Stereocoherence thresholds as a measure of global stereopsis

by

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AUTHOR'S DECLARATION

I hereby declare that I am the sole author of this thesis. This is a true copy of the thesis, including any required final revisions, as accepted by my examiners.

I understand that my thesis may be made electronically available to the public.

Abstract

Purpose: The purpose of this study was to develop a robust and reliable clinical test of stereopsis that is complementary to the conventional disparity threshold tests.

Methods:

Random dot stereograms containing disparity-defined gratings were displayed on a ViewPixx® monitor using LCD shutter glasses. Participants discriminated grating orientation. Form coherence was degraded by assigning random disparities to a variable proportion of dots. The threshold proportion of signal dots required for form discrimination is called the **stereocoherence threshold** (stereoCT). We explored the various stimulus parameters that can affect stereoCT. StereoCT were also measured for a variety of simulated abnormal binocular vision conditions and in patients with amblyopia.

Results: StereoCT was lowest (most sensitive) for a stimulus with a spatial frequency of 1cpd ,a 5.5 arc min dot size, 183 dots/deg^2 dot density and a disparity amplitude of 108 arc sec. StereoCT showed higher sensitivity and reduced variability relative to stereothresholds obtained on conventional disparity thresholds under various simulated abnormal vision conditions (interocular luminance and contrast differences, unilateral blur, and unilateral Bangerter filters). In patients with amblyopia, stereoCT improved with contrast reduction in the fellow eye relative to the amblyopic eye.

Conclusions: StereoCT testing targets the second stage of stereoscopic processing ‘global stereopsis where the local matches of stereoscopic images between two eyes are unified into a global perception of depth. Therefore, stereoCT may provide a useful measure of higher-level stereoscopic vision that is complementary to current tests, which rely on disparity thresholds.

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Dedication

To my loving Parents, Siblings and Friends

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Chapter 1

1.1 Introduction to stereopsis

The term stereoscopic vision has been defined as ‘solid sight’ referring to the three-dimensional view of the world when seen by two eyes[1]. The visual system captures images from the two eyes in two-dimensional forms; the brain uses these images to recover a description of depth. Stereopsis refers to the capacity of the visual system in combining coherently two monocular signals to create a three-dimensional view of the environment[2]. Stereoscopic view depends on binocular, monocular and oculomotor cues. Binocular depth cues arise due to the formation of different retinal images between both eyes, resulting from the horizontal separation between the two eyes[3]. Oculomotor depth cues are of the accommodation and convergence[4]. Monocular cues, also called pictorial cues, arise from aspects of the 2D image that imply depth. The most common cues are size, shade, illumination, texture and color etc[5]. The perception of depth takes into account both pictorial and stereoscopic (binocular and oculomotor) depth cues.

Retinal disparities and corresponding points:

Retinal locations in each eye that have the same visual direction are called corresponding points. Images that fall on corresponding points have zero binocular disparity and produce a sensation of seeing features at the same depth as the point of fixation. Images that fall on non-corresponding points are called disparate images[1]. Disparate images can produce either physiological diplopia or stereoscopic vision.

The empirical horopter is a locus of points, whose images fall on the corresponding points of the two retinas. All objects that are in front or behind the horopter stimulate non-corresponding retinal points creating disparate images. The brain can fuse these disparate images resulting in the impression of three-dimensional single vision. However, there is a finite area around the horopter where disparate images arising from non-corresponding points can be fused into a binocular single image. This area is called Panum's fusional area as described in figure 1. Panum's fusional area was first described by a Danish physiologist Panum. Panum's fusional area is narrow at the center and widens towards the periphery reflecting high resolution and small receptive fields in central vision and low resolution and large receptive fields in the periphery[6]. Binocular visual thresholds have also been found to increase with peripheral stimulation. Stereoscopic resolution deteriorates exponentially with increase in stimulus eccentricity[7]. Ogle et al[8] reported that the vertical extent of Panum's area increases for stimuli placed up to 12 deg from the line of sight along the horizontal meridian. The Veith Muller circle is a theoretical horopter. All points in this circle theoretically stimulate corresponding points and lead to single vision. The Veith-Muller

circle assumes that there is angular symmetry of the corresponding points[9]. The Veith-Muller circle does not match the empirical horopter the locus of corresponding points is an ellipse and not a circle[10]. The difference between the theoretical Veith Muller circle and empirical horopter is called Hering-Hillebrand deviation[10]. Retinal disparity describes the spatial relationship of retinal images with corresponding points. Images falling on corresponding points subtend zero retinal disparity. Images falling on non-corresponding points subtends non zero retinal disparity. Retinal disparity arising from objects that are closer than fixation is called 'crossed disparity'. The images formed by objects closer than fixation lie more towards the temporal retina in each eye. Convergence of the eyes is required to place the images on the fovea. Similarly, retinal disparity arising from objects that are far away from the fixation is called 'uncrossed disparity'. The image formed from objects closer than fixation lie towards the nasal retina in each eye. Divergence of the eyes is required to place these images on the fovea.

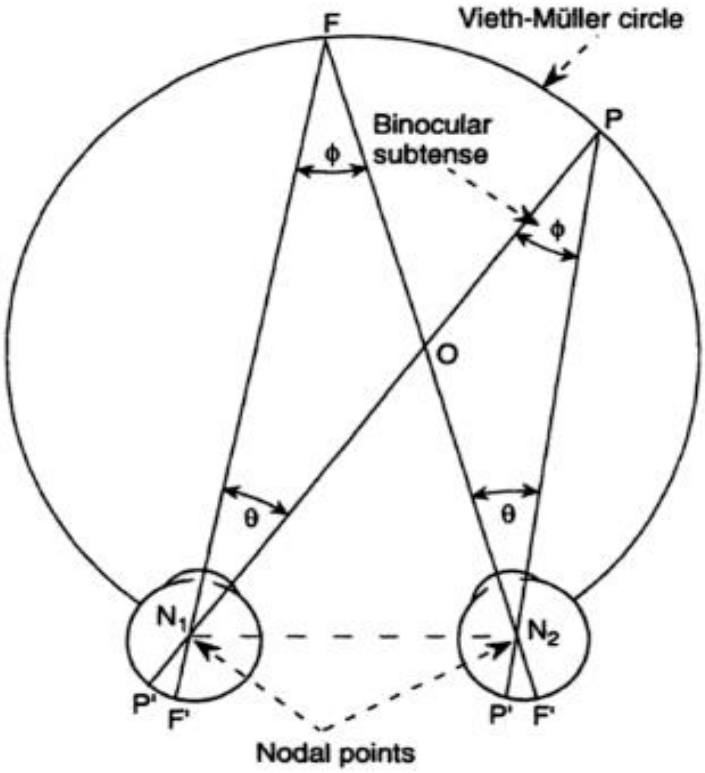

Figure1: Basic geometry of the horizontal horopter. Point F prime falls on the fovea and has zero disparity when the eyes are converged on point F. Images of point P stimulates corresponding points on the retina with respect to point F. The Veith-Muller circle is defined as the locus of all points having zero disparity. Figure adapted from binocular vision and stereopsis by Howard and Rogers[1].

1.2 The physiological basis of stereopsis:

Early work to understand the mechanism of binocular vision and stereopsis was done by Helmholtz, who believed that binocular stereopsis was as a result of a high-level cognitive processes rather than a combination of visual inputs from the two eyes at the early stages of visual processing[2]. Ramon Y Cajal, based upon anatomical investigations, proposed that inputs from corresponding retinal regions converge on what he called "isodynamic cells"[11]. This theory was supported by Hubel and Weisel[12,13] who reported that cells in the cat's visual cortex receive inputs from the two eyes and that the receptive fields of these binocular cells occupy corresponding positions in the two eyes. The primary visual cortex (V1) is the first site at which single neurons can be activated by stimuli in both eyes[14]. The neurons encode information specifically about the relationship between the images in the two eyes. Barlow and Pettigrew[15] were first to describe horizontal disparity sensitive neurons in the primary visual cortex of anesthetized cats and proposed that these may be responsible for stereopsis. Disparity detecting cells have since been found in a range of visual cortical areas including V1, V2, V3, V5 and the medial superior temporal area (MST)[16]. Disparity detecting cells have been classified as near cells which are tuned for crossed disparity, far cells which are tuned for the uncrossed disparity, tuned excitatory cells responding to zero disparity and tuned inhibitory cells responding to all disparities but having a minimal response to zero disparity[11,16].

