thesis show how visual loss from glaucoma influences how patients perceive and react to their visual environment. The principal findings from the studies described in this thesis also show, for the first time, that eye movement analysis could provide a window into the functional deficits associated with glaucoma.

1 Introduction

1.1 Introduction to Glaucoma

Glaucoma is one of the most common causes of irreversible blindness in the world (Quigley and Broman, 2006, Resnikoff et al., 2004, Friedman et al., 2004). It is a collection of irreversible progressive diseases which are currently thought to cause atrophy of the optic nerve by affecting the Retinal Ganglion Cells (RGC) (Quigley, 1996, Quigley et al., 1982). The RGCs play a vital role in vision in that they are responsible for receiving visual information from photoreceptors and transmitting this information via their axons to the optic nerve, and subsequently the brain. Glaucomatous damage and destruction of the RGCs and subsequent damage to the optic nerve occurs gradually over a long period, meaning many individuals may be relatively unaware of their resulting visual loss until a more advanced stage. If left untreated, this progressive damage may ultimately lead to the loss of vision in that eye. It was estimated that in the year 2000 there were 67 million individuals living with glaucoma worldwide (Quigley, 1996) and by 2020 this is expected to have risen substantially (Quigley and Broman, 2006). The increasing life expectancy of the world's population means that this figure is likely to rise further still in the coming years.

Whilst "glaucoma" is a commonly used term there are actually several subtypes which have their own specific characteristics. The most common form is primary open angle glaucoma (POAG). Raised intraocular pressure (IOP; 21mmHg) is an important modifiable risk factor and is commonly used for the detection of POAG and monitoring its likely progression (Pohjanpelto and Palva, 1974, Leske, 1983). Normally, the pressure of the eye is maintained due to a balance between the inset of nutrient-containing aqueous fluid to the anterior chamber and the subsequent removal of this fluid via a series of drainage channels. In general, any blockage to these drainage channels will therefore lead to a build-up of fluid and a subsequent rise in IOP which has knock-on damage to the RGCs and the optic nerve. Although any vision loss that has already occurred as a result of POAG will be irreversible it is possible to slow further progression using therapeutics which attempt to reduce

IOP by either lowering the amount of aqueous fluid or increasing the size of the drainage channels. Laser treatments or trabectulectomy surgery can also be used in an attempt to improve drainage and reduce IOP. Whilst the blockages to the drainage channels leading to POAG occur relatively gradually, acute angle closure glaucoma (AAG) occurs when there is a sudden blockage leading to a sharp and rapid rise in pressure that can often be extremely painful. AAG is much less common than POAG and often requires urgent treatment. An increase in pressure leading to optic nerve damage can also result as a secondary effect of another incident such as another eye disease, an injury or as a result of previous surgery or medication. In this case, the disease is generally termed Secondary Glaucoma. It is worth noting that a raised IOP may also lead to the diagnosis of Ocular Hypertension (OHT), which is not synonymous with glaucoma. This is because in OHT, the raised pressure is not likely to have caused sufficient damage to the optic nerve or any subsequent loss in visual function. Whilst raised IOP is a common feature of the aforementioned neuropathies it is also possible to be diagnosed with glaucoma when the IOP is relatively normal (less than 21mmHg). Such individuals are said to have Normal tension glaucoma (NTG) and have damage to the optic nerve despite no abnormal pressure being recorded.

Whilst raised IOP is an important and common risk factor for glaucoma, there is currently no evidence that it is directly linked to glaucoma. Generally speaking, glaucoma is likely a complex process resulting from a number of interacting components. However, IOP is perhaps the only real measureable variable that may provide a strong indicator that glaucomatous damage has occurred, in addition to directly assessing the optic nerve, perhaps using techniques such as Optical Coherence Tomography (OCT), Heidelberg Retina Tomograph (HRT) and GDx. There are also other factors which are linked to an increased likelihood of having glaucoma, such as age and ethnicity (Tielsch et al., 1991, Klein et al., 1992, Coffey et al., 1993, Mitchell et al., 1996, Dielemans et al., 1994, Leske et al., 1994), family history (Libby et al., 2005), increased blood pressure (Tielsch et al., 1995) and diabetes (Leske, 1983). Hitchings (2000) has conducted a review of the risk factors of glaucoma but ultimately the exact causes of glaucoma are yet to be fully understood.

1.2 Contrast sensitivity

Contrast sensitivity is a vital part of visual performance. If a person cannot detect low contrast objects it may impair their ability to perform tasks such as driving, reading and navigation (Thayaparan et al., 2007) and even their postural stability, potentially leading to a fall (Turano et al., 1994). Reduced contrast sensitivity often is a factor of glaucoma and it is believed that much of the visual disability is caused by this reduction despite normal or near normal visual acuity (Ross et al., 1984).

The gold standard contrast sensitivity test, which is also used throughout this thesis, is the Pelli-Robson chart. It consists of a 16 triplets of letters, each at a lower contrast than the previous, with two triplets per line. The subject must detect 2 of the 3 letters correctly for that level of contrast to be classified as detectable and the final measurement is recorded in terms of log units (logCS). The letters are in the Sloan typeface (which contains 10 letters) and are all of the same size (Pelli et al., 1988). An example of the typeface used is: C D H K N O R S V Z.

Other contrast sensitivity tests that have been proven to be similar or more accurate are the Mars hand held test (Arditi, 2005) and the Vistech CS system (Ginsburg, 1984). The Mars hand held test consists of the same Sloan letters used by the Pelli-Robson chart but each successive letters contrast level is reduced by 0.04 log units. The obvious advantage of this chart is its portability, however this portability does mean the background luminance is likely to change depending on where the test is run which could affect the performance of a subject. This is unlikely to happen with a wall mounted chart such as the Pelli-Robson or Vistech CS system. The Vistech CS system uses gratings rather than letters, which removes the issue of letter detection and potential similarities of the letters (such as C and O or R, K and H). The test consists of 6 different rows of patches with different spatial frequencies (1, 2, 4, 8, 16 and 24 c/deg). There are 9 columns, the first is an example, and then the patches range in contrast from zero to above and below visual threshold by about 0.1 log units. The task is to detect the orientation of the grating in each of the patches, the orientations are: -15°, 0° or 15°. However for this research the Pelli-Robson chart was used as it is the gold standard tool for measuring CS. It is also the most clinically accepted and understandable method.

1.3 Visual fields

Glaucomatous structural damage will usually coincide with a visual field defect. The definition of the visual field (VF) is the area on which light can reach the retina of the eye. This light stimulates the rod and cone cells on the retina which is processed by the ganglion cells within the inner retina. These processed signals are transported along the ganglion cells axon to the brain (Tate and Lynn, 1977, Werner, 1991, Henson, 2000). The normal extent of a healthy subject's visual field from the line of sight is approximately 65° up, 75° down, 100° temporally and 60° nasally for a bright stimulus (Henson, 2000). To perform a VF test a person is asked to fixate on a predetermined point, and stimuli are presented at various locations around their field of view. The subject indicates when they notice the stimuli. VF's are usually conducted monocularly, with one eye occluded whilst the other is tested.

Assessment of visual function is integral to the diagnosis and management of glaucoma and involves measurement of the VF using a technique called perimetry. There are two methods of conducting perimetry: manual and automated, with automated being the most common. Manual perimetry requires highly skilled operators and is very time consuming, the two problems that automated perimetry solves. Computer algorithms perform the test, automatically modifying various properties of the stimuli, such as its luminance, to find the subjects minimum threshold. Katz, et al (1995) established that in glaucoma computerised automated perimetry enhanced assessment of VF's.

The most common type of computerised automated VF perimetry test in glaucoma management is a "white on white" test called standard automated perimetry (SAP). This involves the assessment of a subject's light-difference sensitivity at various locations of their field of view. Two commonly used automated perimeters, certainly in secondary and tertiary care, are the Humphrey Field Analyzer (HFA) (Carl Zeiss Meditec Inc., USA) and the Octopus perimeter (Haag-Streit AG, Koeniz, Switzerland) (Figure 1.1). In the research throughout this thesis the HFA was used to record visual fields and as such the main focus of discussion will be based upon this. The HFA is conducted monocularly in a white bowl perimeter with a luminance of 31.5 apostilbs (A) with the person at a distance of 33cm from the

bowl. The subject is instructed to keep their eye fixated upon a single central point and white circular stimuli (most commonly 0.43° in diameter – Goldman III size) are projected onto the bowl with varying luminance at specific locations which relate to specific regions of the retina. The luminance of the stimuli varies from 0.08 to 10,000A but the HFA represents the minimum luminance the subject can see at that location as a differential threshold in decibel (dB). The formula to calculate these values is:

$$dB = 10 \log_{10}\left(\frac{10000}{A}\right)$$

The dB values range from 0 to 40, with 40 being the least bright stimuli (0.08A) and 0 being the brightest stimuli (10,000A). The primary factors that affect the results from a HFA test are eccentricity and age. Typically the sensitivity in a healthy eye decreases as the eccentricity increases and is represented as the "hill of vision" (Traquair, 1931). Sensitivity also decreases slowly with age, with a reported decrease of 0.1dB/year (Heijl et al., 1991).

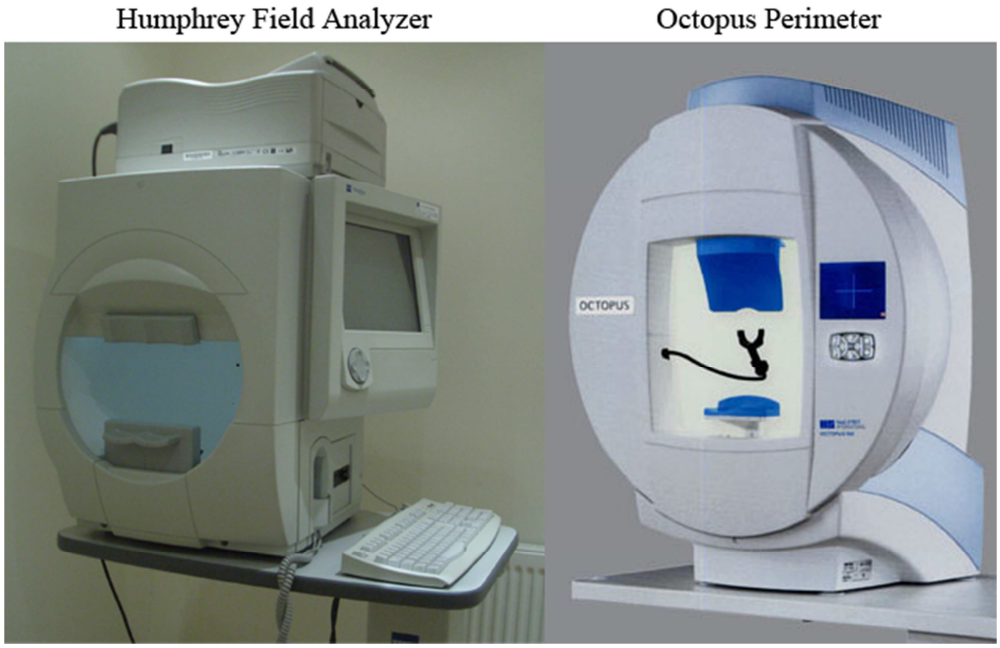


Figure 1.1: The Humphrey Field Analyzer and Octopus Perimeter

HFA SAP tests are carried out in predefined patterns. In this thesis the 30-2, 24-2 and 10-2 patterns are used and therefore only these will be explained in detail. The size of the visual field being tested is represented by the first number (24 in a 24-

2) and this relates to eccentricity in degrees from the centre of the test to the furthest region tested.

Figure 1.2 shows the test patterns for these three VF tests and how they overlap one another. The spacing of the points is 6° starting 3° from the centre in 30-2 and 24-2 VFs and 2° spacing starting 1° from the centre in 10-2 VFs.

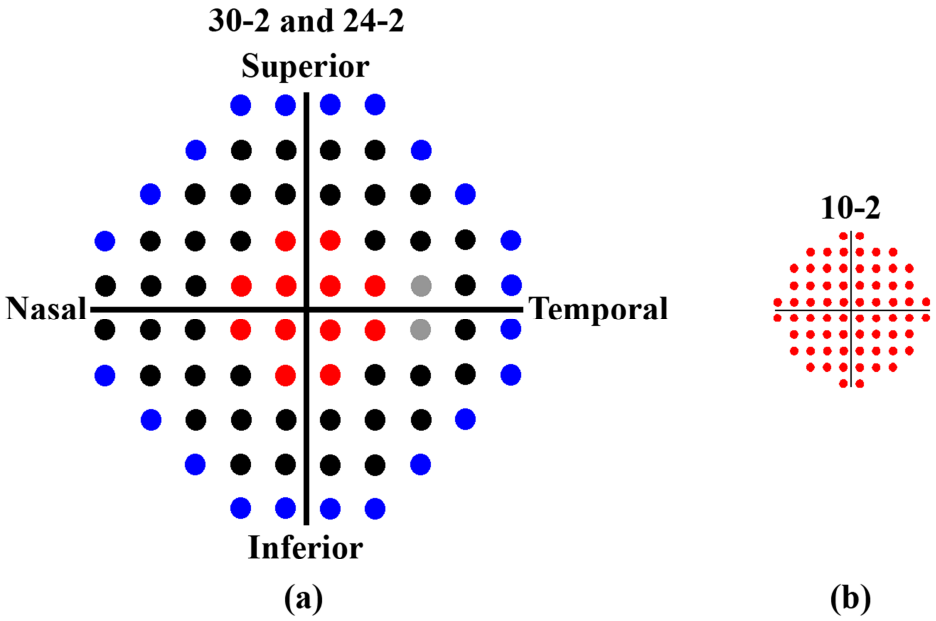


Figure 1.2: Test patterns for the HFA 30-2 (all points), 24-2 (black and red) and the region covered by the 10-2 VFs (represented in red, but it should be noted that these points are not the actual 10-2 test points but the region covered by the 10-2) (a). The grey points are the blind spot location. The points are spaced by 6° in the 24-2 and 30-2 VFs, starting 3° from the centre. The actual test points of the 10-2 are shown in (b). In the 10-2 VF test the points are spaced by 2° starting 1° from the centre.

A person's VF is classified as damaged if their light sensitivity at a specific location is reduced when compared to the average sensitivity at that same location for healthy age-matched controls. In a normally sighted participant the field of view becomes less sensitive the further the distance away from the fovea; this decrease in resolution is due to a reduction in the number of ganglion cells as eccentricity from the fovea increases (Garway–Heath et al., 2000).

Global measures, which try and express various properties of the subject's VF, consist of values such as mean deviation (MD), which informs the reader how much, on average, the points deviate from an age-matched healthy hill of vision.

This value can be slightly misleading if a subject has excessive light scatter, such as in the case of cataract, and to compensate for this the pattern standard deviation (PSD) is used. The PSD describes if the shape of the subject's hill of vision departs from an age-matched hill of vision based on healthy subjects. The glaucoma hemifield test (GHT) gives a measure of whether the VF has glaucomatous traits.

To confirm VF reliability, the fixation losses, false positive errors and false negative errors are examined. Fixation losses are tested by projecting a bright stimulus into the physiological blind spot region of the bowl, if the subject responds it is recorded as a fixation loss. This is shown as the number of fixation losses over the number of times the blind spot check was conducted. Fixation losses of more than 20% will be categorised as poor reliability. False positive errors are checked by adding a purposely long pause between stimuli being projected, if the subject responds to a stimulus during that period it is classified as a false positive. False negative errors are checked by projecting a stimulus at a previously determined location 9dB brighter than the current threshold level of that location. If the subject does not respond it is classified as a false negative. If false negative or false positive percentages go above 33% the VF is classified as being of a poor reliability. All VFs of poor reliability are excluded from this research and repeated (Johnson, 2003).

Examples of all the above measures are shown in Figure 1.3. The interested reader can find more information on perimetry in Henson (2000).

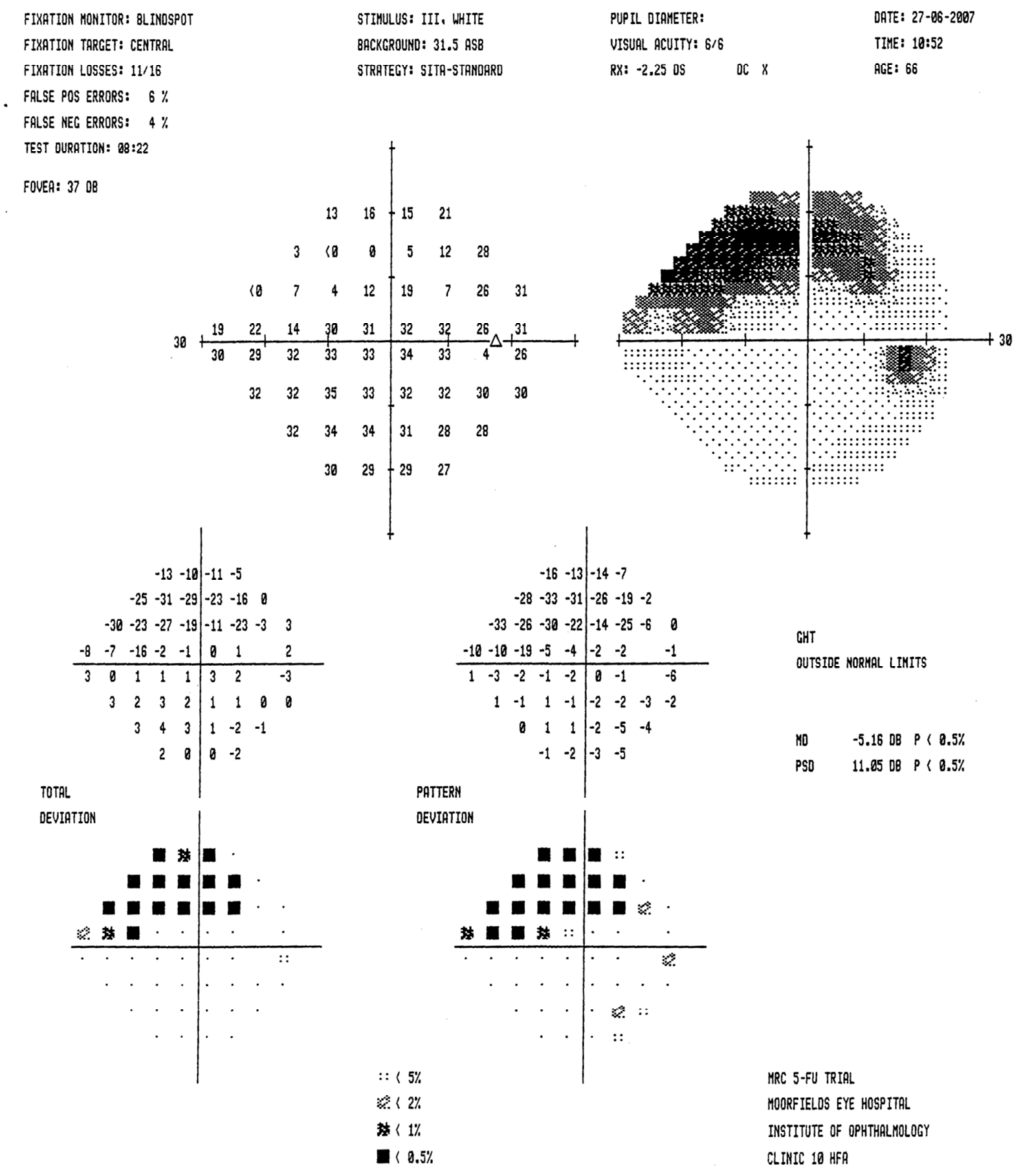


Figure 1.3: Example VF showing the point wise sensitivity levels in dB, GHT, MD, PSD

1.4 Binocular Visual Fields

In the clinic, measurements of the VF play a vital role in monitoring the rate of disease progression in each eye, or determining whether a certain treatment is working or not. However, these measurements offer less information regarding how the individual would function in their everyday life, where both eyes work together to perform visual tasks. A measure of the binocular VF would therefore be more useful in the context of, for example, determining the types of visual disability faced by patients such as their suitability to drive. There is currently only one widely used binocular VF test: the Esterman (Esterman, 1982, Mills and Drance, 1986, Esterman, 1967) (Figure 1.4). Currently the Esterman is conducted on an automated perimeter using a suprathreshold test strategy, which means each point is tested at a fixed brightness (equivalent to 10dB on a HFA visual field test) over a 130° horizontal field of view, with 120 test points. If the stimulus point is missed on its second presentation it is assumed the patient has a sensitivity less than 10dB in that location.

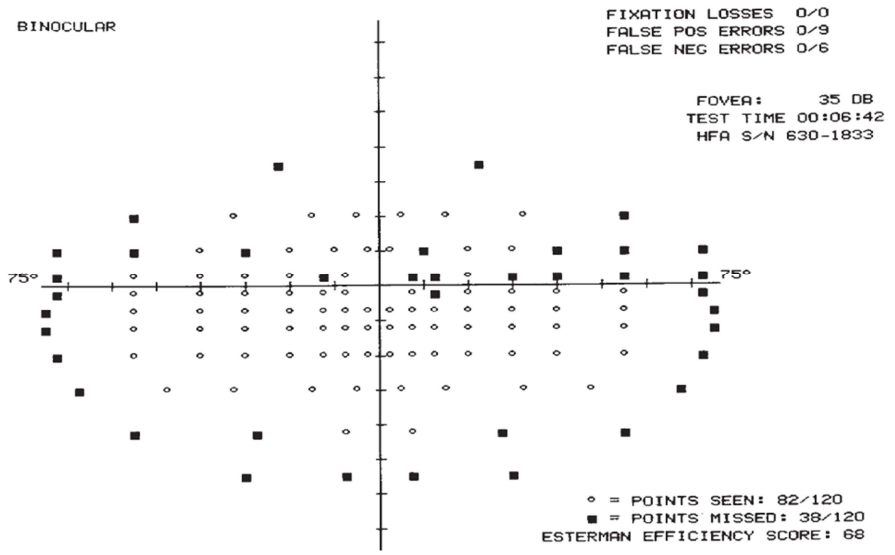


Figure 1.4: Example of an Esterman binocular visual field output: the black points show areas that were not seen by the patient and the circles were detected. Figure taken from (Crabb and Viswanathan, 2005).

An alternative method of gaining an idea of the patient's binocular vision is by combining the two monocular VFs together to give an estimate making the

assumption of perfect binocular alignment. Two main methods are in use to combine monocular VFs: binocular summation and the Integrated Visual Field (IVF). A common form of binocular summation can be calculated by taking the two corresponding points of the left and right VF and calculating the square root of the sum of the squares of those corresponding sensitivities. This method takes into account the binocular "boost" that occurs when both eyes work together, with a maximum "boost" of 40% and minimum of 0%. One down side to this method is it difficult to estimate the binocular VF quickly by eye.

The IVF combines the two monocular visual fields measured using standard clinical procedures to create a binocular representation of that VF. This is conducted by taking each VF point in one eye and comparing it with the corresponding point in the other eye and taking the larger value. If there are no corresponding points at that location (such as in the case of a 24-2 nasal region in the left having no corresponding point in the right) the IVF discards that point. Whilst the IVF is not a direct perimetry test and only offers a simulation of binocular vision, it has been shown to correlate well with the Esterman VF test and with measures of visual disability and may give a better idea of a patient's binocular field in real world contexts (Crabb and Viswanathan, 2005, Crabb et al., 2004, Crabb et al., 1998). This system is very easy to apply when comparing two VFs and therefore is ideal when recruiting patients with specific binocular defects. It does not, however, take into account binocular summation. The IVF can be generated on the PROGRESSOR software (Medisoft Limited, Leeds, UK) for VF analysis (Figure 1.5) (Viswanathan et al., 1997).

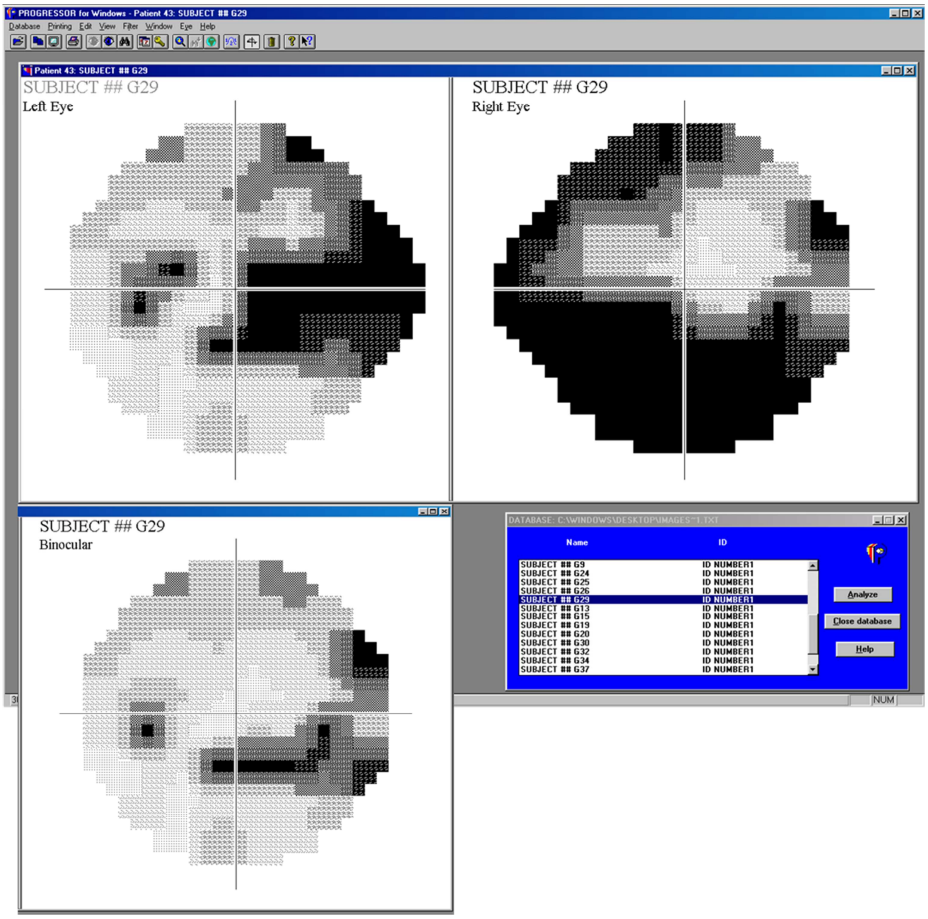


Figure 1.5: Example output for the IVF on PROGRESSOR VF analysis software (Medisoft Limited, Leeds, UK)

1.5 Quality of Life and impairment in Glaucoma

Whilst clinical measures of visual function are useful for gaining an idea of the state of the patient's vision, they do not tell us much about how the patient's visual impairment affects day-to-day activities and their quality of life (QoL). Due to the irreversible nature of glaucoma, any vision loss that has occurred can be expected to have some sort of impact on the patient's life. Studies of QoL are therefore important to determine the ways in which the patient is affected by this visual field loss, and at what stage of disease any changes are likely to occur. QoL is often investigated using self-report questionnaires, interviews or retrospective analysis using medical documents. Self-report questionnaires and interviews are primarily useful in that they are quick and easy to administer and analyse. Furthermore, they are the only feasible method of determining how the patient themselves see the impact of their visual loss and to gain an idea of their experiences, expectations and which activities are the most important to them. This information could be important for devising individual-appropriate management and rehabilitation strategies, especially since clinical time constraints mean it is difficult for the patient to get this information across to their clinician during their standard appointment (Lunnela et al., 2010). There are currently several questionnaires that can be used to measure the QoL of people with glaucoma, ranging from those asking questions relating to more general health to others that were specifically developed with glaucoma in mind (for a review see Spaeth, et al (2006)). However, the self-report methods of measuring QoL have subjective variation. Moreover individuals may change their responses to questions for other reasons, such as fear of losing their driving license and therefore hold back on relevant information about their condition (McGwin et al., 1998). Retrospective studies involving medical records may resolve some of these issues but this technique has its own limitations: for instance, it may be difficult to access old medical records and the information available will be related to socio-economic factors, particularly in countries like the United States where there is a clear link between wealth and access to medical care (Schoen et al., 2010). An alternative approach to gaining insight into the impact of glaucoma on everyday functioning is to objectively measure the individual's actual performance in the types of tasks they would encounter in their normal lives. Although the task may not be as realistic as would

be hoped, it has been found that there is a relationship between how patients perform tasks carried out in the laboratory and their performance in similar tasks in their own home (West et al., 1997). Linking the clinical measurements to how patients are impaired in daily activities is important in the management of the condition; for example, observations of worsening performance in these types of studies may even be another useful way of monitoring disease progression (Haymes et al., 2007, White et al., 2006, Szlyk et al., 2005).

Studies in glaucoma have been limited in number when compared with other chronic conditions (Glen et al., 2011). However, even with this limitation, research shows that patients with glaucoma often suffer with a deteriorated QoL and have problems carrying out everyday vision-based activities. For example, patients with glaucoma appear to have almost a 60% increase in the chance of falls, injuries and fractures and medical records have revealed that they are twice as likely to be placed in a nursing home when compared to normally sighted individuals (Bramley et al., 2008). Various other studies also confirm that people with glaucoma are more likely to fall and have accidents (Haymes et al., 2007, Dolinis et al., 1997, Guse and Porinsky, 2003, Ivers et al., 1998), even with relatively modest visual field defects (Haymes et al., 2007, White et al., 2006, Szlyk et al., 2005). Patients have also self-reported difficulties in tasks such as reading, driving, mobility and searching for objects (Spaeth et al., 2006, McKean-Cowdin et al., 2008, Nelson et al., 2003, Jampel et al., 2002b). Objective studies have also found that patients display deficits in visual activities. Ramulu et al (2009) investigated the effect of glaucoma on reading and found that in patients with advanced bilateral glaucoma there was a decrease in reading speed, although race, education and visual acuity were important predictors of this effect. It has also been shown that patients with glaucoma have difficulties when reaching and grasping for objects (Kotecha et al., 2009), with balance (Black et al., 2008) and navigation (Friedman et al., 2007, Turano et al., 1999). An additional task that is affected by visual impairment caused by glaucoma is driving. Patients are up to 3 times more likely to have a reported motor vehicle accident than people with normal vision (McGwin et al., 2004) and patients have self-reported more problems with driving, particular at night, than controls (Freeman et al., 2008). Patients with increasing

glaucomatous visual field loss also had more accidents when driving using a simulator (Szlyk et al., 2005) and have displayed measured on-road difficulties (Haymes et al., 2008). UK law states that significant loss of binocular vision, as measured by the Esterman binocular VF test, means that the individual is no longer legally fit to drive. The UK Driver and Vehicle Licensing Agency (DVLA) criteria state the following (August 2011):

Acceptable binocular central loss:

- Scattered single missed points
- A single cluster of up to 3 adjoining points

Unacceptable binocular central loss:

- A cluster of 4 or more adjoining points that is either wholly or partly within the central 20 degree area
- Loss consisting of both a single cluster of 3 adjoining missed points up to and including 20 degrees from fixation, and any additional separate missed point(s) within the central 20 degree area
- Any central loss that is an extension of a hemianopia or quadrantanopia of size greater than 3 missed points.

The fact that patients with such binocular VF loss may lose their driving licence presents important issues since it has been shown that some elderly people who stop driving are more likely to have higher rates of depression and a lower QoL (Fonda et al., 2001, Ragland et al., 2005). Problems with other important activities of daily living, such as searching for objects, may also lead to similar feelings of loss of independence and negative effects on QoL.

1.6 Eye movements

Eye movements made whilst carrying out certain visual tasks may shed light on patients' visual function. Although it appears that patients display problems with certain activities of daily living, little is known about the underlying mechanisms that influence how visual loss is perceived and managed by an individual. Studies have suggested that patients can underestimate the true extent of their visual defect (Jampel et al., 2002b, Shaw, 2005). This may be in part related to a series of compensatory brain processes that allow missing visual information to essentially be 'filled in' using the surrounding contextual information in the visual scene (Safran and Landis, 1996, Komatsu, 2006). This means that one eye essentially compensates for the other and this factor may influence how the patient perceives their disease. Investigating the eye movements made by patients as they perceive a visual scene may shed light on the strategies they use as a result of their visual loss and could help develop future studies that attempt to relate the severity, extent and location of a visual field defect to what a patient can and cannot do in terms of real life activities, such as driving and searching for objects. It may even provide a basis for incorporating attention to eye movements into visual rehabilitation and coping strategies for the patient with glaucoma.

To be able to appreciate how eye movements may provide insight into the functional deficits displayed in glaucoma it is necessary to at first summarise the basic principles and the development of eye movement research. The interested reader can find more in Liversedge, et al (2011).

When viewing a static scene, such as a picture or a passage of text, a subject will gaze at a specific area for a period of time, and this is called a fixation. Fixations are interspaced by saccades and blinks. Saccades are very rapid (ballistic) movements of the eye from one area of interest to another, with a peak velocity of about $500°s^{-1}$ (Becker, 1991). The reason eye movements are necessary is due to the natural degradation of a subject's vision as eccentricity from the fovea increases. Moving one's eye allows the individual to move the direction of the fovea (the area of eye with the highest number of ganglion cells and the highest resolution of vision) to different areas of a scene so they are able to see at maximum resolution in that region. When viewing dynamic scenes other types of eye movements may

also be made: a smooth pursuit occurs when an individual tracks a moving object. Optokinetic reflex is similar to a smooth pursuit, whereby an individual tracks an object and once it goes beyond their field of view they move onto tracking the next object. For example, if a person was to sit on a train and look out the window at the trees going by, the eye would track a tree and once it had reached its maximum rotation it would move onto tracking the next tree. Vergence eye movements are the changing of the relative position of the two eyes. Studying different aspects of an individual's eye movements as they view static and dynamic visual scenes will therefore give an insight into the manner in which the individual perceives the world around them and how they may go about performing subsequent vision-based tasks. This may help us decipher what areas of a scene are of most interest to the viewer at a particular point in time. In this thesis the main focus will be on saccades and fixations in the static tasks along with smooth pursuits when looking at dynamic scenes.

1.7 A brief history of eye movement recording

Some of the first studies investigating eye movements involved the use of mirrors which revealed that the eyes move in a series of 'jerks' (Javal, 1879). Clearly this was subjective and thus the recording was essentially only as good as the person making the observations. A more objective method of recording the eye movements was developed by (Delabarre, 1898, Huey, 1898). They separately devised an ingenious (if not slightly painful) method involving the creation of a Plaster of Paris cap with a hole in the middle that was moulded to the shape of the cornea. Since Plaster of Paris can attach firmly and immovably to any moist surface, this device could be attached on to a "cocainised eye". The device was then connected to a recording drum (consisting of a drum, wet piece of paper and a soot pointer) using a wire which enabled horizontal eye movements to be recorded. According to Delabarre the cup would detach after it became tear soaked and the eye recovered after a week, although he could not guarantee no damage had been done! Figure 1.6 shows a schematic of the system created by Huey.

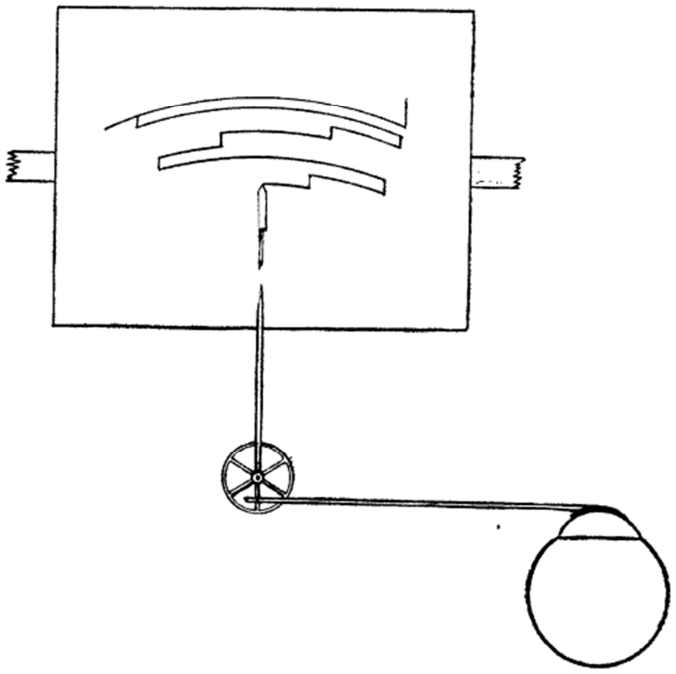


Figure 1.6: Preliminary Experiments in the Physiology and Psychology of Reading, Edmund Burke Huey, 1898 (Huey, 1898)

Huey used his apparatus to study subjects' reading behaviours whilst reading magazines at various distances and found that the 'jerks' were related to the text and changed according to the distance the person viewed. However, these devices restrict eye movements, which in turn strain the eye. Clearly another method was required to be able to validate these results. Dodge and Cline (Dodge and Cline, 1901) therefore devised an eye tracker using photography which for the first time recorded eye movements non-invasively and accurately. Figure 1.7 shows the device they invented with a subject at one end. It worked by shining a vertical slit of light off the cornea of the subject, and by using a photographic film moving at a set speed, recording the reflection of the light through a horizontal slit. This accurately gave the position of the eye horizontally.

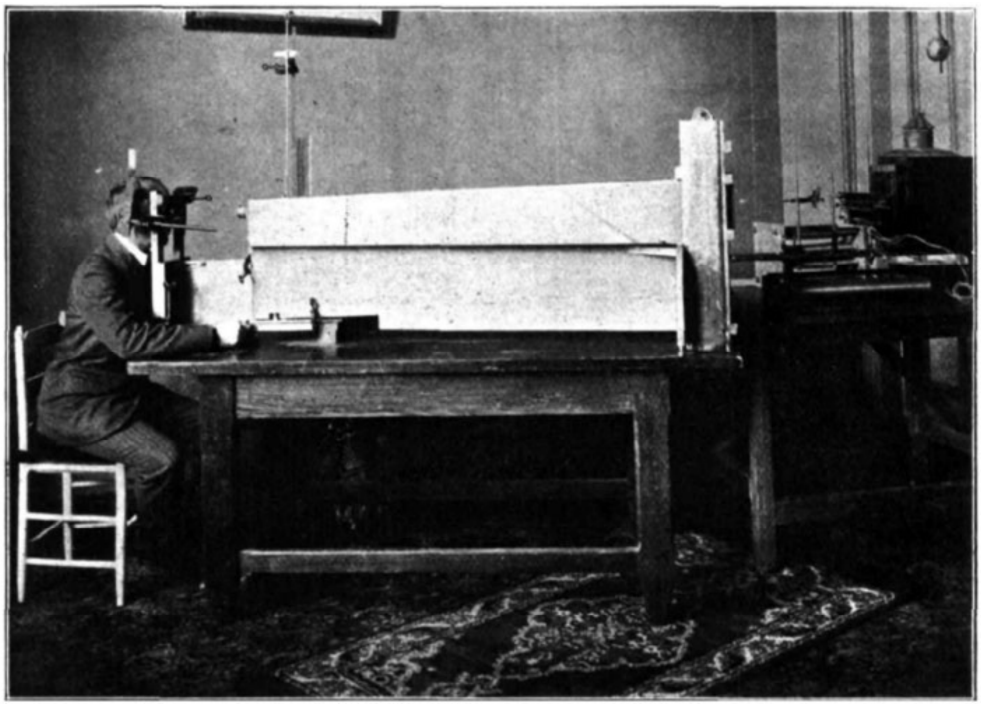


Figure 1.7: The Dodge photomicrograph (DIEFENDORF and DODGE, 1908).

Further developments by Gilliland (1921) recorded both horizontal and vertical eye movements. This technique was enhanced further to allow the measurement of both directions using one eye rather than the two vectors on each separate eye. Some of the first research into two dimensional image viewing was conducted using this method (Buswell, 1935) and a scanpath of his 9th image (in which the

colour has been modified to blue for clarity) by one of the subjects can be seen in Figure 1.8.

