Development and validation of a digital quantitative orthoptics workstation

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ABSTRACT

The objective of the research is to provide the clinician with a simple system for making quantitative measurements that is comparable to the services of a skilled orthoptist. As many optometrists do not possess the necessary equipment for making such assessments, this technology would significantly enhance their referral capabilities. Reviews of the tests involved and instruments available are detailed in Chapter II and III.

Chapter IV presents the various validation experiments carried out on the Tobii X120 eye tracker, concentrating on technical specifications such as, linearity range, optimum measurement distance and setup (with and without chin rest). We also investigated the effect of wearing different types of lens materials and pupil size measurements on the eye tracker system.

We established the inter-examiner agreement of cover test measurements on groups of non-strabismic and strabismic subjects. This study, as detailed in Chapter V, involved collaboration with two clinical orthoptists. We found a good inter-examiner agreement for both the non-strabismic and strabismic cover tests.

We further investigated the use of the eye tracker in providing more reliable findings for cover test measurements as compared to the conventional cover test (Chapter VI). Finally we extended the investigation to a number of different clinical subjects attending the Bristol Eye Hospital (Chapter VII) in order to evaluate our purpose-developed monocular calibration routine.

Performing quantitative eye movement analysis will provide valuable additional information in any clinical investigation of patients with ophthalmological and/or neurological disorders, leading to greater precision in diagnosis. Traditional methods for the evaluation of oculomotor disorders rely on the diagnostic and therapeutic judgements by the examining clinicians and subjective responses from the patient. However, the use of currently available eye movement recording system will provide valuable alternatives for obtaining more objective and quantitative measurements.

LIST OF ABBREVIATIONS

ABBREVIATIONS/SYMBOLS	DESCRIPTIONS
%	percentage
.etd	EBX transfer Data
.tsv	Tab-separated value
<	Value less than
>	Value more than
±	Standard Deviation
Δ / PD	Prism Diopterer
≤	Value less than or equal to
≥	Value more than or equal to
°	Degree
°/s	Degree per second
μm	Micrometer
Cm	Centimetres
CRT	Cathode Ray Tube
D	Dioptre
DC	Direct current
DOS	Disk Operating System
DPI	Dual-purkinje image
DVD	Dissociated Vertical Divergence
e.g.	Exempli gratia (for example)
EMMA	Eye Movement and Analysis System
EOG	Electrooculography
EOM	Extraocular Muscles
ESO	Esophoria/tropia
EXO	Exophoria/tropia
GUI	Graphical User Interface
H	Horizontal
HVID	Horizontal visible iris diameters
Hz	Hertz
i.e	Id est (which means)
ICC	Intraclass Correlation Coefficient
IO	Inferior oblique

IP	Internet Protocol
IR	Infra Red
IR	Inferior rectus
IROG	Infrared oculography
k	kilo
kg-cm	Kilogram per centimetres
LED	Light Emitting Diodes
LOA	Limits of Agreement
LR	Lateral rectus
m	Metres
mm	Millimetres
MR	Medial rectus
mV	Milivolts
nm	Nanometres
ORTHO	Orthophoria
p	probability
PPRF	Paramedian Pontine Reticular Formation
RIN	Rostral Interstitial Nucleus
s	Seconds
SDK	Software Development Kit
SO	Superior oblique
SQL	Structured Query Language
SR	Superior rectus
SSC	Scleral search coil
™	Trademark
TETClient	Tobii Eye Tracking Client
TETServer	Tobii Eye Tracking Server
V	Vertical
v	Volt
VOG	Video oculography

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CHAPTER I

INTRODUCTION

The studies described in this dissertation are aimed at developing a quantitative instrument as means of assessing eye alignment/misalignments using eye tracking instrumentation.

Eye misalignments, such as latent deviation (phoria) and manifest deviation (tropia/strabismus), are fairly common disorders. Phoria exists in most individuals when their binocular fusion is disrupted. The alignment is retained through motor fusion but can voluntarily manifest as a result of fatigue or illness. Eye alignment assessment is important in decompensated phoria as it could lead to problems such as headache, reading difficulties and diplopia (Rajula Karania and Evans 2006). Tropia can arise from neurological problems involving the cranial nerves or can be an indication of systemic problems such as thyroid eye disease, trauma or myasthenia gravis. Previous studies have shown that tropia affects about 2 to 5% of the population, and most cases occur during childhood (Williams et al. 2008; Stidwill 1997). Having a manifest eye misalignment at such an early age can impair the development of binocular vision. Thus, the eye alignment examination in this case is crucial in detecting and diagnosing such conditions and facilitating a suitable optical and/or surgical treatment.

The eye alignment assessment can be performed using subjective (Maddox rod, Maddox wing) or objective (Hirschberg test, Krimsky test and cover test) methods. However, the

cover test has been regarded as the most useful and effective diagnostic procedure in detecting eye misalignment, not only because of the simplicity of the technique but also the information gathered from the test (Eskridge et al. 1991). Evidently, the cover test is the only clinical test that can differentiate between phoria and tropia. Nonetheless, this method involves a fair degree of subjective skills as well as familiarity with the signs of eye movement diseases, which are sometimes difficult to discern. Furthermore, no permanent recording of the test results is made available, making record keeping or monitoring the progress of any treatment difficult.

Eye movement recording systems have been widely used by researchers to investigate various neurological, ophthalmological and psychological diseases (Frohman et al. 2003; Sweeney et al. 2002). This technology dates back to the late 1800s (Jacob and Karn 2003) and utilises eye structures and properties, such as corneal reflection and pupil size, to detect and record eye movements (Ciuffreda and Tannen 1995). The earliest highly precise system, using scleral search coils, was invasive as it involved direct contact with the eyes (Duchowski et al. 2003; van de Geest & Frens 2002). The technology of eye movement recording has since developed to provide increasingly non-invasive measurements with higher precision and sampling rate. Infrared light sources have commonly been used to provide measurements in more natural environments. The instruments developed are increasingly computerised, and the measurement data obtained can be saved to a database for subsequent analysis.

The present research explored the emerging role of infrared eye movement recording systems, in the context of determining the suitability of using one such system as part of a routine clinical eye examination. The ability of the instrument to track eye movements was exploited to detect and quantify eye misalignment during the cover test.

The ultimate aim of this research project was to establish the basis for a digital orthoptics workstation that could provide more objective and quantitative measurements of eye misalignment, i.e. phoria and tropia.

1.1 Thesis organisation

The overall structure of this thesis takes the form of eight (8) chapters, including this introductory chapter. Chapter II begins by laying out the theoretical background of the research and reviewing the basic human visual system as well as the properties and function of eye movements. The conventional methods for detecting eye alignment in a clinical setting are also discussed, including variations of each test and its advantages, disadvantages and limitations. Finally, the discussion extends to currently available instruments for measuring eye movements.

Chapter III describes the methodology used for this study, including details of the instrumentation and experimental setup. Chapter IV presents the experimental study undertaken on the portable infrared eye tracker, the Tobii X120 (Tobii Technology AB, Sweden), to evaluate the technical aspects of the instrument and its suitability for use in a clinical setting. Chapter V describes a study on the agreement of the cover test measurements between clinical examiners. In this chapter, statistical comparisons were made between the measurements taken from two orthoptists and an optometrist on both non-strabismic and strabismic subjects.

Chapter VI presents the findings of the research on eye trackers. First, the chapter focuses on the agreement of the cover test measurements performed by an examiner with two different infrared eye trackers (the Skalar IRIS and the Tobii X120). Secondly, the cover test results from thirty non-strabismic subjects and ten strabismic subjects using the Tobii X120 were investigated, detailing the effect of time of occlusion and phoria variation.

Chapter VII investigates the agreement and accuracy of the cover test measurements in a group of subjects having various abnormal eye movements. Details of the monocular calibration programme developed for this purpose are also described. The final chapter summarises the results of the entire thesis, and in conclusion provides suggestions, critiques, a consideration of limitations and the implications of all of the findings for future research.

CHAPTER II

HUMAN VISUAL AND EYE MOVEMENT SYSTEM

2.1   Eye movement system

2.1.1   Anatomy and physiology

Light is received and transmitted through the complex structure of the human visual system. Light rays entering the eye are refracted as they pass through the anterior and posterior surfaces of the cornea. These surfaces refract the light rays through the pupil, and the combined effect of cornea and lens focuses the rays onto the retina (Tortora and Derrickson 2008).
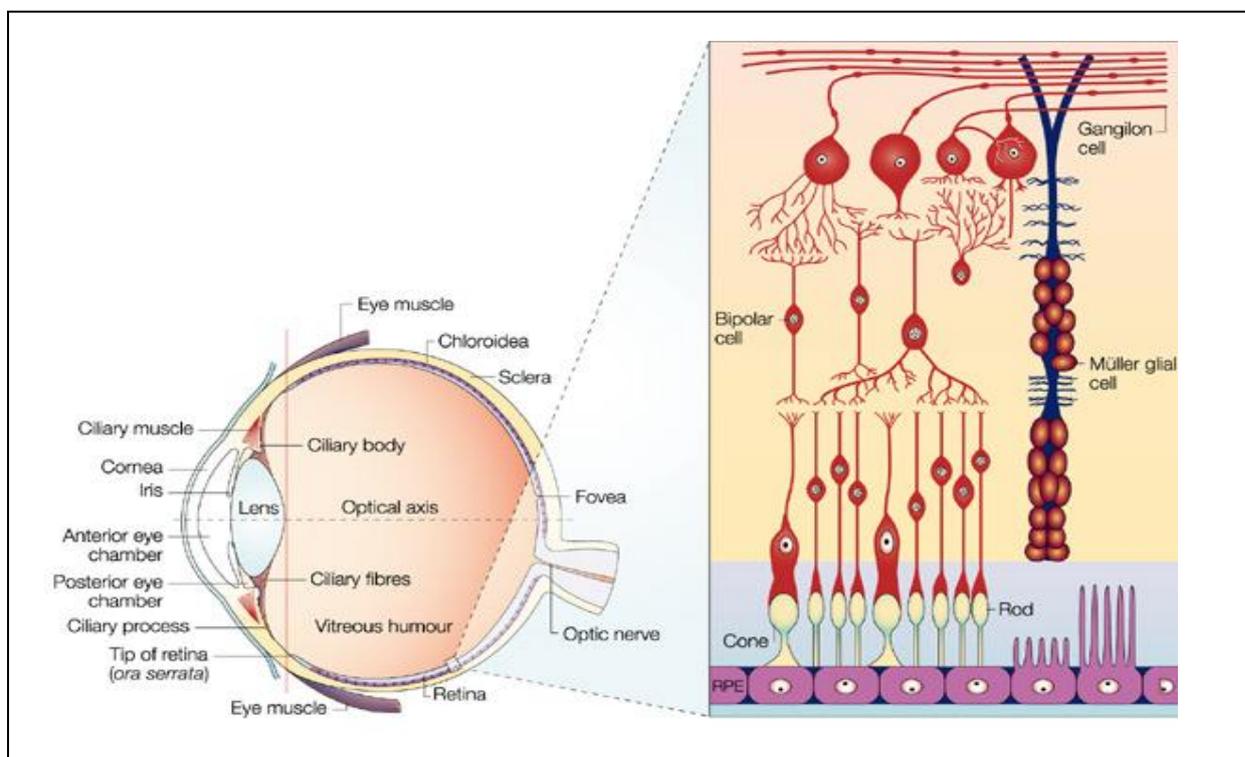
Figure 2.1   Schematic section of an adult human eye (Graw 2003).

The retina, as shown in Figure 2.1, is a multilayered structure containing millions of photoreceptors, which are responsible for capturing light rays and converting them into electrical impulses. There are two types of photoreceptors in the retina, namely cones and rods. Cones are concentrated in the macula, which is the part of the retina that is responsible for central high acuity vision. They are most densely packed within the centre portion of the macula, known as the fovea, function best in bright light, and are responsible for colour vision. Rods are numerous at the periphery of the retina and are more sensitive than the cones in providing vision at lower levels of illumination. Rod density is much greater than cones throughout the retina but the maximum is at the edge of macula and decline sharply at the foveola. Electrical impulses (neural signals) generated from rods and cones ultimately pass through the retinal ganglion cells, which project via the optic nerve to the Lateral Geniculate Nucleus (LGN), where they synapse, and post-synaptic nerves pass on to the visual cortex. The impulses are then transmitted to the higher centres of the brain where higher levels of image processing occur for every stimulus imaged and detected by the eye (Tortora and Derrickson 2008; Adler 2003).

In order to have a clear stable image, regardless of whether the target is static or moving, the reactions of the intraocular and extraocular muscles controlling the shape of the lens and the movements of the eyeball, respectively, must be effective (Tortora and Derrickson 2008; Remington 2005). Eye movements are coordinated by six extraocular muscles (EOMs), which are responsible for ensuring that the visual axes (i.e. the foveae of both eyes) are aligned with each other. These movements, which can be classified as gaze shifting or gaze stabilizing, are coordinated by the oculomotor pathways within the central nervous system (Tortora and Derrickson 2008; Leigh and Zee 2006; Hung et al. 2001). Gaze shifting eye movements are responsible for directing the lines of sight and holding the images of object of interest on the fovea. It can be further classified as saccades, smooth pursuit and vergence. Gaze stabilizing eye movements function by maintaining the images on the retina by compensating for movements of the head and/or the visual world and

consist of reflexive vestibular and optokinetic eye movements (Leigh and Zee 2006; Carpenter 1990).

2.1.1.1 The extraocular muscles

The function of the oculomotor system in controlling eye movements involves the interactions of six EOMs, namely, medial rectus, lateral rectus, superior rectus, inferior rectus, superior oblique and inferior oblique (Wright et al. 2006; Adler 2003) (see Figure 2.2). All four recti muscles arise from the tendinous ring, more commonly known as the annulus of Zinn, which is inserted in the orbital vertex bones. The superior oblique muscle originates from the sphenoid bone, while the inferior oblique muscle has its origin from the maxilla, at the floor of the orbit (Remington 2005).
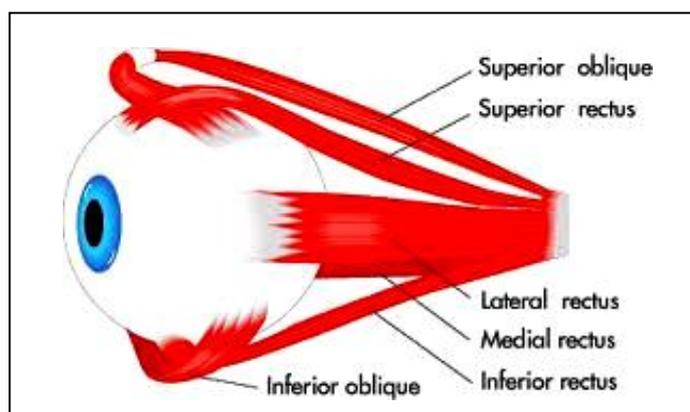
Figure 2.2   View of the extraocular muscles of the left eye (Bianco 2000).

EOMs are classified as skeletal muscles and are among the fastest and most fatigue resistant muscles in the body. Each EOM is divided into two main layers: an inner global layer, bordering the surface adjacent to the globe and containing mainly large muscle fibres, and a surrounding thin orbital layer, composed of small muscle fibres (Yu Wai Man et al. 2005; von Noorden and Campos 2001). The innervation pattern of an EOM consists of both singly innervated muscle 'fast-twitch' fibres (also known as *fibrillenstruktur*) and multiply innervated 'slow-twitch' (or *feldernstruktur*) fibres (von Noorden and Campos 2001; Porter et

al. 1995). These muscles fibres produce fast contraction and slow sustained tonic contraction, respectively, to execute eye movements.

All extraocular muscles receive innervations from cranial nerve III (*oculomotor*) except the lateral rectus and superior oblique muscles, which are innervated by cranial nerve VI (*abducens*) and cranial nerve IV (*trochlear*), respectively (Remington 2005; Adler 2003). The innervation is important in controlling each eye muscle whereby contraction of any of the muscles leads to inhibition of the antagonistic muscle in each eye, which results in muscle relaxation (Sherrington's Law), and co-excitation of the synergistic (yoked) muscle in the other eye (Hering's Law), which ensures conjugate movement of the two eyes.

The primary muscle that moves an eye in a given direction is known as the "agonist". Acting in conjunction with the agonist is the muscle in the same given eye that moves the eye in the same direction, known as the "synergist". "Antagonist" is the muscle in the same eye that moves the eye in the opposite direction to the agonist. According to Sherrington's Law of Reciprocal Innervation, increased innervation to any agonist muscle(s) is accompanied by a corresponding decrease in innervation to its antagonist muscle(s). This law is a classic law that governs all movements of the eyes, in particular the duction system. An understanding of the law is important in interpreting the result of clinical monocular eye movement testing to check for weakness of one or more muscles in a single eye (Pickwell and Evans 2007; von Noorden and Campos 2001). Hering's Law of Equal Innervation states that during conjugate eye movements, equal and simultaneous innervation flows to synergistic, or yoked muscles. Hering's law is particularly useful in explaining abnormalities of oculomotor behaviour seen in tests such as the alternating cover test, which is performed routinely in a primary eye care clinic. The greatest practical significance of Hering's law is its application to the diagnosis of paralytic strabismus. Since the amount of innervation flowing to both eyes is always determined by the fixating eye, the angle of deviation will vary, depending on whether the patient is fixating with the paretic or non-paretic eye. By measuring the

deviation in all the positions of gaze, with each eye fixating in turn, the paretic muscle or muscle groups can be detected (Pickwell and Evans 2007; Adler 2003; Ciuffreda and Tannen 1995).

2.1.1.2 Actions of extraocular muscles

The eye globe, which can be assumed to be a sphere, rotates around three axes that go through the same centre of rotation located approximately at its midpoint. These axes, which are perpendicular to each other, are the horizontal (x-axis), vertical (z-axis) and anteroposterior (y-axis) (von Noorden and Campos 2001).

Rotation of the eye about the x-axis will produce vertical movements, i.e. an upward (elevation) and downward (depression) movement. Rotation about the z-axis will produce a nasal (adduction) and a temporal (abduction) movement. Eye movements about the y-axis (anteroposterior) make the eye rotates temporally and nasally with respect to the superior cornea (known as extorsion and intorsion, respectively). The combination of x-, y- and z-axes allows the eyes to move in different oblique directions (up and nasal, up and temporal, down and nasal and down and temporal).

The action of an eye muscle depends on the direction of its pull with respect to the three axes around which the globe rotates when the eye starts in the primary position (looking straight ahead). Table 2.1 details the muscle actions of each extraocular muscle. The primary action is the main action of the muscles and the secondary and tertiary actions are the subsidiary actions that become increasingly manifest with strong contraction. Medial and lateral recti only have one primary action, which is to mediate the horizontal rotations about the z-axis. The medial rectus is responsible for adducting the eye and the lateral rectus produces abduction movements. On the contrary, the vertical recti and oblique muscles have three actions, which are horizontal, vertical and torsional. For example, the superior

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oblique has a primary action to intort the eye and contributes towards depression (secondary action) and abduction (tertiary action). Nonetheless, to evaluate each muscle action, one has to test the function through the field of action, where the muscle is the primary mover of the eye. Therefore, to evaluate the superior oblique muscle action, the eye has to be moved down and nasally (see Figure 2.3).

Table 2.1   Actions of extraocular muscles from the primary positions (Adler 2003).

Muscles	Primary action	Secondary action	Tertiary actions
Medial rectus (MR)	Adduction	None	None
Lateral rectus (LR)	Abduction	None	None
Superior rectus (SR)	Elevation	Intorsion	Adduction
Inferior rectus (IR)	Depression	Extorsion	Adduction
Superior oblique (SO)	Intorsion	Depression	Abduction
Inferior oblique (IO)	Extorsion	Elevation	Abduction
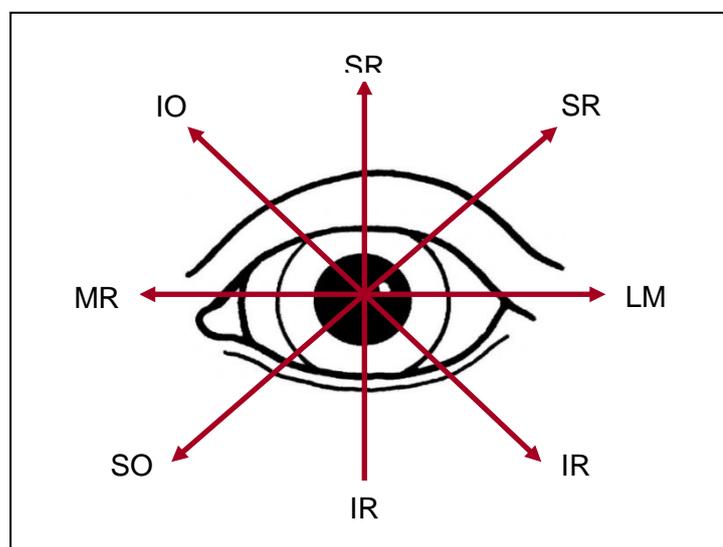
Figure 2.3   Field of actions of extraocular muscles on the left eye. Each arrow points to the quadrant where the specified muscle is the primary mover of the eye. MR=medial rectus, LR=lateral rectus, SR=superior rectus, IR=inferior rectus, SO=superior oblique and IO=inferior oblique (Wright et al. 2006).

2.1.2 Types of eye movements

Eye movements can be considered to have five sub-systems, namely saccadic, vergence, smooth pursuit, vestibular and optokinetic. The types of eye movements that are of particular interest in this study are the saccadic and vergence systems, which will be described in detail below. It was initially thought that these two systems have different properties and were controlled separately (Semmlow et al. 1998). However, recent work has suggested that there are close interactions between the two systems in generating eye movements (Hung et al. 2001).

2.1.2.1 Saccadic movements

Saccades are very rapid conjugate eye movements that can reach velocities of up to 700 degrees per second (°/s) and are elicited to bring images of interest onto the fovea. A saccade is generated in the frontal eye field of Broadmann's area 8, projected to gaze centres in the reticular formation via the superior colliculus. Paramedian pontine reticular formation (PPRF) or horizontal gaze centre, responsible in generating horizontal eye movements while vertical eye movements are generated from rostral interstitial nucleus (RIN) or vertical gaze centre. A pulse-step mechanism is the process responsible for generating a saccadic eye movement (Wong et al. 2008). There are two types of neurons initiating the mechanism in the brainstem, which are known as the burst and omnipause neurons. Burst neurons can be further classified as either excitatory or inhibitory neurons. Excitatory burst neurons (EBN) are responsible for generating the immediate command for a saccadic pulse by activating the neurons that innervate the agonist muscle. Inhibitory motoneurons (IMN), on the other hand, will inhibit the neurons controlling the antagonist muscle. Typically, IMN will be discharged just before or during saccades. The burst neurons will stop firing when the actual eye position matches the desired eye position, and pause neurons will tonically inhibit the burst neurons' activity, causing the saccade to stop.

Saccades can be characterised by different parameters, such as amplitude, latency, duration and peak velocity (Leigh and Zee 2006). The amplitude of a saccade is the size of the eye movement and is measured in degrees (°) and minutes of arc ('). Saccadic amplitude gain, which is the ratio of saccade amplitude to target amplitude, determines the saccade accuracy. Ideally, the response of ocular motor refixation is a single, rapid eye movement that reaches the target and abruptly stops. Bahill et al. (1975) documented that around 85% of naturally occurring saccades are less that 15° in amplitude. Saccade refixation can be either normometric or dysmetric. Normometric saccades consist of a single, accurate movement with appropriate gain and dynamics while a dysmetric saccade is an inaccurate eye movement that can be either too small (hypometric) or too large (hypermetric) with respect to the intended target position (Bahill and Troost, 1979 cited by Ciuffreda and Tannen, 1995). Dysmetric saccades can occur in normal individuals and the error can increase in older subjects or when fatigued. Barnard and Thomson (1995) has highlighted the observation of several patients making more than one eye movement to regain binocular fixation when tested with the unilateral cover test. He linked the outcome of the multiple corrective saccades made with manifested or poorly compensated phoria, which closely related to reported visual fatigue or asthenopia.

Another characteristic of saccades is latency, which is defined as the reaction time from the appearance of a target to the beginning of the saccade. The typical values for saccadic latency in adults are in the range of 200 to 250ms (Yang et al. 2002). However, it can be as low as 100ms or as high as 350ms, depending on the circumstances. It has been shown that the latency of saccades at close viewing distance is shorter than that at far in adults and children. Corrective saccades have also been documented to have a shorter latency (Carpenter 1990). Table 2.2 lists some possible factors that could affect saccadic latency.

Table 2.2   Possible factors that could affect saccadic latency (Ciuffreda and Tannen 1995).

Increase latency	Decrease latency
Very small (<30 min) or large (>10°) target eccentricities	Target predictability
Increased target uncertainty	Increased target luminance
Increased target complexity	Increased target contrast
Increased age in adulthood	Forewarning period
Inability to disengage attention	Heightened attention
Decreased motivation	

Another parameter that is of interest is the duration of saccades, which is defined as the time taken from the start of the saccade to the end of the saccade (Figure 2.4). Typical values of saccade duration are around 30 to 100ms, proportional to the amplitude of the movement, i.e. ranging from 0.5° to 40° (Wong 2008).

Saccadic peak velocity is the maximum speed reached during a saccade. It is usually proportional to the amplitude in small and medium saccades. In normal subjects, the peak velocity ranges from 30 to 700°/s (Wong 2008; Leigh and Zee 2006). The systematic relationship between saccadic amplitude, peak velocity and its duration are best described by the 'main sequence' (Figure 2.5), which has a consistent linear relationship that makes it possible to derive the dynamic characteristic of the saccades and can be used to assess the functions of the oculomotor system (Leigh and Zee 2006).
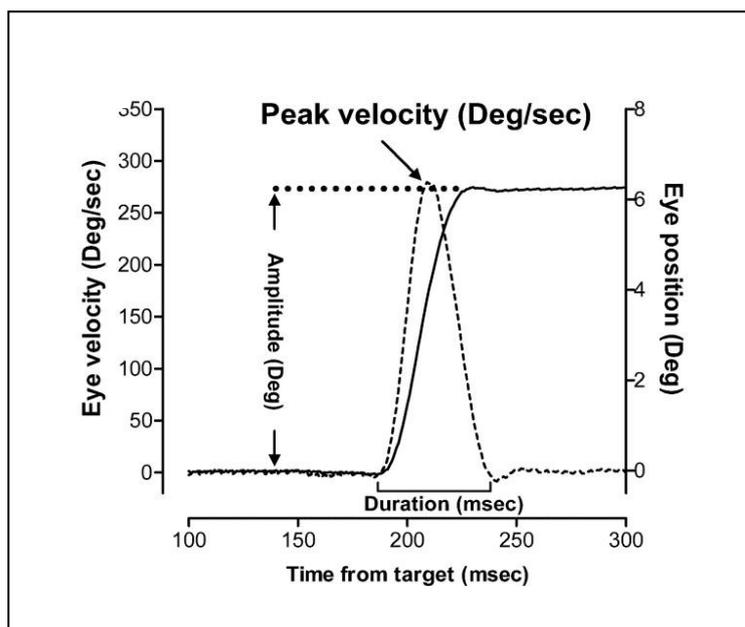
Figure 2.4 Example of eye position and eye velocity changes in a saccade with the solid line representing eye position and the broken line representing eye velocity (Chen et al. 2003).
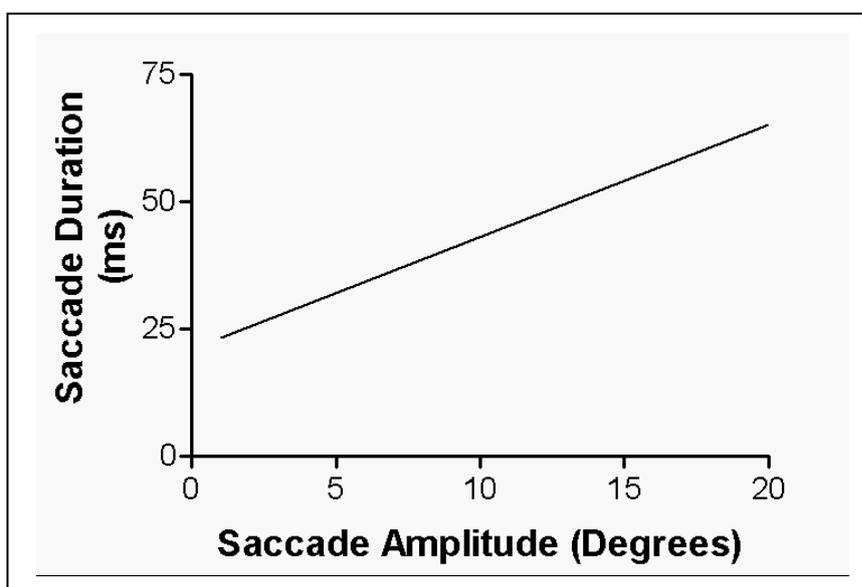
Figure 2.5 Example of the 'Main Sequence' of saccades (http://www.liv.ac.uk /~pcknox/teaching/Eymovs/params.htm).

2.1.2.2   Vergence movements

Vergence eye movements allow the images of a single object at a given distance to be placed on both foveae simultaneously by moving the eyes in opposite directions (convergence and divergence). The movements ensure the proper alignment of the eyes to maintain binocular fixation. Vergence responses are initiated by signals in areas adjacent to the frontal eye fields. There are three types of neurons that are responsible for the control of vergence, known as vergence burst cells, vergence tonic cells and vergence burst-tonic cells. Vergence burst cells are discharged in relation to the vergence velocity (pulse) and act as input to the neural integrator. The vergence tonic cells are activated in relation to the vergence angle (step) and carry the output from the vergence neural integrator. Vergence burst-tonic cells reflect the combined signals of the burst and tonic cells mentioned above. Signals from these cells project directly to both the abducens (cranial nerve VI) and oculomotor (cranial nerve III) nuclei (Leigh and Zee 2006; Wong et al. 2003; Ciuffreda and Tannen 1995).

Maddox (1893), cited by Cooper (1992), classified the vergence system into four components, namely disparity, accommodative, proximal and tonic. Disparity or fusional vergence is elicited by binocular retinal disparity when the images of a single object fall on non-corresponding parts of the two retinas. Crossed and uncrossed retinal disparities will stimulate convergence and divergence movements, respectively, in order to obtain fusion. Previous studies have shown that the amplitudes for fusional convergence movements are greater than those for fusional divergence movements (Leigh and Zee 2006; Borish 2006). Fusional vergence is composed of two subcomponents: fast and slow fusional vergence, which act together to reduce retinal disparity and maintain the vergence response over time (Ciuffreda and Tannen 1995). Fast fusional vergence is responsible for reducing the disparity error to within 1s (Rashbass & Westheimer 1961) while slow fusional vergence maintains binocular alignment with a slower time constant (Schor 1979). During a sustained

vergence gaze, the slow fusional vergence, which responds to the output of the fast fusional vergence system, will increase its output to relieve the fast fusional vergence mechanism. This mechanism will maintain the constant total output of the vergence system, leading to a term described as vergence adaptation (Cooper 1992). Vergence adaptation is a type of compensation mechanism for ocular misalignment, and it is best described using a general adaptation model of vergence and accommodation proposed by Schor (1992). The fundamental feature of this model is that the disparity-driven vergence and blur-driven accommodation are controlled by two negative feedback loops and interactions between the two systems are represented by two feed-forward crosslinks (Jiang 1995). This model combines fast (phasic) and slow (tonic) components. The fast component gives input to the slow component as well as to the crosslinks (see Figure 2.7). During natural viewing, the fast component responds rapidly to the disparity stimuli (retinal disparities). The output from this component is then fed to the slow component, which is responsible for maintaining a stable response through the negative feedback. If the feedback loop is open (i.e. by occluding one eye), the fast component will decay rapidly and the slow component will replace the fast component's response to compensate or adapt to the stress. The magnitude of the crosslink is also reduced. This adaptation will reduce the overall load on the disparity vergence system. Vergence adaptation can be measured clinically using prisms or lenses, and the amount is reported to increase with increased magnitude of the adapting stimulus (Sethi & North 1987).

Accommodative vergence, which is one of the four components in Maddox's vergence classification, also exhibits similar adaptation mechanisms to disparity vergence, as depicted in Figure 2.6. Accommodative vergence is elicited by retinal blur. Reflex accommodation (fast component) acts rapidly in response to the stimulus in order to clear the image and is replaced slowly by the adaptive accommodation (slow component) to maintain the appropriate level of accommodation response. Accommodative convergence can be expressed through the measurement of the AC/A, which is the accommodative vergence to

accommodation ratio. AC/A ratio is typically 4:1 but can range from about 1:1 to 7:1 (Borish 2006). Analysis of the AC/A ratio is important to diagnose and manage binocular vision anomalies. Conversely, the ratio of the accommodation stimulated per prism dioptre of reflex vergence is known as the CA/C (Ciuffreda and Tannen 1995; Hung and Semmlow 1980).
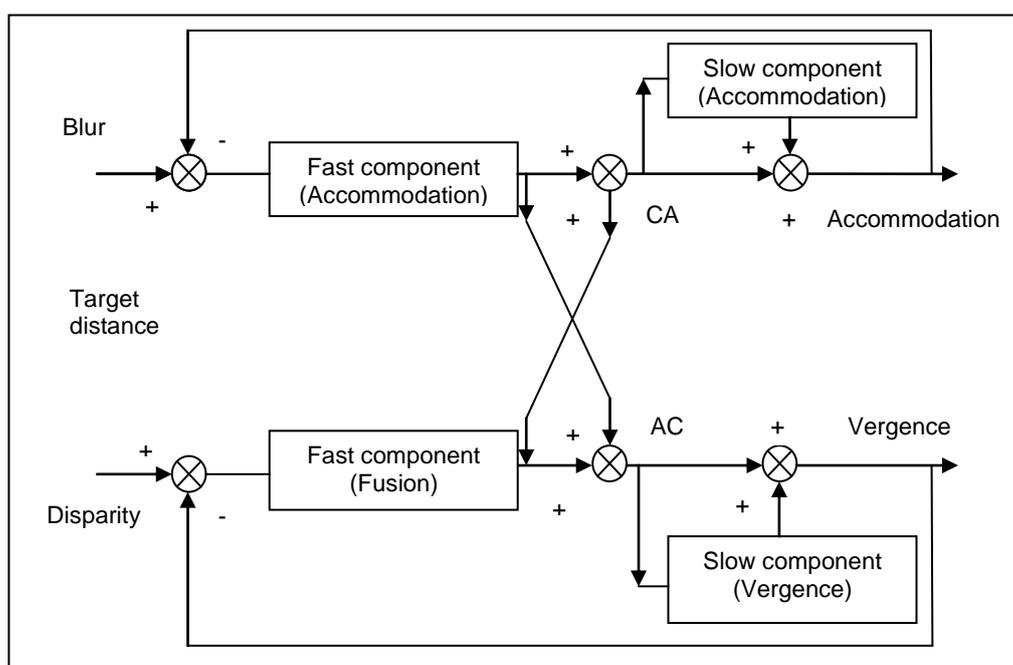
Figure 2.6 A simplified version of Schor's model of accommodation and vergence control. AC represents accommodative convergence, and CA represents convergence accommodation (Jiang 1995).

Proximal vergence is initiated from an awareness of nearness and is thought to provide convergence innervation to the eyes whenever a near object is being viewed. It can also be initiated by other cues such as changes in size (looming), blur-driven and monocular cues as a result of motion parallax and perspective (Leigh and Zee 2006). As proximal vergence is mainly driven perceptually, it is relatively constant and does not change with age (Ciuffreda and Tannen 1995). Proximal vergence contribution towards the overall vergence response is relatively high in the absence of disparity and blur cues. Its impact, however, is less under natural binocular viewing conditions, when both disparity and blur cues are present (Hung et al. 1996).

Tonic vergence represents the underlying resting level of vergence tone (Hung et al. 1994). Tonic vergence innervation converges the eyes from their divergent anatomical position of rest, which is approximately 17 prism dioptre (PD) horizontally, to the physiological position of rest (Borish 2006). This is the vergence angle that eyes would assume in the absence of any muscular innervation. Tonic vergence is significantly correlated to distance heterophoria, and the amount of tonic innervations to the eyes can be influenced by several factors, including the age of the patient, stress, drugs or alcohol, and visual environment (illumination level, retinal eccentricity of stimuli) (Chen et al. 2010; Rosenfield 1997; Ciuffreda and Tannen 1995).

2.1.2.3 Smooth pursuit

The smooth pursuit system generates slow eye movements and functions to keep a moving object on the fovea. This type of eye movement can also be generated by the vestibular and optokinetic system, although the smooth pursuit system can suppress the slow movements made by the other two systems. Although the smooth pursuit neural pathway is not completely understood, it is thought that the movements are mediated by PPRF and motor control centres which are different to the superior colliculus and frontal eye field. Signal goes from retina to parvocellular LGN layers to striate cortex by passing the extrastriate areas, which have direct projections to the brainstem (Stidwell & Fletcher 2011). The cerebellum will then receive input from the brainstem and generate the movement. The peak velocity usually does not exceed 40°/sec, and the latency is reported to be approximately 100ms. The smooth pursuit system will ensure that the eye movement velocity matches the target velocity through its visual feedback control. Any mismatch of the tracking will be corrected by an independently generated saccade (or catch-up saccade) (Ciuffreda and Tannen 1995; Leigh and Zee 1999).

2.1.2.4 Vestibulo-ocular reflex and optokinetic nystagmus

Vestibulo-ocular reflex (VOR) and optokinetic nystagmus (OKN) are two oculomotor systems that have the one common purpose to maintain images steadily on the retina during head movements. VOR generates reflex eye movements at a latency of less than 15ms to stabilise images on the retina during brief head movement. A visual stimulus is not necessary to elicit VOR, hence it functions in total darkness or when the eyes are closed. The OKN system is responsible for generating slow eye movements when the VOR system begins to decrease in activity during continued stimulation i.e. constant head motion. OKN has a longer latency of 140ms, compared to VOR (Leigh and Zee 2006, Ciuffreda and Tannen 1995).

2.2 Anomalies of eye alignments

2.2.1 Phoria

Phoria, or latent strabismus, can be defined as a deviation from the active position when the eyes are dissociated (Pickwell and Evans 2007). It is a reaction to an interruption of the sensory-motor feedback control system. The deviation is not habitually apparent, as fusional vergence will keep the eyes aligned. However, if fusion is broken, for example, as during the application of an occluder in the cover test (see Section 2.3.1.2.3), the eyes move to their natural resting positions. An inward deviation of the line of sight of one eye is termed esophoria and an outward deviation is known as exophoria. Upward and downward deviations are known as hyperphoria and hypophoria, respectively. As a rare occurrence, the eye rotates along the anteroposterior axis when fusion is disrupted. If the eye rotates temporally, it is termed excyclophoria, and if the eye rotates nasally, it is termed incyclophoria. Orthophoria is indicated if there is no movement observed during the dissociation. Phoria can also be classified by the fixation distance at which it occurs or by

assessing whether it is compensated or not, i.e. if the phoria gives rise to any symptoms or to suppression.

Lyle & Bridgemann (1959), cited by Barnard (n.d.), suggested four possible causes of phoria. These comprise anatomical causes, refractive causes, prolonged use of one eye, or trauma. Anatomical causes include abnormality of interpupillary distance, orbital asymmetry, exophthalmos and/or enophthalmos. Refractive causes could be due to problems with the accommodation and vergence system. For instance, there is a tendency to induce a shift towards esophoria in the case of an uncorrected hyperopia. A large majority of myopia cases are associated with exophoria, especially at near distance. Prolonged or repeated use of one eye, such as in the professions of microscopists or watchmaker, has also been suggested as a possible cause of heterophoria. Severe head trauma may result in loss of motor and sensory fusion, which could lead to the development of phoria. A recent study by Wilmer and Backus (2009) on 307 twins revealed that environmental factors such as shared prenatal environment, family, school and societal factors could contribute to the cause of phoria. However, they did not found any relationship between uncorrected refractive errors (genetic factor) and phoria in this longitudinal study.

Tait (1951), cited by Dowley (1987), has reported the distribution of phoria in a sample of 4880 non-symptomatic subjects. He found that there was a high incidence of subjects with orthophoria at distance and that more subjects were exophoric at near. Spierer and Hefetz (1997) reported that there are tendencies to develop more esophoric deviation at distance and exophoric deviation at near with increasing age. The authors monitored the changes from the same group of subjects over 20 years and attributed the changes to the weakening of the extraocular muscles' functions in the presbyopic subjects.

A small, symptomless phoria is common (70-80% of the adult population), although a recent study showed that 20% of patients consulting primary eye care optometrists have a

phoria with possible decompensation signs and symptoms (Rajula-Karania and Evans 2006). Decompensation is the failure of the vergence system to maintain fusion adequately (Stidwell 1998). There are factors that could contribute to the decompensated phoria, such as excessive near work, refractive error, anomalies of accommodation, medication or poor general health (Pickwell 1998). Mon-Williams et al. (1993) also reported clinically significant alterations in heterophoria, in which the subjects complain of asthenopia, following the use of a stereoscopic display. The effort to compensate for a large phoria or weak vergence system could lead to asthenopic complaints, such as headaches, blur, eyestrain or diplopia, which could become pathological (i.e. strabismus) if not treated (Borsting et al. 2003; Sheedy and Saladin 1978).

Phoria measurements are therefore, crucial during eye examination assessment as the findings help in diagnosing binocular vision anomalies that could arise due to the decompensated phoria. Phoria measurements, together with other binocular vision assessments, such as fixation disparity and stereopsis, are also important as they provide a basis for differential diagnosis of eye conditions given that a variety of other defects can lead to similar asthenopic symptoms.

2.2.2 Tropia or strabismus

Tropia is defined as a misalignment of the visual axes when both eyes are viewing a single target (Leigh and Zee 2006; Billson 2003). Tropia can be present at either distance and near vision or at only one distance. It can be generally classified according to the direction of deviation relative to the fixating eye, state of fusion, comitancy or laterality (see Figure 2.7) (von Noorden and Campos 2001). It is categorised as esotropia if the eye deviates nasalward (inward), exotropia (outward), hypertropia (upward), hypotropia (downward), excyclotropia (outward rotation of the globe) or incyclotropia (inward rotation of the globe) (see Figure 2.8).
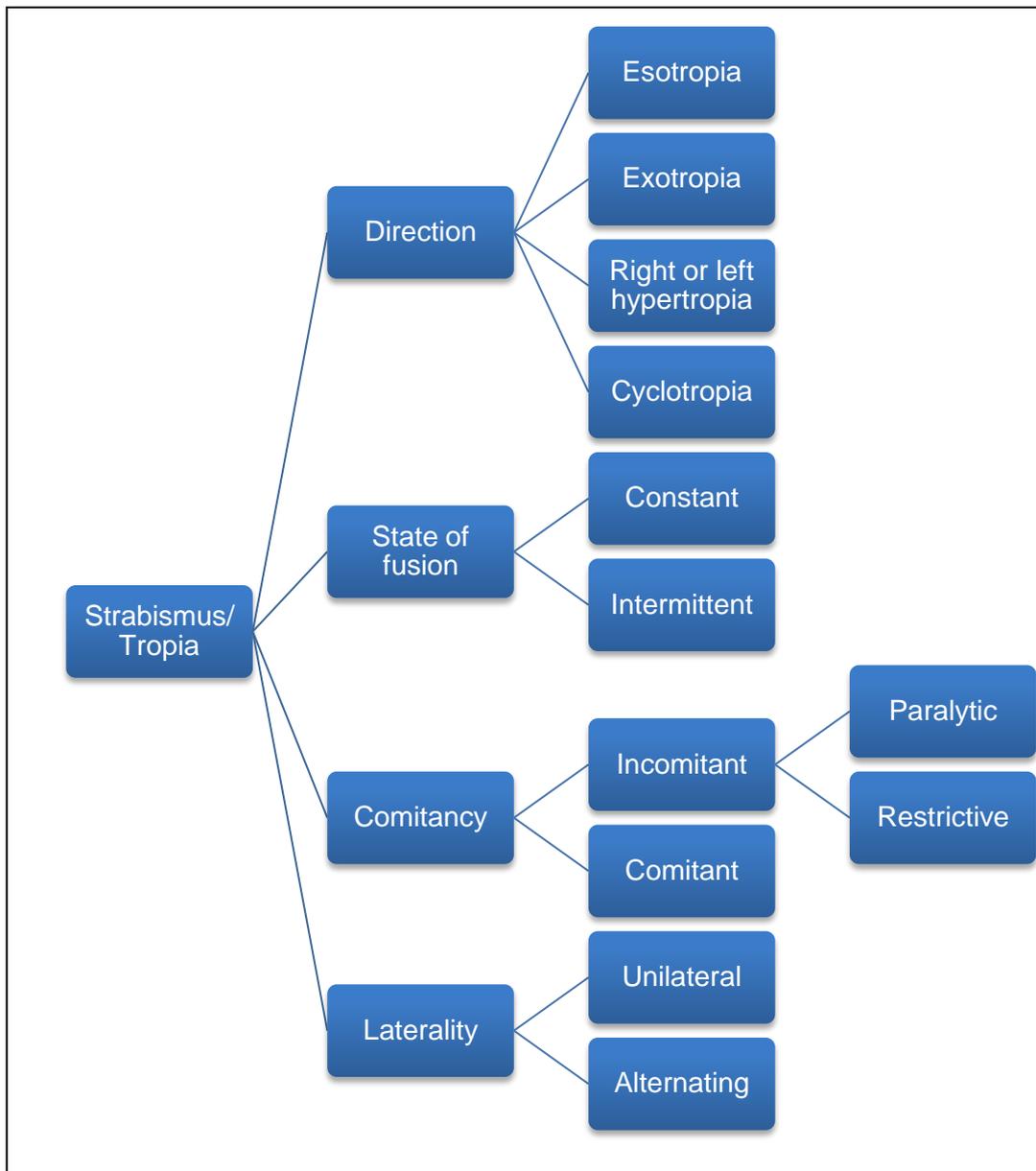
Figure 2.7 Classification of tropia/strabismus (von Noorden and Campos 2001).
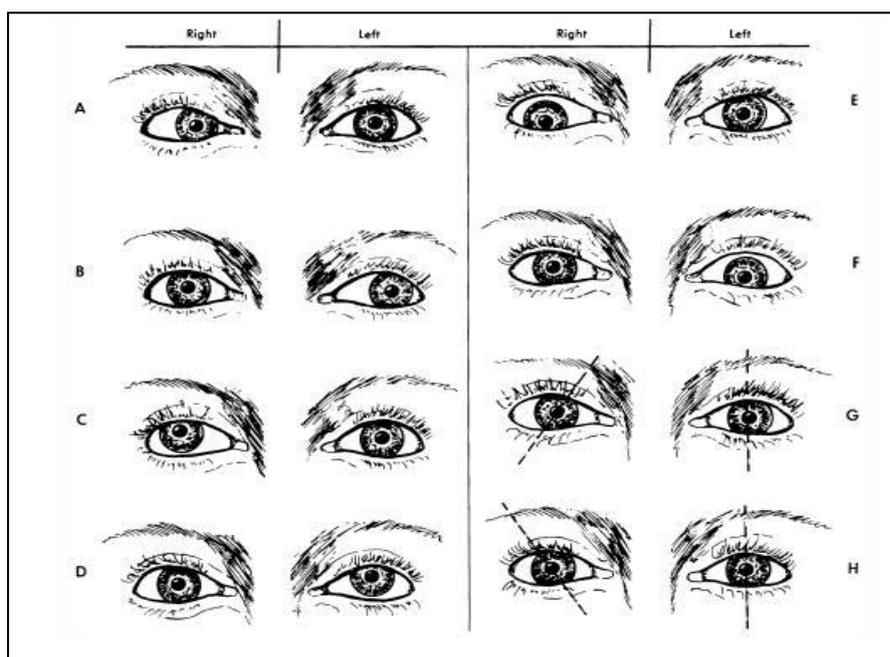
Figure 2.8   Classification of tropia by direction of deviation. A: Right Esotropia; B: Left Exotropia; C: Right hypertropia associated with small exotropia; D: Left hypertropia; E: Right Hypotropia; F: Left Hypotropia; G: Right Incyclotropia; H: Right Excyclotropia (von Noorden and Campos 2001).

Tropia can also be classified according to the state of fusion: manifest or intermittent. The tropia is termed as manifest if the deviation is present at all times and intermittent if the deviation is evident only at certain times. In the latter condition, the fusion mechanism functions in some circumstances and fails in others, for example, under stress, tiredness or illness (von Noorden and Campos 2001).

The deviation can also be classified into two categories, either comitant or incomitant. In the former form, the angle of deviation is the same in all directions of gaze while, in the latter, the angle of deviation varies in different directions of gaze. Comitant deviation commonly presents in congenital tropia. However, certain types of acquired tropia can initially exhibit comitant deviation, for example, in cases of early-onset myasthenia gravis (MG) or chronic

progressive external ophthalmoplegia (Wright 2006). Incomitant deviation occurs as a result of ocular restriction or EOM paresis, which relates to problems such as stiff neck, traumatic muscle damage and neuromuscular disease such as myasthenia gravis. Patients with incomitant tropia show a larger deviation in the direction of action of the underacting or paralytic muscle (von Noorden and Campos 2001). Tropia can also be classified in terms of its laterality. It can occur only in one eye (unilateral) or alternate between the two eyes. Usually, in the alternating condition, the visual acuities of both eyes are the same whereas amblyopia (i.e. reduced vision) is common in the deviating eye in unilateral cases.

Tropia/strabismus is usually first occurs in childhood and is either idiopathic or related to refractive error. Incidence of tropia was documented to be around 3-4% in the population (Stidwell 1997). Sondhi et al. (1988) reported that 70% of normal newborn babies have transient exotropia, which could resolve itself by the age of six months. This has been challenged by Harwood (2003) in her prospective survey on neonatal ocular misalignments, which documented as less than 1% of the children have intermittent esotropia, which ceased spontaneously within two months of age. It is also interesting to note that the study revealed eye professionals often diagnosed exodeviation in infants because of the infant's lack of interest during the examination.

The most common esodeviation in childhood is infantile esotropia, which can be caused by congenital fibrosis of the extraocular muscles, infantile myasthenia gravis or Duane's syndrome. Infantile esotropia comprises less than 1% and transient exotropia accounts for about 70% of incidence at birth (Wright et al. 2006; Lorenz and Brodsky 2005).

There are fewer epidemiology studies concerning the incidence of tropia in adults. Scott et al. (1995), cited by Teed (2009), reported the prevalence of tropia in adults at approximately 4% in the United States. However, most of the patients had developed tropia during childhood. Beauchamp et al. (2003) presented a similar finding with approximately 38% of

the population studied (between 17 and 92 years of age) having a tropia that occurred before the maturation of the visual system. Acquired tropia could be due to nerve paralysis or paresis (paralytic tropia), mechanical restriction of eye movements (restrictive tropia), high refractive error or injury to the eye (e.g. blow-out fracture) (Teed 2009).

Management and treatment of tropia varies from surgical to non-surgical (for example: orthoptic treatments, refractive and prismatic corrections and pharmacological treatment) (Wright 2006; Lorenz and Brodsky 2005; Stidwill 1998). Appropriate treatment is important not only for functional binocularity (i.e. preventing sensory anomalies and restoring the binocular alignment) but also for cosmetic improvement.

2.3   Detection of eye misalignments

2.3.1   Measurements methods in clinical testing

Ocular motor investigation is part of the routine eye examination in the primary eye care clinic. Ocular misalignment can be detected and measured objectively and subjectively using several methods. The test is known as an objective test if there is no perceptual information reported by the subject and the diagnosis depends entirely on the examiner's observation of the patient's eyes (Daum 1991). Subjective tests rely on the subject's response or the estimation of their eyes direction/position when fusion is interrupted. Subjective and objective methods will be discussed in detail in the following sections, with emphasis given to the objective method, the cover test.

2.3.1.1   Subjective methods

2.3.1.1.1   Maddox rod

The Maddox rod is a series of plano-convex cylinders in red or white plastic. It provides phoria measurements when placed in front of one eye of a subject viewing a light source binocularly. The Maddox rod transforms the light source into a streak of light, perpendicular to the axes of the cylinder. Measurement of horizontal deviation involves placing the Maddox rod horizontally, in which the subject will see a vertical streak, and vice versa for vertical measurement. The subject will see two different retinal images formed simultaneously, a spot and a streak of light. The subject has a phoria if the streak of light does not intersect with the spot. Measurement of the magnitude of the deviation can be performed by placing prisms in front of subject's eye until the subject reports seeing the line crossing the spot of light.

The Maddox rod test is considered a dissociative test as there are two different images viewed by the subject, and essentially, there is no binocular vision cue involved. One

disadvantage of this test is the need to control the accommodation as this technique uses a light source as the fixation target. It has been suggested that the subject may overaccommodate when looking at the streak of light and may sometimes fuse the spot and streak (Jones 1983). This will lead to inaccurate measurement of the angle of deviation. However, the problem can be minimised by flashing the light briefly to improve the response from the subject. Perhaps the most serious disadvantage of this method is that it cannot differentiate a phoria from a tropia. The examiner has to distinguish the two by performing an objective test prior to Maddox rod measurements (Wright and Spiegel 2003). Despite the drawbacks, this test is particularly useful in detecting cyclophoria, as the Maddox rod can be oriented obliquely.

Figure 2.9   A Maddox rod.