1.3 Neural basis of stereopsis

Binocular disparities can be encoded as a physical difference in the retinal positions of images or as a phase difference between corresponding points. Binocular neurons use interocular phase or interocular positional differences to encode disparity. In particular, the positional shift model explains that disparity due to positional differences between right and left eye images is computed by a cell with a horizontal shift between the receptive fields of the two eyes whereas the phase shift proposes that it is computed by the difference in arrangement of ON and OFF subunits between the two eyes[17]. Ohzawa& Freeman[18] performed the first quantitative comparison of monocular and binocular responses at different disparities in simple cells in cats visual cortex. They provided evidence that the disparity selectivity might be due to cells having receptive fields in corresponding retinal locations but the shape of the receptive fields is different between the two eyes. Anzai et al[19] compared the monocular and binocular responses of simple cells in adult cats by showing uncorrelated noise patterns to the two eyes. Receptive field profiles were constructed at different locations in the two eyes. They found that binocular interactions depend not only on binocular disparity but also on monocular stimulus phase and positions. Quantitative evidence of the operation of two operational mechanisms and cells showing sensitivity to both phase and positional disparities indicate that encoding happens in a single pathway and both positional and phase signals are combined in the cortical representation. Neurons which respond to binocular stereoscopic depth stimuli also exhibit tuning for disparity and spatial frequency. Neurons that are tuned to low spatial frequencies exhibit poor resolution and respond to a wide range of disparities.

In contrast, neurons tuned to high spatial frequencies exhibit fine resolution properties but are limited to processing narrow range of disparities[19,20]. Trotter et al investigated the neural mechanisms underlying visual localization in 3-D space in area V1 of monkeys. They found that changes in fixation distance modify the response of cortical cells to horizontal disparities[21]. A mixture of different disparity selective cells with different encoding properties indicates that stereoscopic depth perception requires complex neural computation.

1.4 Stereoscopic processing in the brain

Stereoscopic depth processing appears to be a multi-stage process involving both dorsal and ventral stream processing. Both pathways contribute to different stereo computations and perceptual judgments about stereoscopic depth perception[22]. The crucial step of processing retinal disparity is finding where the image of the object is falling on the retina in one eye and defining its corresponding point in the other eye. This is known as the correspondence or matching problem. The initial hypothesis was that stereopsis is a higher-level process where the visual system operates on two retinal images separately performing segmentation, object recognition and comparison for each object in the scene individually. However, the cyclopean RDS stimulus by Bela Julez[3,23] posed a challenge to the correspondence problem as each dot in the RDS potentially has many matches in another eye. The visual system processes the pattern of neighboring dots rather than matching the dots individually. This implies that the correspondence problem must be solved at a ‘global level’; in order to find the correct match one cannot consider the dots

individually, but must also consider the pattern of the neighboring dots. That is, the visual system solves the correspondence problem at a 'global' rather than a purely local level. The local and global stereopsis mechanisms are dissociable. In monkeys, Cowey and Porter[24] reported impaired global stereopsis due to bilateral lesions affecting the inferior temporal cortex whereas removal of portions V1 and V2 that are responsible for central vision elevated the stereothresholds measured on local stereopsis leaving global stereopsis intact. Studies in humans done to understand the processing of local and global stereopsis have revealed contradictory results. In patients, damage to bilateral visual cortices have been associated with loss of three-dimensional vision[25]. Hamsher et al[26] reported selective impairment of global stereopsis with intact local stereopsis in patients with right cerebral hemisphere damage. Ptito et al[27]showed evidence of unaffected local stereopsis when the global stereopsis was impaired due to a temporal lobe excision. The processing of global stereopsis is thought to occur in two stages, the first involves the detection of local disparity and the second involves the integration of this information across large areas of visual information[28]. Poggio et al found neurons responsible for the processing of global stereopsis in V1 and V2 in the foveal cortex of macaque monkeys[29]. The presence of two distinct stereoscopic processing mechanisms highlights the importance of separate measurement in clinical tests. Clinically, different tests are available to measure stereothresholds based on local and global stereopsis. More details are described in chapter 2.3.

1.5 Use of noise to investigate visual functions

Perception of depth is a key task that the visual system has to perform. To achieve this, the visual system must integrate the signal, depth information, and segregate out noise. The ability to process the signal in the presence of noise can be measured psychophysically by altering the ratio of signal dots to noise dots (coherence thresholds) in random-dot visual stimuli. This technique has been used to study global (coherent) motion perception and binocular vision [30,31]. In global motion perception experiments, the subject views a display containing signal dots moving coherently in one direction among noise dots moving randomly. The coherence thresholds are the proportion of the signal to noise dots required to report the direction of coherent motion correctly. The motion coherence task requires integration of local motion signals into a global percept[32,33]. Psychophysical and physiological studies have clearly distinguished global motion processing which is sensitivity to overall direction of motion as opposed to local motion processing which arises from motion sensitivity in a small region of the image[34,35]. In the processing of motion perception, early cortical areas process the local motion components of the object whereas extrastriate areas process motion of the object as a whole.

The segmentation and discrimination properties of disparity processing have been examined by using the signal in noise tasks where an observer is asked to detect a disparity-defined target hidden in a cloud of random dots that mask the target. Uka et al[36]compared neuronal and psychophysical sensitivity to disparity while monkeys discriminated between two coarse disparities (near vs. far) in the presence of noise. The disparity signal was manipulated by varying

the binocular correlation. At 100% correlation, all dots were presented at preferred disparity that elicited a minimal response. At 50% binocular correlation half of the dots were assigned to have random disparities forming a three-dimensional cloud of disparity noise. All correlated dots were assigned fixed crossed vs. uncrossed disparities and noise dots were assigned random disparities between -2 and 2°. Neuronal activity was recorded using extracellular electrophysiological recordings. The average neuronal and behavioral thresholds were found to be nearly identical. The findings indicated that MT was well suited to provide signals that form the basis of perceptual judgments even when stereopsis signals are noisy. Visual noise has also been used in measuring the sensitivity of stereothresholds in human observers. Palmisano et al[37] examined the effect of additive disparity noise on human observer's ability to detect surfaces with periodic corrugations in depth. Noise displays were added to the stereoscopically defined 3D surface by scrambling the signal stimuli along the vertical dimension. The stereoscopic information was preserved while the surface representation of the corrugated surface was disrupted. Additive disparity noise was found to interfere with stereoscopic surface detection for human observers.

External noise has been used widely in investigating visual functions. The quantification of motion perception in noisy signals was taken as a model system to develop a new test based on quantifying depth perception in noise.

Chapter 2

STEREOACUITY

2.1 Depth discrimination thresholds and stereoacuity

The quantification of stereopsis provides information about the binocular vision status of a patient. The depth-discrimination threshold is the smallest depth interval between two stimuli that a subject can detect. Stereoacuity is the depth discrimination threshold expressed in angular terms. Stereoresolution of the human visual system under optimal conditions is as low as few seconds of arc[38,39]. Stereoacuity is a hyperacuity at the fovea; depth differences can be distinguished that are smaller than the diameter of individual photoreceptors[40,41].

In the 19th century, Wheatstone invented the stereoscope which dichoptically presented images containing horizontal disparity between the two eyes using mirrors. This produced retinal disparity and a sensation of depth. Wheatstone's work showed that retinal disparity contributes critically to depth perception and that the brain uses horizontal retinal disparity to estimate relative depth[42]. The processing of stereoscopic information involves local matching of retinal images to obtain an estimate of the absolute disparity of objects relative to the point of fixation. The relative disparity is then computed so that the relative depth of objects is represented independently from the point of fixation[43]. Westheimer et al[41] provided evidence that humans are more sensitive to changes in relative disparity than absolute disparity. Further works found neurons selective to absolute disparities in the primary visual cortex. Neurons selective to relative

disparity were found in area V2[44]. This provided evidence of stereoscopic processing downstream of primary visual cortex.