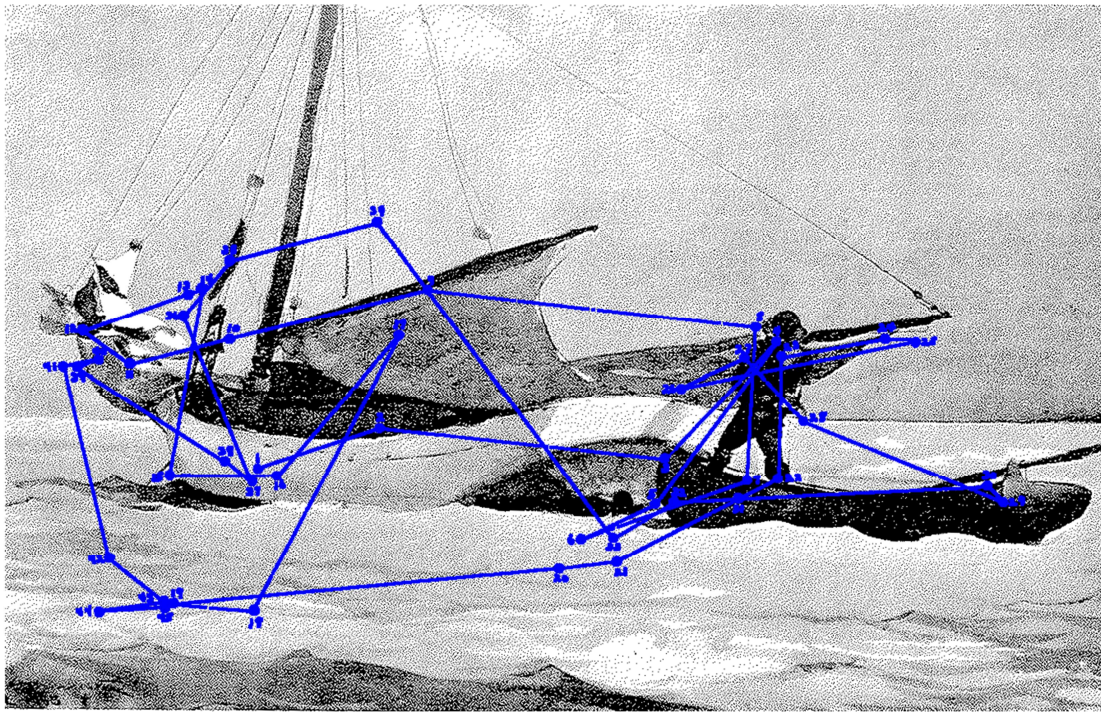


Figure 1.8: Image taken from (Buswell, 1935) (page 2-3) showing the scanpath of a subject viewing an image. The scan path and fixations have been recoloured to blue for clarity.

Eye movement research developed further in the 1960's using suction based contact lenses with mirrors which reflected light projected at the eye towards a camera which subsequently showed the movements and position of the eye (Yarbus, 1967, Riggs et al., 1953, Ditchburn and Ginsborg, 1952, Fender, 1964). Further research used Electro-Oculography, scleral search coils and finally the direct recording of the eye using infrared light. Electro-Oculography uses skin electrodes placed around the eye and by recording the potential differences between the pair the position of the eye can be calculated (Schott, 1922, Mowrer et al., 1935). Scleral search coils consist of a contact lens with two wire coils that disrupt a magnetic field around the head of the subject (Robinson, 1963). The bulges in these lenses can be quite uncomfortable and therefore this technique is now used only for very specific human research and animal research.

Feature detection based methods using video recordings of the eye use infrared light to unobtrusively enlighten the subject's eye and record the corneal refection location (a small bright region appears within the image close to or upon the pupil) and the centre of the pupil. The pupil region is enhanced using one of two methods: bright pupil and dark pupil effect (as demonstrated in Figure 1.9). Both work by increasing the contrast between the iris and pupil. The bright pupil occurs when the light source is being projected directly towards the pupil, and so the eye becomes a 'retroreflector' as the infrared light is reflected from the retina and becomes a very bright area (Merchant et al., 1974). The dark pupil technique projects the light at a different angle and the pupil absorbs the infrared light and the region becomes very dark. Finding the centre of these areas becomes much simpler as even dark irises are clearly separate to the pupil and therefore simple thresholding techniques can be used to locate the pupil and subsequently either elliptical fitting or simple central point fitting can occur. The purpose of the corneal refection is that it stays at a constant location with head movements but its position changes when the eye moves, therefore allowing the subject's point of regard to be calculated even when the subject moves their head.

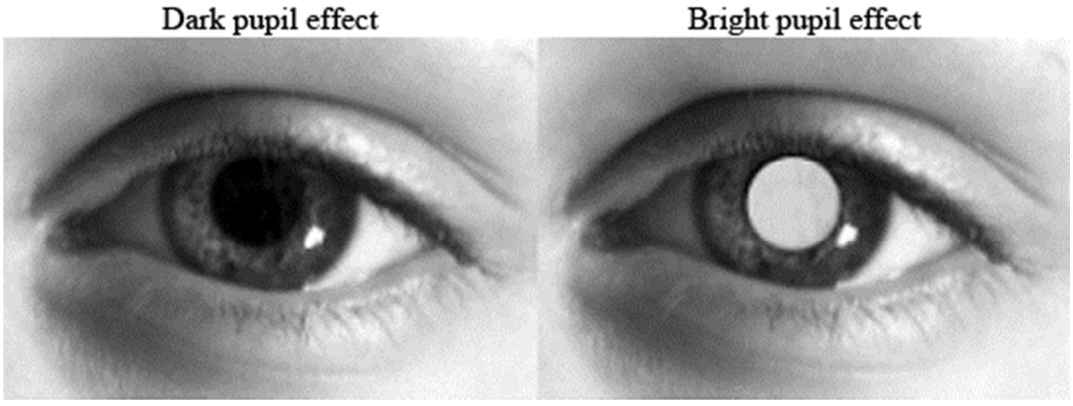


Figure 1.9: Examples of the dark and bright pupil effect commonly used by eye trackers to locate the centre of the pupil. The corneal reflection (CR) can be seen at the bottom right of the pupil. (http://www.archimuse.com/mw2003/papers/milekic/milekic.html; 10/11/2011)

Dual Purkinje eye trackers are a more sensitive eye tracker which records two of the four Purkinje images from the eye. The four Purkinje images are the light projected in to the eye reflecting from the outer (P1) and inner (P2) surface of the cornea and the outer (P3) and inner (P4) surface of the lens. The dual Purkinje eye

tracker uses the reflections from P1 and P4. Infrared eye trackers use the centre of the pupil and often enhance the reliability of the data by combining the central location with the location of P1 (corneal reflection), a scan be seen in Figure 1.9.

In this thesis dark pupil based infrared eye trackers are used; most notably the head mounted EyeLink II (SR Research Ltd., Ontario, Canada) which contains a front facing camera to compensate for the subject's head movements by recording the position of 4 infrared beacons located around the monitor. This device contains two further cameras recording each eye independently at up to 500Hz. The EyeLink II was used for all the eye movement studies in this thesis except when investigating the eye movements in people with glaucoma when performing a hazard perception test (Chapter 6), where an SMI iView X (SensoMotoric Instruments, Teltow, Berlin, Germany) sampling at 240 Hz was used. This SMI iView X is a cold mirror based dark pupil eye tracker, whereby the subject places their head on a chin rest and views a monitor, and between the monitor and subject is a mirror which allows visible light to transfer but infrared light to be reflected. This allows the eye tracker to be located above the subject meaning that they therefore have a good field of view in addition to simplifying the setup procedure since the cameras do not have to be specifically located for the subject's eyes. Images of both these systems can be found in Figure 1.10.

Figure 1.10: The SR Research EyeLink II and SMI iView X eye trackers used in the studies documented in this thesis

1.8 Eye movement research

The study of eye movements has emerged as an interesting and novel approach of improving our understanding as to how 'normal' individuals might perceive the world and how they might function in their day to day activities. How the eye moves as an individual reads is an area that has generated particular interest. Javal (1879) was the first person to discover that eye movements when reading occur in series of fast jumps rather than smoothly across the page. A large amount of research has been conducted in the area of acquisition of information from text, the representation of this text and its understanding which has eventually lead to the development of many different computational models of reading (Rayner, 2009b): Minimal control (Suppes, 1990), Strategy-Tactics (O'Regan, 1990), Word-Targeting (McConkie et al., 1988), SWIFT (Engbert et al., 2002), Glenmore (Reilly and Radach, 2003), Mr. Chips (Legge et al., 2002, Legge et al., 1997), E-Z Reader (Reichle et al., 1998), EMMA (Salvucci, 2000) and Reader (Just and Carpenter, 1980) are just a few example models. Most of these models have had various incarnations but none have managed to represent eye movements during reading perfectly. Nevertheless, it cannot be argued that the study of eye movements has been an immensely valuable tool for increasing our understanding into this vital vision-based skill.

Studying eye movements as a person views natural scenes is also extremely useful for understanding how an individual might perceive the visual information around them. Eye movements during scene perception as an area is generally more difficult to analyse than reading, as in reading there is a clearly defined task, whilst in scene perception the movements are far more variable. Generally speaking, the amount of information that could be viewed within a given moment will be immense, and it is simply not possible for an individual to take in all available information at once. The scan path made by a particular subject will therefore not cover the whole scene, rather individuals will be selective and tend to fixate on the most informative regions of the image and ignore the less informative regions, such as the sky (Rayner, 2009b). Initial work by Buswell (1935) and Yarbus (1967) noted that subjects are drawn to important regions of an image. Much research has followed on from this and tried to quantify where a person is likely to look within a

particular image using saliency models. These suggest that eye movements are partly driven due to several key low-level properties of the image, with the eyes more likely to move towards regions that have, for instance, high levels of contour, contrast, luminance or colour behaviour (Itti and Koch, 2000, Krieger et al., 2000, Acik et al., 2009, Harding and Bloj, 2010, Einhauser and Konig, 2003, Reinagel and Zador, 1999). It has been shown that the gist of an image can be found in a very short space of time (as short as 40ms in monochrome and 80ms in colour images) from a single fixation (De Graef, 2005). This potentially means that a subject may have decided where the following fixations will be in the image within that short period of time.

Whilst a large amount of eye movement research involves the use of healthy participants, several studies have suggested that it might also be a useful tool for understanding functioning within different clinical populations, with evidence showing individuals with various diseases and disorders move their eyes differently to healthy people. Studies have suggested that the smooth pursuit and saccadic eye movements made by patients with schizophrenia differ from those made by healthy individuals (Holzman et al., 1976, Sereno and Holzman, 1995) and when carrying out activities such as face recognition (Manor et al., 1999, Conklin et al., 2002). It has been suggested that eye movement differences could be a functional biomarker for the disease (Lee and Williams, 2000). Patients with Alzheimer's disease have also been shown to demonstrate eye movement impairments; for instance, they find it difficult to produce anti-saccades (the inhibition of eye movements on instruction) (Kaufman et al., 2010). Differences in eye movements have also been observed in patients with other clinical conditions such as Autism (Norbury et al., 2009) and Attention-Deficit Hyperactivity Disorder (ADHD) (Marsh et al., 2000).

The study of eye movements during everyday tasks has also generated some interest with regards to low vision. It has been shown that patients with age-related macular degeneration (AMD) take in less information per forward saccade and make more regressions (backward saccades) when reading which may explain why they have been shown to have slower reading speeds (Rubin and Feely, 2009, Bullimore and Bailey, 1995). There have also been abnormalities with fixation

stability observed and these findings may also help explain some of the impairments with reading displayed by patients with AMD (Crossland et al., 2004). Patients with retinitis pigmentosa (RP) were shown to fixate on different areas when walking a predetermined route compared with people with normal vision (Turano et al., 2001) and this may be one of the reasons behind previously observed difficulties with mobility observed in such patients (Alex et al., 1997). Patients with homonymous hemianopia (who experience loss of vision on one side due to brain damage) have also been shown to change their eye movements; for instance, they produced different scanpaths when viewing visual scenes (Pambakian et al., 2000), and appeared to change their eye movements when searching for objects in scenes relative to those with healthy vision (Machner et al., 2009). Interestingly in the latter study, whilst the eye movement patterns did not correlate with specific details of the defect, there was a significant correlation with defect age. This suggested that patients may have used eye movements as a way of compensating for their visual loss over time, which may imply that similar eye movement adaptations could also occur in patients experiencing visual loss as a result of visual disease.

Some studies have also studied the relationship between eye movement strategies and visual impairment by using artificial scotomas to investigate whether people with normal vision change their eye movements as a result of the loss of parts of their field of view. These studies are in part based on gaze-contingent paradigms which are commonly used in studies of reading and scene perception in healthy subjects. Generally, these paradigms involve masking parts of the field of view and studying how well the individual takes in the available information in terms of the effect on eye movements and performance. This therefore reveals how important a particular part of vision may be for a certain task (for a more detailed review see (Duchowski et al., 2004, Rayner, 1998)). For instance it has been reported that the time to find an object and the length of fixations made are longer when only a small central region is available for visual search (Parkhurst et al., 2000). Another set of experiments also reported that degrading peripheral vision in a controlled manner, so that only a small central window is left, causes individuals to both change the size of their eye movements and take longer to find objects (Loschky

and McConkie, 2000). People will also produce different eye movements when their visual field is restricted in other tasks such as face recognition (Caldara et al., 2010). Based on this reasoning, obstructing the visual field with an artificial scotoma should therefore give similar insight into the implications of visual defects on eye movements and task performance. Cornelissen (2005) researched search times and eye movements when performing a controlled search task (find a letter 'O' in a collection of 'C' distractors) when varying the size of scotomas and found that increasing the size of the peripheral scotoma lead to changes in the size and duration of eye movements made as the participants went about searching for the objects, which coincided with a decreased performance in visual search. Simulating central scotomas and cataract have been shown to lead to difficulties in reading performance, particularly with smaller letter sizes, and to lead to corresponding changes in eye movements relative to normal vision (Fine and Rubin, 1999a). It has also been reported that people with central field loss tend to choose a different region (the Preferred Retinal Locus; PRL) to compensate for the fovea and the application of artificial scotomas using visually healthy participants has helped reveal which region might be best for improving reading speed in patients with central loss (Fine and Rubin, 1999b). On the one hand, simulating scotomas is a useful technique as it allows more control to be asserted as to the location and type of visual field defect. However, this control could also be a major downfall as real life patients do not display identical and predictable defect properties, which in reality will vary in terms of many factors such as size, shape and image distortion (black, blur, etc). This is particularly true in glaucoma where patients can have a wide range of defect types and severities, and different patients may experience their defects in different ways (see Chapter 7). This type of research is also not directly applicable to glaucomatous VF defects as vision is suddenly obscured rather than a patient gradually adapting to their loss. Therefore it is possible that people with glaucoma may function differently in tasks compared with the more controlled situation involving artificial scotomas. Research involving actual people with glaucoma is subsequently needed to be able to clarify how the patients may change their eye movements as they function in real life tasks.

1.9 Aims of thesis

There exist many gaps and unanswered questions with regards to the impact of glaucoma on the patient as they go about their day-to-day life. The aims of this thesis are to expand on the current literature regarding how glaucoma might impact task performance, and to introduce novel ideas regarding eye movements and patient perceptions of their vision in order to gain further insight into the effects of glaucoma on functioning in everyday life. This will involve investigating the performance of people with glaucoma in a variety of situations and comparing this with individuals of a similar age. The outline of the thesis is as follows:

Chapter 2: This chapter describes the key methods of the studies in chapters 3-5 within this thesis and outlines key characteristics relating to the 30 people with glaucoma and 30 age-related controls that took part.

Chapter 3 examines the hypothesis that visual search is impaired in patients with glaucoma, with patients taking longer to locate targets in a 'controlled' search experiment and in photographs of everyday scenes when compared to age-related visually healthy individuals.

Chapter 4 aims to provide further insight into the apparent deficits in visual search performance in glaucoma by investigating whether patients make different eye movements compared with individuals with healthy vision during these tasks. Furthermore, the study will investigate whether any changes in eye movements are related to visual search performance.

Chapter 5 builds on the idea that eye movements are impaired in glaucoma by investigating whether the people with glaucoma display different eye movements to controls when they passively view a selection of naturalistic images.

Chapter 6 examines the eye movements of 14 people with glaucoma and 22 controls when viewing a selection of driving hazard perception test videos. A finding that patients display different eye movement strategies to healthy people could have important implications for determining their fitness to drive.

Chapter 7 aims to gain an increased understanding as to how glaucoma might appear to the affected individual, by asking 50 diagnosed glaucomatous subjects

with a range of HFA visual field defect severities about their perceptions of glaucoma. Patients are shown a selection of images that represent glaucoma in different ways and the patient is asked to choose the image that best illustrates their own visual experiences. The results will give insight as to whether common representations depicting glaucoma in terms of black patches or a black tunnel are the best ways of representing glaucomatous visual field loss.

Chapter 8 concludes this thesis and outlines future work that could be conducted to complement our current understanding of how glaucomatous defects affect eye movements and patient perceptions of their visual field loss.

2 Study design for chapters 3, 4, 5

2.1 Introduction

This chapter's purpose is to introduce the setup and experimental design for the studies in chapters 3, 4 and 5. It then describes the inclusion criteria, visual and demographic properties of the participants that kindly took part in these studies. The final section explains the analysis and bespoke software developed to perform this. These studies were collected at the same time in the same order, but the trials within each study were randomised. It should be noted that the studies in chapters 6 and 7 use completely different setups.

2.2 Participants

Patients were recruited from Moorfields Eye Hospital NHS Foundation Trust, London and the Fight for Sight Optometry Clinic at City University, London. All patients had a clinical diagnosis of glaucomatous optic neuropathy (primary open angle or normal tension glaucoma) with reproducible visual field defects in both eyes. Patients had no ocular disease other than glaucoma. Prior to participation in the studies, patients undertook an eye examination of corrected binocular visual acuity (VA), using an Early Treatment Diabetic Retinopathy Study (ETDRS) chart, and contrast sensitivity (CS) using a Pelli-Robson chart. To be included in the study, patients were required to have a corrected VA of at least 6/12 in each eye. Visual fields (central SITA 24-2 and 10-2 on both eyes) were also recorded on a Humphrey Visual Field Analyzer (HFA, Carl Zeiss Meditec, CA, USA). Patients were identified as having 'overlapping' binocular defects as measured by an estimate of their integrated visual field (IVF) (Crabb et al., 2004, Crabb and Viswanathan, 2005): a simulated binocular visual field in which patients' best point-by-point monocular sensitivity is used (PROGRESSOR software: Moorfields Eye Hospital, London, UK / Medisoft Ltd., Leeds, UK). Specifically, patients had binocular defects with one or more IVF locations with sensitivities of less than 20dB, meaning that they would have significant visual field defects at these 'overlapping' locations in

their monocular VFs. It should be noted that these are only estimates of binocular defects, and not truly measured with both eyes open using something like the Binocular Esterman Test. Visually healthy control people were recruited from university staff, centres for the elderly and the university optometry clinic: prior to participation in the studies they too completed an eye examination of VA, CS and HFA visual fields (central SITA FAST 24-2) to ensure they had no visual field defects which would compromise their role as a control subject in the study. A corrected VA of at least 6/12 was required for each eye in control subjects. Astigmatic error was less than ±2.5 Dioptres in all those recruited. Recruitment of patients and controls was made simultaneously with a specific effort to age-match participants.

Recruitment was restricted to those in good general health ascertained by interview and participants were not enrolled if they were on any significant medication other than that for their glaucoma. ('Significant medication' included anti-depressants, treatment for diabetes or significant use of non-topical β-blocker medication, all of which were deliberately mentioned).

The studies were granted full approval by the National Health Service's (NHS) Research and Ethics department and City University London's School of Health Science Ethics committee. The study conformed to the Declaration of Helsinki and all subjects gave their informed written consent. All data were anonymised before being transferred to a secure computer database at the university.

Sixty participants were recruited for the studies in chapters 3, 4 and 5: thirty people with glaucoma with a mean age of 68.5 (SD: 9.7) years and 30 visually healthy age-related controls with a mean age of 68.4 years (SD: 9.5 years; means not significantly different; P=0.97. Variances not significantly different; P=0.92.). The HFA mean deviation (MD) is a standard clinical measure of the overall severity of a VF defect with more negative values indicating greater VF loss. The MD is calculated as the overall reduction in VF sensitivity relative to a group of healthy age-matched observers and MD is conventionally used as a marker for VF defect severity both in the clinic and in clinical trials. The patients had a range of VF defect severity: average MD was –10.1 (SD: 7.5) dB, –8.2 (SD: 5.2) dB and –6.6 (SD:

4.9) dB in the right eye, left eye and best eye, respectively. Average Pelli-Robson contrast sensitivity values were significantly worse in the patients (mean: 1.80 [SD: 0.16] log units) compared to the control subjects (mean: 1.95 log units [SD:0.04]) using a two-sample t-test ($P<0.001$; 95% confidence interval [CI] for the mean difference of 0.08, 0.20). Mean ETDRS chart corrected binocular LogMAR VA was 0.06 (SD=0.12) and -0.04 (SD=0.10) in the patients and controls respectively. The difference between these mean values was statistically significant ($P<0.001$; two-sample t-test) but the actual size of the average difference, 0.10, was small (95% CI for the mean difference of 0.05 to 0.16).

2.3 Equipment setup

All the studies in chapters 3, 4 and 5 used the same 56cm CRT computer monitor displaying at a resolution of 1600 x 1200 at a refresh rate of 100Hz (Iiyama Vision Master PRO 514, Iiyama Corporation, Tokyo, Japan) to display the images on. The subjects were positioned at a viewing distance of 60 cm and all the images displayed were 40.8 cm (width) x 30.6 cm (height) subtending a half-angle of 20.3° by 14.9°. The screen was calibrated using a Minolta CS-100 luminance meter recording every greyscale combination the system could produce (256). Using these values a table was produced stating the RGB (red, green and blue pixel value) to the luminance value (cd/m^2). Whenever testing or using the monitor for a study, it was always left on for a minimum of half an hour to make sure the screen had "settled down".

The Eyelink II system consists of two computers connected by an Ethernet crossover cable. One computer is used as the display machine and is tasked with displaying all the images/stimuli on the screen at precisely the correct time and sending messages to the eye tracking machine via the Ethernet connection when events (such as key presses, the time images are displayed, the time images are removed, errors, etc.) occur. The second machine is the eye tracking machine, which runs Microsoft Disc Operating System (MS-DOS) (allowing eye position detection to occur in pseudo-real-time with a measurement occurring at every 2ms interval). The eye tracking machine has overall control of the studies, allowing for

aborting trials, recalibrations, etc. but the display machine contains the procedure of the study, including study orders, randomisation of trials, naming of images, drift correction initialisation, and messaging. All applications are coded in C using Microsoft Visual Studio 2005 using the Eyelink Software Development Kit (SDK) to display the stimuli and interface with the eye tracking machine. These applications developed in C were responsible for the randomisation of the trials and the messages required for reordering the data. All the code was written by the author.

Eye movements were recorded using the head-mounted Eyelink II eye tracker. In our setup we used this instrument to sample pupil position monocularly at 500Hz. The instrument claims to measure an average eye position accuracy of better than 0.5° and uses velocity and acceleration thresholds of 30°/s and 8000°/s^2 respectively, to identify saccades and fixations. The reason these values were chosen was to minimise noise. The lower the velocity the more microsaccades will be detected, however this may have added confusion to our analysis due to the subsequent need to merge short fixations into single fixations (or discard altogether). As the focus of this work is to investigate fixations and saccades, microsaccades are likely to confuse the result. This is not to say that microsaccades are not important; they may be very interesting to analyse when comparing between patients and controls, however this type of analysis should involve a more controlled study design as opposed to the more "real-world" perspective taken here. Furthermore, acceleration thresholds reduce the likelihood that noisy data will be classified as saccades. These thresholds have been used in previous studies that used the Eyelink to investigate eye movements when viewing images (Frey et al., 2008, Tatler et al., 2007, Foulsham et al., 2011). On the other hand it is more likely that small saccades will be missed. Noise is difficult to remove in an offline manner and therefore it is far more appealing to try and remove it at an earlier stage. The combination of these values gives us the best situation for reliable data to analyse. Another method used in this research to remove misclassified saccades was to remove all saccades of amplitude less than 0.5°.

A chin rest was used to minimize head movements and patients were asked to keep their head as still as possible. However if any head movements did occur these were compensated for by the EyeLink II's head movement detection system

which adjusts the point of regard accordingly. The EyeLink II proprietary algorithm was used to calibrate and verify the subject's point of regard in relation to the correct location on the display. Verification of calibration accuracy must be stated to be of a "good" level, which in this research required none of the 9 points being verified have an error larger than 1°. Between each trial (image being displayed) a drift correction was performed, and in the case where a large drift was detected, a recalibration and verification performed. In the case of the search tasks (chapter 3 and 4) the participant's point of regard was used to confirm that the participant had found the target stimulus. The trial was stopped at the moment the participant successfully located the target item and the time taken was recorded automatically by the eye tracking system. In all cases the room was in complete darkness but this luminance level was not measured, however the minimum luminance value of the monitor (RGB values set to 0) was 0.98cd/m^2 so it can be assumed the room was equal to this value or less.

All participants wore refractive correction suitable for the viewing distance of 60cm, and the same set of trial frames was worn by each participant (even if they did not need any correction) to ensure that any restriction to the field of view as a result of spectacle frames was equivalent for each person.

2.4 Analysis application

A bespoke analysis application, as shown in Figure 2.3, was developed in C# using Microsoft Visual Studio 2005 for the analysis of eye movements after the data had been exported from the SR Research DataViewer application. The application conducts various tasks, but in this section only the parts that were used in this thesis will be explained.

2.4.1 De-randomisation of trials

All the images used in the research relating to this section were randomised in the display application developed by the author in C. This uses the *rand()* function located in "ctflib.h", which is used to fill an array with random non-repeated numbers the same length as the number of the images in that study. This array is used for randomising the display order of the trial. A message is sent to the eye tracker to state the image displayed and its random order index number. Unfortunately the EyeLink II API does not allow for randomisation, which means bespoke software has to be used to derandomise the data. Another quirk of the EyeLink dataViewer packing is when exporting eye movement data, the messages are not included in this exported data and have to be exported separately. The C# application developed by the author takes the eye movement data and the message data, combines it and then derandomises the data and stores it in a specially designed internal object oriented database.

2.4.2 Formatting data for various statistical tasks

When outputting the data to run various statistical tests, the application reorders the data in a format that is suitable. For instance, for the BCE analysis (used in Chapter 5 and described below) the data can be output as an average or in an ordered per person raw form for easy ANOVA analysis. The program also has various cut off mechanisms to remove data based upon time criteria, such as a trial time limit, limits on saccade amplitude and fixations durations, etc.

2.4.3 Bivariate contour ellipse (BCE) fitting

To calculate the area of the ellipse covering a collection of (x, y) points we use the following formula:

$$BCEA = 2k\pi\sigma_x\sigma_y\sqrt{1-\rho^2}$$

In this formula $\sigma_H\sigma_V$ represent the horizontal and vertical standard deviation over their respective meridians and ρ represents the Pearson correlation (product-moment correlation coefficient) of the (x, y) coordinates. The value k is calculated based upon the probability area to be covered by the ellipse, and this probability is calculated by:

$$P = 1 - e^{-k}$$

In the research in this thesis we always calculate the ellipse to capture approximately 68% of the data points using k = 1.14.

When plotting the ellipse a point is plotted for each degree from 0° to 360°. To calculate this we firstly calculate the two semi-axes by:

$$M_+ = c\sqrt{0.5\left({\sigma_x}^2 + {\sigma_y}^2 + \sqrt{A^2+B^2}\right)}$$

$$M_- = c\sqrt{0.5\left({\sigma_x}^2 + {\sigma_y}^2 - \sqrt{A^2+B^2}\right)}$$

Where the major axis (M_1) is given by the larger of the two values and the minor axis is the smaller (M_2).

A, B and c are given by the following:

$$A = {\sigma_x}^2 - {\sigma_y}^2 \qquad B = 2\rho\sigma_x\sigma_y \qquad c = \sqrt{\chi^2_{(\alpha)}} \text{ on 2 d.f.}$$

To calculate the 360 (x, y) coordinates [X, Y] for the ellipse we perform the following formulae and then plot those points.

$$[X] = \sum_{i=359}^{0} (\bar{x} + M_1 \cos\theta \cos i - M_2 \sin\theta \sin i)$$

$$[Y] = \sum_{i=359}^{0} (\bar{y} + M_1 \sin\theta \cos i + M_2 \cos\theta \sin i)$$

With θ given by:

$$\theta = \frac{\tan^{-1}\left(-\frac{B}{A}\right)}{2}$$

The sections of C# code to perform these formulae are provided in Appendix A and an example of the application running is shown below:

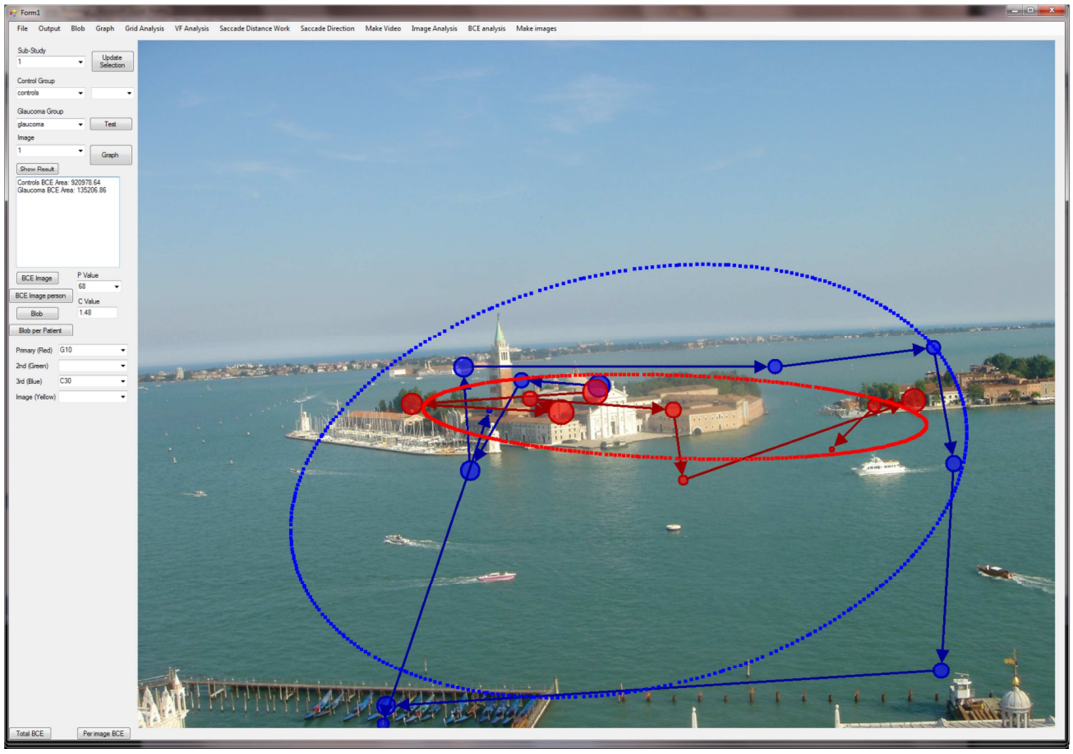


Figure 2.1: Example screenshot of the BCE analysis being executed. This is being run for patient G10 (Red) and control C30 (Blue) using P=0.68 giving a BCEA value in pixels of 920979 for this control and 135207 for the glaucoma patient.

2.4.4 Creating, comparing and overlaying Integrated Visual Fields (IVF) to eye movements

When investigating the eye movement analysis, a way of representing the glaucomatous patient's VF defect is helpful to give an insight into why certain movements may be occurring. The application is capable of combining both 24-2 and 10-2 visual fields to create a dual layer IVF giving a much more precise view of a patient's light sensitivity in comparison to their eye movements. This allows for a semi-transparent region representing the dual layer IVF to be placed upon an image at that patient's point of regard. This can then be created as a film or collection of images. It should be noted that when creating traditional style version of an IVF, PROGRESSOR (section 1.3 for more information) is used, however this cannot integrate 10-2 VF's.

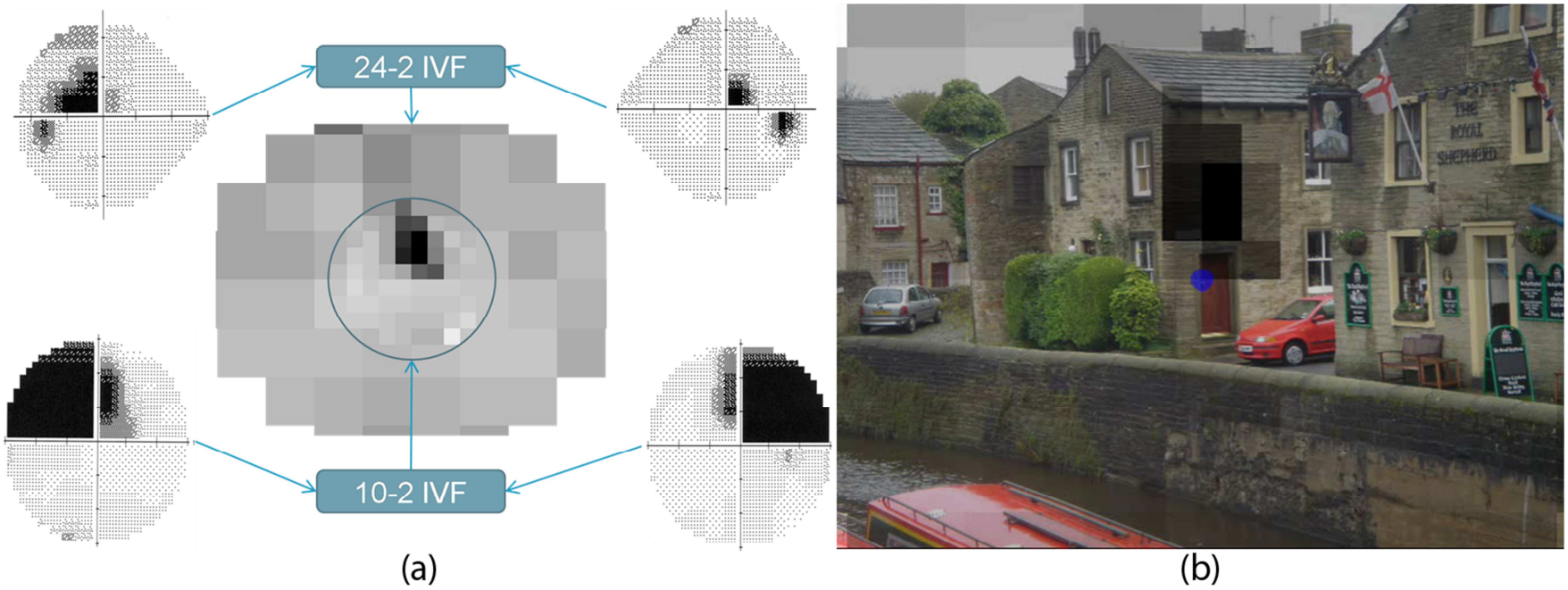


Figure 2.2: Example representing a glaucoma patient's 24-2 and 10-2 visual fields and how the process is used to integrates the two fields (a). This new semi-transparent dual IVF is then overlaid upon the patient's point of regard (b). This output can be created as a film or collection of images.

2.4.5 Quantifying viewing area of subjects

The bivariate contour ellipse provides a general idea of the size of area viewed. However, there may be additional regions of the image that were viewed that were not covered by the ellipse; likewise the points used to fit the ellipse may not necessarily have been viewed by the participant. To quantify a more precise region viewed, rather than a generalised elliptical viewing area, the software can determine whether any of the people with glaucoma may also view different areas of the image to the controls. The application allows for creating regions of interest based on a binary viewing method (1 control views a region then rated as "seen", other regions are "not seen"). The circular area marked as viewed can also be modified in diameter. Figure 2.3 shows a graphical representation of this analysis using 30 controls to create the viewing area in a binary form using a 1.2° marked region (represented as a transparent section). The coloured dots represent the fixations of 3 people with glaucoma, with the size of the points representing their fixation duration. The application, in binary mode, calculates the percentage of fixations within the control region and this is used in chapter 5.

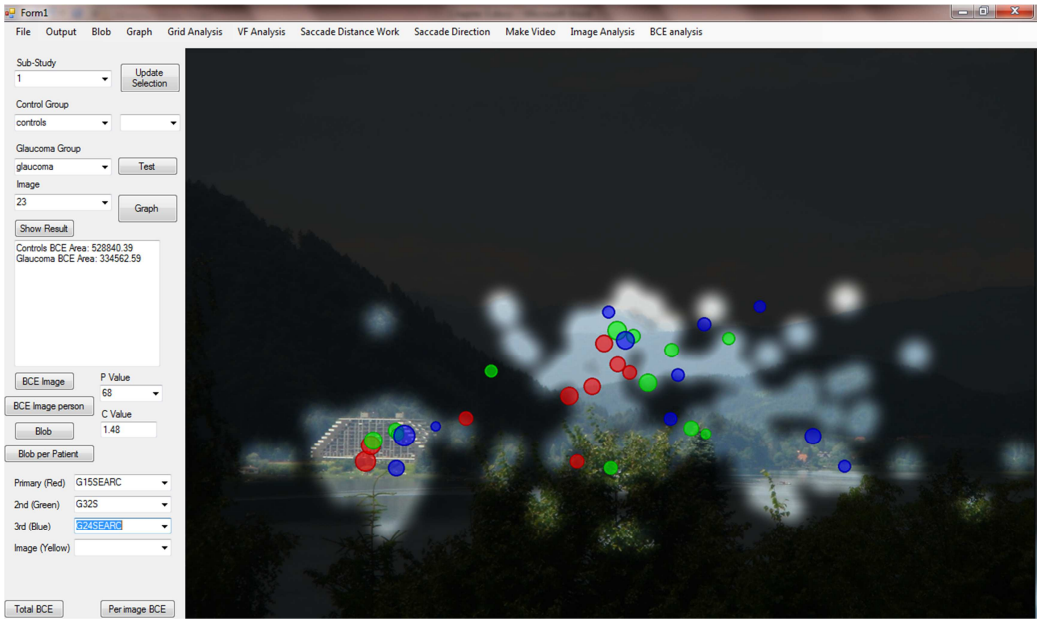


Figure 2.3: A screenshot of the Bespoke C# application analysing the regions of interest when patients passively view images. The coloured dots are three different patients; the size represents their fixation duration. The clouded area represents the control viewing area, where this region is transparent controls have viewed this region once or more. This analysis is used in chapter 5.

3 Visual search in glaucoma

3.1 Introduction

As introduced in chapter 1, tasks such as driving, reading and mobility have been found to be impaired in patients with glaucoma. These data were mainly collected with questionnaires (Jampel et al., 2002a, Nelson et al., 1999, Noe et al., 2003, Bechetoille et al., 2008, Ramulu, 2009, Spaeth et al., 2006). However, individuals' responses on questionnaires about the impact of their condition are likely to be affected by confounding factors such as personality, perception of task difficulty or perceived consequences of admitting accidents (Ormel et al., 1997, Brooks et al., 1990, McGwin et al., 1998, Warrian et al., 2009). More insight might therefore be gained by experiments that observe the patient's performance in everyday tasks, or at least surrogates of those everyday tasks in laboratory conditions (Haymes et al., 2008, Kotecha et al., 2009, Ramulu et al., 2009, Friedman et al., 2007). Ideally, investigations should focus on daily activities that are both important to individuals and are likely to be affected by the disease.