2.3.1.1.2 Modified Thorington test

This test is performed using the Thorington card in conjunction with the Maddox rod test to measure lateral and vertical phoria. The Thorington card consists of rows of targets, horizontal and vertical, for measuring horizontal or vertical phoria, respectively. The spacing of the targets on the Thorington card has been calibrated to be 6cm and 0.4cm apart to represent one prism dioptre when viewed at 6m and 40cm, respectively. Each card has a hole in the middle where the light source is being held. The Maddox rod is placed in front of the right eye and oriented according to either the horizontal or the vertical phoria that is going to be measured. The subject is instructed to look at the 'zero' target at the centre of the card and report the location of the streak of light relative to the zero. The measurement

of the phoria is taken as the closest target where the streak of light passes through the Thorington card. However, issues concerning the control of accommodation also arise as the light is used as the fixation point.
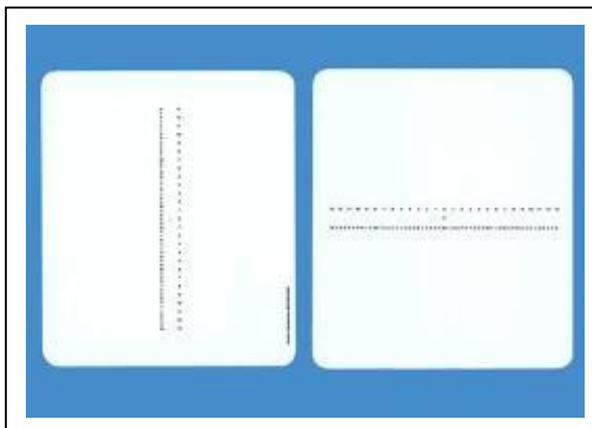
Figure 2.10   The Modified Thorington Card.

2.3.1.1.3 Maddox wing

The Maddox wing is a handheld device for measuring phoria at near. It consists of a septum and two slit apertures that will produce two dissimilar images when viewed binocularly. The subject will see only the white and red arrows with the right eye whilst the left eye will see the horizontal and vertical rows of figures. The white and red arrows provide measurement of vertical and horizontal deviation, respectively. The measurement can be read directly using the horizontal and vertical scales seen by the subject's left eye, which is calibrated in prism dioptre units. The main downside of this test is the limitation of using this instrument only for near measurement and only being useful for measuring a phoria.

Figure 2.11 The Maddox wing.

2.3.1.1.4   von Graefe technique

This technique utilises prisms to dissociate the eyes, and the amount of measuring prism used to achieve alignment of the diplopic images is taken as the measurement of the angle of deviation. Often a vertical Risley prism (oriented base up) in a phoropter unit is used to dissociate the image of the fixation target on one eye and a horizontal base in Risley prism is placed in front of the other eye as the measuring prism. A previous study showed that this test gives the least reliable phoria measurement compared to other methods (Rainey et. al 1998), although this may be due to the patient's difficulty in understanding the procedure involved.

2.3.1.1.5   Synoptophore

A synoptophore is a haploscopic instrument used to measure angle of deviation at horizontal, vertical and oblique gaze positions of tropias and phorias. It has two separate tubes to present different images for each eye. The angle of deviation can be measured subjectively and objectively using a range of foveal, macular and paramacular simultaneous perception slides (Mein and Trimble 1991). The main advantage of a synoptophore is the ability to measure eye misalignment in all gaze positions, especially in the case of cyclophoria and hyperphoria. In spite of this, its accuracy is affected by proximal convergence induced by the instrument.

Figure 2.12 A synoptophore.

2.3.1.2 Objective methods

2.3.1.2.1 The Hirschberg test

The Hirschberg test is one of the objective methods for detecting tropia condition only, but not phoria. A small light source is viewed by the patient at 33cm and the examiner estimates the location of the patient's corneal reflections. The location of the first Purkinje image on both eyes, in relation to the pupil centre, pupil and limbus margin, are compared to determine the relative position of the lines of sights using the formula that 1mm displacement is equivalent to 22PD (Griffin & Grisham 2002, Eskridge et al. 1988). The corneal reflections should be symmetrical between both eyes, although it is normal to have slight nasal displacement of corneal reflexes due to physiological positive angle kappa. Displacement of the corneal reflection relative to the point of the other eye indicates an eye deviation. If the location of the corneal reflection is nasally displaced relative to the reflex in the fellow eye, the patient has an exotropia, whereas, esotropia is diagnosed if the corneal reflection is temporally displaced. This technique is very useful to screen infants or younger children, as it requires little cooperation. Nonetheless, the Hirschberg test has a downside as the corneal reflection is not always discernable for a small angle deviation, even for an experienced examiner. The smallest displacement that can be reliably detected is 0.25mm. However, the sensitivity of this test can be increased using a photographic technique in which the displacement can be distinguished in detail (Griffin & Grisham 2002).

2.3.1.2.2 The Krimsky test

The Krimsky test works similarly to the Hirschberg test but use a prism to neutralise the deviation of the eye. This test is indicated for uncooperative patients (Wright et al. 2006). The drawback of the test is the possible prism adaption that can be induced during the examination.

2.3.1.2.3   The cover test

A cover test is used to evaluate the presence, direction and magnitude of eye deviation (Pickwell and Evans 2007, Wright et al. 2006). It is probably the test most commonly used by optometrists, orthoptists and ophthalmologists to assess the integrity of binocular vision (Barnard and Thomson 1995). This test is dependent on examiner observation of the patient's eye movement in maintaining fixation when each eye is being covered and uncovered in turn using an opaque occluder. However, there is also a subjective evaluation/diagnosis component when the examiner takes into account the patient's response to the target position when performing the cover test (Rainey et.al 1998). The cover test is usually performed at 6m for distance testing and at 25 to 40cm for near testing (Borish 2006). Performed using an accommodative target (usually a Snellen letter chart of one line better than the poorer acuity of both eyes), a cover test has two forms, namely, cover uncover, or better known as unilateral cover test, and alternating cover test.

2.3.1.2.3.1 Unilateral cover test

 A unilateral cover test reveals the presence of a phoria or a tropia and gives additional information about the direction and degree of the deviation. In the case of tropia, the unilateral cover test further classifies the deviation as unilateral or alternating type and characterises it as either constant or intermittent. A unilateral cover test is performed by covering one eye for 2 to 3s while observing the movement of the fixating eye and then observing the movement of both eyes after the cover is removed (Pickwell and Evans 2007). The process is repeated for the other eye and the cycle is repeated several times.

In the case of a phoria, only the eye that is covered will move. In exophoria, the covered eye will move temporally to its tonic vergence position and will be seen to move nasally when the cover is removed. The opposite movement will be seen in the case of esophoria. In

orthophoria, neither eye will move. If the eye moves upwards or downwards upon removal of the cover, it is classified as hypophoria, and hyperphoria, respectively.

In the case of a tropia, the observation is made of the uncovered eye. Principally, in unilateral tropia, no movement is perceived when covering and uncovering the deviating eye. However, when covering the non-deviating eye, the deviating eye will move to take up fixation. As depicted in Figure 2.13 in a case of right esotropia, the non-deviating eye (left eye) remains stationery when the deviating eye (right eye) is covered and uncovered (Figure 2.13 B & C). The deviating eye remains deviated in this stage. When the non-deviating eye is then covered, the deviating eye (right eye) will move to take up fixation (Figure 2.13 D). After the cover is removed, both eyes will move with the non-deviating eye will reassuming fixation and the deviating eye regaining its deviated position (Figure 2.13 E).

In the case of alternating tropia, both eyes are capable take of taking up fixation under binocular conditions. The eye movements seen during the unilateral cover test are the same as in cases for unilateral tropia except the eyes will both remain stationary during the uncovering of the non-deviating eye (Figure 2.13 F).

A: There is esotropia with both eyes viewing (right eye turned in)

B: When the cover is placed before the deviating right eye, no movement occurs; nor does it occur when (C)

C: The cover is removed

D: When the left eye is covered, the right eye must fixate the target and a movement of redress occurs.

E: The left eye again takes up fixation, or

F: The paralyse eye continues to fixate, if the patient is an alternate fixator.

Figure 2.13   The unilateral cover test in detecting esotropia (Leigh and Zee 2006).

2.3.1.2.3.2 Alternate cover test

An alternate cover test is used to reveal the maximum amplitude of deviation (see Figure 2.14). The test is performed by alternately covering one eye for several seconds to dissociate the eyes and then quickly covering the other eye. During this procedure, the examiner has to make sure that one eye is always covered. The test will elicit the presence of phoria and help to bring out the maximal deviation (Leigh and Zee 2006).

Following the dissociation, the deviation can be measured using a prism bar (with the prism pointing to the direction of the deviation) to determine the actual deviation when both eyes are uncovered. The strength of the prism will be increased until no movement of redress is noted or the movement is just reversed (Borish 2006; Leigh and Zee 2006). Table 2.3 lists the type of movement and direction of prism used to measure the deviation of the eye.
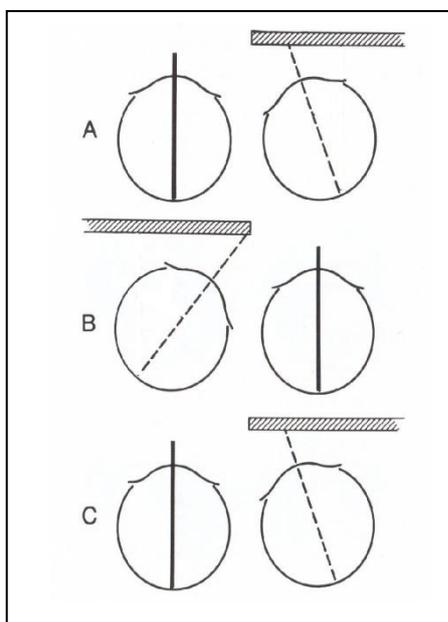
Figure 2.14 The alternate cover test (Leigh and Zee 2006).

Table 2.3   Type of movement when cover is removed and direction of prism used to neutralise and measure the deviation of the eye (Ciuffreda and Tannen 1995).

Type of movement	Type of deviation	Measuring prism
Outward	Esophoria or Esotropia	Base-out
Inward	Exophoria or Exotropia	Base-in
Upward	Hypophoria or Hypotropia	Base-up
Downward	Hyperphoria or Hypertropia	Base-down
Rotary	Cyclophoria or Cyclotropia	Difficult to measure

2.3.1.2.3.3   Simultaneous prism cover test

This variant of cover test is often used to measure the actual tropia angle present under normal seeing conditions i.e. without dissociating the phoria (Wright et al. 2006). The test is performed by placing a loose prism in front of the deviated eye simultaneously as the fixating eye is covered. The simultaneous prism cover test is useful in monofixation syndrome cases in which patients exhibited small angle tropia during alternate cover test but have a smaller angle during normal seeing conditions.

2.3.1.2.3.4   Recording the findings

Recording of the cover test findings is performed by observing the movement and then estimating or measuring the eye movement using prisms or a prism bar. Results are reported for distance and near according to the magnitude in prism dioptre (PD), direction of deviation and type of deviation.

It is also of value to observe the quality of the recovery eye movement for phoria. A guideline (see Table 2.4) for estimating the movement after the cover test has been

published to help in classifying the phoria, i.e. whether it is compensated or not (Pickwell and Evans 2007: Evans 2000). However, this grading system is subjective and depends on the observation of the examiner in classifying the smoothness and speed of movement of the eye recovery. Barnard and Thomson (1995) found that the pattern of eye movements during the recovery phase consisted of a variety of saccadic and vergence movements. They observed that some of their subjects were making multiple corrective saccades after the cover was removed and that they were more likely to report symptoms of asthenopia during near work. They also reported that subjects who made less than two corrective saccades had a well-compensated phoria.

Table 2.4   A grading system to measure the cover test recovery in phoria (Pickwell and Evans 2007).

Grade	Description
1	Rapid and smooth
2	Slightly slow/jerky
3	Definitely slow/jerky but not breaking down
4	Slow/jerky and breaks down with repeat covering, or only recovers after a blink
5	Breaks down readily after one to three covers

2.3.1.2.3.5   Issues concerning cover test

The conventional understanding of a cover test relies on the assumption that the eyes will have to fixate an object of interest with the fovea in order to have a stable and clear image (Borish 2006; Leigh and Zee 2006). In phoria, if one eye is covered, the eye under the cover will move to its heterophoric position and will return to fixation when the cover is removed. It is assumed that the fixing eye will maintain steady fixation, so that there is an asymmetric vergence movement. Contrary to this, Pickwell (1973) revealed that the uncovered eye, or

the fixing eye, often made a small movement and the amount of the movement was documented to be half of the phoria movement detected. Strikingly, he also found that the versional movement of the 'fixing' eye was greater if the dominant eye is covered first (Pickwell 1973). A later study by Peli and McCormack (1983) found similar characteristics of the fixating eye during the cover test. They also noted a difference in the early onset saccade between the two eyes especially with subjects of clear ocular dominancy.

Recovery movement during the cover test is also an integral part of a cover test. Often, a practitioner only observes the recovery movement of the 'covered' eye after the cover is removed. Pickwell (1973) suggested that the recovery movement should be noted in the non-covered and covered eye when administering the cover test. However, it is not possible to note the movements simultaneously in the clinical setting. Therefore, the test should be repeated several times to make this observation (von Noorden and Campos 2001). However, repetition will cause stress to the vergence system, thereby increasing the deviation, and may lead to a phoria breaking down into tropia. It is undeniable that viewing both eyes instead of only one eye helps to increase the information gathered during general clinical exams, and it has long been recognised that an objective eye movement recording system would clearly be able to address the problem (Simons et al. 1978).

It has been proposed that an occlusion period of 2 to 3s should be provided (Pickwell 2007; von Noorden and Campos 2001). However, there are also reports showing that an occlusion period may need to be up to 10s in order for the movement of the occluded eye to reach its maximum amplitude and move to its equilibrium or heterophoric state (Barnard and Thomson 1995; Peli and McCormack 1983). These findings suggest that the practitioner may wish to consider occluding each eye for a period longer than 2s when estimating the amplitude of phoria.

2.3.1.2.3.6   Importance of the cover test

As mentioned earlier, the cover test is useful in detecting and measuring the magnitude of phoria and tropia in a clinical setting. It is also an effective screening protocol and likely to increase the possibility of detecting tropia in children when combined with a test of refraction (The Vision in Preschoolers Study 2007). However, the study also concluded that the test should be done by an eye care professional in order to achieve a precise interpretation for each measurement taken. Additionally, the cover test is the only test useful for differentiating between phoria and tropia (Daum 1991).

The alternate prism cover test has been the gold standard method in measuring tropia in cooperative patients (Billson 2003; von Noorden and Campos 2001). Repeating the test in the nine positions of gaze will also help clinicians to identify and quantify incomitance (Leigh and Zee 2006; Wright et al. 2006).

2.3.1.2.3.7   Limitations and problems

While it is a relatively simple procedure to administer and provides reasonable inter-examiner agreement amongst experienced practitioners (Rainey et al.1998), the cover test has several limitations that can affect the interpretation of the outcome. Some common errors when conducting the cover test have been highlighted, such as failing to fully cover the eye, covering and uncovering too quickly, inappropriate working distance and failing to detect eye movements (Pickwell and Evans 2007).

Although it is possible to perceive a deviation of more than 2PD in a normal subject (Romano and von Noorden 1971, cited by Lam et al. 2005), it is undeniable that the ability to detect the movement depends on the skills and experience of the practitioner. The situation would be particularly difficult if the test were to be administered to patients with poor

cooperation such as a young child, as it may be impossible to maintain fixation or to carry out the occlusion (Mein 1974). Moreover, the outcome of the cover test is rather qualitative (see section 2.2.14). There have been attempts in the past to analyse the eye movements quantitatively during a cover test but these were performed under research laboratory conditions (Barnard and Thomson 1995; Simons et al. 1978). Hasegawa (2003) has addressed the importance of quantifying the eye movement velocity during cover test, in particular for patients with intermittent exotropia, as one of the factors to be taken into consideration before performing eye surgery.

There is also an issue concerning the examiner's position when administering the cover test, as this will affect outcome. Sparks (2002) studied the variations in measuring near phoria with the examiner positioned in the midline and off midline from the patient. The results suggested that larger amounts of phoria, i.e.an average of more than 4PD, will be recorded if the cover test at near is performed from an off-midline position for exophoric patients. However, the examiner position does not affect measurements for patients with esophoria or orthophoria.

2.3.1.3 Comparison between subjective and objective methods

Several studies have been carried out to compare different methods for detecting and measuring ocular misalignment (Lam et al. 2005; Choi and Kushner 1998; Rainey et al. 1998; Schroeder et al. 1996). A comprehensive review of subjective methods in measuring phoria was produced by Schroeder et al. (1996). Comparisons were made between Maddox rod, von Graefe and Thorington tests, where the 95% limits of agreement found was to be between 2 to 4PD. Similar findings were also reported by Casillas and Rosenfield (2006), although measurements performed using a phoropter have wider limits of agreement (1 to 6PD) compared to measurements using a trial frame. The von Graefe technique was found

to be the least repeatable subjective method in measuring phoria, while Maddox Rod and Thorington test gave more reliable results.

When comparing objective methods, the alternate prism cover test has been shown to have a high degree of repeatability compared to Hirschberg and Krimsky. Choi and Kushner (1998) have investigated the accuracy and agreement between the three techniques and found that the alternate prism cover test gave more precise measurements compared to the other two techniques. However, the Krimsky test was more accurate than Hirschberg, although less sensitivity in appreciating differences of below 5PD was noted in this study. They attributed the differences and inaccuracies to the light reflex used in estimating the angle of deviation in the Hirschberg and Krimsky tests. Other studies have also shown that the alternate prism cover test has a high degree of repeatability (Hrynchak et al. 2010; Rainey et al. 1998). High inter- and intra-examiners agreements were observed between measurements with 95% limits of agreement ranging from 2 to 4PD. Rainey (1998) revealed that the correlations between variants of the cover test, i.e. the estimated cover test, the prism neutralized objective cover test and the prism neutralized subjective cover test, were also high.

2.3.2   Measurements methods in the research environment

2.3.2.1 The ideal instrument

There is an extensive array of eye movement recording systems available today, and each can employ different techniques to measure the movement and position of the eyes. In general, the measurement is made possible by manipulating the anatomical landmarks and physical characteristics of the eyes (Ciuffreda and Tannen 1995). The natural colour contrast in the iris/scleral boundary or the pupil/iris margin and the light reflection from the cornea and lens can all be the basis of techniques for detecting eye movements. In the research environment, instruments work by using different principles, with methods of

assessment including, but not limited to, magnetic field (Sprenger et al. 2008), electro-oculography (Wester et al. 2007; Bahill et al. 1975; Young and Sheena 1975), infrared limbal reflection (Träisk et al. 2006; Barnard and Thomson 1995) and video-oculography (van der Geest and Frens 2002).

As knowledge of eye movements has advanced, several instruments have been developed to cater to the urgent needs of this particular research area. Unfortunately, the development of the ideal system is constrained by strict parameters that will later be reflected in the outcome of the recordings. Collewijn et al. (1975) proposed that an ideal instrument should satisfy certain requirements to record precise human eye movements such as having sufficient resolution, linearity and dynamic range as well as the ability to record horizontal, vertical and torsional eye positions simultaneously. The ideal instrument should also have good stability with no baseline drift, be easy to use, non-traumatic and non-invasive in taking measurements (Morimoto and Mimica 2005; Shaunak et al. 1995; Carpenter 1990).

Ultimately, the ideal eye movement device should be consistent in giving precise validated measurements with relative insensitivity to translational head movement, which allows easy application with no interference in behaviour and/or vision (Carpenter 1990; Collewijn et al. 1975). It was proposed that the instrument should have a range of ± 50° for horizontal and vertical plane measurement and ± 20° for torsion to give reliable readings (Carpenter 1990). Furthermore, certain other technical aspects that would lead to achieving consistent measurements should be taken into consideration, such as setting up time, calibration, noise and the cost of the instrument (Duchowski 2007; Morimoto and Mimica 2005; Richards 1990; Reulen et al. 1988).

2.3.2.2   Existing instruments

There are several instruments available for measuring eye movements and eye position although none can satisfy all of the rigid criteria mentioned above. However, it depends on the clinician or researcher to choose the method or instrument that is most suitable for the purpose of the work and fulfils the necessary requirements. Described below are a few different techniques for measuring eye movements and some examples of the instruments that are available on the market.

2.3.2.2.1   Direct contact/attachment to the eyes

The scleral search coil (SSC) is a direct contact method first introduced and developed by Dr. David A. Robinson in 1963 (Carpenter 1990; Robinson 1963). It utilises a scleral contact lens with one or two embedded coils of wire (see Figure 2.15). These contact lenses are inserted into the subject's anesthetised eye(s) and fitted in such a way that the lead wire from the coil leaves at the temporal canthus of the eye, to minimise discomfort (Collewijn et al. 1975). Subject's head is placed inside a set of orthogonal oscillating magnetic fields and the measurement of eye position is obtained by measuring the electric currents induced by the coils.

The scleral search coil method is known for having a high resolution of up to 1 min of arc, thus making measurements of each saccadic oscillations possible. It has proved to have very good linearity, being better than 0.25% for an output signal that is equivalent to the sine of the coil deviation (Träisk et al. 2005; Shaunak et al. 1995). The scleral search coil has the ability to record horizontal, vertical, and possibly, torsional movement simultaneously (Houben et al. 2006; Crawford et al. 1999). It is widely used to measure the three dimensional position of the eye in humans (Houben et al. 2006) and animals, for which

researchers frequently conduct the experiments with the eye coils surgically implanted on the animals' eyes (Crawford et al. 1999).

Figure 2.15   The scleral search coil.

Even though this technique is invasive, takes a long time for setup and needs calibration each time it is used, the scleral search coil method sets a 'gold' standard method for measuring eye movements (Shaunak et al. 1995; Carpenter 1990). However, an experienced clinical practitioner is needed to insert the contact lens/coil, as there is a small risk of incurring corneal abrasion from the use of the contact lens (Irving et al. 2003). This approach, however, would seem rather impractical as well as undesirable for use in infant or child research because of its highly invasive nature and would be too cumbersome to use in the clinical or non-laboratory research. Thus, the techniques described below provide promising alternatives to the scleral search coil.

2.3.2.2.2   Non-contact method/optical method

2.3.2.2.2.1 Infrared oculography (IROG)

Infrared oculography (IROG) works by quantifying the difference between the amounts of infrared light reflected by the sclera between matching infrared light emitting diodes (LED) and phototransistors, which are aimed at the nasal and temporal limbal areas (see Figure 2.16). When the eye moves, the detector located at one side of the cornea will measure an increase in infrared reflection while the other detector measures a decrease in reflection.

The system works by subtracting the nasal and temporal detector voltages for measurements of eye position with respect to head position. Once calibrated, the resultant voltages will be demodulated and amplified to give the angular position of the eye.

The advantage of the IROG technique lies in the use of the infrared detectors, which allows the measurements to be performed even in a dark environment, as the measurements are not markedly influenced by the ambient light. The system also allows measurement of vertical eye movement to be recorded, simply by rotating the detector array to a vertical position (Reulen et al. 1988). Generally, an instrument using the infrared method can have very good spatial resolution of about 0.1° and a temporal resolution of more than 400Hz.

However, the drawback is the possibility of obtaining less precise vertical measurements, due to the nature of the eyelids that sometimes can cover the top and bottom of the limbus (Ciuffreda and Tannen 1995; Young and Sheena 1975). Furthermore, the eyelids could cover the surface of the eye during blinking as the eyes will retract slightly and, thus, alter the amount of light reflected. However, Reulen et al. (1988) proposed that this problem could be eliminated by gently taping the eyelids open.
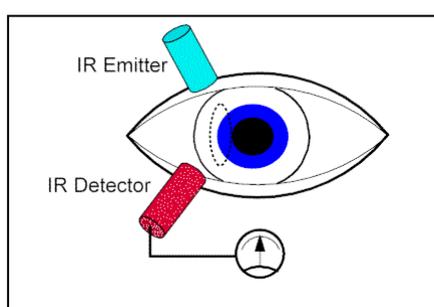
Figure 2.16   Illustration of the infrared oculography technique (http://www.liv.ac.uk /~pcknox/teaching/Eymovs/params.htm).

The discontinued Skalar IRIS (see Figure 2.17) was, until recently, a commercially available eye tracker that utilises this method in detecting the orientation and movement of the eyes.

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Even though the IRIS system has a limited dynamic range of 30° laterally, it has been claimed to be adequate for measuring fixation eye movements, saccades, smooth pursuit and vergence eye movements, producing reliable results (Reulen et al. 1988). Many studies concentrating on eye movement characteristics have been carried out using the system, which has proven to be practical in recording the dynamics of the vergence system (Alvarez et al. 2005; Barnard and Thomson 1995), binocular coordination (Bucci et al. 2002) as well as being suitable for testing adults and children (Bucci et al. 2002; Shaunak et al. 1995). There is also another system developed using the Skalar IRIS, known as EMMA (Eye Movement and Analysis System) for measuring eye movement (Muir et al. 2003). The hardware was designed by combining the IRIS instrument with two computers, an LED bar as a target, a colour video projector and a multi-tone audio generator. Despite the comprehensive system that EMMA comprises, it runs under a DOS operating system that limits the application to a single task and possesses only a plain interface programme. Likewise, the system may not be accessible to the practitioner, as the DOS operating system is now antiquated and difficult to understand, making data analysis complicated. Understandably, as EMMA is not commercially available, users might also need to have some knowledge in programming to be able to use this system.

Figure 2.17   The Skalar IRIS (www.crsltd.com/catalog/skalar).

2.3.2.2.2.2 Video-based methods

Video-based methods rely on the properties of the eye and its optical surfaces to detect and measure eye movements using cameras and image processing hardware (Hansen and Ji

2010; Morimoto and Mimica 2005). Typical sampling frequencies vary between 25 and 300Hz. Instruments that implement higher speed cameras, such as EyeLink from SR Research, can reach up to 2000Hz. Some video-based eye trackers can measure eye movements in the horizontal and vertical planes simultaneously and some can even assess torsional measurements as well. The eye position in the images obtained from the camera(s) is identified and tracked over frames. Generally, this method does not provide point-of-regard measurements. Therefore, multiple ocular landmarks, such as limbal, pupil or corneal reflections, have to be measured to differentiate between the eye and head movements. Alternatively, the instrument can be fixed to the subject's head, in order to match the position of the eye to the head (Duchowski 2003).

Limbus tracking is one of the video-based methods and works by optically detecting the distinct contrast difference between the sclera and iris boundary. The limbus tracking technique is based on the position of the limbus relative to the head position; hence, the instrument has to be fixed to the subject's head. The technique suffers from the fact that the limbus is easily obscured by the eyelids, which will lead to inaccuracies in tracking vertical eye movements (Azam et al. 2009; Richardson and Spivey 2004).

The pupil is one of the common ocular features used for tracking. The principle of this method is to determine the position of the pupil relative to the head, and therefore, there is a need for the instrument to be fixed to the user's head, as with the limbus tracking method. The main advantage of this technique compared to the limbus tracking method is that the pupil margin is darker and sharper than the limbus, thus providing better resolution for detection. This method also allows the detection of vertical eye tracking as the pupil is less likely to be covered by the eyelids, compared to the scleral boundary (Azam et al. 2009).

Another method is based on the **cornea-pupil reflection relationship** and utilises the reflections occurring when a light source is being shone into the eyes. An infrared light

source is commonly used in this technique, instead of visible light, as it does not distract the subject. The positioning of this light source with respect to the optical axis of the camera, can create bright or dark pupil effects (see Figure 2.18). A bright pupil effect occurs when the infrared light source is placed in line with the optical axis, resulting in light being reflected back from the retina. This effect is similar to the 'red eye effect' caused by flash photography. The dark pupil effect occurs when the light source is offset from the optical axis, causing the pupil to appear dark (Marimoto and Mimica 2005; Duchowski 2003). The infrared light source is also responsible for creating the reflections on the eyes. These reflections are known as Purkinje images (Figure 2.20). The 1st and 2nd Purkinje images are from the front and back surfaces of the cornea while the 3rd and 4th Purkinje images are reflections from the front and the back surfaces of the lens. The first Purkinje image, or the 'glint', is the brightest reflection and, therefore, easiest to detect. Sophisticated algorithms are used to calculate and measure eye movements by combining the bright-dark pupil tracking and using the glint, with respect to the pupil, as the eye reference.

The cornea-pupil reflection technique has some distinct advantages, as instruments using this technique generally are comfortable because there is no physical contact with the user's eye or face. Infrared light is used as the illumination source, and therefore, the experiments can be performed over a longer period of time as it is less annoying or disturbing to the patient. Eye movement measurements can be carried out in the most natural way, without the use of any chin rest or bite bar. This is made possible by the use of advanced algorithms and the signal processing involved, which enables larger compensation for head movements (Young and Sheena 1975).

The drawbacks of this method, however, lie in the problems of detecting the glint and capturing a good view when tracking the eyes, as they may at times, be out of the camera's field of view, especially during blinks. Hence, the subject has to be within the range of the infrared illumination and the camera view in order to obtain good eye movement data.

There are a few commercially available instruments based on the cornea-pupil reflection technique, such as Tobii T/X120 and TX300 eye trackers (Tobii Technologies), the ViewPoint eye tracker (Arrington Research), faceLAB (Seeing Machines) and EyeLlink (SR Research).
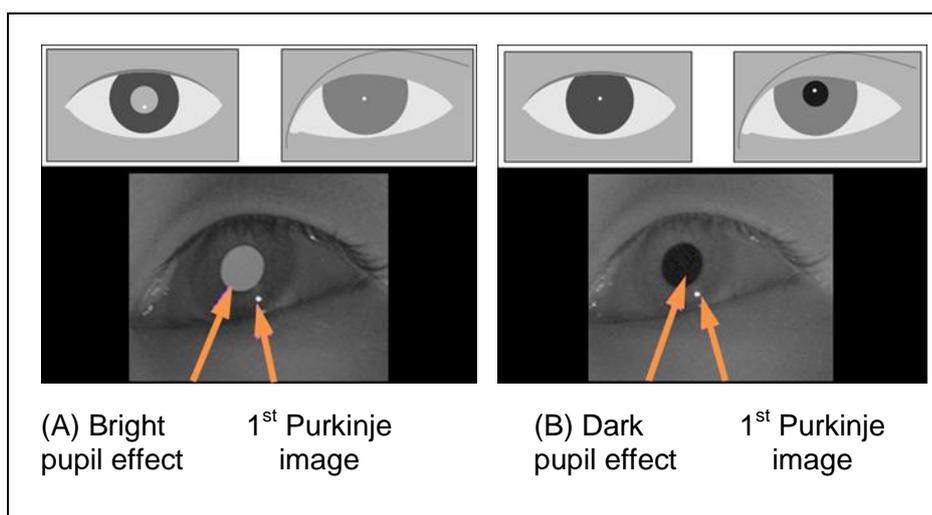
Figure 2.18 Bright and dark pupil tracking (Olsen 2010).
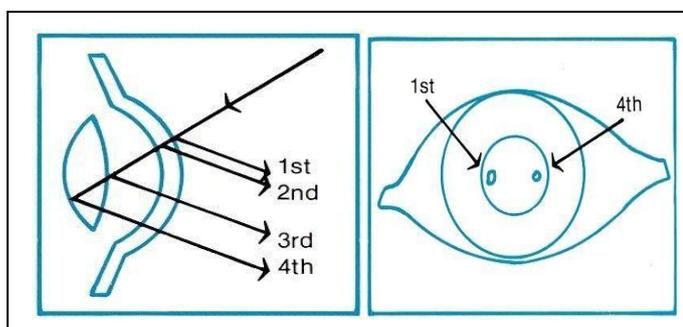
Figure 2.19 Illustrations of Purkinje images. The first (1st) Purkinje image is also known as the glint, which is the reflection from the anterior surface of the cornea; the second (2nd) Purkinje image is the reflection from the posterior surface of the cornea. The third (3rd) and fourth (4th) Purkinje images are formed from the reflection from the anterior and the posterior surfaces of the lens, respectively (Fourward Technologies, Inc. 2001).

The **Dual Purkinje Image (DPI)** technique also utilises the Purkinje images to determine eye position. The spatial positions of the 1st and 4th Purkinje images, which move identically during eye translation and differently during eye rotation, are exploited to differentiate between movements of the eye and head (Duchowski 2003; Deubel and Bridgeman 1995; Clark 1975). The main advantage of this technique is its accuracy and high sampling frequency of 400Hz and above. Despite this, Deubel and Bridgeman (1975) highlighted the fact that the DPI technique may have its limitations because the 4th Purkinje image is rather weak, compared to other Purkinje images. Therefore, to optimise the eye tracking capability, the surrounding lighting has to be controlled. Moreover, a bite bar needs to be used to stabilise head movement (see Figure 2.20).
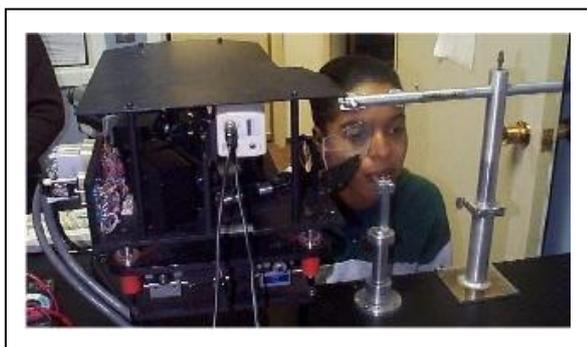
Figure 2.20   Dual Purkinje Image eye tracker (Fourward Technologies, Inc. 2001).

2.3.2.2.3 Electrical potentials

Electro-oculography (EOG) uses electrical potentials measured with skin surface recording electrodes attached to the outer canthus (see Figure 2.21). It works by quantifying the cornea-retinal potential, which is a small voltage between the front and back of the eye, with the cornea being positive relative to the retina. Principally, the retina acts as a dipole with a potential difference of 0.40 to 1.0mV and will create a fluctuating potential relative to the electrodes as the eye moves. After calibration, these potentials will be recorded as measures of eye movements from the surface recording electrodes (Leigh and Zee 2006; Young and Sheena 1975).

EOG has the advantage of being a system that is easy to use and does not interfere with vision. Moreover, the system also permits the patients to wear their own spectacles during the measurement. Another point in favour of the system is that it has a good measurement range of ±60° horizontally and ±40° vertically (Larson 1970), and this technique has been reported to give about ±2° measurement accuracy (Shaunak et al. 1995). Unfortunately, this method is thought to be prone to drift as a result of variation in the corneoretinal potential, which is influenced by the subject's state of alertness and other diurnal variations (Young and Sheena 1975). The signal is influenced by ambient light and the act of occluding one eye produces the effect of a low level of surrounding light (Bahill et al. 1976). EOG is also sensitive to muscle artefacts, including lid interference, that could affect the reliability of the measurement, especially when recording vertical eye movements (Leigh and Zee 2006; Shaunak et al. 1995).

Figure 2.21   The electrooculography (http://www.metrovision.fr/).

2.3.3   Comparison between eye trackers

Several studies have been carried out to evaluate the performance and suitability of the selected tracking methods in measuring eye movements. Many studies compared the selected instrument(s) to the gold standard method, the scleral search coil (SSC) (Schmitt et al. 2007; Imai et al. 2005; Träisk et al. 2005; Deubel et al. 1995). The non-contact instrument using infrared light (e.g. VOG and IROG) source seems to be the most commonly used technique, as it offers an alternative to the SSC in providing reliable eye movement measurements. It was initially shown that the IR eye tracker produces significantly noisier eye movement data compared to the SSC (van der Geest and Frens

2002), but this finding was attributed to the lower sampling rate of the IR system used in this study, which was 250Hz as compared to the 500Hz of the SSC. Similarly, Träisk et al. (2005) reported significant differences in the saccadic main sequence analyses performed with both techniques having the same 500Hz sampling rate. It was thought that the slipping of the coil annulus from the surface of the eyes and changes in the level of the alertness in the subjects wearing the SSC could contribute to the differences found.

Contrary to previous studies, Schmitt et al. (2007) did not find a significant difference between saccadic characteristics investigated using the SSC and IR eye trackers. The comparisons were made between the SSC with a sampling rate of 1000Hz and IR eye trackers with an adjustable sampling rate of 250 to 1000Hz. This study revealed that both techniques produced similar main sequence results and were in good agreement. Imai et al. (2005) also found comparable findings between SSC and IR VOG eye trackers when investigating various eye movements such as smooth pursuit, vestibular and optokinetic. The sampling rate did not influence the results of the eye movement data collected in this study. Comparisons of the different eye movement recording techniques are summarised in Table 2.5.

Table 2.5 Comparison of the eye movement recording techniques.

| Technique | Non-contact method | | | | Electrical potentials (EOG) | Contact method (Scleral search coil) |
| | Infrared oculography | Video based system | | | | |
		Limbus/Pupil tracking	Corneal/pupil relationship	Dual purkinje images		
Subject contact	Head mounted or chin rest	Head mounted or chin rest	None	Chin rest/Bite bar	Electrodes	Contact lens
Accuracy	H : 0.5° - 7° V : 1°-7°	0.003°	0.5-2°	0.017°	±1.5-2°	0.08°
Resolution	0.1°	0.005°	Good	0.25°	About 1°	0.017°
Range	H : ±15-30° V : ±15-20°	H: ±30-40° V: ±20-40°	H : ±12-40° V : ±12-50°	±20-60°	H : ±60° V : ±40°	±25°
Sampling speed	200-4000Hz	50-250Hz	25-2000Hz	Above 400Hz	-	1000Hz
Rotational measurements	X/(Y)	X/Y	X/Y/Z	X/Y	X/Y	X/Y/Z
Pupil diameter measurement	No	Yes	Yes	-	-	No
Advantages	1. Non invasive 2. Minimal discomfort 3. Little noise				1. Non invasive 2. Minimal discomfort 3. Applicable to children and poorly cooperative patients 4. Relatively inexpensive	1. Precise recording 2. Sensitive to less than 1 minute of arc 3. Capable of measuring horizontal, vertical and torsional rotations of eyes and head

Disadvantages	1. Limited range			1. Lens motion artefact 2. Subject's head have to be immobilised by using bite bar	1. Electrical noise 2. Lid artefact 3. Unstable baseline 4. Repeatable calibration 5. Adaptation to ambient lighting 6. Unreliable for vertical eye movements	1. Direct contact method 2. Needs topical anaesthetic drops 3. Large instrument for external coil housing 4. Expensive
Manufacturers (system name)	1. Cambridge research system (Skalar IRIS)	1. ISCAN Inc.	1. Tobii technologies (Tobii T/X series) 2. Seeing machine (FaceLab) 3. Arrington research (Viewpoint) 4. Senso Motoric Instrument (3D VOG) 5. Eyelink (SR Research)	1. Fourward Optical Technologies (DPI Eyetracker)		Skalar medical B.V

Sources: Leigh and Zee 2006; Fourward Technologies, Inc. 2001; Shaunak et al. 1995,Young and Sheena 1975.

2.3.4   Methods/instrument chosen for this project

As mentioned above, each method and instrument has its advantages and disadvantages. None of the eye trackers can fully satisfy all the criteria needed. Some researchers might find certain eye movement parameters to be more important than others. The selection of an appropriate eye tracker is dependent on the criteria chosen, aims of the experiment and perhaps the selection of participants. For example, if the experiment were targeted on children, non-invasive methods would be the obvious choice. When fine eye movements are studied and measurement accuracy is of concern, an instrument with a higher sampling rate has to be selected.

One attempt has been made to incorporate infrared technology to measure eye movements in a clinical setting. Simons et al. (1978) developed an eye movement system combining a minicomputer-based hardware and software to investigate the characteristics of eye movements in the hope of providing an automated clinical test for quantifying eye movements. Although the system seemed to be promising, no further study has since been carried out to test the reliability, repeatability and practicality of such a system in a clinical setting.

In this study, we apply an integrated approach in combining the traditional clinical method of eye alignment measurement, the cover test, with recently available infrared eye trackers. The eye tracking method chosen was based on its invasive nature (non-contact), ease of set up with adequate sampling frequency. The eye tracker system will provide objective and quantitative outcomes of this clinical test and will allow the analysis of eye movements in more detail than is possible under conditions of manual testing. Additionally, the responses are permanently recorded, providing a quantitative basis for monitoring any given treatment to patients.

2.3.5 Specific aims of the project

The goal of this research is to determine the suitability of using the infrared eye tracker as part of the routine clinical eye examination to measure eye misalignment in a more quantitative and objective way. The research was constructed to address the validity and reliability issues of the new eye tracking system, the Tobii X120 (see Chapter IV) in which the methodology and examination procedure involved are detailed in Chapter III. The agreement of the cover test results was first compared between different examiners (see Chapter V) before comparing the cover test results between alternating prism cover test and cover test in front of the eye tracker (see Chapter VI). The eye alignment test was also performed using the eye tracking system on small hospital-based sample patients with abnormal eye movements to identify prospects of implementing such system in a clinical environment (see Chapter VII).

CHAPTER III

METHODOLOGY

3.1   Instrumentation

Two different eye trackers, the Skalar IRIS 6500 and the Tobii X120, were used in this study. As mentioned previously in Chapter II, in spite of the diversity of the eye trackers' functions, the eye trackers in this study were mainly used to perform eye alignment examination. The Skalar IRIS 6500 was utilised in part of the study to compare cover test findings with measurements performed by an optometrist and the second infrared eye tracker, the Tobii X120. The Skalar IRIS is a well-established infrared oculography eye tracker and has been widely used in the research environment. Its applications include many research areas, such as ophthalmology (Bucci et al. 2002), psychology (Gurvich et al. 2007) and neurology (Schon et al. 1999). For the purposes of the comparison investigated here, the Skalar IRIS can be taken as the 'gold standard' in eye tracking. On the other hand, the Tobii X120 has become established in the usability and marketing area, whereas its role in ophthalmological and neurological investigation is limited. Therefore, the potential use of this instrument in this area warrants further investigation (see Chapter IV). The Tobii X120 has distinct advantages over the Skalar IRIS in being portable and less intrusive, especially when examining young children. The Tobii X120 eliminates the inconvenience of wearing a head-mounted device and allows the subject to move their head within a reasonable range, while compensating for the head movement.

3.2   The Skalar IRIS 6500

The Skalar IRIS 6500 (Skalar Medical BV, Delft, Netherlands) consists of a lightweight helmet with two infrared sensors, which are connected to an oscilloscope via a cable. Each sensor consists of nine emitting diodes and nine photosensitive detectors, which are positioned above and below each eye, respectively. The system works by differentiating the infrared light reflection by the iris-sclera boundary. For example, when the eyes move to the left, the voltage of the nasally located detectors is subtracted from the voltage of the detectors located temporally (see Figure 3.1). The voltage difference for each eye is then transformed and amplified resulting in a signal related to the eye's angle of deviation.

RIGHT EYE	**RIGHT EYE**
Emitters	Emitters
Detectors	Detectors
Figure 3.1(a) Right eye in a primary position (looking straight ahead). Both right and left detectors receives equally infrared reflection	Figure 3.1(b) Right eye looking to the left. Note that the right detector receives less infrared reflection than the left detector
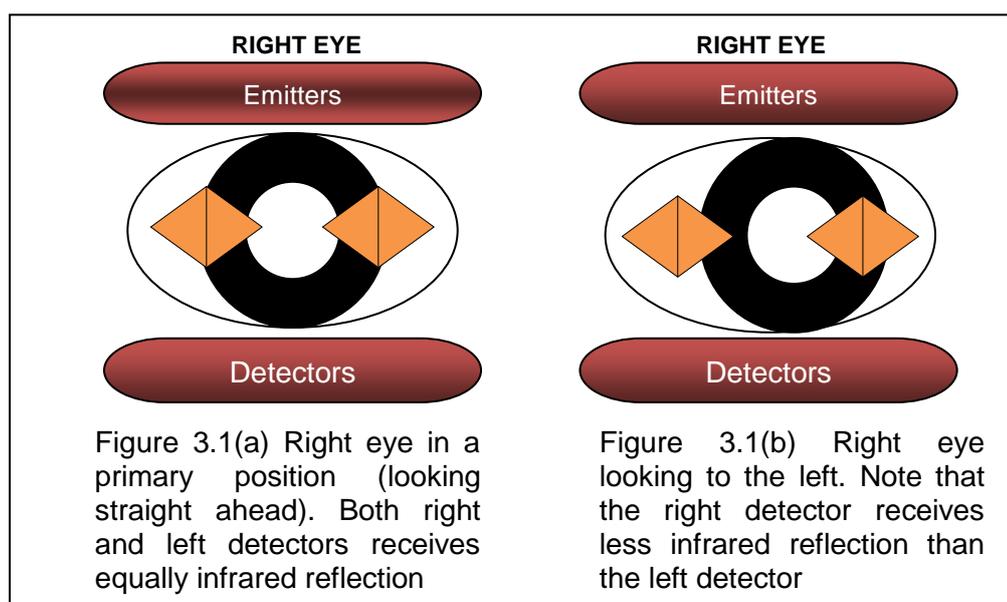
Figure 3.1   Graphical drawings illustrating the principle of eye movement detection using the infrared emitters and detectors of the Skalar IRIS.

The sensors can be adjusted (i.e. rotated) in three perpendicular axes (x, y and z) in order to align the sensors' marker with the pupil centre of each eye (see section 3.2.2). The Skalar IRIS can be used to perform horizontal or vertical eye movement recording of both eyes. However, the measurement can only be done in one plane at a time (Muir

et al. 2001; Skalar Manual n. d.). A recent study has shown that the Skalar IRIS can also be used to measure eye movements at oblique planes with some laboratory modification (Kavasakali et al. 2002).

3.2.1   Software, target stimuli and data handling

In the present study, metrics from the eye tracker's recording were extracted using the vsgEyetrace software programme (Cambridge Research System Limited) which is responsible for generating eye calibration targets as well as presenting the fixation stimulus. This software provides choices of various built-in stimuli to use with further options for different oculomotor experiments, such as saccadic, smooth pursuit, fixation and optokinetic nystagmus eye movements, to name a few. All of the parameters can be changed to suit the desired experiment (see Figure 3.2).
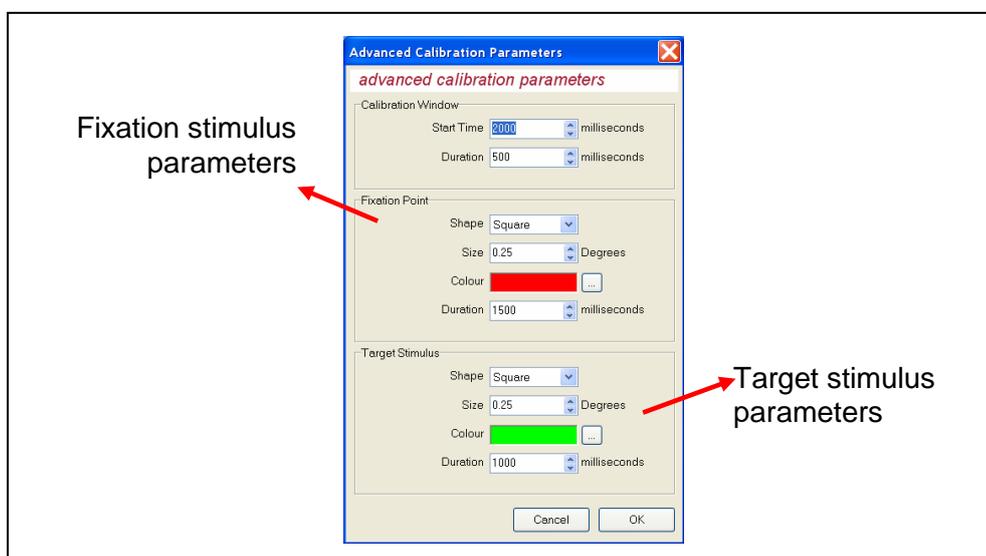
Figure 3.2   Configuration screen for eye movements experiments in vsgEyetrace.

For calibration purposes, a specific saccadic test was set up with black cross targets that were 0.25° in size against a white background. The targets were arranged in the horizontal plane and appeared randomly in 5° eccentricity steps. Upon successful initial setup (see section 3.2.2), subjects were asked to follow the calibration targets

accurately and the data were evaluated using the graphical output from the vsgEyetrace software (see Figure 3.3). For experimental purposes, a fixation target was constructed using a black cross target of similar characteristics to the target used for calibration. Data output files were in the form of *.etd files, which were used to store all the acquired data, together with information about the protocol and any calibration. The data were collected for the eye movement positions for the right eye (channel 1) and the left eye (channel 2). Data from channels 1 and 2 were transferred and saved for offline analyses using a customised MATLAB programme created by Professor Chris Harris (Plymouth University). The calibration and experimental procedure were performed using the targets displayed on a CRT monitor at 40cm and 3m for near and distance cover tests, respectively (see section 3.5).
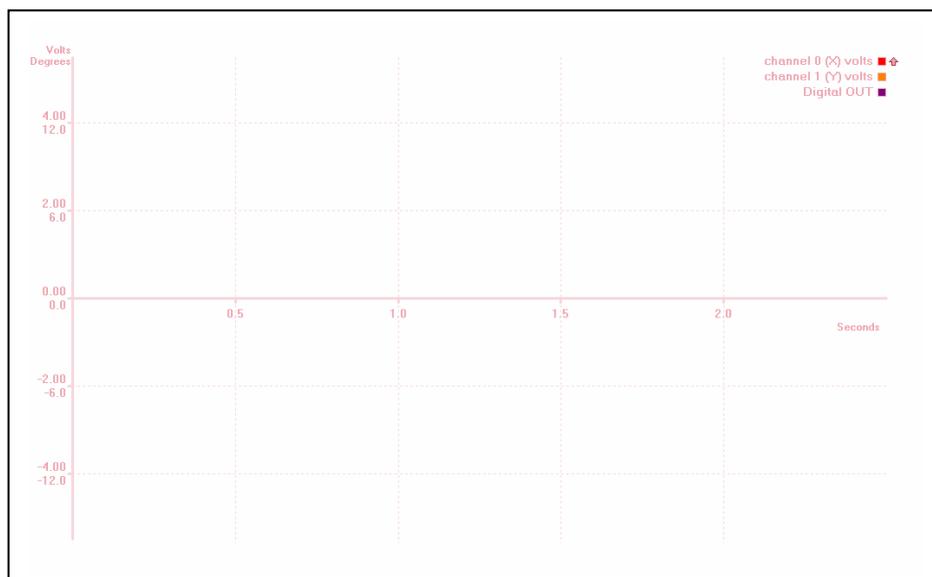
Figure 3.3   Layout of the vsgEyetrace software.

3.2.2   Setup and calibration

The essential criterion for ensuring a proper calibration is aligning the detectors' marker with each pupil centre (see Figure 3.4). The subject was comfortably seated, and the helmet was then fitted on the subject's head. The examiner adjusted the detectors manually so that the horizontal axis (x) marker was perpendicular to pupil centre of each eye and the lower detector was aligned with the lower palpebral margin (vertical axis, y). After adjusting the x- and y-axes, the examiner adjusted the z-axis from the side where the distance from the detector to the subject was set to around 1.5cm to 2cm in order to get optimum IR transmissions. However, appropriate adjustment would have to be made if the subject had long eyelashes or deep-set eyes.
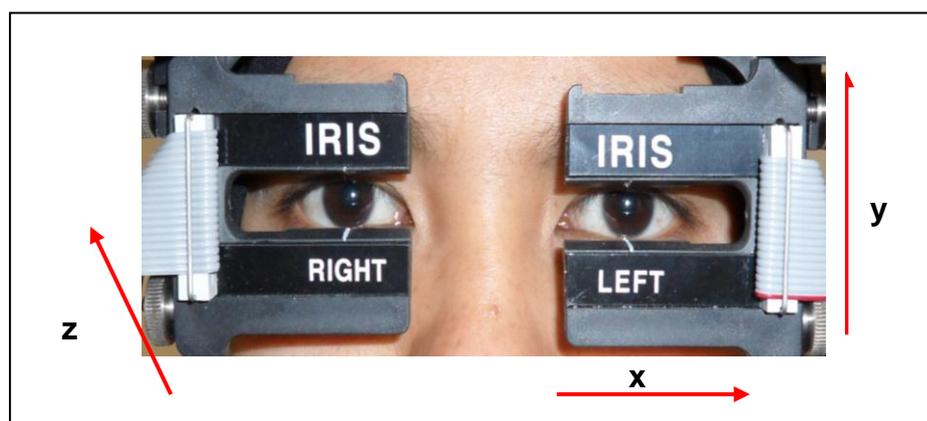
Figure 3.4   Sensors adjustment in three perpendicular axes. X axis refers to horizontal adjustment, y refers to vertical adjustment and z refers to adjustments of the distance of the sensors from the eye.

The next step was to check the synchronisation using IRIS control panel with the eye movements of the subject. The subject was asked to view a target straight ahead and then look at a set of horizontal fixation targets of known angular separation, which were presented randomly. The examiner monitored the eye movements by looking at two green LED indicator lights at the front of the control panel. There were three equally spaced markers in the front panel, one in the centre and one in each side, which

served as guidance for the calibration process (see Figure 3.5). Ideally, the two green LED indicator lights (one for each eye) should be at the central marker when the subject was looking straight ahead and move symmetrically away from the centre when the subject was looking to the right and left by an equal movement. More fine adjustments were made, as necessary using the zero and gain adjustment buttons. This was followed by the computerised calibration procedure detailed in section 3.2.1. The subject's head was stabilised with a chin rest during both the calibration process and the experimental procedure.
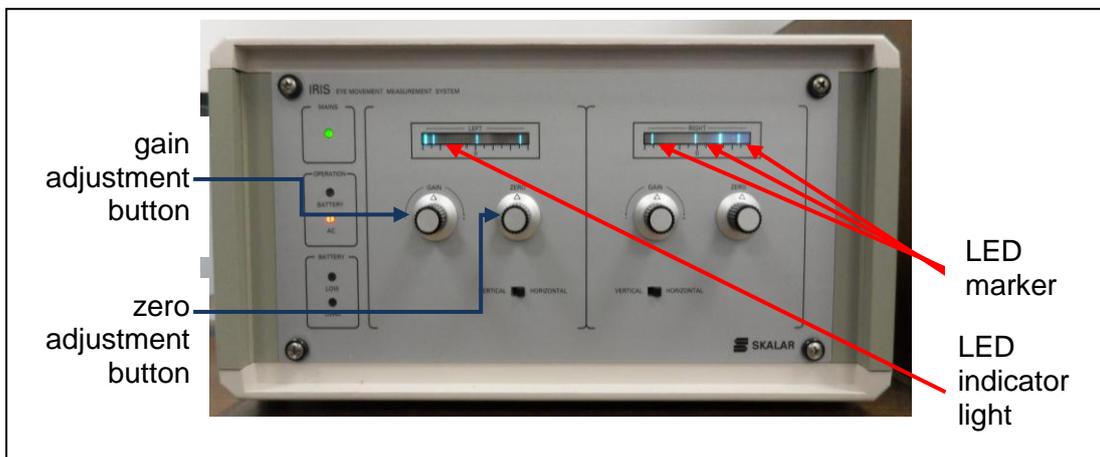
Figure 3.5   Close up control module showing the LED indicator lights, LED marker, gain and zero adjustment button.