2.2 Monocular and binocular cues to depth perception

The perception of depth can be monocularly or binocularly perceived depending on the visual cues available. The relative size, interposition, lightness and shading, motion parallax and linear and aerial perspective of an object are cues giving rise to monocular depth perception[11]. Binocular cues to depth include horizontal binocular disparities and vergence effects[45]. A clear difference in performance under monocular and binocular viewing conditions has been demonstrated for fine motor tasks such as bead threading[46] and reaching and grasping movements[47,48]. Removing binocular information even in the presence of monocular cues can interfere with fine motor task performance.

2.3 Measurement of stereoacuity

Stereoacuity is a measure of stereoscopic performance based on the minimum detectable horizontal disparity. Stereopsis tests have two basic divisions, local and global stereopsis. Local stereopsis depends on horizontal disparity from monocularly detectable patterns whereas global stereopsis consists of cyclopean patterns which are not detectable when viewed monocularly[49]. Therefore, global stereopsis requires local matching of stimulus elements between the two eyes to

recover local depth cues, followed by integration of these local cues into a global, or coherent, percept of form.

There are presently several tests available to assess stereoacuity[50]. A wide variation in stereoacuity has been observed within individual subjects and between stereopsis tests[51]. Real depth tests such as the Howard-Dolman test and the Frisby test create depth by physical separation of test elements. In the Howard-Dolman test, the subject views two vertical rods 1cm in diameter, 6 cm apart, from 6 meters. The subjects judge the relative position of the two rods. The Howard-Dolman test measures stereoacuity thresholds as low as 2 seconds of arc[52]. The Frisby stereo test consists of three transparent plates with different thicknesses: 6mm, 3mm, and 1.5mm. The target is a randomly arranged pattern of arrowheads of various sizes printed on one side of the plate with a circular patterned region printed on the other side of the plate in one of the four quadrants. The subject identifies the disk that differs in depth. The plate creates a binocular disparity of between 15 and 340 arc seconds, depending on its thickness and the viewing distance[53]. Real depth tests have the advantage of not requiring dissociative glasses and give better real world experience[50]. A motion parallax cue is present in real depth stereopsis tests that can be minimized by limiting the movement between patient and test plate[53]. Random dot stereogram tests including the TNO test and Randot tests are used to measure global stereopsis and are widely recommended for detecting abnormal binocular vision. Random dot stereograms (RDS) were first introduced by Bela Julesz in 1960. These stereograms are created by presenting similar random dot patterns to each eye with no apparent shape when viewing monocularly. A

cyclopean shape is created by horizontally shifting a region of dots in one eye creating a disparity with respect to the surrounding dots[10]. The perception of depth is achieved when monocular images containing horizontal disparity are fused[23]. The design of RDS eliminates all non-stereoscopic cues. Clinically, the limitation of RDS test design is longer viewing duration to identify stereoscopic form[54]. Stereoacuity norms for several standard clinical tests have been widely reported. Cooper et al[55] traced the development of stereoacuity in children between 3 to 11 years using Titmus, TNO and Randot sterotests. Adult performance was reached on all the tests by the age of 7 years. Heron et al[56] reported that stereoacuity was higher in children when measured on Frisby stereo test than TNO or Titmus test. Fox et al[57] measured stereoacuity in children using Howard-Dolman apparatus and found mean stereoacuity of 12.6 seconds of arc for a 5 year old participant. Fox concluded that the adult level stereoacuity is achieved at or soon after the age of five years.

The present clinical tests used to quantify stereopsis, which is an important indicator of normal binocular vision, face major limitations. Different test designs have a cap on the maximum stimulus disparity that can be used. Subjects who initially fail to detect the maximum disparity are labeled as having nil stereopsis on the clinical tests (ceiling effect). Stereograms with high disparity are not easier to detect than those with moderate disparity levels in those with impaired binocular vision[58]. This ceiling effect has a major disadvantage as the clinician cannot quantify or report improvements in stereopsis in people with severe loss. Similarly, the clinical test also has limitations on the smallest stimulus disparity that can be measured based on the test design. Under

ideal conditions, the stereothresholds for a normal trained observer can be as low as 2 seconds of arc. However, on clinical stereopsis test, depending on the type of clinical test being used 10 to 40[9,50,59,60] seconds of arc has been reported as a good performance. Given that the lowest disparity thresholds that can be detected are considerably better, a floor effect is observed in many subjects[51].

Most tests available also contain monocular cues that may lead to measuring artificially enhanced stereoacuity or false positive results. Also, most stereopsis tests used in clinical settings are also calibrated for use at a specific testing distance. The alteration of test distance closer or farther from the patient's eye can cause increase or decrease of retinal disparity resulting in overestimation or underestimation of steroacuity[61]. The repeatability of stereoacuity was found to be poor in subjects with poor binocular vision and the clinical stereoacuity tests exhibit reduced agreement indicating that they cannot be used interchangeably[62]. At present, there are no tests for stereopsis that are robust in being able to adequately detect a wide range of binocular visual function, provide good within and between test reliability and provide a useful measurement variability. Redesign of clinical stereoacuity measures without the ceiling and floor effects and with good repeatability could, therefore, provide a more accurate estimate of stereopsis and would be helpful for monitoring improvement and screening in patients with abnormal binocular vision.

2.3.1 Spatial characteristics of stereoacuity

The spatial characteristics of RDS stimuli have been studied extensively. The dot density was defined as the percentage of the total stereogram area that is covered by dots. Tyler[63] measured stereothresholds in random dot stereograms with a range of dot densities and found that for dot densities greater than 43 dots/deg^2, density had very little effect on stereothresholds. Gant et al[64] obtained stereothresholds for a small disparate line segment superimposed on low and high-density flat random dots background. They found optimal thresholds for detecting a stereo pair of vertical bars was 13.8 seconds of arc with a background of 1.77% dot density. The stereothresholds increased two folds (doubled) at lower and higher dot densities with densities that ranged between 1.15% and 15%. They explained that the increase in stereothresholds at low dot densities might be due to increased spacing between elements and attributed the increase in stereothresholds with increased density to crowding effects which might lead to interruptions in disparity averaging mechanisms between the two eyes. The increase in stereothresholds can occur regardless of the discrimination of individual elements in the stereogram[65,66]. The effect of spatial frequency on the perception of corrugated surfaces within RDS was first reported by Tyler[63]. Tyler modulated the disparities of RDS containing sinusoidal gratings. The amplitude (peak to peak) of the wave pattern was varied at different spatial frequencies. Observers were asked to indicate the range of amplitudes at which perception of depth was still noted. Stereo thresholds exhibited decreased thresholds at upper and lower disparities. The variations in depth in the corrugated sinusoidal gratings could not be perceived beyond 5cycles/degree. The optimal

performance was found to be at 1 c/deg. Graham et al[67] found the thresholds for detecting corrugated sinusoidal gratings were lowest at 0.3 to 0.5 c/deg and increased for higher spatial frequencies. Graham et al measured thresholds at six different spatial frequencies 0.05, 0.1, 0.2, 0.4, 0.8 and 1.6 cycles per degree. Graham et al did not observe any floor effects and thresholds were measurable at chosen spatial frequencies. The sensitivity curves for perceiving depth in corrugated sinusoidal gratings agreed well with the results from the previous studies[63]. Fusion was achieved in high and low spatial frequencies. Absolute sensitivity in Tyler's[63] experiments was between 15 and 30 arcsec of the disparity between the peaks and troughs of the corrugations at spatial frequency of 1 cycles/degree which was comparable to the data from Graham et al.

Harwerth et al[54] studied the effect of viewing time on thresholds for depth and form discrimination using random dot stereograms. Stereoscopic stimuli with crossed and uncrossed disparities were presented with viewing times ranging from 0.12 sec to 7 sec. A linear relationship between logarithmic viewing time and disparity threshold for depth discrimination was found. Extended observation times required to detect global stereopsis might indicate the complexity of neural processing[54].