One visual task that plays an important role in daily activities that can be estimated objectively is the ability to search for objects in a scene. Visual search typically involves an active scan of the visual environment for a particular object or feature (the target) among other objects or features (the distractors). An everyday example of visual search could simply be finding a specific item on a supermarket shelf, whereas an example in a controlled experiment might require location of a letter or symbol against a background of distracters. Impaired visual search might put an individual at risk of accidents due to a failure to locate obstacles and hazards. Previously it has been demonstrated that older adults who had difficulty directing attention to target objects placed in different parts of their field of view in a controlled experiment on a computer screen were more likely to have been involved in a higher number of motor car crashes compared to those with unimpaired visual search (Ball et al., 1993). Another study demonstrated a link between performance in a timed search task and difficulty manoeuvring through an obstacle course (Kuyk et al., 1998). There is evidence that performance in

search tasks is compromised in individuals suffering visual loss as a result of age-related macular degeneration (AMD) (Jacko, 2001) or occipital brain lesions (Machner et al., 2009). Another useful study showed that performance in visual search tasks worsens with increasing age and peripheral field constriction (Ball, 1990). These findings suggest that visual search in patients with glaucoma could be particularly affected but there has been little research investigating this directly (Altangerel et al., 2006).

This chapter describes a study that examines the hypothesis that visual search is impaired in patients with glaucoma, with patients taking longer to locate targets in a 'controlled' search experiment and in photographs of everyday scenes when compared to visually healthy individuals of a similar age. Support for this hypothesis may indicate that individuals with glaucoma are forced to employ alternative, more time-consuming strategies to compensate for their visual loss, placing increased demands on their independent lifestyle and subsequently their quality of life.

3.2 Methods

3.2.1 Participants and system setup

The participants and equipment used for this study are described in chapter 2.

3.2.2 Experimental procedure

The first experiment investigated a search task similar to that used by Porter et al (Porter et al., 2007) in which display elements were Landolt C symbols. Each image consisted of one target Landolt C symbol (an upright letter C, which was surrounded by a circle) and a selection of distracters (Landolt C symbols rotated at 90°, 180° or 270°) also encircled. Targets and distracters were equally spaced with their location randomised. As in the aforementioned study, the size of the stimuli and the number of distracters was varied between trials, with the same search images presented to each participant but in a randomised order. In half of the images the diameter of all targets and distracters was 2.07° and in the other half it was 1.15°. For each internal symbol a Landolt C was used (with the break and line width being 1/5 of the diameter). The Landolt C was 50% of the diameter of the outer ring and both the outer ring and Landolt C had the same line width. The background luminance was fixed at 81.9cd/m^2 with the Weber contrast of the display elements set such that each image had a mixture at 9.5%, 25%, 31%, 40% and 98%. In the trials containing display elements of smaller size (1.15°), 5 images contained 100 distracters and 5 images had 50 distracters. For the larger size display elements (2.07°), 5 images contained 30 distracters and 5 images had 50 distracter stimuli. The mean luminance of these images was 68.9 cd/m^2 (SD: 1.5 cd/m^2). Figure 3.1 shows three example search images used in the study. It should be noted that this experiment was not designed with sufficient blocks of trials to examine the effect of the different conditions (display element size and contrast, number of distracters).

After three practice images, 20 images were presented to the participant in random order. Before each image was presented (trial), the participant was asked to fixate on a cross in the middle of a grey screen. Participants were instructed to

verbally tell the experimenter when they had found the target. Eye movements were simultaneously monitored using the EyeLink II system (SR Research Ltd., Kanata, Ontario, Canada) so the experimenter could confirm that the participant had found the target stimulus. The trial was stopped at the moment the participant successfully located the target item and the time taken was recorded automatically by the eye tracking system. If the subject found the incorrect item within the image, they were informed it was incorrect and asked to continue until they found the correct item.

Symbol-like displays do not resemble typical real-world targets such as finding a car key one has dropped or locating a street sign. So the second experiment used images to mimic such 'real-life' situations and participants were presented with 18 photographs of everyday scenes (3 practice trials and 15 images to be used in the analysis). All images were photographs of everyday scenes taken using the same camera (Sony DSC-T1, Sony Corporation, Tokyo, Japan), were displayed at a resolution of 1600 x 1200 pixels and their mean luminance was 9.6 cd/m^2 (SD: 4.0 cd/m^2). Figure 3.2 shows examples of three images used in the study. Before each image was displayed on the computer screen a question would appear which would also be read slowly and clearly to the participant by the experimenter. When the participant acknowledged they had understood the question they were asked to fixate on a target at the centre of a grey screen and then the image would be revealed. Target detection and time to detection was recorded as with the first experiment. All participants viewed the same 15 images but presented in a random order.

3.2.3 Analysis

An average search time was calculated for each participant for each experiment. Individual search times that were longer than 60 seconds were censored at that value. The distribution of response times are typically skewed so the median time across the trials (n=20 for the first experiment and n=15 for the second) was used as the estimate for each participant's average search time. The median of these search times in the patients was then compared to the median search times in the

visually healthy controls by using a non-parametric test, to examine the null hypothesis that average search times were the same across groups. In addition, associations between average search times and Best eye MD (the mean deviation of the better eye visual field), PR log CS (Pelli-Robson contrast sensitivity), ETDRS VA and age were also explored using multiple linear regression in the patient group. Minitab v.14 (Minitab Inc., Pennsylvania, USA) was used for the data analysis.

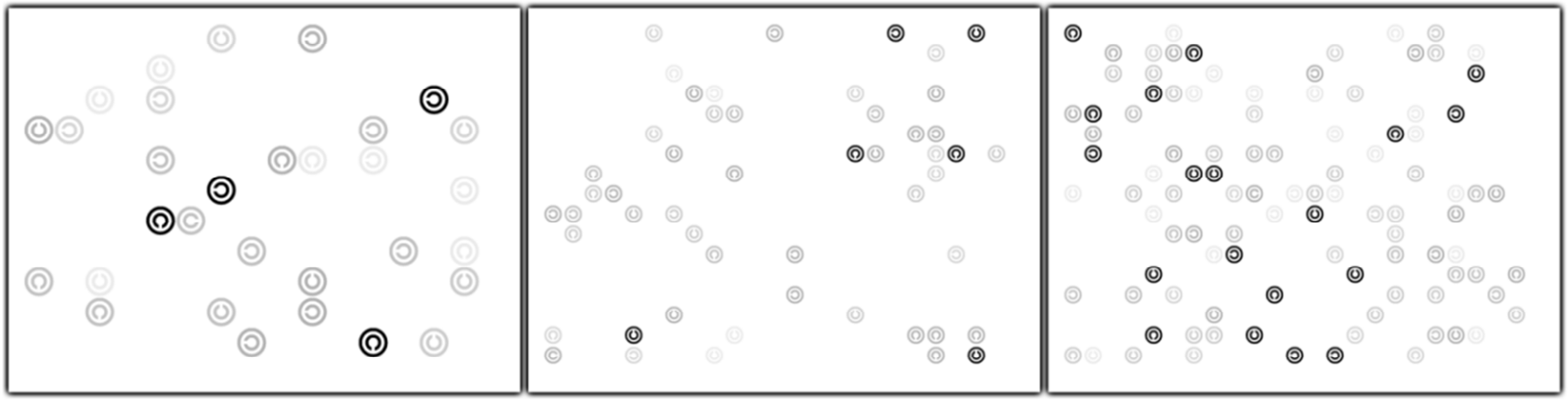


Figure 3.1: Three examples of the Landolt C search task images. Participants were required to locate the correctly oriented letter C (target) in an array of letter C's of different orientations (distracters). All C's, including the target were encircled and the contrast and size of the target varied from image to image.

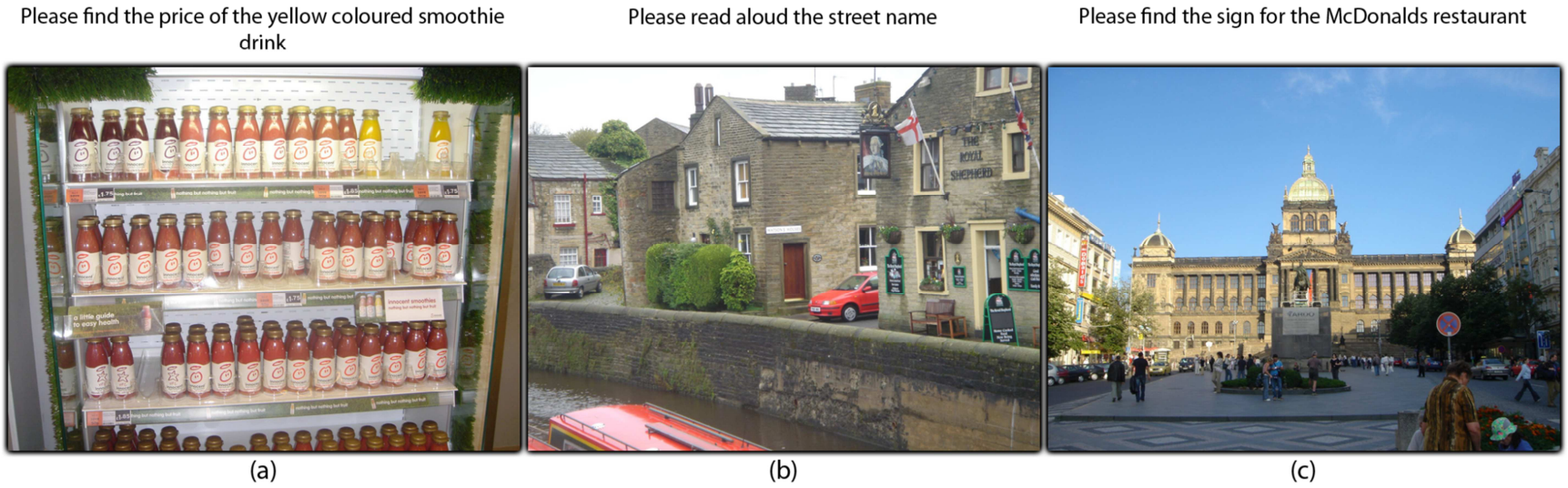


Figure 3.2: Three examples of the photographs used in the 'real-world' search experiment. In each image the study participant was asked to find a target item, the exact text displayed to the patient is shown above. The location of the targets are: [a] located in the top right corner of the image; [b] located in the centre of the image; [c] located towards the middle left of the image.

3.3 Results

In the visual search experiment using the Landolt C symbols, the median search time for the patients and the controls was 13.5 seconds (interquartile range [IQR]: 10.5 – 15.3 seconds) and 12.5 seconds (interquartile range [IQR]: 10.6 – 16.4 seconds) respectively. The difference in these averages was not statistically significant (Mann-Whitney Test P=0.99). In the visual search experiment using photographs of everyday scenes, the median search time for the patients and the controls was 14.2 seconds (IQR: 9.1 – 17.3 seconds) and 8.8 seconds (IQR: 6.5 - 10.3 seconds) respectively: the difference in these averages was statistically significant (Mann-Whitney Test P=0.001) with a 95% CI for this difference ranging from 2.1 to 7.9 seconds. Results from all individual patients are shown in Figure 3.3. The results for the multiple linear regression using average search times for the photographs of everyday scenes as the outcome variable with Best eye MD, PR logCS, Age and ETDRS VA as the independent variables in the patient group is given in Table 3.1. ETDRS VA and age is shown to have no significant effect on average search times whilst there is a significant and equivalent effect of Best eye MD and PR logCS. The % R-squared value for the multiple linear regression equation using Best eye MD and PR logCS is 55%, suggesting that a substantial amount of the variability in average search times for patients is explained by these measurements of visual function alone. However, the magnitude of the average effect of the statistically significant variables on average search times is modest. For example, an average worsening in Best eye MD of 1dB produced an increase of 1.5 seconds in the average search times (95% CI: 0.7 to 2.3 seconds). The sample size is small and some of the explanatory variables (Age and VA) were necessarily fixed in range by the design of the experiment for the primary outcome of difference in search times between patients and controls. Still, this exploratory analysis provides some evidence that visual field and contrast sensitivity measurements have significant and equivalent levels of association with search times in patients with glaucoma, and these associations are stronger than those exhibited by age and visual acuity measures in this group of patients. In addition, there was a no association between search times for the photographs of everyday scenes and search times for the task using Landolt C symbols in this group of patients (Pearson's correlation coefficient= 0.36; R^2 = 12.7%).

Parameter	Estimate	SE	P-value	95% Confidence Interval
Best eye MD	-0.8	0.4	0.05	(-0.002, -1.6)
PR logCS	-37.0	12.5	0.01	(-11.3, -62.8)
Age	-0.1	0.2	0.47	-
ETDRS VA	16.4	16.6	0.33	-

Table 3.1: Results of multiple linear regression of Best eye MD, Pelli-Robson [PR] log CS, ETDRS VA and age on search times using photographs of everyday scenes in the patient group (n=30). The estimates relate to the effect per dB for best eye MD and per log unit for PR logCS.

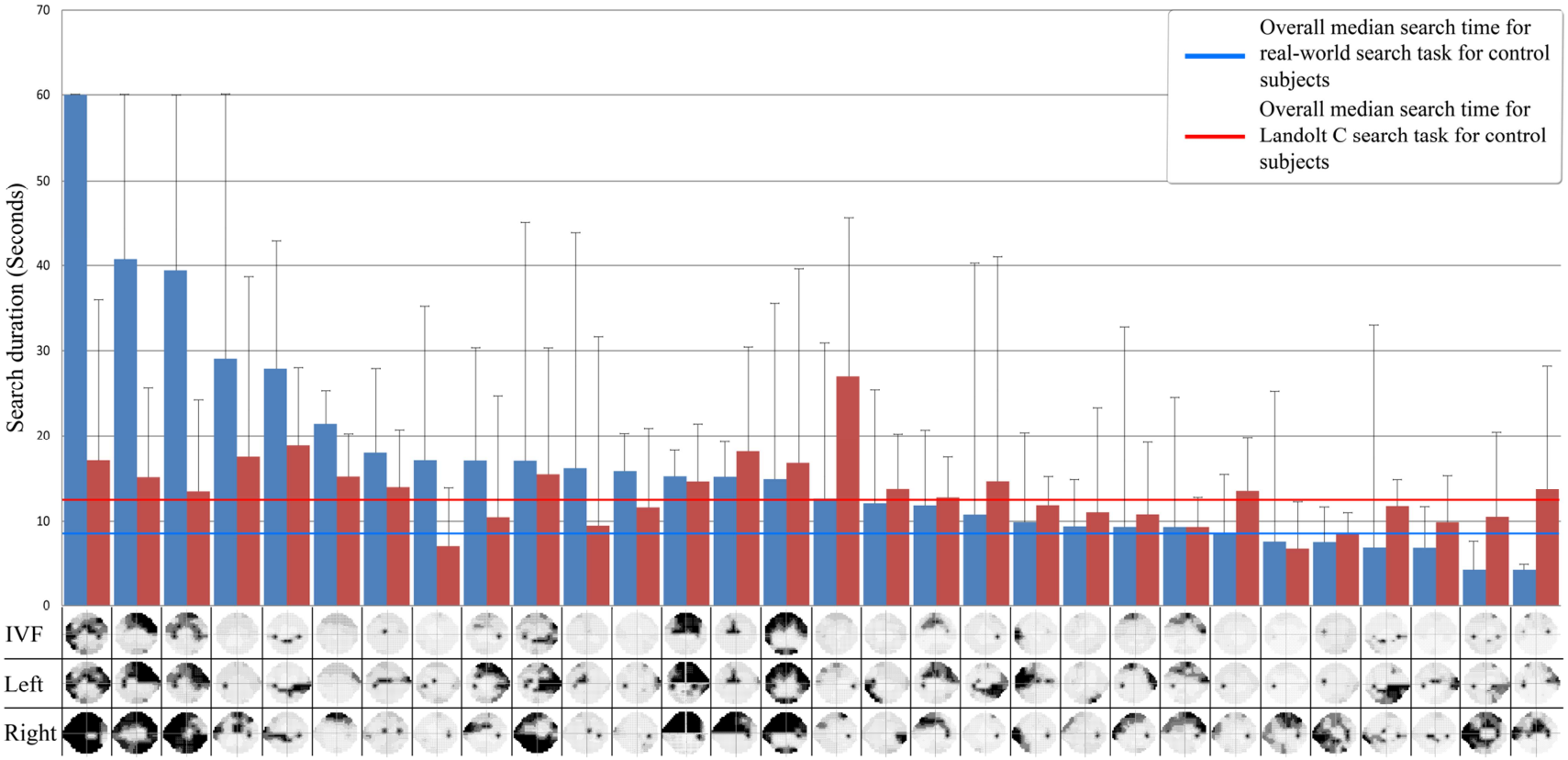


Figure 3.3: Individual average search times for the 30 patients from both experiments. The height of the bars represents median search times (blue denotes real-world search and red denotes the Landolt C search) and the error bars indicate values at the upper quartile. The greyscale of the visual field from the right and left eye is shown for each patient along with their integrated visual field (IVF). Defects are represented by darker regions. All the patients had at least two overlapping binocular VF defects of less than 20dB as estimated by IVF but this may not be obviously apparent on the small greyscale representations. The blue and red horizontal lines denote the overall median search times for the 30 control subjects in the real-world search and Landolt C search tasks respectively.

3.4 Discussion

Searching for something is a task people do many times every day and visual search is a widely studied area in cognitive psychology (Wolfe, 1998) Some attention has been given to the idea that visual search efficiency might be useful for glaucoma detection when incorporated into a psychophysical test (Loughman et al., 2007), but visual search has not been closely studied as a means of evaluating an aspect of visual disability in glaucoma. Results from this study suggest that patients with glaucomatous visual field defects in both eyes find it more difficult to locate target objects when searching photographs of everyday scenes compared to visually healthy individuals of a similar age. In contrast, there was no significant difference in performance between patients and controls when searching images that were more 'controlled' with the Landolt C symbols task.

This difference in performance across the experiments is interesting: it might support the notion that people with glaucoma have difficulties with a task representative of something in their daily life but not when they have a similar challenge in a more controlled functional type test. Of course, finding an object in a computer displayed photograph, albeit of an everyday scene, is not the same as searching for something in real-life. Nevertheless, these results are compatible with the observation that patients with glaucoma commonly self-report difficulty with this type of task. For example, responses about difficulty searching for dropped items had the highest association with binocular visual field loss when compared to other activities in a study of a large sample of patients with glaucoma (Viswanathan et al., 1999). Likewise, in an insightful interview study on the impact of glaucoma on everyday activities, patients frequently and eloquently described the frustration they experienced when searching for things (Green et al., 2002). Moreover, Altangerel et al (Altangerel et al., 2006) directly tested the performance of glaucoma patients on different activities and identified searching for objects as one of the tasks most related to the extent of visual field loss.

Visual search is a complex task involving both foveal and peripheral vision (Ball et al., 1988). The results from this study prompt speculation that the increased average search time experienced by the patients in the photographs of everyday scenes may be partially related to an inability to sufficiently utilise prior

(Theeuwes et al., 2006) and salient information (Cave and Wolfe, 1990) in their peripheral vision due to their restricted field of view. For instance, evidence suggests that people normally integrate prior knowledge with visual properties to aid object detection (Theeuwes et al., 2006): simply put, an individual searching for a street sign, for example, will already know that signs are usually located in a certain place (on posts or at the corner of a road) and will thus apply this prior knowledge to aid their search for the object in their peripheral vision. However, the peripheral visual field defects experienced by people with glaucoma may obscure such a landmark, making it more difficult to successfully utilise their previous knowledge to locate the sign connected to it. Reduced CS also appeared to play an important part role in a patient's ability to search for real-world objects; possibly making them second guess the target. We did not measure colour vision, but one potential explanation for the difference between patients and controls could be colour recognition deficiencies in glaucoma (Austin, 1974, Kalmus et al., 1974, Pacheco-Cutillas et al., 1999); objects should appear highly salient but may not to a patient with these functional deficits. The colourful, realistic images used in this study contrast greatly from typical standard functional measurement that are acquired in the glaucoma clinic and the conjecture about colour vision deficiencies in the patients might explain some of the results.

It is interesting that average search time for patients with the 'controlled' Landolt C search task were, however, not significantly different to those average search times in the healthy controls of similar age. Perhaps the facility to integrate prior knowledge with visual properties of the 'scene' to aid object detection is more ambiguous with this type of image. The largest distance between objects in the Landolt C search task was 3° and therefore it is likely to be a somewhat simpler task for both controls and patients to locate the position of the next potential item to look at, meaning the search becomes more systematic and relies less on peripheral vision. Simply put, the everyday images might require a fuller field of view to perform the search task optimally. Likewise, the impact of prior information and saliency in the Landolt C search task, compared to the photographs of everyday scenes, is probably less. Results from other visual search experiments indicate that older adults find it more difficult to locate items when

the target is more similar to distracter stimuli (Scialfa et al., 1998). Since this study primarily involved elderly subjects in both the patients and controls, it might be expected that both groups would find the Landolt C search task equally difficult due to the lack of distinctive information that could be utilised to optimise their performance. Of course, the two tasks are not directly comparable in everything except that one comprises an unnatural scene (Landolt Cs) while the other consists of natural scenes. For example, the two tasks cannot be exactly matched for target size or contrast. Unsurprisingly there was some association between the average search times for the Landolt C search task and the search times using photographs of everyday scenes in the patient group. Still, the results simply highlight that patient performance is equivalent to age-related visually healthy subjects in a search task using optotypes, but it is worse when searching more 'natural scenarios' represented in this instance by the photographs of everyday scenes.

The patients and controls had similar age so this cannot explain the differences in search performance with the photographs of everyday scenes. All participants were required to have a corrected VA of at least 6/12 in each eye but average binocular ETDRS VA was slightly better in the controls. The difference in performance in the search task might be best explained by the differences in visual field defect or by differences in contrast sensitivity. The latter supports the belief that a decrease in contrast sensitivity in glaucoma patients may account for much of the visual disability from the condition despite normal or near normal visual acuity (Ross et al., 1984). Performing the same experiment on other visually healthy subjects but lowering the contrast of the images might be informative here. Results from multiple linear regression indicated that visual field and contrast sensitivity measurements have significant and equivalent levels of association with search times of the photographs of everyday scenes in this small patient group. A selection criterion for good general health of the participants was used but not all may have reported use of mild anti-hypertensive or statins or other commonly used drugs in an elderly population. Also, the groups were not deliberately matched for a test of cognitive ability. More trials in the experiment may have yielded better estimates of average search times, but the number was minimised to avoid fatigue effects in elderly participants.

The cases in this study are representative of patients with glaucoma in both eyes and many exhibited visual field defects that would be described as at least moderately severe. The patients did not have early stage glaucoma. For example, if any of these patients were drivers then they would be obliged to notify the Driver and Vehicle Licensing Agency to have a full binocular visual field assessment in order to examine their legal fitness to drive in the UK. The integrated visual fields provide a good estimate of the patient's central binocular field of view from the monocular results and these suggest that some of the patients would be visually disabled to the extent that they would not be legally fit to drive (Crabb et al., 2004). Inspection of the greyscales of the visual fields (monocular and IVF) when compared to individual search times (Figure 3.3) hints that the link between severity of defect and search times is an ambiguous one, although results from multiple linear regression provide some evidence of an association between the level of damage, as estimated by the MD in the best eye, with search performance. Firm conclusions about patient's visual search performance being linked to specific types of defect and stage of disease severity cannot however be inferred from these data; this awaits further investigation.

Impaired visual search performance will probably place an increased burden on the glaucomatous patient's independent lifestyle, and may be partially linked to the higher number of falls and accidents reported by these patients (Haymes et al., 2007). The main finding in this exploratory study, disclosing the difficulty patients with bilateral glaucoma have in searching for an item in a photograph of an everyday scene, should stimulate other investigations into the impact of the disease on visual search performance, including perhaps surveillance of eye movements (Crabb et al., 2010). Identification of the problems experienced by glaucoma patients when carrying out such tasks is an important step towards a better understanding of the impact of the condition in everyday life, and may prove helpful for developing future methods of disease monitoring and even rehabilitation.

3.5 Conclusion

Some patients with glaucomatous visual field defects in both eyes found it especially difficult to locate objects in photographs of everyday scenes when compared to visually healthy individuals of a similar age. However in a more controlled Landolt C search task, where stimuli are located close together, patients performed similarly to the visually healthy controls. These findings therefore suggest that searching for objects is an additional challenge that could be faced by people with glaucoma in their day-to-day life.

4 Eye movements during visual search

4.1 Introduction

As shown in chapter 1, it appears that this visual loss can have a detrimental impact on the quality of life of the patient; for instance, patients have reported that they experience problems with tasks such as reading, walking and face recognition in addition to experiencing more falls and motor vehicle accidents (Nelson et al., 2003, Jampel et al., 2002b, Haymes et al., 2007, McGwin et al., 2004). Studies have also more objectively examined the performance of patients in laboratory based simulations of a variety of 'everyday' vision-based tasks and found that patients with glaucoma displayed significant impairments in these tasks compared with people with normal vision (Ramulu et al., 2009, Kotecha et al., 2009, Szlyk et al., 2005), although studies investigating how glaucoma actually impacts visual functioning in the everyday world are generally underrepresented in the literature (Glen et al., 2011). In chapter 3 it was found that some patients' ability to locate objects in pictures of everyday scenes is compromised. In that study, it was found that patients with glaucoma were significantly slower to locate the target object in computer displayed naturalistic images, but not in a controlled task involving greyscale 'Landolt C' stimuli. These results suggested that when searching for items in real-life situations where the visual scene is more complex patients with glaucoma may not be able to rely on the same strategies as those with healthy vision. They may instead be forced to employ alternative, more time consuming techniques for perceiving the scene as a result of their visual loss. However, little is known about the underlying mechanisms and strategies that could be influencing this apparent impairment.

This chapter aims to provide further insight into the apparent deficits in visual search performance in glaucoma by investigating whether patients make different eye movements compared with individuals with healthy vision in the aforementioned search tasks. Furthermore, do any changes in eye movements influence their performance? Abnormal eye movement behaviour has been observed in patients with functional deficits as a result of other eye disorders; for

instance, evidence suggests a link between eye movements and impaired reading speed in age-related macular degeneration (AMD) (Rubin and Feely, 2009, Crossland and Rubin, 2006). Eye movement strategies have also been investigated in terms of the mobility difficulties observed in retinitis pigmentosa (RP), with patients with increasing visual field loss tending to fixate downwards or at nearby objects instead of towards their intended goal, as persons with normal vision did when walking an unfamiliar route (Turano et al., 2001). Moreover, eye movements have subsequently been applied to a rehabilitation setting, in that training the individual to alter their eye movement behaviour has been shown to lead to improvements in their task performance (Seiple et al., 2005, Pambakian et al., 2005). In terms of glaucoma, there has been very limited research; though the work presented in chapter 5 indicates that patients change their eye movements relative to healthy control subjects when viewing static naturalistic images and chapter 6 discusses dynamic driving scenes. Simulated and actual peripheral field loss has also been shown to disrupt the build-up of accurate spatial representations of the surrounding visual world (Fortenbaugh et al., 2008) and lead to more restricted scanning behaviour whilst walking, likely due to a lack of visual stimulation in the wider locations of their visual field (Vargas-Martin and Peli, 2006) which may be a factor behind the difficulties experienced by such patients.

4.2 Methods

4.2.1 Participants and system setup

The sixty participants that took part in this research are described in detail in chapter 2 and their search duration results can be found in chapter 3. The system setup and eye tracker is described in full in chapters 2 and 3. All saccades of amplitude less than 0.5° were removed so as to exclude noise within the eye movement data.

4.2.2 Experimental procedure

The methods are identical to those described in chapter 3 with the exception that the eye movements were being analysed rather than just used to confirm the subject had found the correct target. To briefly summarise: Two studies were performed, the first consisted of a selection of 18 real-world natural and urban scenes, 3 of which were used as a practice and the further 15 were shown in random order and were used in the analysis. Before each image was displayed, the target was described in text form on the screen and this was also read aloud to the patient by the experimenter. Two examples showing the image displayed, text displayed to the subjects and scan paths are shown in Figure 4.1.

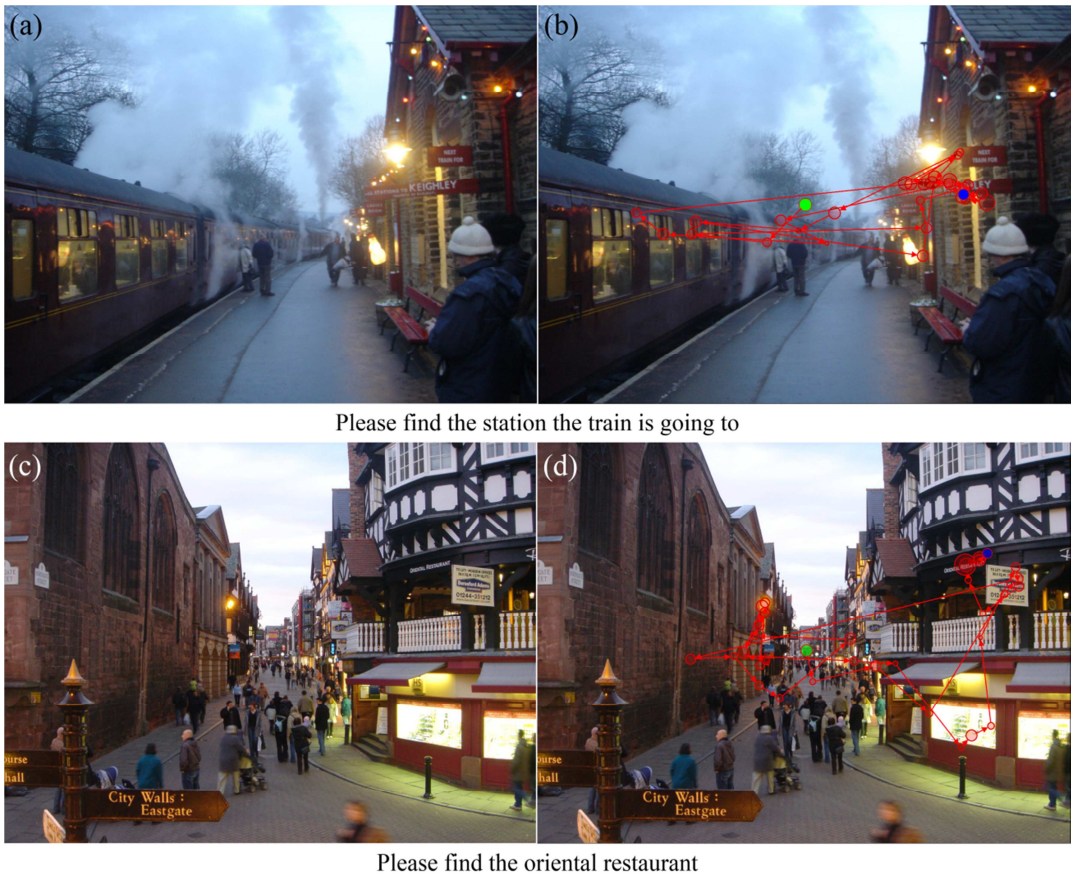


Figure 4.1: Two example scan paths by two different patients in the real-world search task. The text displayed to the participant is shown below the image. The first image (a) shows the unmodified version of the image and the patient's scan path can be seen in section (b), the green fixation point denotes the start point and the blue shows the final fixation (which is on the sign stating the station name the train is going to). The red dots are the fixations, with the size relating to the fixation duration and the lines between each dot a saccade. A different image is shown in (c) and a different patient's fixations and saccades are shown in image (d) in the same fashion as in (b). Larger versions of figure (b) and (d) can be found in appendix B.

The second study was a Landolt C search task, which consisted of one correctly oriented Landolt C and a selection of incorrectly oriented C. The target and distractor were encircled by an outer ring. There were 23 trials, 3 were practices and then the further 20 were randomly displayed and these results were analysed. Of the 20 trials analysed, 10 contained stimuli that were larger (2.07° in diameter with 30 or 50 distractors and one target) and 10 contained stimuli that were smaller in size (1.15° in diameter with 50 or 100 distractors and a single target) and in each of these trials the contrast was varied (Webber contrasts of: 9.5%, 25%, 31%, 40% and 98%). Both studies displayed the images on a 56cm CRT computer monitor using the same setup as described in chapter 2. In both studies,

prior to each image presentation (trial), the participant was asked to fixate on a cross in the middle of a grey screen. Eye movements were simultaneously monitored using the EyeLink II system (SR Research Ltd., Kanata, Ontario, Canada) and the subject's point of regard was used to confirm that the participant had found the target stimulus. The trial was stopped at the moment the participant successfully located the target item. The eye movement setup is described in more detail in chapter 2.

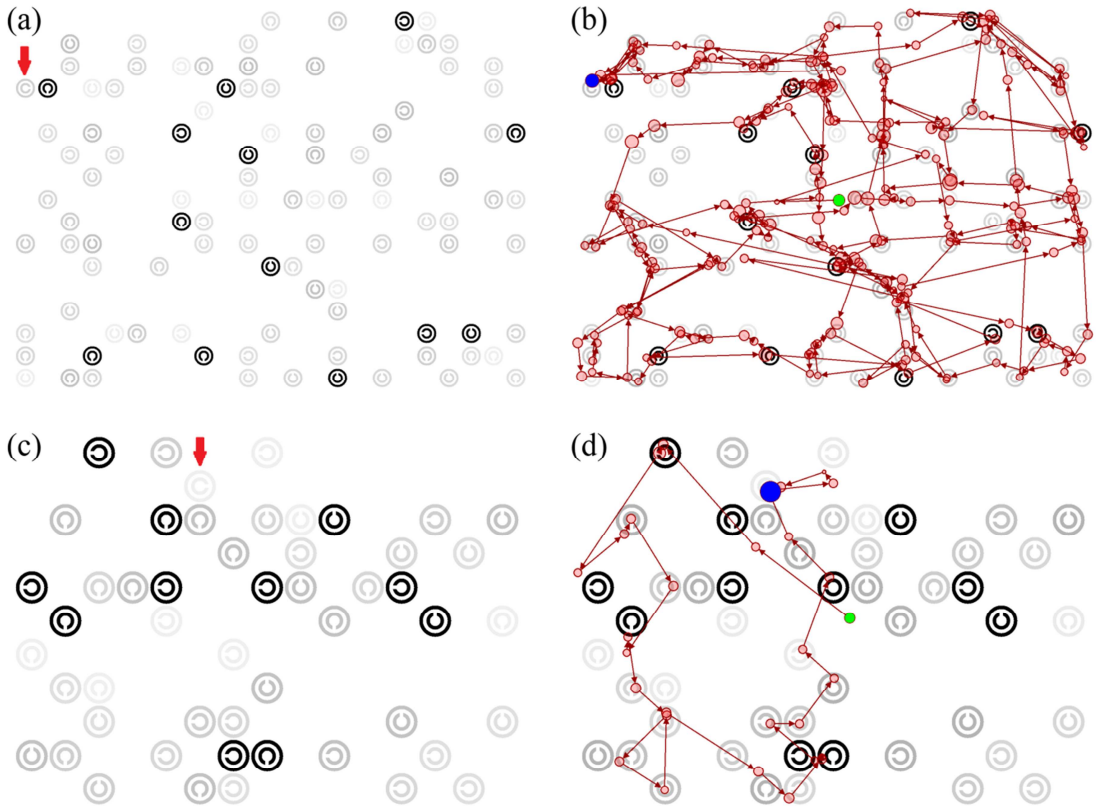


Figure 4.2: Landolt C search examples. Images (a) and (c) are the original images shown to the subjects; the targets have a red arrow beside to make them clearer to the reader. Images (b) and (d) show the fixations and saccades using the same method as in Figure 4.1. Images (a) and (b) are the 1.15° diameter and (c) and (d) are the 2.07° diameter stimuli. Larger versions of figure (b) and (d) can be found in appendix B.

Due to the exclusion of saccades less than 0.5°, as explained in section 4.2.1, 9.7% of glaucomatous and 9.5% of control data were removed in the real world search task. When investigating the Landolt C search task 6.4% of glaucomatous data and 5.1% of control data were excluded.

4.2.3 Analysis

The experimental design meant all participants viewed the same images, displayed in random order, in both studies (20 for the Landolt C and 15 for the real-world search tasks), so these were assumed to be repeat measures. A mixed two-way analysis of variance (ANOVA) (accommodating missing data by the method of median imputation) using a General Linear Model (GLM) to assess each of three different eye movement parameters (response variables). The software package SPSS 18 (IBM Corporation, Somers, NY, USA) was used to perform these statistics. In this two-way ANOVA arrangement, variation in the response variable (each eye movement parameter) was expected to be different across the images and across the participants, with the primary null hypothesis of there being no difference in the average value for the eye movement parameters between the patients and controls examined (F test on the main factor, participant group, from the ANOVA). Averages across the whole experiment (means for each eye movement parameter across all 20 and 15 images) were also calculated for each participant and were plotted to illustrate overall effects, including overall variability within groups.

In addition, univariate associations between the eye movement parameters against severity of visual field defect as measured by the Best Eye MD and severity of contrast sensitivity (PR log CS) were explored using Spearman's rho correlation coefficient in the patient group. To examine the relationship between eye movements (saccades per second and saccade amplitude) and search performance (search duration) Spearman's correlation coefficient was again used. The proportion of variation in search performance explained by these factors was explored using multiple linear regression.

4.3 Results

Each of the three eye movement parameters considered was assessed using a mixed two-way GLM ANOVA with the images (trials) representing repeated measures. The departure of the F statistic from 1 summarises the extent of a difference in the main factor (patients versus controls) and the P-value refers to the null hypothesis of no effect, or no difference, in that main factor. No obvious departure from normality was observed in any of the average response variables as assessed by the Kolmogorov-Smirnov test. The degrees of freedom were corrected using the Greenhouse-Geisser method where Mauchly's test indicated that the assumption of sphericity did not hold. On average patients had a significantly lower saccade rate (saccades/second) when compared to controls ($F_{1,58}$ = 4.1; P=0.047) and there was no significant interaction term ($F_{9,496}$ = 1.0; P=0.47; groups by image) indicating that the effect was almost always consistent across all the 15 repeat measures (trials). There was also statistical evidence that patients had longer average fixation duration compared to controls ($F_{1,58}$ = 5.8; P=0.02) with again no significant interaction term ($F_{5,270}$ = 0.3; P=0.71) meaning that the effect was consistent irrespective of the image viewed. There was no statistical evidence for a difference in the mean saccade amplitude between the groups ($F_{1,58}$ = 0.9; P=0.34).

There are no statistically significant differences in any of the eye movement parameters in the Landolt C search task when comparing the two groups (saccades per second $F_{1,58}$ = 1.8; P=0.19, saccade amplitude $F_{1,58}$ = 1.6; P=0.21 and fixation duration $F_{1,58}$ = 1.1; P=0.29).

Figure 4.3 (a, b, c) illustrates the results from the real-world search task by plotting overall mean values for the three eye movement summary measures for each participant in the experiment. The overall mean number of saccades/second per trial was 2.6 (SD: 0.4) and 2.8 (SD: 0.3) for patients and controls respectively, equating to an average reduction in saccade numbers of 6.0% (95% CI: 0.1 to 12.0%). The overall mean fixation duration (ms) was 314 (SD: 43) and 295 (SD: 27) for patients and controls, giving, as expected, an equivalent percent difference between patients and controls. The overall mean saccade amplitude (in degrees) was 4.6 (SD: 0.6) and 4.8 (SD: 0.5) for patients and controls and there was no

difference in variance between the two groups (P=0.44; F-test on variances). Figure 4.3 (d, e, f) shows the results from the Landolt C search task. The overall mean number of saccades/second per trial was 3.3 (SD: 0.4) in the patient group and 3.5 (SD: 0.3) in the control group, which gives an average reduction in saccade numbers of 5.1% (95% CI: -0.4 to 10.5%). The overall mean fixation duration (ms) was 251 (SD: 39) and 238 (SD: 23) for patients and controls, giving, as expected, an equivalent percent difference between patients and controls. The overall mean saccade amplitude (in degrees) was 4.4 (SD: 0.8) in the patients and 4.7 (SD: 0.7) for the controls.