3.3   The Tobii X120 eye tracker

The Tobii X120 eye tracker (Tobii Technology AB, Sweden) is a portable, eye-tracking unit (see Figure 3.6). It offers flexibility in recording eye movements regardless of any stimulus arrangements or display setup. The Tobii X120 is equipped with its own software, Tobii Studio™, which offers a fully automatic eye calibration procedure and accurate tracking with a large freedom of head movement (Tobii X60 & X120 Eye Tracker Product Brochure 2008).

This eye tracker utilises infrared as a light source to illuminate the eyes, and the Purkinje images I (anterior corneal reflection) are captured by two image sensors in the built-in camera of the eye tracker unit. The Tobii X120 uses both dark and bright pupil illumination settings to maximise its ability to track the eye position. Dark pupil illumination is achieved when the illumination source is placed offset from the optical axis, resulting in the pupil appearing darker than the iris. If the illumination source is coaxial with the camera, the pupil will appear to be brighter than the iris (bright pupil tracking) because of retinal reflection (i.e. red eye). While bright pupil tracking works best on individuals with light irides, it is less suitable for subjects with darker irides. In such cases, dark pupil tracking method will be automatically chosen by the eye tracker to produce the greater pupil/iris contrast. The pupil images captured by the sensors are translated as eye gaze positions in real time using image processing algorithms and a physiological 3D model of the eyes (Tobii Eye Tracking White Paper 2010).

Figure 3.6   The Tobii X120 (Tobii Technology AB, Sweden).

_____Chapter III

3.3.1   Software, target stimuli and data handlings

Tobii Studio™ is an analysis software that provides a comprehensive platform for calibration, target presentation and analysis. The Tobii eye tracker, integrated with the Tobii Studio™ software, has an option to perform binocular calibration in either automatic or manual mode. It is also equipped with a built-in infant calibration involving a more attention-grabbing target that can also be used as a fixation target. The interface is easy to use and facilitates in the design of any experiment using different media such as videos, pictures or web recordings with the drag and drop function (Tobii Studio™ Product Brochure 2009). Once designed, the test can be easily set up and the quality of the eye movement data collected during an experiment can be evaluated during playback, before exporting the data to an Excel spreadsheet for further analysis.

For calibration purposes, we used the Tobii Studio™ built-in 9-point automated calibration programme before each experiment. This programme involved the subject following a target as it moved to nine random points across the screen while the Tobii X120 gathered eye position data at each point for data mapping (see section 3.3.2). For the experimental cover test study, we constructed a black cross fixation target of 0.25º in size against a white background, similar to that used with the Skalar IRIS.

The data generated were in the form of *.tsv files. Useful raw data output consisted of a timestamp, X and Y gaze coordinates, relative pupil size and distance from the eye tracker to the subject. All data were exported to Microsoft Excel, and the information was displayed in columns that could be plotted as graphs for ease of interpretation (see Figure 3.7). The raw data were filtered from the system noise and blinks using validity codes. These codes are the built-in estimation of the eye tracker's confidence that the data captured for a given eye actually belong to that eye. This validity code ranges

from 0 to 4, where 0 represents reliable data and 4 corresponds to missing data. Full explanations of the validity codes and possible combinations of the codes for the two eyes are detailed in Tables 3.1 and 3.2. Data from the eye tracker were all filtered so that only a combination code of 0-0 was accepted before further analyses were undertaken.

Table 3.1   Interpretation of the validity codes for one eye.

Validity code	Interpretation
0	The eye tracker is certain that the data for this eye is correct. There is no risk of confusing data from the other eye.
1	The eye tracker has only recorded one eye, and has made some assumptions and estimations regarding which is the left and which is the right eye. However, it is still very likely that the assumption made is correct. The validity code for the other eye is in this case always set to 3.
2	The eye tracker has only recorded one eye, and has no way of determining which one is the left eye and which one is the right eye. The validity code for both eyes is set to 2.
3	The eye tracker is fairly confident that the actual gaze data belong to the other eye. The other eye will always have validity code 1.
4	The actual gaze data are missing or definitely belong to the other eye.

Table 3.2   Possible combination of validity codes for two eyes.

Validity codes combination	Description
0-0	Both eyes found. Data are valid and correctly identified for both eyes.
0-4 or 4-0	One eye found. The system correctly identifies which eye is being captured. Gaze data are the same for both eyes.
1-3 or 3-1	One eye found. The system is estimating which eye is being captured. Gaze data are the same for both eyes.
2-2	One eye found. The system is uncertain of which eye is being captured. Gaze data are the same for both eyes.
4-4	No eye found. Gaze data for both eyes are invalid.

Graphs were plotted using columns 'GazePointXRight' and 'GazePointXLeft' against time to show the subjects' eye movements when looking at the horizontal targets on the screen. The graph shown in Figure 3.8 represents the eye movements in pixels. Upwards on the graph denotes rightward eye movements and downwards refers to leftward eye movements. The same graph was plotted using column 'GazePointYRight' and 'GazePointYLeft' against time to represent the data for vertical gaze (see Figure 3.9). The upwards tracings represent the eye position while looking down and vice versa. For both graphs, the red line corresponds to the right eye and the blue line is for the left eye.

Figure 3. 7 The raw data from the eye movement recording in the .tsv file after being converted to an *.xsl file. Columns in green represent data for Left Eye and columns in orange correspond to Right Eye. Highlighted columns refer to horizontal eye positions and outlined columns are for the vertical eye positions.
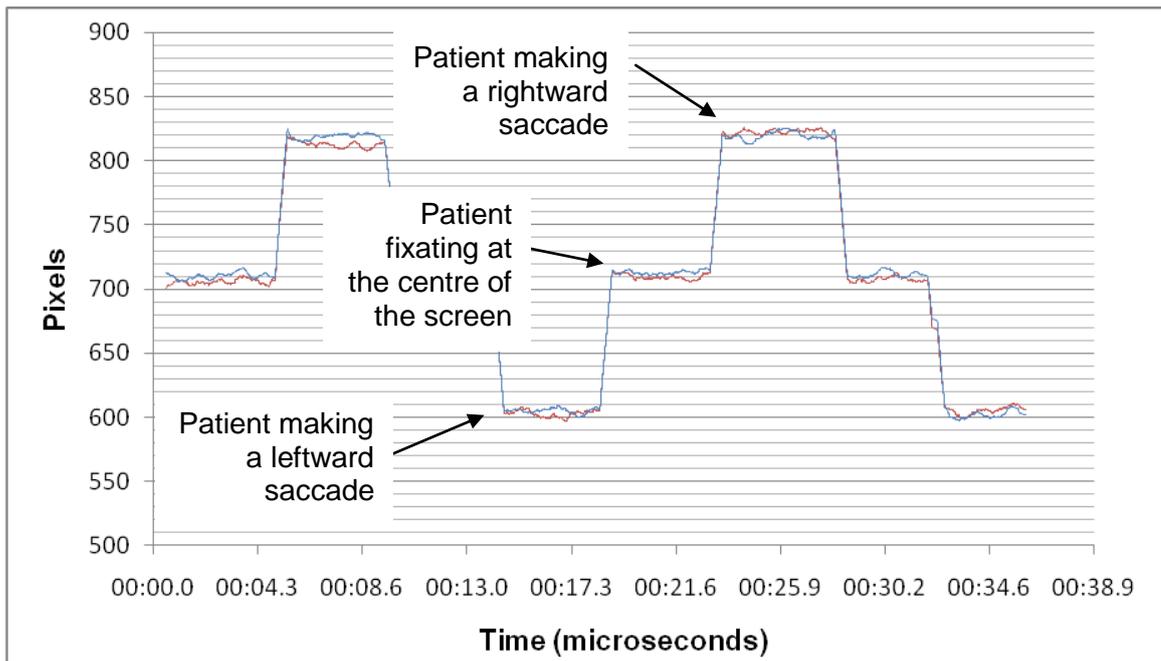
Figure 3.8 The horizontal eye movements plot in pixels against time (microseconds) for subject MA. The red and blue lines represent the right and left eye movements, respectively.
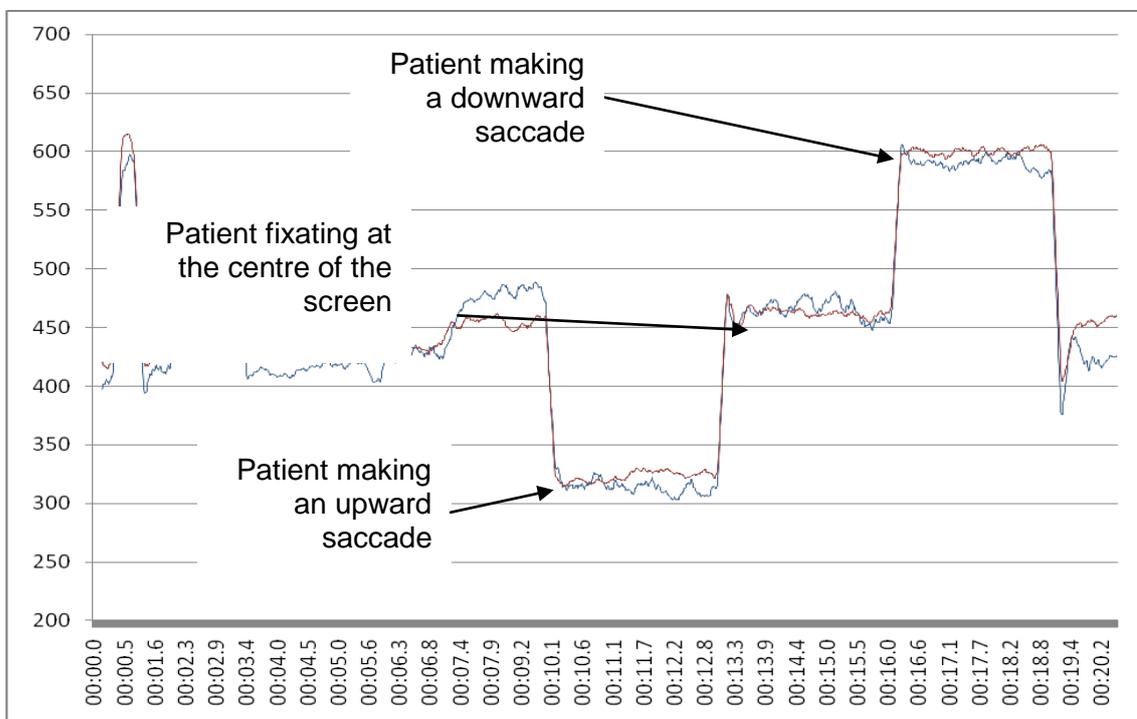
Figure 3.9 The vertical eye movements plot in pixels against time (seconds) for subject MA. The red and blue lines represent the right and left eye movements, respectively.

Unlike the output data from the vsgEyetrace programme, raw output data from the Tobii X120 are computed in pixels, which is relative to the resolution of the viewing/display device used, such as a monitor screen. The eye movement's data produced by the system therefore needed to be converted into degrees or prism diopters in order to produce a meaningful data set. We performed a pilot study to determine the conversion by using a simple trigonometry calculation and formula, as shown in Figure 3.10.
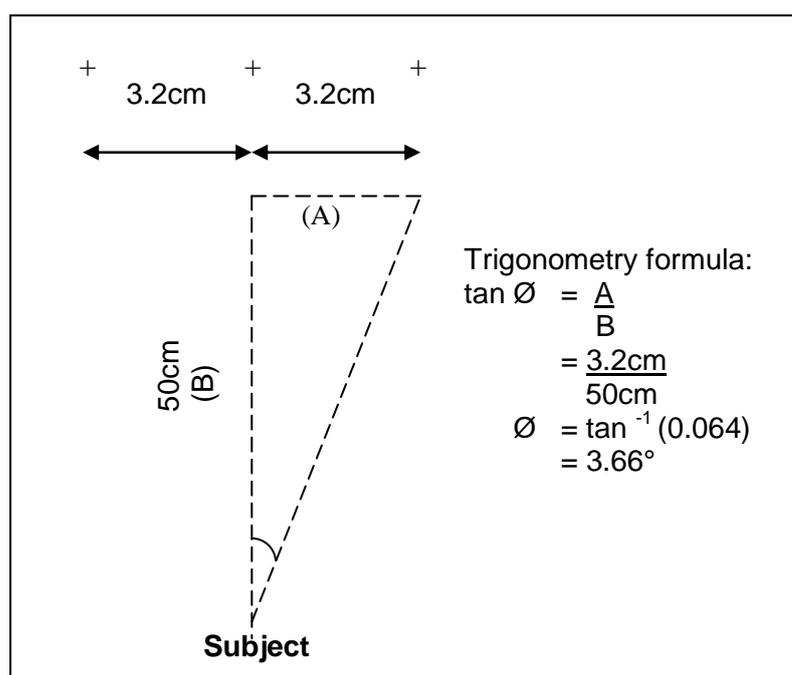
Figure 3.10   Representation of the trigonometry projection for calculating the pixels to degree conversion from the Tobii X120 raw data output. The measurements here are not scaled.

In the experiment, subjects were asked to make saccades to targets on the right and left (of known target separation), where the difference for the right and left saccade peaks from the central fixation target was measured. For example, in Figure 3.6, subject MA's average centre fixation is 710.311 pixels, while the saccade to the right is 820.166 pixels and the left saccade is 600.451 pixels. The difference from each

saccade to the centre fixation point is 153.86 pixels. We then calculated the amplitude

of the saccadic eye movements (in visual degree), to the right or left of the centre

fixation point using a simple trigonometry formula, as shown in Figure 3.11. Using the

basic formula of a conversion from degrees to prism dioptres which is 0.57° = 1PD, the

pixels to prism dioptre unit was derived from the formula as shown below, with the final

conversion being calculated as 24 pixels for an equivalent of 1 prism dioptre.

If 0.57° = 1PD; So, 3.66°= 6.42PD = 153.86 pixels Therefore, 1PD = 153.86 pixels/6.42PD   = 24 pixels

Figure 3.11   The conversion formula for pixels to prism dioptre.

3.3.2   Setup and calibration

Physical adjustments had to be made to the Tobii X120 setup, as the accuracy of its

measurements was heavily dependent on the parameters entered into the

configuration tool setup. Emphasis had to be placed on measuring the angle between

the eye tracker (Figure 3.12 A) and the display (Figure 3.12 B), distance to the display

screen (Figure 3.12 C), size of the display (Figure 3.12 D), and the height of the eye

tracker to the display (Figure 3.12 E). These measurements were all important as the

Tobii X120 is a standalone portable eye tracker and the algorithm embedded in the eye

tracker requires the input from the parameters mentioned above to ensure its proper

alignment to the screen and the subject. A digital angle measure (Skil Europe BV,

Netherlands; Model 0580) was used to determine precisely the eye tracker and the

display angles. In our study, we configured two separate settings, i.e. for experiments

at a distance of 3m and 40cm, at which different displays were used. These

parameters were saved to the configuration files and retrieved when performing any eye tracking experiment at the respective distance.
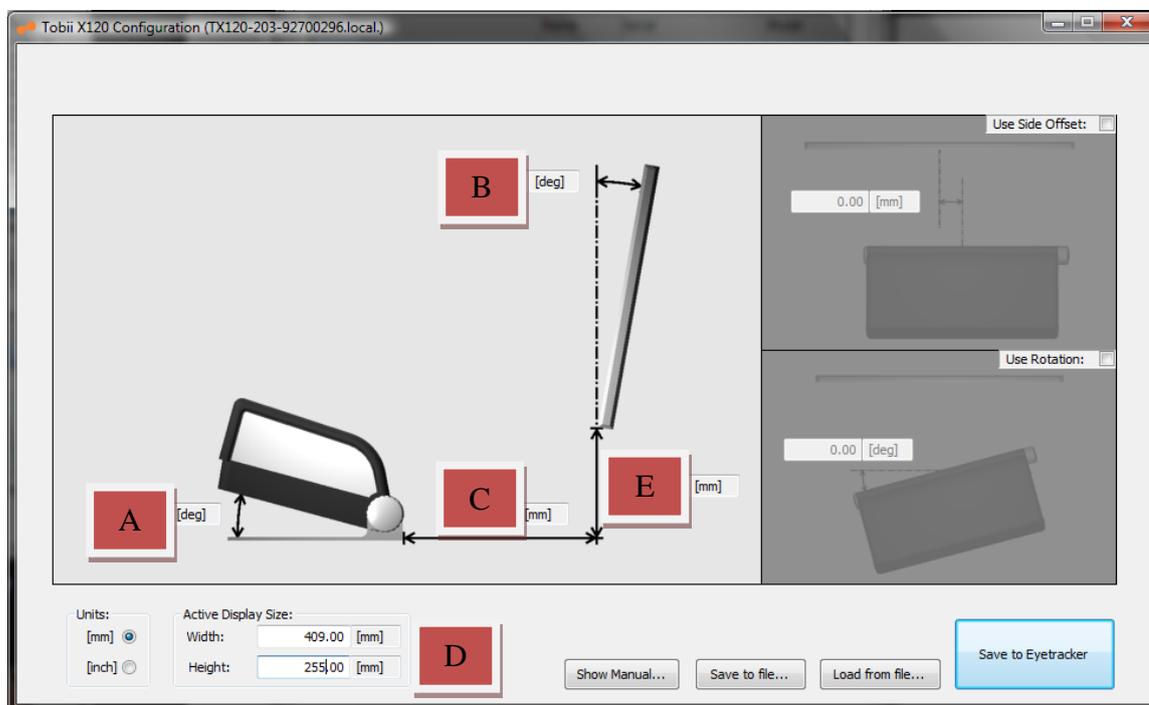
Figure 3.12 The schematic figure above represents the parameters that need to be specified in the Tobii X120 configuration setup to ensure accurate eye tracking.

The subject was seated comfortably on a chair, which was raised or lowered to make sure the stimulus and the eyes were at the same level. The subject was positioned in front and in the middle of the eye tracker and the monitor screen. No chin rest or bite bar was required as the Tobii eye tracker can compensate for head movements of about 30x22x30cm for the eye tracker running at 120Hz (see Section 4.4). The regular automated calibration would involve the subject following a moving red dot to specific points on the screen. The eye tracker tracks both eyes simultaneously and automatically determined the right or left eyes. The quality of the calibration was presented by green lines displayed on the screen with respect to the actual target points, which were depicted as grey spots in the calibration window (see Figure 3.13). The lengths of the green lines indicate the offset of the eye fixations made by a subject

from the centre of each of the calibration points. This provided an indication to the examiner whether the calibration needed to be repeated. A proper calibration as shown in Figure 3.13 (left), results in green lines within the grey spots, whereas an inaccurate calibration (see Figure 3.13 (right)) produces large offsets and correspondingly longer green lines. Several factors contribute to these offsets, such as the eye tracker was not configured properly or the subject was not fixating on the calibration points properly. Recalibration can be performed for any selection of points as needed. Once a proper calibration was obtained for all points, it could be reused without the need for another calibration.
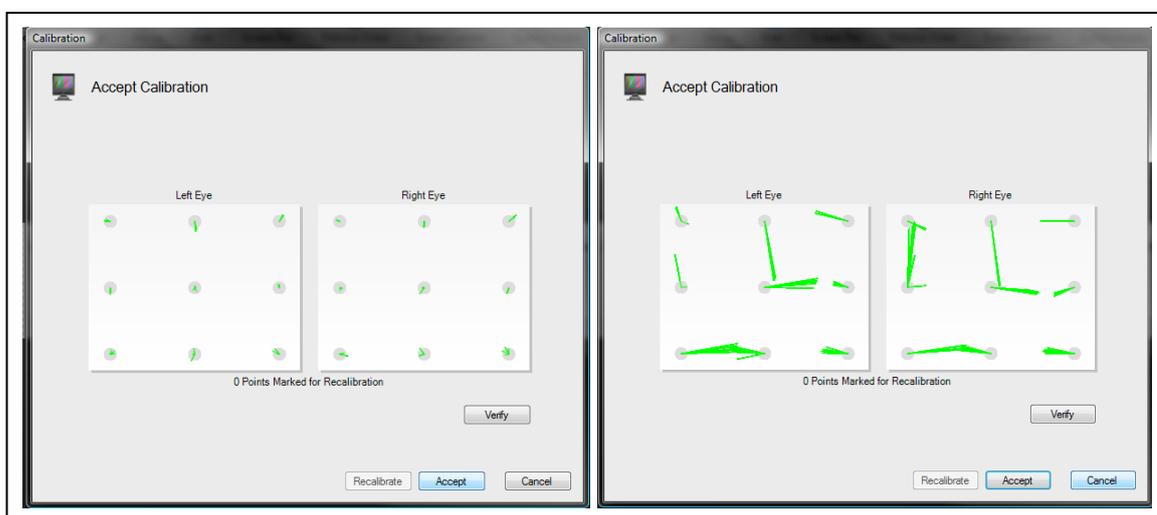
Figure 3.13   Example of a desired (perfect) calibration (left) and an offset calibration (right).

The similarities and differences between the Skalar IRIS and the Tobii X120 are detailed in Table 3.3.

Table 3.3 Similarities and differences of the Skalar IRIS 6500 and the Tobii X120 eye tracker .

Requirements	Specifications	
	Skalar IRIS	**Tobii X120**
Type	Limbus tracking IR system	Purkinje image I and bright and dark pupil detection
Setup & recording system	Fixed, Head-mounted system	Portable, Video-based system
Calibration	1. Manual calibration 2. The following 2-step calibration process are performed: • Looking at 3 fixation points of known angle separation to determine the gain and zero adjustments • Calibration through vsgEyetrace software using fixation targets of known angular separation 3. Duration time depends on subject's cooperation and sensor's alignment (15 minutes)	1. Automatic or manual calibration 2. The calibration consisted of an automated process generated using the Tobii Software Development Kit • Subject instructed to follow a set of fixation targets that appear in random manner • The software analyses the fixation gaze position automatically 3. Duration time was approximately less than 5s depending on subject's attentiveness
Temporal resolution/ sampling frequency	Temporal resolution is 250Hz but can be enhanced to 1000Hz from the system software	This instrument can be set at 60Hz or 120Hz as the sampling frequency

Reliability	Reliability of this system largely depends on the alignment of the sensors. As long as the sensors stay fixed in relation to subject's eye, the calibration should stay stable	The same calibration can be used repeatedly as the infrared sensors are fixed in the eye tracker relative to the tracking plane
Invasiveness	It is not invasive but poses a restriction to subject's head movement, as subject's head needs to be strapped firmly on the chin/head rest to minimise movement	This eye tracker is not invasive and does not require any headgear with sensors attached.
Data coverage/eye movement positions	Able to record only horizontal or vertical eye movements at one time	Horizontal and vertical movements are recorded simultaneously

3.4   Semi-automated occluder

Developing an automated occluder is desirable to accompany the eye movement system as part of the workstation development in order to provide a reliable and repeatable occlusion time during the cover test. Simons et al. (1978) were the first to report a fully integrated cover test administration system. The principle of the system was to utilise servomechanisms to insert occluders using rotary actuators driven by brushless DC torque motors. Both automated occluders were contained in a test unit attached to the eye movement recording system in which they were controlled by a computer programme. The principal problem with this approach was the complexity of the system and the fact that it did not facilitate viewing fixation at different distances, i.e. far (6m) and near (40cm).

In 1983, Peli and McCormack published a paper in which they described the use of electromechanical occluders controlled by a manual switch. Although the setup proved to serve the objective of the study undertaken, no detailed specification of the electromechanical occluders was given. Barnard and Thomson (1995) also used the same approach in their study to analyse characteristics of eye movements during the cover test. They combined the use of polystyrene covers driven by stepper motors and controlled the movement by a different computer to that recording the eye movements. The potential use of the polystyrene covers for the present study was excluded, as it would interfere with the measuring principle of one of the eyetrackers used in this study, the Tobii X120. The Tobii X120's sensors and detectors are housed in a standalone unit enclosing the light source and cameras. Any obstruction between the eye tracker and the eye, as in the application of an opaque occluder, would block the infrared light transmission.

As the use of a conventional opaque occluder was excluded, other options such as photographic shutters, ferro-electric and liquid crystal shutters were considered. The potential of using photographic shutters was rejected, as this would produce an unwanted proximal accommodation to subjects. Moreover, the shutters are made of an opaque material and this would pose the same problem as using any other conventional occluder with the Tobii X120 eye tracker. The option of using ferro-electric shutters was also excluded. These advanced materials have a slab of ferroelectric crystal located between polarizers and open to pass light when activated by a pulse of up to 100volts. They are usually controlled by synchronisation with the computer's refresh rate. The shutters would not only interfere with the setup of the Skalar IRIS, as they usually come in the form of goggles or glasses, but also the Tobii X120, as the materials are polarised. Polarised material would absorb the infrared light and, therefore, degrade the tracking ability of the instrument (Henderson 2011). The possibility of using liquid crystal materials was also rejected, as the dark state is not as opaque as a conventional occluder is, and the time in the opaque state is too short.

Flitcroft (2006) has patented an eye examining system to measure eye deviations using a corneal reflex technique. The system combines the use of a portable head-mounted eyetracker and an occluder made of a material that is visually opaque but allows infrared light to pass through. The use of such material as an occluder would satisfy the requirement for both eye tracker systems used in this study. Therefore, it was decided that the best method to adopt for this research was mechanically driven occluders or shutters with the use of a servomotor, and an occluder made from an infrared transparent material.

3.4.1   Occluder properties and design

To satisfy the requirements of both systems, infrared filters (Optolite IR) made of broadband acrylic were used as the occluders (see Figure 3.14). The filters are opaque to visible light but have the ability to transmit infrared light of up to a maximum of 90% in the infrared region from 850nm to 2000nm (InstrumentPlastics, http://www.instrumentplastics.co.uk/product.php 2010).   The   material   used   has excellent transmittance of infrared radiation at wavelengths greater than 750nm. The filters, originally supplied with dimensions of 100 x 100mm and 1.5mm in thickness, were manually cut out into the shape of a conventional occluder, measuring 75mm in diameter and 125mm long to ergonomically fit in the servo arms and for ease of use and handling.

Figure 3.14   Infrared filters (Optolite IR).

3.4.2 Servo and controller

Servo is a mechanical motorised device that has the ability to rotate its wheel or arm to a specific position. The servo used in this study has a torque of 4.1kg-cm with a speed of 0.16s / 60° at 6V (Dynam, Model: B2232) and specifically was made for this project by our school's technician, Mr. Rob O'Donovan. It was controlled by a DC motor, linked to an internal position feedback potentiometer that ensured accurate rotation when the switch was initiated.

The position of the servo's rotation was controlled by a toggle switch using a modified servo controller. Two fixed resistors, 8k2 ± 5% and 1k0 ± 5%, were used to drive the servo to preset positions (see Figure 3.15).
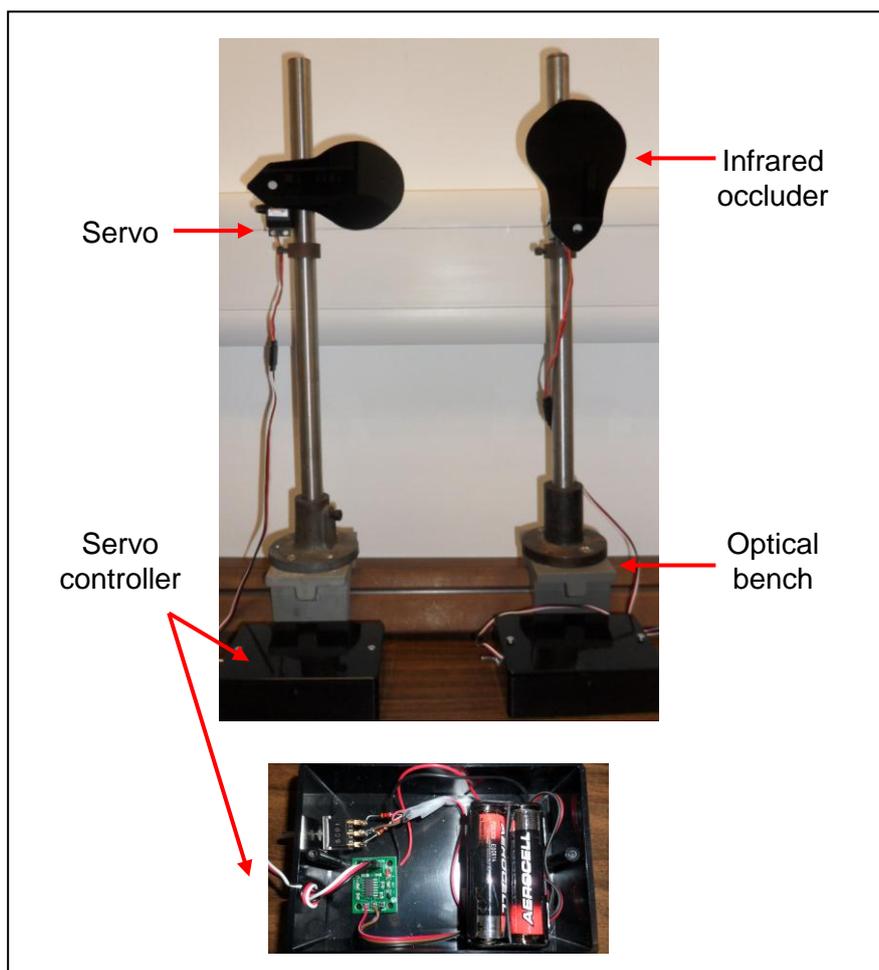
Figure 3.15   Semi-automated occluder unit.

The occluders were attached to the servos and mounted on an optical bench with two rods. An initial experiment was performed to evaluate the use of this set up. The major problem encountered was that the occlusion time and speed were highly dependent on the servo unit and battery life. Thus, the speed appeared to be inconsistent over time, and the fact that the set up could not be integrated with the eyetrackers' software posed a major difficulty in the implementation of the system. However, with the further advancement of eye tracking technology, this application would ultimately prove useful if the servo unit could be integrated with and controlled by the software used to capture the eye movements.

3.5   Laboratory setup

The potential of running the eye movement recording simultaneously using both eye trackers was excluded as the Skalar IRIS emitters would interfere with the infrared transmission of the Tobii X120 eye tracker system and the Skalar IRIS detectors might pick up the infrared light source. We established two different laboratory setups for the Skalar IRIS and the Tobii X120 eye trackers.

For the Skalar IRIS experimental set up, a computer was used to control the eye tracker (Skalar IRIS) and linked to a CRT monitor, responsible for presenting the stimulus. The CRT monitor was placed on a wheeled table so that the distance from the monitor to the subject could be changed between 3m to 40cm for distance and near settings, respectively (see Figure 3.16).

For the experimental set up using the Tobii X120, we positioned the eye tracker below and to the rear of the monitor screen that was used to present the near stimulus. This monitor screen was mounted on a monitor arm that could be swung to the side to allow the subject to also view the target presentation from a projector on

the wall for experiments at distance. The Tobii X120 and the Skalar IRIS were controlled by different computers (see Figure 3.17).
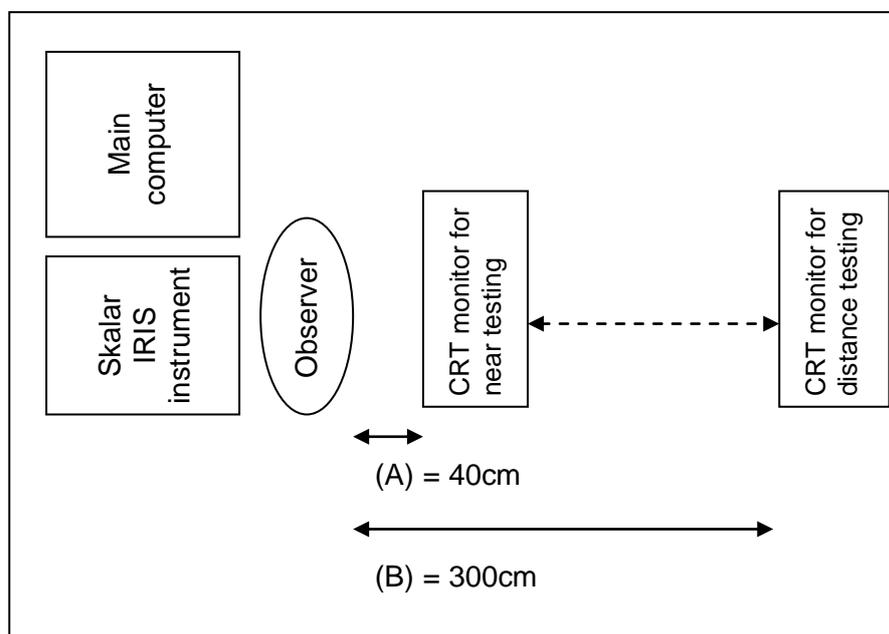
Figure 3.16   Schematic diagram of the set up for the Skalar IRIS eye tracker, showing the distance from the observer to the monitor screen for experiment at near (A) and at far (B).
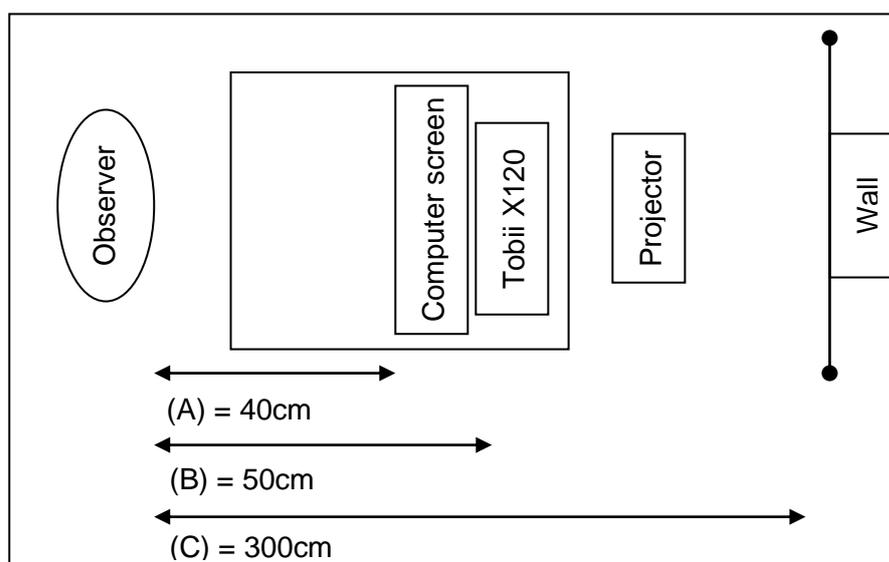
Figure 3.17   Schematic diagram of the set up for the Tobii X120, showing the distance from the observer to: the eye tracker (B), the stimulus on the computer screen (A) and the stimulus on the wall projection (C).

3.6 Summary

This chapter has been concerned with the methodology used for this study. It has detailed the technical aspects of the eye trackers used and the associated laboratory examination setup. The following chapter and its various subsections describe technical factors influencing the eye movement measurements using the Tobii X120.

CHAPTER IV

VALIDATING THE USE OF THE TOBII X120

4.1   Description

The Tobii X120 is a portable infrared eye tracker, mainly used for marketing research such as in web usability studies and evaluating advertisements. It offers a comprehensive eye movement recording programme, from test setup and calibration to data recording, visualisation and data analysis, through its robust software, the Tobii Studio™ (see Chapter III). However, the application of this commercially useful eye tracker to the research, and ultimately, clinical environment warrants further evaluation. There are a few technical aspects that, because they could influence the experimental setup and data analyses, need to be addressed and evaluated. These issues are discussed in the following sections.

4.2   Linearity range of the Tobii X120 eye tracker system

4.2.1   Objective

The aim of this study is to establish the range over which linear eye movement recordings can be achieved in both horizontal (180°) and vertical (90°) directions of gaze using the Tobii X120 eye tracker. It is essential to know if the system gives linear measurements across the planes tested in order to be certain that the eye positions recorded do not differ significantly from the actual gaze positions.

4.2.2   Methods

4.2.2.1 Participants

Five subjects took part in this study (age range=20-33 years). Three of them were aware of the objective of the study, and the other two were naïve about the procedures. There were three emmetropic subjects, and two were myopic. The myopic subjects wore their habitual correction (contact lenses) during examination. All subjects had visual acuities of at least 6/6 for both eyes and had normal binocular vision based on preliminary tests (cover test, ocular motility tests and stereopsis) performed prior to the eye movement recording. None had any ocular diseases, strabismus or was on medication/alcohol that could affect eye movements.

4.2.2.2 Stimuli and experimental setup

Stimuli consisting of a set of cross fixation targets were constructed in the Tobii Studio™ software (see Figure 4.1). A black cross against a white background was presented randomly in steps of 5° in the horizontal (5°, 10°, 15°, 20° and 25°) plane with return to zero in each case. The same target was also presented in the vertical plane (5°, 10° and 15°). Each cross was 0.2cm in height and 0.2cm in width, corresponding to 0.3° when viewed at 40cm.

The subject was asked to sit in front of the eye tracker at a distance of 40cm from the monitor screen. Subjects performed a routine calibration process using the Tobii Studio™ built-in programme (as described in Chapter III) before the stimuli were presented. After a successful calibration, the subject was instructed to fixate the targets as they appeared, as accurately as possible. The same procedure was performed for a set of vertical targets. The eye movement data recorded were exported to a spreadsheet in Microsoft Excel for off-line analysis.
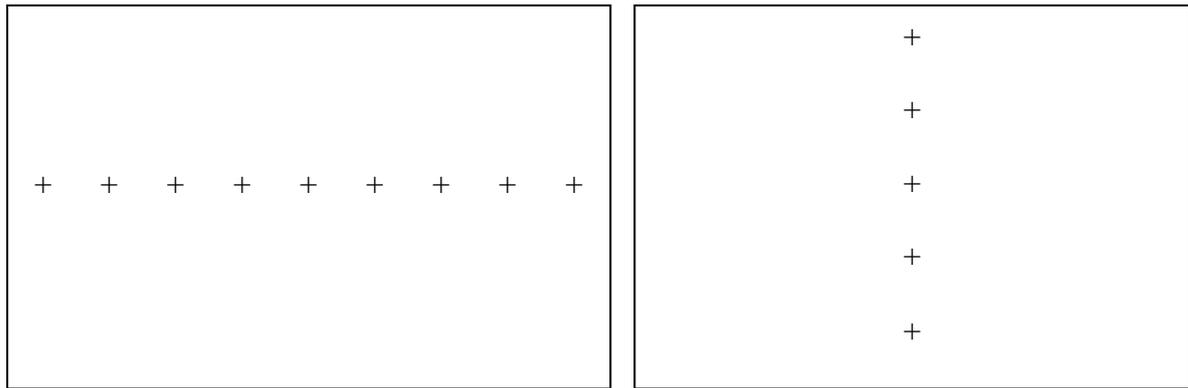
Figure 4.1   Target representations of the stimuli used for the linearity range study, corresponding to 5⁰ separation in the horizontal plane (left) and the vertical plane (right).

4.2.2.3 Analysis

The eye movement data were filtered according to the validity codes mentioned previously in Chapter III (see Section 3.3.1) and sorted manually according to the target positions for further analysis. The mean values of the measured eye movement amplitudes were tested for normality distribution using the Shapiro-Wilk test. Linear regression analyses were applied to all data to evaluate the relationship between the eye movements and target positions.

4.2.2.4   Results and discussion

A Shapiro-Wilk test revealed that the data for the right and left eyes for all subjects were normally distributed ($p > 0.05$). Linear regression analyses were applied to all data sets of each subject in the horizontal and vertical planes. Figures 4.2 and 4.3 show the relationship between target position and eye position (monocularly) for horizontal and vertical eye movements performed by each subject, respectively. The results from the linearity range experiment showed that the system is linear up to ± 25° in the horizontal plane and up to ± 15° in the vertical plane. The goodness of fit revealed an R squared of more than 0.99 for every linear regression calculated (see Figures 4.2 and 4.3). The mean differences between the target position and measured eye movements for horizontal and

vertical targets are listed in Tables 4.1 and 4.2, respectively. 'Mean position error' refers to the difference between eye positions from the target positions and 'mean alignment error' refers to the difference between right and left eye positions data at target position. The calculated percentage of the differences between target position and measured eye movements revealed that the deviations from linearity were less than 0.29% for saccades smaller than 25° (horizontally) and 0.17% for saccades smaller than 15° (vertically). The larger deviations from linearity observed in the horizontal plane could be due to the flat monitor screen used in the experiment, when in fact the visual system of human is designed to operate in depth (i.e. along a fixed radii or distance curve). It can be seen that, as the angle of the target position increased, the eye movement deviated more from linearity. However, the misalignment errors between the two eyes were relatively small (≤0.30°).

Table 4.1   Mean differences between target positions and measured eye positions, averaged from all subjects for horizontal targets (all in degrees).

Actual target position	-25	-20	-15	-10	-5	0	5	10	15	20	25
Mean position error	4.35	3.45	2.35	1.30	0.35	0.14	-0.29	-1.55	-2.20	-3.50	-4.20
Mean alignment error	-0.10	0.30	0.30	0.20	0.10	-0.02	0.02	-0.10	-0.20	-0.20	-0.40

Table 4.2   Mean differences between target positions and measured eye positions, averaged from all subjects for vertical targets (all in degrees).

Actual target position	-15	-10	-5	0	5	10	15
Mean position error	2.40	1.20	0.25	0.19	-0.20	-1.25	-1.95
Mean alignment error	-0.20	0.80	-0.10	-0.26	0.20	0.30	0.30
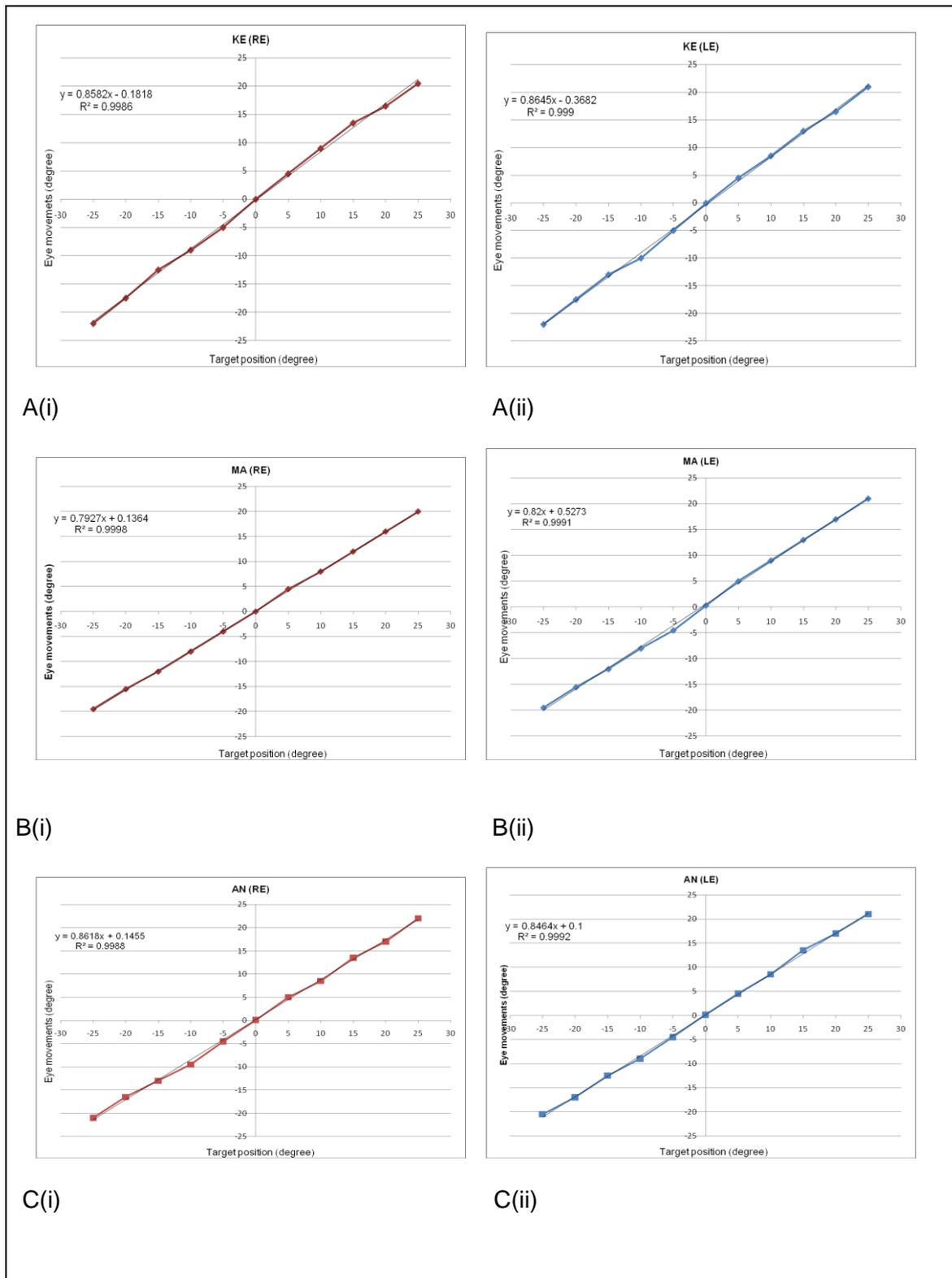
Figure 4.2 (A)-(C) Linear regression graphs showing the average values in horizontal position for right eye (i) and left eye (ii) of subjects KE(A), MA(B) and AN(C).

D(i)   D(ii)

E(i)   E(ii)
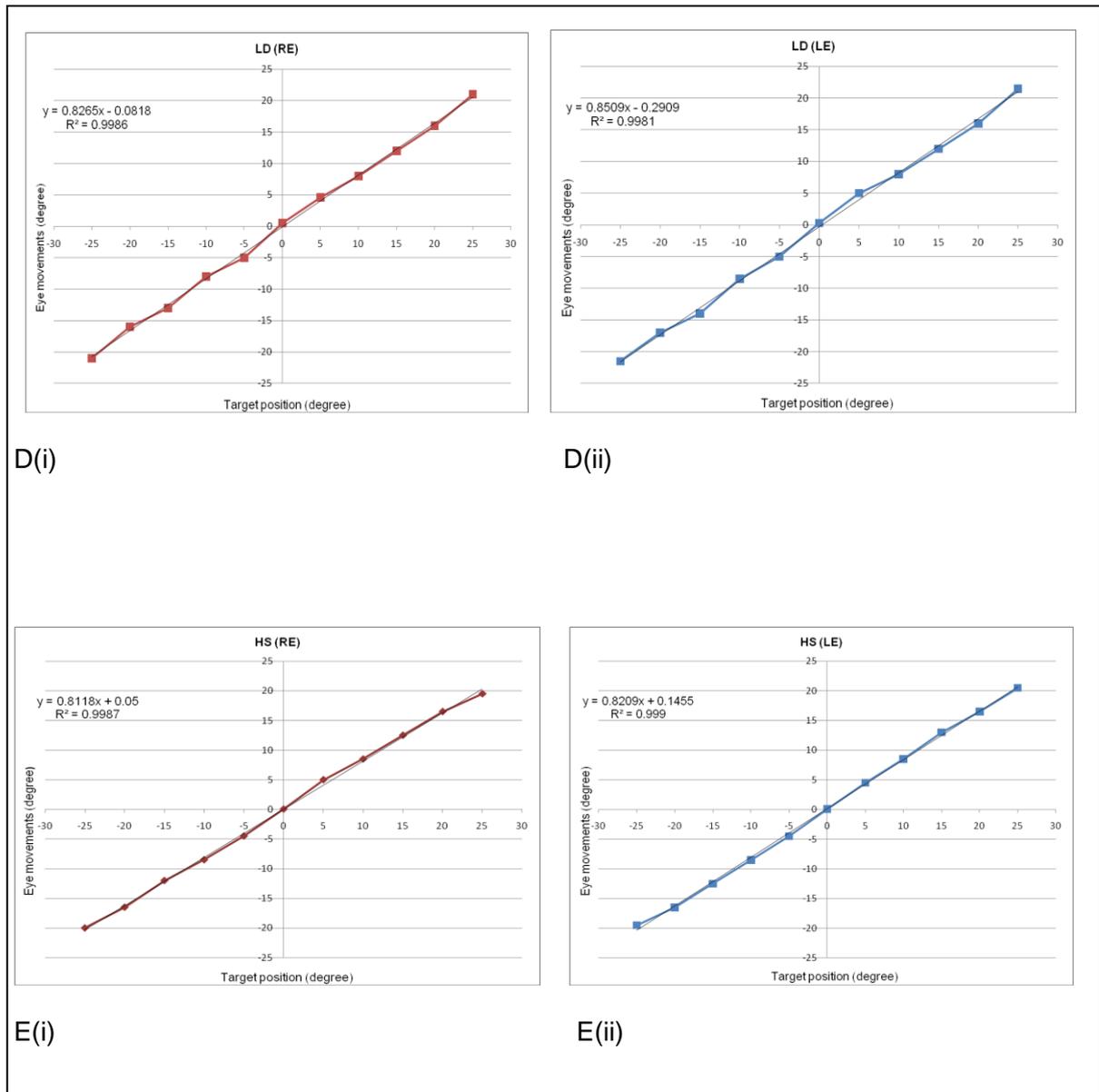
Figure 4.2 (D)-(E)   Linear regression graphs showing the average values in horizontal position for right eye (i) and left eye (ii) of subjects LD(D) and HS(E).
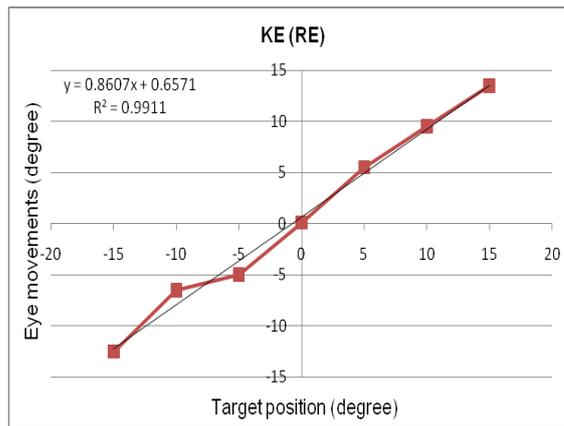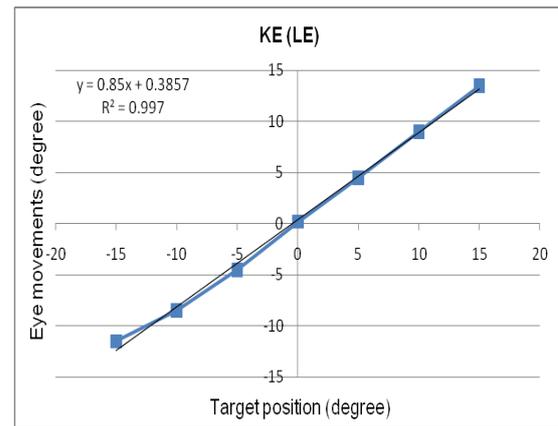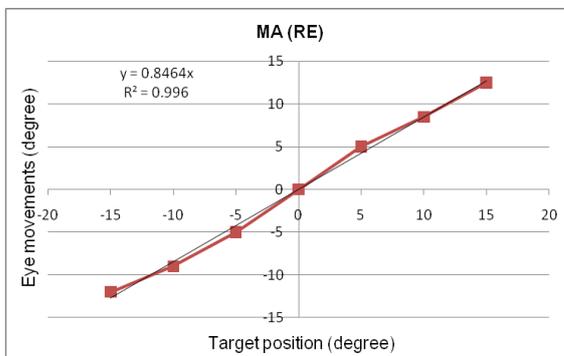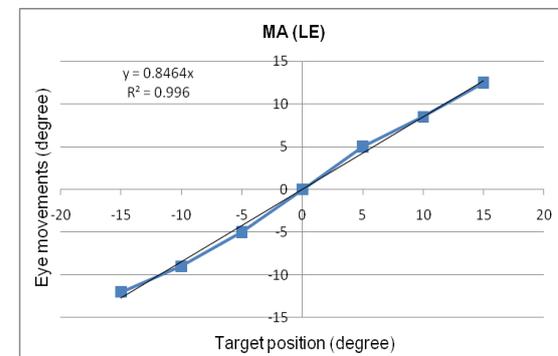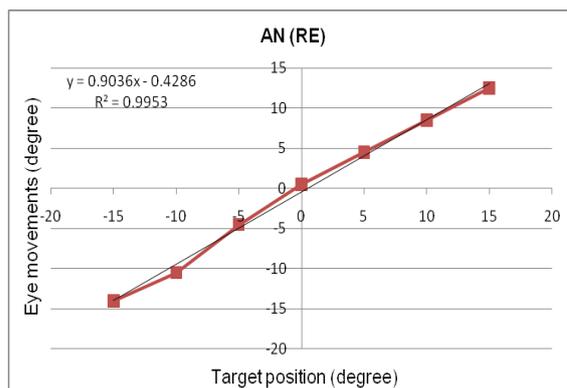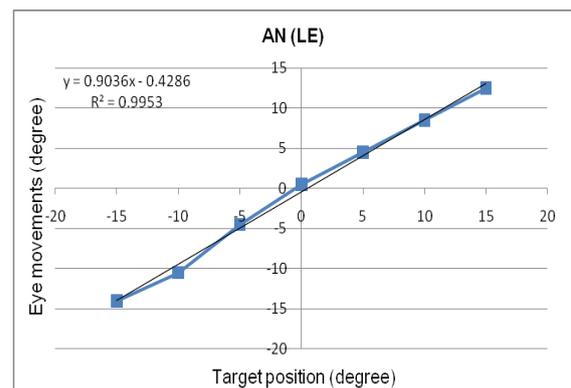
Figure 4.3 (A)-(C) Linear regression graphs showing the average values in vertical position for right eye (i) and left eye (ii) of subjects KE(A), MA(B) and AN(C).