2.3.2 Effect of interocular differences on stereoacuity

Binocular vision and stereoscopic processing mechanisms are affected by inter-ocular differences in contrast and luminance[68–70]. Halpern and Blake[68] measured stereothresholds as a function of

interocular contrast difference using the method of adjustment. The observers adjusted the retinal disparity of a narrowband stimulus until it appeared in the depth plane defined by two flanking reference lines. When the fixed contrast was high, stereo acuity deteriorated steadily as the contrast in one eye was decreased. This effect was greatest at the lowest spatial frequency tested. When the fixed contrast was low, however, small increases in the contrast to one eye had no deleterious effect on stereo acuity. In addition, reducing contrast to only one eye impairs stereo acuity more than an equivalent contrast reduction to both eyes[68,71] while having essentially no effect on fusion limits[71].

The mean luminance in both eyes and one eye was manipulated using neutral density filters by Alexandre et al[72] to investigate the effects of luminance on stereopsis. Disparity processing was minimally affected by a binocular change in luminance but was greatly affected by a luminance mismatch between the two eyes. Stereothresholds remained constant until ~1.5 ND but grew exponentially to approximately three-fold with an increase in luminance mismatch between two eyes >1.5 ND filter. Stereothresholds also progressively degraded with the addition of dioptric blur and by diffusing blur using a Bangerter filter over one eye[73,74]. Stereothresholds are sensitive to mismatch of luminance, contrast and spatial frequency between the two eyes. The reduced sensitivity might be due to inter-stimulus suppression where the stimulus with higher luminance or contrast suppresses the weaker stimulus. Location shifts have also been attributed as the cause where a brighter stimulus causes shifts in the apparent location of the dimmer stimulus reducing the disparity between them[10]. Loss of stereothresholds due to unequal illumination between the

two eyes might be due to the latency differences between the stimuli. With unequal illumination, visual inputs from the two eyes arrive at the visual cortex at different times causing asynchrony. Stimulus asynchrony could directly interfere with the detection of disparity[72]. Stereothresholds also show sensitivity to unilateral defocus. Peters et al[75] found that 80% of subjects show deterioration of stereothresholds for 1D of monocular defocusing. The degree of tolerance of monocular defocus also differs between local and global stereopsis. The tolerance to defocus is better for global stereopsis than local stereopsis[76].

Human stereopsis has been shown to have constraints in detection due to spatial characteristics of the stimulus as described above. The maximum and minimum disparities that can be detected provide a background in understanding these constraints.

2.4 Stereopsis and amblyopia

Amblyopia is defined as a neuro-developmental disorder of the visual cortex that arises from abnormal visual experience early in life[77]. It presents with a number of impairments in spatial vision such as reduced visual acuity, impaired contrast sensitivity, impaired global motion integration, reduced stereopsis and reduced visual acuity with crowding[78]. The risk of developing amblyopia is associated with strabismus, significant refractive error, and conditions that may cause form vision deprivation. Amblyopia is clinically significant because it is one of the most

prevalent visual disorders in children affecting 4.7% of children in Canada[79]. The key to successful treatment depends on detecting amblyogenic risk factors by measuring impairments in spatial vision, specifically, reduced visual acuity and/or stereopsis. The importance of an accurate and precise clinical test to measure stereopsis is essential in screening for amblyopia. Stereopsis measures can also reveal the effectiveness of therapy and be helpful in monitoring the disease. Impaired stereopsis has real-world implications for patients with amblyopia including reduced performance on a wide range of visuomotor tasks[80–82]and visually guided hand movements[83]. Improved stereoacuity has also been associated with better reading ability[84].

Stereoscopic perception is strongly depended on well-balanced input from the two eyes[68,85,86]. Under conditions of normal vision, balanced binocular vision is maintained due to symmetric suppression between the two eyes. Imbalance of suppression leads to abnormal binocular vision. In amblyopia, the dominant eye or the fellow fixing eye (FFE) exerts stronger suppression over the non-dominant eye or the amblyopic eye (AE) resulting in disrupted binocular vision[87,88]. Suppression of the amblyopic eye has been implicated as a possible cause of amblyopia and loss of stereopsis in humans[30,89,90]. A modern binocular approach has been used to reducing suppression by rebalancing the information between the two eyes. Binocular treatment is based on evidence that patients with amblyopia have functionally suppressed binocular visual systems under normal viewing conditions and the visual system in amblyopia can combine information between the two eyes if suppression is reduced[30,91,92]. The treatment involves reduction of contrast in the fellow dominant eye while presenting the amblyopic eye with full contrast. Many recent

studies have explored contrast balanced binocular treatment to improve visual function[91,93–95]. Significant improvements in visual acuity and stereopsis were observed on in adults and children[92]. Ding et al[96]measured the recovery of stereopsis in stereo blind individuals through perceptual learning (PL) on contrast balanced visual stimuli between the two eyes. The best stereo performance for normal observers occurred when two eyes were presented with identical contrast. All observers with stereothresholds of less than 100 seconds of arc showed substantial improvements of on both psychophysical and clinical stereothreshold tests after perceptual learning on contrast balanced targets. Hess et al[90] showed improvement of stereopsis on a dichoptic, video-game-based iPod treatment called Tetris. Tetris stimuli comprise high and low contrast blocks. The high contrast blocks are falling blocks that are seen by the amblyopic eye. The players have to change the position and orientation of the falling blocks to form tessellated rows of blocks at the bottom of the screen. Low contrast blocks are seen by the fellow fixing eye. The contrast offset between the two eyes is increased overtime by 10% of its starting value. Stereothresholds improved significantly by 0.61 log units post treatment. In some patients, stereopsis that could not be measurable clinically was improved to fine or coarse levels after treatment. Hess et al[97] investigated the residual stereothresholds of patients with strabismic amblyopia by using motion in depth targets. Amblyopic patients who had no stereoscopic function were retested by placing a neutral density filter (ND) in front of the fellow fixing eye. The idea behind this was to reduce the suppressive influence of the normal eye and balance binocular input between the two eyes to reveal the presence of any latent stereo function. Stimuli

were dynamic random dot stereograms consisting of red and green dots distributed on a dark background. The dynamic random dot stereogram was made up of disparity defined square shapes with crossed and uncrossed disparity. Temporally correlated and uncorrelated dynamic random dot stereograms were used. Subjects were asked to indicate whether the disparity-defined square in the left or right side of the screen was closer. The use of an ND filter in front of the fixing eye significantly improved performance in a selected group that exhibited chance performance without filters. This residual stereopsis was called latent stereopsis. However, the similar comparison made on static stereoacuity tests such as Randot and TNO tests did not reveal improved stereopsis in this group. The authors suggested latent stereopsis is specific for dynamic stimuli in strabismic amblyopia. In chapter 6, we focus on measuring global stereothresholds using noise coherence and disparity thresholds by balancing the contrast between eyes for randot stereograms in a small set of participants with amblyopia.

2.5 Objective and aims of the study

The perception of global stereopsis in RDS is a two-stage process, the first stage involves processing of local disparity signals and the second stage involves the integration of local stereoscopic information into a global coherent form[15,98,99]. The overall purpose of our research was to develop a novel measure of stereopsis that targets global integration. This was achieved by degrading orientation discrimination of a depth defined sinusoidal grating within random dot

stereograms by randomizing the depth position of a proportion of dots (noise dots). We call the thresholds obtained by this novel measure as stereocoherence thresholds or stereoCT.

The specific aims were:

Aim 1

Spatial stimulus characteristics for stereoCT

The first aim was to identify appropriate spatial parameters for a stereoCT stimulus that consisted of an RDS depicting a depth-defined sinusoidal grating. We focussed on four main spatial parameters: the density and dot size of the RDS, the spatial frequency of the sinusoidal grating in the RDS and finally the peak-to-peak disparity of the sinusoidal grating. We also evaluated the test-retest repeatability of the stereoCT at variable stimulus disparities.

Aim 2

The second aim of the study was to investigate the effects of disrupted binocular vision induced with to uniocular blur, uniocular fogging and with differences in interocular contrast and in luminance on stereoCT in normal individuals. The hypothesis was that the stereoCT measures would exhibit increased sensitivity to binocular disruption and reduced variability in healthy individuals compared to conventional disparity thresholds under conditions of disrupted binocular vision.

Aim 3

The final aim was to examine stereoCT in patients with amblyopia. StereoCT were measured with a suprathreshold stimulus disparity determined by conventional disparity thresholds and retested with different levels of penalisation of the dominant eye. The hypotheses were that the stereoCT would improve at the same optimum contrast reduction in the fellow eye as disparity thresholds and that stereoCT would be more sensitive and less variable than similar measurements using conventional disparity thresholds.