Table 4.1 shows the relationship between the eye movement parameters investigated and severity of visual field loss (best eye MD in dB) and severity of contrast sensitivity damage (PR Log CS) in the patient group (n=30). It is interesting that in the real-world search task the only association that can be drawn up is between saccade rate and contrast sensitivity (Spearman's rho: 0.43). However in the Landolt C search task (which has no significant differences between the control subjects and patients) had good associations between BEMD and saccade amplitude (rho: 0.51) and between contrast sensitivity and saccade rate (rho: 0.51), saccade amplitude (rho: 0.53) and fixation duration (rho: -0.40). This indicates that patients with worse BEMD and contrast sensitivity make smaller saccades and lower contrast sensitivity indicates lower saccade rates along with longer fixations.

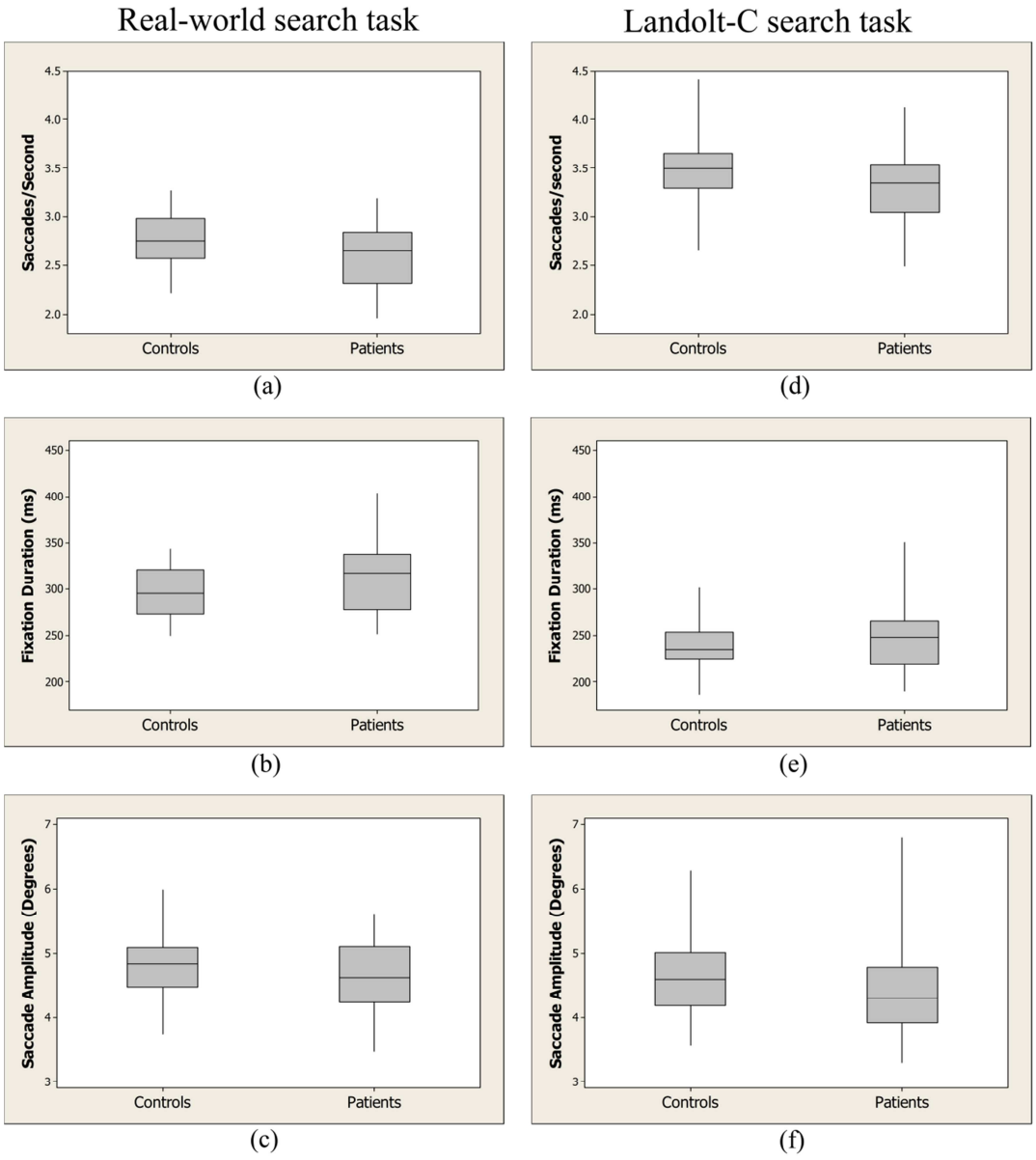


Figure 4.3: Box plots showing the results from three eye movement parameters being analysed for the two tasks. Plots (a, b, c) show the real-world search task and (d, e, f) show the Landolt C search task. There is a statistically significant difference between the controls and the patients when investigating the average number of saccades per second (a) and the fixation duration (b) during the real-world search. There is no significant difference in the average saccade amplitude in either task or the number of saccades per second and fixation duration in the Landolt C search task.

	Number of Saccades	Saccade Amplitude	Fixation duration
Real-world search BEMD	0.25 (P>0.05)	0.33 (P>0.05)	-0.07 (P>0.05)
Real-world search Contrast sensitivity	0.43 (P=0.02)	0.09 (P>0.05)	-0.30 (P>0.05)
Landolt C search BEMD	-0.07 (P>0.05)	0.51 (P=0.004)	-0.12 (P>0.05)
Landolt C search Contrast sensitivity	0.51 (P=0.004)	0.53 (P=0.003)	-0.40 (P=0.03)

Table 4.1: Spearman's rank correlation coefficient (rho) for the three eye movement parameters against severity of visual field loss (best eye MD) and severity of contrast sensitivity damage (PR Log CS) in the n=30 patients.

Table 4.2 and Figure 4.4 indicates that there exist good associations between performance and both the number of saccades and fixation duration. Stepwise multiple regression was performed to find which combination of variables produce the predictors in this model. The criteria used were that variables could be removed from the model if they caused a reduction in the r^2 value that had an associated p-value greater than 0.1. The model indicates the largest proportion of the variance in search times could be explained by a combination of both the rate at which patients perform saccades (P<0.01) and the size of those saccades (P=0.01) (multiple regression: P<0.01; R2=59%). The 5% and 95% confidence interval of the slope coefficient when performing the regression are -31.6 to -14.5 and -12.1 to -1.6 for saccade rate and saccade amplitude respectively. Fixation duration was not included in the model most probably because of its orthogonal relationship with saccade rate (indicated by its highly significant spearman's correlation [rho: -0.87]).

There are no significant eye movement predictors of search duration in the control group. No eye movement parameters appeared to predict search speed in the glaucomatous group when performing the Landolt C search task (P>0.05), but in the control group there appeared to be a mild link between saccades rate and search time. Table 4.2 shows these results in further detail for both studies and Figure 4.4 and Figure 4.5 shows the scatter plots relating to the three eye movement parameters in the real-world and Landolt C search tasks respectively.

	Saccades	Saccade Amplitude	Fixation duration
Controls Real-world search time	-0.19 (P>0.05)	-0.05 (P>0.05)	0.13 (P>0.05)
Controls Landolt C search time	-0.38 (P=0.04)	0.10 (P>0.05)	0.21 (P>0.05)
Real-world search time	-0.68 (P<0.01)	-0.34 (P>0.05)	0.52 (P<0.01)
Landolt C search time	-0.26 (P>0.05)	-0.26 (P>0.05)	0.21 (P>0.05)

Table 4.2: Spearman's rank correlation coefficient (rho) for the three eye movement parameters against search times in the two tasks for n=30 controls and n=30 patients.

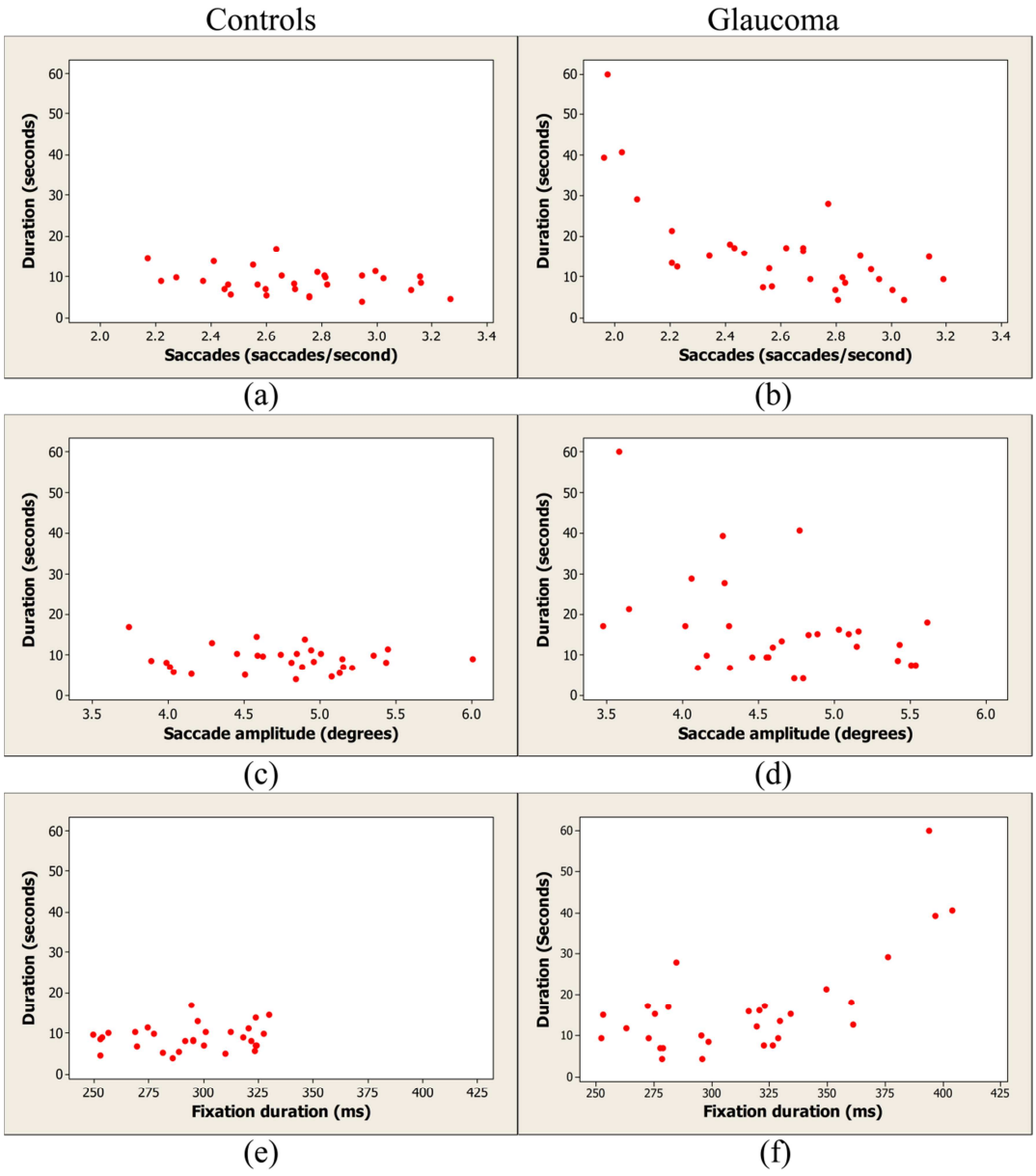


Figure 4.4: Duration to find the target within the image compared to saccades per second (a, b), fixation duration (c, d) and saccade amplitude (e, f) in the real-world search task for the n=30 controls and n=30 patients respectively.

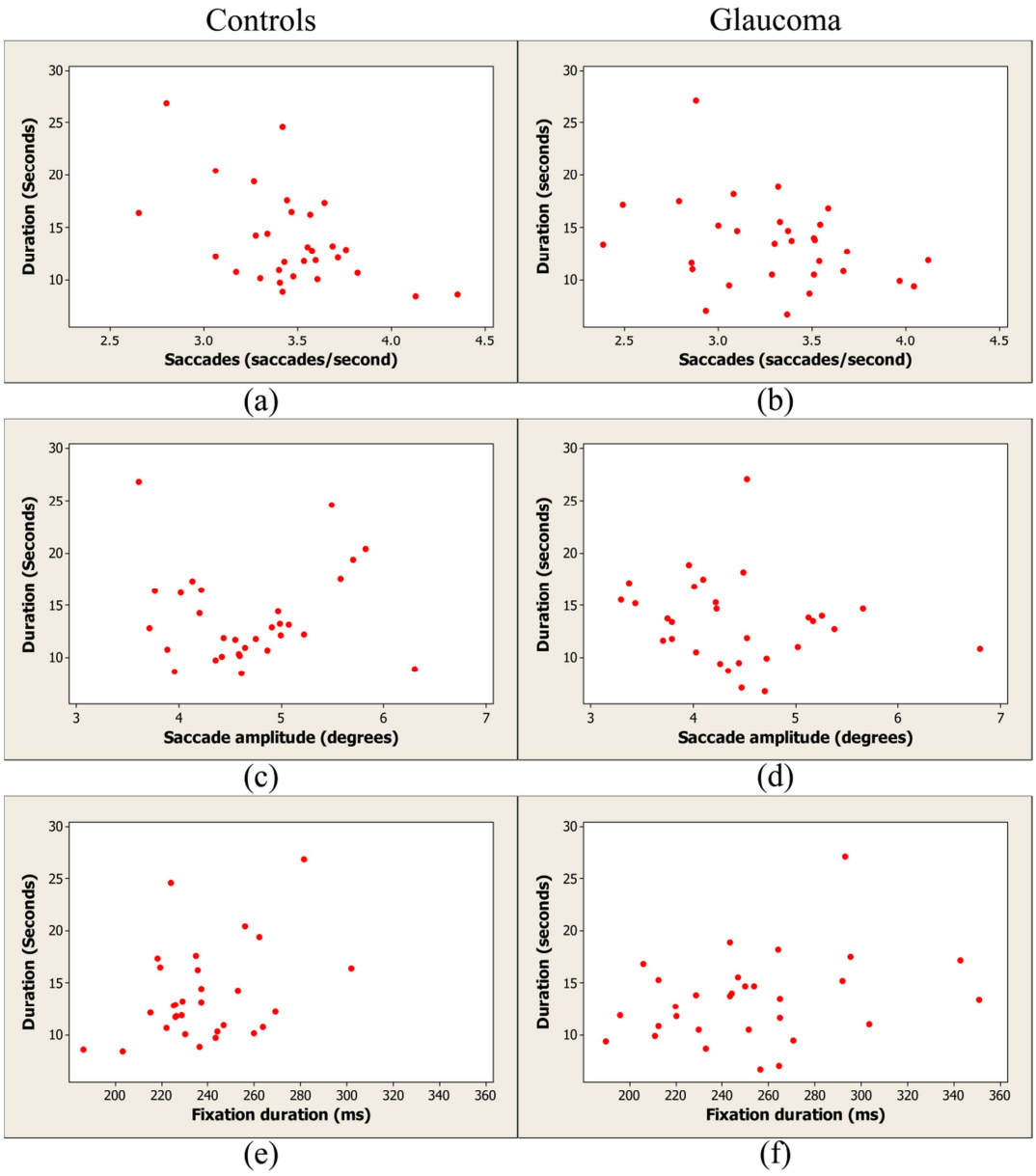


Figure 4.5 : Duration to find the target within the image compared to saccades per second (a, b), fixation duration (c, d) and saccade amplitude (e, f) in the Landolt C task for the n=30 controls and n=30 patients respectively.

4.4 Discussion

Searching for objects is a task that is conducted effortlessly many times a day by the average individual as they go about their day-to-day life. For instance, looking for one's car keys, food shopping and finding the correct money to pay for said items in the supermarket will all require the swift detection of the 'target' object from amongst an array of irrelevant 'distractor' items. It appears that visual loss as a result of glaucoma impairs the individual's ability to successfully conduct this 'everyday' activity, as reported in chapter 3, patients with glaucoma were slower to locate target items in naturalistic images than controls of a similar age with healthy vision. The current research adds to this finding, in that it was discovered that patients also produced different eye movement behaviour when searching for objects in these same 'real-world' images. More specifically, it was found that the patients produced significantly fewer saccades per second, and therefore fixated for longer, than the control subjects. It is well documented that peripheral vision plays a key role in eye movement behaviour, in that it is necessary for detecting the objects of most functional importance so that a subsequent saccade can be made towards it, bringing the item onto the fovea for more detailed inspection (Hooge and Erkelens, 1999). Therefore the finding that patients produced fewer saccades than the controls may reflect the degradation of peripheral vision as a result of glaucomatous damage, meaning the patient struggles to detect the most salient items around them. Instead, the patient may be forced to employ more erratic and inefficient scanning strategies to locate the object of interest. By producing fewer saccades, the patients also by default fixated on visual information for a significantly longer period of time. It may be that increased fixation duration is the patient's way of compensating for their visual loss, as it allows them to concentrate for longer on certain items of information. Research suggests that normally individuals will adapt the duration of their fixations in accordance with how difficult the visual task is (Rayner, 2009a), with an increased fixation duration generally improving performance in more difficult search tasks (Watson et al., 2010). When the vision of normal subjects is obstructed with an artificial scotoma, however, it appears that whilst this strategy is still employed, it is no longer optimal (Cornelissen et al., 2005). The employment of a similar eye movement strategy by individuals with glaucoma may therefore explain why patients were

previously slower to detect the target objects than the controls with full visual fields, as the loss of vision occurring as a result of the disease affects the quality of scene perception and the visual system's subsequent ability to select the most appropriate eye movement behaviour. At the moment these assumptions need to be researched more fully, as there are solid associations between CS and saccade rate. Further research needs to separate out eye movement differences caused by glaucomatous CS loss and glaucomatous VF degradation.

Whilst patients displayed impairments with search behaviour when viewing naturalistic images, the eye movement behaviour of the patients during the Landolt-C search task was not any different on average to that employed by the controls. This finding echoes the results from the previous chapter that indicated that despite being slower to find objects in naturalistic scenes, the patients performed similarly to controls when the situation was more controlled. The reason for these conflicting results may reflect the characteristics of the images used and how glaucomatous visual field loss restricts the important regions of the image. In the Landolt-C search task the target and distractors are similar and placed relatively close together. The role of peripheral vision for selecting the most salient items will therefore be minimal and the individual will likely benefit by taking a systematic approach to viewing the images, directing their saccades to each item in a controlled and purposeful manner. Whether the patient has defects in their peripheral vision will thus be largely irrelevant, and only very central visual field defects are likely to affect the task. On the contrary, the real-world images are much more complex and the areas of interest are often further apart and less predictable. The individual will be much more reliant on their peripheral vision to select the most important items to bring onto the fovea via a saccade. A VF defect in any location is thus more likely to affect the efficiency of the search task, even in the case of peripheral defects, as the full picture cannot be seen and therefore the most useful item may be unavailable (Mackworth and Morandi, 1967).

Subsequent correlational analyses were used to provide further insight as to which visual characteristics may be most important in dictating the eye movement behaviour of the patients during the search tasks. It was found that contrast

sensitivity was the factor that was most associated with all three eye movement parameters in the more naturalistic search task. CS loss often coincides with glaucomatous damage (Hawkins et al., 2003, Stamper, 1989) and so its influence on the eye movement strategies used by the patients is not all that surprising. Stimulus contrast is an important visual property for dictating eye movement behaviour, with evidence suggesting that stimuli with higher contrast are more likely to be selected for fixation (Acik et al., 2009). A patient with diminished contrast sensitivity will subsequently be less likely to detect such key items and will thus likely require more time to build up a detailed representation of the visual scene. Worsening contrast sensitivity loss was also associated with the different eye movement behaviour produced by people with glaucoma when passively viewing similar naturalistic scenes, thus reinforcing its importance in dictating how the glaucomatous patient may view the world (see chapter 7). However, although contrast sensitivity was related to eye movements, there was no significant relationship between best eye MD and eye movements during the naturalistic search task, which is somewhat surprising given the previously discussed role a wide visual field should have when searching for objects. The lack of relationship here may perhaps reflect the simple reality that MD alone is not a sufficient measure for encapsulating the full extent of the glaucomatous damage and loss. Visual field data, for example, is inherently noisy between measurements in primary open-angle glaucoma (Heijl et al., 1989). The visual fields included in the current study were recorded on only one occasion, and it is possible that the values used in the current analysis would not necessarily reflect those given had the data been recorded on a different date or time. Furthermore, HFA 24-2 visual fields are recorded separately in each eye, and yet the current tasks were conducted using both eyes as would be the case when searching for objects in real life. A measure of the binocular visual field would likely be most appropriate for this type of research but unfortunately there is not an entirely suitable test in existence at present. The suprathreshold Esterman visual field gives an idea of whether a patient can see the target within that region of their binocular vision, but does not give us an idea of the level of light sensitivity within that region of their visual field as the HFA VFs do (Esterman, 1967, Esterman, 1982). We feel the mean deviation in the best eye is therefore the most practical simulation of real life

vision that is available, with the integrated visual field also serving as a simple simulation, but not a direct measurement, of the patients binocular sensitivity (Crabb et al., 2004, Crabb and Viswanathan, 2005). However this method does not take into account which parts of the visual field are most affected in real-life, which is likely to be an important factor for understanding eye movement behaviour. Several studies involve the use of simulated defects, which are advantageous in that it is possible to exert control over the size and location of defect. However, artificial scotomas are not truly reflective of the experiences of real life people with glaucoma who have visual loss that is far less predictable, therefore complicating the task of determining the influence of such VF loss on eye movement behaviour. The relationship between defect location and eye movements during visual search should be a subject of future research in the context of the everyday functioning of patients with glaucoma.

Nevertheless, although there was no significant difference between the eye movements of the patients and controls on average during the Landolt-C search task, the correlational analyses revealed that saccade amplitude was actually modestly correlated with BEMD in this task, with the patients with a worst BEMD appearing to make smaller saccades than those with better BEMD. Patients with a low MD value in their best eye are likely to have a large amount of visual field damage which will most probably impinge upon central, as well as peripheral parts of the visual field. Given that central visual loss will likely be more debilitating during the controlled task, where the physically similar targets and distracters are separated by only a small margin of around 3° and a wide field of view serves little purpose in the initiation of saccades, it may be that those patients with more central loss are making small compensation saccades as is the case in AMD, a disease characterised by central scotomas (Bellmann et al., 2004, Crossland and Rubin, 2002). This effect is however not likely to have been strong enough to have influenced the results once the data for all patients was averaged. Furthermore, the decrease in saccade amplitude may also be a by-product of the nature of the stimuli in this task, whereby properties such as stimulus contrast and the number of distracters were manipulated. For instance, decreasing stimulus contrast has been shown to lead to the production of smaller saccades (Näsänen et al., 2001).

Contrast sensitivity was significantly correlated with the three types of eye movement in the search task involving controlled Landolt C stimuli, but it is likely that diminished contrast sensitivity as a result of glaucoma would be even more detrimental for those trials where the target was a stimulus of low contrast anyway. In hindsight it would have been beneficial to investigate in more detail the relationship between the stimulus properties and the eye movement strategies used by the patients versus the controls to determine whether this was indeed the case. However, unfortunately the design of the study did not allow for this as there were unequal numbers of trials representative of each of the stimulus property types, a feature we accept to be one of the main limitations of the current work.

Correlational analyses between eye movements and search times revealed that the eye movements produced in the naturalistic search task, and to a lesser extent in the controlled Landolt C task, were linked to how long the patient took to locate the target item. For instance, the fewer saccades made by a patient per second, the longer it took them to find the target. On the other hand, there was not any real relationship between eye movement strategies and search performance in the control subjects. The convincing relationships between eye movements and search times reported here provide important evidence that the compensatory eye movement strategies used by patients with glaucoma may underlie some of the visual disabilities, in this case searching for objects, that are displayed by many patients as a result of the disease and the strategy the patient chooses can influence how well they are able to deal with their visual loss. Furthermore, these findings may subsequently hint at a potential rehabilitation method that could teach the patient to view the visual scene differently in an attempt to improve their functional performance. For instance, it was found that by training patients with AMD to make increasingly large eye movements in reading tasks that gradually increased in difficulty throughout an 8 week period eventually lead to improvements in reading speed (Seiple et al., 2005). Also, training individuals with hemianopia to make larger saccades in their blind regions has been shown to increase the field of view for visual search and subsequently improve performance (Kerkhoff et al., 1992, Zihl, 1988). It may be that encouraging certain people with glaucoma to perhaps look around an image more frequently in addition to making

wider eye movements could increase their chance of finding objects more quickly and therefore help compensate for their field loss, although this should be the subject of a more focused and purposely designed investigation.

Whilst this study provides promising evidence that the eye movements of people with glaucoma change relative to healthy controls when searching for objects in real-world scenes, it should be remembered that these images were static and therefore not entirely reflective of the more fast-paced and changeable nature of the real world. The finding that patients produced different eye movements when searching for objects in less predictable naturalistic images, but not in a grey scale and generally more controlled laboratory task, nevertheless highlights the importance of taking a more real-world perspective when considering how glaucoma actually manifests itself as the individual goes about their daily life outside of the clinic. In future studies perhaps gaze could be monitored as the patient searches for real-life objects within a controlled normal environment to further determine how patients may carry out this task in their normal lives. In the meantime, this study provides an important next step into our understanding of how glaucoma actually manifests itself as the patient goes about their normal activities.

4.5 Conclusions

This patient group exhibited an average of 2.6 saccades/second that was significantly lower than that exhibited by a control group of age-related visually healthy people (2.8 saccades/second) when searching for objects in naturalistic images. This in turn meant the patient group performed longer fixations in this task. It must be noted that the size of this reduction in saccade rate is small (6%) and there is a large amount of variability. There was no difference in the average eye movement behaviour of the patients compared with the controls in the more controlled search task involving Landolt-C stimuli. These changes in eye movements appear to be related to their search performance and therefore give an interesting insight into why patients with worsening glaucoma appear to be worse at the real-world search task. The lower a glaucomatous patient's saccade rate the worse they are likely to perform in these tasks, which begs the question: Would encouraging people with glaucoma to change their saccade rate improve their performance at these search tasks? This research in the meantime further increases our understanding of the visual functioning of people with glaucoma in their everyday lives.

5 Eye movements of people with glaucoma when passively viewing images

5.1 Introduction

As introduced previously, it is important to consider how any measured visual loss impacts the individual in their daily life beyond the clinic. Studies that objectively measure the patient's performance in surrogates of vision-based tasks help quantify complaints made by patients and have revealed that patients display difficulties in many everyday tasks. However, little is known about the underlying mechanisms influencing these impairments. Chapter 4 suggested that important insight for this may lie in patients' eye movements, and how they may differ from visually healthy individuals. Efficient eye movements are a necessity for successful everyday visual functioning, by allowing the individual to scan available visual information before selecting the objects of most functional importance and bringing them onto the fovea for more detailed analysis. A finding that patients with eye disease move their eyes differently to visually healthy individuals could therefore help underpin the nature of the functional impairment. The link between eye movements and visual functioning has already received some clinical interest in amblyopia (Kanonidou et al., 2010), retinitis pigmentosa (Turano et al., 2001) and age-related macular degeneration (AMD) (Bullimore and Bailey, 1995). Individuals with contrast sensitivity loss were also found to produce abnormal eye movement behaviour as they manoeuvred complex routes through their natural environment (Vivekananda-Schmidt et al., 2004). Furthermore, the potential of such eye movement behaviour research with regards to the development of future low-vision rehabilitation strategies is beginning to be recognised (Seiple et al., 2005). With regards to glaucoma, chapter 4 showed that patients appeared to make different eye movements when performing visual search within real-world images. Chapter 6 discusses the finding that some patients produced different eye movement behaviour when viewing films of road and traffic scenes filmed from the

perspective of a driver compared with visually healthy individuals of a similar age. This provides some evidence to support previous research findings that individuals with more severe peripheral visual field defects tend to make more fixations, more errors and take longer to find objects than control subjects (Coeckelbergh et al., 2002). Little is known regarding the impact of glaucomatous visual field loss on eye movement behaviour in other visual scenarios. Evidence suggests that eye movements can be driven by the nature and complexity of the task (Andrews and Coppola, 1999, Rayner, 2009a, Henderson, 2003, Bertera and Rayner, 2000) and as such, it is of worth to consider the eye movement behaviour produced in a variety of naturalistic situations in order to gain a wider insight into the functioning of those with visual field loss.

The principal aim of this chapter is to use eye tracking to examine the hypothesis that patients with bilateral glaucomatous field defects exhibit significant differences in eye movement characteristics as compared to age-related healthy control subjects when naturally viewing a series of images of everyday scenes. The results should provide further insight into the nature of compensatory mechanisms used by people with glaucoma when perceiving the world around them, which could in turn pave the way for additional educational and management strategies.

5.2 Methods

5.2.1 Participants and system setup

The participants that took part and system setup for this study are described in chapter 2. All saccades of amplitude less than 0.5° were removed so as to exclude noise within the eye movement data; 2.8% of the patient data and 2.7% of the control eye movement data on average were consequently removed.

5.2.2 Procedure

A slide-show of 28 images was shown to each participant. The images were presented on the system described in chapter 2. The images were photographs of natural or urban scenes taken using the same camera (Sony DSC-T1, Sony Corporation, Tokyo, Japan) and were presented in random order at a resolution of 1600 x 1200. Each image within the slide-show was displayed for exactly 3.2 seconds. Every participant was given the following instruction before starting the study: "Please view these images as you would a slide show of photographs, like if you are viewing a photo album. You can move your eyes around as much as you like". They were invited to comment on the pictures during the breaks between each image presentation, and were encouraged to offer an opinion about each photograph such as whether they found it pleasant or recognised the location at which the photograph was taken. This was to ensure that the participants were actually viewing the images, but still allowed for the existence of a 'passive' component in that they were able to view any part of the image that they wished and did not feel that they were being 'tested'. Examples of three of the images with superimposed eye movement data (scanpaths) for three patients and three controls are shown in Figure 5.1.

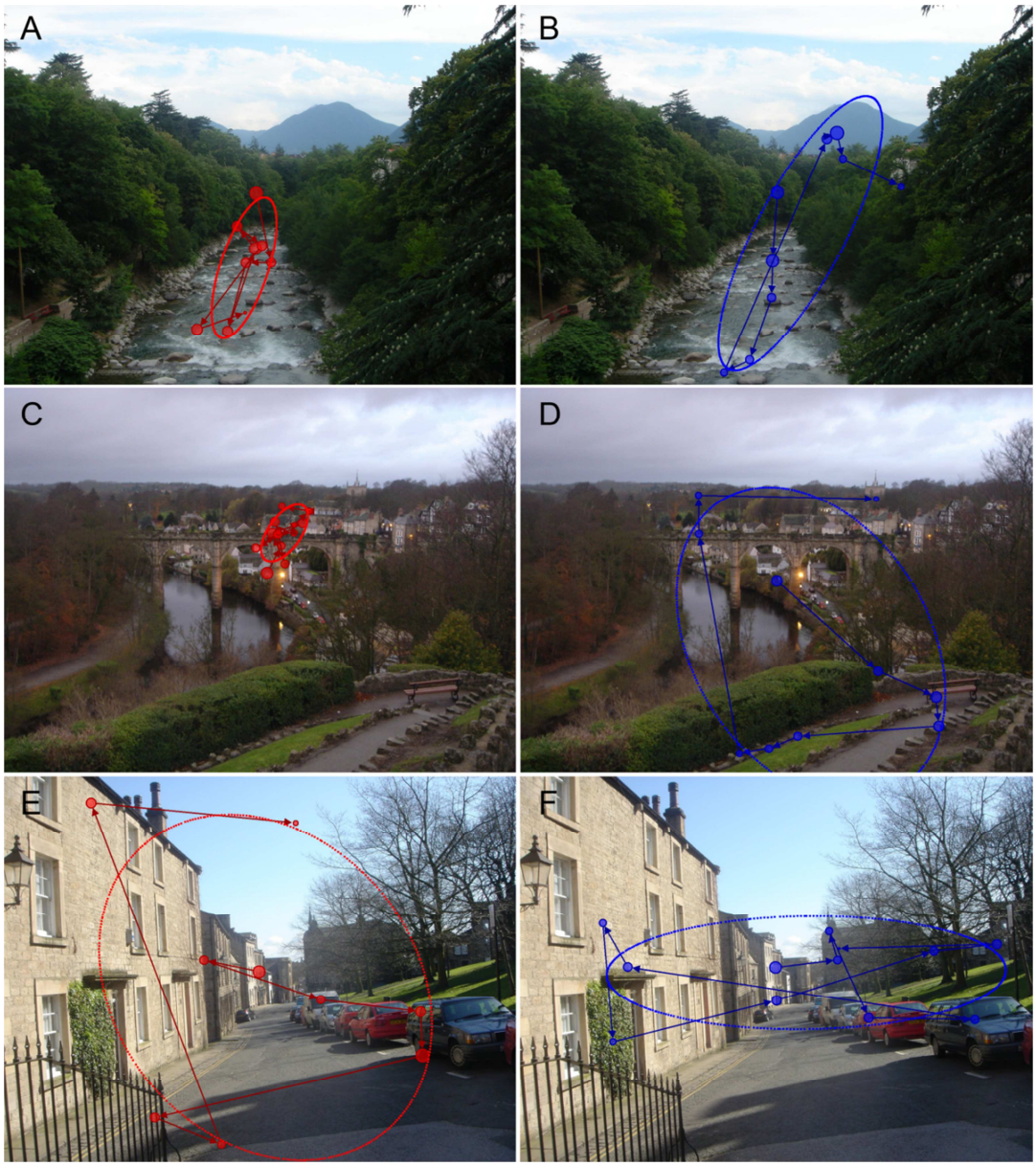


Figure 5.1: Images A, C and E show three of the images (out of 28) with superimposed scanpaths of eye movements from three of the glaucoma patients. Images B, D, F are the same images showing different control subjects viewing the same images. The dots represent the location of fixations, with the size of the dot representative of the fixation duration. The saccades are represented by the connecting lines and the bivariate contour ellipse (BCE) is shown encompassing approximately 68% of the individual's viewing area calculated, in this instance, for the single image.

5.2.3 Primary analysis

The eye tracker automatically extracts and records a number of eye movement parameters. For this study, number of saccades per second per trial, average fixation duration (ms) per trial and average saccade amplitude (degrees) per trial were considered. These summary eye movement parameters were calculated for each image as viewed by each participant.

The experimental design meant all participants viewed the same 28 images, albeit in random order, so these were assumed to be repeat measures. A General Linear Model (GLM) was used to perform a mixed two-way analysis of variance (ANOVA) (accommodating missing data by the method of median imputation) to assess each of three different eye movement parameters (response variables) using the statistical software package SPSS 18 (IBM Corporation, Somers, NY, USA). In this two-way ANOVA arrangement, variation in the response variable (each eye movement parameter) was expected to be different across the images and across the participants, with the null hypothesis of real interest being no difference in the average value for the eye movement parameters between the patients and controls examined (F test on the main factor, participant group, from the ANOVA). Averages across the whole experiment (means for each eye movement parameter across all 28 images) were also calculated for each participant and were plotted to illustrate overall effects, including overall variability within groups.

In addition, univariate associations between the eye movement parameters against severity of visual field defect as measured by the Best Eye MD (the mean deviation of the better eye 24-2 visual field) and severity of contrast sensitivity (PR log CS) were explored using Spearman's correlation coefficient in the patient group alone. As a consequence of the 'real world' nature of the study, monocular visual fields for the patients were also merged to form a binocular integrated visual field (IVF) for every patient. This method has been previously used and validated in the context of disability produced by visual field loss (Crabb and Viswanathan, 2005, Crabb et al., 2004) and arguably helps represent the link between loss of vision and behaviour in an everyday environment without the use of additional binocular VF testing. Greyscale representations of these binocular integrated visual field plots were directly compared to the BCEA for each patient.

5.2.4 Secondary analysis

In order to assess the size of the average viewing area for an individual across the slide-show, all fixations (point of regards) were extracted from the software for each participant across all 28 images. Then, to quantify the spatial coincidence of the point of regard location for each participant, the best-fit bivariate contour ellipse (BCE) of the points was calculated. The BCE area has been previously used to quantify fixation eye movement stability in patients with macular degeneration (Crossland and Rubin, 2002, Bellmann et al., 2004, González et al., 2006) and to quantify viewing areas for subjects as they watch movies (Goldstein et al., 2007, Crabb et al., 2010). In short, the centre of the BCE represents the mean 'point of regard', with the spatial extent of the ellipse being one standard deviation from this centre along two principal axes, theoretically affording 'coverage' of approximately 68% of the 'point of regard' locations. The BCE area (BCEA in degrees squared) therefore provides a summary measure of the spatial extent of a participant's gaze over the entire set of images. These values are then compared between groups to examine the hypothesis that patients may or may not have a more restricted viewing area compared to controls. Univariate associations between BCEA and best eye MD, PR log CS and IVF were also explored.

BCEA provides a summary of the spatial extent of the observer's fixations over the entire set of images but it does not represent the regions of interest that the observer focussed on. The next secondary analyses attempted to determine if some of the patients failed to look at parts of the image that were typically viewed by the visually healthy controls. This required a novel analysis and the development of a bespoke computer program in C#. For each of the 28 images, every fixation made by the visually healthy control subjects was plotted on a grid of the same size as the image (1600 by 1200 pixels). Each fixation was assumed to subtend a diameter of 1.2 degrees (the size of the foveola) and these were represented on the grid. This leads to a map where each and every pixel is represented by dichotomous values as 'seen' or 'not seen'. 'Not seen' would mean that pixel would never be covered by any of the control subjects' (n=30) fixations. The next step involved consideration of the fixations made by each of the individual patients in relation to this map. For each patient, the program records the percentage of fixations that fall

within the regions of interest generated by the sample of control subjects. A low value for this metric would indicate that the patient has fixated in areas of the image that none of the control subjects would have fixated on. The computer program produces a visualization of the normal observer or region of interest map. Examples of these are shown in Figure 5.2. The darker, semi-transparent region represents the area that no control subjects viewed, and the fully transparent regions are where at least one of the control subjects fixated on something that was of interest. Fixations made by two people with glaucoma for the two images in Figure 5.2 (A, C) are displayed as green and red dots in Figure 5.2 (B, D). Many of the fixations from these patients are not in the region of interest generated by the controls. A summary measure of failure to fixate on regions of interest from the control map was calculated across the entire image set for each patient. These secondary analyses would then allow a test of the hypothesis that this 'unusual' viewing pattern would be more apparent in patients with worse VF defect and worse CS. This was examined by looking at associations between the metric from the analysis and Best eye MD and CS. This novel analysis therefore gives an idea about whether patients are more likely to look 'outside' of the areas of the image chosen for fixation by normally sighted individuals.