D(i)

D(ii)

E(i)

E(ii)
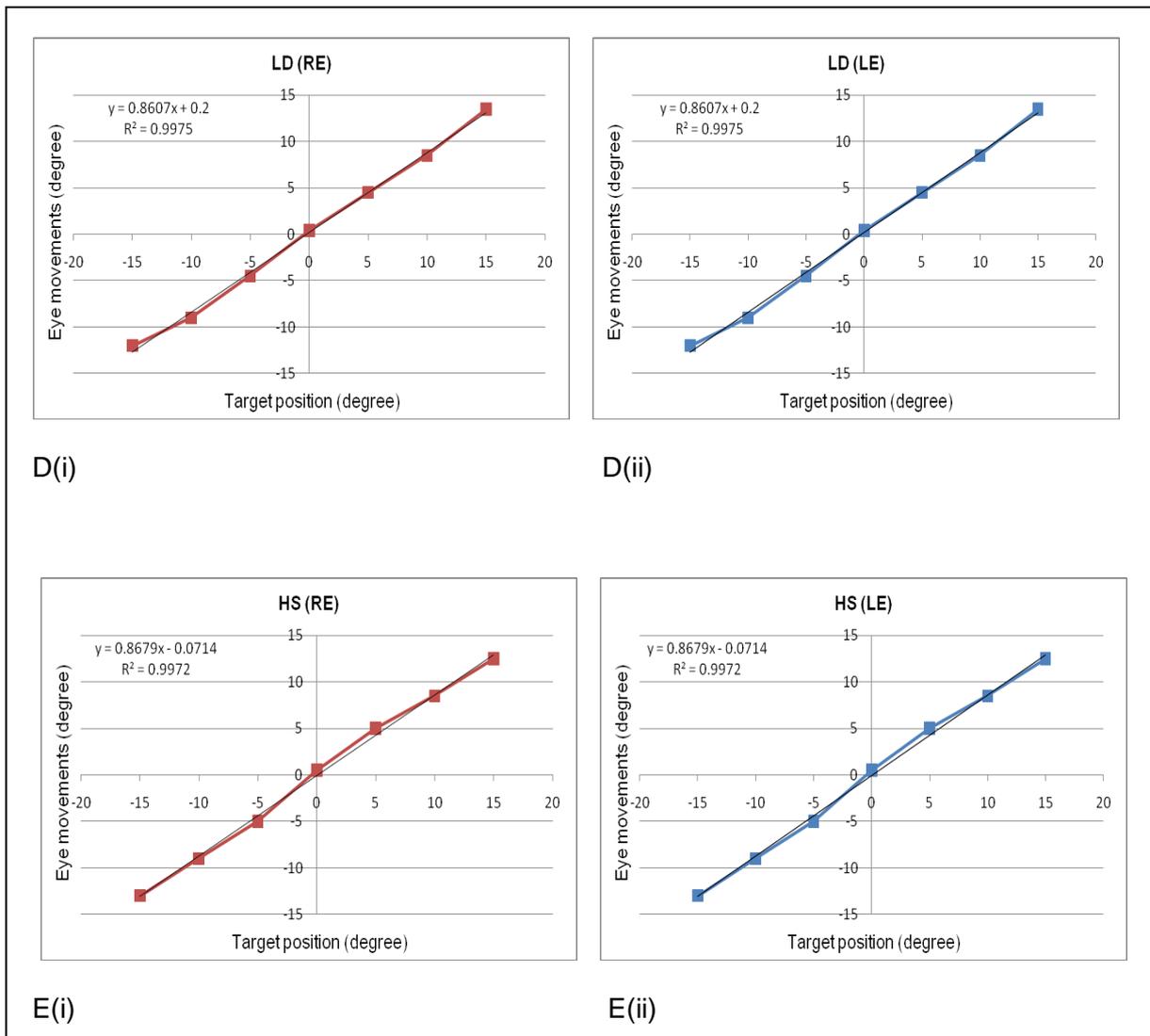
Figure 4.3 (D)-(E) Linear regression graphs showing the average values in vertical position for right eye (i) and left eye (ii) of subjects LD(D) and HS(E).

4.3   Eye movement measurements with varying distances

4.3.1 Objective

This study was carried out to evaluate the appropriate distance for good infrared signal/reflection from a subject's eyes to the Tobii X120 eye tracker. The manufacturer's guide suggests that the best distance for any experiment is within a range of 50 to 80cm from the eye tracker. This ensured a strong green bar in the calibration window screen, which indicates a good eye position for successful tracking (see Figure 4.4). If a subject was positioned too near or too far away from the eye tracker, the bars turned red and the pupils could not be tracked/detected. The quality of the eye movements sampled during a recording is provided by looking at the validity values from the replay section of the Tobii Studio™ software. The validity values are the information given by the eye tracker representing the calculation of the number of eye tracking samples that were correctly identified by the eye tracker. The maximum value, i.e.100%, indicates that both eyes were successfully detected during the recording (see Chapter III). A validity sample of 50% could suggest that either both eyes were found during half of the recording time or only one eye was found during the full recording session (Tobii Studio™ 2.2 User Manual 2010). However, the manufacturer does not provide any guidance on the optimum validity sample one should expect from any recording. Because of our aim to run all experiments at 40cm (which is the typical near distance for the cover test), it is important to know whether our experimental setup would permit sufficient infrared signal.

4.3.2 Methods

The eye tracker was positioned beneath and to the rear of the monitor screen (see Chapter III). This allowed subjects' eyes to be tested at distances of 50cm to 70cm from the eye tracker. We evaluated three distances from the Tobii X120, 50cm (nearest to the screen), 60cm (in the middle) and 70cm (farther away from the screen), which are

equivalent to 40, 50 and 60cm when measured from the subject's eyes to the monitor screen, respectively. Henceforth, we will only mention the distances from the subject to the eye tracker, which are 50, 60 and 70cm, to avoid confusion. Five subjects (age range=20 to 29 years) were recruited for this pilot experiment. Three subjects were emmetropic and the other two subjects were myopic and wearing contact lenses (i.e. habitual correction) during the experiment. All subjects had at least 6/6 vision in both eyes with correction (when necessary). The experiment was conducted using a set of 'cross' fixation targets in the horizontal plane, as in Figure 4.5. Each fixation target appeared for 5 seconds, and the subjects were instructed to fixate the target as soon as it appeared. The order of the distances tested was randomized to eliminate any possible fatigue effects during the experiment. Calibrations were performed and repeated at the beginning of each experiment for each distance.
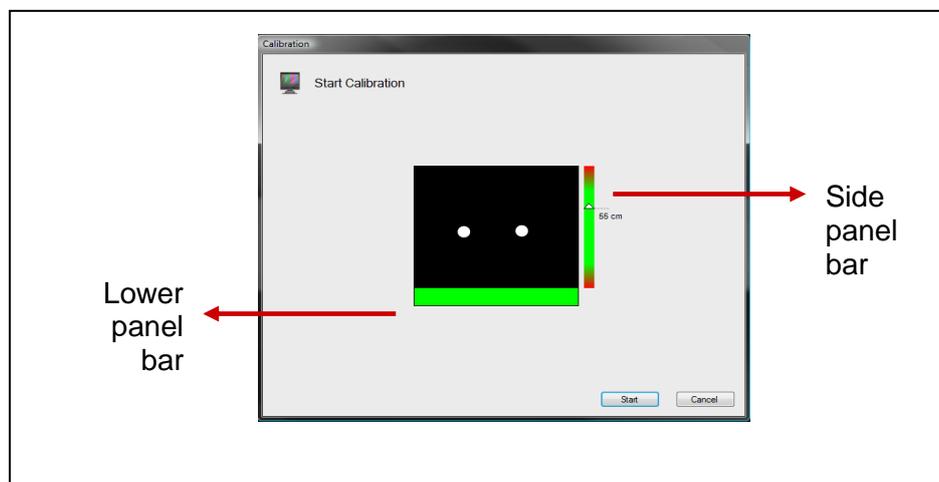
Figure 4.4   Initial set up prior to calibration to determine the subject's distance from the eye tracker. The calibration window will automatically give the distance measurement from the eye tracker to the subject's eyes, as shown at the side panel bar. Lower panel bar represents the strength of the infrared transmission.
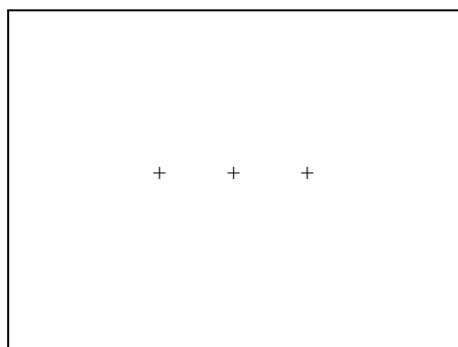
Figure 4.5   The layout of cross fixation targets used in this experiment.

4.3.3 Analysis

Data were plotted using Microsoft Excel for all subjects for each of the test distances. Quantitative analyses were performed using Shapiro-Wilk to test for normality distribution and, as appropriate, either ANOVA or Friedman test was used to compare the differences of the percentage validity obtained for the distances tested.

4.3.4 Results

Figure 4.6 presents the percentage of sampled data for each subject at the three viewing distances. All eye movement data sampled had validity scores above 80%. Overall, data sampled for 50 and 60cm were clearly better than 70cm. A viewing distance of 70cm resulted in the lowest percentage validity for all subjects.

The Shapiro-Wilk test revealed that the data were not normally distributed (p<0.05). A Friedman test performed on the validity values showed that there is a statistically significant difference between the quality of the eye movements recorded for the three distances (z=10, p=0.007).

	1	2	3	4	5	Subject
50cm	94	94	95	94	95	
60cm	96	95	97	94	96	
70cm	87	88	82	88	88	
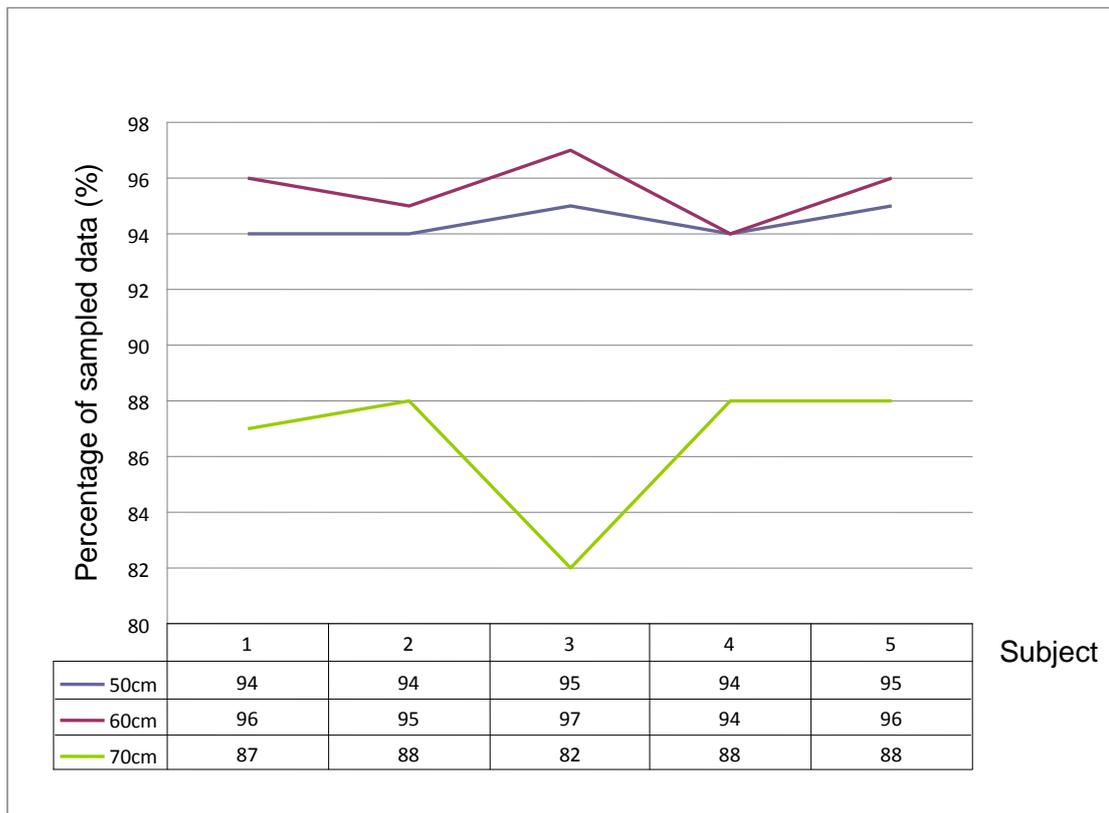
Figure 4.6 Validity percentages for eye movements sampled by the Tobii X120 at three different distances.

4.3.5   Discussion

The validity percentage represents the quality of the eye movement sampled on each recording. This measure provides a valuable indication for the examiner concerning whether or not the eye movement recording needs to be repeated, without having the need to export and analyse the data after the experiment. Observations made during the experiment showed that the eye tracker struggled to track subjects' eyes when the viewing distance was 70cm, i.e. the farthest away from the monitor screen tested. Although the calibration and experiments can be performed, the quality of the eye movements sampled by the eye tracker was much lower as compared to those recorded at 50 and 60cm.

Quantitative analyses of the percentages of the validity sampled data support these qualitative observations. Overall, the results showed that subjects performed better at 50cm (median=94; interquartile range=2) and 60cm (median=96; interquartile range=2) as compared to 70cm (median=88; interquartile range=4). Nevertheless, all validity percentages were more than 80%. The results support the use of the Tobii X120 for our intended experiment at distance of 40cm between the subject and the monitor screen.

4.4   Eye movement measurements with and without a chin rest

4.4.1   Objective

The Tobii X120 eye tracker system has an embedded algorithm that allows a large freedom of head movement, i.e. 30 x 22 x 30cm, for the system running at a 120Hz sampling rate. This permits any experiment being carried out while allowing more natural behaviour, as there is little restriction in head movement. The manufacturer claims that no chin rest/headrest or bite bar is needed when performing any experiment. It was of interest in this study to evaluate whether the eye movement output varies significantly depending on whether the measurements are performed with or without head immobilisation, i.e. with or without the use of a chin rest.

4.4.2   Methods

Ten visually normal subjects (visual acuity of 6/6 or better in both eyes) were recruited for this experiment (age range=19-21 years). Seven subjects were emmetropic and three subjects were myopic. Two subjects were wearing spectacle corrections and one subject was wearing contact lenses during the experiment. For the head immobilisation experiment, an adjustable chin rest mounted on a wheeled table was used. The chin rest was set up in front of and in the middle of the monitor screen, taking advantage of the fact that the table and/or chin rest height could be adjusted separately. For the experiment without the use of a chin rest, the subject was seated comfortably in front of the monitor screen and was instructed to perform the experiment while minimising their head movement. The stimuli presented were fixation crosses at nine fixation points, as presented in Figure 4.7. Each fixation target appeared sequentially for 5s from the top left of the monitor screen to the bottom right. All subjects performed the test twice, once with the use of a chin rest and once without the chin rest.
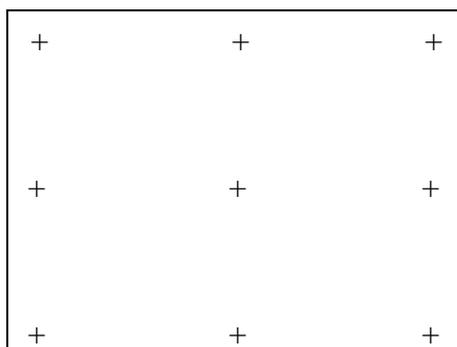
Figure 4.7   The layout of nine fixation crosses used in this experiment.

4.4.3   Analysis

The analyses were carried out by looking at the quality of eye tracking performed by all subjects, with and without the use of a chin rest, by plotting the percentages of the validity of the successful eye movement tracked by the Tobii X120. The data were further analysed by testing the normality of the distribution using the Shapiro-Wilk test. Depending on the distribution of the data, the possible differences between the data collected were tested either using a paired t-test or a Wilcoxon test. Analysis was also performed to compare the position of each subject's fixation with the target position.

4.4.4   Results

The Shapiro-Wilk test showed that the data were normally distributed ($p > 0.05$). Figures 4.8 and 4.9 present typical examples of the eye movement for Subject 5 when the experiment was performed with and without the use of a chin rest. Right and left eye movements are indicated by the red and blue lines, respectively. Dashed lines represent the target positions (top, middle and bottom from the screen). Visual inspection of both graphs reveals that this subject performed slightly better without the use of chin rest, and this observation is confirmed by the validity value reported by the eye tracker during the experiment (see Figure 4.10).
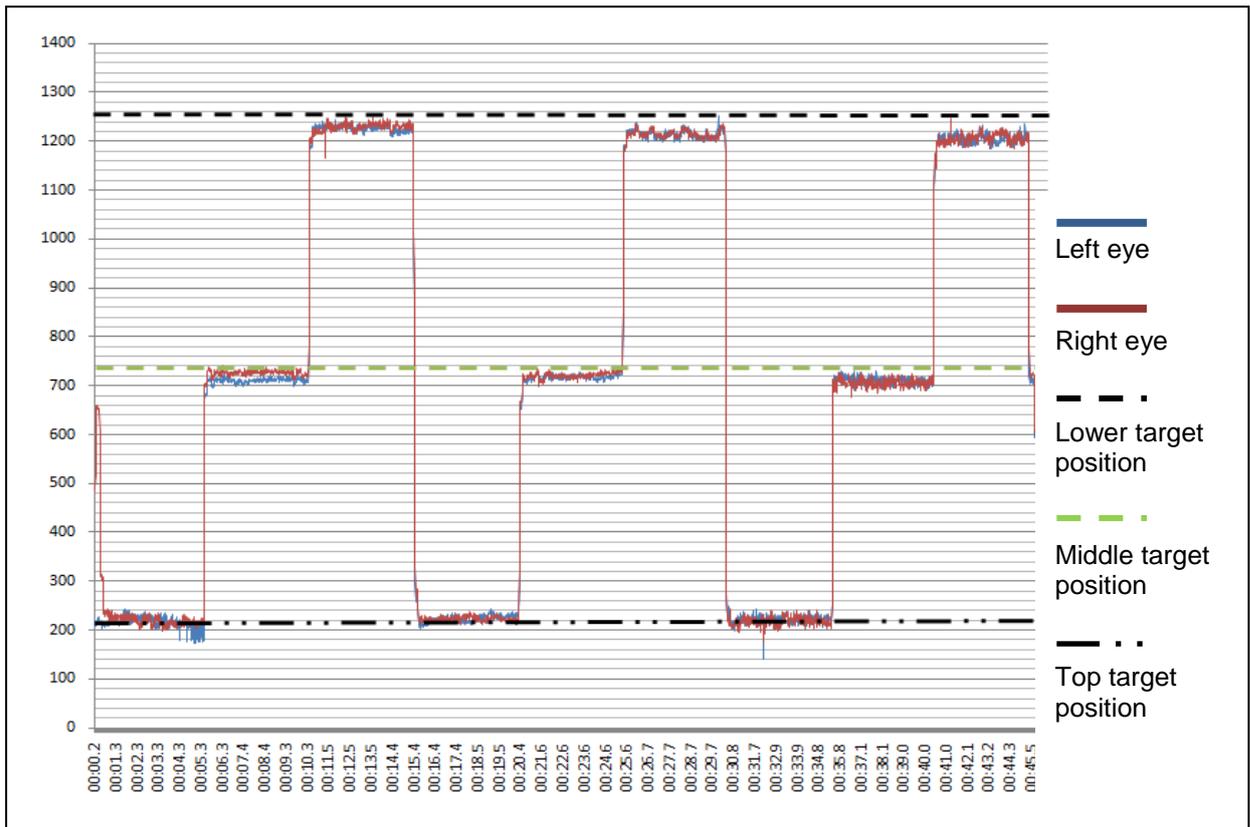
Figure 4.8 Example plot of a recording using a chin rest performed by a subject.
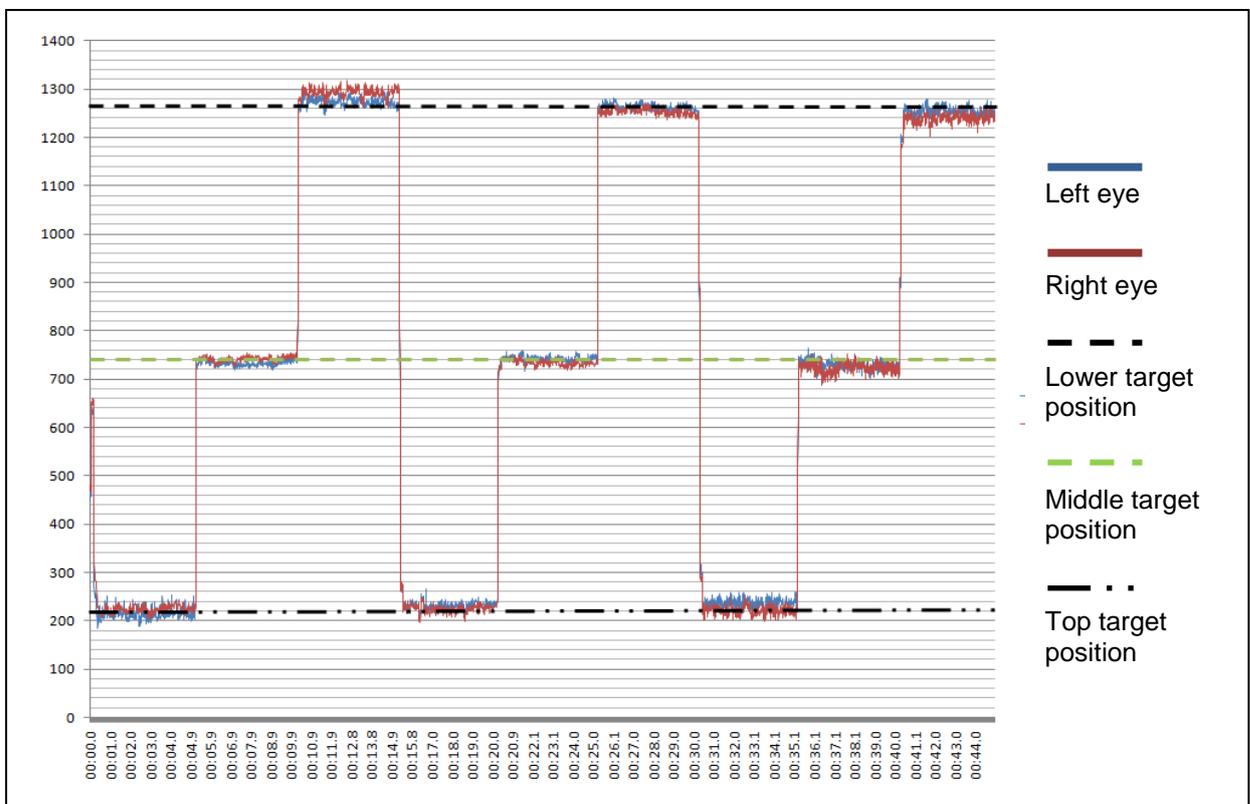
Figure 4.9 Example plot of a recording without using a chin rest performed by a subject.

The percentages of the validity of the eye movements detected by the Tobii X120 eye tracker are plotted for all subjects in Figure 4.10. The validity percentages of the sampled data were all above 85%. Only Subject 4 exhibited a large difference between the experiment with the use of a chin rest (95%) and without a chin rest (85%). A paired t-test performed on the validity values revealed that there is no significant difference between the experiment performed with and without the use of a chin rest (t=0.29, p=0.78).

	1	2	3	4	5	6	7	8	9	10	Subject
Chin rest	91	92	95	95	95	88	89	95	98	98	
Without chin rest	91	96	94	85	98	94	88	93	98	95	
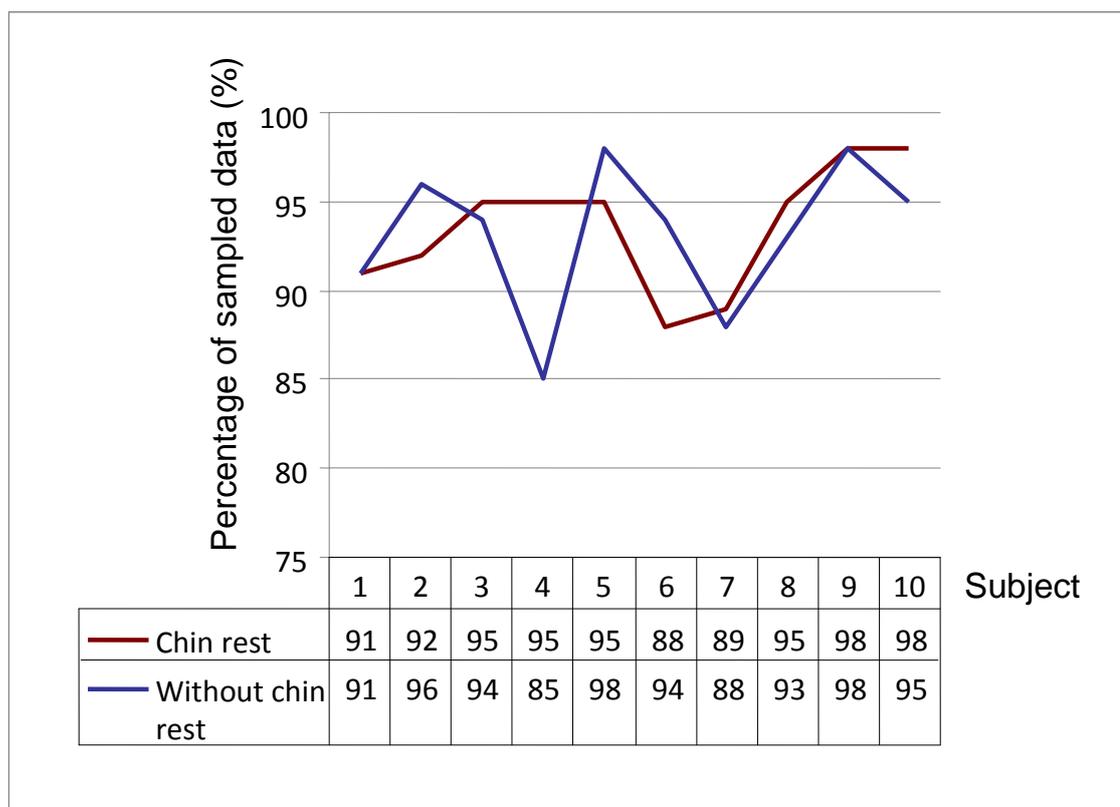
Figure 4.10 Graphs showing the validity data (percentages) from all subjects when the recordings were performed with and without the use of a chin rest.

We computed the difference between the eye movements made by each subject to the known target positions to reveal the accuracy of the eye movements performed with and without the use of a chin rest. The mean differences for top, middle and lower targets were averaged and are plotted in Figure 4.11. 'A' and 'B' denote the average differences in the eye movements performed with and without the use of a chin rest, respectively. The target

positions were numbered from 1 to 9 for ease of interpretation: 1=top left, 2=top middle, 3=top right, 4=middle left, 5=middle middle, 6=middle right, 7=lower left, 8=lower middle, and 9=lower right target.
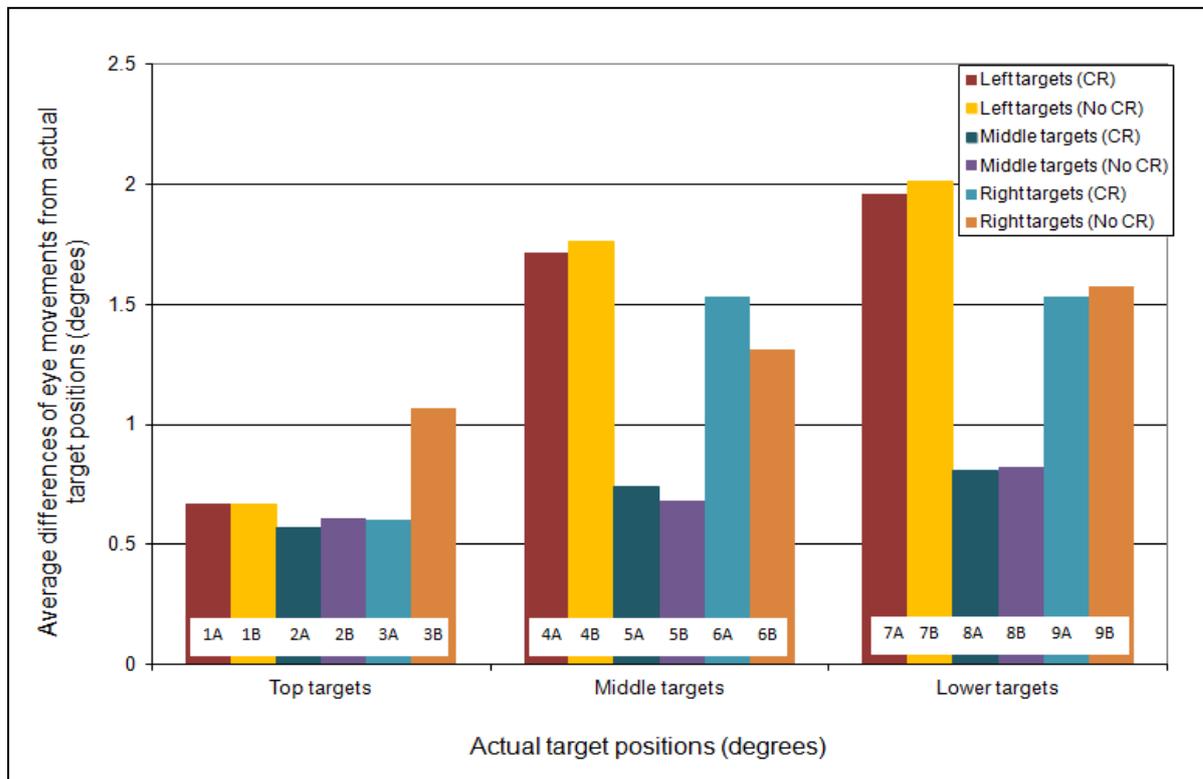
Figure 4.11 Average differences between eye movements and actual target positions. 'A' and 'B' represent the average difference of eye movements performed using a chin rest (CR) and without using a chin rest, respectively. 1 to 9 denotes the target positions: 1=top left, 2=top middle, 3=top right, 4=middle left, 5=middle middle, 6=middle right, 7=lower left, 8=lower middle, and 9=lower right target.

Overall, eye movement appeared less accurate when performed without the use of a chin rest with the exception of target positions 5 and 6. Paired t-tests were performed on the data from each target position in both conditions, i.e. with and without the use of a chin rest. Although the mean difference for target position 3 (top left) of -0.46 ± 0.92° was found to be slightly higher than the rest, the results showed that there was no significant difference between the two sets of data for all targets with p values of >0.05 at each position.

4.4.5   Discussion

The Tobii X120 eye tracker is designed to be used without immobilising the head using either a chin/head rest or a bite bar. It has robust algorithms, aided by the stereo data processing of input from the two cameras embedded in the eye tracker, which compensate for head movement within a 'cube' of space measuring 30 x 22 x 30cm (Tobii Studio™ 2.2 User Manual 2010). The results from this study support the manufacturer's assertion that eye movement recording can be accurately performed without the use of a chin rest to allow for more normal head posture/movement behaviour. Although there are small discrepancies in the eye movements performed by the subjects when compared with the actual target position, the differences were not statistically significant ($p > 0.05$). Nonetheless, care has to be taken in interpreting the results as this experiment was carried out on cooperative adults only. The outcome might be different if the system were tested on children or uncooperative subjects, in which the control of head movements could be an issue.

4.5   Eye movement measurements with different types of lens material

4.5.1   Objective

The aim of this study was to assess the performance of the Tobii X120 eye tracker when measuring eye movements of subjects wearing spectacles with different lens materials. It is important to take this point into consideration as patients' refractive correction will vary greatly both in the material used for their spectacles and the refractive power itself. It is desirable to examine patient's eye movements in their habitual correction as is the case in the real clinical environment. It would be important to know if the Tobii X120 eye tracker can perform the measurements reliably, i.e. within a certain degree of accuracy, on patients regardless of the lens material used for their correction.

4.5.2   Methods

Five different lens materials (see Table 4.3) were used in this study. All lenses were plano, and each was glazed in identical plastic frames. Ten healthy emmetropic subjects (age range=20-29 years) participated in this study. Stimuli used in this experiment consisted of a set of fixation crosses at nine positions of gaze, similar to the targets used in section 4.4.2. Every subject had to repeat the experiment six times, one trial with every lens material and one occasion without any spectacles on (i.e. their habitual emmetropic condition). The order of the lens materials was randomised. Extra care was taken to make sure that the lenses were clean before the start of each experiment. The eye movement data from all subjects were exported to an Excel spreadsheet for further analysis.

Table 4.3   Different lens materials used in this study.

LENS MATERIAL
Glass (Uncoated)
Glass Multi Anti-Reflection (MAR) Coating
Plastic 1.5 refractive index (Uncoated)
Plastic 1.5 refractive index (MAR)
Plastic 1.6 refractive index (MAR)

4.5.3   Analysis

The distribution of the data was tested using a Shapiro-Wilk test and the appropriate parametric (repeated-measures ANOVA) or non-parametric (Friedman) test was performed to evaluate any difference in fixation error for all subjects using different lens materials. We also looked at the difference of the percentage of sampled data (validity) from all subjects.

4.5.4   Results

Results from the Shapiro-Wilk test revealed that the data were normally distributed ($p>0.05$). A repeated-measures ANOVA was performed on each fixation point to measure the effect that different materials had on the fixation error. The means and standard errors are presented in Table 4.4. Glass with MAR coating had the least fixation error (mean=-0.02 ± 0.14°) and plastic 1.6 had the highest fixation error of 0.10 ± 0.05° compared to other lens types. However, no significant effects of the different lens materials used were revealed from the analysis of repeated-measures ANOVA ($p>0.05$).

Analysis of the validity data was also performed (see Table 4.4), and graphs of the percentages of sampled data (validity) with glass and plastic materials are presented in Figures 4.12 and 4.13, respectively. All validity outputs were more than 86%. Repeated-measures ANOVA revealed that there was no significant effect on the percentage of sampled data with different lens materials (p=0.61). It is also evident in the graphs, that there is no clear pattern found to indicate that any of the lens materials affected the eye tracking ability of the Tobii X120.

Table 4.4   Mean and standard error of fixation error and validity data with different types of lens materials.

Lens material	Mean ± standard error of fixation error (degree)	Mean ± standard error of validity data (%)
No Glasses	0.05 ± 0.04	94.80 ± 1.19
Glass	-0.03 ± 0.14	94.50 ± 1.22
Glass MAR	0.05 ± 0.07	94.60 ± 1.01
Plastic 1.5	-0.05 ± 0.11	95.00 ± 0.93
Plastic 1.5 MAR	0.09 ± 0.05	95.00 ± 1.03
Plastic 1.6	0.10 ± 0.05	95.40 ± 0.69
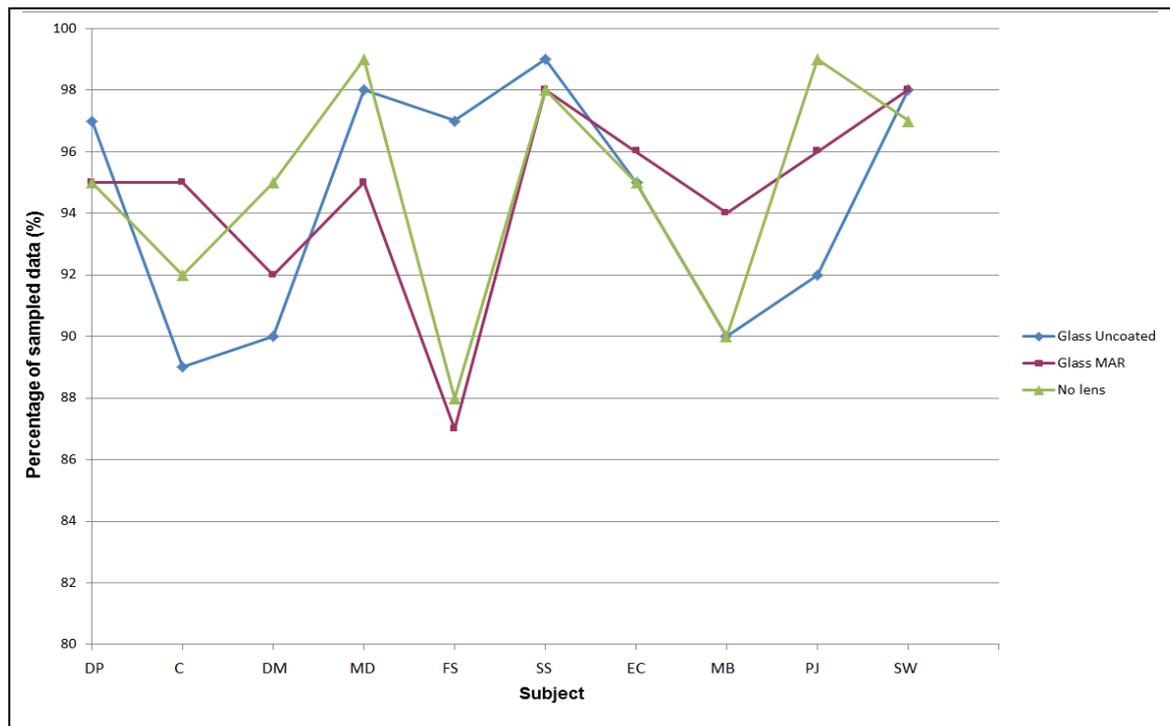
Figure 4.12 Percentage of sampled data (validity) from all subjects when the recordings were performed with glass lens materials (uncoated and coated with MAR) as compared to normal viewing (without any lens).
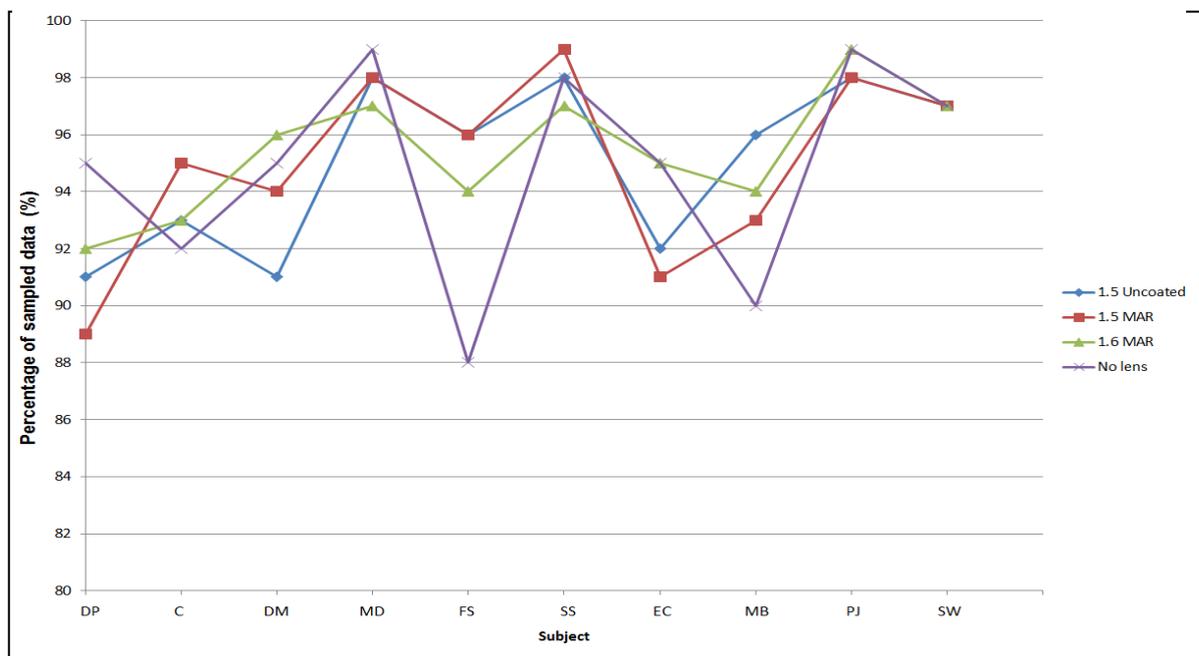
Figure 4.13 Percentage of sampled data (validity) from all subjects when the recordings were performed with different types of plastic lens materials as compared to normal viewing (without any lens).

4.5.5   Discussion

In order to use an eye tracker in a clinical environment, it is desirable to perform any test with a patient's habitual correction. Thus, it is important to evaluate its tracking performance with various types of lens materials, as patients present in the clinic wearing different types of lenses. Tobii Technology AB, the manufacturer of the Tobii X120, claimed that the instrument performs well with subjects wearing spectacles or contact lens with the exception of some bifocal lenses, which can block the eye tracker's view of the user's eyes (Tobii Studio™ 2.X Product description 2010.).

Both glass and plastic are common lens material types and are all said to transmit near infrared well (Bennett 2008). It might be expected that lens material with multi anti-reflection coating (MAR) would perform better than uncoated lenses, as MAR reflect the light better. However, we did not observe any significant difference in either the fixation error results or the validity data from the different lens materials used in this study.

Nonetheless, the results have to be interpreted cautiously, as the experiment only involved plano lenses as subjects were emmetropic and had normal binocular vision. The finding could be different if different lens powers were to be tested.

4.6 Pupil size measurements

4.6.1 Objective

One of the Tobii X120's features is its ability to measure pupil size. The localisation of the pupil and a determination of its orientation are the principal basis of eye detection used in this video-based eye tracking system. As the information on the distances between the eyes and the eye tracker's sensors are also measured continuously, the Tobii X120 eye tracker's firmware can calculate the pupil size by measuring the diameter of the pupil images registered by the optical sensors, and multiplying them with appropriate scaling factors (Tobii Eye Tracking White Paper 2010).

Pupil size measurements are very important for making a non-invasive diagnosis of many different diseases such as Alzheimer's disease (Richman et al. 2004), sleep disorders (Oroujeh et al. 1995), and effects on the consumptions of medicines, alcohol and other drugs in humans (Uetake et al. 2000). Measurements of pupil size are also essential in eliminating post-surgery visual complaints such as halos and ghost images (Kohnen et al. 2003). Unequal pupil sizes between two eyes, clinically known as anisocoria, could be a sign of disease, such as Horner's syndrome or Holmes-Adie pupil. However, there have been reports stating that anisocoria could be of a physiological origin, with about 20% of the normal population exhibiting the sign. A difference between the two pupils of more than 0.4mm is regarded as clinically significant (Ettinger et al. 1991).

The main motivation for this study arose from anecdotal reports that some patients had trouble using the Tobii P10 usability device, which is another Tobii system that relies on the same eye tracking principle as the Tobii X120. The patients have dilated pupils as a result of their required medication, and this adversely affected the calibration process and subsequent use of the device. Typical pupil sizes for human eyes are between 2 to 4mm, but it can be as large as 8mm in low illumination (Borish 2006). Hence, we stimulated

physiological dilation and constriction of the pupils in normal subjects using different background illuminations (see Section 4.6.2.2) to evaluate the accuracy and performance of the Tobii X120 system when compared with pupil measurements performed using an external CCTV infrared video camera (Concept Pro DSP 300, Videcon PLC).

4.6.2   Methods

4.6.2.1 Set up

Different set ups were investigated to find the best way to capture independently the pupil size for both eyes so that their sizes could be compared with the pupil size measurements produced in the raw data output from the Tobii X120 eye tracker. Trials with three different camera configurations were carried out to determine the one most suitable. These involved: (1) mounting the camera on the side of the monitor screen, (2) using a half silvered mirror and camera to the side of the subject, and (3) placing the camera above the monitor screen. Although it was possible to get a close up view of the pupils with the first set up, a parallax error was introduced in image analysis as a result of the offset position of the camera. To eliminate this problem, we experimented with the second set up using a half-silvered mirror, angled at 45° in front of the subject's eyes. Although we managed to get a frontal view of the subject's pupil, the Tobii X120 pupil measurement was compromised because the set up blocked the infra red transmission from the eye tracker. We resorted to the third setup by positioning the CCTV camera above the monitor screen to get a clear frontal view of the subjects' pupil diameters without affecting the eye tracker's ability to detect the eyes.

The CCTV camera was set at a frame rate of 25 frames per second. In order to capture pupil size regardless of ethnicity, we set the camera to capture images in 'night mode' to enhance the pupil images' contrast, especially for darker irides, which could be difficult to image using the normal camera setup. The video recording was performed using

VirtualDub version 1.9.8 (Lee 2009) and the image analysis was carried out using ImageJ version 1.42 (Rasband 2008).

4.6.2.2 Stimulus

Target presentation was constructed as a sequence of four fixation crosses with changing target and background colours to stimulate differences in pupil size for a total presentation time of 40s (see Figure 4.14). The cross fixation target used was 0.4cm in height and width, making it 0.67° in size when viewed at a distance of 40cm. An image of a white fixation cross at the centre of the screen with a black background was introduced for 10s to produce pupil dilation followed by an image with the inverse features (i.e. white background) to initiate pupil constriction. The sequence was continued with the presentation of a white target against a black background for another 10s and a black target on a white background for the last 10s.
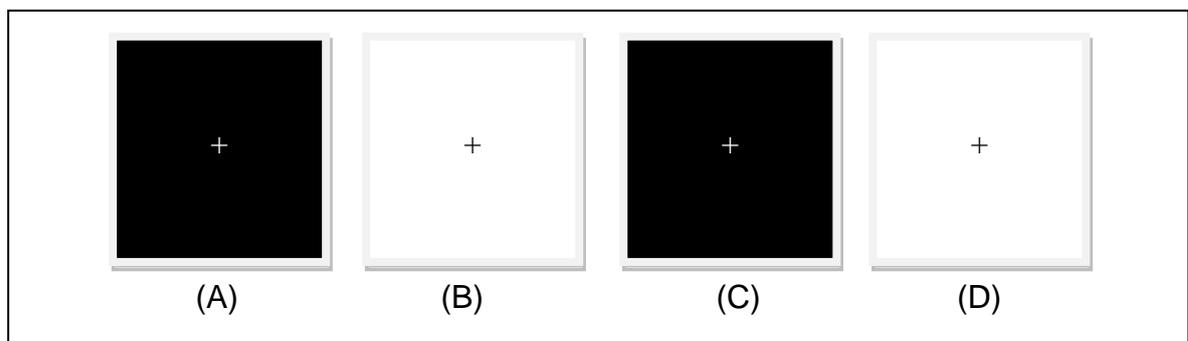
Figure 4.14   Target presentation on different backgrounds for the pupil test. Note the change of the black background (A & C) to white background (B & D) to stimulate pupil dilation and constriction, respectively.

4.6.2.3 Subjects and testing procedure

Eleven subjects (8 Caucasians and 3 Asians) with age ranges from 20 to 50 years, participated in this experiment. 8 subjects were emmetropic and 3 subjects were myopic and wore their contact lenses during the examination. All subjects were healthy and had a visual acuity of 6/6 in both eyes.

Calibration was performed under the Tobii Studio™ prior to data collection. Following a successful calibration, the VirtualDub programme was activated to start video recording from the CCTV camera before commencing the stimulus presentation under Tobii Studio™. The test was performed by asking the subject to fixate at the centre of the cross binocularly. All subjects were made aware that the stimulus' background colour would automatically change after 10s for each target presentation and were asked to continue fixating on the target as accurately as possible throughout the test. All video recordings were saved for off-line analysis. The horizontal visible iris diameters (HVID) for each subject were also measured prior to examination using a milimeter rule with magnified view using the Burton lamp.

4.6.3   Analysis

Pupil measurements from the Tobii X120 raw data output were exported to an Excel spreadsheet for analysis, which involved extracting and filtering the pupil data, in which both the right and left eye's pupil diameters were plotted.

Pupil images from the CCTV camera recordings were segmented and time stamped in VirtualDub to correlate temporally with the recordings in Tobii Studio™. Analyses were performed frame by frame using ImageJ software. The horizontal diameter of each pupil was marked to obtain its measurement in pixels. Taking Figure 4.15 as an example, the

diameter for subject MS's right pupil was 27 pixels (123 pixels – 96 pixels) and 23 pixels for the left pupil's diameter. The results were further analysed and plotted under Microsoft Excel, in which, the readings were converted into millimetres based on the horizontal visible iris diameter for each subject, using the simple calculation presented in Table 4.5.

Table 4.5   Formula derived to determine the pupil diameter using ImageJ analysis.

Subject's HVID (X) in mm	**=**	Horizontal visible iris diameter (HVID) measured on each subject
Subject's HVID (Y) in pixels	**=**	Horizontal visible iris diameter (HVID) measured from ImageJ output
Subject's pupil diameter (Z) in pixels	**=**	ImageJ output (pupil diameter at a time point in the image sequence shown in Figure 4.14)
Formula for conversion:	**=**	Pupil diameter (image sequence) in mm = Z x (X/Y)

The distributions of the data sets were analysed using a Shapiro-Wilk test before the appropriate parametric or non-parametric tests were performed. Analyses on the mean/mean rank differences were performed using either a paired t-test or a Wilcoxon test to compare the overall pupil test results from the Tobii X120 and those determined by image analysis from the CCTV camera. The same analysis was also performed to compare pupil size during the first and second dilation and the first and second constriction phases obtained from the two techniques. A Bland and Altman analysis was also performed to evaluate the agreement of pupil measurement using both techniques, in which the averages of pupil diameter measurements were plotted against their differences.
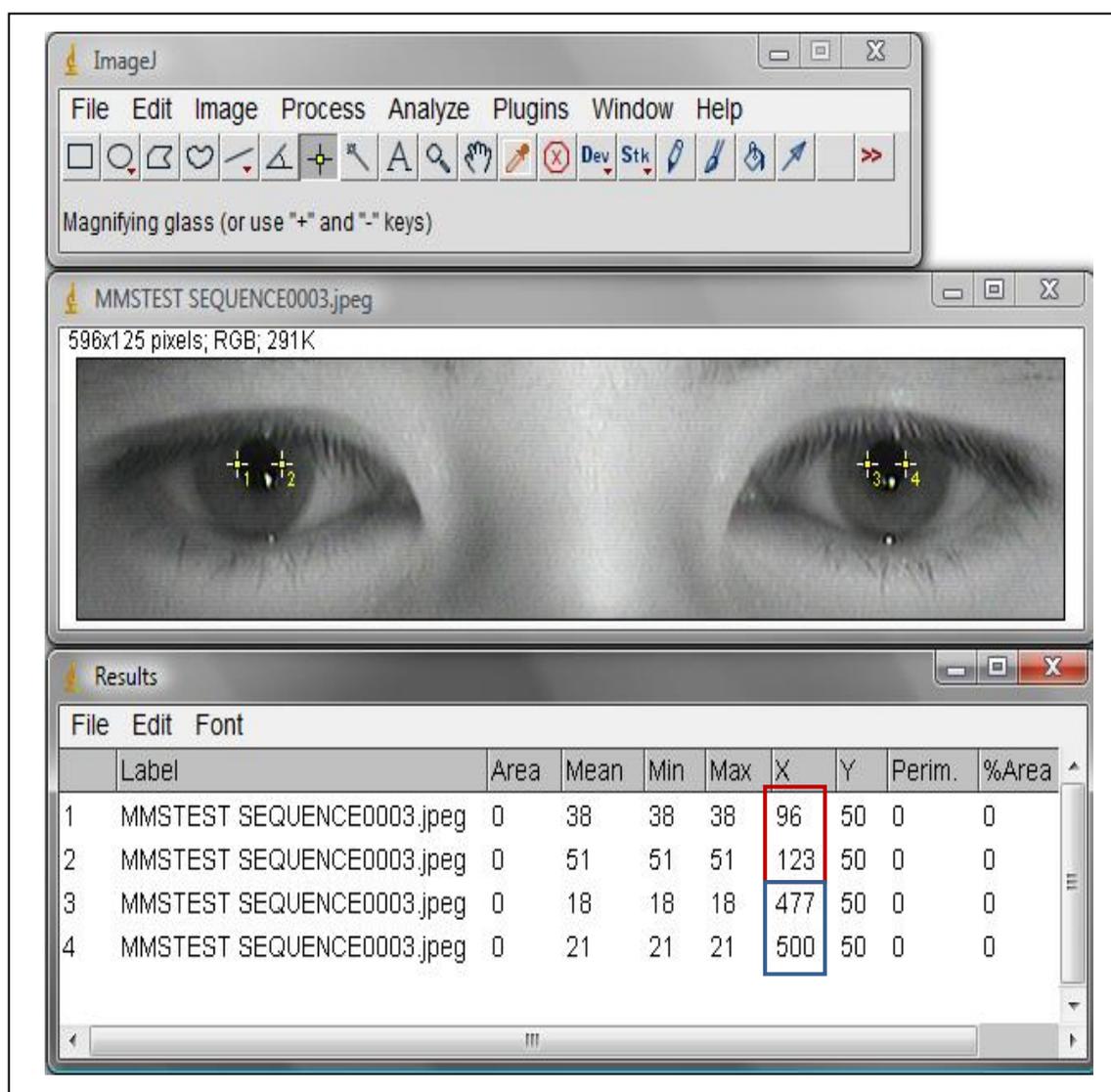
Figure 4.15   Representation of the image analysis using ImageJ software. Results in the red box refer to the measurements (in pixels) of points 1 and 2 for the right pupil's diameter. Findings for points 3 and 4 are shown in the blue box.