Chapter 3

Overview of methods, apparatus, and procedures

3.1 Introduction:

The research undertaken comprises a series of studies. Firstly, pilot studies to define the normal parameters of stereopsis with conventional thresholds and stereoCT. The main studies utilized artificially degraded vision to characterize the impact of visual degradation on stereo thresholds. Finally, the stereopsis tests were used to explore binocularity on a small series of individuals with amblyopia.

In this chapter, the strategies for measuring stereoCT are explained and the overall methods and apparatus are outlined.

3.2 Experimental stimuli

3.2.1 Software description and instrumentation

Stimuli were created in MATLAB (The Math Works; CA) with the Psychophysics toolbox[100] and displayed on a gamma-corrected VPixx 3D monitor (VPixx technologies, Vision Science Solutions) at a viewing distance of 600 cm. Each pixel subtended 0.15 arc minutes at this viewing distance. Subjects viewed the stimulus wearing VPixx LCD shutter glasses, which operated on an active shutter (frame sequential) principle providing a single stereoscopic image. Between

presentations, the observer fixated a central white dot, presented dichoptically (zero disparity), against a gray background (35 cd/m^2). Figure 5 shows a similar stimulus that can be viewed using red: green filters to separate the eyes. The stimuli comprised two interleaved images of RDS that were presented within a central square area of 2.86 degree X 2.86 degree. The random dot stereogram consisted of randomly distributed white dots (5.5 arcmin diameter dot size; dot density of 183 dots/deg^2 and 1 cpd spatial frequency). All the signal dots formed a corrugated sinusoidal grating. A similar corrugated surface can be seen in Figure 3 using red-green glasses. The noise dots were dots that had similar stimulus properties such as dot size and contrast equal to those of the signal dots. The noise dots were positioned randomly within the disparity range defined sinusoidal grating. The proportion of noise dots to the signal dots could be varied and staircase procedures were used to determine thresholds based on observer's responses[101,102]. The stimuli for measuring conventional disparity thresholds comprised of two interleaved images of a RDS (2.86 deg X 2.86 deg) presented dichoptically on the VPixx screen. Coherent random dots contained a sinusoidal corrugated surface. A range of stimulus disparities were introduced based on positional differences between the two half images necessary to give rise to binocular disparity. The minimum change in stimulus disparity that could still give rise to the perception of depth was recorded as disparity threshold in seconds of arc. We added 10% random noise dots to the conventional (100% coherent) disparity threshold stimulus to minimize floor effects. This was a novel method to overcome the test limitation.

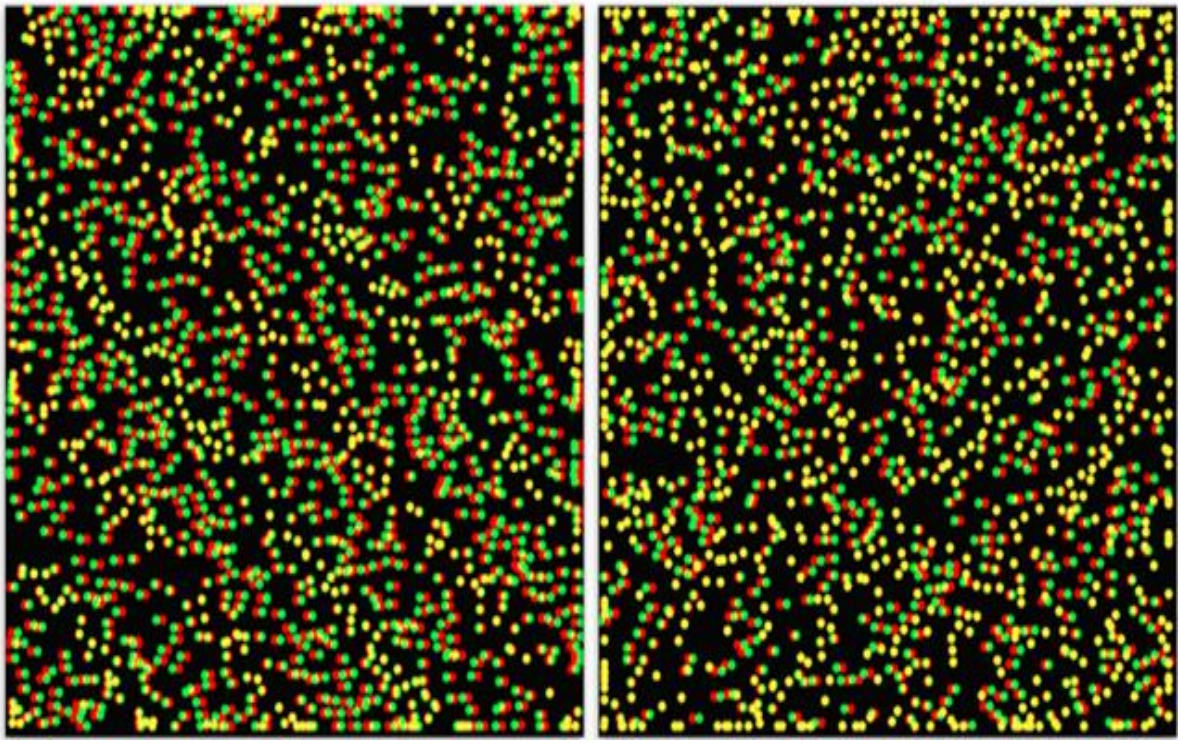

Figure 2: A red-green stereogram presented above illustrates stimuli similar to those used in the study. (In the study monocular gray dots were separated between the eyes using LCD shutter goggles.) The image on the left shows RDS with 100% coherence and the image on the right shows a RDS with 60% coherence (40% noise dots). The disparity of the sinusoidal grating is the same in the right and left images but the image on the right has a less coherent form due to an increase in the proportion of noise dots.

3.2.2 VPixx display Luminance calibration

VPixx monitors have better performance than CRTs because of their superior temporal and spatial characteristics[103]. Calibration and luminance readings for the VPixx monitor were made using a computer-controlled spectrophotometer. The sensor of the spectrophotometer is first calibrated using a standard white calibration plate. The spectrophotometer is then placed against the screen to block any stray light (i1, X-Rite, VPixx technologies); the i1Pro photometer can measure spectral data between 380 nm and 730 nm at 10 nm intervals.

3.2.3 Psychophysical Thresholds:

StereoCT

A two alternative forced-choice staircase procedure was used to estimate the stereoCT and disparity thresholds. A coherence of 100% means that all dots are signal dots; while a coherence of 0 means that all dots are noise dots. The stereothresholds were reduced after four consecutive correct responses and increased after one wrong response that corresponded to a criterion of 85.84% correct[102]. The reduction rate in disparity or coherence was 20% before the first reversal and 10% after the 1st reversal, while the increase rate was always 5% of the incorrect response. Each session was terminated after five reversals and the threshold was computed from the mean of the last three reversals. Observers were asked to detect the orientation of sinusoidal gratings,

which was oblique towards either the left or right side. At the end of each presentation, the observer made a forced-choice decision about the orientation of the disparity target. The stimulus was presented for one second and the observers had 30 seconds to respond.

Disparity thresholds

Disparity thresholds followed a similar threshold measuring procedure in terms of step size, number of reversals and presentation time. The disparity amplitude was modulated using a one up and four down staircase. The stereoacuity was first assessed using the stereo fly test and this information was used to present the initial largest disparity on the test to determine thresholds.