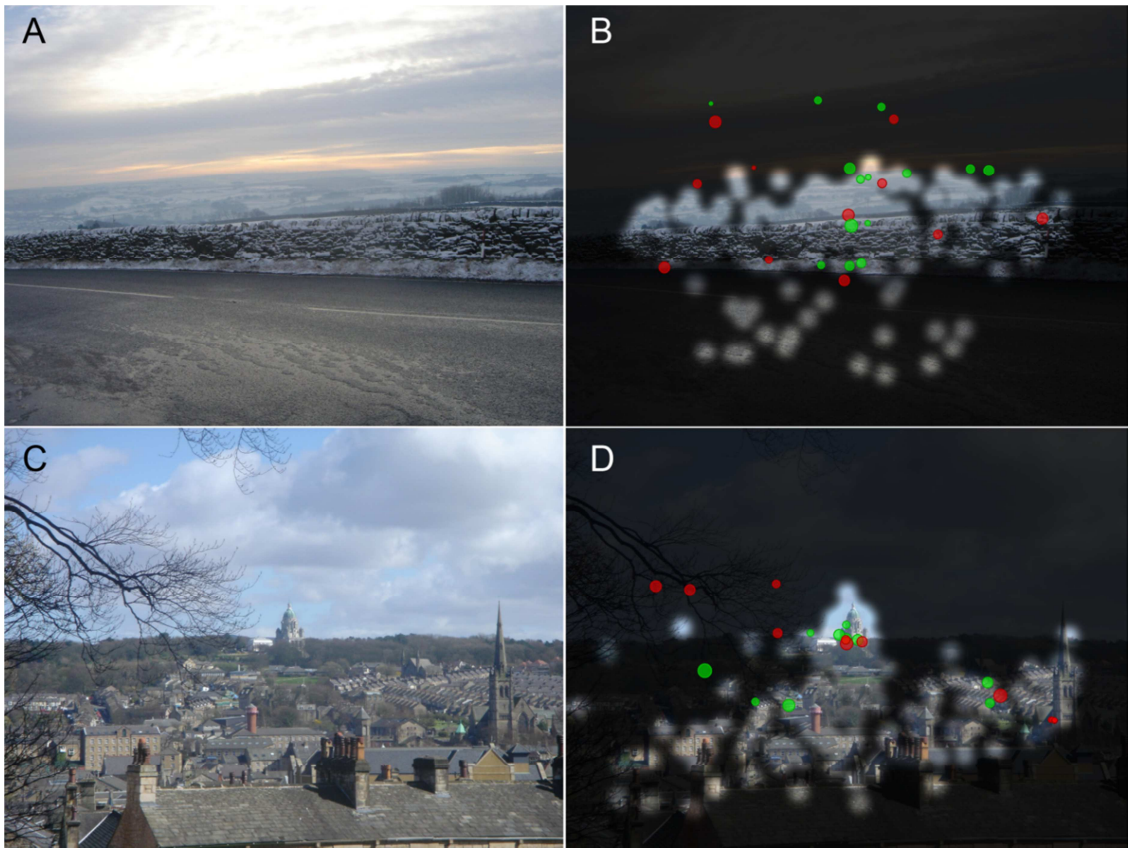


Figure 5.2: Images A and C show original images and B and D show the control 'region of interest' (generated by the fixations of the 30 controls) superimposed as the transparent regions of the image. If no control views a region the area is darkened. The fixations of two different patients (represented by the red and green dots respectively) are displayed in image B and D: many of the fixations made by these patients fall in areas of the image that were never viewed by any of the 30 age-matched controls.

5.3 Results

5.3.1 Primary results

Each of the eye movement parameters considered was assessed using a mixed two-way GLM ANOVA with the images (trials) representing repeated measures. The departure of the F statistic from 1 summarises the extent of a difference in the main factor (patients versus controls) and the P-value refers to the null hypothesis of no effect, or no difference, in that main factor. No obvious departure from normality was observed in any of the average response variables as assessed by the Kolmogorov-Smirnov test. In the case where Mauchly's test indicated that the assumption of sphericity did not hold, degrees of freedom were corrected using the Greenhouse-Geisser method. There was statistical evidence that on average patients made fewer saccades per second when compared to controls ($F_{1,58}$=6.2; P=0.016) and there was no significant interaction term ($F_{16,931}$=1.6; P=0.07; groups by image) meaning that the effect was almost always consistent across all the 28 repeat measures (trials). Following this, as would be expected, there was also statistical evidence that patients had longer average fixation duration compared to controls ($F_{1,58}$=8.1; P=0.006) with again no significant interaction term ($F_{5,270}$=1.4; P=0.23) meaning that the effect was consistent irrespective of the image viewed. There was, however, no statistical evidence for a difference in the mean saccade amplitude between the groups ($F_{1,58}$=2.3; P=0.14).

Figure 5.3 (a, b, c) illustrates the results by plotting overall mean values for the three eye movement summary measures for each participant in the experiment. The overall mean number of saccades/second per trial (each lasting 3.2 seconds) was 3.1 (SD: 0.4) and 3.3 (SD: 0.3) for patients and controls respectively; an average reduction in saccade numbers of 6.7% (95% CI: 2.6 to 10.8%). The overall mean fixation duration (ms) was 297 (SD: 52) and 265 (SD: 35) for patients and controls, giving, as expected, an equivalent percent difference between patients and controls. The overall mean saccade amplitude (in degrees) was 5.4 (SD: 1.5) and 5.8 (SD: 0.8) for patients and controls. Whilst the ANOVA indicated no significant difference in the average values for saccade amplitude it is clear from Figure 5.3 (c) that there was a greater spread and variation in the between-person

saccade amplitude parameter for the patients compared to the controls; this effect was statistically significant (P=0.001; F-test on variances).

Results from the exploratory univariate analysis of association between the eye movement parameters and severity of visual field loss (best eye MD in dB) and severity of contrast sensitivity damage (PR Log CS) in the patient group (n=30) are shown in

Table 5.1. There is no evidence of any statistically significant correlations, suggesting that level of visual field damage or level of contrast sensitivity impairment is not associated with the eye movement parameters.

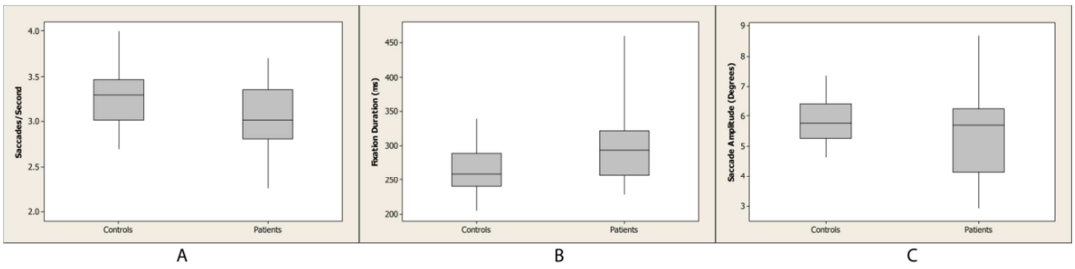


Figure 5.3: Boxplots showing average number of saccades (A), fixation duration (B) and saccade amplitude (C) for the controls and patients (whiskers on plots are set at the minimum and maximum values). The average number of saccades is decreased in the patient group. Although the average saccade amplitude is similar in both groups, the between-person variability (illustrated by the width of the boxes) is significantly larger in the patients compared to the controls.

5.3.2 Secondary results

The BCEA summarises the magnitude of the overall viewing region for a participant across all the images. The mean BCEA was 317 (SD: 89) and 244 (SD: 100) degrees squared for the controls and the patients respectively. Therefore, the average BCEA for the patients was 23% smaller than the average BCEA for the controls (95% CI: 11 to 35%) and this difference was highly significant (P=0.004; two-sample t-test). Results for the people with glaucoma and control subjects can be viewed in Figure 5.4. Results from the exploratory univariate analysis of association between the BCEA and severity of visual field loss (best eye MD in dB) and severity of contrast sensitivity damage (PR Log CS) in the patient group (n=30) are shown in

Table 5.1. There was no evidence of any statistically significant correlations, suggesting that level of visual field damage or level of contrast sensitivity impairment is not associated with the size of BCEA in this group of patients.

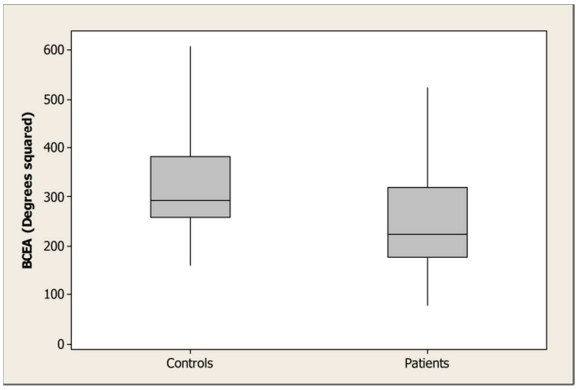


Figure 5.4: Boxplots showing overall bivariate contour ellipse area (BCEA in degrees squared) for the patients and the controls. The patients tend to view a more restricted region of the images when compared to the controls.

However, when investigating the number of fixations viewed within the control region there appears to be some association with MD which is close to statistical significance (Spearman's rho: 0.35; p=0.06) and contrast sensitivity (rho: 0.39; p<0.05). Scatterplots for these two results are shown in Figure 5.5. This finding suggests that those patients with a worsening MD in the best eye and a decline in contrast sensitivity are more likely to spend time looking at different regions of the image than the controls.

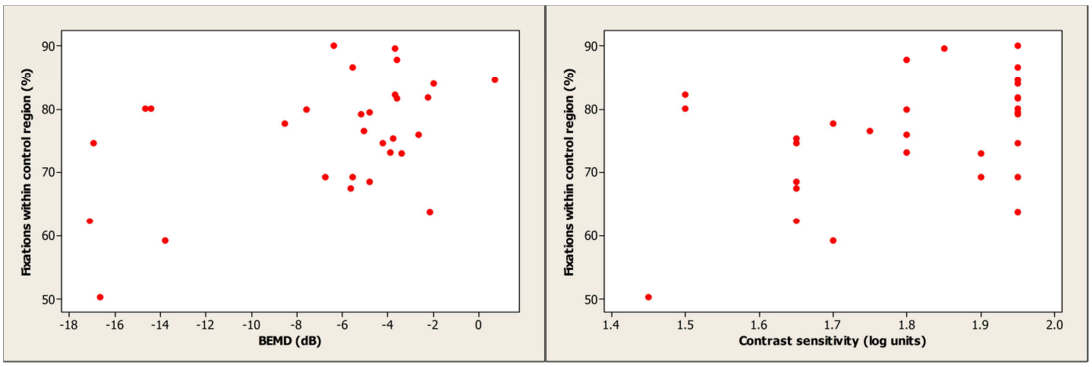


Figure 5.5: Scatter plots showing the relationship between the percentage of fixations made by the patients within the control 'region of interest' against best eye MD and contrast sensitivity.

	Number of Saccades	Saccade Amplitude	Fixation Duration	BCEA	Fixations within control region
BE MD	0.01	0.05	0.01	-0.10	0.35
PR Log CS	0.17	-0.15	-0.20	-0.24	0.39

Table 5.1: Spearman's rank correlation coefficient (rho) for the three eye movement parameters, BCEA and saccades within control region against severity of visual field loss (best eye MD) and severity of contrast sensitivity damage (PR Log CS) in the n=30 patients.

Figure 5.6 shows greyscale representations of each patient's central binocular integrated visual field (IVF). These binocular VFs cover field of view of about 20º (being composed of monocular 24-2 HFA VFs) and the scaled BCEA for each patient is superimposed on each VF to give an idea of how this varies by individual. Summary measures for the eye movement parameters are given for each patient too.

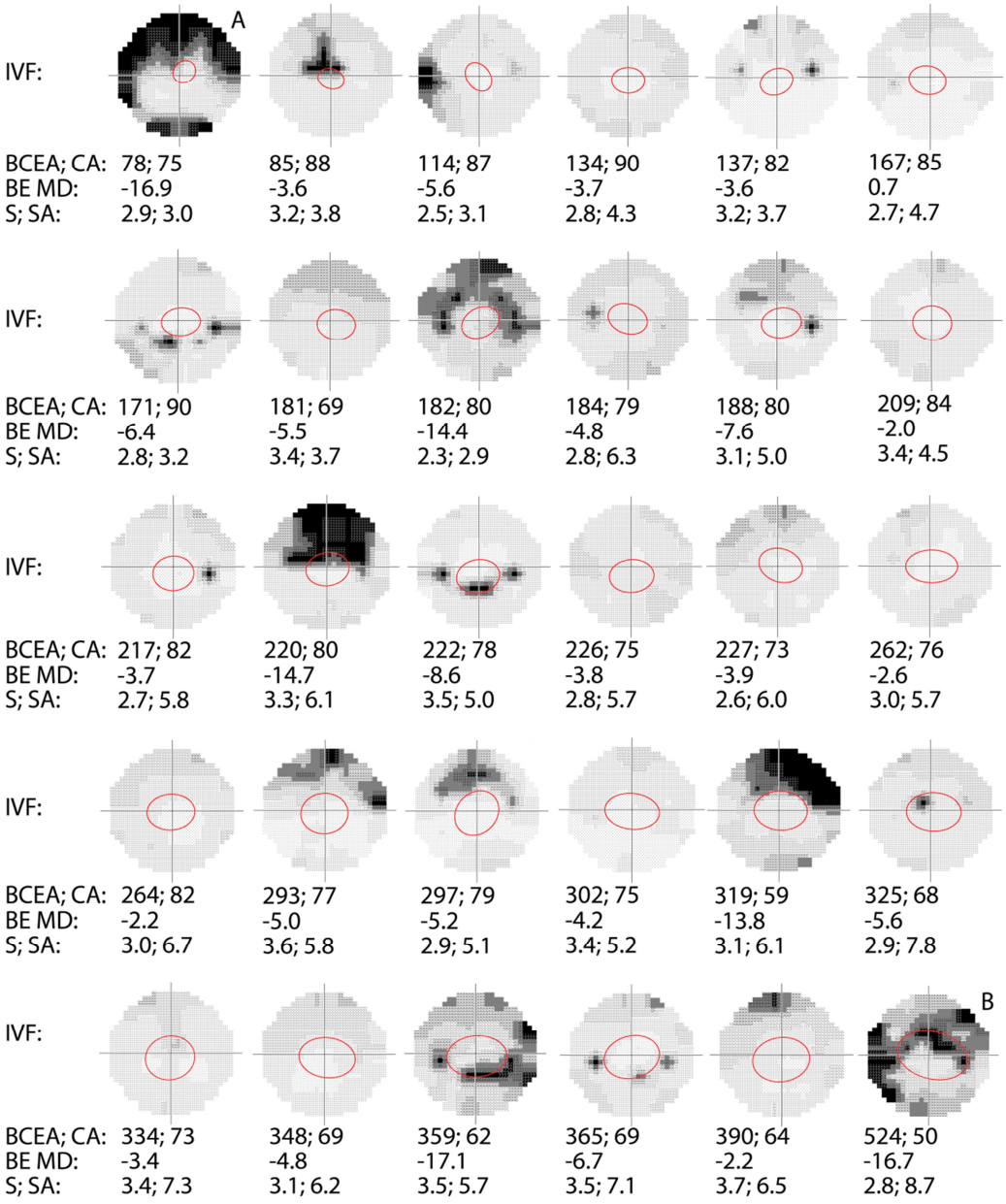


Figure 5.6: Greyscales of binocular integrated visual fields (IVF) for all the patients with their bivariate contour ellipse (BCE) scaled and superimposed. Overall BCE area (BCEA) is given in degrees squared and the patients are ranked in order of this value. The average percentage of the control area per image viewed by each patient is also stated (CA). Each patient's best eye MD (BE MD) is specified in dB. The average number of saccades (S) and saccade amplitude (SA) in degrees per image is stated for each of greyscales.

5.4 Discussion

Results from this study provide some evidence to suggest that individuals with bilateral glaucoma produce different eye movements compared to visually healthy individuals of a similar age when passively viewing images of natural scenes. For instance, the patient group made fewer saccades and consequently fixated for longer, than the control subjects when viewing the images. Since new information can only be acquired during fixations (when the eyes hold still) (Matin, 1974), and it is not possible to develop a sufficiently detailed percept from one glance alone (Irwin, 1991); the finding that the patients made fewer saccades suggests they were subsequently unable to process as much of the visual scene as their visually healthy counterparts during the specified time period. An increased number of saccades (and fixations) will also normally compensate for the fact that the quality of information naturally falls off from the central point of regard (Henderson, 2003), and so the fact that fewer saccades were made in a condition characterised by peripheral loss further suggests that the perceptual quality of each scene was not as fruitful for some of the people with glaucoma as compared to visually healthy people. Nevertheless, as was also observed in the previous chapter, the production of fewer saccades by default enabled the participant to fixate for longer on selected information, and this finding may be the first indicator of the employment of an alternative strategy as a result of the reduction in visual field in an attempt to ensure the most important visual information is not missed. For instance, evidence suggests that the time spent looking at a particular area is related to how informative the individual believes that information to be (Antes, 1974, Henderson, 2003). Therefore, it may be that by spending longer focusing on a particular aspect of the image, the glaucomatous patient either consciously or subconsciously hopes to focus on only the more useful information. Moreover, the observation could, perhaps, simply reflect a difference in the temporal processing of information between people with glaucoma and individuals with normal vision, but this should be the subject of further investigation. The finding of an increased fixation duration in the patient group also adds weight to the results in that it suggests that the result that less saccades were produced by the patients reflected a genuine change in eye movements and was not simply a fact of poor eye movement recording in one group or other personal factors such as whether

patients tended to blink more throughout the task. In addition, this study also introduced investigation into more spatial aspects of eye movement behaviour in terms of the size and general location of the fixations made. According to the results of the BCEA analysis, fixations made by the patients when they viewed the images naturally (and therefore could view any part of the image they liked) were restricted to narrower regions of the image on average compared with the controls, again implying that the patients were only able to gain a limited interpretation of the image in front of them. When perceiving visual scenes, it is believed that a much wider area of visual field is required to sufficiently gather information than in other visual tasks such as reading (Rayner, 2009a). Loss of VF will therefore limit the amount of information that is able to be processed in a certain length of time; a finding supported by research showing that masking increasing areas of the field of view will largely impair an individual's ability to recognise features of a scene (Saida and Ikeda, 1979). Despite this result, there was surprisingly no significant difference when comparing the mean saccade amplitudes of the patients with the controls in this study. This is likely due to the large between-person variability in eye movements observed in the patients compared with the controls; for instance, some individual patients recorded average saccade amplitude around three times larger than other patients. This variability may still serve as an indicator that glaucoma may interfere with the strategies normally employed by healthy individuals, and force some patients to utilise alternatives that are very different to others. The strategy chosen could have important implications for real-life situations during which the rapid scanning of the visual field is required; for instance, for making judgements when crossing the road or during a driving manoeuvre when the immediate visual scene must be taken into consideration.

Furthermore, the exploratory analysis revealed that patients with a worsening VF defect severity (as measured by the MD in the best eye) and worsening contrast sensitivity (as measured by PR CS) were less likely to fixate the same parts of the image as the controls. This result further suggests that there is something specific to glaucoma that is causing the patients to perceive the image differently to the controls. Peripheral information is thought to be used to help filter visual

information so that the eyes are directed to more useful items (Mackworth and Morandi, 1967), and it may be the case that the nature of the typically peripheral defects seen in glaucoma somewhat compromises this ability, thus decreasing the likelihood that the patient will fixate on the same areas as the controls. Moreover, low level visual properties including contrast levels have been shown to influence fixation, with a higher proportion of fixations being made on regions of increased luminance-contrast (Reinagel and Zador, 1999, Krieger et al., 2000, Einhauser and Konig, 2003). Diminished contrast sensitivity – which often coincides with glaucomatous visual field loss (Hawkins et al., 2003, Stamper, 1989) - is therefore likely to impede ability to detect these regions and thus drive the individual to fixate on other, perhaps less salient areas.

Explaining the differences in eye movements observed between groups in terms of the basic parameters and BCEA is more complex, as unlike when considering the spatial locations observed, there was no evidence of a direct association between these variables and MD in the best eye or PR CS. The patients and controls were all elderly and carefully selected to have similar age so this cannot explain the differences in the eye movements. All participants were required to have a corrected VA of at least 6/12 in each eye but average binocular ETDRS VA was slightly better in the controls. VF defects are very difficult to quantify and although summary measures like MD are used clinically they are only a 'blunt' measure of the VF and tell us little about the topography or spatial nature of glaucomatous VF defects. Despite the patients performing differently to the controls on the whole, it should be reiterated that there was still a large amount of variation in eye movement behaviour across the patients. Closer examination of individual cases can help to decipher what additional factors relating to vision may be driving the results. Particular cases of note are patients A and B (Figure 5.6), who despite having similar MD values in their best eye VF recorded the largest and smallest BCEA respectively. Closer examination of the VFs of the aforementioned patients hints that defect location may also be an important factor in determining the development of compensatory patterns; for instance, it can be seen that patient A's VF defect is more peripheral than that of patient B, who has severe central loss in the upper right hemisphere. Perhaps patient A is less aware of their defect than

patient B during everyday functioning, and has therefore not adopted compensatory eye movement strategies within a central 20°. Defect awareness is likely to encompass a wide range of characteristics including years since diagnosis, rate of progression and the stage of disease at which the individual was diagnosed, in addition to personal expectations and experiences. A limitation of this study was that this type of data was not collected. Investigation of the spatial relationship between gaze patterns and VF defects thus awaits further investigation.

Of course there may still have been some additional demand characteristics in existence in this study; for example, since the photographs used in the current study depicted a variety of different scenes taken on different dates, weather types and lighting conditions, it was not possible to control for factors such as saliency, contrast and pattern features of objects which are thought to influence saccadic behaviour (Itti and Koch, 2000, Krieger et al., 2000, Acik et al., 2009, Harding and Bloj, 2010). Nevertheless, the sample of images could be said to be reflective of natural scenes, and since there was found to be no statistically significant interaction term in the eye movements between images, it appears that the nature of the task was still relatively consistent throughout the duration of the study. An additional anomaly relates to whether the participants were actually paying sufficient attention to the images. Care was taken by the experimenter to ask the participants informal questions about the images between presentations but there was not an explicit performance measurement. We wanted the participant to view any part of the image that they wished; perhaps as they would when encountering a visual scene for the first time so as to capture 'natural' eye movements removed from increased task demand. Nevertheless it may be have been that some observed eye movements were in response to visual scenes generated during mind-wandering as opposed to those that were being driven by the real-life scene (Brandt and Stark, 1997).

This study provides some new evidence about how patients with bilateral glaucoma view pictures of natural and everyday scenes. Further studies into the eye movement patterns of patients with glaucoma when carrying out other more cognitively demanding visual tasks, such as reading, are undoubtedly needed before an accurate understanding of the functional deficits experienced by patients

with glaucoma can be gained. The variability in patient response in the data presented in this study suggest that other experiments consider whether fixation patterns may be adaptive, in the sense that there could be increased probability that scan paths will include fixations in damaged parts of the visual field. Such studies require innovative quantitative approaches of the eye movement patterns beyond, for example, simply counting the number of saccades and the size of the saccades. Examining whether patients with unilateral glaucoma produce different eye movement behaviour in their diseased eye may also be helpful. The idea that some patients make different eye movements to visually healthy control people opens up the idea of thinking how this information might be used in rehabilitation of visual impairment. This has received attention in other retinal diseases such as age-related macular degeneration (AMD) where some eye movement research rehabilitative techniques for visual impairment, with evidence to suggest that reading ability can improve following training focusing on eye positioning and movements (Seiple et al., 2005). Providing auditory feedback about eye movements is also thought to help improve task performance (Hall, 2001). Identifying optimal strategies for patients with glaucoma may help improve performance in other visual tasks (Vukicevic, 2009), and to serve as a way to educate the patient about their defect. We hope that the results from this study may stimulate future investigations which may also make such interventions a reality for people with glaucoma in an attempt to improve their understanding of their condition and their ability to independently go about their daily activities.

5.5 Conclusions

This exploratory study provides some new evidence that patients with bilateral glaucoma exhibit different eye movement behaviour compared to visually healthy subjects of a similar age when viewing images of everyday scenes. These results should stimulate further eye movement studies in glaucoma and these might provide a new 'window' into understanding the functional deficits of the disease. We speculate that understanding such 'real world' visual function deficits in glaucoma is perhaps a first step towards designing appropriate strategies for patient education about the impact of a visual field defect and potential rehabilitation. Further studies in eye movements and glaucoma are already underway in our laboratory.

6 Eye movements of people with glaucoma when performing a driving hazard perception test

6.1 Introduction

As explained earlier in this thesis, more insight is needed into how VF defects manifesting at different stages in the disease process impact on patients' everyday visual function. Chapter 3 showed that glaucoma patients have issues with visual search, with chapter 4 and 5 showing how eye movements are inhibited when performing real-world visual search and passively viewing images. In this chapter the effect glaucomatous defects have on patients' eye movements when performing a video based driving hazard perception test will be explored.

Glaucoma undoubtedly impacts on an individual when VF loss causes the removal of a driving licence (guidelines can be found in section 0), and several studies of varying experimental design have shown that certain glaucomatous visual field defects are not compatible with safe driving (Haymes et al., 2007, Haymes et al., 2008, Johnson and Keltner, 1983, McGwin et al., 2004). The issue of driving with glaucoma is a serious one, with a significant proportion of patients suffering visual loss that results in driving ineligibility, certainly in the UK (Ang and Eke, 2006, Owen et al., 2008). Moreover, it has been demonstrated that patients perceive this particular potential outcome of their disease to be as serious to them as the long-term risk of blindness (Bhargava et al., 2006).

The Hazard Perception Test (HPT) was introduced as an element of the UK driving licence theory test in 2003 as a measure to encourage appropriate visual scanning of the road or highway and to develop the ability to recognise at the earliest opportunity that a potentially dangerous driving situation might arise. In this context a 'learner driver' is shown a film of a real driving scene, seen from the perspective of the driver, with the task being to detect potential 'hazards': these are defined as something that would make the camera car take evasive action, such

as braking for an oncoming cyclist or a pedestrian unexpectedly crossing the road/street. Primarily, it is a useful educational tool allowing learner drivers to encounter 'on road' driving scenes from the safety of a computer monitor. A subject's performance on the HPT is clearly dependent on instruction, prior experience and perception of what represents a driving hazard, and HPT performance in terms of simply detecting a hazard in visually healthy subjects is certainly variable (Chisholm et al., 2008). Previously the HPT, as a simple reaction test to hazards, was investigated as a potential proxy measure for identifying visual defects that would impinge on fitness to drive, and was found to have limited value for this purpose (Rauscher et al., 2007). Whether the HPT is an indicator of subjects' visual strategies when driving under the conditions in which they are most likely to have an accident is open to debate, and is not the subject of this study. Rather, for the purposes of this study, this realistic and relevant visual scenario can be 'played out' on a computer screen allowing for accurate gaze tracking in a controlled laboratory setting, thus making it most suitable for examining the eye movement behaviour of people with glaucoma compared to control subjects whilst viewing an everyday scene.

The aim of the work described in this chapter is to perform eye tracking on subjects as they simultaneously view a series of HPT film clips to examine the hypothesis that patients with binocular glaucomatous field defects exhibit significant differences in eye movement characteristics to healthy control subjects. Moreover, in the context of visual field defects and fitness to drive, the data can also be used to examine qualitatively how these patients' eye movements relate to the events and hazards in the video sequences.

6.2 Methods

6.2.1 Participants

This retrospective study took advantage of some of the data collected as part of a UK Department for Transport (DfT) funded study conducted at City University London, fully reported elsewhere (Chisholm et al., 2008, Rauscher et al., 2007). In short, this UK DfT study aimed to examine the agreement between the outcome of conventional visual field tests and proxy measures of driving safety in subjects with binocular paracentral scotoma, resulting from a range of visual disorders, but preserved visual acuity (VA). One experiment in this study, not performed on all study participants, examined the performance of subjects on the HPT whilst eye movements were simultaneously recorded. Glaucoma patients were recruited from the Central Middlesex Hospital (North West London Hospitals NHS Trust), Moorfields Eye Hospital Foundation Trust London and the Fight for Sight Optometry Clinic at City University London. Data from these patients, along with those from a group of visually healthy control subjects, are the subject of this study.

All patients had a clinical diagnosis of glaucomatous optic neuropathy (primary open angle glaucoma) in both eyes and are, therefore, representative of those patients who should undergo further testing to satisfy the visual field requirements for legal fitness to drive in the UK (Chisholm et al., 2008, Crabb et al., 2004). Prior to inclusion in the study, all patients had a full eye examination including central visual fields (24-2 or 30-2 SITA Standard) recorded on a Humphrey Visual Field Analyzer (HFA, Carl Zeiss Meditec, CA, USA). Patients were excluded if they produced unreliable fields at this first visit. VA of at least 6/9 was required in both eyes, with no other significant ocular disease reported other than glaucoma. Visually healthy control subjects were recruited from University staff, centres for the elderly and the University optometry clinic. A full eye examination, including HFA visual fields, was carried out to exclude any abnormality before a volunteer was accepted into the study. A VA of at least 6/9 was required for each eye.

The subjects in this study consisted of 14 people with glaucoma and 22 visually healthy controls (these are a different group of participants to the previous chapters). The mean age of the patients was 66.7 (SD=19.0) years compared to a mean age of 48.9 (SD=13.8) years for the control subjects (averages significantly different; P=0.003; two sample t-test). The patients had a range of visual field defect severity: average HFA mean defect (MD) was -9.2 (SD=9.7) dB, -8.0 (SD=9.0) dB and -10.5 (SD=9.6) in the right eye, left eye and worse eye, respectively. Five of the patients (36%) and five of the controls (23%) had never driven (proportions not significantly different; P=0.46; Fisher's exact test). The self-reported average number of years actively driving was 21 (SD=13) and 16 (SD=11) for the patients and the controls respectively (averages not significantly different; P=0.50; two sample t-test).

The study was approved by the ethics committee of each of the participating institutions where subjects were recruited (Moorfields and Whittington Research Ethics Committee, London; School of Community and Health Sciences Research and Ethics Committee, City University London). All participants were asked about their general health and were excluded if they were on any significant medication (other than that for their glaucoma). Written informed consent, according to the tenets of the Declaration of Helsinki, was obtained prior to examination from each subject. All the data, with patient identifiers removed, were transferred to a secure computer at the university.

6.2.2 System Setup

The HPT film clips used in this study have been used elsewhere (Grayson and Sexton, 2002) and consisted of 26 short films (range 40-73 seconds) showing a range of driving environments (e.g. dual-carriageway or divided highway, rural lane, busy urban streets). Each film contained between one and three 'hazardous driving events'. The films were digitised (with a standard mpeg codec running at 25 frames per second) and shown on a 42 inch plasma widescreen monitor (1280 by 1024 pixel resolution) in a rectangle of width 824 mm and height 512 mm. Participants were seated at a chin rest 120cm from the screen and the image

subtended 39° horizontally and 25° vertically. Eye movements were monitored using a SMI iView X eye tracker (SensoMotoric Instruments, Teltow, Berlin, Germany) sampling at 240 Hz. The SMI eye tracker has reported spatial accuracy better than 0.5°. Calibration, drift correction, and validation were performed using the algorithms provided by the instrument.

6.2.3 Procedure

Participants were all given the same verbal instructions: that they should look out for events that would cause the camera-car to take evasive action such as braking or evasive steering. They held a response button in their preferred hand, and were instructed to press the button whenever they judged one of these hazards as imminent. This 'press button' performance in the actual hazard detection task was not considered in this study because previous analysis indicated large variability in 'press button' scores and the influence of subject specific definition of what constitutes a hazard (Rauscher et al., 2007). Following calibration of the eye tracker, each subject was shown two introductory films prior to the commencement of data collection, to allow them to familiarise themselves with the task. The film clips were presented in random order with occasional rest periods between films.

Participants were asked if they were current drivers or had ever been a driver, and if so were asked to estimate the number of years they had been actively driving. These data were not used to exclude or include participants in this study. None of the participants had previously performed the HPT and all were therefore naïve to the task.

6.2.4 Primary analysis

The eye tracker yields an enormous amount of raw data: essentially a trace of 'gaze' recorded as (x, y) coordinates related to the viewing area every 4.2ms for each film. The results from this experiment contained more than 13 million of these data points. A bespoke application written in Microsoft Visual C# was developed by the author for analysing these time series. The following briefly describes the techniques employed in the main analysis.

Eye movements were divided into fixations, saccades and 'smooth pursuits' using a velocity based criterion. One difficulty is correctly separating these movements from the variability in the measurement process. Therefore, a noise removal technique was first applied to the data which filters out highly variable non-physiological measurements (high frequency noise) by taking a window or block of 50 (x, y) coordinate eye gaze positions (around 210ms) and calculates the speed of any eye movement between the positions recorded at time point t and t+1. If more than 75% of the recordings within that window move at 30°/s or more then the whole window is removed from the trace because these measurements are assumed less likely to be physiological movements and are more likely attributed to measurement variability. The window moves along the trace to perform the same procedure on the next 50 samples. On completion, an eight sample median filter is passed over the remaining data to remove or dampen 'low frequency' noise. Blinks (denoted by zero value data), gaze outside the viewing area and other eye tracking failures were identified then removed from the traces. Films in which less than 40% of the recordings remained were discarded to ensure that we were not removing too much data per film, following a previously used protocol (Crossland and Rubin, 2002).

Once the data are filtered, saccades were defined as the proportion of the trace where the velocity of the eye movement is faster than 30°/s. This criterion of 30°/s or higher for identifying saccades is common in eye movement studies and eye tracking instrumentation, since this is considered the upper limit of pursuit eye movement speed (van der Geest, 2002, Hsiao and Cottrell, 2008, Stampe, 1993). Any saccade exceeding a duration of 120ms or is less than 10ms were excluded from the analysis. In addition saccades that originate or terminate outside the

confines of the dimensions of the display of the film (calibration errors) were excluded from the analysis. Fixations were defined as the proportion of the trace where gaze was 'still' and the velocity of the eye movement is less than 1.5°/s. We defined periods of the trace where the speed was greater than 1.5°/s but less than 30°/s to be 'pursuit' movements, where gaze was most likely 'tracking' a moving object in the film. In truth, these pursuit movements are very difficult to quantify even with a sophisticated eye tracker operating at a high frame rate, but we shall refer to them as possible 'smooth pursuits' lacking the stability characteristic of a fixation, but without being fast enough to be classified as a physiological saccade. The algorithm then automatically records the number of fixations, the number of saccades and the number of smooth pursuits per minute of film. It also yields average fixation duration (ms), average 'smooth pursuit' duration (ms) and average saccade amplitude (size in degrees). These six summary eye movement parameters were recorded for each film as viewed by each subject.

The experimental design aimed to minimize the between subject variability in the eye movement parameters with all participants viewing the same films, so these were assumed to be the blocks in the experiment. A General Linear Model (GLM) was used to perform univariate analysis of variance (ANOVA) with an unbalanced design (accommodating missing data by the method of median imputation) to assess each of six different eye movement parameters (response variables) using the statistical software package Minitab v.14 (Minitab Inc., Pennsylvania, USA). In this two way ANOVA arrangement, variation in the response variable (each eye movement parameter) was expected to be different across the films and across the subjects, with the null hypothesis of real interest being no difference in the average value for the eye movement parameters between the patients and controls examined (F test on the main factor, participant group, from the ANOVA).

6.2.5 Secondary analysis

A 'point of regard' analysis was also implemented. The eye tracking sequence is co-registered to the film sequence with each frame of the film equating to nine eye-tracking samples; a mean of these (x, y) points is defined as the 'point of regard' for that frame. This is repeated for all the control subjects such that each film frame has a sample of 'points of regard' (x, y), one for each control subject, for that particular frame. To quantify the spatial coincidence of the point of regard location for all the control subjects, we calculated the best-fit bivariate contour ellipse (BCE). The BCE area has been previously used to quantify fixation eye movement stability in patients with macular degeneration (Crossland and Rubin, 2002, Bellmann et al., 2004, González et al., 2006) and to quantify viewing areas for subjects as they watch films (Goldstein et al., 2007). For our application we implemented the method as described by Goldstein et al (Goldstein et al., 2007) but in a novel development we also plotted the ellipse on each frame of the film, as explained in section 0, (Altman, 1978, Healy, 1972) thus giving a dynamic visual representation of the region of interest for the control subjects. The centre of the BCE represents the mean 'point of regard' of the controls, with the spatial extent of the ellipse being one standard deviation from this centre along two principal axes, theoretically affording 'coverage' of approximately 68% of the 'point of regard' locations in a given frame. The percentage of patients' points of regard falling inside the BCE should be 68% under a null hypothesis that the people with glaucoma were, on average, viewing the same parts of the driving scene as the visually healthy subjects.

Monocular visual fields for the patients were merged to form an integrated visual field (Crabb and Viswanathan, 2005, Crabb et al., 2004): a simulated binocular visual field in which patients' best point-by-point monocular sensitivity is used (PROGRESSOR software: Moorfields Eye Hospital, London, UK / Medisoft Ltd., Leeds, UK). The software application developed in this work then aligns and scales a greyscale of this binocular field of view to the gaze point for each patient; this provides a dynamic illustration of a patient's restricted field of view as the film sequence runs, giving an insight into the difficulty of the task from the patient's perspective.

6.3 Results

6.3.1 Primary results

A small number of eye movement traces from the films were excluded for the 14 patients and 22 control subjects due to corrupt data or particularly noisy sequences where more than 60% of the data were removed by the filtering: a threshold used in previous studies (Crossland and Rubin, 2002). This affected results from two controls and two people with glaucoma, but none of these had fewer than 23 films available for analysis. Prior to settling on the numbers for this study, other subjects (3 patients and 4 controls) had several films (more than 12) where a large proportion of data were corrupt, missing, poorly calibrated or had more that 60% removed by the filtering algorithm: these subjects (some of whom had reported difficulty with the task or eye tracking failures) were not included in the final 36 assessed.

Each of the eye movement parameters was assessed in a GLM ANOVA: the departure of the F statistic (on 1 and 25 degrees of freedom) from 1 summarises the extent of a difference in the main factor (patients versus controls) and the P-value refers to the null hypothesis of no effect, or no difference, in that main factor. (No obvious departure from normality was observed in any of the response variables as assessed by the Kolmogorov-Smirnov test). There was considerable statistical evidence that on average patients made more saccades per second ($P<0.001$; $F_{1,25} = 22.7$; mean increase 8.6%; 95% confidence interval [CI]: 4.8 to 12.4%), more fixations per minute ($P<0.001$; $F_{1,25} = 33.8$; mean increase 11.8%; 95% CI: 7.8 to 15.8%) and more smooth pursuits per second ($P=0.001$; $F_{1,25} = 14.6$; mean increase 8.2%; 95% CI: 3.5 to 12.9%) than the control subjects. There was no evidence for a difference in saccade amplitude ($P=0.15$; $F_{1,25} = 2.3$) and no evidence for a difference in average duration of the fixations ($P=0.09$; $F_{1,25} = 3.1$), but there was some evidence of average duration of smooth pursuits being significantly greater in the controls compared to the patients ($P=0.002$; $F_{1,25} = 12.6$; mean difference of 6.3%; 95% CI 2.7 to 9.9%). These results are further illustrated in Figure 6.1: each graph considers a different eye movement parameter, with each point in the graph being the result from each of the 26 films. If the average value

for an eye movement parameter for the patients was identical to the controls then the point would fall exactly on the line of unity. The relative position of the points either below or above this line of unity gives a graphical indication of the magnitude and direction of the experimental effect and illustrates the ANOVA results.

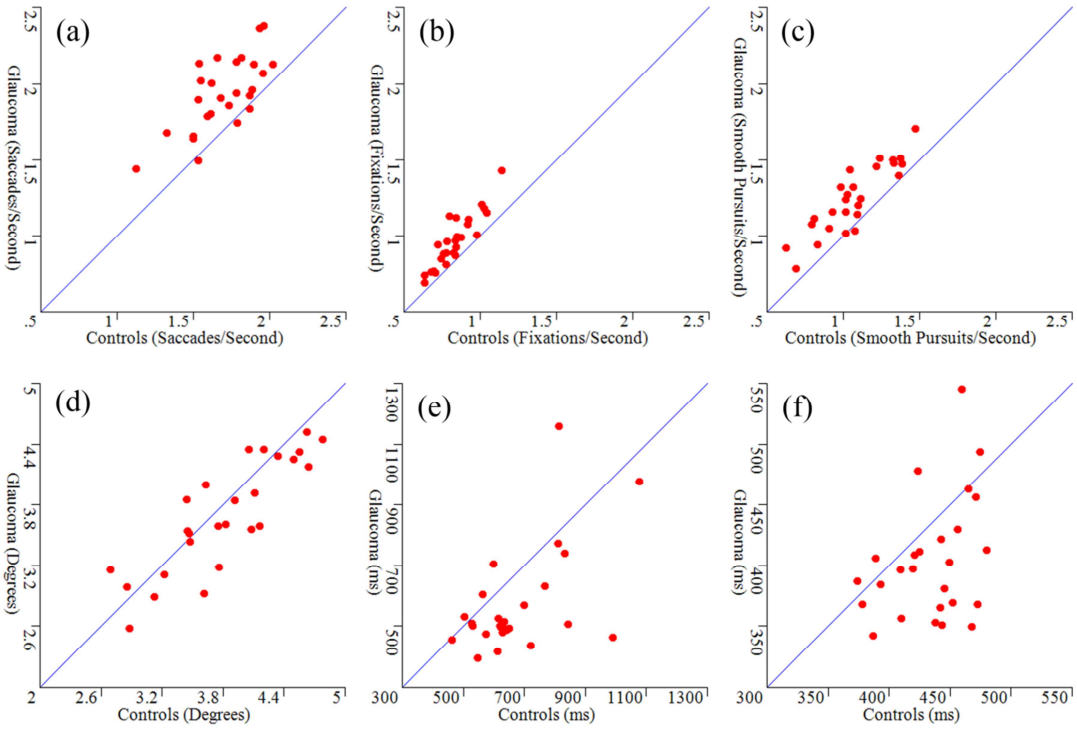


Figure 6.1**:** Graphs showing the average response in each eye movement parameter for the patients and the controls with (a) average number of saccades per second; (b) average number fixations per second; (c) number of smooth pursuits per second of film; (d) average saccade amplitude (size in degrees); (e) average fixation duration (ms); and (f) average 'smooth pursuit' duration (ms). Each symbol represents the results from one of the 26 films. If there were no differences in the averages then symbols would fall exactly on the line of unity. For example, (a) indicates that the patients made, on average, more saccades across the films than the control subjects.