4.6.4   Results

Data from all but one subject (AC) were successfully analysed using both techniques. Data from subject AC (age=50 years) had to be rejected because his pupils were too small to be analysed through manual inspection using ImageJ. His pupil diameters were consistently small even during the dilation phases. Aging is presumed to cause a reduction

in sympathetic innervation, leading to smaller pupil size (Borish 2006). Hence, data analyses were only carried out on ten subjects.

A Shapiro-Wilk test revealed that the data were normally distributed (p > 0.05). The mean pupil diameters measured using the Tobii X120 and the CCTV camera are shown in Table 4.6. It can be seen from the standard deviations that values varied more with the CCTV camera measurements than with the Tobii X120. Mean pupil diameter measurements during constriction phases were less variable for both techniques (Tobii X120=2.96 ± 0.39mm; CCTV camera=3.10 ± 0.57mm) than the measurements during dilation phases (Tobii X120=4.09 ± 0.60mm; CCTV camera=4.22 ± 0.79mm).

A paired t-test was performed to compare the difference between means of the pupil diameter measured using the Tobii X120 and those captured with the CCTV camera. Analyses showed that the differences between the pupil diameter measurements using the two methods were not significant during the first dilation phase (t=-0.12 ± 0.72, p=0.62), first constriction phase (t=-0.12 ± 0.47, p=0.45), second dilation phase (t=-0.13 ± 0.67, p=0.56) and second constriction phase (t=-0.15 ± 0.44, p=0.29). The paired t-test also revealed non-significant results when comparisons were performed between the first and second dilation/constriction phases. The Tobii X120 produced results of t=-0.06 ± 0.14, p=0.21 and t=-0.04 ± 0.15, p=0.48 for dilation and constriction phases, respectively. CCTV camera findings revealed non-significant findings for first and second dilation phase (t=-0.05 ± 0.19, p=0.41) and first and second constriction phase (t=-0.02 ± 0.20, p=1.00) (see Table 4.7 and 4.8).

We constructed the Bland and Altman plot on the measurements taken by the two techniques and found that both techniques showed good agreement during the first dilation phase (mean difference=-0.12 ± 0.72mm), second dilation phase (mean difference=-0.13 ± 0.67mm), first constriction phase (mean difference=-0.12 ± 0.47mm)

and second constriction phase (mean difference=-0.15 ± 0.44mm). We observed that the limits of agreement (LOA) during constriction phases were narrower than the dilation phases (see Figure 4.16).

Table 4.6   Mean pupil diameter measurements with the Tobii X120 and the CCTV camera for dilation and constriction phases (N=10).

Instrument/Phase	Mean pupil diameter measurement ± standard deviation (mm)
Tobii X120	
• **First dilation phase**	4.13 ± 0.59
• **Second dilation phase**	4.06 ± 0.63
○ **Mean dilation**	4.09 ± 0.60
○ **Maximum and minimum pupil measured**	5.20/3.18
• **First constriction phase**	2.98 ± 0.41
• **Second constriction phase**	2.94 ± 0.39
○ **Mean constriction**	2.96 ± 0.39
○ **Maximum and minimum pupil measured**	3.75/2.45
CCTV camera	
• **First dilation phase**	4.24 ± 0.82
• **Second dilation phase**	4.19 ± 0.81
○ **Mean dilation**	4.22 ± 0.79
○ **Maximum and minimum pupil measured**	5.70/2.90
• **First constriction phase**	3.10 ± 0.60
• **Second constriction phase**	3.10 ± 0.57
○ **Mean constriction**	3.10 ± 0.57
○ **Maximum and minimum pupil measured**	4.15/2.00

Table 4.7 The paired t-test findings on pupil diameter measurements for dilation and constriction phases between the Tobii X120 and the CCTV camera (N=10).

Pupil diameter results between the Tobii X120 and the CCTV camera	t value	P value
First dilation phase	-0.12 ± 0.72	0.62
First constriction phase	-0.12 ± 0.47	0.45
Second dilation phase	-0.13 ± 0.67	0.56
Second constriction phase	-0.15 ± 0.44	0.29

Table 4.8 The paired t-test findings on pupil diameter measurements between first and second dilation and constriction phases for the Tobii X120 and the CCTV camera (N=10).

Pupil diameter results between first and second dilation/constriction phases		t value	P value
Tobii X120	First and second dilation phases	-0.06 ± 0.14	0.21
	First and second constriction phases	-0.04 ± 0.15	0.48
CCTV camera	First and second dilation phases	-0.05 ± 0.19	0.41
	First and second constriction phases	-0.02 ± 0.20	1.00
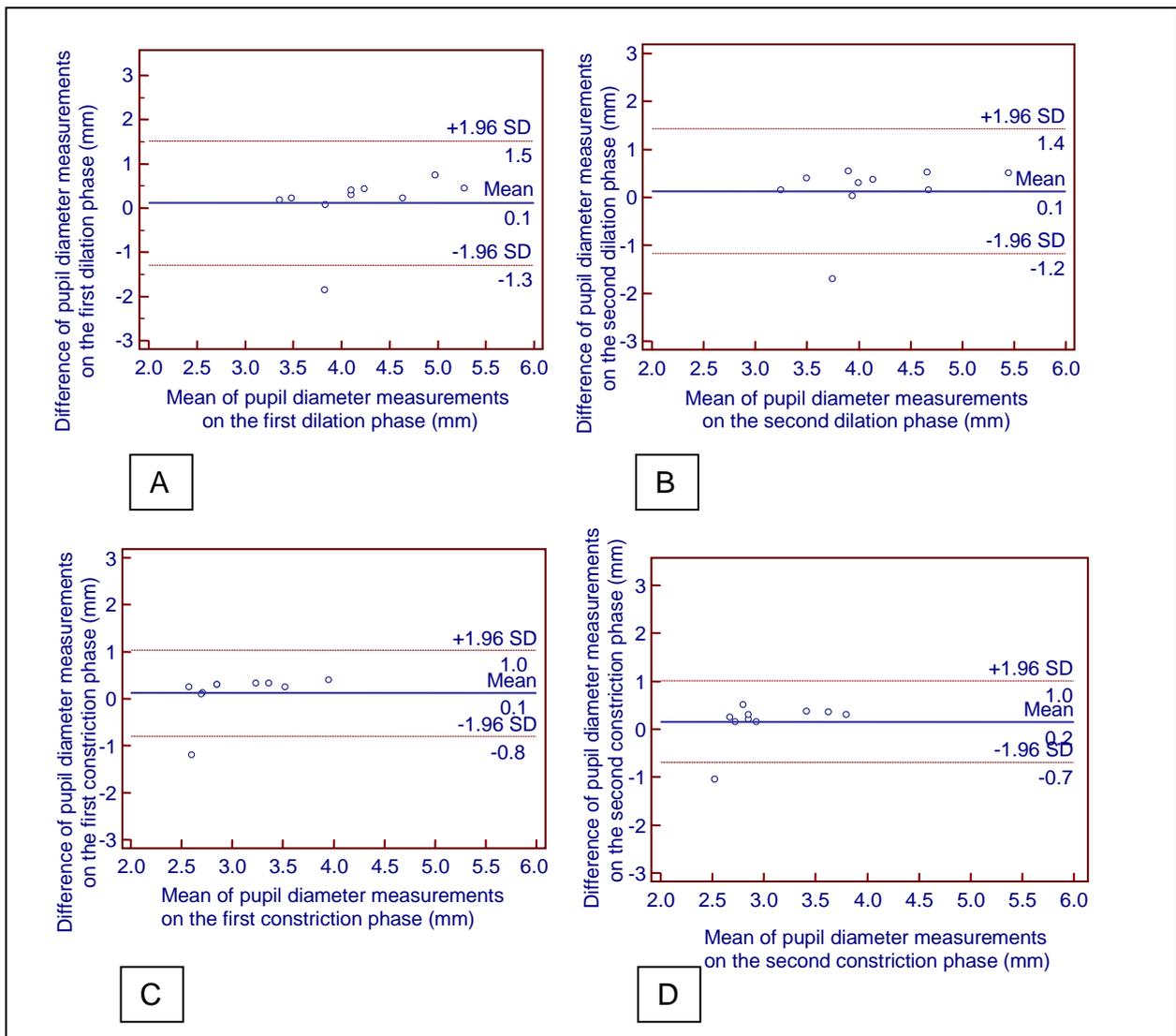
Figure 4.16   Bland and Altman plot comparing the pupil diameter measurements between the Tobii X120 and the CCTV camera (ImageJ analysis). A and B are the first and second dilation phases, respectively, C and D represent the first and second constriction phases.

4.6.5   Discussion

The maximum pupil diameter measured using the Tobii X120 was 5.20mm and the minimum pupil diameter was 2.45mm. The CCTV camera measured a maximum and minimum pupil diameter of 5.70mm and 2.00mm, respectively. The differences between pupil diameter measurements observed using these two techniques could be due to the fact that the Tobii X120 measured the longest possible diameter, i.e. corresponds to elliptical shape (Tobii™ SDK User Manual), while analysis using ImageJ for images from CCTV camera were performed on the horizontal visible iris diameter, which corresponds to a circular shape. Nonetheless, when examining each image, we found that all subjects had limited validity of the vertical pupil dimension, as it was covered by the upper lid. This is likely to influence the eye tracker to measure the same dimension (i.e. HVID) as that measured/performed manually using ImageJ.

Although pupil diameter measurements from the Tobii X120 were less variable than the CCTV camera, the differences between two techniques were not significantly different as revealed by the paired t-test analyses. The paired t-test revealed that the means for pupil diameter measurements were comparable between dilation/constriction phases (see Tables 4.7 and 4.8). We also compared the agreement between the Tobii X120 and the CCTV camera for the pupil diameter measurement using a Bland and Altman plot. For our entire set of measurements, we found that the agreements between pupil diameter measurements for the two techniques were excellent. Limits of agreements showed that the measurements were all within ± 1.50mm. The findings demonstrated that the pupil diameters detected by the two techniques were comparable.

4.7 Summary

This chapter has concentrated on the validity of the Tobii X120 eye tracker in performing various measurements. The findings should be interpreted in light of technical aspects limitations inherent to the eye tracker. Ultimately, we propose to develop and validate a workstation for assessing the oculomotor system, especially eye alignment. A quantitative comparison of the standard clinical measure of eye alignment, the cover test, between different examiners will be discussed in Chapter V, followed by clinical applications using the Tobii X120 eye tracker in Chapters VI and VII.

CHAPTER V

INTER-EXAMINER AGREEMENT OF COVER TEST MEASUREMENTS

ON NON-STRABISMIC AND STRABISMIC SUBJECTS

5.1 Objective

The principal objective of this study was to evaluate the agreement of cover test measurements between examiners on the same group of non-strabismic and strabismic subjects. The aim was twofold: to validate the author's cover test and to provide the basis for the next step of the research, which was to assess the cover test findings by the eye trackers. A comparison was made between two orthoptists and between each orthoptist and an optometrist (author). This chapter is divided into two parts: firstly, comparison of the cover test measurements in non-strabismic subjects and secondly, in strabismic subjects.

5.2 Non-strabismic subjects

5.2.1 Participants

Fifty non-strabismic subjects were recruited from the students and staff of Cardiff University. Subjects' age ranges from 19-42 years (mean age=24.62 years) and 64% of them were female. Informed consent was obtained from all subjects, and the study was approved by the School of Optometry and Vision Sciences' Human Research Ethical Committee. No subjects had a history of ocular or systemic health problems; all had 6/6 or better Snellen visual acuity in both eyes (with correction), and all exhibited stereoacuity of at least 60 sec of arc with the Titmus Fly test.

5.2.2   Protocols and procedures

An optometrist (author), who henceforth will be referred to as Examiner 1 (E1), and two clinical orthoptists (Examiner 2 (E2) and Examiner 3 (E3)) examined the subjects. The cover test measurements were taken at the primary position for distance (6m) and near (40cm). All examiners assessed each subject independently in random order during the same session. Subjects wore their habitual correction during the examination. Any deviation was quantified using a prism bar with the alternating prism cover test. The measurements were based on the prism increment of a 2 prism dioptre (PD) step for measuring deviation of less than 20PD, and a 5PD step for prism ranges from 20 to 50PD. The examiners were masked to each other's results and no specific instructions on how the testing should be done were given to the examiners. This was to mimic routine clinical testing as closely as possible.

5.2.3   Analysis

Data management and analysis were performed using Microsoft Excel, SPSS 16.0 and MedCalc. The normality of data distribution was tested using a Shapiro-Wilk test. Descriptive analysis was used to determine the range of phoria magnitude for the cover test results for all three examiners. Signed mean was also calculated because of the nature of the phoria data, where positive indicated esophoria and negative denoted exophoria. By taking this into account, the sign differences represented the true value of the phoria findings. The Friedman test was performed to assess the differences between measurements performed by the three examiners at distance and at near, and p-value was set at the level of 0.05.

Analysis of the degree of agreement between the measurements of the three examiners was performed using the Intraclass Correlation Coefficient (ICC) and the Bland-Altman plot (Bland and Altman 1986; Shrout and Fleiss 1979). The model chosen for ICC analysis was a two-way fixed model in which the systematic difference between examiners was relevant to the measured outcome and absolute agreement was expected, as opposed to consistency

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(Bravo and Potvin 1991; Shrout and Fleiss 1979). The value for ICC ranges from 0 (no agreement) to 1 (total agreement). Further classification on a five point scale was adapted from Landis and Koch (1977), in which the degree of agreement is considered as poor if the ICC value is 0.00, slight (0.01-0.20), fair (0.21-0.40), moderate (0.41-0.80) and excellent (0.81-1.00). Although the ICC can be used to assess agreement between two or more examiners, we measured the degree of agreement between all three examiners and between pairs of examiners. This analysis was performed to compare the evaluation of ICC with the limits of agreement (LOA) from the Bland-Altman plots.

Bland-Altman plots evaluate the degree of agreement by calculating the mean difference between two measurements in the same subjects and the standard deviation of the differences. Approximately 95% of these differences will scatter between the mean differences of ± 1.96 standard deviations of these differences. This analysis is not influenced by the variance of the assessed parameters and, therefore, will give a better assessment of the inter-examiner repeatability of cover test measurements (Bland and Altman 1986).

5.2.4   Results

The Shapiro-Wilk test revealed that the cover test data for distance and near measurements are not normally distributed (p<0.05). The magnitudes of phoria measurements for subjects at distance and at near are presented in Figure 5.1 and 5.2. Phoria for each subject was calculated by averaging the results from all three examiners. The units are all in prism dioptres (PD). The range for phoria magnitude at distance was between 1PD esophoria to -5PD exophoria and from 3PD esophoria to -19PD exophoria for near cover test findings. All subjects exhibited only horizontal phoria. The results obtained from the descriptive analysis for distance and near cover tests are shown in Table 5.1.

Results of the Friedman's chi-square test showed a value of 1.921 (p=0.383) for cover test measurements at distance, and a value of 0.203 (p=0.903) for cover test at near. The results,

as presented in Table 5.2, are not statistically significant (p>0.05). Hence, there is no evidence that the distributions of the measurements made by the three examiners were different from each other.

The agreement of the cover test measurements between examiners was evaluated using the ICC and the Bland-Altman plots. Table 5.3 presents the degree of agreement between the measurements using the ICC method. The analysis revealed excellent correlations for measurements by all three examiners at distance and at near with values of 0.84 and 0.96, respectively. Degrees of agreement were also tested between pairs of examiners. ICC for cover test at distance between E1-E2 was 0.70, E1-E3 was 0.78, E2-E3 was 0.83 and E1 to average of measurements performed by E2 and E3, was 0.78. ICC for cover test at near between all pairs of measurements were 0.94 (E1-E2), 0.95 (E1-E3), 0.95 (E2 and E3) and 0.96 (E1 to average of measurements performed by E2 and E3).

The inter-examiner agreements were also analysed using Bland-Altman and the results presented in Table 5.3. Bland-Altman plots were also constructed to show the limits of agreement between any pair of examiners for the cover test results for non-strabismic subjects. Figure 5.3 to Figure 5.6 presents the Bland-Altman plots for distance cover test findings, and Figure 5.7 to Figure 5.10 provides the comparisons for near cover test. There were no significance systematic biases observed for all measurements as shown by the mean differences i.e. all being close to zero. The calculated 95% LOA were approximately between ± 3PD and ± 4PD for E1 & E2 at distance and at near fixation. The 95% LOA for E1 & E3 were about ± 2PD for distance and ±4PD for near. When the measurements were compared for E2 & E3, the 95% LOA showed approximately ± 2PD and ± 4PD for distance and near cover test, respectively. Calculations for E1 and the average results for E2 and E3 showed 95% LOA of approximately ± 2PD (distance cover test) and ± 3PD (near cover test).
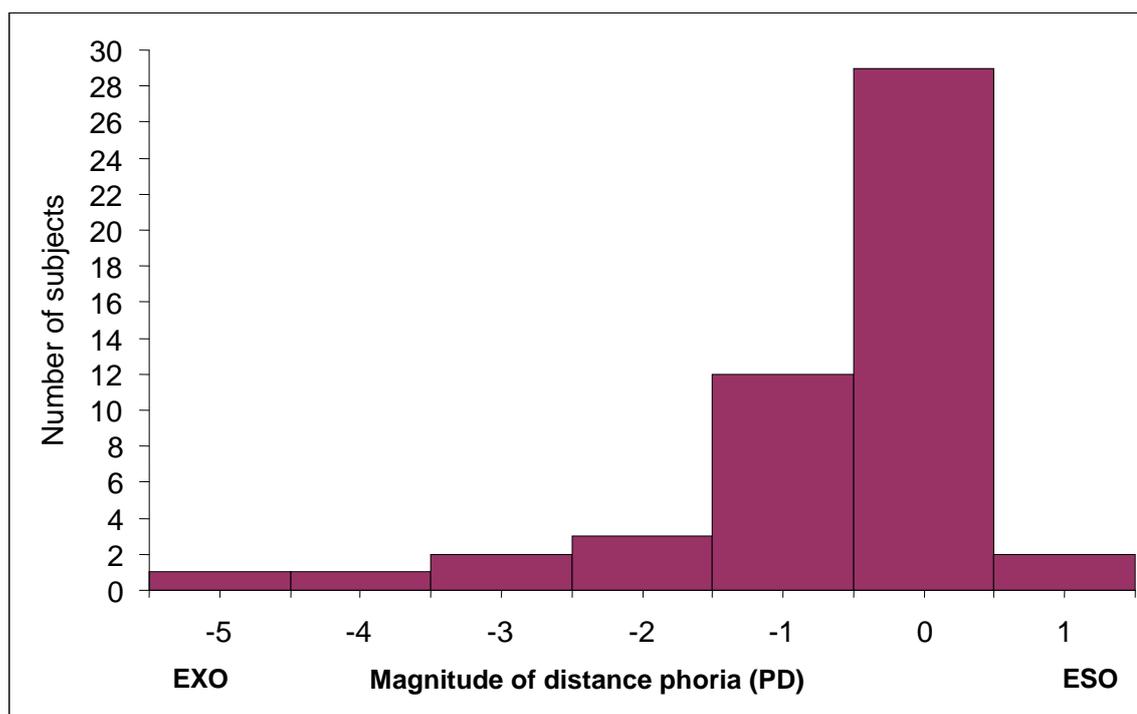
Figure 5.1 Distribution of phoria magnitude for distance cover test measurements. The phoria magnitude was derived by averaging the results from each examiner for each subject. Minus (-) sign denotes exophoria and plus (+) sign denotes esophoria.
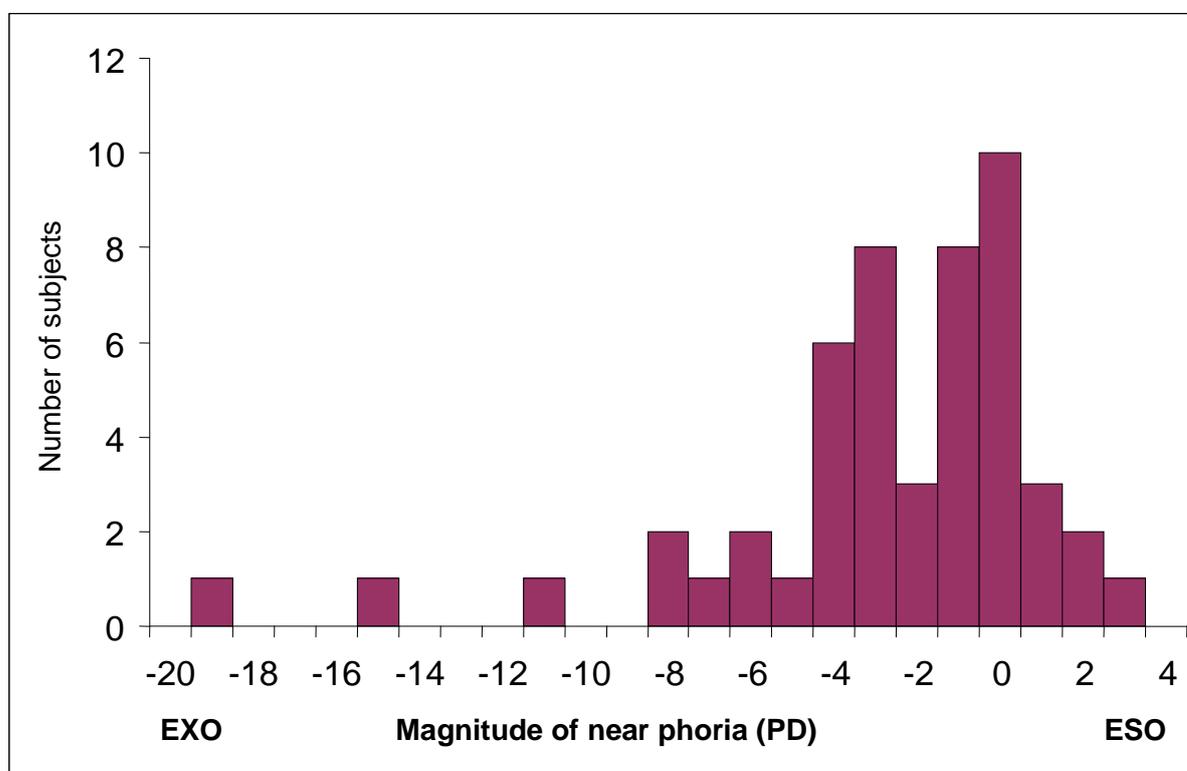
Figure 5.2 Distribution of phoria magnitude for near cover test measurements. The phoria magnitude was derived by averaging the results from each examiner for each subject. Minus (-) sign denotes exophoria and plus (+) sign denotes esophoria

Table 5.1   Descriptive analysis results (median, interquartile range, minimum and maximum) for the cover test measurements between three examiners.

Cover test	Median	Interquartile range	Minimum	Maximum
Distance	0.00	1	-5	1
Near	-1.83	4	-19	3

Table 5.2   Friedman test detailing the chi-square values and p-values for the cover test measurements results between three examiners at distance and at near.

Cover test	Mean rank			Chi-Square value	p-value
	Optometrist	**Orthoptist 1**	**Orthoptist 2**		
Distance	2.09	1.92	1.99	1.921	0.383
Near	1.96	2.03	2.01	0.203	0.903

*Not significant; p-value>0.05

Table 5.3   Degree of agreement using the Intraclass Correlation Coefficient and the Bland-Altman calculation between examiners.

Examiner	ICC	Bland & Altman	
		Mean difference	**95% Limits of Agreement**
Cover test at distance			
E1-E2	0.70	0.18	-2.41 to 2.77
E1-E3	0.78	0.20	-1.93 to 2.33
E2-E3	0.83	0.02	-2.13 to 2.17
E1-E2/3 (Average)	0.78	0.19	-1.92 to 2.30
E1-E2-E3	0.84	-	-
Cover test at near			
E1-E2	0.94	-0.08	-3.81 to 3.65
E1-E3	0.95	0.02	-3.77 to 3.81
E2-E3	0.95	0.10	-3.70 to 3.90
E1-E2/3 (Average)	0.96	-0.03	-3.27 to 3.21
E1-E2-E3	0.96	-	-

* **E1**= Optometrist; **E2**= Orthoptist 1; **E3**= Orthoptist 2
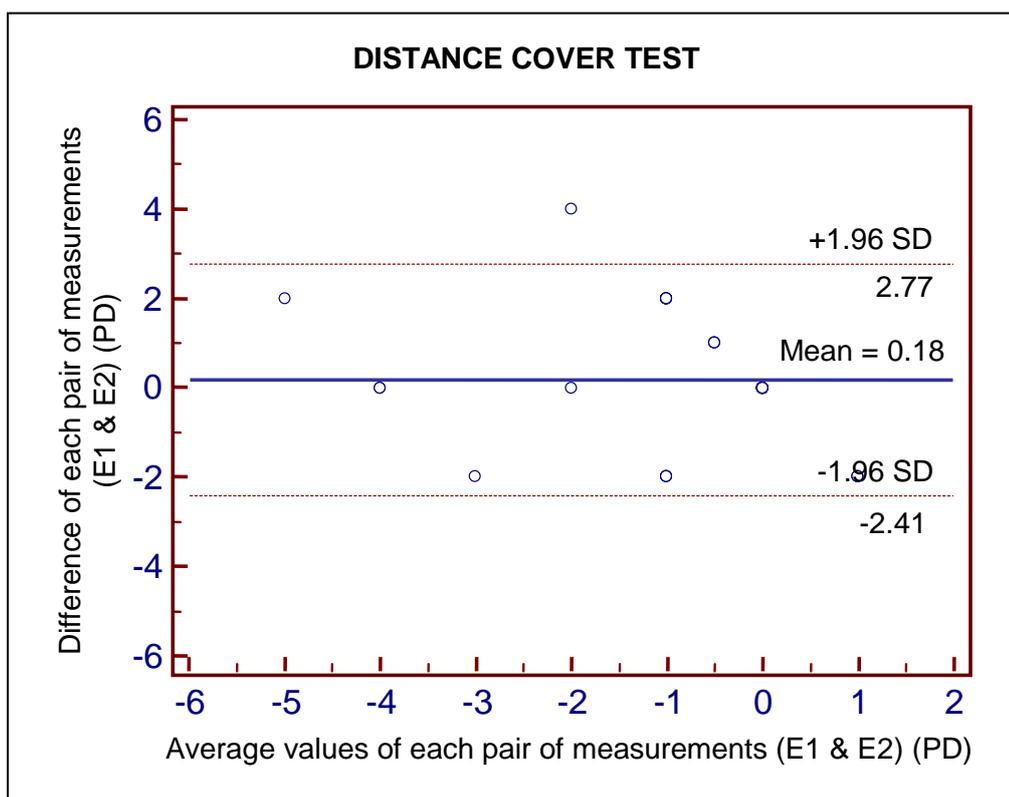
Figure 5.3   Bland-Altman plot of difference between Optometrist (E1) and Orthoptist 1 (E2) for distance cover test. The solid blue line indicates the mean difference and the red dashed lines represent the 95% limits of agreement at ± 1.96 standard deviation.
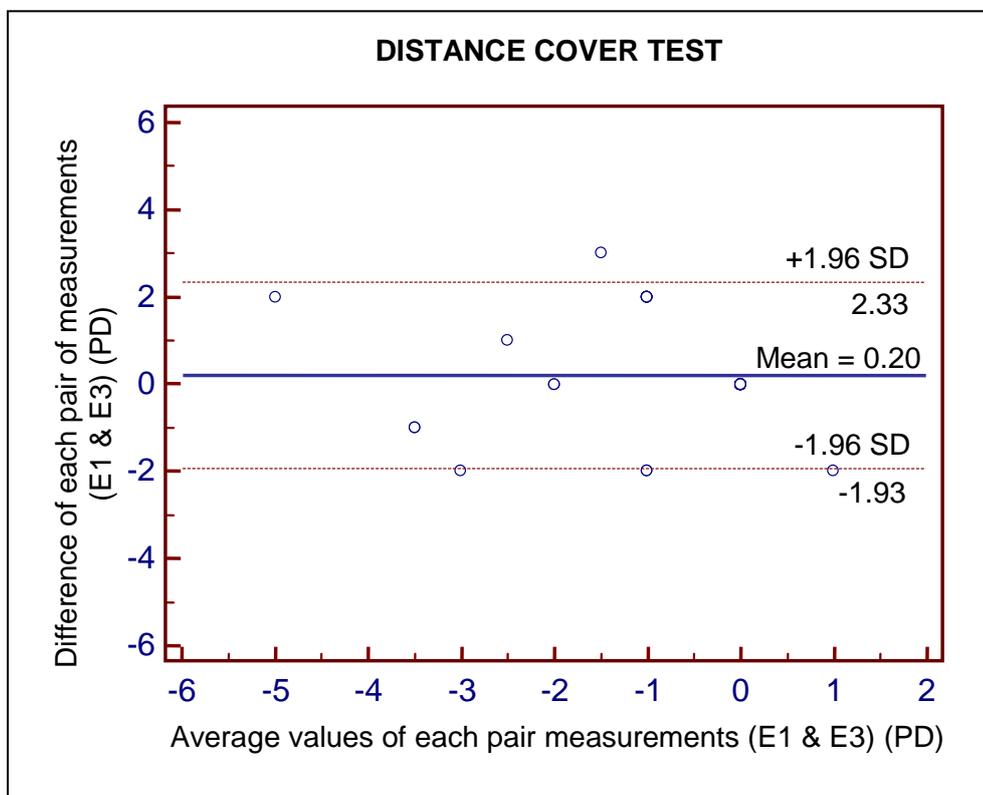
Figure 5.4   Bland-Altman plot of difference between Optometrist (E1) and Orthoptist 2 (E3) for distance cover test. The solid blue line indicates the mean difference and the red dashed lines represent the 95% limits of agreement at ± 1.96 standard deviation.
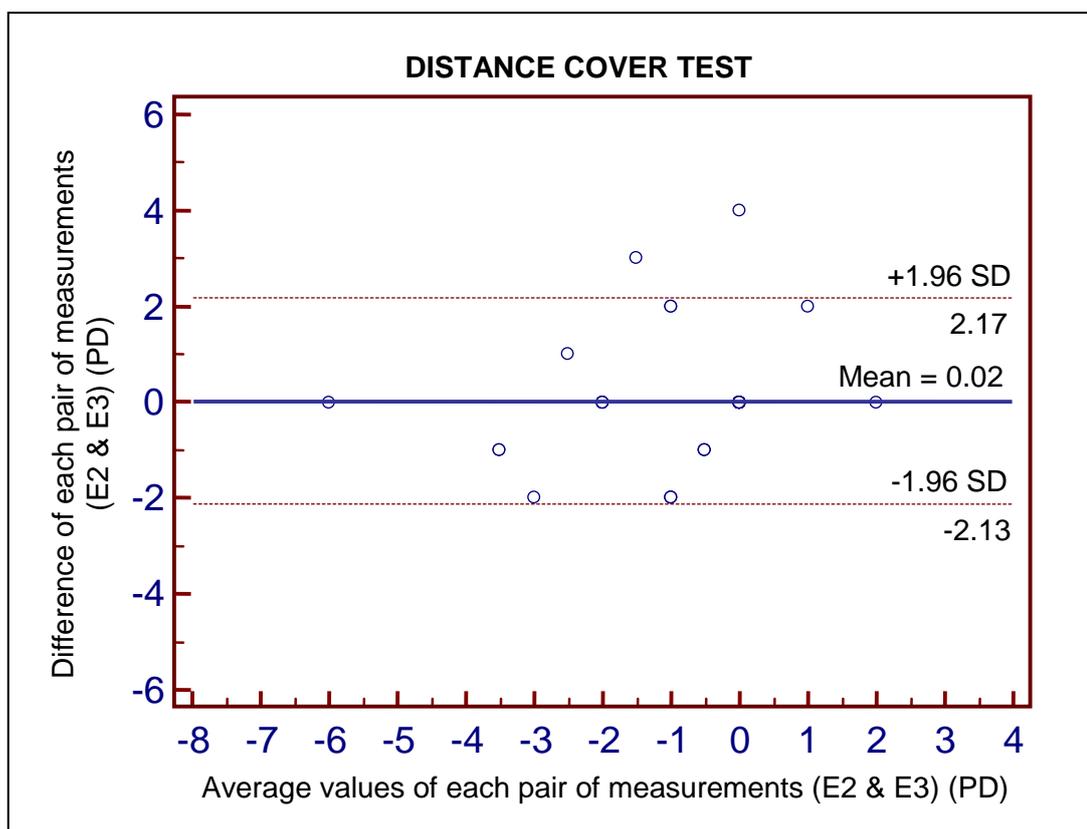
Figure 5.5 Bland-Altman plot of difference between Orthoptist 1 (E2) and Orthoptist 2 (E3) for distance cover test. The solid blue line indicates the mean difference and the red dashed lines represent the 95% limits of agreement at ± 1.96 standard deviation.
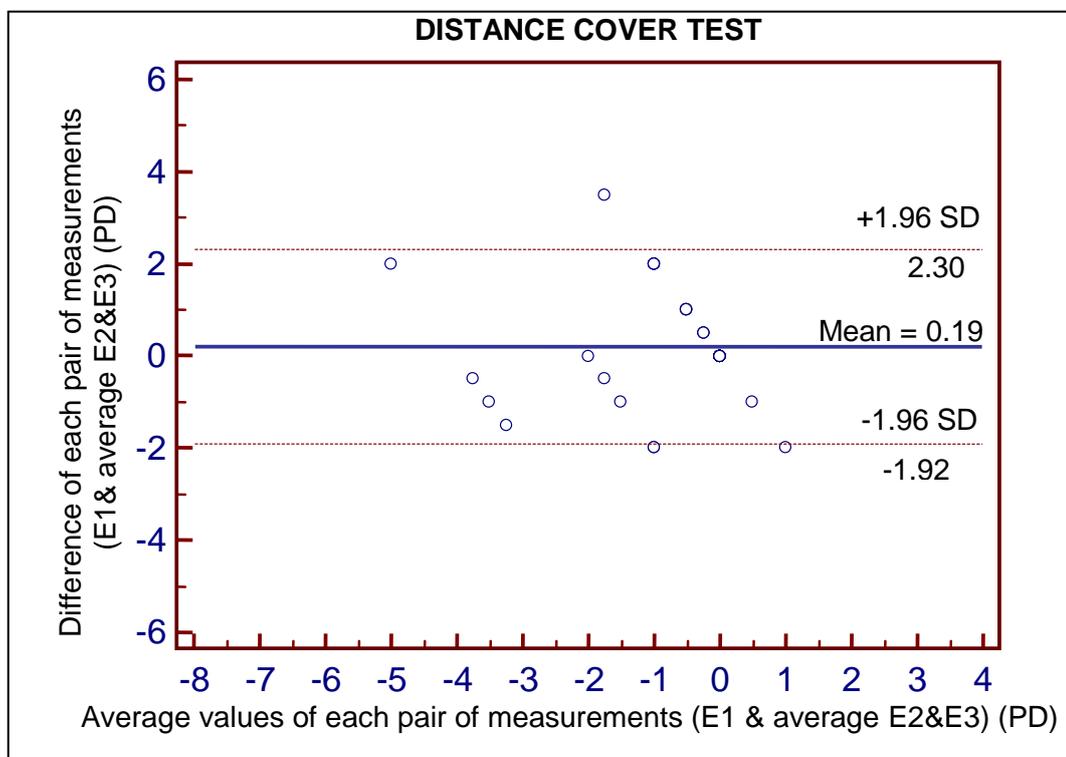
Figure 5.6 Bland-Altman plot of difference between Optometrist (E1) and average orthoptists' measurements (E2&E3) for distance cover test. The solid blue line indicates the mean difference and the red dashed lines represent the 95% limits of agreement at ± 1.96 standard deviation.
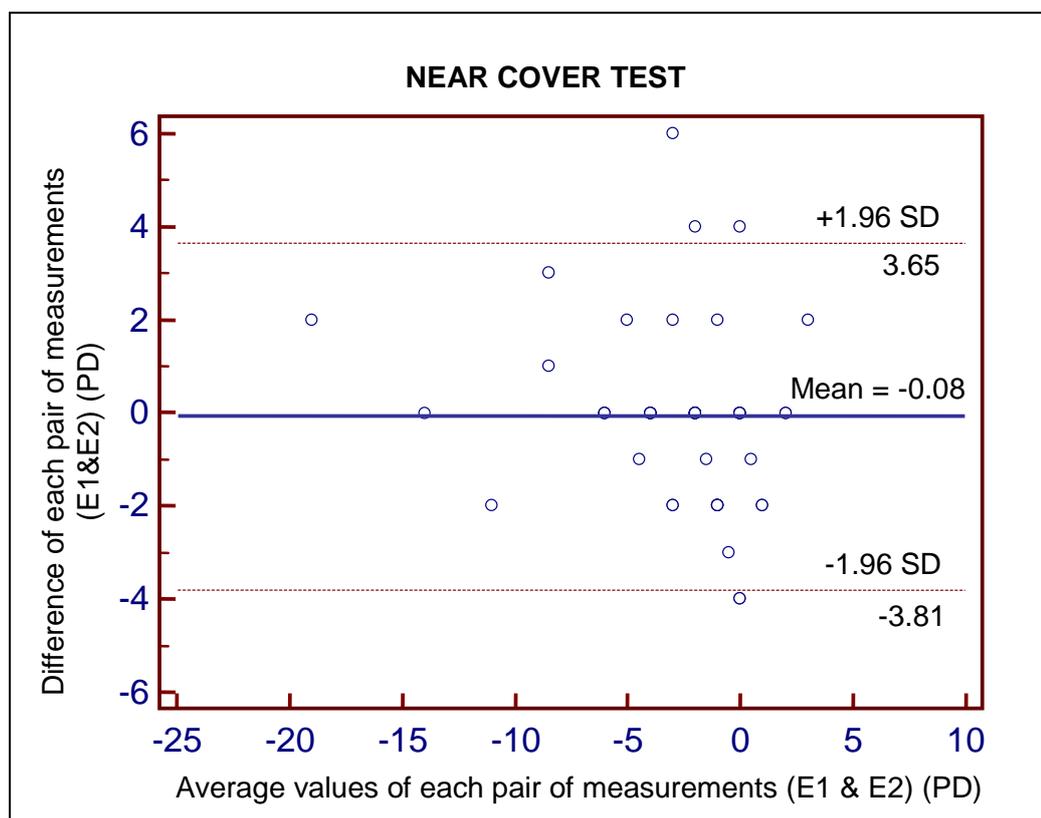
Figure 5.7   Bland-Altman plot of difference between Optometrist (E1) and Orthoptist 1 (E2) for near cover test. The solid blue line indicates the mean difference and the red dashed lines represent the 95% limits of agreement at ± 1.96 standard deviation.
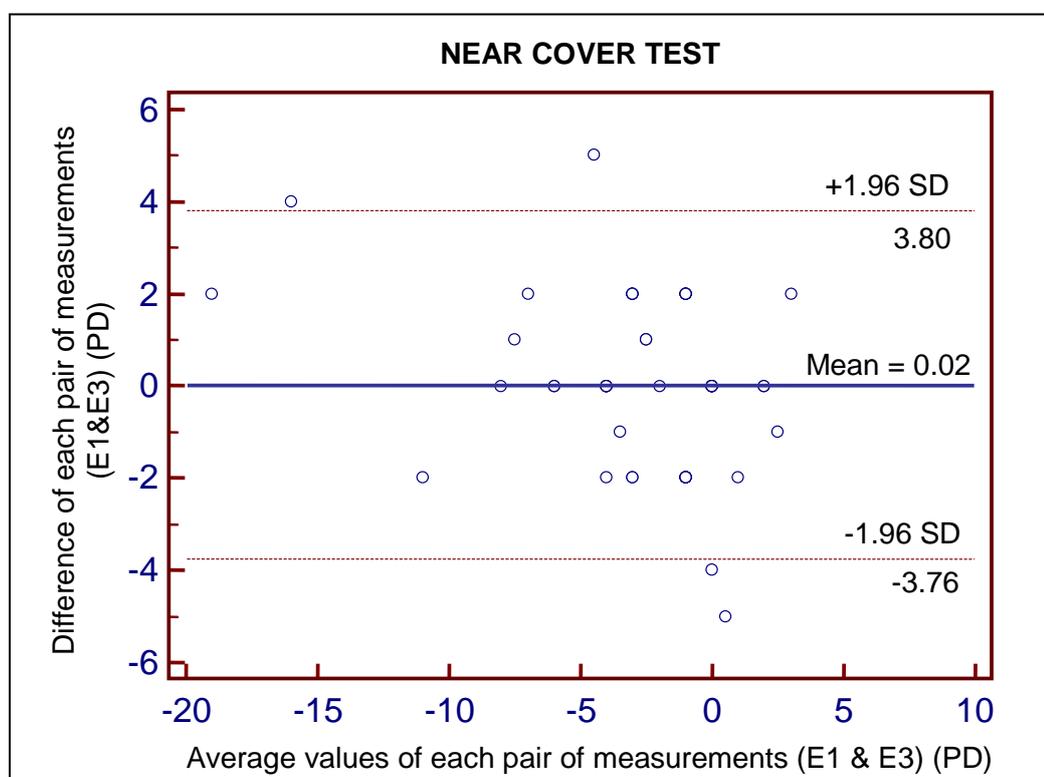
Figure 5.8   Bland-Altman plot of difference between Optometrist (E1) and Orthoptist 2 (E3) for near cover test. The solid blue line indicates the mean difference and the red dashed lines represent the 95% limits of agreement at ± 1.96 standard deviation.
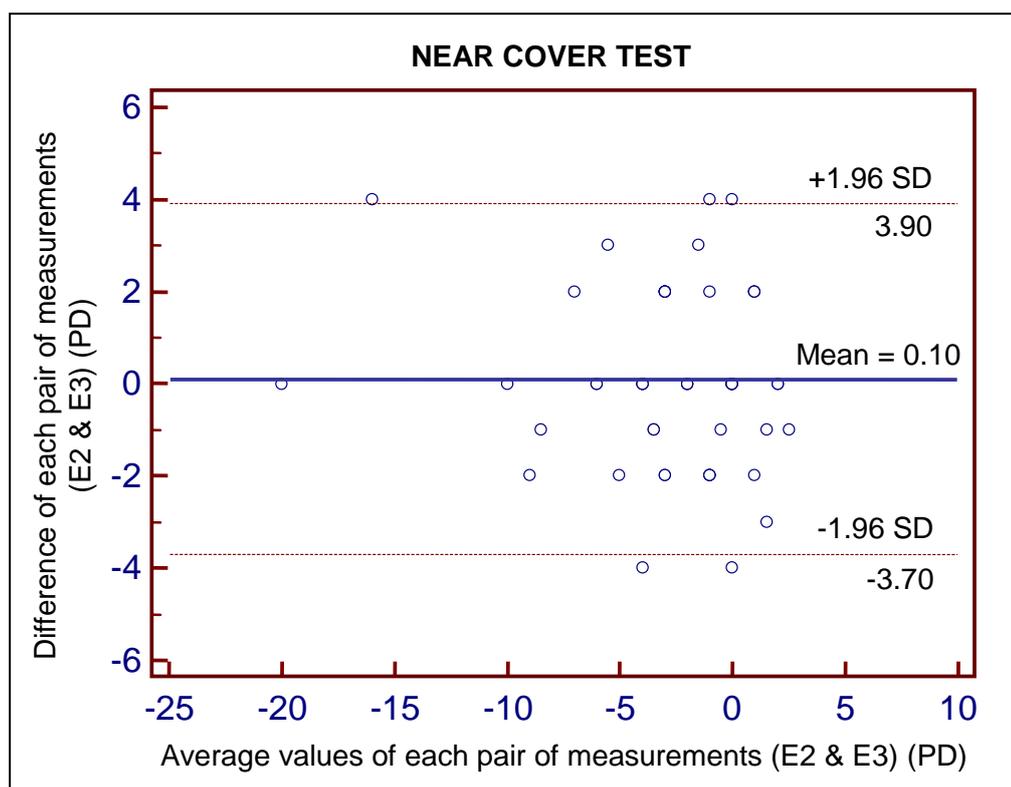
Figure 5.9 Bland-Altman plot of difference between Orthoptist 1 (E2) and Orthoptist 2 (E3) for near cover test. The solid blue line indicates the mean difference and the red dashed lines represent the 95% limits of agreement at ± 1.96 standard deviation.
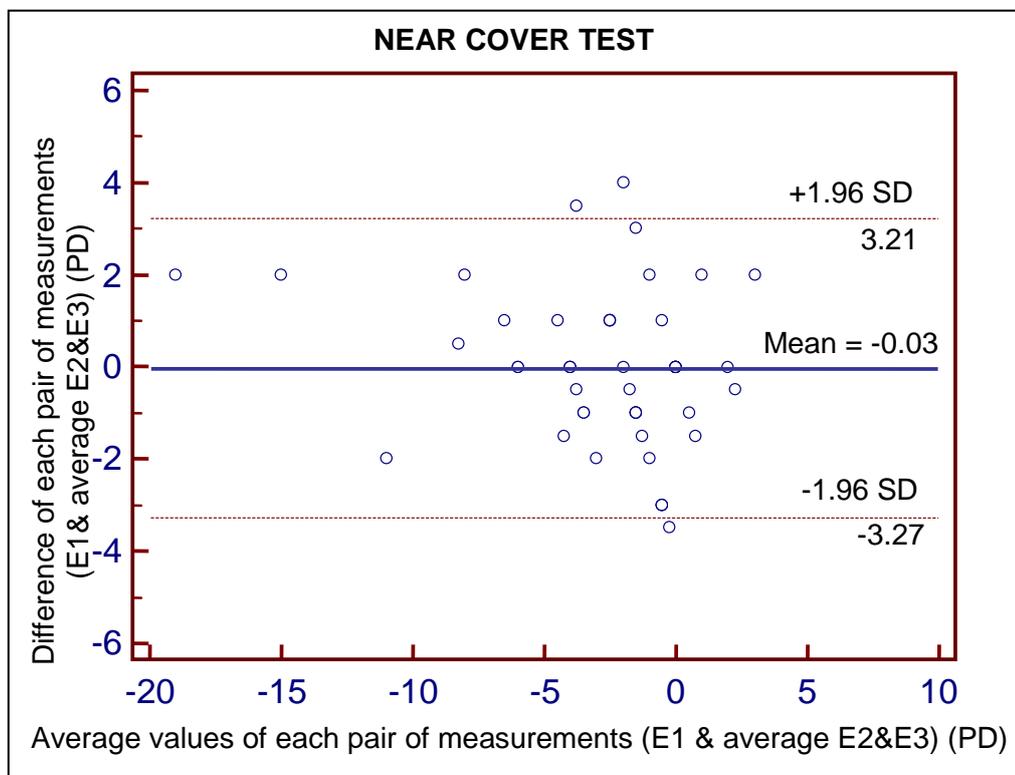
Figure 5.10 Bland-Altman plot of difference between Optometrist (E1) and average orthoptists' measurements (E2 & E3) for near cover test. The solid blue line indicates the mean difference and the red dashed lines represent the 95% limits of agreement at ± 1.96 standard deviation.

5.2.5   Discussion

Although inter-examiner reliability of the cover test measurement has been reported in the literature (Holmes et al. 2008; Rainey et al. 1998) (see Chapter II), we know of no previous attempt to compare the measurements between orthoptists and optometrists. Both eye care practitioners work hand in hand in diagnosing and treating binocular vision problems. Therefore, it is important to know if the measurements performed by different examiners are comparable to each other to ensure reliable measurements are obtained. This study was designed to evaluate the agreement between the measurements made by an optometrist (author) and the two orthoptists.

Distribution of the phoria findings, as presented in Figure 5.1 and 5.2 reflects the normal phoria distribution in the population (von Noorden and Campos 2001). The results showed the range of phoria findings at distance were smaller than at near. This suggests that the phoria in this group of non-strabismic subjects were less variable and the distribution was narrower at distance than at near. Analysis of the mean rank using the Friedman test revealed that the measurements between examiners did not differ significantly, either at distance (p=0.383) or at near (p=0.903). The p-values for both measurements were all more than 0.05, indicating that the measurements were comparable.

It is interesting to note that some of the previous studies used the Pearson correlation coefficient to evaluate agreement of cover test measurements between examiners. This test does not account for any potential systematic difference between measurements. Moreover, good correlation does not always imply good agreement. In this study, we have chosen ICC to evaluate the inter-examiner agreement between measurements. The ICC values estimate the variability of the quantitative measurements by the examiners compared to the total variability across all readings and subjects. There are a few models of ICC that can be used.

We performed our calculation based on the two-way fixed model, in which the subjects are randomly ordered and the same examiners perform the cover test measurements [ICC 3,1].

We also performed the analysis using Bland-Altman plots to measure the degree of agreement. It is beneficial to measure the inter-examiner agreement using different methods, as emphasised by Luiz et al. 2005, because no one method gives an accurate representation of the results as each has its own advantages and disadvantages. The Bland-Altman method assesses the agreement by plotting the differences in the measurements made by two examiners against average values of the measurements. Good agreement is indicated if the limits of agreement (LOA) i.e. the ± 1.96 x the standard deviations of the mean of the differences are narrow. Although both the ICC and the Bland-Altman plot give the measurements of the degree of agreement, the ICC gives quantitative measures of the degree of agreement. Moreover, ICC made possible the comparison between three examiners whereas the Bland-Altman test only permits a comparison of any two means. However, Bland-Altman analysis is useful in providing a qualitative assessment through its limits of agreement (LOA) and graphical output. The interpretation of the results, however, depends on an understanding of the clinical importance of the obtained range (Bland and Altman 1986).

The overall results from the ICC analysis showed moderate to excellent inter-examiner agreement for cover test measurement at distance (ICC=0.70 to 0.84) and at near (ICC=0.94 to 0.96). It is apparent from the results presented in Table 5.3 that the ICC values for near measurements showed higher agreement compared to the ICC values for distance measurements. Degree of agreements was higher when the comparison was made between all three examiners compared to any pair of examiners. This implies that there is little variation between the prism cover test measurements for each subject by the three examiners. The most striking result to emerge from the data is that the agreement seemed to be higher between orthoptists (E2-E3) than between optometrist (E1) and either orthoptist

(E2 or E3). Interestingly, the ICC between E1 and E3 (ICC=0.78; 0.95) were slightly higher than the ICC between E1 and E2 (ICC=0.70; 0.94), for both distance and near cover test measurements. Although the ICCs obtained in any paired comparison were all in excellent agreement, the slight differences found could be attributed to experience and the methods used in performing the cover test procedure. Examiners 2 and 3 are both working as clinical orthoptists in the hospital and therefore could have been exposed to the same routine and measurement techniques, in contrast to examiner 1. There have been reports highlighting the effect of an examiner's experience when performing the cover test. Hrynchak (2010) compared cover test measurement between two experienced optometrists and two optometry students on fifty non-strabismic subjects and found a mean difference of 0.8 ± 3.5PD between the experienced and the novice examiners. An earlier report from Rainey et al. (1998), on two optometry faculty members' cover test measurements on seventy two non-strabismic subjects, revealed a mean difference of -1.0 and 95% LOA of ± 3.5PD. The mean differences from these studies were all less than 2PD. The findings were deemed not significant clinically as 2PD is considered to be the smallest eye movement that can be detected when performing the cover test (Fogt et al. 2000; Romano and von Noorden 1971). in all of the studies mentioned above, however, the examiners compared were all from the same background or profession.

In contrast to the findings of Hrynchak et al. (2010) and Rainey et al. (1998), a recent study by Anderson et al. (2010) revealed a significant difference between the measurements made between experienced and inexperienced examiners. In this study, the experienced examiners trained selected inexperienced examiners, who were naïve to the cover test procedure and who did not have any knowledge of eye care or optometry. The results showed that 40% of the overall absolute mean differences in measurements between examiners were more than 2PD, implying that it is possible to attain significant differences between the measurements of different examiners. However, direct comparison with the present study cannot be made as the ICC was not used in the analyses of Anderson's results.

Findings from Bland-Altman analyses in our study showed low average discrepancy when measurements were compared between examiners, in which the absolute mean signed differences found were all less than 0.5PD for distance and near cover test measurements. The 95% LOA found from this study were approximately ± 3PD for distance cover test and ± 4PD for near cover test. These findings are consistent with those of Johns et al. (2004) and Rainey et al. (1998), who found LOA to be in the same range. The wide LOA obtained in this present study may be explained by the fact that the measurements relied on the 2PD increment of prism bar used. Moreover, there was no specific instruction given to each examiner on determining the neutralising point when performing the prism cover test. The testing distance, especially at near, was not measured prior to each examination, although all examiners were aware that the near cover test should be performed at 40cm. It is possible that the findings could be dependent on the experience of the examiners and the method used, as mentioned above. However, it has been shown that the subjective prism cover test measurements give narrower LOA compared to the objective prism cover test, which is the method that was used in this present study (Rainey et al. 1998).

5.3 Strabismic subjects

5.3.1 Participants

Twenty strabismic subjects (8 female and 12 male) were recruited from staff, students and clinical patients from Cardiff University. The mean age of this group of subjects was 34.10 (age range:20-68 years). Informed consent was obtained from all subjects where the ethical permission was approved by the School of Optometry and Vision Sciences' Human Research Ethical Committee.