3.2.4 Screening Tests

Clinical visual acuity and stereoacuity

Best-corrected visual acuity was measured using the Freiburg Visual Acuity test, an automated procedure measurement of visual acuity[104]. Landolt-Cs were presented on a monitor in one of eight orientations. The subjects were asked to respond to the orientation of the Landolt-Cs using a keypad. Acuity thresholds were determined by the ‘‘Best Probability Estimation of Sensory Threshold’’ (PEST) staircase. The BEST-PEST algorithm estimates visual acuity in adaptive steps starting with large optotypes and closing in on the thresholds by reducing the step size based on the observer's response[105]. Stereoacuity was measured using the Stereo Fly Test. This test was

performed at 40 cm with the subject wearing polarizing spectacles. The Stereo Fly test consists of line stereograms of a housefly with large disparity, animals with disparities of 400 to 100 seconds of arc, and nine sets of circles with disparities of 400 to 20 seconds of arc. The stereo fly test evaluates both gross and fine stereopsis from 800 to 20 seconds of arc. The fly was shown first. If a positive response was given, the subjects proceeded to identify the perception of depth in animals and circles respectively. The lowest disparity that the subject was able to detect was recorded as their stereo thresholds in seconds of arc.

Cover/uncover test and alternate cover test

Ocular alignment was assessed using a cover/uncover test and alternate cover test for both a distance (6 m) and near (50 cm) target. In the cover/uncover test the participant is asked to look at a fixation target placed at a distance or near. A cover paddle is used to switch between binocular fixation (uncover) and monocular fixation (cover) by occluding the participant's right eye and then left the eye. The examiner observes the un-occluded eye to determine if re-fixation occurs. The alternate cover test was performed by switching occlusion between the left and right eye for 1 to 2 seconds without allowing binocular fixation to occur. A deviated eye will show refixation when uncovered. If strabismus (manifest deviation) or heterophoria (refixation on the alternating cover test) was detected, the deviation was neutralized using prism bar. Normal subjects showed heterophoria within normal limits according to Morgan's norms[106,107].

Worth four-dot test

The Worth-four dot test is a subjective test to determine the presence of binocular fusion or suppression. The testing target consists of four illuminated dots; two dots are green, one is red, and one is white. The participant views the target through red-green glasses that consist of a red filter in front of one eye and a green filter in front of the other. Monocularly, the participant sees two red dots through the red filter and three green dots through the green filter. Binocularly, however, the fused perception results in the participant seeing four dots because the white dot is seen as either a single red or green dot, according to which eye is dominant.

Test for eye dominance (Hole in a card test)

Eye dominance was determined by instructing the subject to binocularly fixate one letter on a visual acuity chart (20/200) at distance through a 'hole' between their hands. The subject was asked to report from which eye the target was visible while the examiner occluded each alternately. The dominant eye was the eye that could maintain the view of the letter centered in the hole. Eye dominance was measured to simulate amblyopic vision by placing neutral density filters over the non-dominant eye. Zhou et al[69] replicated the strong binocular imbalance between two eyes observed in patients with amblyopia by manipulating interocular luminance using neutral density filters placed over the non-dominant eye.

3.2.5 Participants

All studies were designed as cross-sectional studies. Subjects were recruited through University of Waterloo bulletin boards, email lists, and the University of Waterloo graduate studies website. The total number of normal participants in the study was 50 and 4 participants had amblyopia. All subjects were screened using the test described in detailed below

Table 1: Characteristics of healthy participants

Participants	Median Age	Median VA	Median stereoacuity
Normals	27	-0.1	20

Inclusion criteria for healthy participants

- Best corrected visual acuity 0.1 Log MAR or better in each eye.
- Stereoacuity 25 seconds of arc or better on the stereo fly test.
- Heterophoria within normal limits based on Morgan's norms[106,107].
- The absence of strabismus and other ocular diseases.

Participants with visual acuity worse than 0.1 Log MAR or stereoacuity worse than 25 seconds of arc on the stereo fly test were excluded from the study unless they met the criteria for amblyopia (see Chapter 6). The subjects gave informed written consent before participating and the study was approved by University of Waterloo office of Research Ethics (see Appendix 1).

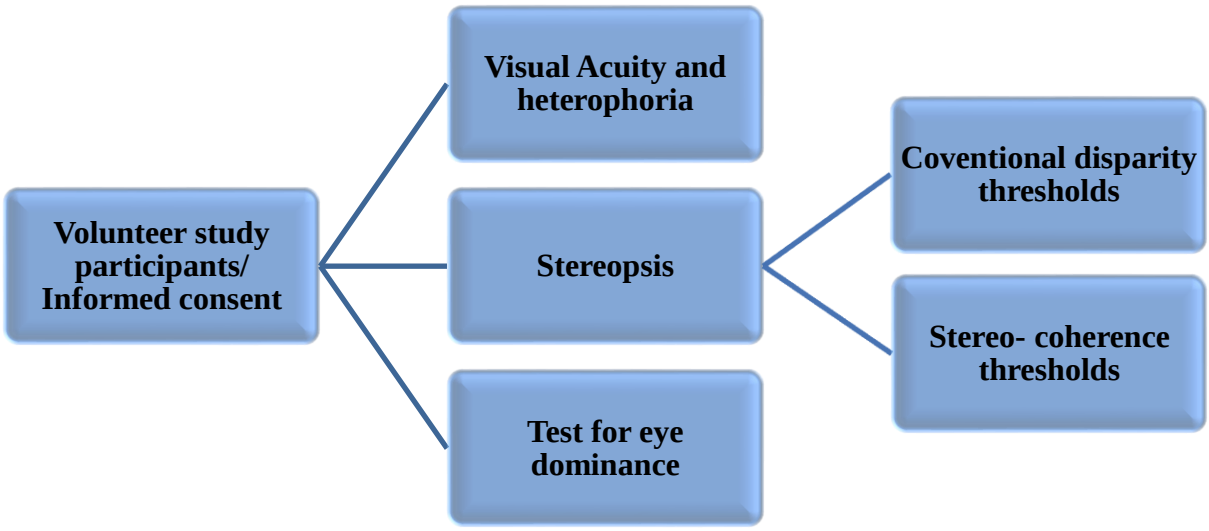

Figure 3 Depicts the hierarchy of the experimental procedure. All healthy participants and participants with amblyopia underwent routine clinical evaluation and if they were eligible, conventional disparity threshold and stereoCT were obtained using the experimental stimulus.

3.3 Statistical Analysis

Statistical analysis was performed using the commercial software SPSS (version 24). Descriptive statistics included mean and SD for normally distributed variables and median and interquartile range (IQR) for non-normally distributed variables. The Shapiro-Wilk test was used to check for the normality of distribution. A p-value of ≤ 0.05 was considered statistically significant.

3.3.1 Paired comparisons of means

The paired t-test calculates the difference within each before-and-after pair of measurements, determines the mean of these changes, and reports whether this mean of the differences is statistically significant. The paired t test assumes that the variance between groups is equal. Our data revealed unequal variances between conditions. We used post hoc paired Tamhanee T2 test corrected p values. This test is used when the variances between paired groups are unequal[108].This method is based on the student t-distribution. It uses the Sidak test to set the alpha level and the Welch procedure to determine degrees of freedom.

3.3.2 Variance calculations

An F test[109] is used to measure statistical differences if variances of the two populations are equal. Variances are a measure of dispersion or scatter of data from the mean. Larger values represent greater dispersion.

3.3.3 Test-retest Repeatability

Test-retest repeatability was assessed using the intraclass correlation coefficient (ICC). The ICC is a measure of the reliability of measurements or ratings. The ICC is calculated with variance estimates obtained through analysis of variance. The benchmark values of <0.75 ICC indicate poor to moderate reliability, Values >0.75 indicate good reliability[110].

In Chapter 4 spatial stimulus parameters including dot density, dot size, spatial frequency and stimulus disparity were varied for conventional disparity thresholds and stereoCT. The main studies are elaborated in Chapters 5 and 6. In chapter 5, the stimulus parameters were fixed and binocular vision was disrupted with uniocular contrast and luminance differences and with uniocular fogging and optical blur, using Bangerter filters and blur respectively. The effects of these disruptions on stereothresholds were studied for both conventional disparity thresholds and stereoCT. Chapter 6 describes in detail stereothresholds obtained by both tests on participants with amblyopia.

Chapter 4

Pilot study: Spatial stimulus characteristics for stereoCT

4.1 Introduction to the pilot studies:

The perception of depth in a random dot stereogram is purely cyclopean and has been shown to be affected by spatial stimulus characteristics. Spatial stimulus characteristics such as spatial frequency, the density of dots in an RDS and size of the dots effect disparity thresholds [63,64,111–113] (see Chapter 2, section 2.3, subsection 2.3.1.) We evaluated the effect of these parameters on stereoCT to identify the optimal stimulus for subsequent experiments. In addition, the stereoCT stimulus is constructed from a suprathreshold disparity-defined sinusoidal grating. Therefore, we also varied the maximum disparity of the grating.