The potential confounding effect of age on eye movement parameters was assessed on the control group. The association between each eye movement parameter (averaged across films) and age in the 22 subjects was calculated. None of the resulting six correlation coefficients were statistically different from zero and were all very small in magnitude ranging from r=0.05 (P=0.82) to r=0.24 (P=0.28). Therefore, from this experiment there was no evidence that the eye movement parameters varied with age.

6.3.2 Secondary Results

The BCE analysis attempted to compare the overall viewing region of the two groups (Figure 6.2). The mean number of points of regard that fell in the BCE was calculated for each patient with the overall average for the glaucomatous group being 63.2% (SD 9.6%). This average was clearly not significantly different from the theoretically expected value (68%) generated from the control group (P=0.49; one sample t-test). In some films, this average value was as high as 84.3% and in others as low as 55.2% but there did not seem to be any observed pattern of viewing region in the patients departing from that of the controls being associated with the type of driving scene (e.g. rural, urban, divided highway/dual carriageway).

In short, participants tended to view the same overall region of the driving scene whether they were glaucomatous or not, but this was on average, and considering the group as a whole. By using the software developed for this study it was possible to follow the viewing pattern of individual patients as they viewed the different films and compare this view with the pattern from all the control subjects simultaneously. Although difficult to quantify, there were several very revealing examples of individual patients clearly not following the control viewing pattern and unambiguous cases where the patient was unaware of emerging hazards. These examples became more informative when the integrated visual field defect of the patient was superimposed on the films giving a perspective of the patient's 'struggle' with their restrictive binocular central field defect. Two cases are shown as montages in Figure 6.3.

Figure 6.2**:** Examples of the BCE 'point of regard' analysis superimposed on frames from some of the HPT films. The centre of the red ellipse represents the mean 'point of regard' of the controls with the spatial extent of the ellipse being one standard deviation from this centre along two principal axes, theoretically affording 'coverage' of approximately 68% of the 'point of regard' locations in a given frame. Note how the location and spatial extent of this ellipse changes with each frame of the film as the control subjects' view is drawn to different aspects of the changing road scene. For each frame the number of patients' points of regard (blue symbols) 'captured' by the ellipse can be automatically counted and compared to the expected value under the null hypothesis that the average 'viewing area' is the same in the two groups. Note that not all 14 patients are recorded in each frame because of blinks, loss of data, and variable responses. Also, note that in the UK vehicles are driven on the left hand side of the road.

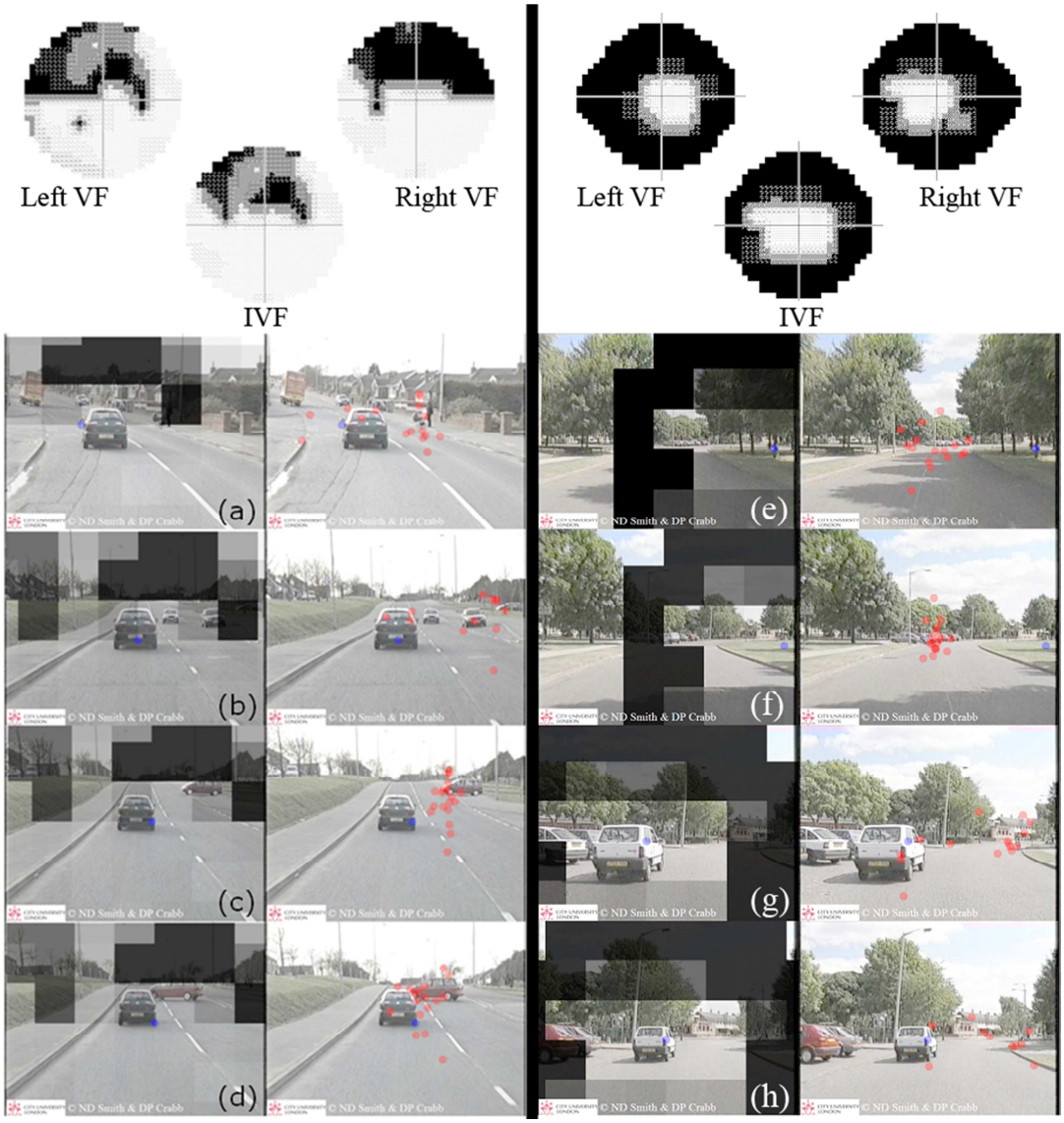


Figure 6.3**:** Two example patient's visual fields, 'point of regard' and HPT films. Images a-d represents the first patient viewing a film and e-h represents the second patient viewing a different film. HFA greyscales for the first and second patient's monocular (30-2 and 24-2 respectively) and IVF are shown above the set of images. In each image the IVF is scaled and superimposed on the point of regard to represent the restricted field of view. In (a) whilst most of visually healthy subjects (red symbols) fixate on the pedestrian with a pram/pushchair, seeing them as a potential hazard, the patient (blue symbol) fails to alter their gaze. Similarly in (b) and (c) most of control subjects quickly move their fixation towards the the car hazardously turning on to the main street from the right intersection. The patient's view of this hazard is masked by their defect and they do not alter their gaze at any point, even when the camera car 'brakes' to take evasive action (d). This patient has a binocular visual field that would probably be on the borderline of satisfying the UK guideline for visual field fitness to drive. In the second example image (e) the patient is actively scanning the road ahead in an attempt to predict the next hazard. In doing so the patient, unlike the controls, fails to see the pulling out unexpectedly from the left due to their restricted field of view (f and g). Similarly the patient's advanced binocular defect prevents them from seeing pedestrians about to cross the street from the curb (h). This patient would not satisfy the UK guideline for visual field fitness to drive.

6.4 Discussion

These results provide some new evidence that some characteristics of eye movements in people with glaucoma with binocular visual field defects are different to those of healthy control subjects when performing the HPT. On average, the patients made more saccades and more fixations than controls. With this task we speculate that patients are, unconsciously or otherwise, making more saccades to search the image as a 'compensation' for their restricted field of view. Since a binocular visual field defect reduces the amount of visual information available, this might suggest fewer eye movements (Cornelissen et al., 2005), but this was not the case when patients were viewing these moving images. Our results also indicate that fixation duration was, on average, shorter with patients compared to controls. In contrast, it has been previously shown that fixation duration increases with the size of absolute central scotomas, but this was in a study using artificial scotomas on healthy subjects and a different task (searching a static image) (Cornelissen et al., 2005). Others have shown a reduction in fixation duration when an artificial scotoma is used to block foveal vision. (Henderson et al., 1997)

The BCE analysis indicated that patients were, on average, looking at the same areas as control subjects in the HPT films. Despite the novelty and computational difficulty of this analysis it is probably too insensitive to the subtle departures in patient gaze as compared to the controls. Looking at individual cases viewing individual films was more revealing but provides little quantitative information about how the patients differ from a normal viewer. A better post-hoc analysis might mark out areas in the frames that are of interest, perhaps associated with the looming hazards, and then quantify the patient's gaze falling in these areas. Such an analysis would probably need larger sample numbers than made available for this study to provide an adequate comparison.

Eye movement studies in 'real world' or simulated 'real world' environments have tended to focus on experiments with artificial scotomas or, when carried out in patient groups, with retinitis pigmentosa (RP) (Vargas-Martin and Peli, 2006, Turano et al., 2001) and age-related macular degeneration (MD) (Crossland and Rubin, 2006). Few studies have previously examined eye movement behaviour in

glaucomatous subjects. An elegant study by Cheong et al (Cheong et al., 2008) examined 'traffic gap' judgement and eye movements in subjects with peripheral visual field loss, including three subjects with glaucoma, as compared to healthy subjects. They reported restricted gaze patterns using the BCE approach but little evidence of difference in saccade amplitudes, or fixation duration. Eye tracking experiments by Geruschat et al (Geruschat et al., 2006) demonstrated that on average people with glaucoma (n=12) had similar fixation patterns as compared to controls when crossing a street. Coeckelbergh et al (Coeckelbergh et al., 2002) measured eye movements on a simple static search task and attempted to relate these to an actual on-road driving test in 50 subjects with field loss, some of whom were glaucomatous (number not given in the study). The number of fixations in the search task increased as a function of the size of the peripheral visual field defect, a finding consistent with our results. They reported some association between fixation duration and severity of central field defect but then indicated that eye movement parameters recorded during a simple static search task did not predict viewing behaviour in the actual task of driving. This is not surprising since gaze patterns are intrinsically related to the specific task: their patterns obtained from a static search task are likely to differ from patterns for a 'driving' task. Indeed eye movement patterns for the latter have been shown to be extremely complex (Land and Lee, 1994).

The HPT was previously studied as a possible surrogate for the UK visual field standard for fitness to drive (Rauscher et al., 2007). The main measurement considered was the press button response which yielded the percentage of hazards missed and the mean hazard response time. The main finding from this study was that the HPT, when using detection and speed of detection of the hazard, was of limited value when used alone in identifying subjects with visual field loss incompatible with current UK driving standards. Our current interest in the HPT is quite different: for the purpose of our current study, the HPT is used as a realistic, dynamic, visually challenging 'scene' whilst eye movements are simultaneously recorded.

As in any case-control study, especially when data are examined retrospectively, it is prudent to highlight potential confounders. For example, the patients were, on

average, older than the control group. However, previous work with the HPT and eye movement analysis in healthy subjects has shown there is little evidence of an age-related decline in scene search performance when detecting hazards (Underwood et al., 2005).The lack of association between the eye movement parameters and age in our normal sample supports this. It has been previously shown that experienced drivers demonstrate more extensive scanning than the novices in performing the HPT (Underwood et al., 2002, Underwood et al., 2003). In our study the patient group had a slightly higher proportion of non-drivers compared to the control group but, on average, the patients had more years of self reported driving experience than the controls (none of the differences reached statistical significance). Therefore, the groups were fairly well matched for this potential confounder.

Other caveats to be considered when interpreting the results from this study include the difficulty in truly identifying and separating the different types of eye movement, especially delineating saccades from smooth pursuits when the participant observes a moving image. This is a challenging task even with modern eye tracking instrumentation. We took the approach of excluding some subjects and removing significant sections of eye movement traces where it was not possible to identify clearly the different movements using an algorithm based on eye movement velocity developed for the purpose. The experiment was not an easy one for some subjects to perform, taking around 30 minutes to view all the film clips, and this probably contributed to the variability in the measurements. Furthermore, the patient group for our study was small, meaning population inference should be treated cautiously, but the sample size was certainly equivalent to or greater than those used in many experimental eye movement studies in the literature.

Anecdotally, some patients criticize the current static binocular visual field test (Esterman Test) used to establish legal fitness to drive in the UK for not allowing 'scanning' for a target. An eye movement and HPT task might be useful as a test for visual field restriction and fitness to drive. The set up would benefit from films shown on a larger screen, equivalent to that 'view' from a vehicle, and an eye tracker device that allows for natural movements. Such a test would not be reliant

on press-button defined hazard detection but could simply monitor the patient's natural gaze. A post-hoc analysis of gaze patterns, compared to visually healthy control subjects, as illustrated in this study, could determine if patients 'saw' hazards, road/traffic signs and events that might provide evidence for them being visually 'safe' drivers. Taken alone it is very unlikely that such an idea would solve the difficulty of determining the vision standard for fitness to drive, the skills for which are so multifactorial that it defies one simple standard. Besides, the low task demand of watching a film may give an impression of competent driving performance that may not be maintained if someone is controlling a vehicle. Nevertheless, given the debate about current visual field standards for driving (Kotecha et al., 2008, Westlake, 2000) such an approach may warrant further investigation.

The films showing, frame by frame, a patient's gaze pattern diverging from those of a number of visually healthy subjects provide a revealing insight into the visual impairment caused by glaucoma. This is particularly striking when the individual binocular visual field defects, made dynamic by aligning them to the moving point of regard, are superimposed on the films. One significant output from this work has been the use of these films in educational/awareness programmes for glaucoma in the UK and the subsequent interest they have generated, including a feature on the BBC (British Broadcasting Corporation) News (BBC, 2008).

6.5 Conclusion

This exploratory study provides some new evidence that patients with bilateral glaucoma exhibit different eye movement behaviour compared to visually healthy subjects when viewing a driving scene. It is interesting to note that some of the findings presented in the current study were orthogonal to the results described previously in chapters 4 and 5. In the current chapter, it is reported that there was no difference in the size of viewing area between patients and controls but that patients produced more, and thus shorter, fixations than the controls when searching for hazards in the Hazard Perception Test. However, the previous studies reported a *reduced* saccade rate in patients when they view or search for objects within naturalistic images. It has previously been reported that participants will alter their eye movements in situations where the quantity of visual information is heightened and the task becomes more cognitively demanding (Greene and Rayner, 2001, Bertera and Rayner, 2000, Vlaskamp and Hooge, 2006). In the passive viewing task (chapter 6), cognitive demands were minimal in that participants were presented with static, consistent information whereby any object could be chosen for fixation during the known time period. The participants were in effect tasked to simply 'enjoy' the images. Conversely the HPT was dynamic and as such the viewer was faced with a huge array of changing information every second, Consequently, the participants in the HPT were under pressure to not only find a target object, but to do so during a very limited time period. We therefore suggest that these inconsistencies may be related to the task complexity and quantity of visual information that was available to the participants.

It is hoped that these results from this exploratory study will at least stimulate investigations into the idea that eye movement studies, perhaps coupled with work on patient's adaption to visual field defects, might provide a new 'window' into understanding the functional deficits of glaucoma. It is speculated that understanding such 'real world' visual function deficits in glaucoma is perhaps a first step towards designing appropriate strategies for patient education about the impact of a visual field defect and potential rehabilitation.

7 How Does Glaucoma Look? Investigating Patient Perception of Visual Field Defects

7.1 Introduction

Currently, the majority of our understanding with regards to visual functioning in glaucoma comes from clinical measures such as visual fields, which assign numerical values to symbolise how well the individual is able to see in different areas of their vision. One of the main aims of this thesis has been to move away from this 'clinic-based' perspective and gain an increased understanding of how glaucoma actually affects visual functioning in real-life. In chapter 3 it was shown that glaucoma can impair performance in visual activities and chapters 4, 5 and 6 showed that the eye movement strategies the patient uses as they go about certain everyday activities change due to their glaucomatous defects. However, an additional area to consider when investigating the impact of glaucoma on real world functioning is how the patient themselves perceive their vision and to what extent they are aware of these functional impairments. The reality currently appears to be some sort of a 'mismatch' between how patients perceive their vision compared with what appears to be their actual visual loss. For instance, patient perceptions of their vision have been found to be poorly correlated with clinical assessments of their visual function (Jampel et al., 2002b, Nelson et al., 1999). Moreover, patients often appear to be unaware as to the extent of their visual loss, perhaps due to the asymptomatic nature of glaucoma in its earlier stages (Robin DiMatteo et al., 2002), which in turn appears to have a negative influence on treatment compliance (Shaw, 2005, Schwartz and Quigley, 2008). There are also discrepancies between the clinician and patient with regards to the effects of glaucoma, with one study finding ophthalmologists underestimate the impact of loss of vision on quality of life compared with the views of the patient (Brown et al., 2000).

In addition, it seems that many patients are simply unaware that there is anything wrong with their vision whatsoever. One qualitative study investigating patient perceptions of their diagnosis and subsequent life with glaucoma found that many patients were 'surprised' to find there was something wrong with their vision, or had attributed any noticed changes to 'bad glasses' or the normal ageing process. In addition, several patients noted that they knew little about glaucoma prior to their diagnosis (Green et al., 2002).

Since a staggering 50% of those with glaucoma in developed countries are thought to be living without awareness of their condition (Quigley, 1996), there is clearly a need for new and improved strategies for informing both diagnosed patients and the general public as to what having glaucoma is actually like. Such increased awareness may subsequently educate patients as to what changes to their lives they should prepare for, and motivate those individuals who would not have otherwise realised that they had a problem to make that crucial appointment with their optician. Awareness of glaucoma from an early stage may also help limit the burdens of the types of functional impairments that coincide with glaucoma that have been discussed in the previous chapters of this thesis.

One key method of raising awareness of glaucoma may be to focus on the development and communication of more accurate representations as to what it actually 'looks like'. Currently, the common depiction of glaucoma, particularly in the media, is in terms of a 'tunnel' or 'black patches' in the regions where there is loss of vision (Figure 7.1).

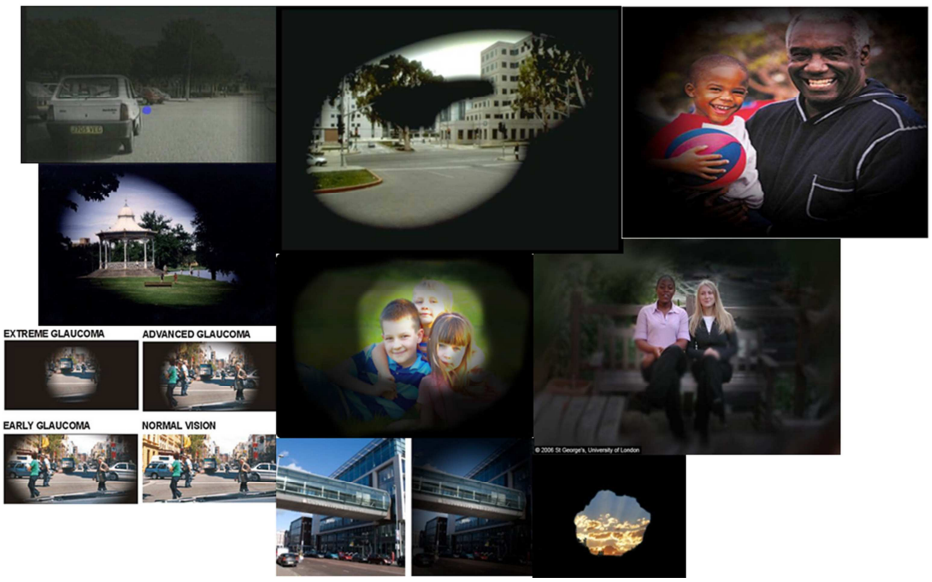


Figure 7.1: Collection of images representing glaucoma found using Google images (http://www.google.co.uk/images).

Aspects of our own previous research may even have contributed to this convention; for instance, when the findings of chapter 6 were reported by the BBC (BBC, 2008), the article was accompanied by a video showing a patient watching the hazard perception test, with the transparency of the image manipulated in an attempt to demonstrate which areas of the visual field were impaired for that patient and which were relatively 'normal'. Thus, those impaired parts of the visual field appeared darker than those parts that had little damage. Whilst the intended purpose of this manipulation was simply to demonstrate that there were parts of the visual field that the patients could not see properly as they were driving, it would be understandable if this video was to be misinterpreted as a direct representation of what the visual scene would look like 'through the eyes' of a patient with glaucoma. It may be that representations such as these are not sufficient illustrations of how some or even all of those with the glaucoma recognise their impairment, meaning that many are subsequently left unaware of the presence or extent of developing visual loss. The current study therefore aims to gain an increased understanding as to how glaucoma might appear to the affected individual, by giving diagnosed glaucomatous subjects with a range of HFA visual field defect severities the chance to talk about their perceptions of glaucoma

and to choose the representation that they feel best illustrates their visual experiences.

7.2 Methods

7.2.1 Participants and system setup

Patients were recruited from Moorfields Eye Hospital Foundation Trust London and the Fight for Sight Optometry Clinic at City University London. All patients had received a clinical diagnosis of glaucomatous optic neuropathy (primary open angle or normal tension glaucoma) with resulting visual field defects in both eyes. All patients took part in an eye examination prior to participation in the study consisting of corrected binocular visual acuity (VA) using an ETDRS chart and contrast sensitivity (CS) using a Pelli-Robson chart. All patients were required to have a corrected VA of at least 6/9 in each eye, with no other ocular disease other than glaucoma. In addition, visual fields (central SITA 24-2 and 10-2 on both eyes) were recorded on a Humphrey Visual Field Analyzer (HFA, Carl Zeiss Meditec, CA, USA). To be included in the study, patients were required to have 'overlapping' binocular defects as measured by an estimate of their integrated visual field (IVF) (Crabb et al., 2004, Crabb et al., 1998): a simulated binocular visual field in which patients' best point-by-point monocular sensitivity is used (PROGRESSOR software: Moorfields Eye Hospital, London, UK / Medisoft Ltd., Leeds, UK). Specifically patients were required to have two or more IVF locations with sensitivities of less than 20dB.

The mean age of the 50 patients was 70 (SD: 7) years. The patients had a range of visual field defect severity: average 24-2 HFA mean defect (MD) was -8.7 (SD: 5.8) dB, –10.5 (SD: 7.1) dB and –7.3 (SD: 5.7) in the right eye, left eye and best eye, respectively. The mean binocular contrast sensitivity and visual acuity of the patients was 1.8 (SD: 0.18) PR log CS and 0.07 (SD: 0.10) logMar.

All participants were claimed to be in good general health during an interview and participants were not enrolled if they were on any significant medication other than that for their glaucoma. ('Significant medication' included anti-depressants or treatment for diabetes or significant use of non-topical β-blocker medication, all of which were deliberately mentioned).

To take part in this study the subjects were sat in front of a laptop with a 13.3 inch LCD screen at a distance of 40cm, covering the full area of the screen, and audio recordings of the patients making their selection were made on the laptop.

7.2.2 Procedure

Initially six images, as shown in Figure 7.2, were shown to the patients and they were asked to choose the image that most closely represents their vision with glaucoma. The same image was used but was manipulated in various different ways to represent glaucoma. Image A is the traditional black tunnel vision manipulation, image B is the exact same region using a Gaussian blur, C shows black patches (located in common glaucomatous regions), D is the Gaussian blur version of C, E uses a filling in method (combination of context aware tool, recolouring and replication of regions of the image; Adobe Photoshop CS5, Adobe Systems Incorporated, CA, USA) and F is the unmodified image.

Patients were then asked three questions about their experience with glaucoma and their responses were recorded:

1) In your own words could you describe how your glaucoma affects your vision?

2) Are you aware of your visual field defect?

3) When you are aware of your visual field defect, can you describe how it looks or how it impacts on your field of vision?

Figure 7.2: A is the traditional black tunnel vision manipulation, image B is the exact same region using a Gaussian blur, C shows black patches (located in common glaucomatous regions), D is the Gaussian blur version of C, E uses a filling in techniques to replace missing areas of the image and F is the unmodified image.

7.2.3 Primary analysis

The responses from the six images shown to the patients were counted and percentages calculated.

7.2.4 Secondary analysis

The answers to the three questions about the patients' experiences with glaucoma were audio recorded and transcribed. These transcripts were then processed and verbs relating to the subject's positive description (any instance where a patient describes their vision without a negative in front – for example: "my vision is not blurry" would not be included whilst "my vision is blurry" would be included) were highlighted. For each patient a list was created containing these descriptions of their vision. The number of times a patient uses a word is not considered, either a word is said one more times and placed in the list, or it is not said (and therefore not placed in the list).

7.3 Results

7.3.1 Primary results

Four percent (CI: 0% - 9%) of the patients chose image B (blurred tunnel), 54% (CI: 40% - 68%) chose image D (blurred patched), 16% (CI: 6% - 26%) chose image E (filling in) and 26% (CI: 14% - 38%) chose image F (no difference) from Figure 7.2. No patients chose the images with black filling in.

Table 7.1 shows the breakdown of the patients' BEMD, CS, VA, age and IVF, image selection and the distribution of BEMD values for each image. The patients who chose the image with a tunnelled blur effect have a far more severe BEMD (-12.8dB; SD: 2.1) than the patients who chose the no change image (3.7dB; SD: 4.1. p=0.03; independent 2-sample t-test), as demonstrated in Figure 7.3. There is also a significant difference when comparing the patients who chose the no change image against the blurred patches image (-7.9; SD: 5.8. p=0.002; independent 2-sample t-test).

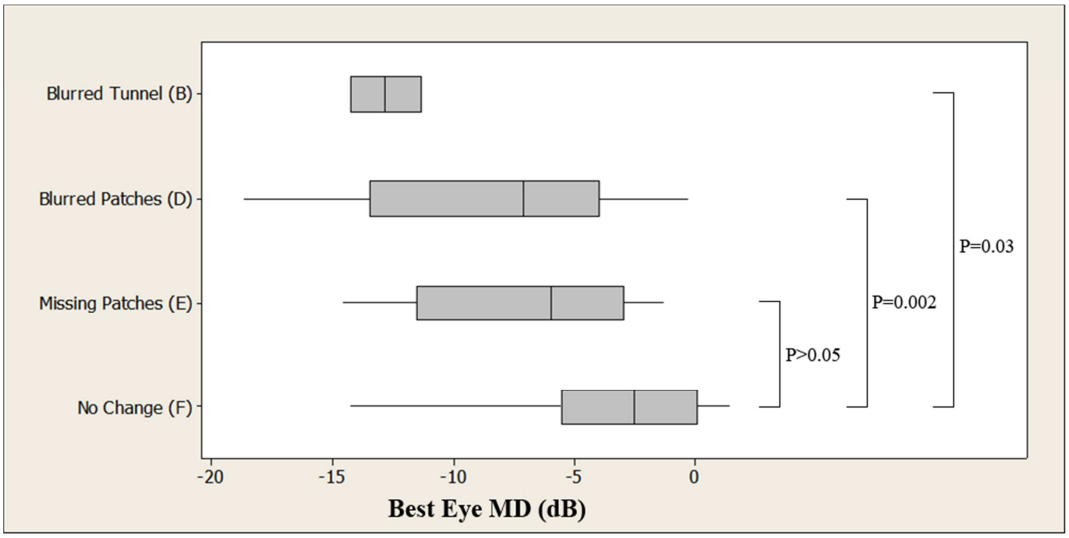


Figure 7.3: Box plot showing the distribution of best eye MD values for the patients who chose each image. The level of significance (independent t-test) between the mean BEMD of the patients that chose "no change" compared with that of the other images is shown on the right. There is no significant difference between (F) and (E), however there are significant differences between (F) and both (B) and (D). Results from Image A and C are not shown as no patients chose those images. The whiskers represent the range of the data.

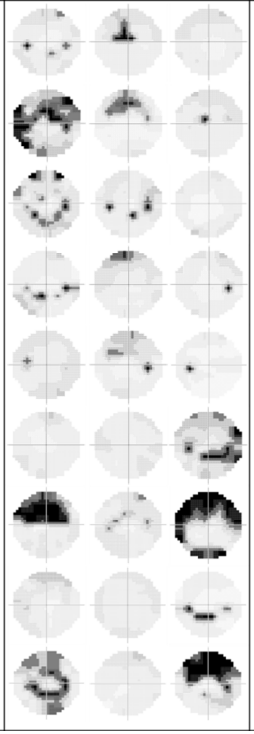
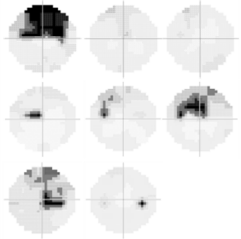
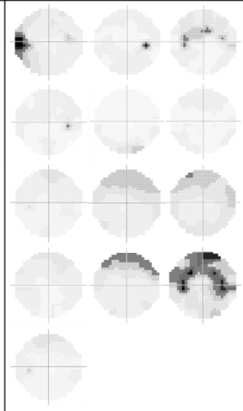
Image selected	Black Tunnel (A)	Blurred Tunnel (B)	Black Patches (C)	Blurred Patches (D)	Missing Patches (E)	No Change (F)
Number of Patients	0 (0%)	2 (4%)	0 (0%)	27 (54%)	8 (16%)	13 (26%)
Best Eye MD (dB)		-12.8 (2.1)		-7.9 (5.8)	-6.8 (4.8)	-3.7 (4.1)
Contrast Sensitivity (LogCS)		1.65 (0.4)		1.8 (0.2)	1.8 (0.2)	1.87 (0.16)
Visual Acuity (LogMar)		0.15 (0.04)		0.08 (0.08)	0.06 (0.08)	0.02 (0.12)
Age (Years)		79 (1)		70 (7)	68 (6)	66 (7)
Integrated Visual Field						

Table 7.1: Breakdown of the images chosen by each patient along with best eye MD, contrast sensitivity, visual acuity, age and integrated visual field.

7.3.2 Secondary results

The most frequent words used by patients in this study to describe their defect were “miss” (16 patients), “dark” (9 patients), “light” (7 patients), “clear” (6 patients) and “blur” (6 patients). “Miss” was used when a patient experienced missing something, “dark” was used by 8 of the 9 patients when talking about issues in the dark, whilst the other patient initially stated they see dark patches, however later in the conversation this was reworded as a “hazy” patch. “Light” was used in a variety of different ways: for instance, patients claimed to find dim light, or bright lights from cars, difficult to deal with, or claimed to require good light to read, and some even referred to missing lights during the visual field test. When patients used the word “clear”, it was always in the context of finding things difficult to see clearly. Table 7.2 shows the words used by patients when describing their defect in a negative light, the number of patients who used each word and the average severity of VF defect (in terms of MD in the best eye) of the patients who used said word. Figure 7.4 graphically represents the descriptive words used by the patients using a Wordle (http://www.wordle.net). This technique demonstrates the frequency of a word’s use by manipulating the size of the word in the diagram; the larger the word appears in the Wordle, the more often it was used by the patients. So, the word “miss”, as shown in Table 7.2, is the most commonly used word by the patients when describing their defect, appears largest in the Wordle diagram. It is also interesting to note the appearance of the word “black” in the Wordle diagram, given that the previous results suggested that none of the patients chose the images that represented their defect in terms of a black tunnel, or black patches. The context of this word’s use should therefore be clarified; one out of the two patients using the word said their vision was “blacked out” and the other stated their vision was “black” and then later in the conversation stated was “there’s nothing there”. This provides further support for the idea that ‘black’ can be used as a symbol of something that is ‘not there’ as opposed to a direct description of vision.

Word	Frequency	BEMD	Word	Frequency	BEMD
miss	16	-10.5 (5.3)	fuzzy	3	-7.0 (0.9)
side	12	-10.0 (6.6)	distance	3	-10.9 (6.0)
dark	9	-9.9 (5.1)	blind	3	-11.5 (5.2)
light	7	-6.4 (6.0)	worse	2	-9.6 (7.6)
compensate	6	-7.6 (5.1)	tired	2	-12.1 (9.5)
clear	6	-11.1 (6.7)	spot	2	-10.0 (6.3)
blur	6	-6.9 (5.6)	slow	2	-15.0 (2.8)
focus	5	-7.0 (6.4)	scan	2	-9.8 (6.3)
double-vision	4	-5.6 (5.2)	foggy	2	-15.1 (5.2)
move	4	-5.4 (2.4)	fill	2	-7.5 (0.2)
down	4	-10.4 (7.9)	dim	2	-5.9 (0.3)
disappear	4	-7.7 (5.2)	colour	2	-9.7 (4.7)
peripheral	3	-4.9 (2.0)	black	2	-9.5 (2.6)
nothing	3	-12.6 (4.6)			

Table 7.2: The number of patients that used specific words to describe their visual field defect in a negative way. Only frequencies larger than 1 are shown.

Figure 7.4: Wordle showing the words used by patients to describe their vision in a negative way (all words were used one or more times by at least one patient). The larger the word the more frequently it was used.

Figure 7.5 gives further insight into the visual experiences of some of the patients by displaying interesting quotes alongside a greyscale of that patient's IVF. There appears to be some relationship between the severity and location of binocular defects and description of their vision.

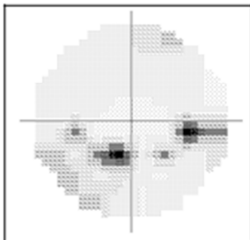
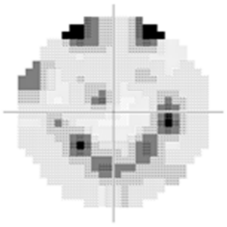
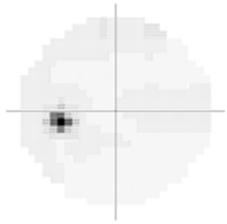
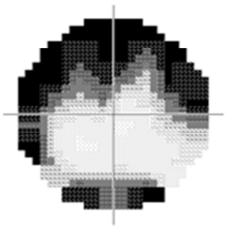
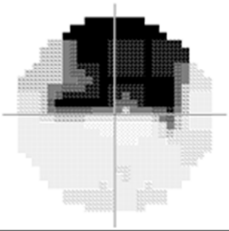
	I don't often do it because it frightens me to see what I've got missing, but the other day when I was sitting in the garden I looked down and I thought oh gosh there's a great big chunk missing, and it depends how close you are to something or how far away you are...
	It's very difficult because nobody can tell you what your sight is like, and it's very difficult to describe
	there's no sort of black, not like that, not with me anyway, not like that, no, no not at all. It's blurred, it's not... But as I say there are areas of blur and then ordinary, it's difficult to describe it sometimes really
	when I usually first get up in the mornings I get very much blurred, like a mist, and I keep cleaning my glasses but it's not there. It's like a mist you know
	When I saw a bus coming towards me I thought it was a single decker and it turned out to be a double decker. So I'm aware of that and I sort of adjust, I am aware of it I have a blind bit about here

Figure 7.5: Example passages by patients describing their experience with glaucoma along with their corresponding IVF.

7.4 Discussion

Evidence suggests that public knowledge about glaucoma is poor (Baker and Murdoch, 2008), and that as many as half of the individuals with the disease don't actually realise that they have it (Quigley, 1996). There are also clear issues regarding treatment compliance in glaucoma, with many patients needing active involvement in the disease management processes to be convinced that there is something wrong with their vision (Hamelin et al., 2002, Shaw, 2005). Attempts have been made within the media to raise awareness of the conditions, with one of the most common educational strategies consisting of images representing glaucoma in terms of a black tunnel or black patches across the normal visual scene (Figure 7.1). Yet in contrast to the images often distributed in the media depicting glaucomatous loss as 'black', the most striking finding of the current study was that not a single patient chose the images featuring black (Figure 7.2, images A and C) as the best representation of their actual vision. Instead, the most commonly chosen images were those containing blurred patches (Figure 7.2, image D), or missing parts (Figure 7.2, image E). This finding strongly suggests that the current message regarding the 'appearance' of glaucoma may be flawed, and that how the patient actually perceives their visual field defect in real life is different to this representation. This apparent misinterpretation may therefore be an underlying factor of the lack of awareness of glaucoma experienced by many individuals with the disease and the general public.

Further investigation revealed that there may be some sort of link between how glaucoma 'looks' and the stage of disease (Figure 7.3). Several individuals with less severe glaucomatous defects picked the image that depicted no change; therefore implying they believe their vision to be perfectly 'normal'. This finding is in line with the traditional idea that glaucoma is asymptomatic until later stages. Nevertheless, there is some evidence that glaucoma can display effects even in earlier disease stages (McKean-Cowdin et al., 2008, Viswanathan et al., 1999), suggesting that it is important for these patients to better understand their disease even at mild severity. Perhaps these patients would notice some change to their vision should they be encouraged to focus on it more. The creation of more realistic images may therefore help them realise how their vision could worsen,

and encourage treatment compliance. On the other hand, patients with a worse MD in their best eye VF were more likely to choose an alternative modified picture to best represent their visual experience, but contrary to the common media depictions of a black tunnel or patches, the majority of patients chose either blurred patches, or the image with 'missing parts'. The former image implies that the most affected areas of visual field may appear distorted to the patient or of poorer definition. These are supported by direct quotes from some of the patients (Figure 7.5). On the flip side, the image depicting missing parts suggests that whilst the quality of the image appears 'normal', the patient sometimes recognises that what they are 'seeing' may not add up to the actual visual information around them. For instance, they may become aware of an additional object at a later stage that they did not notice before (Figure 7.5). This experience may relate to the phenomenon whereby items simply disappear and are 'filled in' by their surroundings (Ramachandran and Gregory, 1991, Komatsu, 2006). This cortical plasticity is known to cause individuals to ignore or underestimate their visual field defects and this lack of awareness may lead to functional impairments in certain individuals (Safran and Landis, 1996). Perhaps how the patient recognises their glaucoma may be related to how much the individual is concentrating on their vision and is subsequently aware of their visual loss. Future studies should look at the link between awareness and functional performance. There is also the possibility that a person with glaucoma may find the images displayed further degraded than intended due to their functional degradation. However, it must be considered that glaucomatous VF defects move with a person's eye rather than being static within the image and therefore it will be clear what is the simulated degradation and their own field loss. Nevertheless this matter could be addressed in more detail with a more controlled monocular study design using people with one eye with advanced glaucomatous scotomas and the other with relatively good vision viewing the selection of images.