5.3.2 Protocols and procedures

The experiment follows the protocols detailed in section 5.2.2. The measurements were performed at primary position at the same fixation distances. Taking into consideration the degree and nature of the strabismus, standard loose prisms were used instead of prism bar to measure the angle of deviation. The individual prisms increased in power from 1PD to 10PD in single unit increments, from 10 to 20PD in 2 unit increments and 20 to 50PD in 5 unit increments. This is necessary to ensure ease of measurements as there is a need to stack the prisms if the measurement involves deviation in two meridians, i.e. horizontal and vertical. Although there is no specific instruction given to each examiner, the deviations were recorded as the value of the closest prism that can neutralise the misalignment. The examiners first determined the type of deviation using a unilateral cover test and then followed this by an alternating prism cover test to measure the angle of deviation.

5.3.3 Analysis

The same statistical analysis tests were performed as in section 5.2.3. The analyses were also extended to measure the deviation of both the horizontal and vertical components of the deviation, if present.

5.3.4   Results

The range of strabismic subjects seen in this study are detailed in Table 5.4. Distributions of the average cover test findings from all examiners are presented in Figures 5.11 (distance cover test) and 5.12 (near cover test) and Table 5.5. The normality test using Shapiro-Wilk revealed that the average results for cover test at distance (p=0.012) and at near (p=0.032) were not normally distributed (p<0.05). Comparison of the mean rank difference of the measurements between three examiners using the Friedman test (Table 5.6) showed chi-square values of 0.298 (p=0.862) and 3.125 (p=0.210) for distance and near cover test measurements. It is apparent from these results that the findings were all not significant (p>0.05), reflecting the fact that the measurements were comparable.

The inter-examiner agreements for the cover test results at distance and at near were analysed using the ICC and Bland-Altman. The results obtained from the analyses are presented in Table 5.7. Excellent degree of agreements (ICC= 0.94 to 1.00) were found for all pairs of measurements except for the distance cover test findings for vertical component, which was shown to have moderate ICC (ICC=0.74) for all three examiners.

Our results from the Bland-Altman analyses showed that the mean differences were less than 1PD for both distance and near cover test measurements. The 95% LOA for cover test at distance ranged from ± 2PD to ± 7PD. On visual inspection, there were trends observed in the plots in which the difference between methods tends to get larger as the average measurements increase, in particular towards more exophoric deviation.
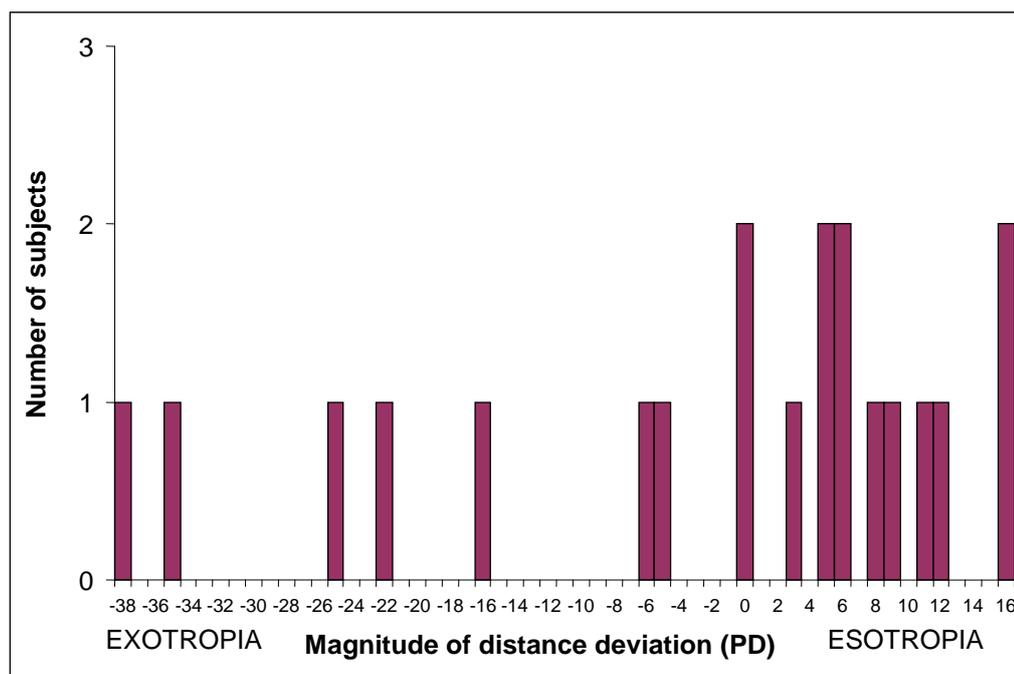
Figure 5.11 Distribution of strabismic magnitude for distance cover test measurements. The magnitude was derived by averaging the results from each examiner for each subject (PD). Minus (-) sign denotes exophoria and plus (+) sign denotes esotropia.
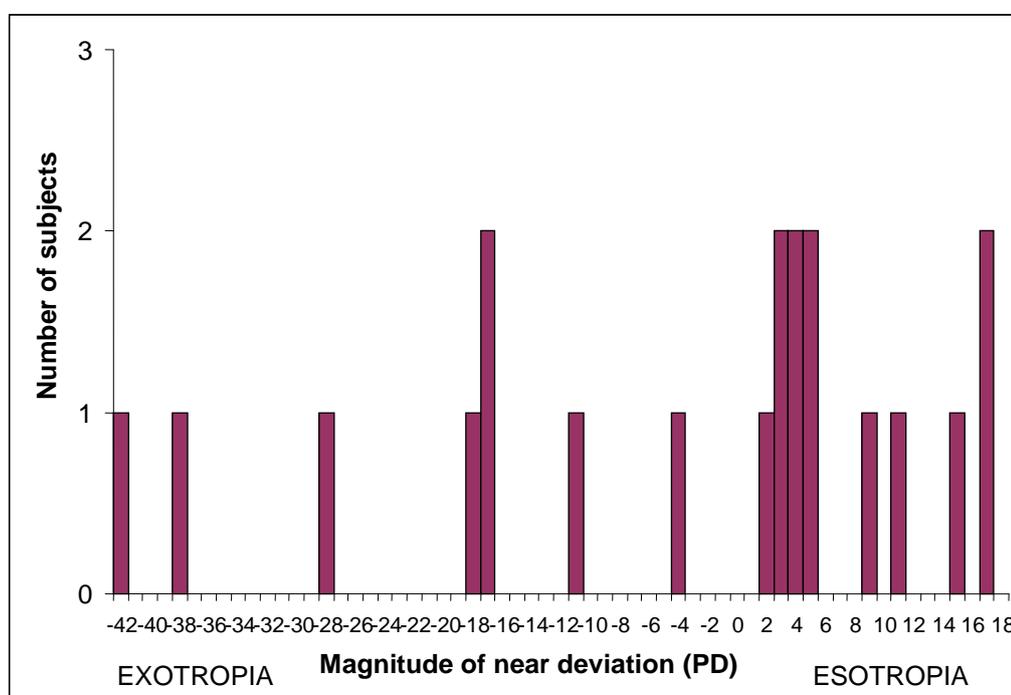
Figure 5.12 Distribution of strabismic magnitude for near cover test measurements. The magnitude was derived by averaging the results from each examiner for each subject (PD). Minus (-) sign denotes exotropia an plus (+) sign denotes esotropia.

Table 5.4 Summary of the number of the strabismic subjects and their diagnosis.

Number of subjects	Diagnosis
5	Right esotropia
4	Left esotropia
2	Right exotropia
3	Left exotropia
1	Alternating esotropia
1	Alternating exotropia
2	Right exotropia with right hypertropia
1	Right esotropia with left hypertropia
1	Left exotropia at near only

Table 5.5 Descriptive analysis results (median, interquartile range, minimum and maximum) for the cover test measurements between three examiners on strabismic subjects.

Cover test	Median	Interquartile range	Minimum	Maximum
Distance	4.17	23	-38	16
Near	3.00	25	-42	17

Table 5.6 Friedman test detailing the chi-square values and p-values for the cover test measurements results between examiners at distance and near.

Cover test	Mean rank			Chi-Square value	p-value
	Optometrist	Orthoptist 1	Orthoptist 2		
Distance	1.98	2.08	1.95	0.298	0.862
Near	2.00	1.75	2.25	3.125	0.210

*Not significant; p-value > 0.05

Table 5.7 The degree of agreement for inter-examiner cover test measurements at distance and at near, using the Intraclass Correlation Coefficient (ICC) and the Bland-Altman test.

Examiner	ICC	Bland & Altman	
		Mean difference (PD)	Limits of Agreement (PD)
Cover test at distance (Horizontal deviation)			
E1-E2	0.99	-0.65	-6.95 to 5.65
E1-E3	1.00	-0.05	-4.52 to 4.42
E2-E3	0.99	0.60	-6.23 to 7.43
E1-E2/3 (Average)	1.00	-0.35	-4.62 to 3.91
E1-E2-E3	0.99	-	-
Cover test at distance (Vertical deviation)			
E1-E2	0.86	-0.33	-3.33 to 2.66
E1-E3	-0.50	0.00	-3.39 to 3.39
E2-E3	0.47	0.00	0.00 to 0.00
E1-E2/3 (Average)	0.82	-0.17	-2.63 to 2.30
E1-E2-E3	0.74	-	-
Cover test at near (Horizontal deviation)			
E1-E2	1.00	0.75	-3.37 to 4.87
E1-E3	0.99	-0.20	-6.25 to 5.85
E2-E3	0.99	-0.95	-5.98 to 4.08
E1-E2/3 (Average)	1.00	0.28	-4.25 to 4.80
E1-E2-E3	1.00	-	-
Cover test at near (Vertical deviation)			
E1-E2	1.00	0.00	0.00 to 0.00
E1-E3	0.94	0.00	-3.92 to 3.92
E2-E3	0.94	0.00	-3.92 to 3.92
E1-E2/3 (Average)	0.98	0.00	-1.96 to 1.96
E1-E2-E3	0.97	-	-

* **E1**= Optometrist; **E2**= Orthoptist 1; **E3**= Orthoptist 2
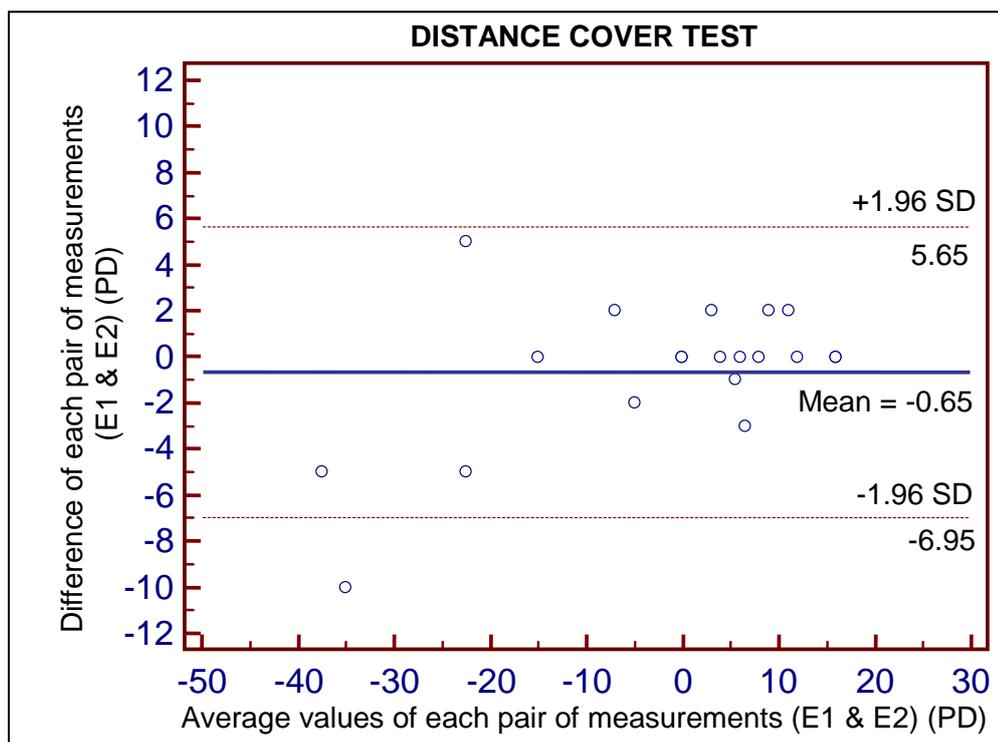
Figure 5.13 Bland-Altman plot of difference between Optometrist (E1) and Orthoptist 1 (E2) for distance cover test (horizontal deviation). The solid blue line indicates the mean difference and the red dashed lines represent the 95% limits of agreement.
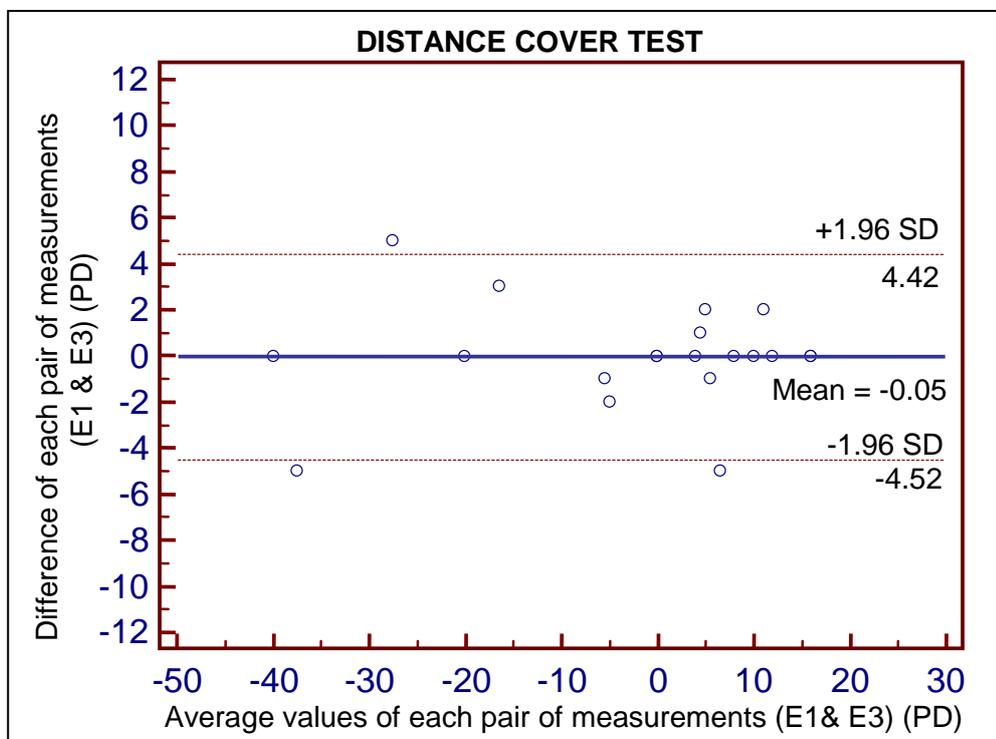
Figure 5.14 Bland-Altman plot of difference between Optometrist (E1) and Orthoptist 2 (E3) for distance cover test (horizontal deviation). The solid blue line indicates the mean difference and the red dashed lines represent the 95% limits of agreement.
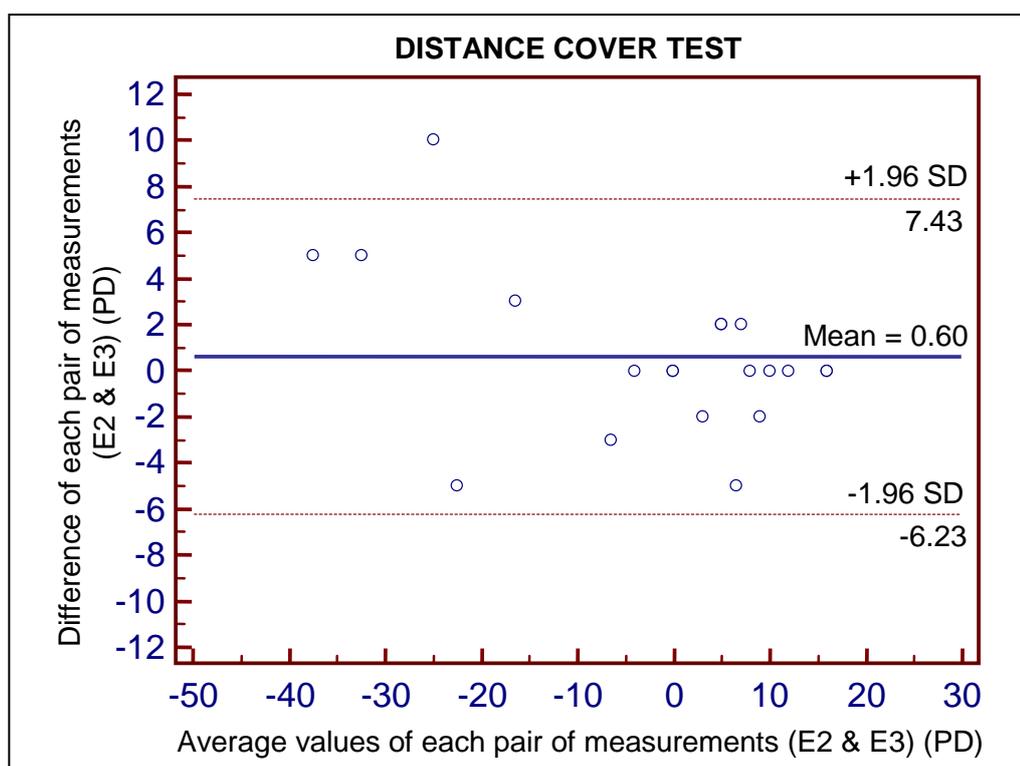
Figure 5.15 Bland-Altman plot of difference between Orthoptist 1 (E2) and Orthoptist 2 (E3) for distance cover test (horizontal deviation). The solid blue line indicates the mean difference and the red dashed lines represent the 95% limits of agreement.
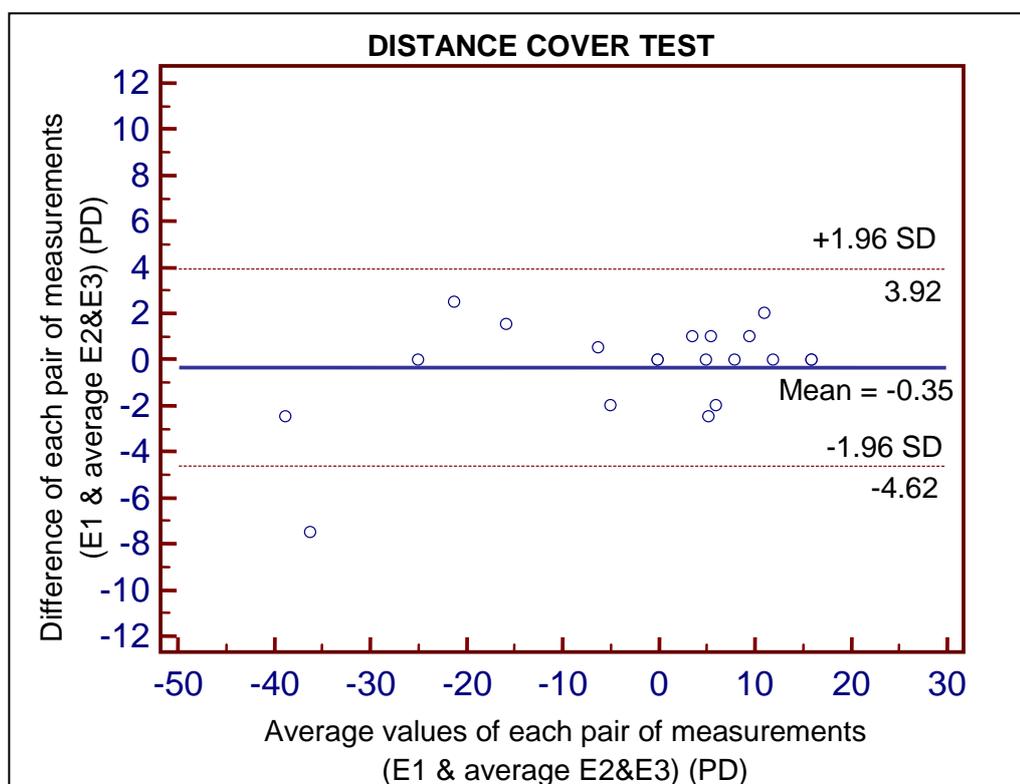
Figure 5.16 Bland-Altman plot of difference between Optometrist (E1) and average orthoptists' measurements (E2&E3) for distance cover test (horizontal deviation). The solid blue line indicates the mean difference and the red dashed lines represent the 95% limits of agreement.
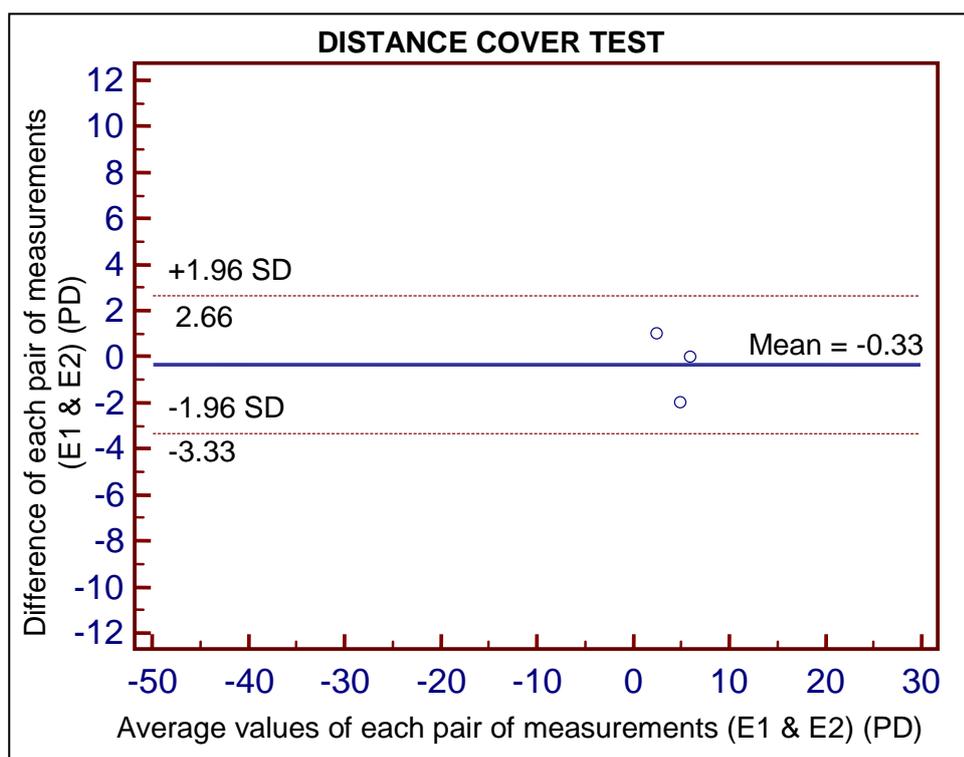
Figure 5.17   Bland-Altman plot of difference between Optometrist (E1) and Orthoptist 1 (E2) for distance cover test **(vertical deviation)**. The solid blue line indicates the mean difference and the red dashed lines represent the 95% limits of agreement.
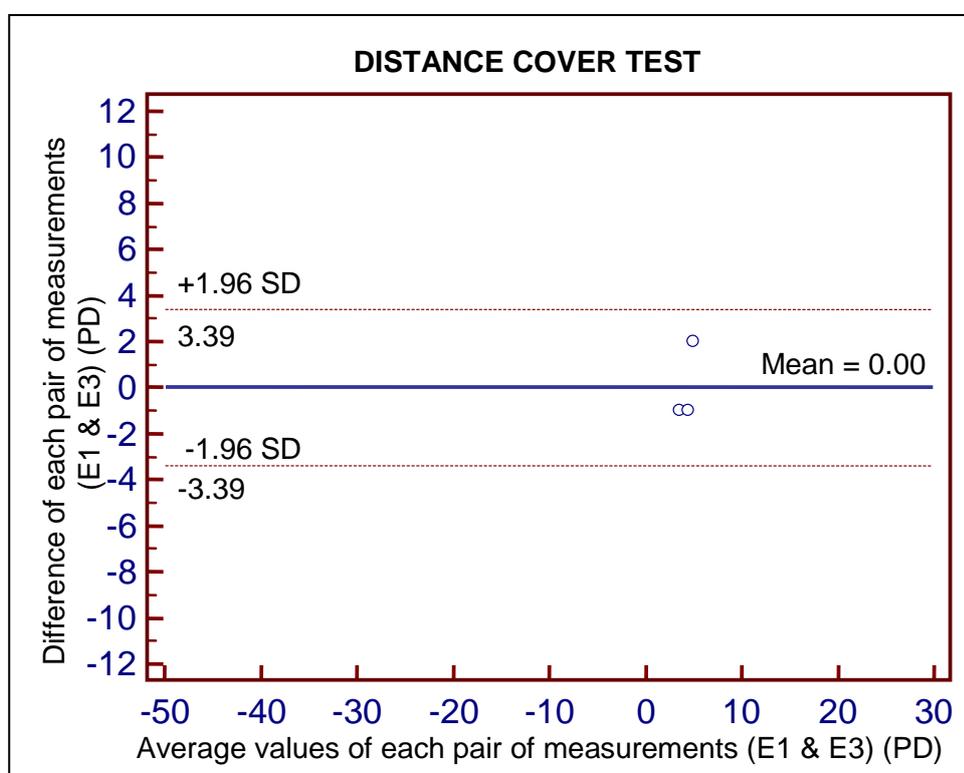
Figure 5.18   Bland-Altman plot of difference between Optometrist (E1) and Orthoptist 2 (E3) for distance cover test **(vertical deviation).** The solid blue line indicates the mean difference and the red dashed lines represent the 95% limits of agreement.
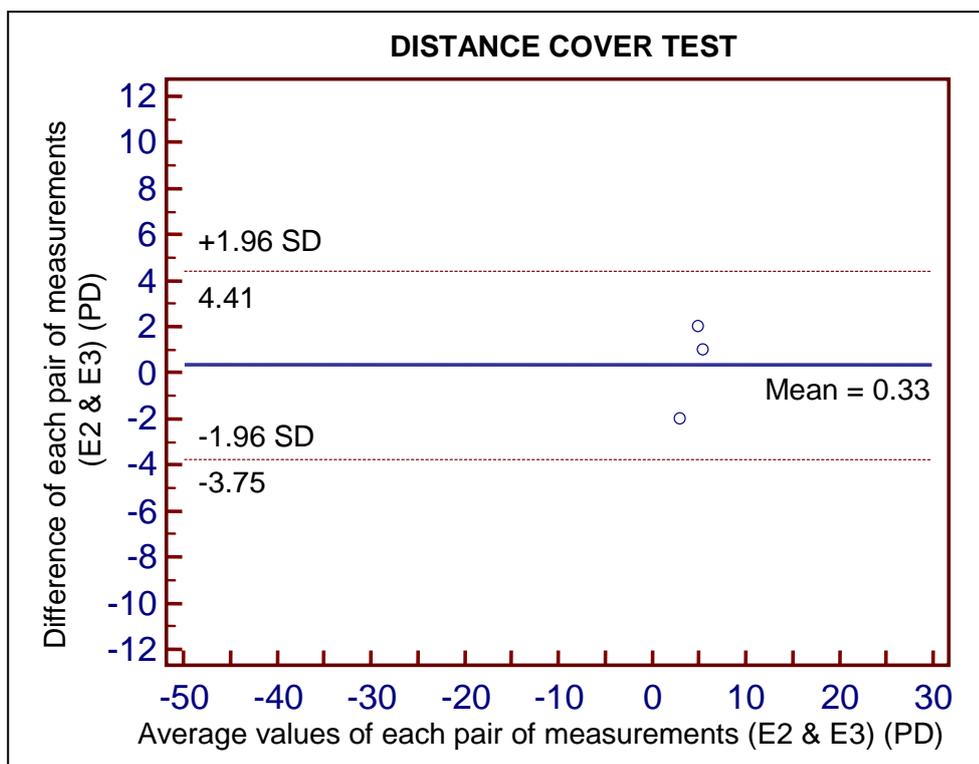
Figure 5.19   Bland-Altman plot of difference between Orthoptist 1 (E2) and Orthoptist 2 (E3) for distance cover test **(vertical deviation).** The solid blue line indicates the mean difference and the red dashed lines represent the 95% limits of agreement.
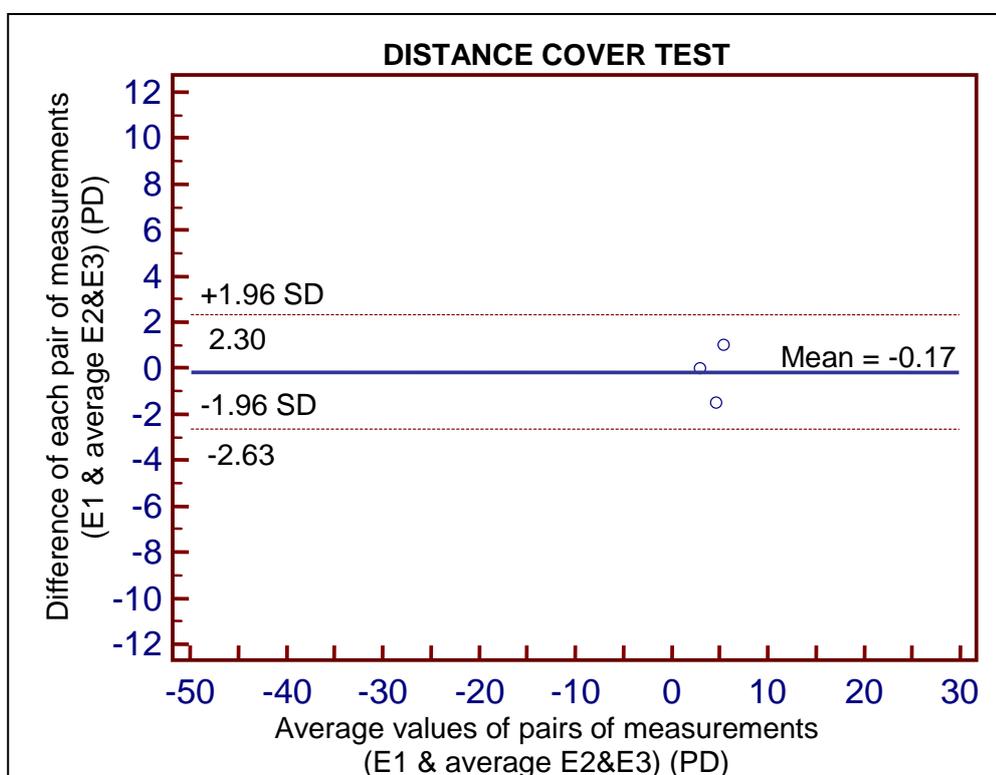
Figure 5.20   Bland-Altman plot of difference between Optometrist (E1) and average orthoptists' measurements (E2&E3) for distance cover test **(vertical deviation).** The solid blue line indicates the mean difference and the red dashed lines represent the 95% limits of agreement.
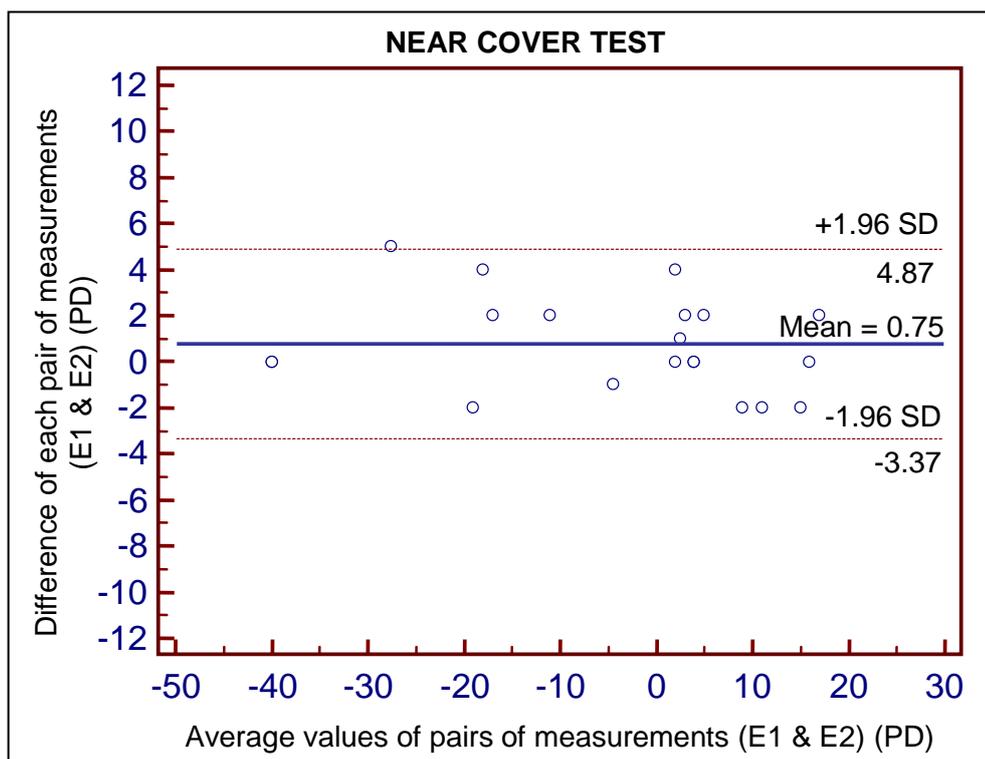
Figure 5.21 Bland-Altman plot of difference between Optometrist (E1) and Orthoptist 1 (E2) for near cover test. The solid blue line indicates the mean difference and the red dashed lines represent the 95% limits of agreement.
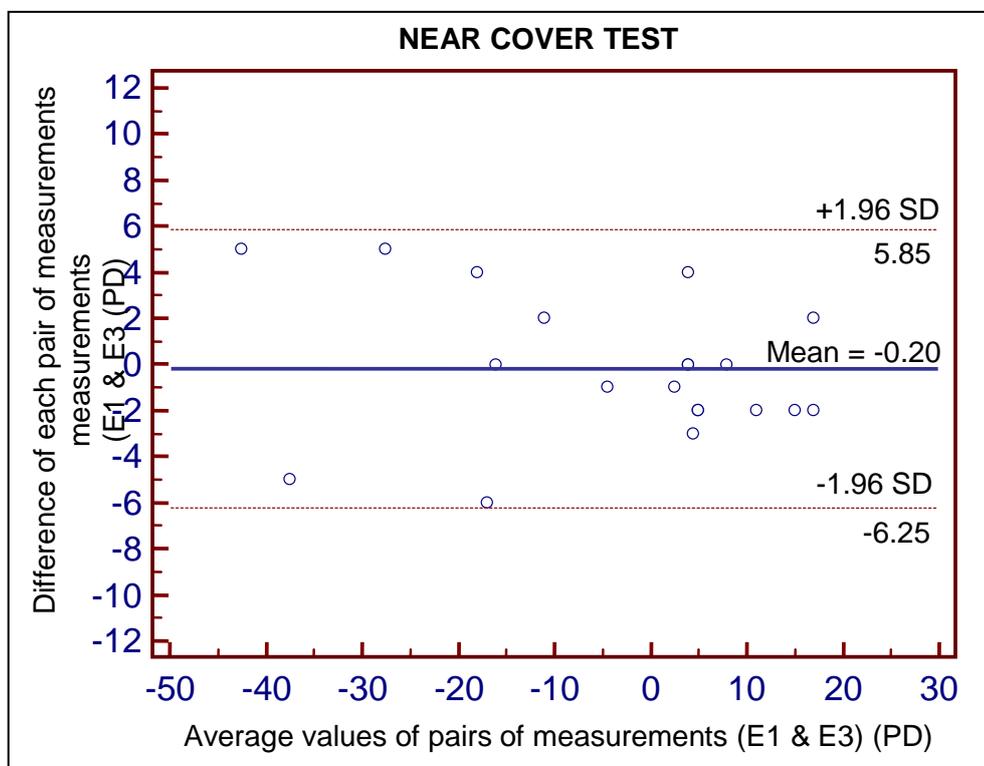
Figure 5.22 Bland-Altman plot of difference between Optometrist (E1) and Orthoptist 2 (E3) for near cover test. The solid blue line indicates the mean difference and the red dashed lines represent the 95% limits of agreement.
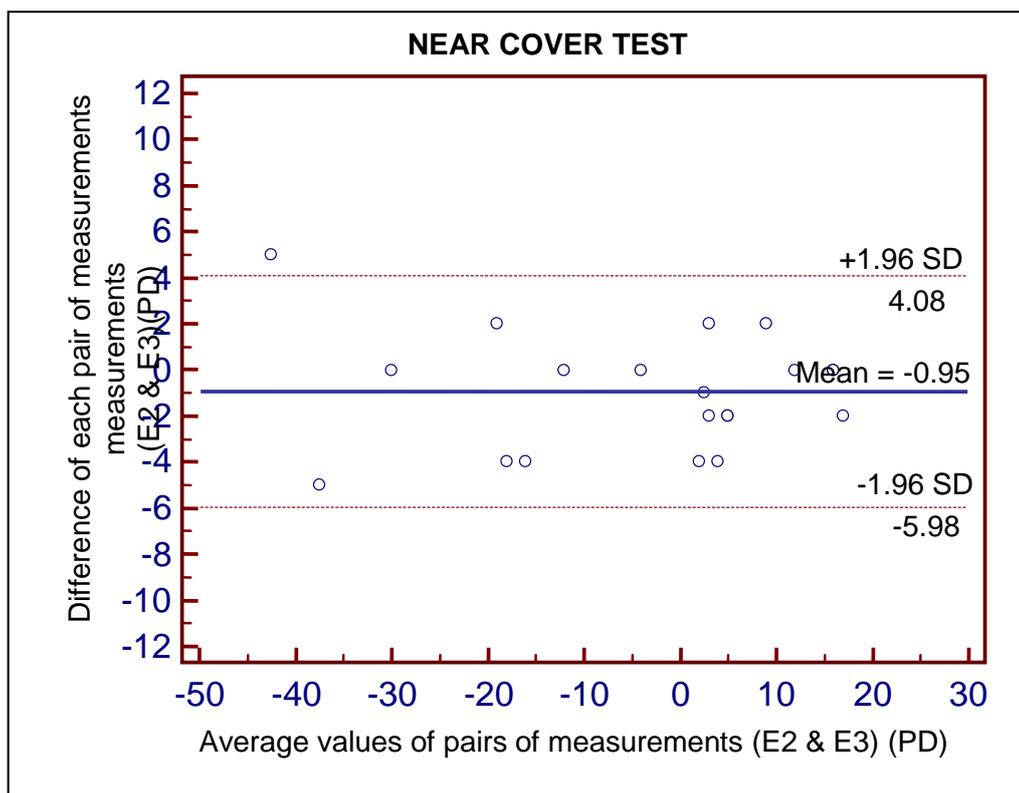
Figure 5.23 Bland-Altman plot of difference between Orthoptist 1 (E2) and Orthoptist 2 (E3) for near cover test. The solid blue line indicates the mean difference and the red dashed lines represent the 95% limits of agreement.
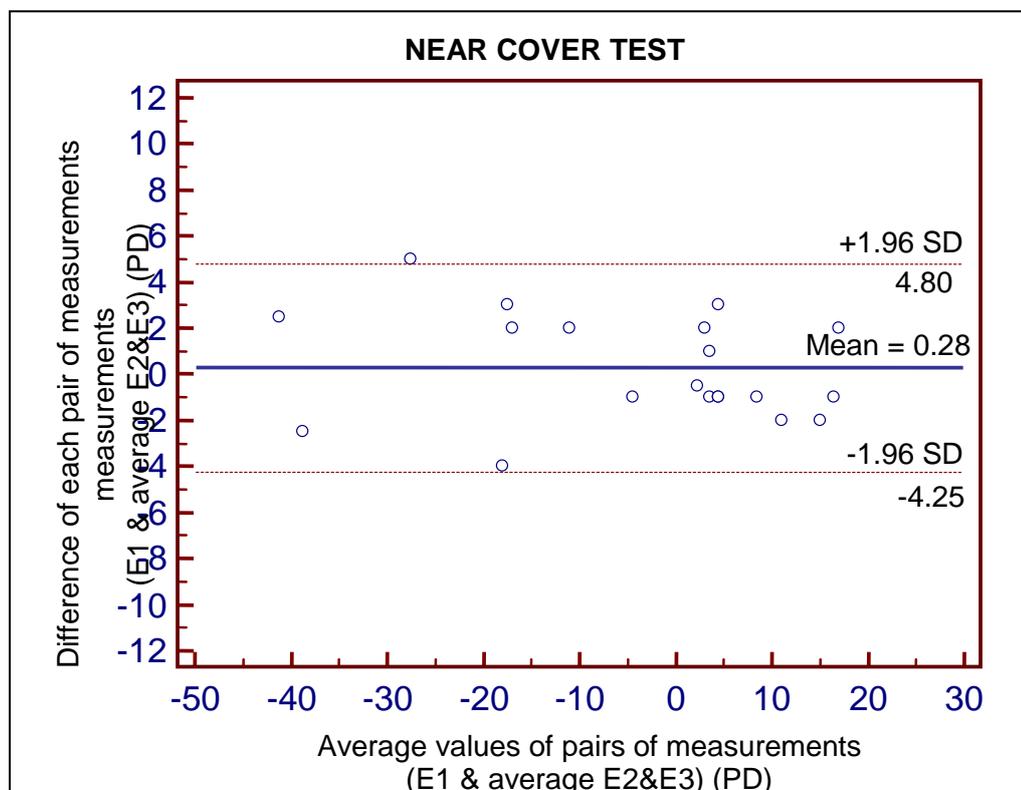
Figure 5.24 Bland-Altman plot of difference between Optometrist (E1) and average orthoptists' measurements (E2&E3) for near cover test. The solid blue line indicates the mean difference and the red dashed lines represent the 95% limits of agreement.
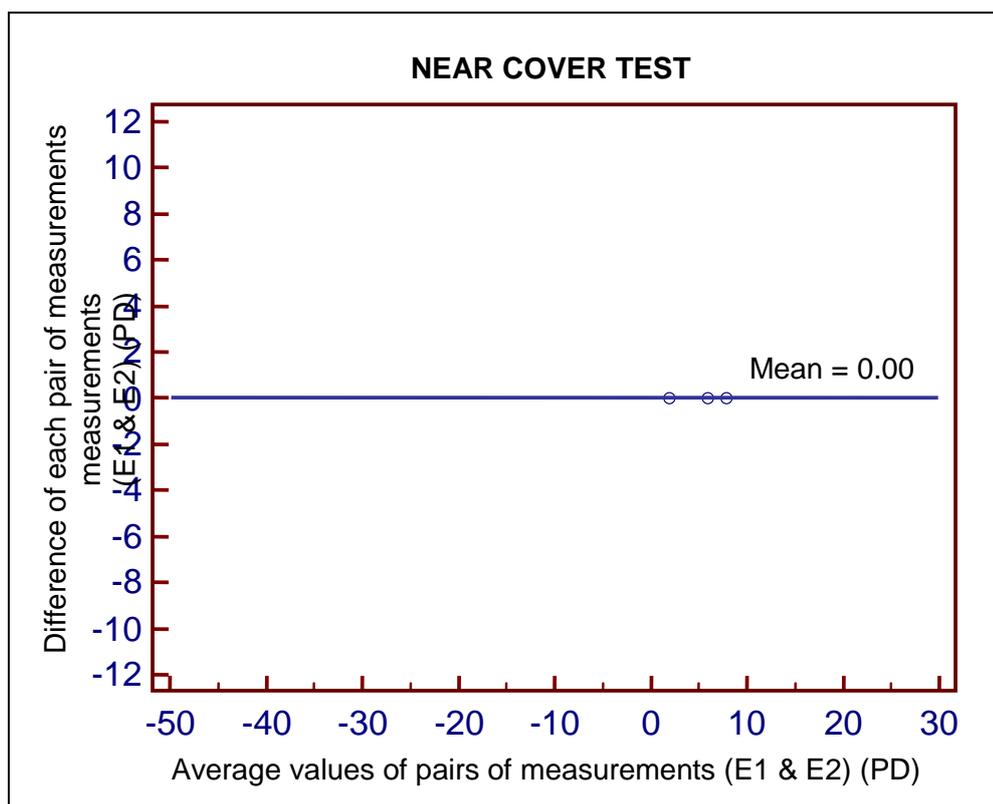
NEAR COVER TEST

Figure 5.25 Bland-Altman plot of difference between Optometrist (E1) and Orthoptist 1 (E2) for near cover test **(vertical deviation).** The solid blue line indicates the mean difference and the red dashed lines represent the 95% limits of agreement.
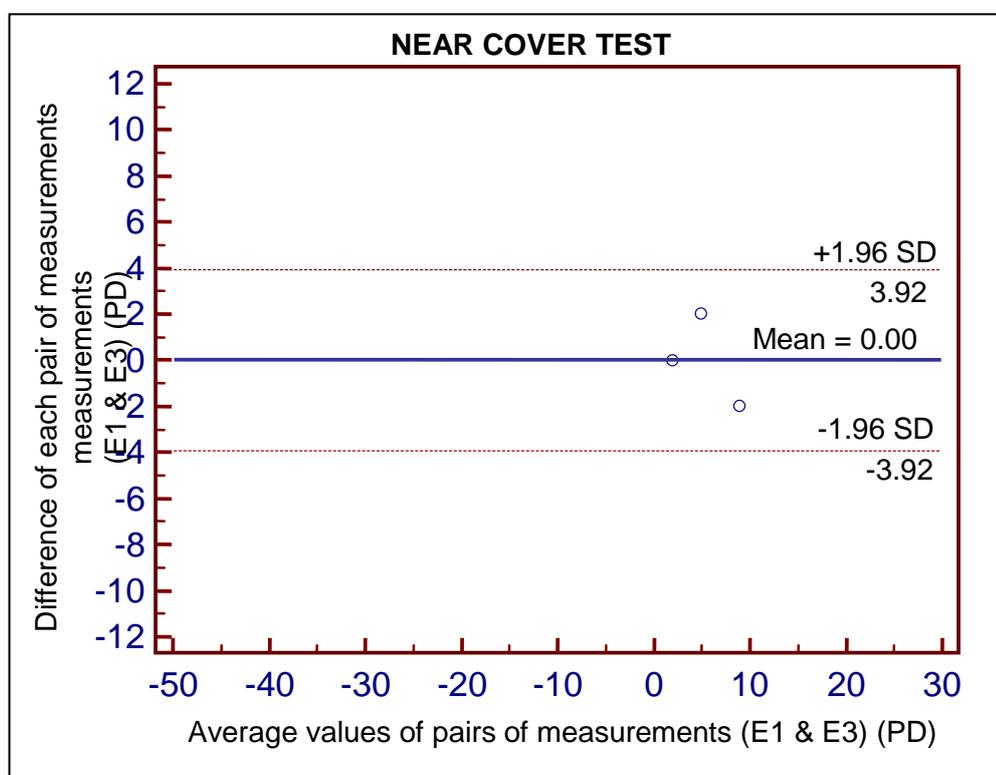
NEAR COVER TEST

Figure 5.26 Bland-Altman plot of difference between Optometrist (E1) and Orthoptist 2 (E3) for near cover test **(vertical deviation).** The solid blue line indicates the mean difference and the red dashed lines represent the 95% limits of agreement.
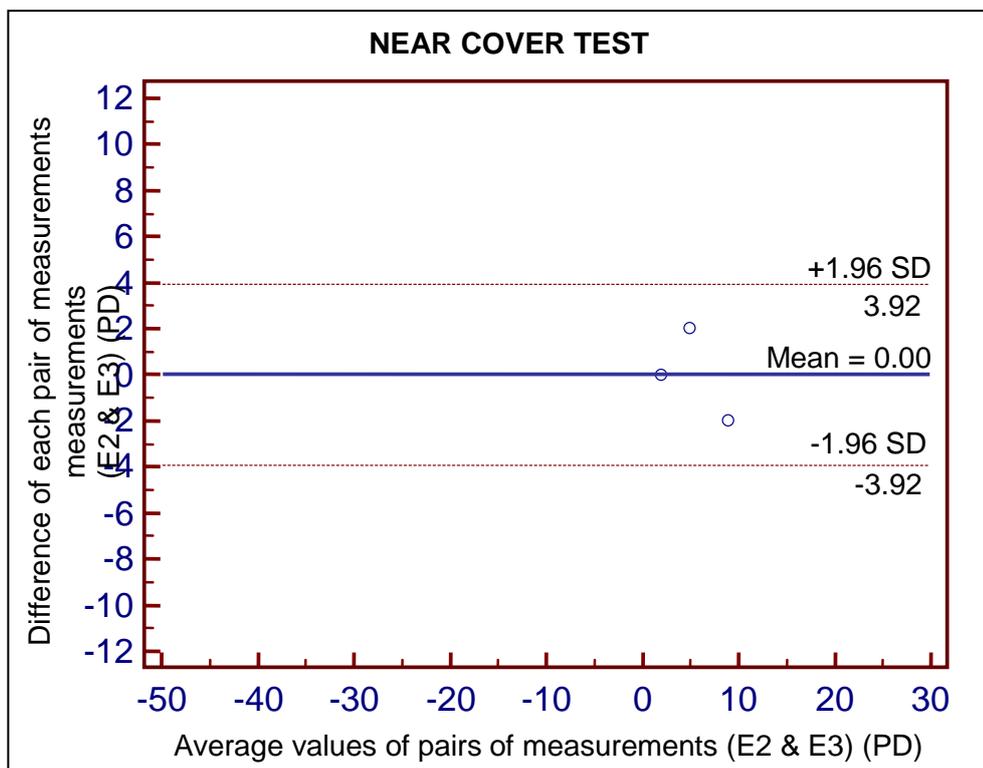
Figure 5.27 Bland-Altman plot of difference between Orthoptist 1 (E2) and Orthoptist 2 (E3) for near cover test **(vertical deviation).** The solid blue line indicates the mean difference and the red dashed lines represent the 95% limits of agreement.
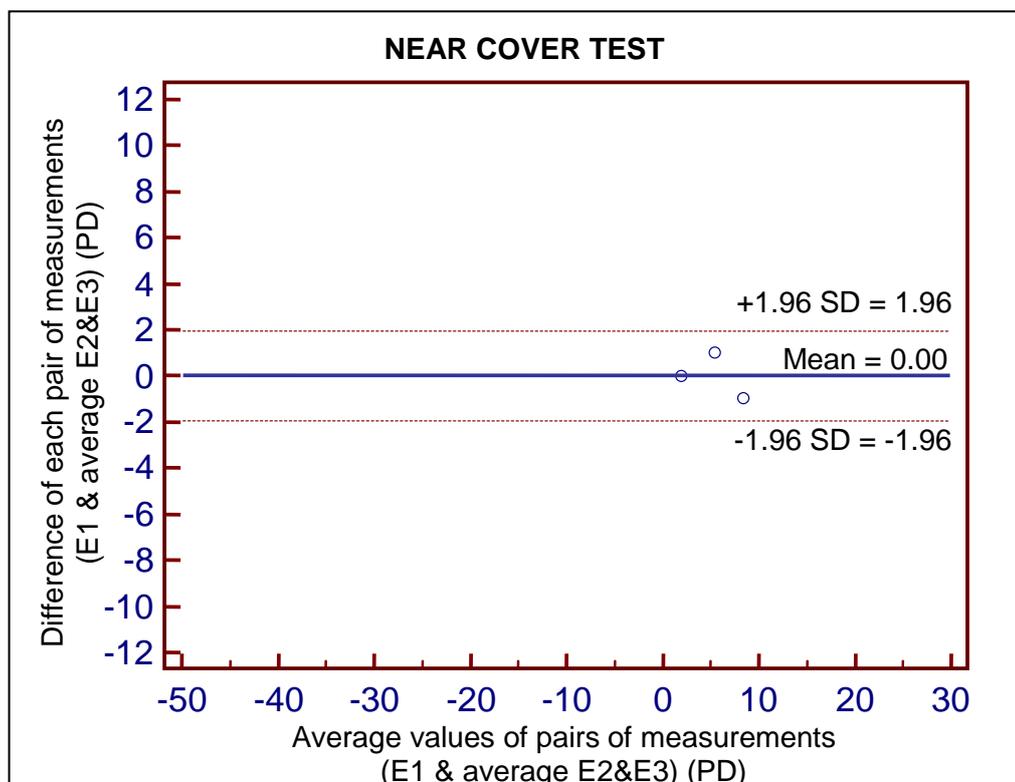
Figure 5.28 Bland-Altman plot of difference between Optometrist (E1) and average orthoptists' measurements (E2&E3) for near cover test **(vertical deviation)**. The solid blue line indicates the mean difference and the red dashed lines represent the 95% limits of agreement.

5.3.5   Discussion

All types of strabismus were included in this study as limiting the study to one type of strabismus would have restricted the usefulness and generality of the experiment. In reviewing the literature, several studies have been carried out to investigate the agreement of cover test measurements in non-strabismic subjects (Anderson et al. 2010; Hrynchak et al. 2010; Johns et al. 2004; Rainey et al. 1998). However, there is still insufficient data on the degree of the inter-examiner agreement on measurements of strabismic subjects. Comparison has been made of the average of the cover test results in subjects with constant manifest esotropia (Deacon et al. 2001). However, that study only concentrated on the difference in the techniques used by the two examiners, and paired t-tests were performed, and did not take into account the reliability and agreement between the measurements. A recent study by Holmes et al. (2008) has investigated the inter-examiner agreement on 23 patients with sixth nerve palsy. They performed the ICC and Bland-Altman analyses and found the ICC to be excellent and the 95% LOA to be of 10.2PD and 9.2PD for distance and near cover test measurements, respectively.