Chapter 4 includes four different pilot studies:

Study 1: Effect of dot density and dot size on stereoCT

The aim of this study was to determine the effect of varying dot density and dot size on stereoCT and to find the dot density and dot size that allowed for the lowest stereoCT.

Study 2: Effect of spatial frequency on conventional disparity thresholds and stereoCT

The aim of this study was to determine the effect of spatial frequency of the disparity defined sinusoidal grating on stereothresholds measured by both conventional disparity thresholds and stereoCT.

Study 3: Effect of stimulus disparity on stereoCT

The aim of this study was to determine the effect of changing the maximum disparity of the disparity-defined grating on stereoCT.

Study 4: Test-retest repeatability of stereoCT

The aim of the final pilot study was to determine the test-retest repeatability of stereoCT and assess whether this varied with the maximum disparity of the disparity defined gating.

4.2 Pilot Study 1: Effect of dot density and dot size on stereoCT:

The goal of this study was to examine which RD density and dot size would show best stereothresholds for subsequent application as the test stimulus for our main studies.

Methods:

Participants were healthy volunteers (n=10) who were screened for normal vision and binocularity as explained in chapter 3, section 3.2, sub-section 3.2.4. Stimulus presentation and psychophysical thresholds were obtained using a two alternative forced choice staircase as described in chapter 3, section 3.2, and sub-section 3.2.3. A constant stimulus disparity of 108 seconds of arc was used to measure stereoCT. The stimulus characteristics of dot density and dot size were manipulated in this experiment. Three different dot densities were tested at three different dot sizes (dot densities: 367, 183 and 122 dots/deg square at dot sizes of 1.3, 5.5 and 7.9 arcmin). These dot densities and dot sizes were chosen to cover the range of the stimulus parameters that could be presented on the test screen. Stimulus order was randomized across participants.

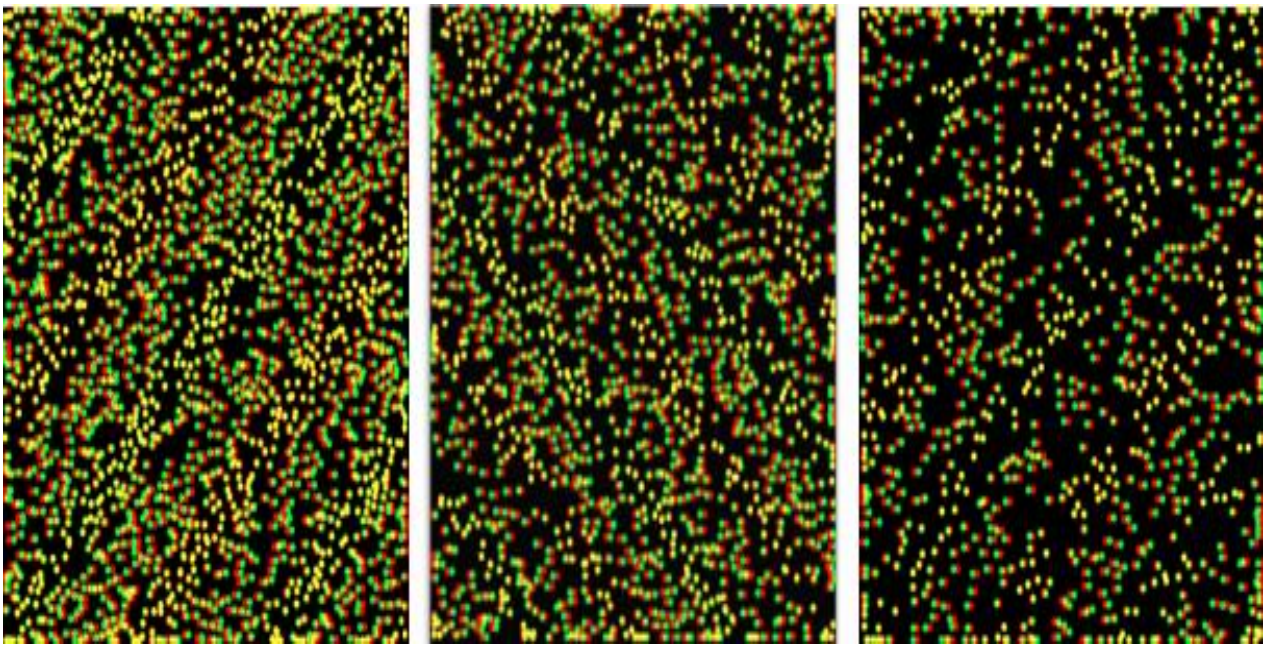

Figure 4 Image presented in a red-green stereogram for illustration (stimuli used in the studies contained white dots separated using liquid crystal shutter goggles). Image 1, 2 and 3 are RDS with a similar dot size but with varying dot densities. For a full screen at 6 meters this dot size was 5.5 arc min. The target disparity is similar in all three images (sinusoidal grating, 108 sec of arc, 1 cycle/deg spatial frequency when presented on the VPixx screen 6 meters from the participant). This dot density (183 dots/deg^2) was found to have better stereoCT for further analysis.

Results

The results are seen in Figure 5. We plotted mean stereoCT as a function of dot density with different dot sizes.

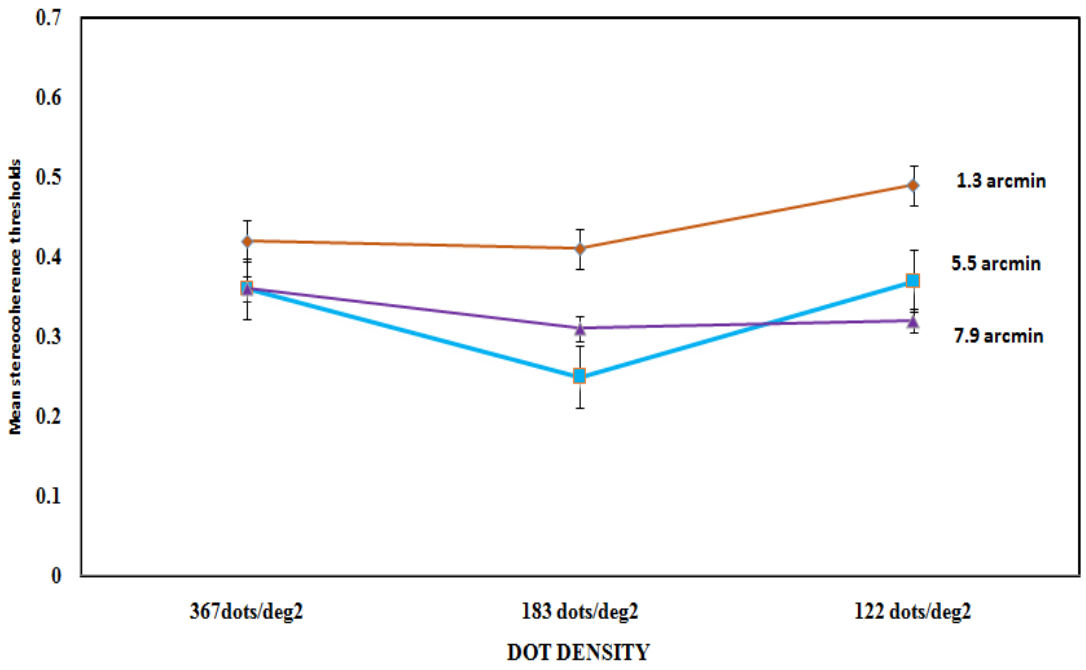

Figure 5: Mean stereoCT for depth discrimination (y-axis) as a function of dot density (x-axis) for different dot sizes. Orange diamonds, blue squares and purple triangles represent dot widths of 1.3, 5.5 and 7.9 arcmin respectively. Error bars represent 1SEM.