Whilst quantitative techniques in Ophthalmological research are normal, the potential for qualitative methods for improving healthcare is beginning to be recognised. Although there are certain types of bias that can be introduced when considering data yielded from notes and transcripts due to subjective influences

from the sides of both the participant and the experimenter, novel questions and trends may emerge from the data in a way that would not be possible in a more numerical-based dataset. Qualitative research can produce vast amounts of data, which requires labour intensive analysis and interpretation. It was therefore deduced that interviewing the patients, and analysing the transcripts in a systematic manner, would enable further information regarding their experiences with glaucoma to be revealed. One simple technique of summarising such data is to use simple counts to yield information regarding the most common themes and traits (Pope et al., 2000). Analysis of transcripts from the conversations revealed that the most commonly used words to describe their vision were in line with the most popular images chosen by the participants. For instance, 16 patients used the word 'miss' as a description of their experiences, in the context that objects were just 'not there' but there was no noticeable change to the quality of the image. "Blur" and words synonymous with this unclear, low resolution effect ("hazy", "double vision", "clear", "fuzzy", "foggy") were also commonly used by the patients to describe their vision. Furthermore, several insightful comments were made by the patients during the study session, which enabled them to reveal details regarding their perceptions of their condition that would not have been possible during a normal clinic appointment (Lunnela et al., 2010). An example of this is a patient described how on one occasion she did not notice the arrival of her bus at the bus stop, because she could not see the top deck (Figure 7.5, final example). Interestingly the location of the binocular field loss of this patient coincided with the area of the visual field where the top deck of the bus would have appeared. A more individualised perspective on each patient's visual field loss and subsequent experiences in everyday life may help develop programs developed to that individual's specific needs and even help improve their QoL.

It is worth noting that the word "black" was also mentioned by the patients a small number of times, which was surprising in the context of the finding that none of the patients felt the images using black to represent areas of visual loss were the most adequate representations of their actual vision. However, analysis of the transcripts allowed clarification of the context in which the word was used, and revealed that it was actually used by one patient in the context of 'blacked out' (i.e.

a commonly used expression to describe the phenomenon whereby visual information disappears) and likewise was used by the other individual as a way of describing that there was "nothing there". The confusion in these statements highlights the limitations of this work in that the experiences of the patients are subjective and therefore difficult to verify, in addition to the fact that visual experience is ultimately something that is extremely difficult for one to eloquently put into words. As one patient put it "it's very difficult, as nobody can tell you what your sight is like, it's very difficult to describe" (Figure 7.5). Finally, the aforementioned patients reaffirm the idea that black is often used as a solution to the awkward task of representing something that is not actually there. However, this does not ultimately appear to be an optimal strategy in terms of representing what glaucoma "looks like" as the results of the current paper show that patients with glaucoma do not see black in their field of view. Using black as a method to represent areas of "nothingness" or less defined vision in the field of view could be unsurprisingly be misinterpreted as showing a direct view of how a person of glaucoma would see the world and as such, on viewing this image in a similar mindset, it is not unreasonable to suggest that many people with glaucoma may have deduced that their either did not have glaucoma, or that it is not that severe, as how they see the world does not coincide with the apparent depiction in the images. The current study suggests instead that moving towards images with blurriness and/or missing regions may be a more appropriate method of representing how a glaucomatous defect may be perceived. Of course it should be reinforced that these images are never going to be able to perfectly represent glaucoma. Each individual undeniably perceives the world differently, and as such, the development of the 'perfect' image depicting what having glaucoma is like is most probably an impossible task. However, working together with patients with glaucoma and actively involving them in the development process will allow for the creation of more realistic representations of visual loss and should ultimately help increase awareness of glaucoma amongst both diagnosed patients and the general public.

7.5 Conclusion

Patients with glaucoma do not perceive their visual field defect as 'black patches' or as a 'tunnel' effect masking their field of view. The lack of patients choosing the 'tunnel' effect choice maybe down to our sample not having advanced glaucomatous defects. These findings are important in the context of depicting the effects of the disease and raising awareness for detection and case finding. People with glaucoma in earlier disease stage are unlikely to notice their defect or any symptoms and therefore picked the picture with no change. However, more severe patients were more likely to notice something but would most commonly refer to blur and choose the blurred patches picture or refer to things simply 'not being there' and therefore choose the image with missing 'filled in' patches as the best depiction of this. No patient chose either image with black regions.

8 Conclusions and further work

Current measurements of glaucomatous visual loss are useful for monitoring the severity and progression of disease in a clinical environment. Unfortunately little is currently known about how VF defects actually impact on the patient's day-to-day performance on 'visual tasks'. The overall aim of this thesis was to increase our understanding as to how patients with glaucoma function in their everyday lives, and in particular whether they might change their eye movements relative to people with healthy vision. The work in this thesis subsequently contributes the following new findings to the research literature:

The study in Chapter 3 explored the performance of people with glaucoma in an important under-investigated visual task: searching for objects. This involved comparing the average time taken for a group of patients diagnosed with glaucoma to find target objects in controlled and naturalistic images with that of age-related controls. It was reported that, although the groups did not perform any differently in the more controlled search task, the people with glaucoma displayed significantly more impairment on average when searching for objects in a more naturalistic environment. Contrast sensitivity and visual field defect severity were associated with search time in the patients. Hence patients with glaucoma could display disability when searching for objects in their day-to-day lives as a result of worsening aspects of their visual loss.

The study described in Chapter 4 utilised the study of eye movements as a potential method for understanding how patients with glaucoma function as a result of their visual loss. The study investigated whether there may be some relationship between the observed deficits in visual search task performance and the eye movements the patients make as they carry out the task. The eye movements of patients were measured using an Eyelink II as they carried out the search tasks described in Chapter 3 and compared with those made by visually healthy subjects. It was found that patients with glaucoma produced significantly fewer saccades on average than the controls when searching for target objects, with saccade rate linked to both the severity of visual field defect and contrast

sensitivity. There was also a correlation between eye movements and task performance, with those patients who produced fewer saccades per second also performing worse in the task. This effect was not present in the participants with normal vision. This may suggest that the eye movements patients make could be an underlying factor relating to the functional deficits they can experience in everyday tasks such as visual search.

The work presented in Chapter 5 sought to investigate whether the eye movement differences observed in the patients who took part in the previous search task also exist in other naturalistic settings with differing task demands. This study observed the eye movements of patients with glaucoma and visually healthy subjects as they passively viewed photographs of everyday scenes. There was therefore no real task demand- they simply had to 'enjoy' the pictures; in an attempt to isolate eye movements that might occur as a patient views a scene for the first time. It was found there was a small but significant reduction in the number of saccades made by the patients on average compared with the controls. There was also a small effect in terms of how they viewed the image in that the patients tended to view more restricted areas of the field of view than the participants with normal vision. This may suggest that the peripheral field loss typically experienced by patients with glaucoma restricts the eye movements they make and therefore means that they cannot build up as fruitful a representation of the visual world around them as people with healthy vision. Furthermore, it was shown that patients with worsening VF defect severity and worsening contrast sensitivity are less likely to fixate the same parts of the image as controls. This result further suggests that there is something specific to glaucoma that is causing the patients to perceive the image differently to the controls.

The study described in Chapter 6 examined how the eye movements produced by people with glaucoma as they viewed a driving scene compared to those made by control subjects with normal vision. Driving is a topic of much relevance in glaucoma given, for example, the legal fitness to drive requirements in the UK. This study found that patients also move their eyes differently when searching for hazards; a finding that could have additional implications for determining fitness to drive. In contrast to the studies in the previous chapters when participants

passively viewed and searched for items within naturalistic images, this study found that patients produced significantly *more,* and thus shorter, fixations on average compared with the controls. It is speculated that this discrepancy is related to task demands; this study involved viewing a face-paced dynamic scene whereas the other tasks involved simpler, static images. These results therefore also indicate the importance of considering the nature of the tasks when considering the eye movements made by patients with glaucoma.

The study in Chapter 7 aimed to investigate patient perceptions of their vision and how a visual field defect might appear to the patient in real life. The effect of glaucoma on vision is commonly represented as appearing like a black tunnel or as black patches but this study found that none of the patients described their defect as appearing in this way. Instead, many patients claimed their defect appeared more 'blurred' or that there may be some 'missing parts' of their vision where information has been filled in by contextual surroundings. This information is important for educating patients and clinicians as to the effects of glaucoma and the development of more improved representations could encourage better diagnosis and treatment compliance.

In short, this thesis has contributed to our understanding as to the effects of glaucoma on the patient's everyday life, firstly by showing that patients are on average slower to find objects in everyday scenes than people with healthy vision of a similar age. This suggests they could face disability with visual search tasks in their real life. Furthermore, a particular emphasis of the thesis was to highlight novel findings that patients with glaucoma appear to display different eye movements as they carry out various real-world tasks. A key finding was that patients reduce their saccade rate when searching for objects compared with controls, and that there was a link between saccade rate and the length of times patients took to find the objects in the search tasks. This suggests that eye movement strategies may underlie some of the functional deficits, such as with visual search, displayed by some patients with glaucoma. The reduced saccade rate displayed by patients on average compared with healthy age-related people was also observed when patients were free to view any part of an image that they wished. Further evidence also suggested that patients on average view more

restricted areas of visual scenes and look at different parts of the scene compared with controls. This suggested that the peripheral defects often seen in glaucoma may affect their ability to build up a fruitful representation of a visual scene, and affect which visual information they deem to be most important. Patients also changed their eye movements when viewing dynamic driving videos, but this time patients increased their fixation rate to deal with the task. Finally, it was also shown that current understanding regarding the 'appearance' of glaucoma to the patient in their everyday lives may differ from how the patient actually perceives it. By highlighting that patients do not perceive their defect as a 'black tunnel' or 'black patches' in their vision, this study emphasises the need for new and improved representations to help better explain how glaucoma might affect the patient in everyday life.

However, despite these contributions, there are still many unanswered questions and therefore scope for further research. Ideas for future research are therefore as follows:

- Pictures of everyday scenes displayed on a computer screen are not the same as the real thing. Future research could therefore examine whether patients with glaucoma are slower and produce different eye movements when searching for real-life objects or carrying out other tasks in a naturalistic setting.
- Patients were shown to have different levels of awareness of their defect and the impact it had on their day-to-day functioning. Perhaps how aware patients are of their defect influences the types of eye movements they make in an attempt to compensate for their visual loss? Future studies should also consider the link between other characteristics of the VF defect, such as the specific location of the defect, and how this might influence eye movements and task performance.
- Although patients use both eyes to function in the real-world, our current understanding and techniques for measuring binocular visual function are somewhat limited. For instance, we don't fully understand exactly how the known 'filling in' effects occur or how one eye compensates for another, and although useful, the only clinically available test of binocular visual field, the

Esterman, is limited in the degree of information it is able to give regarding the actual levels of sensitivity. It is therefore equally difficult to infer exactly why eye movements may be occurring in binocular tasks. Since visual fields are currently measured monocularly, perhaps measuring eye movements in each eye separately could help us better understand exactly what is happening to the eye movements as a result of the type and location of the visual loss.

- The findings reported in this thesis could also be used to produce more accurate educational tools regarding what having glaucoma is actually like, by developing images and videos that incorporate the new information regarding how glaucoma appears to the patient and the eye movements patients may make as they study visual scenes (Figure 8.1).

Figure 8.1: Using the findings in Chapter 7 a more representative version of one of the images shown in Figure 6.3a (also shown in a and b) has been created and is shown in c.

Appendix A – Sample C# code

C# code to calculate Bivariate Contour Ellipse Area (BCEA)

```
public double ellipseArea(double probabilityArea)
{
	double[,] ellipse = largeProbabilityEllipse(probabilityArea);
	double SDPointLocOverMeridianX = SDPointLocOverMeridian(xIn);
	double SDPointLocOverMeridianY = SDPointLocOverMeridian(yIn);
	double pearsonResult = pearson(xIn, yIn);
	double a = Math.Pow(SDPointLocOverMeridianY, 2) - Math.Pow(SDPointLocOverMeridianX, 2);
	double b = 2 * pearsonResult * SDPointLocOverMeridianX * SDPointLocOverMeridianY;
	double theta = 0.5 * Math.Atan(-b / a);
	double[] m1m2 = m1andm2(probabilityArea, SDPointLocOverMeridianX, SDPointLocOverMeridianY, pearsonResult);
	double meanX = meanValues(xIn);
	double meanY = meanValues(yIn);
	double m1 = m1m2[0], m2 = m1m2[1];

	if (SDPointLocOverMeridianX < SDPointLocOverMeridianY)
	{
		m1 = m1m2[1];
		m2 = m1m2[0];
	}

	if (SDPointLocOverMeridianX < SDPointLocOverMeridianY)
	{
		double adj = (double)m1m2[1] * (double)Math.Cos(theta);
		double opp = (double)m1m2[1] * (double)Math.Sin(theta);
		theta += Math.PI / 2;
		double adj2 = (double)m1m2[0] * (double)Math.Cos(theta);
		double opp2 = (double)m1m2[0] * (double)Math.Sin(theta);
		double newY = Math.Sqrt(Math.Pow((meanX - (adj + meanX)), 2) + Math.Pow((meanY - (opp + meanY)), 2));
		double newX = Math.Sqrt(Math.Pow((meanX - (adj2 + meanX)), 2) + Math.Pow((meanY - (opp2 + meanY)), 2));
		return Math.PI * newX * newY;
```

```
        }
        else
        {
                double adj = (double)m1m2[0] * (double)Math.Cos(theta);
                double opp = (double)m1m2[0] * (double)Math.Sin(theta);
                theta += Math.PI / 2;
                double adj2 = (double)m1m2[1] * (double)Math.Cos(theta);
                double opp2 = (double)m1m2[1] * (double)Math.Sin(theta);
                double newY = Math.Sqrt(Math.Pow((meanX - (adj + meanX)), 2) + Math.Pow((meanY - (opp + meanY)), 2));
                double newX = Math.Sqrt(Math.Pow((meanX - (adj2 + meanX)), 2) + Math.Pow((meanY - (opp2 + meanY)), 2));
                return Math.PI * newX * newY;
        }
}
```

C# code to calculate (X, Y) coordinates to plot Bivariate Contour Ellipse

```
public double[,] probabilityEllipse(double probabilityArea)
{
	double SDPointLocOverMeridianX = SDPointLocOverMeridian(xIn);
	double SDPointLocOverMeridianY = SDPointLocOverMeridian(yIn);
	double correlation = 0;
	double[] m1m2;
	double meanX = meanValues(xIn);
	double meanY = meanValues(yIn);

	if (SDPointLocOverMeridianX < SDPointLocOverMeridianY)
	{
		SDPointLocOverMeridianX = SDPointLocOverMeridianY;
		SDPointLocOverMeridianY = SDPointLocOverMeridian(xIn);
		correlation = pearson(yIn, xIn);
		m1m2 = m1andm2(probabilityArea, SDPointLocOverMeridianX, SDPointLocOverMeridianY, correlation);
		double[,] results = new double[360, 3];
		double a = Math.Pow(SDPointLocOverMeridianY, 2) - Math.Pow(SDPointLocOverMeridianX, 2);
		double b = 2 * correlation * SDPointLocOverMeridianX * SDPointLocOverMeridianY;
		double theta = 0.5 * Math.Atan(-b / a);
		double r = Math.Sqrt(1 - Math.Pow(correlation, 2));
		double loopSize = probabilityArea * correlation * SDPointLocOverMeridianX;
		double m1 = m1m2[1], m2 = m1m2[0];
		if (m1m2[0] > m1m2[1])
		{
			m1 = m1m2[0];
			m2 = m1m2[1];
		}

		for (int i = 0; i < 360; i++)
		{
			results[i, 1] = meanY + m1 * Math.Cos(theta) * Math.Cos(i) - m2 * Math.Sin(theta) * Math.Sin(i);
			results[i, 0] = meanX + m1 * Math.Sin(theta) * Math.Cos(i) + m2 * Math.Cos(theta) * Math.Sin(i);
		}
	return results;
	}
```

```
        else
        {
                correlation = pearson(xIn, yIn);
                m1m2 = m1andm2(probabilityArea, SDPointLocOverMeridianX, SDPointLocOverMeridianY, correlation);
                double[,] results = new double[360, 3];
                double a = Math.Pow(SDPointLocOverMeridianY, 2) - Math.Pow(SDPointLocOverMeridianX, 2);
                double b = 2 * correlation * SDPointLocOverMeridianX * SDPointLocOverMeridianY;
                double theta = 0.5 * Math.Atan(-b / a);
                double r = Math.Sqrt(1 - Math.Pow(correlation, 2));
                double loopSize = probabilityArea * correlation * SDPointLocOverMeridianX;
                double m1 = m1m2[1], m2 = m1m2[0];
        if (m1m2[0] > m1m2[1])
        {
                m1 = m1m2[0];
                m2 = m1m2[1];
        }

        for (int i = 0; i < 360; i++)
        {
                results[i, 0] = meanX + m1 * Math.Cos(theta) * Math.Cos(i) - m2 * Math.Sin(theta) * Math.Sin(i);
                results[i, 1] = meanY + m1 * Math.Sin(theta) * Math.Cos(i) + m2 * Math.Cos(theta) * Math.Sin(i);
        }
        return results;
        }
}
```

C# common functions

Calculate major and minor axis

```
private double[] m1andm2(double probabilityArea, double SDPointLocOverMeridianX, double SDPointLocOverMeridianY, double correlation)
{
	double[] results = new double[2];
	double a = Math.Pow(SDPointLocOverMeridianY, 2) - Math.Pow(SDPointLocOverMeridianX, 2);
	double b = 2 * correlation * SDPointLocOverMeridianX * SDPointLocOverMeridianY;

	results[0] = probabilityArea * Math.Sqrt(0.5 * ((Math.Pow(SDPointLocOverMeridianX, 2) + Math.Pow(SDPointLocOverMeridianY, 2))
+ Math.Sqrt(Math.Pow(a, 2) + Math.Pow(b, 2))));
	results[1] = probabilityArea * Math.Sqrt(0.5 * ((Math.Pow(SDPointLocOverMeridianX, 2) + Math.Pow(SDPointLocOverMeridianY, 2))
- Math.Sqrt(Math.Pow(a, 2) + Math.Pow(b, 2))));
	return results;
}
```

Calculate Pearson correlation

```
private double pearson(double[] x, double[] y)
{
	double meanx = meanValues(x);
	double meany = meanValues(y);
	double sxx = 0, syy = 0, sxy = 0;

	for (int i = 0; i < x.Length; i++)
	{
		sxx += Math.Pow((x[i] - meanx), 2);
		syy += Math.Pow((y[i] - meany), 2);
		sxy += (x[i] - meanx) * (y[i] - meany);
	}
	return sxy / Math.Sqrt(sxx * syy);
}
```

Calculate Standard Deviation over meridian

```
private double SDPointLocOverMeridian(double[] data) //gives σx and σy
{
	double[] dataMinusMean = new double[data.Length];
	double mean = meanValues(data);
	for (int i = 0; i < data.Length; i++)
		dataMinusMean[i] = data[i] - mean;

	double results = SDit(dataMinusMean, meanValues(dataMinusMean));
	return results;
}
```

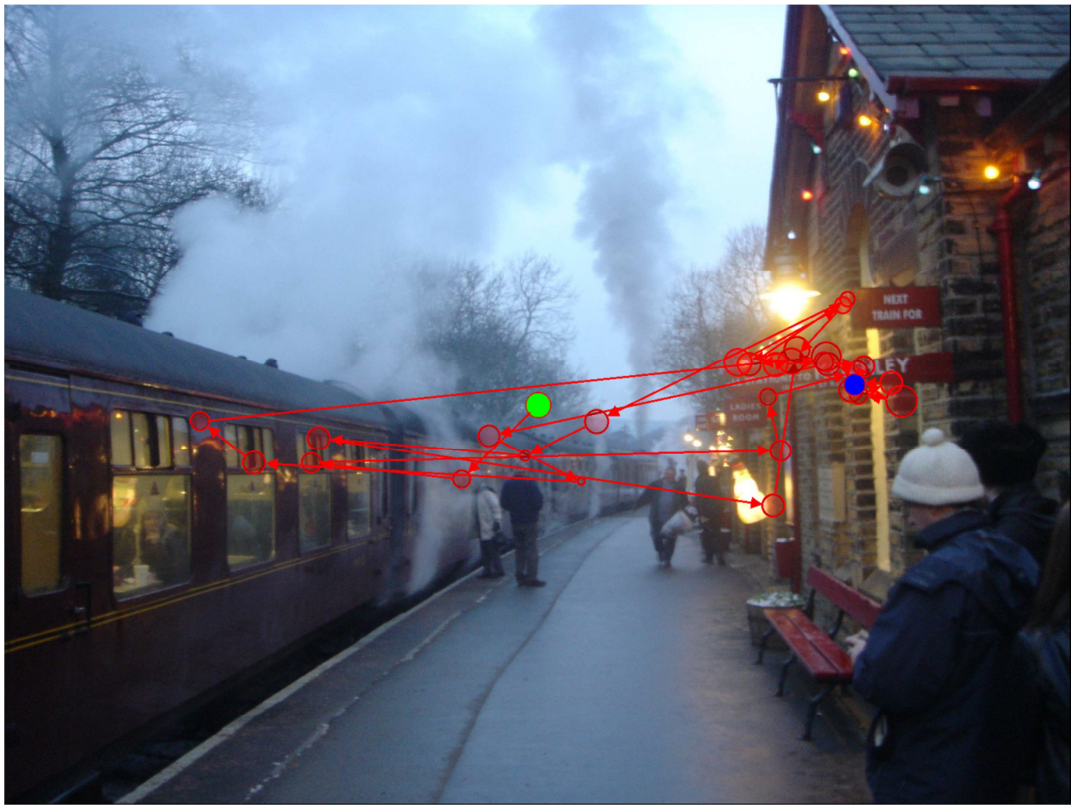
Calculate mean

```
private double meanValues(double[] meanArray)
{
	double mean = 0;
	for (int i = 0; i < meanArray.Length; i++)
		mean += meanArray[i];
	mean /= meanArray.Length;
	return mean;
}
```

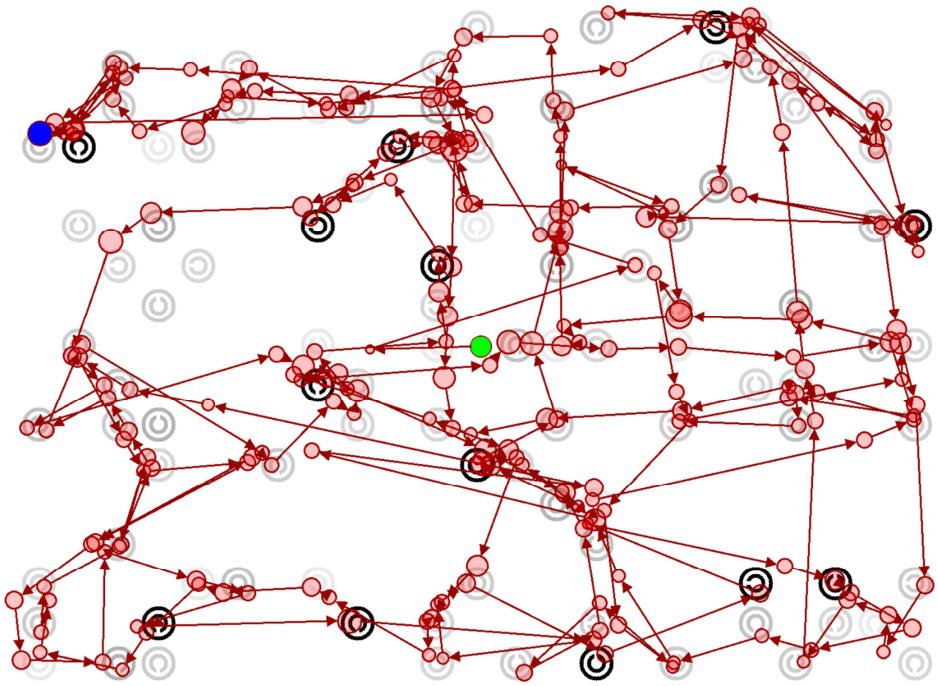
Calculate Standard Deviation

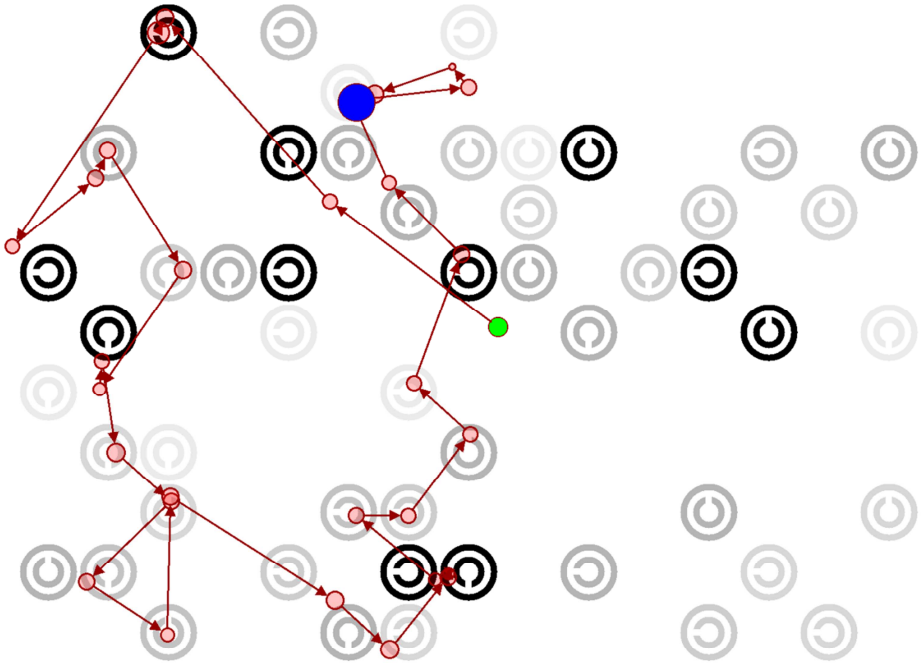
```
private double SDit(double[] dataToSD, double mean)
{
	double sd = 0;
	for (int i = 0; i < dataToSD.Length; i++)
		sd += Math.Pow((dataToSD[i] - mean), 2);
	double temp1 = (double)1 / ((double)dataToSD.Length - 1);
	sd *= temp1;
	sd = Math.Sqrt(sd);
	return sd;
}
```

Appendix B – Larger versions of eye movement traces from Chapter 5




City Walls :
Eastgate





Appendix C – Participant details

Control participant details

Control number	Age	Sex	Right MD	Left MD	BEMD	VA	PRlogCS
1	78	F	-0.67	-0.78	-0.67	-0.1	1.95
2	56	M	0.53	0.59	0.59	-0.1	1.95
3	82	M	-0.27	1.2	1.2	0.1	1.75
4	68	F	-0.39	-1.75	-0.39	0	1.95
5	62	F	0.45	-0.05	0.45	0	1.95
6	73	M	-1.41	-1.07	-1.07	-0.1	1.95
7	77	F	-0.1	-0.15	-0.1	-0.1	1.95
8	76	M	1.52	0.87	1.52	0	1.95
9	73	F	-1.29	-1.32	-1.29	0	1.95
10	64	F	0.63	0.81	0.81	0.1	1.95
11	68	F	1.52	1.25	1.52	-0.2	1.95
12	69	F	-2.27	-1.37	-1.37	0.1	1.95
13	71	M	1.26	1.7	1.7	0.2	1.95
14	68	F	0.92	0.66	0.92	-0.1	1.95
15	33	F	-0.16	0.53	0.53	-0.3	1.95
16	74	F	1.95	0.75	1.95	0	1.95
17	68	M	1.86	1.38	1.86	-0.1	1.95
18	56	F	-0.1	-0.03	-0.03	-0.04	1.95
19	62	F	1.66	1.22	1.66	-0.14	1.95
20	63	M	-0.05	-0.63	-0.05	-0.14	1.95
21	64	M	-0.84	-3.94	-0.84	-0.04	1.95
22	74	F	0.5	0.36	0.5	-0.08	1.95
23	76	M	-0.45	-0.33	-0.33	-0.08	1.95
24	74	F	-1	-2.61	-1	0	1.95
25	71	M	0.54	0.93	0.93	0.2	1.95
26	75	M	-1.06	-2.83	-1.06	-0.08	1.95
27	79	F	-0.95	-1.79	-0.95	0	1.95
28	64	M	-1.17	-0.06	-0.06	0	1.95
29	70	F	0.59	-0.19	0.59	0.02	1.95
30	75	M	1.54	0.36	1.54	-0.12	1.95

Glaucoma participant details

Patient number	Age	Sex	Right MD	Left MD	BEMD	VA	PRlogCS
1	59	M	-11.32	0.72	0.72	-0.18	1.95
2	65	F	-4.24	-5.68	-4.24	-0.12	1.95
3	75	F	-6.39	-13.48	-6.39	-0.04	1.95
4	71	M	-3.78	-5.74	-3.78	0.18	1.65
5	64	M	-1.99	-5.98	-1.99	0.02	1.95
6	73	M	-26.16	-14.41	-14.41	0.12	1.5
7	77	F	-18.41	-16.93	-16.93	0.18	1.65
8	78	M	-5.56	-12.89	-5.56	0.06	1.95
9	77	F	-3.61	-2.24	-2.24	0.16	1.95
10	82	F	-4.98	-3.89	-3.89	0.12	1.8
11	68	M	-4.32	-2.64	-2.64	-0.06	1.8
12	76	M	-19.76	-13.81	-13.81	0.24	1.7
13	66	F	-8.55	-9.02	-8.55	0.18	1.7
14	71	M	-13.79	-3.59	-3.59	0.24	1.8
15	61	M	-3.4	-5.71	-3.4	0.06	1.9
16	35	F	-11.06	-3.61	-3.61	-0.1	1.95
17	60	F	-19.36	-6.73	-6.73	-0.18	1.9
18	74	M	-7.77	-4.82	-4.82	0.16	1.65
19	79	F	-3.69	-10.64	-3.69	0.16	1.5
20	58	F	-4.53	-2.15	-2.15	0.02	1.95
21	77	F	-14.65	-17.75	-14.65	0.02	1.95
22	79	F	-5.61	-6	-5.61	0.04	1.65
23	68	F	-7.81	-5.03	-5.03	-0.04	1.75
24	65	M	-29.27	-16.66	-16.66	0.04	1.45
25	58	F	-3.68	-5.54	-3.68	-0.08	1.85
26	66	F	-5.16	-11.18	-5.16	0.08	1.95
27	66	M	-7.57	-12.12	-7.57	0.14	1.8
28	58	M	-17.23	-4.82	-4.82	0.14	1.95
29	78	F	-5.63	-5.54	-5.54	0.18	1.95
30	72	F	-22.51	-17.1	-17.1	0.18	1.65

Appendix D - Peer reviewed papers

Crabb DP, Smith ND, Rauscher FG, Chisholm CM, Barbur JL, Edger DF & Garway-Heath DF (2010). Exploring Eye Movements in Patients with Glaucoma When Viewing a Driving Scene. PLoS ONE 5(3): e9710.

Smith ND, Crabb DP & Garway-Heath DF (2011). An exploratory study of visual search performance in glaucoma. Ophthalmic and Physiological Optics, 31, 225–232.

Smith ND, Crabb DP; Glen FC; Burton R & Garway-Heath DF (2012). Eye movements in patients with glaucoma when viewing images of everyday scenes. Seeing and Perceiving. Accepted for publication

Meeting abstracts

Smith ND, Rauscher FG, Chisholm CM, Edgar DF, Barbur JL, Garway-Heath DF & Crabb DP (2007). Eye Movements in Patients with Glaucoma When Viewing a Driving Hazards Perception Test. Invest Ophthalmol Vis Sci; 48: E-Abstract 4450.

Smith ND, Rauscher FG, Chisholm CM, Edgar DF, Barbur JL, Garway-Heath DF, Rubin GS & Crabb DP (2007). Eye Movement analysis in Glaucoma When Viewing a Driving Hazards Perception Test. European Conference of Eye Movements (ECEM), Potsdam

Smith ND, Rubin GS, Garway-Heath DF & Crabb DP. (2008). Exploring Eye Movements in Glaucomatous Patients When Viewing Natural Photographs. *Invest Ophthalmol Vis Sci*; 49: E-Abstract 1110

ND Smith, GS Rubin, DF Garway-Heath, DP Crabb (2009). How does glaucoma affect eye movements when searching and passively viewing photographs? British Congress of Optometry and Vision Science (BCOVS), Brighton

ND Smith, GS Rubin, DF Garway-Heath, DP Crabb (2009). What do patients with glaucoma do when they search and look at everyday scenes? UK and Eire Glaucoma Society Meeting (UKEGS), Dublin

ND Smith, GS Rubin, DF Garway-Heath, DP Crabb (2009). What do patients with glaucoma do when they search and look at everyday scenes? Royal College of Ophthalmologists (RCO) Annual meeting, Birmingham

ND Smith, GS Rubin, DF Garway-Heath, DP Crabb (2010). What do patients with glaucoma do when they search and look at everyday scenes? European Association for Eye and Vision Research (EVER), Portoroz

Smith ND, Crabb DP & Garway-Heath DF (2011). How Does Glaucoma Look? A Study of Patient Perception Of Visual Field Defects. Invest Ophthalmol Vis Sci; 52: E-Abstract 4414

Smith ND (2011). Eye movements in Glaucoma. European Conference of Eye Movements (ECEM), Marseille

References

ACIK, A., ONAT, S., SCHUMANN, F., EINHAUSER, W. & KONIG, P. 2009. Effects of luminance contrast and its modifications on fixation behavior during free viewing of images from different categories. *Vision Res,* 49**,** 1541-53.

ALEX, B., JAN, E. L.-K., RUSSELL, L. W., NICOLE, A., JOHN, B. & JANE, M. 1997. Mobility performance with retinitis pigmentosa. *Clinical and Experimental Optometry,* 80**,** 1-12.

ALTANGEREL, U., SPAETH, G. L. & STEINMANN, W. C. 2006. Assessment of function related to vision (AFREV). *Ophthalmic Epidemiol,* 13**,** 67-80.

ALTMAN, D. G. 1978. Plotting Probability Ellipses. *Applied Statistics,* 27**,** 347-349.

ANDREWS, T. J. & COPPOLA, D. M. 1999. Idiosyncratic characteristics of saccadic eye movements when viewing different visual environments. *Vision Research,* 39**,** 2947-2953.

ANG, G. S. & EKE, T. 2006. Lifetime visual prognosis for patients with primary open-angle glaucoma. *Eye,* 21**,** 604-608.

ANTES, J. R. 1974. The time course of picture viewing. *Journal of Experimental Psychology,* 103**,** 62-70.

ARDITI, A. 2005. Improving the design of the letter contrast sensitivity test. *Invest Ophthalmol Vis Sci.,* 46**,** 2225-9.

AUSTIN, D. J. 1974. Acquired colour vision defects in patients suffering from chronic simple glaucoma. *Trans Ophthalmol Soc U K,* 94**,** 880-3.

BAKER, H. & MURDOCH, I. E. 2008. Can a public health intervention improve awareness and health-seeking behaviour for glaucoma? *British Journal of Ophthalmology,* 92**,** 1671-1675.

BALL, K., OWSLEY, C., SLOANE, M. E., ROENKER, D. L. & BRUNI, J. R. 1993. Visual attention problems as a predictor of vehicle crashes in older drivers. *Invest Ophthalmol Vis Sci,* 34**,** 3110-23.

BALL, K., OWSLEY, C., BEARD, B. 1990. Clinical visual perimetry underestimates peripheral field problems in older adults. *Clin. Vision. Sci.,* 5**,** 113-125.

BALL, K. K., BEARD, B. L., ROENKER, D. L., MILLER, R. L. & GRIGGS, D. S. 1988. Age and visual search: expanding the useful field of view. *J Opt Soc Am A,* 5**,** 2210-9.

BBC Breakfast. Clip available at: http://news.bbc.co.uk/1/hi/health/7660570.stm, Year. TV. Directed by BBC. UK.

BECHETOILLE, A., ARNOULD, B., BRON, A., BAUDOUIN, C., RENARD, J. P., SELLEM, E., BROUQUET, Y., DENIS, P., NORDMANN, J. P., RIGEADE, M. C., BASSOLS, A., BENMEDJAHED, K., GUILLEMIN, I. & ROULAND, J. F. 2008. Measurement of health-related quality of life with glaucoma: validation of the Glau-QoL 36-item questionnaire. *Acta Ophthalmol,* 86**,** 71-80.

BECKER, W. 1991. Saccades. *In:* CARPENTER, R. H. S. (ed.) *Eye Movements.* London: Macmillan Press.

BELLMANN, C., FEELY, M., CROSSLAND, M. D., KABANAROU, S. A. & RUBIN, G. S. 2004. Fixation stability using central and pericentral fixation targets in patients with age-related macular degeneration. *Ophthalmology,* 111**,** 2265-2270.

BERTERA, J. & RAYNER, K. 2000. Eye movements and the span of the effective stimulus in visual search. *Attention, Perception & Psychophysics,* 62**,** 576-585.

BHARGAVA, J. S., PATEL, B., FOSS, A. J. E., AVERY, A. J. & KING, A. J. 2006. Views of Glaucoma Patients on Aspects of Their Treatment: An Assessment of Patient Preference by Conjoint Analysis. *Invest. Ophthalmol. Vis. Sci.,* 47**,** 2885-2888.

BLACK, A. A., WOOD, J. M., LOVIE-KITCHIN, J. E. & NEWMAN, B. M. 2008. Visual impairment and postural sway among older adults with glaucoma. *Optom Vis Sci,* 85**,** 489-97.

BRAMLEY, T., PEEPLES, P., WALT, J. G., JUHASZ, M. & HANSEN, J. E. 2008. Impact of vision loss on costs and outcomes in medicare beneficiaries with glaucoma. *Arch Ophthalmol.,* 126**,** 849-56.

BRANDT, S. A. & STARK, L. W. 1997. Spontaneous Eye Movements During Visual Imagery Reflect the Content of the Visual Scene. *Journal of Cognitive Neuroscience,* 9**,** 27-38.

BROOKS, W. B., JORDAN, J. S., DIVINE, G. W., SMITH, K. S. & NEELON, F. A. 1990. The impact of psychologic factors on measurement of functional status. Assessment of the sickness impact profile. *Med Care,* 28**,** 793-804.

BROWN, G. C., BROWN, M. M. & SHARMA, S. 2000. Difference between ophthalmologists' and patients' perceptions of quality of life associated with age-related macular degeneration. *Can J Ophthalmol,* 35**,** 127-33.

BULLIMORE, M. A. & BAILEY, I. L. 1995. Reading and Eye Movements in Age-Related Maculopathy. *Optometry & Vision Science,* 72**,** 125-138.

BUSWELL, G. T. 1935. *How people look at pictures: A study of the psychology of perception in art.,* Chicago, University of Chicago Press.

CALDARA, R., ZHOU, X. & MIELLET, S. B. 2010. Putting Culture Under the 'Spotlight' Reveals Universal Information Use for Face Recognition. *PLoS One,* 5**,** e9708.

CAVE, K. R. & WOLFE, J. M. 1990. Modeling the role of parallel processing in visual search. *Cogn Psychol,* 22**,** 225-71.

CHEONG, A. M. Y., GERUSCHAT, D. R. & CONGDON, N. 2008. Traffic Gap Judgment in People with Significant Peripheral Field Loss. *Optometry and Vision Science,* 85**,** 26-36.

CHISHOLM, C. M., RAUSCHER, F. G., CRABB, D. C., DAVIES, L. N., DUNNE, M. C., EDGAR, D. F., HARLOW, J. A., JAMES-GALTON, M., PETZOLD, A., PLANT, G. T., VISWANATHAN, A. C., UNDERWOOD, G. J. & BARBUR, J. L. 2008. Assessing visual fields for driving in patients with paracentral scotomata. *Br J Ophthalmol,* 92**,** 225-230.

COECKELBERGH, T. R. M., W. CORNELISSEN, F., H. BROUWER, W. & C. KOOIJMAN, A. 2002. The effect of visual field defects on eye movements and practical fitness to drive. *Vision Research,* 42**,** 669-677.