Our findings for horizontal deviation, which showed ICC values of 0.99 for cover test at distance and at near, seem to be consistent with the findings of Holmes et al. (2008). However, our analysis on the vertical component of the deviation has revealed poor to moderate agreement at distance measurement (ICC for E1-E2-E3=0.74; ICC for E1-E2=0.86; ICC for E1-E3=-0.50; ICC for E2-E3=0.47; ICC for E1-average E2/E3=0.82). The reason for this is not clear, but it may be attributed to the small sample size in this study for the vertical component (n=3). It seems possible that these results are also due to measurement techniques/errors in stacking the prisms to neutralise the horizontal and vertical deviation. Interestingly, negative ICC was observed for measurements between E1 and E3 for vertical deviation. There is very little literature on interpreting a negative ICC effect on agreement analysis. Some authors suggest that negative ICC could indicate that there may be more variation observed in the set of data than is expected by chance (Taylor 2009). In any event,

a direct comparison to Holmes et al. (2008) findings cannot be made as their measurements only involved horizontal deviation.

Our Bland-Altman analyses revealed mean differences of less than 1PD for all pairs of examiners. The 95% LOA between paired measurements showed a wider range compared to the results obtained from the non-strabismic subjects in this study. The results, which vary between ±4 to ±7PD for distance and ±3 to ±6PD for near, are comparable to those reported by Holmes et al. (2008). The findings could be due to factors such as the distribution and degree of deviation noted on the strabismic subjects varies widely, compared to the non-strabismic subjects. Moreover, the measurements were performed using loose prism with increment of 5 PD for deviation more than 20PD, which could also contribute to the wide LOA observed in the measurement. We also noticed that the 95% LOA for the vertical component were narrower than the horizontal component, both at distance (±3PD) and at near (±4PD). It is also interesting to note that the difference between methods tend to get larger as the average measurements increase especially on more exophoric measurements, although the findings were only noted on the horizontal deviation measurements. It could be due to the fact that the occurrence of vertical deviation in the sampled subjects were low compared to the horizontal deviation.

Nevertheless, caution must be applied, as the findings for the cover test results on the strabismic subjects might not be transferable to the whole population because of the relatively small sample size (N=20). Moreover, the experiment only involved cooperative adult subjects with various type of strabismus. The findings could be different if data from child subjects were included. Additionally, the current study was not specifically designed to evaluate intra-examiner agreement of the cover test measurements. It was initially thought that the results would not be truly masked as the orthoptists would be most likely to remember the previous measurements as most of the participants were the clinical patients attending the orthoptic clinic.

5.4   Overall conclusions

Although previous studies of the degree of agreement of the cover test measurements have thus far have been limited to non-strabismic subjects, we demonstrated that good to excellent agreement could be obtained with strabismic subjects.

Overall, the results of the studies reported here showed that the inter-examiner agreement on the cover test results at distance and at near:

- did not differ significantly for either non-strabismic or strabismic subjects
- demonstrated that the cover test performed by the author is not significantly different to, and has good agreement with, the orthoptists. Therefore, it is possible to rely on the author's cover test measurements for the next step of the research.

CHAPTER VI

THE COVER TEST MEASUREMENT PERFORMED WITH THE TOBII X120 ON NON-STRABISMIC AND STRABISMIC SUBJECTS

6.1 Cover test examination performed with the Tobii X120

We have shown that the inter-examiner agreements of cover test results were excellent for both non-strabismic and strabismic subjects (see Chapter V). The aim of this study was to use the Tobii X120, in conjunction with the conventional cover test performed by the author, to measure the angle of deviation. The cover test performed with the Tobii X120 was entirely objective, in which little cooperation and input was needed from the subjects. Technically, the eye tracker can measure the position of the eye, at a frequency of 120Hz, without the need for the examiner to observe the state of the eye dissociation. The fact that the cover test was performed using the infrared transparent occluder made it possible to record the eye movement behind the occluder simultaneously during the test. This chapter will concentrate on a series of examinations of groups of non-strabismic subjects as detailed below:

1. Analysis of eye movement recordings performed using the infrared eye tracker, the Tobii X120

2. The cover test protocols: unilateral and alternating cover test

    a. Experiment 1: Occlusion time

    b. Experiment 2: Phoria variation over time

3. Comparison of the cover test measurements performed with the alternating prism cover test and the Tobii X120

6.2   Analysis of eye movement recordings performed using the Tobii X120 eye tracker

6.2.1   Determination of the optimum occlusion time

For each cover test experiment performed using the Tobii X120, 'event logs' were created and defined to identify the start and the end of each occlusion time before raw data were exported to MATLAB programme for further analysis (see Table 6.1). These 'event logs', created using the Coding Scheme feature in the Tobii Studio™ programme, were assigned to individual keyboard keys. To mark the start and end of each occlusion, the keyboard keys were manually logged by the author during the playback of the recording. The accuracy of the manual log can be ascertained by looking at the pupil diameter profile of each Tobii X120's output recording. For example, in Figure 6.1(B), whenever the occluder is held in front of one eye, the pupil diameter of that eye will increase rapidly as the retinal illumination is reduced, and the diameter will decrease after the occluder is taken out, thus giving an indication of the accuracy with which the occlusion is measured.

Table 6.1   Description of the event logs used to mark the occlusion start and end time during the cover test experiment.

Description		Event log
Unilateral cover test	Start of occlusion on right eye	Occ IN_RE
	End of occlusion on right eye	Occ OUT_RE
	Start of occlusion on left eye	Occ IN_LE
	End of occlusion on left eye	Occ OUT_LE
Alternate cover test	Occlude right eye	Alt_RE
	Occlude left eye	Alt_LE
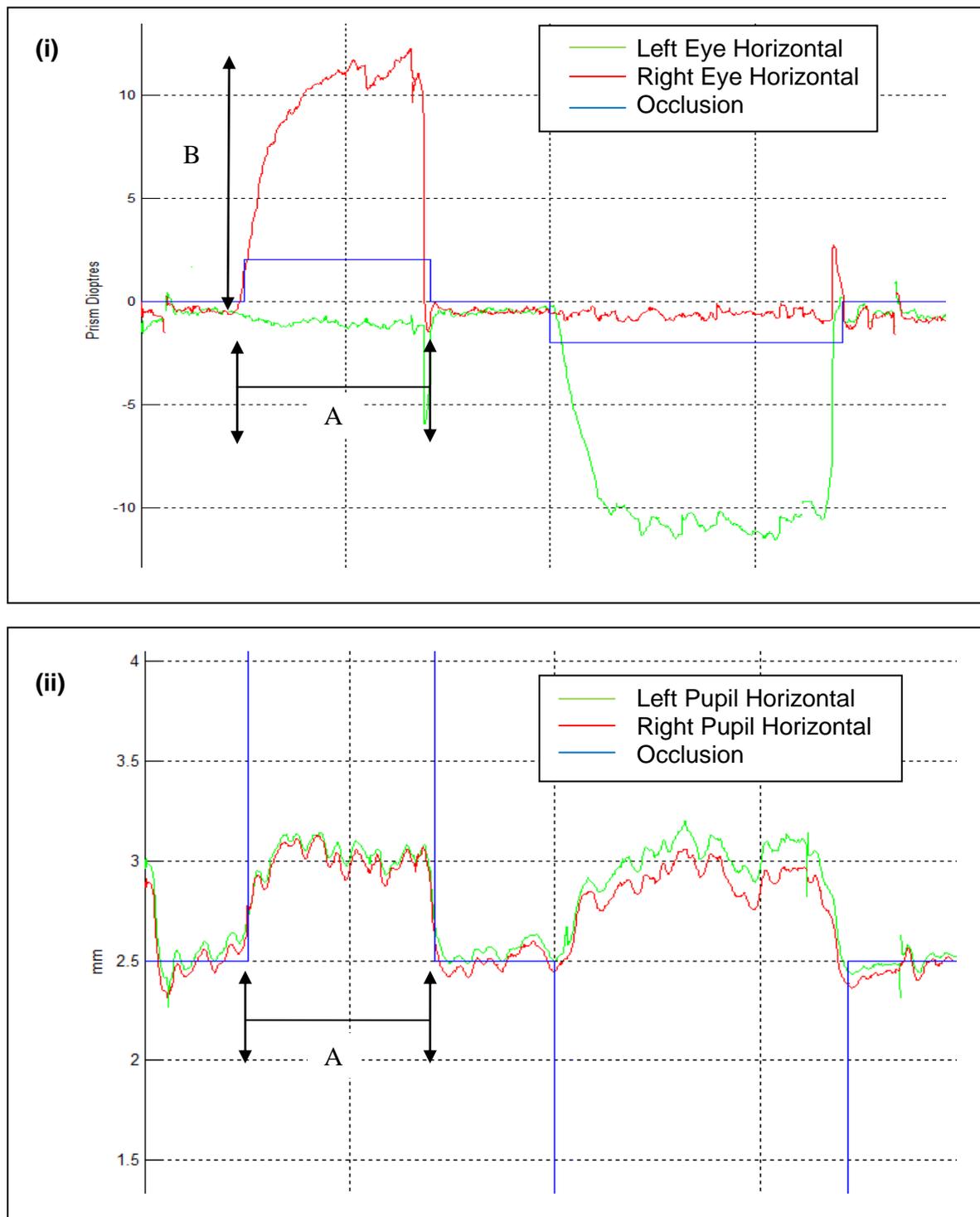
Figure 6.1   **(i)** Upper figure shows a typical eye movement recording analysis using a MATLAB programme showing the parameter extracted during the 10s unilateral cover test on subject SA. 'A' represents the start and end of occlusion time and 'B' shows the maximum phoria amplitude during the cover test. **(ii)** Lower figure shows the accuracy of the event log can be confirmed by looking at the pupil constriction and dilation during the occlusion time.

6.2.2   Determination of phoria amplitudes

Eye movement recordings of the cover test performed using the Tobii X120 were analysed using a MATLAB programme, especially written for this study by our collaborator, Professor Chris Harris (Plymouth University). A graphical presentation of the data generated by the MATLAB programme consists of continuous eye position and occlusion time traces that have been colour coded for ease of interpretation. Figure 6.1 shows a typical output of this programme, in which right and left eyes are identified by red and green lines, respectively. The occlusion times are coded as blue traces. Upward traces on the output graph denote rightward movements and downward traces for leftward movements. The MATLAB programme automatically marked the 'event logs' according to which eye they were assigned to. For example, if 'Occ IN_RE' and 'Occ OUT_RE' were logged, the MATLAB programme will assign the occlusion traces in upwards traces (right eye), as presented in Figure 6.1 (A).

The maximum phoria amplitude (B) was determined by looking at the position of the eye at the beginning of a saccade generated when the eye was occluded during a cover test, to its position at fixation, i.e. the end of a saccade. In the Tobii Studio™ programme, saccades were separated from fixations using algorithms that detect abrupt changes in the means of the eye movement sample (Tobii Studio™ 2.2 User Manual 2010). Phoria amplitudes observed during each cover test were extracted (by averaging the amplitude peaks observed during the occlusion period) and recorded in a Microsoft Excel spread sheet for statistical analysis using Excel and SPSS software.

6.2.3   Experiment 1: The effect of occlusion time on the phoria measurements

6.2.3.1 Objective

The aim of this experiment was to determine the time of occlusion during unilateral cover test that is sufficient to reveal the maximum phoria amplitude.

6.2.3.2 Methods

Five visually asymptomatic subjects (age range: 20-30 years old) participated in this study. All subjects had at least 6/6 visual acuity in both eyes with a stereo acuity of at least 40 seconds of arc using the Titmus Fly test. None of the subjects had any binocular vision problems. The experiment follows the calibration protocol as detailed in Chapter III. Subjects were instructed to fixate the target on the screen during the course of the examination while the examiner performed the cover test using a various occlusion times: 2, 5, 10 and 30s at 40cm. The first test was performed with the left eye covered for 2s and uncovered (fixation with both eyes) for 2s to allow the eyes to realign before the right eye was then occluded for 2s. The tests for an occlusion time of 5, 10 and 30s followed the same protocol as mentioned above with the exception that the binocular fixation period was longer (5s) to allow the eyes to regain binocular fusion. The test for each occlusion time was separated by at least five minutes between sessions to minimise the possibilities of breaking the subject's phoria state or inducing a fatigue effect.

The distribution of the phoria amplitude in each eye was tested using the Shapiro-Wilk test. The phoria amplitudes for each pair of eyes were also compared for each session, either using a paired t-test or a Wilcoxon signed rank test, depending on the data distribution. In the event of no significant difference between the two eyes, data for right and left eyes were averaged and an ANOVA or a Friedman analysis was performed to compare each mean/mean rank of the difference of occlusion time on the phoria amplitude.

6.2.3.3 Results

The phoria amplitudes were normally distributed (p>0.05). The amplitudes of the phoria, as measured after 2, 5, 10 and 30s occlusion time on each eye are presented in Table 6.2. A paired t-test performed on the phoria amplitude for each subject revealed that there were no differences detected between the right and left eye for each occlusion time, where a 2s cover test revealed a p-value of 0.70, 5s cover test (p=0.61), 10s cover test (p=0.13) and 30s cover test (p=0.96). The average of the phoria amplitudes for every subject were calculated and plotted against occlusion time (Figure 6.2). ANOVA analysis on the average phoria amplitudes revealed that the means differ significantly to each other with F-value=7.34, p=0.003. It is apparent from Figure 6.2 that phoria amplitude for all subjects increased rapidly from 2 s to 10s occlusion time. Phoria amplitude of two subjects reached a plateau after 10s, while the other three subjects exhibited a more gradual increase in phoria amplitude. The mean increase in phoria amplitude from 2 to 30s occlusion time was -1.90PD.

Table 6.2 Phoria amplitude in both eyes for all subjects during various occlusion times.

Subject	Occlusion time (seconds)							
	2		5		10		30	
	R (PD)	L (PD)	R (PD)	L (PD)	R (PD)	L (PD)	R (PD)	L (PD)
1	-1.4	-1.4	-2	-1.5	-2.6	-2.8	-2.6	-3.7
2	-0.5	-0.7	-1.1	-1.1	-2.1	-2.3	-2.1	-2.3
3	-0.8	-0.8	-1.7	-1.8	-2.0	-2.5	-2.5	-2.5
4	-2.5	-2.1	-2.8	-2.1	-3.2	-3.1	-5.4	-4.0
5	-1.5	-1.5	-1.5	-2.0	-3.5	-3.4	-3.5	-3.5

R = Right eye occluded; L = Left eye occluded

	Average 2 seconds	Average 5 seconds	Average 10 seconds	Average 30 seconds
Subject 1	-1.4	-1.8	-2.7	-3.2
Subject 2	-0.6	-1.1	-2.2	-2.2
Subject 3	-0.8	-1.8	-2.3	-2.5
Subject 4	-2.3	-2.5	-3.2	-4.7
Subject 5	-1.5	-1.8	-3.5	-3.5
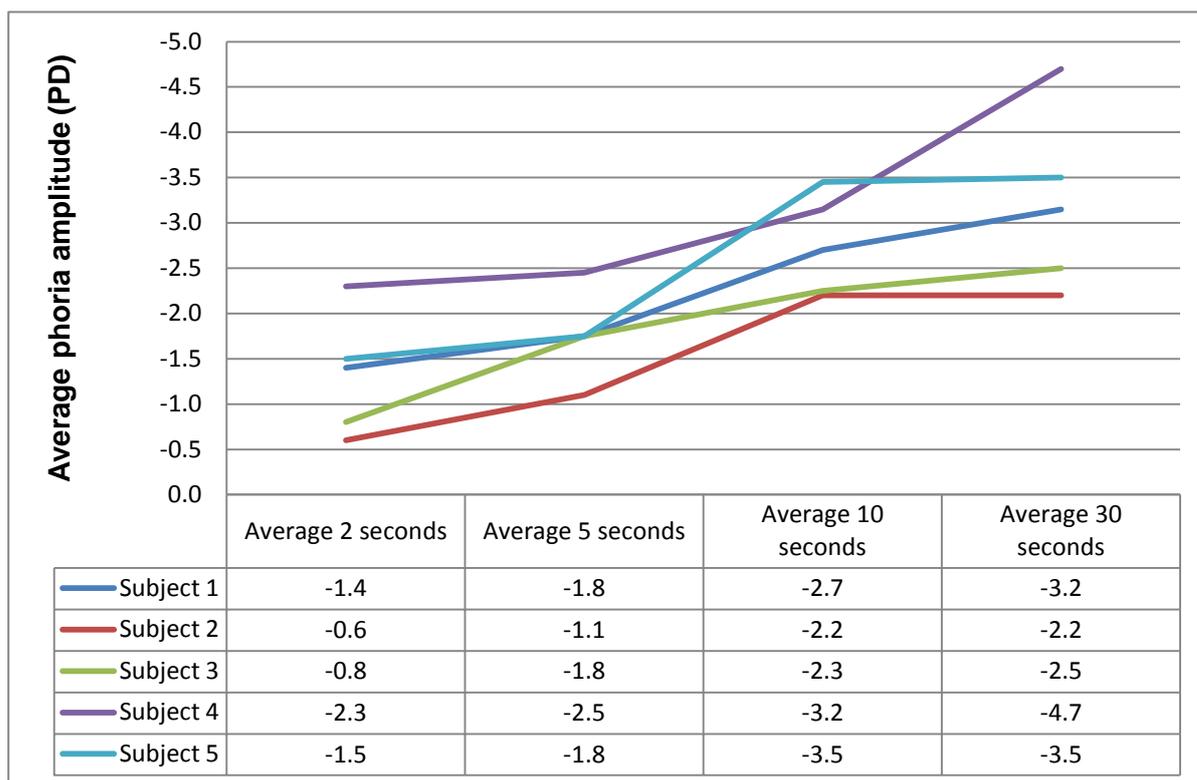
Figure 6.2 Average phoria amplitude for all subjects as measured after 2, 5, 10 and 30s of occlusion.

6.2.3.4 Discussion

It was always assumed that phoria amplitude between the right and left eye are the same during a cover test. This assumption held true in this experiment where the analysis performed using a paired t-test revealed no significant differences between the two eyes (p>0.05).

The 2s occlusion time has been considered as standard when measuring phoria during a unilateral cover test. It was suggested that 2s will create a brief disruption to binocular vision, in which the vergence feedback loop was 'open'. The fast fusional vergence was stimulated and the output was then fed into the slow fusional vergence system, which made the covered eye move to its heterophoric position. However, it is often noted that the phoria amplitude during this brief dissociation time is not stable, as it was only fast fusional

vergence that decayed rapidly, with minimal effect on the slow fusional vergence system (Cooper 1992). Peli and McCormack (1983) reported that the eyes might take up to 8s to reach equilibrium/balance during the cover test. Barnard and Thompson (1995) also reported a significant difference between phoria amplitude measured during 2s and 10s of dissociation time. They suggested that at least 5s was required to reveal the complete phoria amplitude. They concluded that the conventional 2s occlusion time was not sufficient to elicit maximum phoria amplitude due to the prolonged decay of slow fusional vergence. Rosenfield et al. (1997) suggested that approximately 25 minutes of dissociation time is required to eliminate slow fusional vergence and hence, provide more accurate phoria measurements. This study by Rosenfield et al. (1997) was in agreement with previous work by Marlow (1920), who had also demonstrated a much longer occlusion time of up to 27 days was required to fully eliminate the slow fusional vergence component in measuring phoria.

In our study, we found that the phoria amplitude varies with occlusion time. All subjects showed an increase in phoria amplitude with two subjects reaching an equilibrium state after 10s of occlusion time while the other three subjects still exhibiting a slower increase in phoria amplitude after 10s.

However, this study was limited due to its small sample size and the fact that only studied subjects with low exophoria amplitude were investigated. Although there was still an increase in phoria amplitude at 30s, it was thought that implementing a 30s occlusion time would constitute an impractically long examination time. Accordingly, we decided to compare 2s to 10s occlusion times for the unilateral cover test. However, it was interesting to note that the phoria at 30s occlusion times appears to be approximately doubled the amount of phoria measured at the initial 5s in each subject.

6.2.4   Experiment 2: Measurements of phoria variation over time using the Tobii X120

6.2.4.1 Objective

We investigated whether phoria amplitudes and recovery times varied during the day in a group of non-strabismic subjects. The objective of this experiment was to give us an indication of whether if it is important to specify the time of day in performing the cover test examination. The experiment would also determine if visual fatigue at the end of working day had an effect on a subject's phoria level.

A previous study by Yekta et al. (1987) demonstrated that there was a statistically significant difference between mean dissociated phoria measured at the beginning and at the end of a normal working day (p<0.001) on 84 non-strabismic subjects. They reported a mean increase in dissociated phoria of 0.79PD from -4.38 ± 2.89PD at the start of the working day to -5.17 ± 3.10PD at the end of the working day. However, 43% of the subjects had the same phoria level while 8% had decreased phoria at the end of the day.

6.2.4.2 Methods

Ten subjects were recruited for this experiment. The subjects were between 20 to 29 years old, and all had a visual acuity of at least 6/6 in both eyes and a stereoacuity of at least 40 seconds of arc. None of the subjects had amblyopia or strabismus. Three subjects were myopic (mean spherical equivalent=-2.75 ± 0.50DS) and wore their normal correction (contact lenses) during the examination.

The alternating prism cover tests were performed first, followed by the alternating cover test in front of the eye tracker at 40cm. On the Monday and Friday of the same week, the examinations were conducted between 9.30am to 10.30am for the morning session and between 4.00am to 5.00am for the evening session. The phoria amplitudes from the

alternating prism cover test and from the eye movement recording were extracted and analysed using Excel and SPSS software. Data distributions were tested using the Shapiro-Wilk test before appropriate comparison between morning and evening sessions and between early and end of the week sessions were performed on all subjects using a paired t-test or a Wilcoxon Signed rank test.

Additional validity statistics were applied to the data to test for the agreement between the two methods. The analysis was performed by determining the mean difference (bias) and 95% limits of agreement (LOA) as described by Bland and Altman (1986).

6.2.4.3 Results

The Shapiro-Wilk test showed that the data were normally distributed (p>0.05). Mean phoria amplitudes measured from the alternating prism cover test and extracted from the Tobii X120 were presented in Table 6.3, with the raw data plotted in Figure 6.3. Generally, the mean phoria amplitudes in the morning sessions were lower than in the evening sessions. For the prism cover test, mean phoria amplitude was -2.60 ± 1.90PD compared to -3.00 ± 1.94PD at the start of the week (Monday), and the mean phoria amplitude on Friday morning was -2.80 ± 1.69PD compared to -3.60 ± 2.07PD on Friday evening. The mean phoria amplitudes extracted from the eye movement recordings performed by the Tobii X120 showed mean phoria amplitudes of -2.55 ± 1.62PD for the morning session and -2.75 ± 1.55PD for the evening session on Monday. The mean phoria amplitudes during sessions on Friday were   -3.30 ± 1.93PD (morning session) and -3.50 ± 2.21PD (evening session).

Table 6.3 The mean phoria measurements from conventional alternating prism cover tests and eye movement recordings performed with the Tobii X120.

Subject	Monday morning		Monday evening		Friday morning		Friday evening	
	PCT	Tobii X120	PCT	Tobii X120	PCT	Tobii X120	PCT	Tobii X120
Mean phoria (PD)	-2.60	-2.55	-3.00	-2.75	-2.80	-3.30	-3.60	-3.50
Standard deviation (PD)	1.90	1.62	1.94	1.55	1.69	1.93	2.07	2.21

*PCT=prism cover test
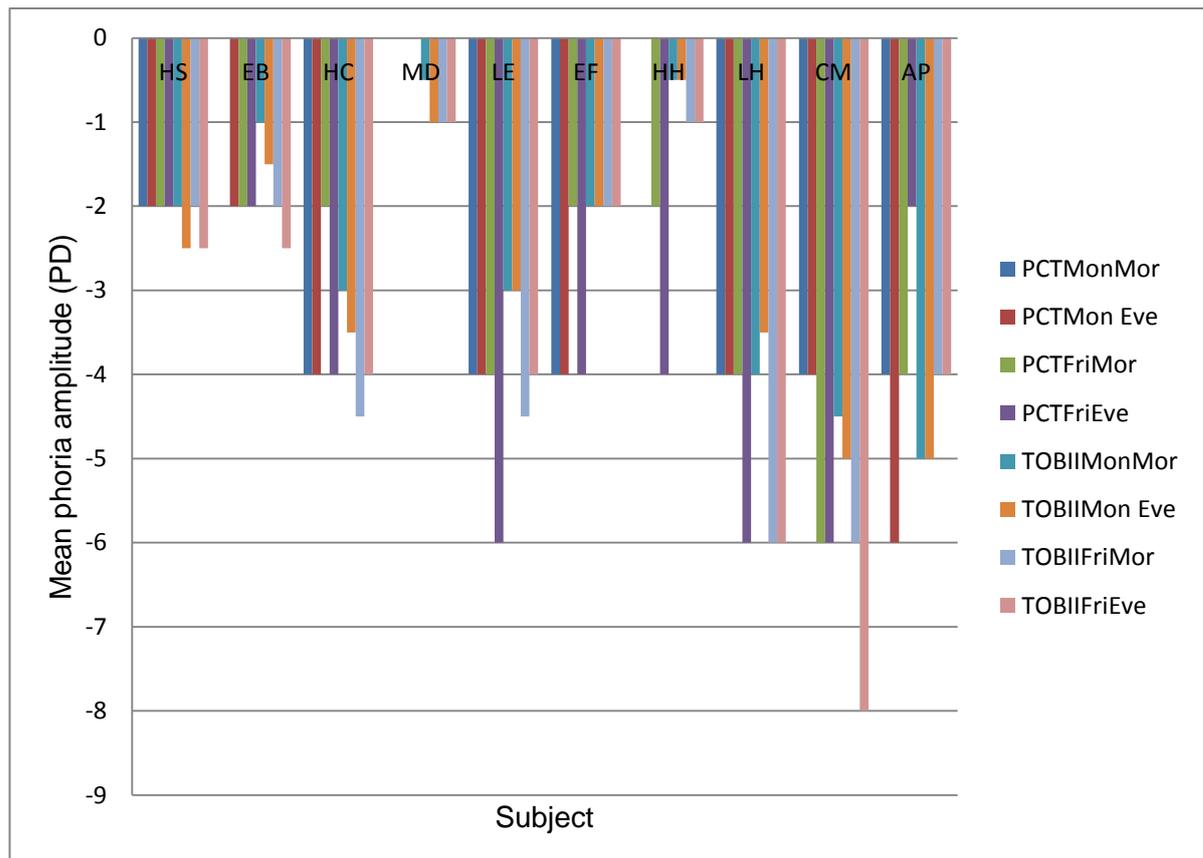
Figure 6.3 Bar charts showing the distribution of mean phoria amplitude measured using prism cover tests and eye movement recordings from the Tobii X120 for all subjects across sessions.

Table 6.4 The paired t-test findings between the alternating prism cover test and the cover test measurements using the Tobii X120 (N=10).

The alternating prism cover test and the cover test using the Tobii X120	Prism cover test		Cover test using the Tobii X120	
	t-value	p-value	t-value	p-value
Morning-evening session				
• **Monday**	1.50	0.17	-1.81	0.10
• **Friday**	1.81	0.10	-0.89	0.40
Early-end of week session				
• **Mornings**	-0.43	0.68	-2.58	0.03*
• **Evenings**	-0.90	0.39	-1.97	0.08

*significant p<0.05

The paired t-tests were conducted to compare the alternating prism cover test measurements and the results are presented in Table 6.4. The measurements were not significantly different between morning and evening sessions, either on Monday (t=-1.50, p=0.17) or on Friday (t=-1.81, p=0.10). Comparison between early and end of the week sessions, between Monday-Friday morning session (mean=-0.20 ± 1.48PD; t=-0.43, p=0.68) and Monday-Friday evening session (mean=-0.60 ± 2.12PD; t=-0.90, p=0.39) were also not significant.

The paired t-tests performed to compare the cover test using the Tobii X120 also showed no significant difference between morning-evening sessions. Results for morning-evening sessions for Monday (mean=-0.20 ± 0.35PD; t=-1.81, p=0.10) and Friday (mean=-0.20 ± 0.71PD; t=-0.89, p=0.40), respectively. Comparisons between early-end of the week sessions were also performed between Monday-Friday morning session (mean=-0.75 ± 0.92PD; t=-2.58, p=0.03) and Monday-Friday evening session (mean=-0.75 ± 1.21PD; t=-1.96, p=0.08). The results revealed a significant finding for Monday-Friday morning session only.

A Bland-Altman analysis was used to assess the level of agreement between the alternating prism cover test and the cover test using the Tobii X120 results. Analysis indicates that the 95% limits of agreement (LOA) between the two methods ranged from -1.98 to 1.88PD (Monday morning), -2.17 to 1.67PD (Monday evening), -1.57 to 2.57PD (Friday Morning) and -3.26 to 3.46PD (Friday evening). The mean differences were equal or less than 0.50PD for all sessions. Table 6.5 summaries the agreement of the cove tests findings using the Bland and Altman analysis.

Table 6.5   The degree of agreement between the alternating prism cover test and the cover test measurements using the Tobii X120 (N=10).

The alternating prism cover test and the cover test using the Tobii X120	Bland & Altman	
	Mean difference (PD)	**Limits of Agreement (PD)**
Monday morning	-0.05	-1.98 to 1.88
Monday evening	-0.25	-2.17 to 1.67
Friday morning	0.50	-1.57 to 2.57
Friday evening	0.10	-3.26 to 3.46

6.2.4.4 Discussion

Generally, the mean phoria findings measured using both techniques for all subjects increased towards the end of the week. The mean phoria recorded for alternating prism cover test findings showed a slightly lower value than that of the Tobii X120, except for Friday evening session. This differences could be attributed to the protocols of the study, in which the alternating prism cover test is always performed first prior to the cover test assessment with the eye tracker. Randomisation of tests may eliminate the problem to exclude possibility of fatigue in vergence system. However, we did a random check to some of the patients by performing the alternating prism cover test before and after the assessment with the eye tracker. It is unlikely that randomisation could affect the findings as

the alternating prism cover test performed did not show any increment. Moreover, the differences recorded for every session are less than 1PD.

The paired t-tests performed on both techniques between morning and evening session and between early and end of the week session also showed insignificant findings, except for phoria findings during Monday-Friday (morning) session using the Tobii X120. The Bland and Altman analysis showed good agreement between the prism cover tests and cover tests performed using the Tobii X120 on all session. The two methods showed consistent bias of ≤0.50PD as shown by the mean differences for all session. The findings are not clinically significant as 2PD is considered to be the smallest eye movement that can be detected when performing the cover test (Fogt et al. 2000; Romano and von Noorden 1971). The LOA was narrower when measured on Monday session (-2.17-1.88PD) compared to Friday session (3.26-3.46PD), which also could be due to the protocol of the study. The small sample size (N=10) limits us to generalise the reason, although the differences could be due to fatigue effect. Larger sample size is needed to confirm the findings.

In conclusion, the alternating prism cover test and the cover using the Tobii X120 can be performed at any time during the week as time variation has little effect to the findings reported.

6.3   The cover test protocols

The unilateral and the alternating cover tests were performed in front of the eye tracker using the setup detailed in Chapter III. After a successful calibration process, the subject was seated comfortably in front of the monitor screen. A cover test was performed using an occluder while the subject fixated a cross fixation target on the monitor screen, which subtends 0.3^o when viewed at 40cm (0.2cm in height and 0.2cm in width). The occluder used is opaque but allows infrared light to pass through the material, hence, enabling us to also monitor the behaviour of the eye behind the occluder. This will provide valuable insights into the eye movements' dynamics during the cover test. The occlusion was performed manually and the occlusion periods for the cover test procedure were based on a digital timer. Video recording was also performed simultaneously during the cover test experiment to 'event log' the occlusion time (see Section 6.2.1).

6.3.1   Unilateral cover test

The unilateral cover test was performed using protocols detailed in Table 6.6. We compared 2, 5, 10 and 30s occlusion period on a group of subjects (see section 6.2) and decided to compare the conventional clinical 2s time for occlusion with 10s for our unilateral cover test routine. Barnard and Thompson (1995) had found statistically significant differences in the phoria amplitudes when the cover test was performed with occlusion times of 2s and 10s. Their study suggested that the conventional 2s occlusion time was not long enough to reveal full phoria amplitude and proposed an occlusion time of at least 5s.

The procedure began with the subject fixing on the fixation target for 4s before the cover was held first in front of the left eye for 2s. After 2s, the subject fixated binocularly on the fixation target for another 2s and the cover was then held in front of the right eye. This procedure was repeated again for the left and rights eye before then covering the left eye for

a 10s occlusion time. During the 10s cover test, binocular fixation times were increased to 5s to allow the eyes to regain fixation. The procedure ended with binocular fixation for another 4s, allowing the subject to resume their baseline fixation. In this protocol, the occluder was always held over the left eye first to standardise the procedure. The subject's dominant eye was not tested prior to examination.

Table 6.6   Diagram represents unilateral cover test protocol.

Covered	Unilateral cover test (occlusion time (s))								
eye		2	2	2	2	10	10	10	10
Left	FIXATE (4s)		FIXATE (2s)		FIXATE (2s)		FIXATE (2s)		FIXATE (2s)		FIXATE (5s)		FIXATE (5s)		FIXATE (5s)		FIXATE (4s)
Right									

6.3.2   Alternating cover test

The alternating cover test protocol was performed for five times. The procedure was started by instructing the subject to fixate the fixation point for 4s before the occluder was alternately moved to cover the left and then the right eye for 2s for each cover period. Table 6.7 illustrates the process involved in this alternating cover test.

Table 6.7   Diagram represents alternating cover test protocol

Covered	Alternating cover test (occlusion time (s))										
eye		2	2	2	2	2	2	2	2	2	2
Left	FIXATE (4s)											FIXATE (4s)
Right											

6.4 Comparison of the alternating prism cover test and the alternating cover test performed using the Skalar IRIS 6500 and the Tobii X120 on non-strabismic subjects

6.4.1 Objective

This study was carried out to evaluate the agreement between the cover test performed using the Skalar IRIS 6500 and the Tobii X120 on a small group of non-strabismic subjects. The comparison is important to establish if the Tobii X120 could produce reliable findings as that of the Skalar IRIS 6500 for oculomotor assessments.

6.4.2 Methods

Five subjects were recruited for this experiment. The subjects were between 20 to 30 years old (mean age= 23.67 ± 4.84 years). All had a visual acuity of at least 6/6 in both eyes and a stereoacuity of at least 40 seconds of arc. None of the subjects had amblyopia or strabismus. Two subjects were emmetropic and three subjects were myopic (mean spherical equivalent=-2.00 ± 0.75DS) and wore their spectacles during examination.

The examiner performed an alternating prism cover test prior to the cover test measurement using the infrared eye trackers, the Skalar IRIS and the Tobii X120. The cover test was performed at 40cm (near measurement) and 3m (distance measurement). The protocols for alternating cover test as detailed in section 6.3.2 were carried out in front of the eye tracker using an infrared transparent occluder. The study was performed after consent had been obtained from all subjects. We performed statistical analysis to check for normality of data distribution using the Shapiro-Wilk test. We compared the alternating prism cover test and the alternating cover test results with the eye tracker using either an ANOVA test (normally distributed data) or a Friedman test (not-normally distributed data). We also performed the

Intraclass Correlation Coefficient (ICC) analysis to assess the level of agreement between the alternating prism cover test and the alternating cover test using the eye trackers.

6.4.3 Results

The Shapiro-Wilk test revealed that the data are normally distributed (p>0.05). Table 6.8 presents the phoria findings at distance and at near for the alternating prism cover test and the alternating cover test performed using the Tobii X120 and the Skalar IRIS. The mean phoria findings for the cover test at distance for prism cover test, the alternating cover test using the Tobii X120 and the Skalar IRIS 6500 were -1.20 ± 1.79PD, -0.99 ± 0.46PD and -0.77 ± 0.46PD, respectively. Near cover test results were -2.33 ± 2.94PD (the prism cover test), -2.05 ± 1.99PD (the alternating cover test using the Tobii X120) and -2.04 ± 2.04PD (the alternating cover test using the Tobii X120). There were no statistically significant differences between group means as determined by one-way ANOVA test for distance cover test (F=0.33, p=0.73) and near cover test (F=0.19, p=0.82). The Intraclass Correlation Coefficient analysis showed good degree of agreement among the three techniques for distance (ICC=0.72) and near cover test measurements (ICC=0.95) (Table 6.9).

Table 6.8   The ANOVA test detailing the mean and p-values for the cover test measurements results between the prism cover test, the alternating cover test using the Tobii X120 and the Skalar IRIS 6500 at distance and at near (N=5).

Cover test	Mean (PD)			F-value	p-value
	Prism cover test	**Tobii X120**	**Skalar IRIS 6500**		
Distance	-1.20 ± 1.79	-0.99 ± 0.46	-0.77 ± 0.46	0.33	0.19
Near	-2.33 ± 2.94	-2.05 ± 1.99	-2.04 ± 2.04	0.19	0.68

*Significant; p-value<0.05

Table 6.9   Degree of agreement using the Intraclass Correlation Coefficient between the prism cover test, the alternating cover test using the Tobii X120 and the Skalar IRIS 6500, at distance and at near (N=5).

Cover test	Intraclass correlation Coefficient (ICC)	
	ICC	**95% Confidence Interval**
Distance	0.72	-0.59 to 0.97
Near	0.95	0.79 to 0.99

6.4.4 Discussion

The range of phoria tested for this study was smaller and all subjects were more exophoric at near compared to distance cover test. The mean phoria recorded at distance and at near were higher for the alternating prism cover test compared to the alternating cover test using both eye trackers. The differences could be attributed to the increment of prism strength used during the alternating prism cover test as the measurements using the eye trackers did not involve any use of prism bar. The ANOVA analysis revealed that the means are not significantly different between the three methods for cover test measurements at distance (F=0.33, p=0.19) and at near (F=0.19, p=0.68). The ICC analysis also showed moderate to excellent inter-examiner agreement for cover test measurement at distance (ICC=0.72) and at near (ICC=0.94).

The results from this study showed comparable findings for all three methods. Although each eye tracker employs different techniques to detect eye movements (see Chapter III), the statistics analysis revealed that the measurements were approximately equal and less variation was seen for the cover test measurements by the Tobii X120.

6.5   Comparison of the unilateral cover test and alternating cover test performed using the Tobii X120 on non-strabismic subjects

6.5.1   Objective

We have shown that time factors (morning or evening) do not have any significant effect on the measurements of phoria in our selected group of subjects. Therefore, the data collection can be performed at any time during the week. We also established that the cover test performed using the Skalar IRIS 6500 and the Tobii X120 was comparable. This section will concentrate on the results of the cover test performed on a larger group of subjects to assess the agreement of cover test results performed manually and using the Tobii X120 eye tracker.

6.5.2   Methods

Thirty subjects, aged between 20 to 38 years (mean = 25.17 years), participated in this study. All subjects had normal binocular vision and had at least 6/6 or better visual acuity with their current prescriptions. In this study, ten subjects were tested while wearing their spectacles (mean spherical equivalent=-2.75 ± 1.31DS), and two subjects wore their soft contact lenses (mean spherical equivalent=-2.81 ± 0.24DS). The remaining eighteen subjects were emmetropic and did not wear any spectacles or contact lenses.

The examiner performed a alternating prism cover test prior to the cover test measurement using the infrared eye tracker, the Tobii X120. The cover test was performed at 40cm (near measurement) and 3m (distance measurement). The protocols detailed in section 6.4 were carried out in front of the eye tracker using an infrared transparent occluder. The unilateral cover test was performed first and followed by an alternating cover test. The study was performed after consent had been obtained from all subjects. We performed statistical analysis to check for normality of data distribution using the Shapiro-Wilk test. We compared

the unilateral cover test of 2s and 10s occlusion times and the alternating prism cover test and alternating cover test results with the eye tracker using either the paired t-test (normally distributed data) or the Wilcoxon Signed Rank test (not-normally distributed data). We also performed a Bland and Altman analysis to assess the level of agreement between the two methods, the alternating cover test using the Tobii X120 to the established prism cover test findings. Additional statistical analyses were also performed to evaluate if the level of dissociation between unilateral 10s occlusion time and alternating cover test have any significant difference on the measured phoria.

6.5.3 Results

The Shapiro-Wilk test confirms that the data are normally distributed (p>0.05). The results obtained from the unilateral cover test of 2s and 10s occlusion times can be compared in Table 6.10**.** It is apparent from the table that phoria measured at distance were similar for both occlusion times. However, the near unilateral cover test assessment showed a slight increment of 1.40PD exophoria when comparing the 2s occlusion time to 10s occlusion time. Further analysis using a paired t-test revealed that the measurements did not differ significantly at distance (t=-0.21, p=0.84) but showed a significant difference at near (t=-4.45, p<0.05), in which the phoria measured were more exophoric.

Table 6.10   Comparison of phoria findings from unilateral cover test of 2s and 10s occlusion times.

Cover test	2s occlusion time (mean ± SD) (PD)	10s occlusion time (mean ± SD) (PD)	Paired t-test
Distance	-1.05 ± 0.96	-1.01 ± 1.41	t=-0.21, p=0.84
Near	-2.12 ± 2.61	-3.52 ± 3.10	t=-4.45, p<0.05*

*statistically significant p<0.05

A comparison between the alternating prism cover test and alternate cover test performed with the Tobii X120 was also carried out using paired t-tests and the results are presented in Table 6.10. The alternating prism cover test revealed a mean of -1.67 ± 1.75PD for distance cover test and a -3.33 ± 2.75PD for near cover test. The cover test assessment using the Tobii X120 showed a -1.18 ± 1.24PD and a -3.55 ± 3.15PD for distance and near cover tests, respectively. As shown in Table 6.11, the mean phoria was higher for the distance alternating prism cover test compared to the alternating cover test performed using the Tobii X120 for distance measurement. However, the mean phoria for alternating prism cover test at near was lower than the alternating cover test performed using the Tobii X120. It is also apparent from the table that the ranges of phoria findings at distance and at near using the eye tracker are wider than the alternating prism cover test measurements (Figure 6.4).

Bland-Altman analysis was also performed to test the degree of agreement between the two methods of cover test measurements. For cover test at distance, the 95% limits of agreement ranged from -2.90 to 1.92PD with a mean difference of -0.49PD. Near cover test showed a 95% limits of agreement ranged from -3.13 to 3.55 and a mean difference of 0.21PD.

A paired t-test and a Bland and Altman test were also performed to determine if there is any significance difference between unilateral 10s occlusion time and alternating cover test. The findings are summarised in Table 6.12 and Figure 6.5. Paired t-tests revealed non significance differences between measurements at distance (t=1.09, p=0.28) and at near (t=-0.11, p=0.91). Bland and Altman analysis showed that a mean difference of 0.17 (95% LOA=-1.47 to 1.80) for distance cover test measurement and a mean of 0.21 with the 95% LOA of -2.11 to 2.16 for near cover test measurement.

Table 6.11   Comparison of the phoria findings between alternating prism cover test and the alternating cover test performed with the Tobii X120 using paired t-tests and Bland and Altman analysis on non-strabismic subjects (N=30).

Cover test	Alternating prism cover test (PD)	Alternate cover test using the Tobii X120 (PD)	Paired t-test (PD)	Bland and Altman (PD)
Distance				
• **Mean**	-1.67	-1.18	t=2.18	Mean difference=-0.49
• **SD**	1.75	1.24	p=0.04*	95% LOA=-2.90 to 1.92
• **Range**	-4.00 to+2.00	-3.75 to+3.75		
Near				
• **Mean**	-3.33	-3.55	t=-0.68	Mean difference=0.21
• **SD**	2.75	3.15	p=0.50	95% LOA=-3.13 to 3.55
• **Range**	-8.00 to +2.00	-11.40 to +1.05		

*statistically significant p<0.05
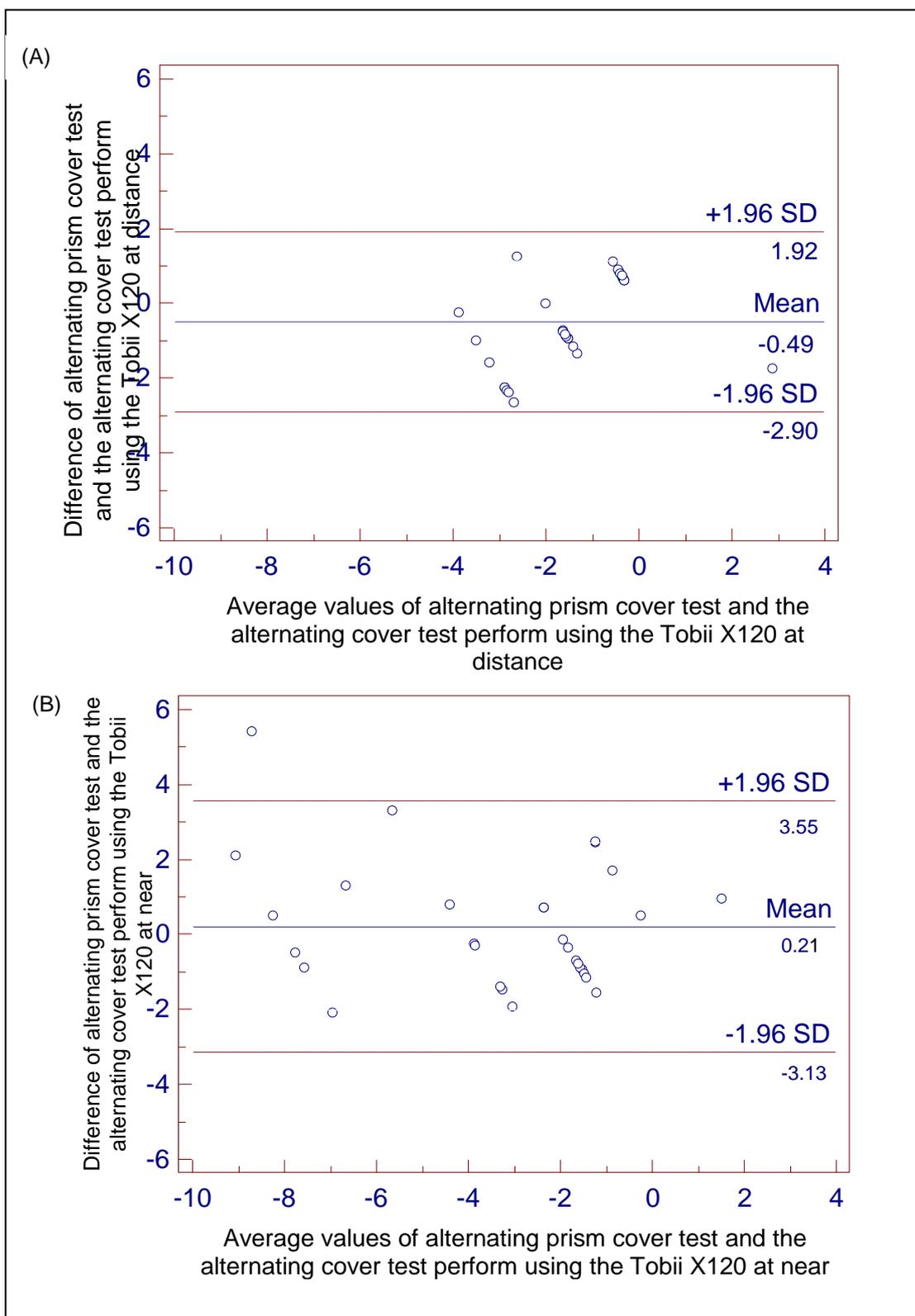
Figure 6.4 Bland-Altman plot of difference between alternating prism cover test and the alternating cover test perform using the Tobii X120 for distance cover test (A) and near cover test (B) on non-strabismic subjects (N=30). The solid blue line indicates the mean difference and the red dashed lines represent the 95% limits of agreement.

Table 6.12 Comparison of the phoria findings between unilateral 10s cover test and alternating cover test, both performed with the Tobii X120 using paired t-tests and Bland and Altman analysis on non-strabismic subjects (N=30).

Cover test	Unilateral 10s cover test using the Tobii X120 (PD)	Alternate cover test using the Tobii X120 (PD)	Paired t-test (PD)	Bland and Altman (PD)
Distance				
• **Mean**	-1.01	-1.18	t=1.09	Mean difference=0.17
• **SD**	1.41	1.24	p=0.28	95% LOA=-1.47 to 1.80
Near				
• **Mean**	-3.52	-3.55	t=-0.11	Mean difference=0.21
• **SD**	3.10	3.15	p=0.91	95% LOA=-2.11 to 2.16
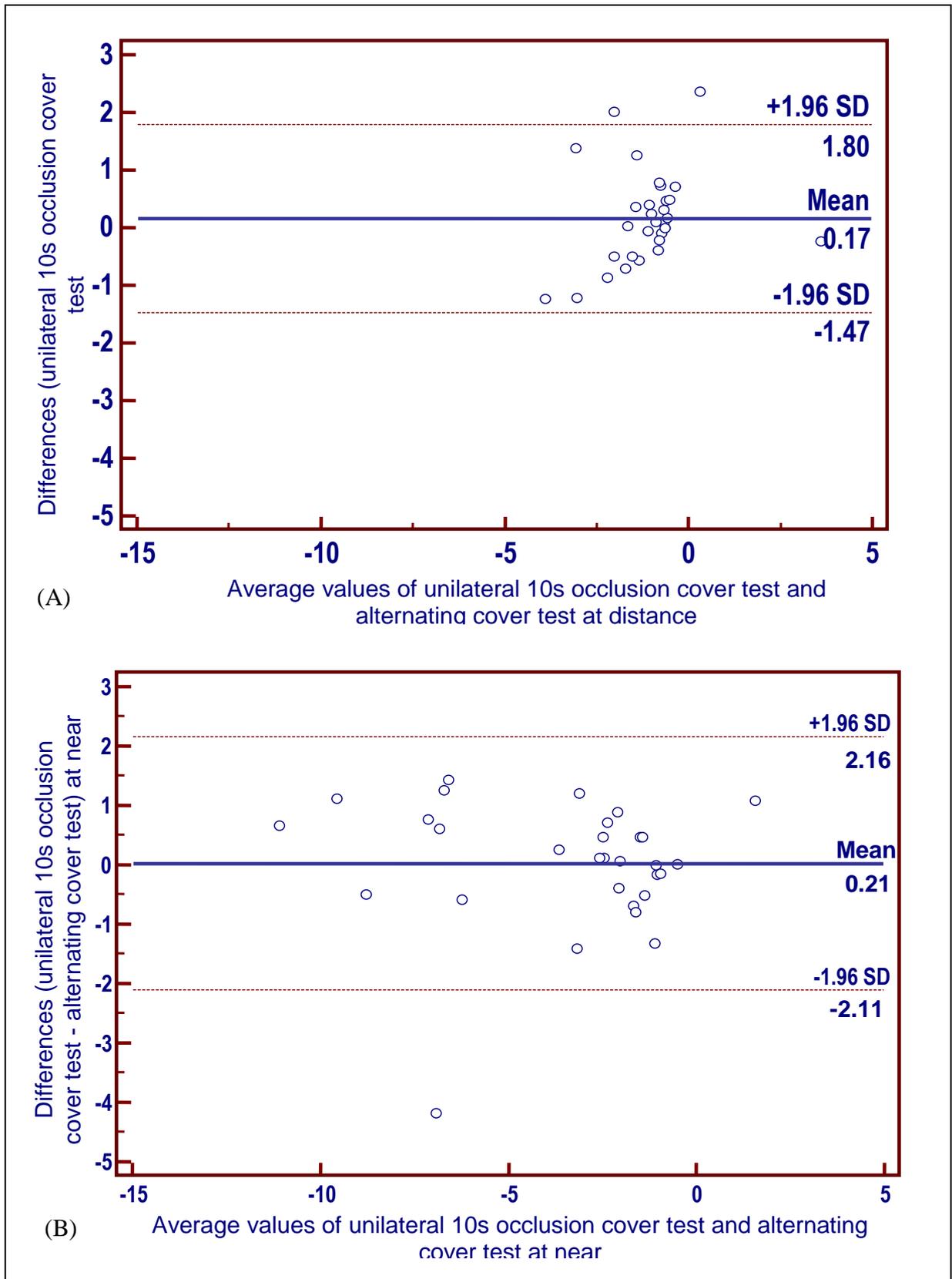
Figure 6.5 Bland-Altman plot of difference between unilateral 10s occlusion cover test and the alternating cover test perform using the Tobii X120 for distance cover test (A) and near cover test (B) on non-strabismic subjects (N=30). The solid blue line indicates the mean difference and the red dashed lines represent the 95% limits of agreement.

6.5.4 Discussion

This study was designed to determine the differences between unilateral cover tests with 2s and 10s occlusion times and to evaluate the degree of agreement between the alternating prism cover test findings and alternating cover test values from the eye tracker. Different occlusion times during the unilateral cover test at distance did not affect the phoria level as showed by the paired t-test result. However, mean phoria increased to more exophoric findings after 10s of occlusion time. It is interesting to note that the mean phoria for a unilateral 10s occlusion time (-3.52 ± 3.10PD) was similar to mean phoria recorded for the alternating prism cover test at near (-3.33 ± 2.75PD) and alternating cover test at near from the Tobii X120 eye tracker (-3.55 ± 3.15PD). Cooper (1992) suggested that phoria amplitude would increase during the alternating cover test, which allows the full extent of the deviation to be seen. It is a consensus among practitioners to perform the cover test with a brief occlusion time of 1 or 2s (von Noorden & Campos 2001) for unilateral and alternating cover tests. However, previous studies have shown otherwise. Peli and McCormack (1983) reported that some subjects in their study took up to 8s to reach an equilibrium position during a cover test. This finding is supported by Barnard & Thompson (1995), who showed that 5s was adequate for the eyes to reach a stable position. Similarly in this study, we found that mean phoria increased from 2s to 10s occlusion time during the unilateral cover test. The results may suggest that the unilateral cover test performed with a 10s occlusion time is needed when estimating the amplitude of phoria and would likely to be the same as the alternating cover test results.

When comparing the alternating prism cover test result with those from the eye tracker using a paired t-test, we found a significant difference for findings at distance (t=2.18, p=0.04). Mean phoria findings for the alternating prism cover test at distance were more exophoric than those of the cover test from the eye tracker. A paired t-test for cover test at near showed no significant differences (t=-0.68, p=0.50). Difference of the mean phoria for cover

test findings at distance could be due to a factor that relates to the technical and instrumentation aspects. Firstly, the alternating prism cover test at distance was performed with the examiner just off the midline of the patient's view of the distance target while, during the alternating cover test performed using the Tobii X120, the eye tracker was directly in front of the subject. As reported by previous studies from Johnson et al. (2004) and Clark et al. (2003), phoria findings tend to have an exo shift if the examiner's position is on the side of the patient's midline. It is difficult to explain this result, but it might be related to prism orientation during the cover test procedure and induced parallax error. Nevertheless, the difference in the mean phoria findings between the two methods was 0.49PD, which is within the limits of minimal detectable eye movement by an examiner (2PD) (Fogt et al. 2000). Although a paired t-test showed a significant difference between the two methods, further analysis using Bland and Altman showed that alternating prism cover test and alternating cover test using the Tobii X120 consistently showed minimal bias. Mean differences of -0.49PD for distance cover test and 0.21PD for near cover test measurements were all less than 0.50PD. 95% limits of agreement for distance and near cover tests also showed a narrow range of less than ±4PD. These results need to be interpreted with caution as subjects recruited were all exophoric subjects except for one esophore. A different outcome might be expected if a greater variety of phoria subjects were recruited.

When the unilateral 10s occlusion cover tests were compared to the alternating cover test, we found an interesting results from the paired t-test in which the cover test results were not significantly different. Further analysis with the Bland and Altman plot revealed a narrow LOA with mean differences of 0.17 (distance cover test) and 0.21 (near cover test). This could imply that the unilateral 10s occlusion has the dissociative effect as the alternating cover test and further investigation could be performed to larger subject sample.

6.6   Comparison of the alternating prism cover test and cover test performed using the Tobii X120 on strabismic subjects

6.6.1   Objective

Previous section detailed the examination performed on non-strabismic subjects. The aim of this study is to investigate and to compare the alternating prism cover test findings to the alternating cover test performed using the Tobii X120 on a small group of strabismic subjects.

6.6.2   Methods

Ten strabismic subjects (6 female and 4 male) from students, staff and clinical patients from Cardiff University participated in this study. The mean age of this group of subjects was 33.40 years old (age range: 20-68 years). Clinical characteristics of each patient are presented in Table 6.13. Seven subjects were myopic and three subjects were hyperopic. Eight of them wearing spectacles and the other two wore their contact lenses during examination. The corrected visual acuity was 6/12 or better for both eyes for all subjects. The protocol for this study was approved by School of Optometry and Vision Sciences' Human Research Ethical Committee and the patients gave their informed consent prior to participation. The cover test protocols and analysis of test results follow those detailed in section 6.4.2.

Table 6.13   Clinical characteristics of strabismic subjects.

Subject ID	Age	Diagnosis
TQ	20	Intermittent exotropia
ST	20	Alternating esotropia
TN	20	Intermittent exotropia
SAM	21	Right esotropia
GW	21	Left esotropia
GC	30	Left exotropia
SM	35	Right exotropia
AS	45	Left exotropia
TF	54	Left exotropia
MD	68	Right esotropia

6.6.3   Results

The Shapiro-Wilk test showed that the data are normally distributed (p>0.05). Table 6.14 presents the mean deviation findings for the alternating prism cover test and the alternating cover test performed with the Tobii X120 on strabismic subjects for distance and near measurements. The mean deviation for the alternating prism cover test recorded at distance (-3.60 ± 17.04PD) was higher than the findings from the eye tracker (-1.54 ± 20.76PD). The near alternating prism cover test revealed a lower mean deviation of -4.65 ± 18.53PD as compared to -6.72 ± 16.29PD from the cover test using the eye tracker. It is also apparent from Table 6.14 that the range of deviation recorded for the alternating prism cover test was narrower than that of the eye tracker for distance measurement but wider for near measurement.

Table 6.14 Comparison of cover test findings between alternating prism cover test and the alternating cover test performed with the Tobii X120 using paired t-tests and Bland and Altman analyses on strabismic subject (N=10).

Cover test	Alternating prism cover test (PD)	Alternate cover test using the Tobii X120 (PD)	Paired t-test (PD)	Bland and Altman (PD)
Distance				
• **Mean**	-3.60	-1.54	t=1.33	Mean difference=-2.06
• **SD**	17.04	20.76	p=0.22	95% LOA=-11.67 to 7.55
• **Range**	-35.00 to +16.00	-40.00 to +23.89		
Near				
• **Mean**	-4.65	-6.72	t=-1.97	Mean difference=2.07
• **SD**	18.53	16.29	p=0.08	95% LOA=-4.46 to 8.60
• **Range**	-41.00 to +16.00	-40.12 to +11.29		

The paired t-tests performed to determine any differences between the data sets revealed no significant differences between the results from the distance cover test (t=1.33, p=0.22) and near cover test (t=-1.97, p=0.08). The Bland and Altman tests showed a mean difference of -2.06PD, with 95% limits of agreement that ranges from -11.67 to 7.55PD for distance measurements and a mean difference of 2.07PD with 95% limits of agreement ranges from -4.46 to 8.60PD for near measurements. The Bland and Altman plots for both distance and near cover test measurements are presented in Figure 6.6.
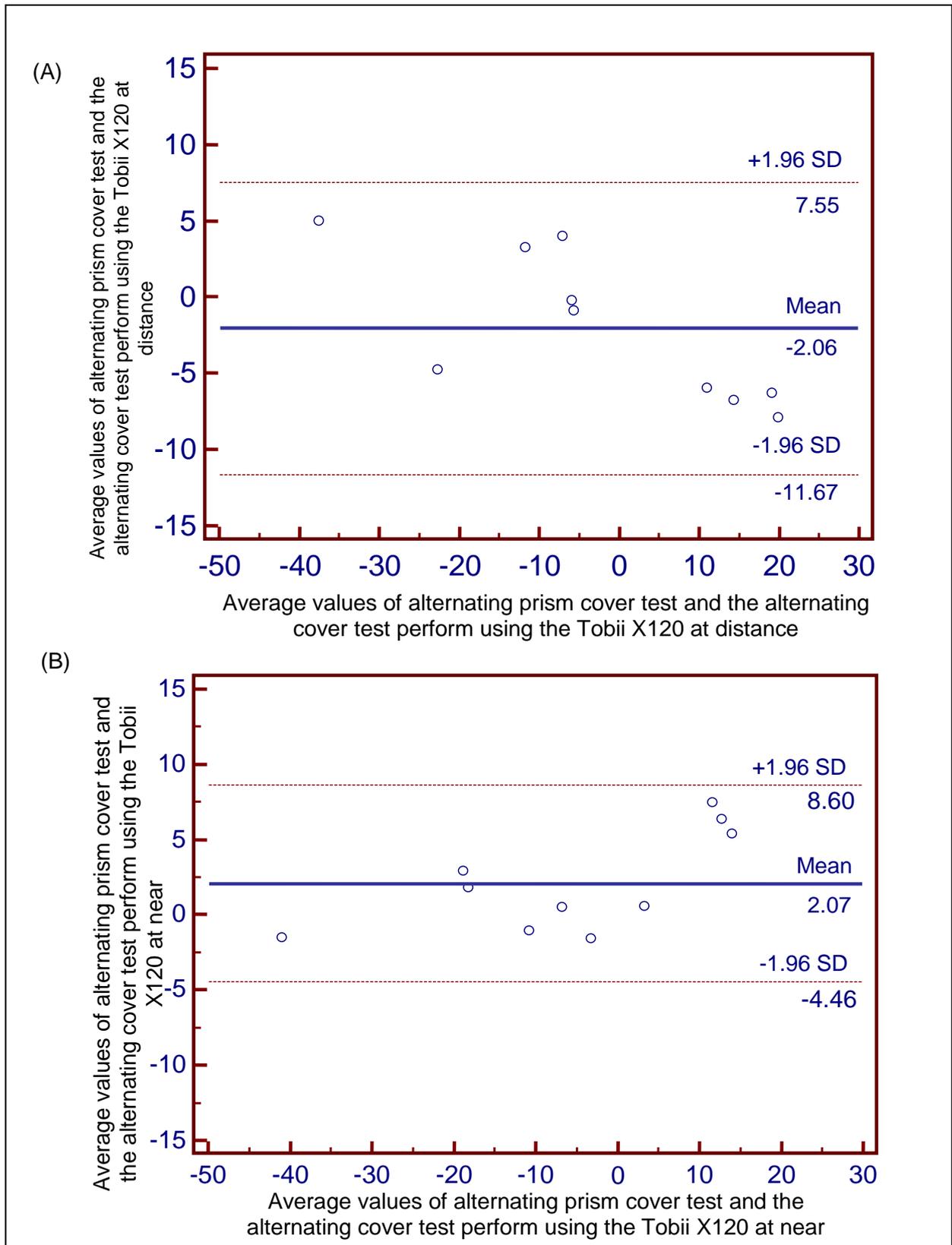
Figure 6.6 The Bland-Altman plot of difference between alternating prism cover test and the alternating cover test perform using the Tobii X120 for distance cover test (A) and near cover test (B) on strabismic subjects (N=10). The solid blue line indicates the mean difference and the red dashed lines represent the 95% limits of agreement.

6.6.4   Discussion

Despite the fact that the mean deviations recorded for distance and near measurements were different between the alternating prism cover test and the alternating cover test with the eye tracker, the paired t-test analysis have shown that none of the differences are statistically significant (distance cover test, t=1.33, p=0.22; near cover test, t=-1.97, p=0.08). The Bland and Altman analysis also showed a good agreement between the two methods in measuring deviations at distance and at near. A mean differences of -2.06PD (distance cover test) and 2.07PD (near cover test) with 95% limits of agreement of ±11.67PD for distance and ±8.60PD for near cover test are similar to results reported by Holmes et al. 2008, who found a 95% limits of agreement of ±10.2PD for distance and ±9.20PD for near cover test. Nevertheless, our findings should be interpreted with caution because the data were collected for only ten subjects with different types and degree of strabismus. We did not perform a separate analysis for lower and larger deviations nor did we perform a test for the reliability of the measured deviations with the two techniques. Lack of published data contrasting the measurements made by conventional cover tests with those made using a computerised method makes it difficult to determine if our findings can be generalised.

6.6.5   Conclusion

We have shown that it is feasible to perform cover test measurements using the eye tracker, and the results are shown to be comparable to the conventional prism cover test. Although the data revealed no significant differences between the two methods, we observed some inconsistency in the eye movement data output of some individual patients. This could be due to the fact that the initial calibration was based on the standard built-in binocular calibration programme embedded in the Tobii Studio™ software, which led us to develop our own monocular calibration routine to overcome the problem (see Chapter VII).

CHAPTER VII

EXAMINATION OF EYE MOVEMENTS USING THE TOBII X120 ON SUBJECTS WITH ABNORMAL EYE MOVEMENTS –

CASE STUDIES

7.1 Introduction

The aim of this chapter is to demonstrate the practicality of using the Tobii X120 in a clinical setting. Taking advantage of the strong clinical, teaching and research links that are already well established between the Bristol Eye Hospital (BEH) and the Cardiff School of Optometry and Vision Sciences, we established the 'proof of concept' in implementing the use of this modern, non-invasive eye tracker for the cover test assessment of patients in BEH, possessing a range of eye movement problems. In this chapter, we will be discussing:

1. The monocular calibration programme developed to provide more accurate eye tracking measurements in clinical patients.

2. Case studies of subjects seen during visits to BEH.

3. The evaluation of the use of the eye tracker in a clinical setting: implementation, constraints and limitations.

7.2 Development of the monocular calibration programme

Tobii Studio™ performs a calibration under binocular viewing conditions by measuring certain characteristics of the subject's eyes (e.g. pupil, etc.). The information gathered is then used to calculate eye gaze direction using proprietary algorithms and a physiological three dimensional eye model. The binocular calibration procedure assumes that both eyes are looking at the same point, which works exceptionally well with most normal subjects. However, in a case of manifest eye misalignment, such as in patients with strabismus, the eyes are not normally aligned, which will lead to an inaccurate calibration. We therefore proposed a monocular calibration procedure to ensure that each of the subject's eyes will be fixating on the target as precisely as possible. As mentioned previously, all our subjects had good visual acuity in both eyes and could fixate the target monocularly.

We developed a new method with the original Tobii Software Development Kit (SDK), using Microsoft Visual Studio as a platform. We modified the basic Tobii SDK components and then utilised them to execute a monocular calibration for each eye. The procedure consisted of creating an individual monocular calibration file, adding components and coding, changing the Graphics User Interface (GUI), and finally uploading the merged calibration file, including monocular calibration data, to Tobii Studio™ before starting any eye movement experiments. The processes involved are detailed in Sections 7.2.1 to 7.2.4.

7.2.1 Creating and adding monocular calibration files

A new modified programme was created in Microsoft Visual Studio 2010 with the help of our collaborator, Dr. Nathan Bromham. Microsoft Visual Basic was used as the programming language for adding and modifying the existing codes. Separate right and left eye calibrations were added to the SDK using the Tobii Eye Tracking Client *(TETClient)* command. This command enables the monocular calibration routine to communicate with the eye tracker through the *TETServer*, which is the software controlling the eye tracker hardware. A 'merge' calibration command line was also added to extract the separate right and left eye calibrations and combine them into a new (merged) calibration file. The individual calibration files (RightCalibration, LeftCalibration and MergeCalibration) were written as text files, and stored on the computer.

7.2.2 Modification of the GUI

The original GUI consists of three main functions: track status, calibrate and track start/stop. New buttons were added to the original 'calibrate' part of the GUI and assigned to each command line for the monocular calibration files (i.e. right and left eyes) mentioned above (Figure 7.1). The hostname (which is the IP address) of the specific eye tracker used was also added to the GUI to ensure automatic detection of the eye tracker system. When each calibration procedure was being executed, the outcome was shown as a graphical calibration plot (Figure 7.2) and will automatically be changed/rewritten when a new calibration is performed. Each calibration performed could be verified by referring to the text files stored for each calibration. The examiner had an option to perform the calibration process with 2, 5 or 9 points, simply by clicking on the relevant button on the GUI.
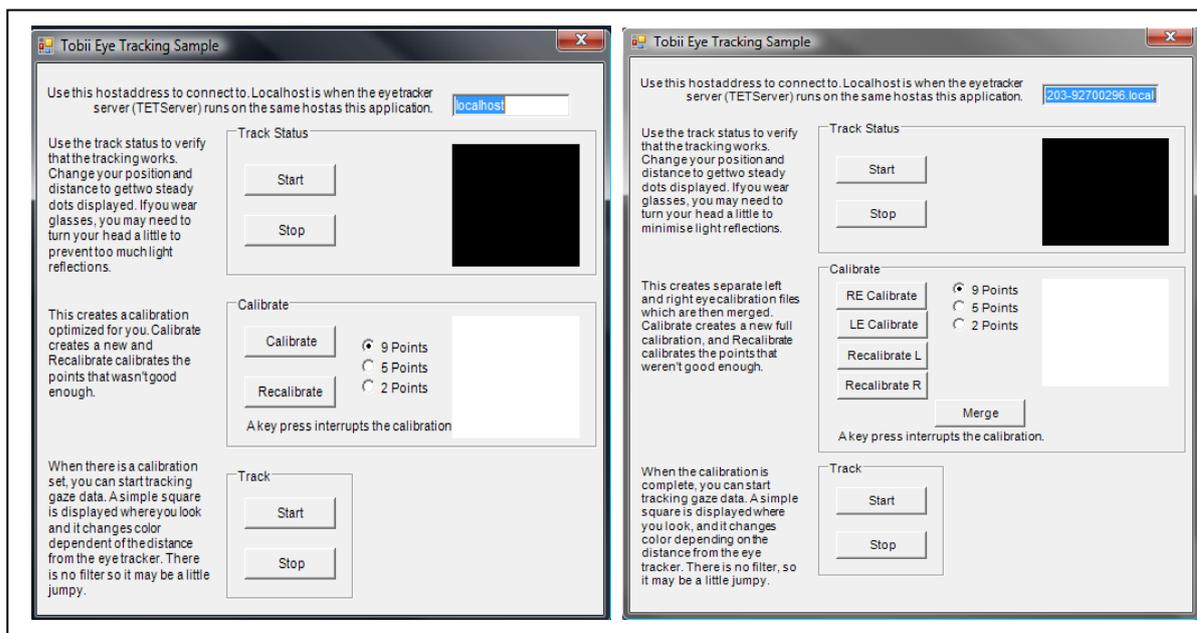
Figure 7.1   Original GUI in Tobii SDK sample files (left) and modified GUI for monocular calibration routine (right).
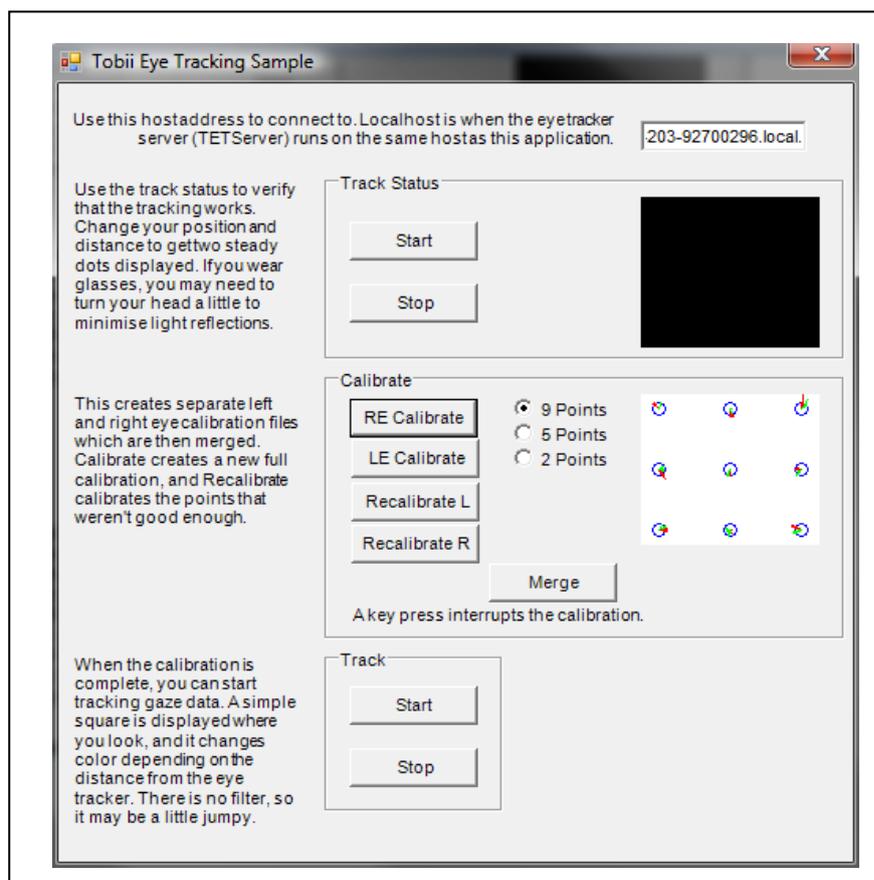
Figure 7.2   Calibration plot sample for right eye calibration of a subject.

7.2.3 Uploading the calibration

The monocular and merge calibration routines were controlled within the Visual Basic programme, and the gaze data from the calibration saved as text files. These files, in particular the merge calibration file, were uploaded to the Tobii Studio™ software using the database created for the specific project. The database could then be accessed using a Structured Query Language (SQL) manager, which is a computer language platform that allows data modification and control of an SQL database. Because of the complex design of the Tobii Studio™ programming, the automatic Studio calibration had to be performed first for any new subjects, followed by the monocular-merge calibration using GUI. The latter calibration file was then manually uploaded to Studio database using SQL Manager by inserting the file into the specific patient's CalibrationData column (see Figure 7.3), thus replacing the initial automatic Tobii (binocular) calibration data.
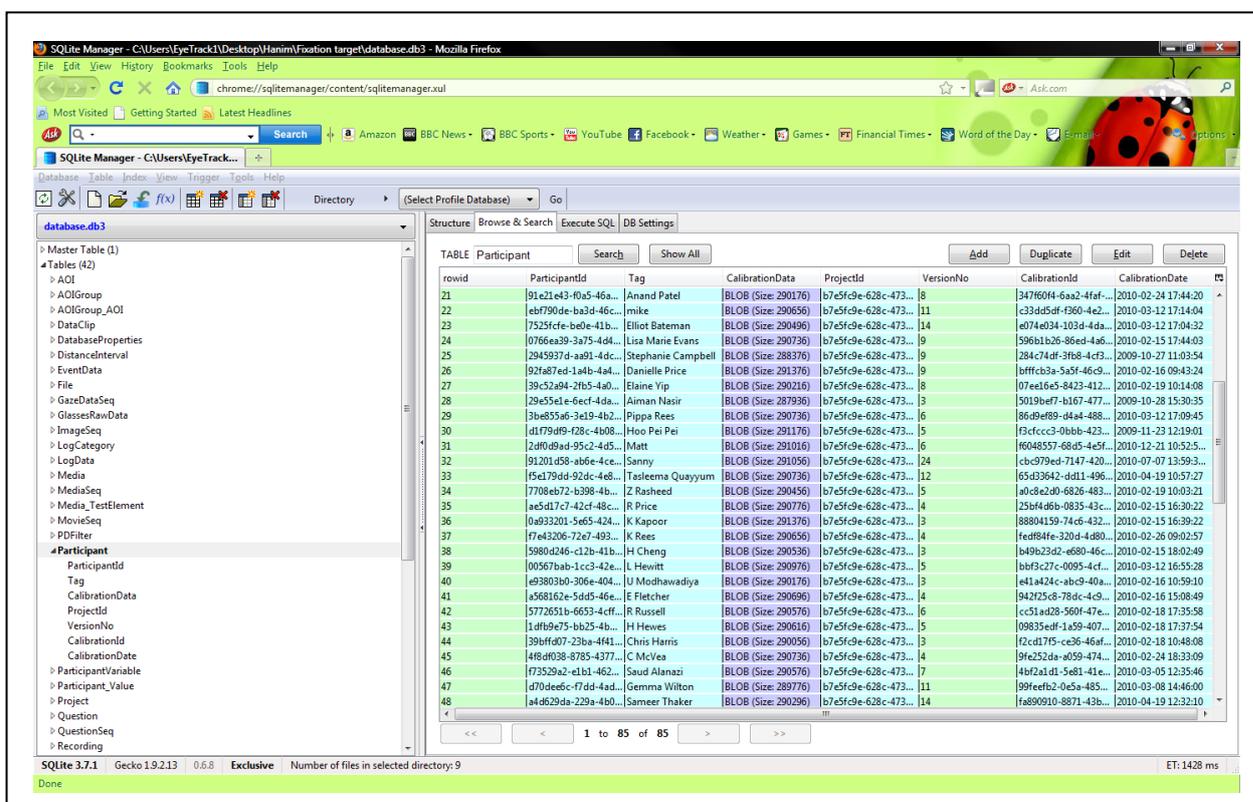
Figure 7.3 SQL Manager programme to upload the merge calibration files to Tobii Studio™ database.

7.2.4   Verifying the uploaded calibration

Simple experiments were then carried out to test whether the merged calibration file based on the two monocular calibrations had been transferred successfully to the Studio database. This process was crucial, as the new calibration files were needed as an accurate baseline for gaze data from each eye for the subsequent experiment(s). Although the monocular calibrations could be verified through the calibration plots in the GUI and the registered text files, it did not provide a quantification of the validity of the calibration performed. The aim of the test was to confirm that the correct calibration was extracted, merged and uploaded to the Studio database (see Figure 7.4).
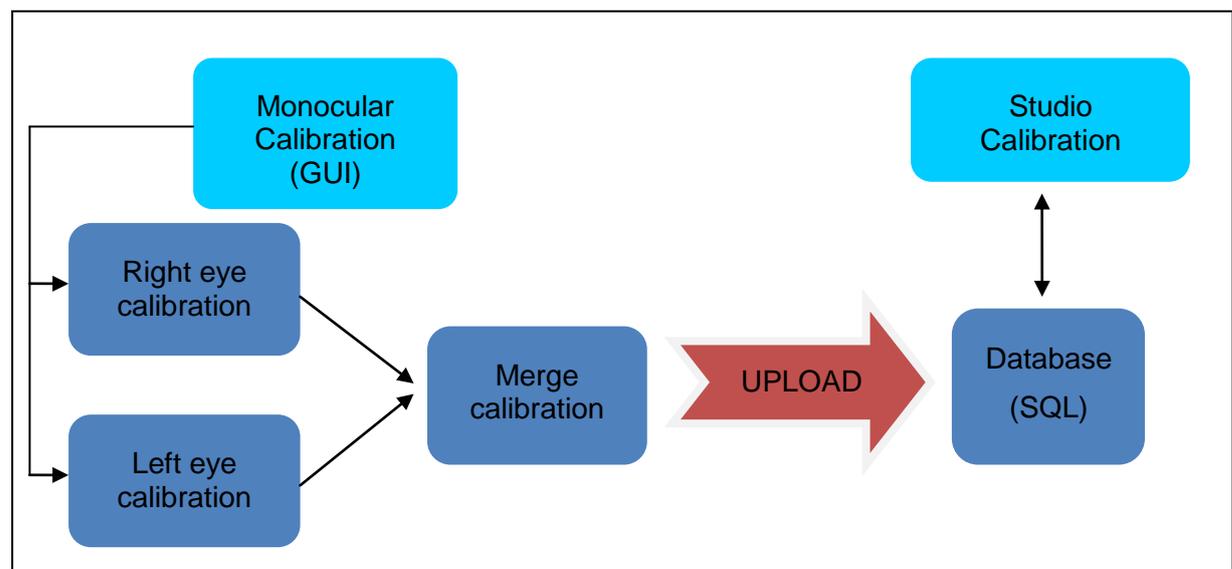
Figure 7.4   Flow chart of the monocular calibration programme.

The experiment was conducted using a vertical prism to dissociate the eyes. It involved performing a Studio calibration with the prism in front of the right eye (8PD) and then running the monocular-merge calibration under the GUI without the prism. Eye movement recording was later performed with the prism in front of the subject's right eye. The subject was asked to fixate at a centre fixation cross for 10 seconds. Finally, the recording was exported to a MATLAB programme for subsequent data analysis. Three visually normal

subjects participated in this preliminary study. It was expected that the eye movement outcome would show that the two eyes were not fused (as a result of the use of the prism) if the successful monocular-merge calibration file was uploaded.

Figure 7.5 shows the results obtained from one of the subjects, demonstrating the expected deviation of the right eye while the left eye maintained accurate fixation on the fixation target while the prism was held in front of the right eye.
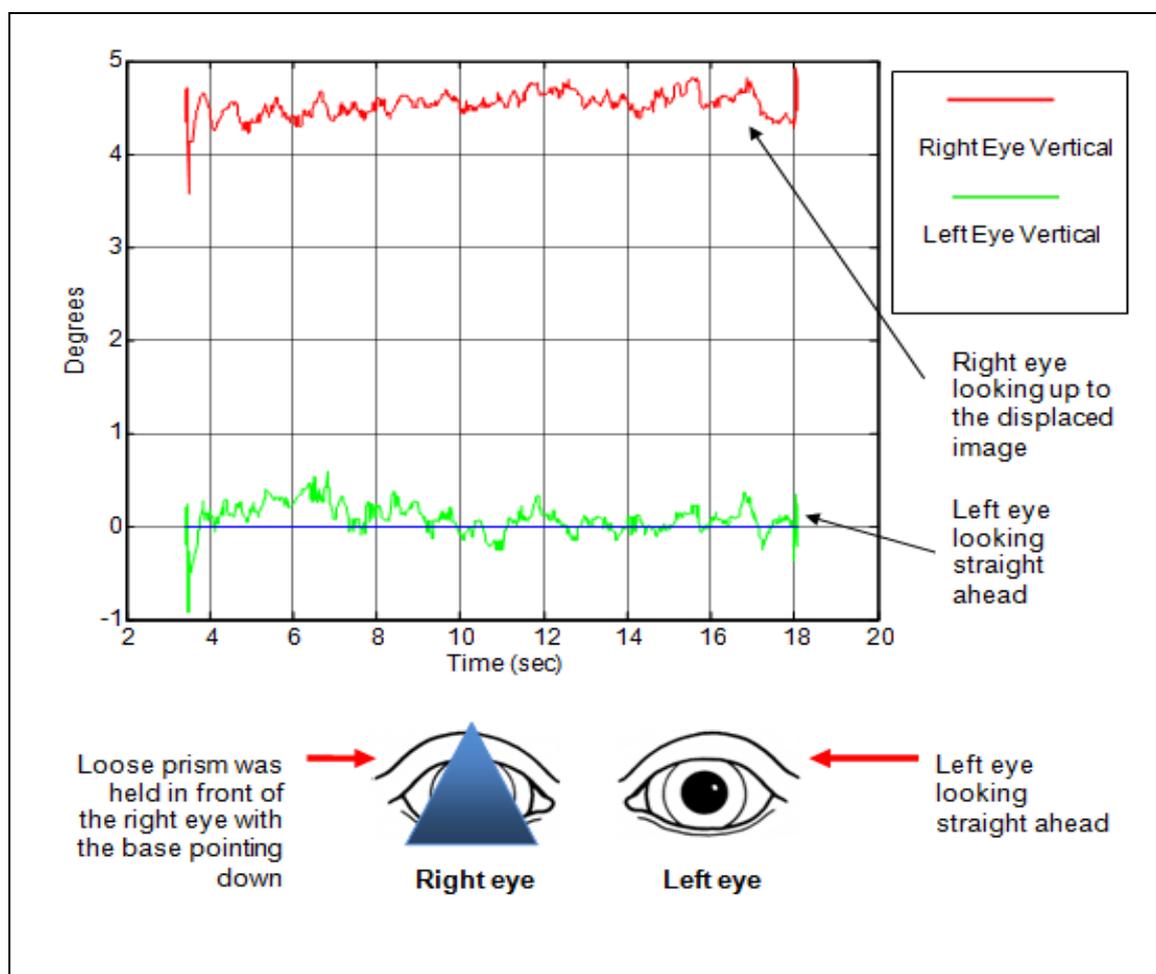
Figure 7.5   Eye movement data output confirming the successful upload of the monocular calibration routine. An 8PD base down prism was held over the right eye during this experiment. The resultant output showed that the left eye (no prism) was fixating on the target while the right eye (loose prism) was looking upwards to the direction of the displaced image.

7.3 Evaluation of the use of the eye tracker in the clinical setting

A temporary eye movement recording testing station was set up in BEH. This visit was the first attempt to use the eye tracker unit in a clinical setting. One purpose was to identify further aspects that need to be considered for the implementation of such an instrument.

7.3.1   Setting up

In the laboratory environment, the Tobii X120 eye tracker is set up on a height adjustable table with an adjustable chair. This arrangement ensures that the subject is always seated at the proper height to view the stimulus target and that his/her eyes are within range of the infrared light transmission of the eye tracker (see Figure 7.6). During the visit to BEH, the eye tracker had to be assembled on a regular office table that was a little lower than it should have been, and therefore an adjustment had to be made to increase the height of the instrument to the appropriate level. Because of the ongoing building renovation at the time of the visit and considering the volunteered patients have to see other eye specialists during their visit, we only performed the monocular calibration routine and near cover test for each patients.

Figure 7.6   Optimum setup for the Tobii X120 eye tracker (Tobii Studio™ 2.2 User Manual 2010).

7.3.2   Case studies

7.3.2.1 Post-surgical squint

A 58-year-old male (G.C.) presented in the clinic for a post-surgical squint appointment. He recently had a left recession of the inferior oblique muscle. During his clinical assessment, he reported that his diplopia state was unchanged since the surgery. On initial examination by the orthoptist, his distance and near visual acuities were found to be 6/4.8 and -0.1, respectively in each eye, with a LogMAR chart. He wore a progressive lens of +4.00DS in front of his right eye and +4.25DS on his left eye with the addition of +2.00DS for each eye. He exhibited a stereoacuity of 55 seconds of arc and a near point of convergence of 8cm.The cover test performed by the orthoptist showed that this subject had a 12PD exophoria and a 10PD left hyperphoria at distance and a 10PD exophoria and a 16PD left hyperphoria at near.

We then performed a near cover test using the Tobii X120 on G.C. During the examination, the subject was looking through his near prescription and had to tilt his head back in order to view the fixation target presented on the screen clearly. A few runs of the Tobii Monocular-Merge calibration routine had to be performed to get usable calibration data prior to the cover test assessment. On playback, the validity sample was only marginally good (51%). This could be due to the thickness of the lens and/or the spectacle frame interfering with eye recording. From data analysis, the alternate cover test using the eye tracker revealed a 14PD exophoria and 17PD left hyperphoria at near. These differences could be due to G.C's viewing posture as he has to look through the near portion of his progressive lenses. It also could be due to the thickness of the lens which possibly poses problems for the eye tracker in the detection of the corneal reflections.

7.3.2.2 Decompensating exophoria

Patient S.W., a 22-year-old female, has had right lateral rectus recession on 9th March 2007. She came for a follow-up appointment with complaints of experiencing headaches after close work and having difficulties reading. She also reported being aware that her eye drifts outward when she feels tired. She did not wear any refractive correction. S.W.'s general health is otherwise unremarkable.

S.W.'s visual acuity was good for the right eye and left eye, acuities were exhibited 6/6^{-2} and 6/6, respectively. Near point of convergence was at 6cm, normal stereoacuity with Frisby (55 seconds of arc) and no abnormality was detected during extraocular motility test. The prism cover test performed showed a 16PD exophoria at distance and a 14PD exophoria at near. From the examination performed by the orthoptist, all the symptoms reported by S.W. were not manifested during the time of examination. S.W. was diagnosed as having decompensated exophoria. No eye exercises were given as she showed good eye control and good convergence. She was advised to have short episodes of close work with regular breaks to help with her problem.

The Tobii Monocular-Merge calibration routine was a success with S.W. Validity data showed a good eye recording of 89%. Findings from the near cover test performed were 14.1PD exophoria. The results were similar to the cover test findings performed by the orthoptist.

7.3.2.3 Hashimoto Thyroiditis and mild thyroid eye disease

M. H., 75-year old white female, presented to the clinic for a follow up appointment. She has previously been diagnosed as having Hashimoto Thyroiditis, bilateral idiopathic chronic dacryoadenitis and mild thyroid eye disease. M.H. had right posterior subcapsular aspiration with intraocular lens implant on January 2011. She did not report any vision complaints and was compliant with her medication regime. She has a pair of progressive spectacle lenses and a pair of reading spectacles. Her reading spectacles have an 11PD base out prism incorporated in the prescription. Distance visual acuities measured with habitual progressive spectacles, RE +1.50/-1.75 x 160 and LE +1.50/-1.75 x 70 (Addition: +2.50DS), were $6/7.5^{-2}$ and $6/24^{-1}$, respectively. Vision for her left eye improved to $6/12^{+2}$ with pinhole test. Vision at near was -0.10 for both eyes using both reading and progressive spectacles. Cover test showed a 2PD left exotropia at distance and near through the habitual reading prescription. Extraocular motility testing showed bilateral senile restriction in up gaze with some discomfort reported.

Near cover test using the Tobii X120 was performed with M.H.'s reading spectacles. Results using the eye tracker showed a finding of 2PD exotropia consistent with the cover test performed by the orthoptist.

7.3.2.4 Left IVth Nerve palsy with right Internuclear Ophthalmoplegia, secondary to Multiple Sclerosis

S.H. is a 28-year-old female who attended the clinic for a follow up appointment after having been diagnosed as having left IVth nerve palsy secondary to multiple sclerosis. S.H. reported having intermittent diplopia, which gradually increased in frequency and severity, when compared to her last visit to hospital. She has previously been prescribed distance spectacles to correct her myopia (RE -5.00/-2.50 x 165 and LE -4.75/-2.00 x 170). Her corrected vision was 6/3.8^{-1} for right and left eyes, when tested with a LogMAR chart. Cover test showed a 7PD exophoria with left hyperphoria at distance and a 6PD exophoria at near through her habitual prescription. Extraocular motility testing showed an abducting nystagmus on laevoversion. She was prescribed an 8PD base up prism for the right lens of her spectacles to help with her symptoms and would be reviewed again in two weeks' time.

We performed the cover test with her spectacles (without prism). Our near cover test assessment with the eye tracker revealed a 6.1PD exophoria with the initial calibration performed using the Tobii Monocular-Merge calibration routine. Thus, the result was consistent with the findings from the orthoptist.

7.3.2.5 Residual right exotropia

K.G. is a 44-year-old lady attending the clinic for a post-operative follow up appointment. She had a left eye lateral rectus muscle recession and medial rectus muscle resection on 24th January 2011. K.G. was happy with her cosmetic appearances but complained of pain around her left eye without experiencing any diplopia. Habitual visual acuities for right and left eyes were 6/15^{+2} and 6/12^{+2}, respectively. Near point of convergence was 18cm. Extraocular motility testing showed left eye restriction during adduction and abduction. The prism cover test showed a 16PD exotropia at distance and a 14PD exotropia at near.

During our cover test examination using the Tobii X120 eye tracker, we found a 12PD exotropia using the Tobii Monocular-Merge calibration routine, an underestimation of 2PD compared to the orthoptist's finding. However, the result is not clinically significant as the magnitude of prism change that is likely to represent a real change in eye deviation is regarded as changes of more than 10PD (Holmes et al. 2008).

7.3.2.6 Intermittent right exotropia-well controlled

Patient C.S., a 42-year-old female, presented to the clinic for a regular follow up appointment. She was previously diagnosed as having intermittent right exotropia with well-controlled muscles. She had a patching treatment before undergoing squint surgery at the age of 3 years old. She was in good health and has no vision complaints. She is currently wearing only reading glasses. On examination by the orthoptist, C.S.'s visual acuities in the right and left eyes were 6/12^{-2} and 6/7.6^{-1}, respectively. Near point of convergence was 8cm and her stereoacuity with Frisby was 55 seconds of arc. Prism cover test at distance and near showed an 18PD exotropia and a 25PD exotropia, respectively.

Our near cover test assessment with the eye tracker revealed a 17PD exophoria using the Tobii Monocular-Merge calibration routine. The finding slightly underestimates the results from the orthoptist's cover test by 8PD. It is possible that the difference was due to the inappropriate adjustment of the table/chair height to correctly align the patient's eye with the computer screen. It was not possible at the time of examination to obtain an adjustable chair, and the table height was fixed. This resulted with C.S. sitting slightly higher than the intended position. It is possible that this poor position alignment interfered with the ability of the eye tracker to detect the corneal reflection, resulting in the observed discrepancy.

7.3.2.7 Consecutive left exotropia

C.R., a 55-year-old female, attended the clinic for her annual follow up appointment. She had had a bilateral strabismus surgery when she was a child. C.R. complained of soreness in both her eyes. She currently has two pairs of spectacles, one for distance vision (RE +1.25DS and LE +0.75DS) and one for near (+4.25DS in right eye and +3.75DS in left eye). Her distance visual acuities were 6/4.8 and a 6/7.5[+2] for her right and left eyes, respectively. Her near vision was N5 on both eyes. Cover test showed a 30PD left exotropia at distance and an 8PD left exotropia at near using her habitual prescription. The Frisby test showed a negative result with no stereopsis. Extraocular motility testing showed no abnormality.

The cover test assessment using the Tobii X120 showed a 6.1PD exotropia (Tobii Monocular-Merge calibration routine). The cover test findings were 1.9PD lower when compared to the prism cover test measurement by the orthoptist. The difference was too small to be considered as a real change in cover test measurement (Holmes et al. 2008).

7.3.2.8 Intermittent left exotropia

S.A.R is a 23-year-old female, who presented to the clinic for a follow up appointment to monitor her intermittent left exotropia. The patient reported having transient diplopia without her glasses but otherwise her general and ocular histories were unremarkable. She was wearing her myopic prescription of RE -0.75DS/-0.25DC x 10 and LE -0.75DS. Her visual acuities were RE 6/4.8 and LE 6/6 when tested with a LogMAR chart. Her near vision was N5 in both eyes. The prism cover test showed a 4PD left exotropia at distance and a 12-14PD left exotropia at near.

Upon assessment with the Tobii X120 eye tracker, S.A.R's cover test showed a 14.2PD left exotropia at near, which is in accordance with the prism cover test results obtained by the orthoptist.

7.3.2.9 Sturge Weber Syndrome with residual amblyopia and divergent squint on the left eye

Mr. I.P, a 46-year-old gentleman, came to the clinic for a regular follow up check-up. He was diagnosed as having Sturge Weber Syndrome with residual amblyopia and exotropia on the left eye. I.P's visual acuities were RE 6/4.8 and LE 6/19, no improvement with pinhole). His near vision was N6 in both eyes. The prism cover test revealed a 25PD exotropia for both distance and near. Extraocular motility showed a restricted movement in her left eye when attempting adduction and laevoversion.

During our attempt to perform the cover test assessments using the Tobii X120 eye tracker, we encountered problems due to a disruption of the electrical supply in the building, as detailed in section 7.3.3.3 below. This unforeseen situation resulted in the Tobii Monocular-

Merge calibration routine failing to work. Although the calibration programme could be executed, the data could be uploaded to the eye tracker as a result of a hardware/software internal problem, attributable to the sudden loss of power.

7.3.2.10 Duane Syndrome Type I with marked head turn to the left

Mrs. A.I., a 46 year-old female came to the clinic after being referred from the **Royal United** Hospital Bath to discuss possible surgical options to centralise binocular single vision. She was previously diagnosed with Duane Syndrome Type I with acquired partial 3rd nerve palsy. Her vision was RE 6/6 and LE $6/9.5^{+2}$ improvement with pinhole to $6/7.6^{+2}$. A.I.'s near point of convergence was 6cm. Prism cover test at distance and near showed a 40PD esotropia and a 23PD esotropia, respectively. Her extraocular motility test showed a restricted movement in the left eye with no abduction beyond the midline and up gaze restriction. It was also apparent that her left palpebral fissure widened on abduction and narrowed on adduction. She had an abnormal head posture with a marked head turn to the left.

In an effort to perform a cover test assessment on A.I using the Tobii X120, we implemented a few modifications. With A.I.'s abnormal head posture, eye movement calibration proves to be challenging. We experimented using manual and automated calibrations, using a calibration with fewer fixation points and adjusting the speed of the calibration points to get the optimum calibration data points. We also tried examining A.I. with and without her abnormal head posture. However, the eye tracker consistently experienced difficulties in detecting A.I's eye movements. This could be due to her extreme head turn, making detection of the corneal reflex barely possible, as the nose bridge obscured the infrared light (see section 7.3.3.2). The experiment had to be stopped and the patient had to be discharged as she had another clinic to attend.

Table 7.1   Summary of cases that attended Bristol Eye Hospital.

No	ID	Gender	Age	Diagnosis
1	GC	M	68	Post-operative squint surgery reporting double vision problems
2	SW	F	22	Decompensating exophoria
3	MH	F	75	Hashimoto Thyroiditis and mild Thyroid Eye Disease
4	SH	F	28	Left IVth Nerve palsy with right Internuclear Ophthalmoplegia secondary to Multiple Sclerosis
5	KG	F	44	Residual right esotropia
6	CS	F	42	Intermittent right exotropia-well controlled
7	CR	F	55	Consecutive left exotropia
8	SAR	F	23	Intermittent squint
9	IP	M	46	Sturge Weber Syndrome with residual amblyopia and divergent squint of the left eye.
10	AT	F	46	Duane Syndrome Type I with marked head turn to the left

Table 7.2   Summary of the cover test findings by cases.

Patient ID	Alternating Cover test findings	
	Orthoptist	Tobii Monocular-Merge calibration
GC	10 XP	14 XP
SW	14 XP	14 XP
MH	2 XT	2 XT
SH	6 XP	6.1 XP
KG	8 ET	12 ET
CS	25 XT	17 XT
CR	8 XT	6 XT
SAR	14 XP	14.2 XP

7.3.3   Data collection (constraints and limitations)

7.3.3.1 Use of spectacles

Although we have successfully carried out studies with subjects wearing spectacles and contact lenses before (see Chapter IV), we had never tested subjects with thick plus lenses, which may be used by some patients for reading. Although it is not impossible to detect the eyes through such lenses, the Tobii X120 eye tracker clearly had difficulties tracking the eyes, making the calibration procedure difficult. Taking into consideration that the experiments cannot be performed without proper calibrated data points, this difficulty poses a problem in the case of patients wearing thick lenses.

We also encountered the same problem with subjects who wore progressive lenses. Since the experiments were conducted at a near distance, subjects needed a near prescription to view the fixation targets. Subject G.C, for example, had to tilt his head slightly upwards in order to view through the near prescription. This problem was exaggerated if the patient was wearing full frame spectacles because the rim interfered with the eye tracker's infrared transmission, which led to difficulties in detecting the eyes. The same problem was also experienced with subjects who wore spectacles fitted with a Fresnel prism as the grooves in the Fresnel prism deflected the infrared light incident on the spectacles (Møller and Trabjerg 2005).

7.3.3.2   Anatomical features

The eye tracker works by detecting the corneal reflexes and uses the pupil centre-corneal reflection technique (Tobii Eye Tracking White Paper 2010). Eye position needs to be in the maximum coverage area of the infrared transmission. Any aspects that prevent/prohibit the transmission will make detection of these reflexes impossible. We also examined one

subject (AT) with a distinct head turn to the left due to hereditary Duane's Syndrome. The subject had diplopia and her double vision was markedly decreased in the head turn position. Therefore, we tested the subject in this position, but this created a problem as the eye tracker could only detect one eye because of the nose bridge, which obscured the view of the other eye. Enough calibration data points could not be obtained to set a baseline before starting the experiment. We tried to calibrate the subject's eye movement using the Tobii Monocular-Merge calibration routine, purposely developed for this exchange study. However, the interface programme again failed to perform the calibration for the same reasons.

7.3.3.3 Unforeseen constraints and problems encountered

During the visit, we experienced a few technical problems related to the eye tracker hardware and the application that we developed (i.e. Tobii Monocular-Merge calibration routine). The eye tracker failed to operate as usual after we encountered an interruption of power supply in the hospital building, which at the time of examination was having a renovation. The eye tracker also failed to connect to the computer as a result of a faulty LAN adapter. Fixing these problems involved installing updated Tobii Studio™ software and license, which required assistance from the manufacturer. This problem also caused the Tobii Monocular-Merge calibration routine to malfunction as it was not compatible with the newly installed Tobii Studio™ software.

7.4 Conclusion

Despite the difficulties encountered, this exchange visit has helped greatly in evaluating the Tobii X120 eye tracker as a tool for examining eye alignment in a clinical setting. It has given us the opportunity to demonstrate the use of the eye tracker in patients with a wide variety of eye movement problems. The constraints and problems that occurred during

these exchange visits have enlightened us about the possible problems that can occur and therefore have helped us anticipate the additional requirements needed to implement such a system when measuring the eye movements of patients with different conditions.

CHAPTER VIII

CONCLUSION

This project was undertaken to evaluate the use of eye trackers as an alternative to give a more objective and quantitative outcome of the cover test findings. Emphasis has been given to the application using the Tobii X120 as it has several qualities as a promising instrument for the purpose mentioned above. Apart from being non-invasive and using infrared as a light source for detecting the eye, the Tobii X120 is also a stand-alone portable unit, making it easy to set up according to the requirements of any tests. Moreover, it is considered a 'patient-friendly' infrared eye tracker as it does not involve the use of any contact coils or helmets to track the eyes. The potential of this eye tracker is extensive, not only because it is quick and does not need highly trained personnel to operate the system, but also because it could possibly be used as a screening tool in a primary eye clinic or as a teaching tool in optometry/ophthalmology courses.

This study has demonstrated that it is possible to record eye movements and alignment objectively under an infrared cover/occluder. The added value when using this type of occluder is that it blocks visible light (as in conventional occluder) while at the same time, allowing near infrared light through. Eye movement under the occluder can easily being tracked and assessed in a way never before possible under clinical conditions. The quantitative results of the cover test findings we performed in this study are also comparable with the prism strengths used to determine the angle of deviation when performing the cover test.

8.1 Limitations of the study

This study has a number of limitations that need to be considered as detailed below:

8.1.1 Eye tracker limitation

Studies performed in this research are more focussed on the use of the Tobii X120 eye tracker. As highlighted in previous chapters, the Tobii X120 stands out as being a patient-friendly instrument, compared to other eye trackers commonly used in laboratory and research environment, which mainly utilise head gear or chin rest to restrain head movement.

The main drawback of the Tobii X120 eye tracker, however, is that the speed and frequency was limited to 120Hz. Although the sampling frequency was acceptable for investigating the amplitude of eye deviation, it would be interesting to investigate the recovery movements of the eyes being occluded during the cover test as this information is useful to determine whether the phoria level is compensated or not. At present, recovery movements cannot be analysed qualitatively or quantitatively because of the low sampling frequency. Additionally, having a higher sampling rate is desirable for quantification of eye movement parameters in other eye condition/disease especially, for example, nystagmus. This would determine the dynamics of eye movements in certain gazes and help in identification of difficult eye movement problems, including but not limited to, nystagmus, diplopia and vertical strabismus. This study was also limited by the eye tracker's standard calibration process, which only can be performed binocularly. Calibration is crucial when using any instrument to ensure accurate findings. Initial monocular alignment of each eye separately needs to be established prior to any eye movement experiments. While the calibration seemed to work fine with phoria patients, it is however, difficult to determine the eye gazes for strabismic patients. Although we have successfully developed a monocular calibration routine (see

Chapter VII), the procedure is liable to instability and requires further research and development.

In terms of software, the Tobii X120 is fully equipped with its own comprehensive software, the Tobii Studio™. This software is able to record and generate graphical output of eye movement data in scan path plot, bee-swarm and heat gaze map, to name a few. Although the data produced were convenient and useful, it is less informative for the interpretation of oculomotor assessment. In this study, evaluation was based on raw eye movement data, which have to be analysed manually to produce a relevant data set. It would be more practical if the eye movement data could be extracted automatically and displayed in real-time. It would also be convenient to have a display showing the instantaneous eye position to facilitate any adjustments. Clinical algorithms can also be integrated within the analysis software to give a conclusive diagnosis and aid in the management of the patients, as some of the ocular disorders have distinctive characteristics. For example, gaze evoked nystagmus indicates cerebellar disease and slow vertical saccades suggest progressive supra nuclear palsy. However, this would take some time to develop and collaborative work between engineers, developers and eye care professionals has to be initiated to make a fully functional instrument.

8.1.2 Research subjects

Another limitation of this study is that the numbers of patients were relatively small, in particular the study which was carried out in the Bristol Eye Hospital, due to limitations of time and patient availability. Small sample size means that the results have to be interpreted carefully. Although the results cannot be used to characterise the whole population, certainly the findings documented in this thesis will be a resource that adds to the body of knowledge in the oculomotor field/area. Preferably, power calculations for a targeted sample should be made prior to research, to make the results more valuable.

8.1.3   Experimental limitation

In addressing our objective to assess eye alignment, automated occluders were developed. However, we experienced technical and programming difficulties in integrating the system with the software used by the eye tracker. The process involved took longer than anticipated. Due to practical time constraints, using a manual occluder to perform the cover test procedure seemed to be the best option to move forward.

8.2   Future plans

The application of a non-invasive eye tracker has more potential in the clinical environment. The initial study in this project, as described in Chapter VI, can be further expanded to look at the effect of eye dominancy in the cover test and eye behaviour in the prism cover test. This will not only contribute to the knowledge of the test but also allows the dynamics of eye movements behind the cover to be documented and tested. Additionally, this instrument could also be used to aid teaching and would help in developing students' interest in the research environment.

One study has documented the use of the Tobii1750, i.e. the previous model of the Tobii eye tracker, for visual field testing. The application seemed feasible to be carried out in children. Therefore, it would be interesting to evaluate the same approach using latest Tobii eye tracker on adults and children.

The Tobii X120 is also portable enough to be set up easily as a screening tool for school children. Having a simple device that can be operated without requiring training and clinical expertise may provide a promising solution to the false positive referral cases involving eye movement anomalies.

8.3   Overall conclusion

As the technology advances, the application of the infrared eye tracker will be expanded greatly where the clinical possibilities are extensive. It is always desirable to have an instrument that is non-invasive, comfortable and easy to use, especially when children are to be assessed.

This study has shown the potential of using such instrument in various groups of patients. Future work on larger cohorts of patients might more fully validate this eye tracking system and established its usefulness and practicality in clinical practice.

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APPENDICES

i   Oral presentations

Seminar: Young Neuroscientists' Day, Bristol, United Kingdom
Date: 4th November 2010

ii   Poster presentations

Conference: Association for Research in Vision and Ophthalmology's 2010 Annual Meeting (ARVO), Fort Lauderdale, United States of America
Date: 2nd – 5th May 2010

Conference: 15th European Conference on Eye Movements 2009 (ECEM), Southampton, United Kingdom
Date: 23-27 August 2009

Postgraduate Research Day
School of Optometry and Vision Sciences, Cardiff University, United Kingdom
Date: 24th April 2009