COFFEY, M., REIDY, A., WORMALD, R., XIAN, W. X., WRIGHT, L. & COURTNEY, P. 1993. Prevalence of glaucoma in the west of Ireland. *Br J Ophthalmol,* 77**,** 17-21.

CONKLIN, H. M., CALKINS, M. E., ANDERSON, C. W., DINZEO, T. J. & IACONO, W. G. 2002. Recognition memory for faces in schizophrenia patients and their first-degree relatives. *Neuropsychologia,* 40**,** 2314-2324.

CORNELISSEN, F. W. P., BRUIN, K. J. P. & KOOIJMAN, A. C. P. 2005. The Influence of Artificial Scotomas on Eye Movements during Visual Search. *Optometry & Vision Science,* 82**,** 27-35.

CRABB, D. P., FITZKE, F. W., HITCHINGS, R. A. & VISWANATHAN, A. C. 2004. A practical approach to measuring the visual field component of fitness to drive. *Br J Ophthalmol,* 88**,** 1191-1196.

CRABB, D. P., SMITH, N. D., RAUSCHER, F. G., CHISHOLM, C. M., BARBUR, J. L., EDGAR, D. F. & GARWAY-HEATH, D. F. 2010. Exploring eye movements in patients with glaucoma when viewing a driving scene. *PLoS One,* 5**,** e9710.

CRABB, D. P. & VISWANATHAN, A. C. 2005. Integrated visual fields: a new approach to measuring the binocular field of view and visual disability. *Graefes Arch. Clin. Exp. Ophthalmol.,* 243**,** 210-216.

CRABB, D. P., VISWANATHAN, A. C., MCNAUGHT, A. I., POINOOSAWMY, D., FITZKE, F. W. & HITCHINGS, R. A. 1998. Simulating binocular visual field status in glaucoma. *Br J Ophthalmol.,* 82**,** 1236-41.

CROSSLAND, M. D., CULHAM, L. E. & RUBIN, G. S. 2004. Fixation stability and reading speed in patients with newly developed macular disease. *Ophthalmic and Physiological Optics,* 24**,** 327-333.

CROSSLAND, M. D. & RUBIN, G. S. 2002. The use of an infrared eyetracker to measure fixation stability. *Optometry and Vision Science,* 79**,** 735-739.

CROSSLAND, M. D. & RUBIN, G. S. 2006. Eye movements and reading in macular disease: further support for the shrinking perceptual span hypothesis. *Vision Res,* 46**,** 590-7.

DE GRAEF, P. 2005. Semantic effects on object selection in real-world scene perception. *In:* UNDERWOOD, G. D. M. (ed.) *Cognitive processes in eye guidance.* Oxford, UK: Oxford University Press.

DELABARRE, E. B. 1898. A Method of Recording Eye-Movements. *The American Journal of Psychology,* 9**,** 572-574.

DIEFENDORF, A. R. & DODGE, R. 1908. AN EXPERIMENTAL STUDY OF THE OCULAR REACTIONS OF THE INSANE FROM PHOTOGRAPHIC RECORDS. *Brain,* 31**,** 451-489.

DIELEMANS, I., VINGERLING, J. R., WOLFS, R. C., HOFMAN, A., GROBBEE, D. E. & JONG, P. T. 1994. The prevalence of primary open-angle glaucoma in a population-based study in The Netherlands. The Rotterdam Study. *Ophthalmology,* 101**,** 1851-1855.

DITCHBURN, R. W. & GINSBORG, B. L. 1952. Vision with a Stabilized Retinal Image. *Nature,* 170**,** 36-37.

DODGE, R. & CLINE, T. S. 1901. The angle velocity of eye movements. *Psychological Review,* 8**,** 145-157.

DOLINIS, J., HARRISON, J. E. & ANDREWS, G. R. 1997. Factors associated with falling in older Adelaide residents. *Australian and New Zealand Journal of Public Health,* 21**,** 462-468.

DUCHOWSKI, A. T., COURNIA, N. & MURPHY, H. 2004. Gaze-contingent displays: a review. *Cyberpsychol Behav.,* 7**,** 621-34.

EINHAUSER, W. & KONIG, P. 2003. Does luminance-contrast contribute to a saliency map for overt visual attention? *Eur J Neurosci.,* 17**,** 1089-97.

ENGBERT, R., LONGTIN, A. & KLIEGL, R. 2002. A dynamical model of saccade generation in reading based on spatially distributed lexical processing. *Vision Research,* 42**,** 621-636.

ESTERMAN, B. 1967. Grid for Scoring Visual Fields: I. Tangent Screen. *Arch Ophthalmol,* 77**,** 780-786.

ESTERMAN, B. 1982. Functional scoring of the binocular field. *Ophthalmology.,* 89**,** 1226-34.

FENDER, D. H. 1964. CONTACT LENS STABILITY. *Biomed Sci Instrum.,* 2**,** 43-52.

FINE, E. M. & RUBIN, G. S. 1999a. The effects of simulated cataract on reading with normal vision and simulated central scotoma. *Vision Research,* 39**,** 4274-4285.

FINE, E. M. & RUBIN, G. S. 1999b. Reading with simulated scotomas: attending to the right is better than attending to the left. *Vision Research,* 39**,** 1039-1048.

FONDA, S. J., WALLACE, R. B. & HERZOG, A. R. 2001. Changes in Driving Patterns and Worsening Depressive Symptoms Among Older Adults. *The Journals of Gerontology Series B: Psychological Sciences and Social Sciences,* 56**,** S343-S351.

FORTENBAUGH, F. C., HICKS, J. C. & TURANO, K. A. 2008. The Effect of Peripheral Visual Field Loss on Representations of Space: Evidence for Distortion and Adaptation. *Investigative Ophthalmology & Visual Science,* 49**,** 2765-2772.

FOULSHAM, T., TESZKA, R. & KINGSTONE, A. 2011. Saccade control in natural images is shaped by the information visible at fixation: evidence from asymmetric gaze-contingent windows. *Atten Percept Psychophys.,* 73**,** 266-83.

FREEMAN, E. E., MUNOZ, B., WEST, S. K., JAMPEL, H. D. & FRIEDMAN, D. S. 2008. Glaucoma and quality of life: the Salisbury Eye Evaluation. *Ophthalmology,* 115**,** 233-8.

FREY, H.-P., HONEY, C. & KÖNIG, P. 2008. What's color got to do with it? The influence of color on visual attention in different categories. *Journal of Vision,* 8.

FRIEDMAN, D. S., FREEMAN, E., MUNOZ, B., JAMPEL, H. D. & WEST, S. K. 2007. Glaucoma and mobility performance: the Salisbury Eye Evaluation Project. *Ophthalmology,* 114**,** 2232-7.

FRIEDMAN, D. S., WOLFS, R. C., O'COLMAIN, B. J., KLEIN, B. E., TAYLOR, H. R., WEST, S., LESKE, M. C., MITCHELL, P., CONGDON, N. & KEMPEN, J. 2004. Prevalence of open-angle glaucoma among adults in the United States. *Arch Ophthalmol.,* 122**,** 532-8.

GARWAY–HEATH, D. F., CAPRIOLI, J., FITZKE, F. W. & HITCHINGS, R. A. 2000. Scaling the Hill of Vision: The Physiological Relationship between Light Sensitivity and Ganglion Cell Numbers. *Investigative Ophthalmology & Visual Science,* 41**,** 1774-1782.

GERUSCHAT, D. R., HASSAN, S. E., TURANO, K. A., QUIGLEY, H. A. & CONGDON, N. G. 2006. Gaze Behavior of the Visually Impaired During Street Crossing. *Optometry and Vision Science,* 83**,** 550-558.

GINSBURG, A. P. 1984. A new contrast sensitivity vision test chart. *American Journal of Optometry and Physiological Optics,* 61**,** 403-7.

GLEN, F., CRABB, D. & GARWAY-HEATH, D. 2011. The direction of research into visual disability and quality of life in glaucoma. *BMC Ophthalmology,* 11**,** 19.

GOLDSTEIN, R. B., WOODS, R. L. & PELI, E. 2007. Where people look when watching movies: Do all viewers look at the same place? *Computers in Biology and Medicine,* 37**,** 957-964.

GONZÁLEZ, E., TEICHMAN, J., LILLAKAS, L., MARKOWITZ, S. & STEINBACH, M. 2006. Fixation stability using radial gratings in patients with age-related macular degeneration. *Can J Ophthalmol,* 41**,** 333-339.

GRAYSON, G. & SEXTON, B. 2002. Hazard Perception Test. *Transport Research Laboratory,* TRL558.

GREEN, J., SIDDALL, H. & MURDOCH, I. 2002. Learning to live with glaucoma: a qualitative study of diagnosis and the impact of sight loss. *Soc Sci Med,* 55**,** 257-67.

GREENE, H. H. & RAYNER, K. 2001. Eye-movement control in direction-coded visual search. *Perception,* 30**,** 147-57.

GUSE, C. E. & PORINSKY, R. 2003. Risk factors associated with hospitalization for unintentional falls: Wisconsin hospital discharge data for patients aged 65 and over. *Wmj.,* 102**,** 37-42.

HALL, E. C., CLUFFREDA, K.J. 2001. Eccentric viewing training in macular degeneration using auditory ocular motor biofeedback. *Journal of Behavioral Optometry,* 12**,** 87-93.

HAMELIN, N., BLATRIX, C., BRION, F., MATHIEU, C., GOEMAERE, I. & NORDMANN, J. P. 2002. [How patients react when glaucoma is diagnosed?]. *J Fr Ophtalmol,* 25**,** 795-8.

HARDING, G. & BLOJ, M. 2010. Real and predicted influence of image manipulations on eye movements during scene recognition. *Journal of Vision,* 10**,** 8 1-17.

HAWKINS, A. S., SZLYK, J. P., ARDICKAS, Z., ALEXANDER, K. R. & WILENSKY, J. T. 2003. Comparison of contrast sensitivity, visual acuity, and Humphrey visual field testing in patients with glaucoma. *Journal of Glaucoma,* 12**,** 134-8.

HAYMES, S. A., LEBLANC, R. P., NICOLELA, M. T., CHIASSON, L. A. & CHAUHAN, B. C. 2007. Risk of Falls and Motor Vehicle Collisions in Glaucoma. *Invest. Ophthalmol. Vis. Sci.,* 48**,** 1149-1155.

HAYMES, S. A., LEBLANC, R. P., NICOLELA, M. T., CHIASSON, L. A. & CHAUHAN, B. C. 2008. Glaucoma and On-Road Driving Performance. *Invest. Ophthalmol. Vis. Sci.,* 49**,** 3035-3041.

HEALY, H. J. R. 1972. Drawing a Probability Ellipse. *Applied Statistics,* 21**,** 202-204.

HEIJL, A., LINDGREN, A. & LINDGREN, G. 1989. TEST-RETEST VARIABILITY IN GLAUCOMATOUS VISUAL-FIELDS. *American Journal of Ophthalmology,* 108**,** 130-135.

HEIJL, A., LINDGREN, G. & LINDGREN, A. 1991. Normal variability of static perimetric threshold values across the central visual field. *Arch Ophthalmol,* 105**,** 1544-1549.

HENDERSON, J. M. 2003. Human gaze control during real-world scene perception. *Trends in Cognitive Sciences,* 7**,** 498-504.

HENDERSON, J. M., MCCLURE, K. K., PIERCE, S. & SCHROCK, G. 1997. Object identification without foveal vision: Evidence from an artificial scotoma paradigm. *Perception & Psychophysics,* 59**,** 323-346.

HENSON, D. B. 2000. *Visual Fields, 2nd ed*, Oxford University Press.

HITCHINGS, R. 2000. *Glaucoma,* London, BMJ Publishing Group.

HOLZMAN, P. S., LEVY, D. L. & PROCTOR, L. R. 1976. Smooth Pursuit Eye Movements, Attention, and Schizophrenia. *Arch Gen Psychiatry,* 33**,** 1415-1420.

HOOGE, I. T. C. & ERKELENS, C. J. 1999. Peripheral vision and oculomotor control during visual search. *Vision Research,* 39**,** 1567-1575.

HSIAO, J. H. & COTTRELL, G. 2008. Two Fixations Suffice in Face Recognition. *Psychological Science,* 19**,** 998-1006.

HUEY, E. B. 1898. Preliminary Experiments in the Physiology and Psychology of Reading. *The American Journal of Psychology,* 9**,** 575-586.

IRWIN, D. E. 1991. Information integration across saccadic eye movements. *Cognitive Psychology,* 23**,** 420-456.

ITTI, L. & KOCH, C. 2000. A saliency-based search mechanism for overt and covert shifts of visual attention. *Vision Research,* 40**,** 1489-1506.

IVERS, R. Q., CUMMING, R. G., MITCHELL, P. & ATTEBO, K. 1998. Visual impairment and falls in older adults: the Blue Mountains Eye Study. *J Am Geriatr Soc.,* 46**,** 58-64.

JACKO, J. A., SCOTT, I.U., BARRETO, A.B., BAUTSCH, H.S., CHU, J.Y.M., FAIN, W.B. Year. Iconic visual search strategies: A comparison of computer users with AMD versus computer users with normal vision. *In:* Ninth International Conference on Human Computer Interaction, 2001 New Orleans.

JAMPEL, H. D., FRIEDMAN, D. S., QUIGLEY, H. & MILLER, R. 2002a. Correlation of the Binocular Visual Field with Patient Assessment of Vision. *Invest. Ophthalmol. Vis. Sci.,* 43**,** 1059-1067.

JAMPEL, H. D., SCHWARTZ, A., POLLACK, I., ABRAMS, D., WEISS, H. & MILLER, R. 2002b. Glaucoma patients' assessment of their visual function and quality of life. *Journal of Glaucoma,* 11**,** 154-63.

JAVAL, E. 1879. Essai sur la Physiologie de la Lecture. *Annales D'Oculistique*.

JOHNSON, C. A. 2003. Perimetry. *In:* MORRISON, J. C. & POLLACK, I. P. (eds.) *Glaucoma: Science and Practice.* New York: Thieme.

JOHNSON, C. A. & KELTNER, J. L. 1983. Incidence of visual field loss in 20,000 eyes and its relationship to driving performance. *Arch Ophthalmol,* 101**,** 371-375.

JUST, M. A. & CARPENTER, P. A. 1980. A theory of reading: From eye fixations to comprehension. *Psychological Review,* 87**,** 329-354.

KALMUS, H., LUKE, I. & SEEDBURGH, D. 1974. Impairment of colour vision in patients with ocular hypertension and glaucoma. With special reference to the "D and H color-rule". *Br J Ophthalmol,* 58**,** 922-6.

KANONIDOU, E., PROUDLOCK, F. A. & GOTTLOB, I. 2010. Reading strategies in mild to moderate strabismic amblyopia: an eye movement investigation. *Invest Ophthalmol Vis Sci,* 51**,** 3502-8.

KATZ, J., TIELSCH, J. M., QUIGLEY, H. A. & SOMMER, A. 1995. Automated perimetry detects visual field loss before manual Goldmann perimetry. *Ophthalmology,* 102**,** 21-6.

KAUFMAN, L. D., PRATT, J., LEVINE, B. & BLACK, S. E. 2010. Antisaccades: a probe into the dorsolateral prefrontal cortex in Alzheimer's disease. A critical review. *J Alzheimers Dis,* 19**,** 781-93.

KERKHOFF, G., MUNSSINGER, U., HAAF, E., EBERLE-STRAUSS, G. & STOGERER, E. 1992. Rehabilitation of homonymous scotomata in patients with postgeniculate damage of the visual system: saccadic compensation training. *Restor Neurol Neurosci.,* 4**,** 245-254.

KLEIN, B. E., KLEIN, R., SPONSEL, W. E., FRANKE, T., CANTOR, L. B., MARTONE, J. & MENAGE, M. J. 1992. Prevalence of glaucoma. The Beaver Dam Eye Study. *Ophthalmology,* 99**,** 1499-1504.

KOMATSU, H. 2006. The neural mechanisms of perceptual filling-in. *Nat Rev Neurosci,* 7**,** 220-231.

KOTECHA, A., O'LEARY, N., MELMOTH, D., GRANT, S. & CRABB, D. P. 2009. The Functional Consequences of Glaucoma for Eye-Hand Coordination. *Invest. Ophthalmol. Vis. Sci.,* 50**,** 203-213.

KOTECHA, A., SPRATT, A. & VISWANATHAN, A. 2008. Visual function and fitness to drive. *Br Med Bull,* 87**,** 163-174.

KRIEGER, G., RENTSCHLER, I., HAUSKE, G., SCHILL, K. & ZETZSCHE, C. 2000. Object and scene analysis by saccadic eye-movements: an investigation with higher-order statistics. *Spatial Vision,* 13**,** 201-14.

KUYK, T., ELLIOTT, J. L. & FUHR, P. S. 1998. Visual correlates of mobility in real world settings in older adults with low vision. *Optom Vis Sci,* 75**,** 538-47.

LAND, M. F. & LEE, D. N. 1994. Where we look when we steer. *Nature,* 369**,** 742-744.

LEE, K.-H. & WILLIAMS, L. M. 2000. Eye movement dysfunction as a biological marker of risk for schizophrenia. *Australian and New Zealand Journal of Psychiatry,* 34**,** S91-S100.

LEGGE, G. E., HOOVEN, T. A., KLITZ, T. S., STEPHEN MANSFIELD, J. & TJAN, B. S. 2002. Mr. Chips 2002: new insights from an ideal-observer model of reading. *Vision Research,* 42**,** 2219-2234.

LEGGE, G. E., KLITZ, T. S. & TJAN, B. S. 1997. Mr. Chips: An ideal-observer model of reading. *Psychological Review,* 104**,** 524-553.

LESKE, M. C. 1983. The epidemiology of open-angle glaucoma: a review. *American Journal of Epidemiology,* 118**,** 166-191.

LESKE, M. C., CONNELL, A. M., SCHACHAT, A. P. & HYMAN, L. 1994. The Barbados Eye Study. Prevalence of open angle glaucoma. *Arch Ophthalmol,* 112**,** 821-829.

LIBBY, R. T., GOULD, D. B., ANDERSON, M. G. & JOHN, S. W. 2005. Complex Genetics of Glaucoma Susceptibility. *Annu Rev Genomics Hum Genet,* 6**,** 15-44.

LIVERSEDGE, S., GILCHRIST, I. & EVERLING, S. (eds.) 2011. *The Oxford Handbook of Eye Movements,* Oxford: OUP Oxford.

LOSCHKY, L. C. & MCCONKIE, G. W. 2000. User performance with gaze contingent multiresolutional displays. *Proceedings of the 2000 symposium on Eye tracking research \& applications.* Palm Beach Gardens, Florida, United States: ACM.

LOUGHMAN, J., DAVISON, P. & FLITCROFT, I. 2007. Open angle glaucoma effects on preattentive visual search efficiency for flicker, motion displacement and orientation pop-out tasks. *British Journal of Ophthalmology,* 91**,** 1493-1498.

LUNNELA, J., KÄÄRIÄINEN, M. & KYNGÄS, H. 2010. The views of compliant glaucoma patients on counselling and social support. *Scandinavian Journal of Caring Sciences,* 24**,** 490-498.

MACHNER, B., SPRENGER, A., SANDER, T., HEIDE, W., KIMMIG, H., HELMCHEN, C. & KOMPF, D. 2009. Visual search disorders in acute and chronic homonymous hemianopia: lesion effects and adaptive strategies. *Ann N Y Acad Sci,* 1164**,** 419-26.

MACKWORTH, N. H. & MORANDI, A. J. 1967. The gaze selects informative details within pictures. *Perception and Psychophysics,* 2**,** 547-552.

MANOR, B. R., GORDON, E., WILLIAMS, L. M., RENNIE, C. J., BAHRAMALI, H., LATIMER, C. R., BARRY, R. J. & MEARES, R. A. 1999. Eye movements reflect impaired face processing in patients with schizophrenia. *Biological Psychiatry,* 46**,** 963-969.

MARSH, P. J., LAZZARO, I., MANOR, B. R., HARRIS, A. W. F., WILLIAMS, L. M., GORDON, E. & DAVIDSON, D. 2000. Facial expressions of emotion and visual scanpaths in attention-deficit hyperactivity disorder (ADHD) and first-episode psychosis (FEP). *Schizophrenia Research,* 41**,** 288-288.

MATIN, E. 1974. Saccadic suppression: A review and an analysis. *Psychological Bulletin,* 81**,** 899-917.

MCCONKIE, G. W., KERR, P. W., REDDIX, M. D. & ZOLA, D. 1988. Eye movement control during reading: I. The location of initial eye fixations on words. *Vision Res.,* 28**,** 1107-18.

MCGWIN, G., JR., MAYS, A., JOINER, W., DECARLO, D. K., MCNEAL, S. & OWSLEY, C. 2004. Is Glaucoma Associated with Motor Vehicle Collision Involvement and Driving Avoidance? *Invest. Ophthalmol. Vis. Sci.,* 45**,** 3934-3939.

MCGWIN, G., JR., OWSLEY, C. & BALL, K. 1998. Identifying crash involvement among older drivers: agreement between self-report and state records. *Accid Anal Prev,* 30**,** 781-91.

MCKEAN-COWDIN, R., WANG, Y., WU, J., AZEN, S. P. & VARMA, R. 2008. Impact of visual field loss on health-related quality of life in glaucoma: the Los Angeles Latino Eye Study. *Ophthalmology,* 115**,** 941-948 e1.

MERCHANT, J., MORRISSETTE, R. & PORTERFIELD, J. L. 1974. Remote Measurement of Eye Direction Allowing Subject Motion Over One Cubic Foot of Space. *Biomedical Engineering, IEEE Transactions on,* BME-21**,** 309-317.

MILLS, R. P. & DRANCE, S. M. 1986. Esterman disability rating in severe glaucoma. *Ophthalmology.,* 93**,** 371-8.

MITCHELL, P., SMITH, W., ATTEBO, K. & HEALEY, P. R. 1996. Prevalence of openangle glaucoma in Australia. The Blue Mountains Eye Study. *Ophthalmology,* 103**,** 1661-1669.

MOWRER, O. H., RUCH, T. C. & MILLER, N. E. 1935. THE CORNEO-RETINAL POTENTIAL DIFFERENCE AS THE BASIS OF THE GALVANOMETRIC METHOD OF RECORDING EYE MOVEMENTS. *American Journal of Physiology -- Legacy Content,* 114**,** 423-428.

NÄSÄNEN, R., OJANPÄÄ, H. & KOJO, I. 2001. Effect of stimulus contrast on performance and eye movements in visual search. *Vision Research,* 41**,** 1817-1824.

NELSON, P., ASPINALL, P. & O'BRIEN, C. 1999. Patients' perception of visual impairment in glaucoma: a pilot study. *Br J Ophthalmol,* 83**,** 546-52.

NELSON, P., ASPINALL, P., PAPASOULIOTIS, O., WORTON, B. & O'BRIEN, C. 2003. Quality of life in glaucoma and its relationship with visual function. *J Glaucoma,* 12**,** 139-50.

NOE, G., FERRARO, J., LAMOUREUX, E., RAIT, J. & KEEFFE, J. E. 2003. Associations between glaucomatous visual field loss and participation in activities of daily living. *Clin Experiment Ophthalmol,* 31**,** 482-6.

NORBURY, C. F., BROCK, J., CRAGG, L., EINAV, S., GRIFFITHS, H. & NATION, K. 2009. Eye-movement patterns are associated with communicative competence in autistic spectrum disorders. *J Child Psychol Psychiatry,* 50**,** 834-42.

O'REGAN, J. K. 1990. Eye movements and reading. *In:* KOWLER, E. (ed.) *Eye movements and their role in visual and cognitive processes.* New York: Elsevier.

ORMEL, J., KEMPEN, G. I., PENNINX, B. W., BRILMAN, E. I., BEEKMAN, A. T. & VAN SONDEREN, E. 1997. Chronic medical conditions and mental health in older people: disability and psychosocial resources mediate specific mental health effects. *Psychol Med,* 27**,** 1065-77.

OWEN, V. M. F., CRABB, D. P., WHITE, E. T., VISWANATHAN, A. C., GARWAY-HEATH, D. F. & HITCHINGS, R. A. 2008. Glaucoma and Fitness to Drive: Using Binocular Visual Fields to Predict a Milestone to Blindness. *Invest. Ophthalmol. Vis. Sci.,* 49**,** 2449-2455.

PACHECO-CUTILLAS, M., EDGAR, D. F. & SAHRAIE, A. 1999. Acquired colour vision defects in glaucoma-their detection and clinical significance. *Br J Ophthalmol,* 83**,** 1396-402.

PAMBAKIAN, A., CURRIE, J. & KENNARD, C. 2005. Rehabilitation Strategies for Patients With Homonymous Visual Field Defects. *Journal of Neuro-Ophthalmology,* 25**,** 136-142.

PAMBAKIAN, A. L., WOODING, D. S., PATEL, N., MORLAND, A. B., KENNARD, C. & MANNAN, S. K. 2000. Scanning the visual world: a study of patients with homonymous hemianopia. *J Neurol Neurosurg Psychiatry,* 69**,** 751-9.

PARKHURST, D., CULURCIELLO, E. & NIEBUR, E. 2000. Evaluating variable resolution displays with visual search: task performance and eye movements. *Proceedings of the 2000 symposium on Eye tracking research \& applications.* Palm Beach Gardens, Florida, United States: ACM.

PELLI, D. G., ROBSON, J. G. & WILKINS, A. J. 1988. The design of a new letter chart for measuring contrast sensitivity. *Clinical Vision Sciences,* 2**,** 187-199.

POHJANPELTO, P. E. J. & PALVA, J. 1974. OCULAR HYPERTENSION AND GLAUCOMATOUS OPTIC NERVE DAMAGE. *Acta Ophthalmologica,* 52**,** 194-200.

POPE, C., ZIEBLAND, S. & MAYS, N. 2000. Analysing qualitative data. *BMJ,* 320**,** 114-116.

PORTER, G., TROSCIANKO, T. & GILCHRIST, I. D. 2007. Effort during visual search and counting: insights from pupillometry. *Q J Exp Psychol (Colchester),* 60**,** 211-29.

QUIGLEY, H. A. 1996. Number of people with glaucoma worldwide. *British Journal of Ophthalmology,* 80**,** 389-393.

QUIGLEY, H. A., ADDICKS, E. M. & GREEN, W. R. 1982. Optic Nerve Damage in Human Glaucoma: III. Quantitative Correlation of Nerve Fiber Loss and Visual Field Defect in Glaucoma, Ischemic Neuropathy, Papilledema, and Toxic Neuropathy. *Arch Ophthalmol,* 100**,** 135-146.

QUIGLEY, H. A. & BROMAN, A. T. 2006. The number of people with glaucoma worldwide in 2010 and 2020. *Br J Ophthalmol,* 90**,** 262-7.

RAGLAND, D. R., SATARIANO, W. A. & MACLEOD, K. E. 2005. Driving cessation and increased depressive symptoms. *J Gerontol A Biol Sci Med Sci,* 60**,** 399-403.

RAMACHANDRAN, V. S. & GREGORY, R. L. 1991. Perceptual filling in of artificially induced scotomas in human vision. *Nature,* 350**,** 699-702.

RAMULU, P. 2009. Glaucoma and disability: which tasks are affected, and at what stage of disease? *Current Opinion in Ophthalmology,* 20**,** 92-98.

RAMULU, P. Y., WEST, S. K., MUNOZ, B., JAMPEL, H. D. & FRIEDMAN, D. S. 2009. Glaucoma and Reading Speed: The Salisbury Eye Evaluation Project. *Arch Ophthalmol,* 127**,** 82-87.

RAUSCHER, F., CHISHOLM, C. & CRABB, D. 2007. Central scotomata and driving. *Road safety research report 79, compiled for UK Department for Transport*.

RAYNER, K. 1998. Eye movements in reading and information processing: 20 years of research. *Psychological Bulletin,* 124**,** 372-422.

RAYNER, K. 2009a. Eye movements and attention in reading, scene perception, and visual search. *The Quarterly Journal of Experimental Psychology*.

RAYNER, K. 2009b. Eye movements and attention in reading, scene perception, and visual search. *The Quarterly Journal of Experimental Psychology,* 62**,** 1457-1506.

REICHLE, E. D., POLLATSEK, A., FISHER, D. L. & RAYNER, K. 1998. Toward a model of eye movement control in reading. *Psychological Review,* 105**,** 125-157.

REILLY, R. & RADACH, R. 2003. Foundations of an interactive activation model of eye movement control in reading. *In:* HYÖNÄ, J., RADACH, R. & DEUBEL, H. (eds.) *The mind's eye: Cognitive and applied aspects of eye movements.* Elsevier.

REINAGEL, P. & ZADOR, A. M. 1999. Natural scene statistics at the centre of gaze. *Network: Computation in Neural Systems,* 10**,** 341-350.

RESNIKOFF, S., PASCOLINI, D., ETYA'ALE, D., KOCUR, I., PARARAJASEGARAM, R., POKHAREL, G. P. & MARIOTTI, S. P. 2004. Global data on visual impairment in the year 2002. *Bulletin of the World Health Organization,* 82**,** 844-851.

RIGGS, L. A., RATLIFF, F., CORNSWEET, J. C. & CORNSWEET, T. N. 1953. The Disappearance of Steadily Fixated Visual Test Objects. *J. Opt. Soc. Am.,* 43**,** 495-500.

ROBIN DIMATTEO, M., GIORDANI, P. J., LEPPER, H. S. & CROGHAN, T. W. 2002. Patient Adherence and Medical Treatment Outcomes: A Meta-Analysis. *Medical Care,* 40**,** 794-811.

ROBINSON, D. A. 1963. A METHOD OF MEASURING EYE MOVEMENT USING A SCLERAL SEARCH COIL IN A MAGNETIC FIELD. *IEEE Trans Biomed Eng.,* 10**,** 137-45.

ROSS, J. E., BRON, A. J. & CLARKE, D. D. 1984. Contrast sensitivity and visual disability in chronic simple glaucoma. *British Journal of Ophthalmology,* 68**,** 821-827.

RUBIN, G. S. & FEELY, M. 2009. The Role of Eye Movements During Reading in Patients with Age-Related Macular Degeneration (AMD). *Neuro-Ophthalmology,* 33**,** 120-126.

SAFRAN, A. B. & LANDIS, T. 1996. Plasticity in the adult visual cortex: implications for the diagnosis of visual field defects and visual rehabilitation. *Current Opinion in Ophthalmology,* 7**,** 53-64.

SAIDA, S. & IKEDA, M. 1979. Useful visual field size for pattern perception. *Percept Psychophys,* 25**,** 119-25.

SALVUCCI, D. D. 2000. An interactive model-based environment for eye-movement protocol analysis and visualization. *Proceedings of the 2000 symposium on Eye tracking research \& applications.* Palm Beach Gardens, Florida, United States: ACM.

SCHOEN, C., OSBORN, R., SQUIRES, D., DOTY, M. M., PIERSON, R. & APPLEBAUM, S. 2010. How Health Insurance Design Affects Access to Care and Costs, by Income, in Eleven Countries. *Health Affairs Web First*.

SCHOTT, E. 1922. Über die Registrierung des Nystagmus und anderer Augenbewegungen vermittels des Saitengalvanometers. *Dtsch Arch Klin Med,* 140**,** 79-90.

SCHWARTZ, G. F. & QUIGLEY, H. A. 2008. Adherence and Persistence with Glaucoma Therapy. *Survey of Ophthalmology,* 53**,** S57-S68.

SCIALFA, C. T., ESAU, S. P. & JOFFE, K. M. 1998. Age, target-distractor similarity, and visual search. *Exp Aging Res,* 24**,** 337-58.

SEIPLE, W., SZLYK, J. P., MCMAHON, T., PULIDO, J. & FISHMAN, G. A. 2005. Eye-Movement Training for Reading in Patients with Age-Related Macular Degeneration. *Investigative Ophthalmology & Visual Science,* 46**,** 2886-2896.

SERENO, A. B. & HOLZMAN, P. S. 1995. Antisaccades and smooth pursuit eye movements in schizophrenia. *Biological Psychiatry,* 37**,** 394-401.

SHAW, M. E. 2005. Increasing compliance with glaucoma therapy: "so, convince me I have something wrong with my eyes". *Insight,* 30**,** 7-9.

SMITH, N. D., CRABB, D. P. & GARWAY-HEATH, D. F. 2011. An exploratory study of visual search performance in glaucoma. *Ophthalmic and Physiological Optics,* 31**,** 225-232.

SPAETH, G., WALT, J. & KEENER, J. 2006. Evaluation of Quality of Life for Patients With Glaucoma. *American Journal of Ophthalmology,* 141**,** 3-14.

STAMPE, D. M. 1993. Heuristic filtering and reliable calibration methods for video based pupil tracking systems. *Behavior Research Methods, Instruments, and Computers,* 25**,** 137-142.

STAMPER, R. L. 1989. Psychophysical changes in glaucoma. *Surv Ophthalmol,* 33 Suppl**,** 309-18.

SUPPES, P. 1990. Eye-movement models for arithmetic and reading performance. *In:* KOWLER, E. (ed.) *Eye movements and their role in visual and cognitive processes.* New York: Elsevier.

SZLYK, J. P., MAHLER, C. L., SEIPLE, W., EDWARD, D. P. & WILENSKY, J. T. 2005. Driving Performance of Glaucoma Patients Correlates With Peripheral Visual Field Loss. *Journal of Glaucoma,* 14**,** 145-150.

TATE, G. W. & LYNN, J. R. 1977. *Principles of quantitative perimetry: Testing and interpreting the visual field,* New York, Grune & Stratton.

TATLER, B. W., WADE, N. J. & KAULARD, K. 2007. Examining art: dissociating pattern and perceptual influences on oculomotor behaviour. *Spatial Vision,* 21**,** 165-184.

THAYAPARAN, K., CROSSLAND, M. D. & RUBIN, G. S. 2007. Clinical assessment of two new contrast sensitivity charts. *Br J Ophthalmol.,* 91**,** 749-52. Epub 2006 Dec 13.

THEEUWES, J., REIMANN, B. & MORTIER, K. 2006. Visual search for featural singletons: No top-down modulation, only bottom-up priming. *Visual Cognition,* 14**,** 466 - 489.

TIELSCH, J. M., KATZ, J., SOMMER, A., QUIGLEY, H. A. & JAVITT, J. C. 1995. Hypertension, perfusion pressure, and primary open-angle glaucoma. A population-based assessment. *Arch Ophthalmol,* 113**,** 216-221.

TIELSCH, J. M., SOMMER, A., KATZ, J., ROYALL, R. M., QUIGLEY, H. A. & JAVITT, J. 1991. Racial variations in the prevalence of primary open-angle glaucoma. The Baltimore Eye Survey. *The journal of the American Medical Association,* 266**,** 369-374.

TRAQUAIR, H. M. 1931. Perimetry in the study of glaucoma. *Trans Ophthalmol Soc UK,* 51**,** 585-599.

TURANO, K., RUBIN, G. S., HERDMAN, S. J., CHEE, E. & FRIED, L. P. 1994. Visual stabilization of posture in the elderly: fallers vs. nonfallers. *Optometry and vision science : official publication of the American Academy of Optometry,* 71**,** 761-9.

TURANO, K. A., GERUSCHAT, D. R., BAKER, F. H., STAHL, J. W. & SHAPIRO, M. D. 2001. Direction of Gaze while Walking a Simple Route: Persons with Normal Vision and Persons with Retinitis Pigmentosa. *Optometry & Vision Science,* 78**,** 667-675.

TURANO, K. A., RUBIN, G. S. & QUIGLEY, H. A. 1999. Mobility Performance in Glaucoma. *Invest. Ophthalmol. Vis. Sci.,* 40**,** 2803-2809.

UNDERWOOD, G., CHAPMAN, P., BOWDEN, K. & CRUNDALL, D. 2002. Visual search while driving: skill and awareness during inspection of the scene. *Transportation Research Part F: Traffic Psychology and Behaviour,* 5**,** 87-97.

UNDERWOOD, G., CHAPMAN, P., BROCKLEHURST, N., UNDERWOOD, J. & CRUNDALL, D. 2003. Visual attention while driving: sequences of eye fixations made by experienced and novice drivers. *Ergonomics,* 46**,** 629-646.

UNDERWOOD, G., PHELPS, N., WRIGHT, C., LOON, E. & GALPIN, A. 2005. Eye fixation scanpaths of younger and older drivers in a hazard perception task. *Ophthalmic and Physiological Optics,* 25**,** 346-356.

VAN DER GEEST, J. 2002. Recording eye movements with video-oculography and scleral search coils: a direct comparison of two methods. *Journal of Neuroscience Methods,* 114**,** 185-195.

VARGAS-MARTIN, F. & PELI, E. 2006. Eye Movements of Patients with Tunnel Vision While Walking. *Invest. Ophthalmol. Vis. Sci.,* 47**,** 5295-5302.

VISWANATHAN, A. C., FITZKE, F. W. & HITCHINGS, R. A. 1997. Early detection of visual field progression in glaucoma: a comparison of PROGRESSOR and STATPAC 2. *Br J Ophthalmol.,* 81**,** 1037-42.

VISWANATHAN, A. C., MCNAUGHT, A. I., POINOOSAWMY, D., FONTANA, L., CRABB, D. P., FITZKE, F. W. & HITCHINGS, R. A. 1999. Severity and Stability of Glaucoma: Patient Perception Compared With Objective Measurement. *Arch Ophthalmol,* 117**,** 450-454.

VIVEKANANDA-SCHMIDT, P., ANDERSON, R. S., REINHARDT-RUTLAND, A. H. & SHIELDS, T. J. 2004. Simulated Impairment of Contrast Sensitivity: Performance and Gaze Behavior during Locomotion through a Built Environment. *Optometry & Vision Science,* 81**,** 844-852.

VLASKAMP, B. N. & HOOGE, I. T. 2006. Crowding degrades saccadic search performance. *Vision Res,* 46**,** 417-25.

VUKICEVIC, M., FITZMAURICE, K. 2009. Eccentric viewing training in the home environment: Can it improve the performance of activities of daily living? *Journal of Visual Impairment and Blindness,* 103**,** 277-290.

WARRIAN, K. J., SPAETH, G. L., LANKARANIAN, D., LOPES, J. F. & STEINMANN, W. C. 2009. The effect of personality on measures of quality of life related to vision in glaucoma patients. *Br J Ophthalmol,* 93**,** 310-5.

WATSON, M., BRENNAN, A., KINGSTONE, A. & ENNS, J. 2010. Looking versus seeing: Strategies alter eye movements during visual search. *Psychonomic Bulletin & Review,* 17**,** 543-549.

WERNER, E. B. 1991. *Manual of Visual Fields,* New York, Churchill Livingstone Inc.

WEST, S. K., RUBIN, G. S., MUNOZ, B., ABRAHAM, D., FRIED, L. P. & THE SALISBURY EYE EVALUATION PROJECT, T. 1997. Assessing Functional Status: Correlation Between Performance on Tasks Conducted in a Clinic Setting and Performance on the Same Task Conducted at Home. *J Gerontol A Biol Sci Med Sci,* 52A**,** M209-217.

WESTLAKE, W. 2000. Another look at visual standards and driving. *BMJ,* 321**,** 972-973.

WHITE, S. C., ATCHISON, K. A., GORNBEIN, J. A., NATTIV, A., PAGANINI-HILL, A. & SERVICE, S. K. 2006. Risk factors for fractures in older men and women: The Leisure World Cohort Study. *Gender Medicine,* 3**,** 110-123.

WOLFE, J. M. 1998. *Visual search,* Hove, U.K., Psychology Press.

YARBUS, A. L. 1967. *Eye Movements and Vision,* New York, Plenum.

ZIHL, J. 1988. Methodische Voraussetzungen der neuropsychologischen Rehabilitation. *In:* ZIHL, J. & CRAMON, V. (eds.) *Neuropsychologische Rehabilitation - Grundlagen-Diagnostik-Behandlungsverfahre.* Berlin: SpringerVerlag.