There was a significant main effect of dot size on stereoCT ANOVA F=3.4, (p=0.03). Lowest stereoCT were observed for a random dot size of 5.5 arc minutes at 183 dots/deg^2 dot density (figure 5). At this density and dot size thresholds averaged approximately 0.25 (25% signal dots, 75% noise dots). When the dot size was decreased from 5.5arc min, stereoCT increased significantly (post hoc LSD 0.02,). A Larger dot size of 7.9 arc min did not reveal any significant difference from the optimum size. Dot densities did not have any significant effect on measured thresholds.

Discussion

The lowest stereoCT were observed for a random dot size of 5.5 arc minutes at 183 dots/deg^2 dot density. We tested the coherence thresholds at three different densities 367, 183 and 122 dots/deg^2. Based on the dot sizes, we calculated the percentage of the total stereogram area that was covered by dots. The percent area covered ranged from low density of 7% to higher densities of 83%. We found lowest stereoCT at around 29% RDS densities but varying dot density did not have much effect on stereoCT. Gantz et al[114] measured stereothresholds for a random dot stereogram superimposed on a line segment. Stereothresholds were measured with varying dot densities ranging between 1.15% and 15% density. Lowest stereothresholds were found when the dot density was 1.77% and approximately doubled for lower and higher dot densities. The results are not comparable as there is a fundamental difference in the stimulus disparity amplitude at which the thresholds were obtained between both studies. The lowest disparity that could be

measured by our stimuli was 18 seconds of arc. We measured the effect of dot density for a corrugated sinusoidal grating, which had maximum disparity amplitude of 108 seconds of arc. The reason we did not find significance with varying density might be because the background sinusoidal grating had a larger disparity amplitude and increasing density might not have affected the stereothresholds as much. Moreover, stereoCT may be affected by interactions between dot size and dot density. If the RDS is covered densely with signal dots adding more noise might disrupt the stereoscopic perception much faster provided that the presented stimulus disparity is at threshold. Studies have reported a decrease in stereothresholds with increasing dot density due to crowding[39,115,116]. Studies have also reported elevation of stereothresholds at low dot densities attributed to increased spacing between elements[64] which makes it harder to integrate the surface. We found significant increase in thresholds with smaller dot sizes. This might have to do with the detection of stereoscopic surface in the presence of smaller dots and a greater effect of noise dots making it harder to integrate the stereoscopic surface. If the dot size is larger, it might provide better stereoscopic resolution of the background sinusoidal grating making it easier to integrate the surface.

4.3 Study 2: Effect of spatial frequency on stereoCT:

The aim of this study was to measure the stereothresholds as a function of spatial frequency. We hypothesized that the stereothresholds obtained by conventional disparity thresholds and noise based stereoCT would worsen at very high and very low spatial frequencies due to spatial constraints exhibited by stereoscopic processing mechanisms (more details in chapter 2, section 2.3, subsection 2.3.1).

Methods:

Participants for this pilot study were healthy volunteers with normal binocular vision. Stereothresholds were obtained using conventional disparity thresholds (n=7) and stereoCT (n=10). Stimulus presentation and psychophysical thresholds were obtained using a two alternative forced choice staircase as described in chapter 3, section 3.2, sub-section 3.2.3. A constant stimulus with a maximum disparity of 108 seconds of arc was used to measure stereoCT. The spatial frequency of the stimulus was manipulated in this experiment. Stereothresholds were tested with five different spatial frequencies 0.5, 1, 2, 4 and 8 cycles/degree. These spatial frequencies were chosen to cover the range of low and high spatial frequencies similar to previous experiments on conventional disparity thresholds[63,111,117]. All the measurements were made in one session; the spatial frequencies were presented in random order.

Results:

The results are seen in Figure 6a and 6b. In Figure 6a, we plotted stereoCT as a function of spatial frequency in bar graphs. In figure 6b, conventional disparity thresholds are plotted as a function of spatial frequency in box and whisker plots. The results of Figure 6a are normally distributed and 6b are not normally distributed.

Fig 6a **Fig 6b**

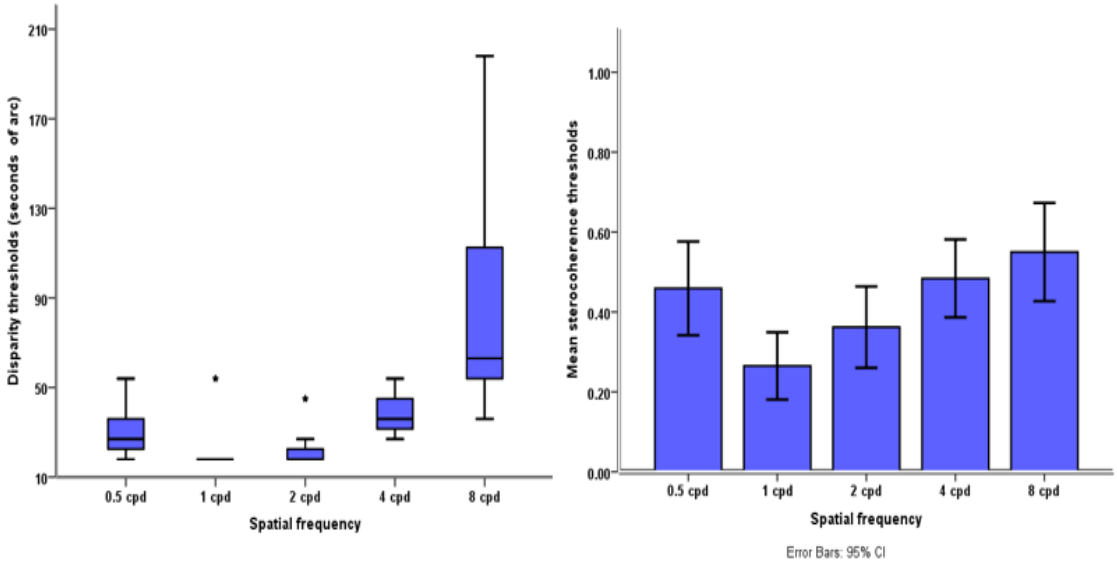

Figure 6b: Global stereoCT plotted as a function of spatial frequency (n=10). Error bars represent 95% CI. Coherence thresholds were measured at five different spatial frequencies (0.5, 1, 2, 4 and 8 cycles/degree). **Figure 6a** shows box and whisker plots with median values with interquartile range (n=7) of disparity thresholds (conventional test) plotted as a function of spatial frequency for comparison.).

The stereoCT versus spatial frequency function for is U-shaped, with the lowest threshold occurring at 1cpd (figure 6a). The main effect of spatial frequency on stereoCT was significant F (4) =5.7, p=<0.001, two-factor ANOVA. StereoCT gradually increased with increase in spatial frequency. The stereoacuity versus spatial frequency function for disparity thresholds showed some floor effects with lowest thresholds (median 18 sec of arc) at spatial frequencies of 1 and 2 cpd.

Table 2: Paired comparisons between spatial frequencies of random dot stereograms for stereoCT and disparity thresholds

StereoCT				Disparity thresholds
Spatial frequency groups	Mean difference	Std. Error	Sig. (p value)	Sig. (p value)
0.5 vs 1 cpd	0.19	0.06	0.07	0.27
0.5 vs 2 cpd	0.09	0.06	0.85	0.27
0.5 vs 4 cpd	-0.02	0.06	1.00	0.16
0.5 vs 8 cpd	-0.09	0.07	0.93	0.02*
1 vs 2 cpd	-0.09	0.05	0.70	1.00
1 vs 4 cpd	-0.21	0.05	0.01*	0.04*
1 vs 8 cpd	-0.28	0.06	0.005*	0.01*
2 vs 4 cpd	-0.12	0.06	0.49	0.02*
2 vs 8 cpd	-0.18	0.07	0.15	0.01*
4 vs 8 cpd	-0.06	0.06	0.007*	0.02*

Paired comparisons

Post hoc paired comparisons with bonferroni correction showed that significant differences in stereoCT were observed at 4 and 8 cpd spatial frequency when compared to 1 cpd (paired t-test $p<0.05$) for which the thresholds were lowest. Disparity thresholds were not significantly different

between lower spatial frequencies up to 4 cpd and were significantly increased for the higher spatial frequencies of 4 and 8 cpd from the spatial frequency with lowest stereoCT ($p<0.05$, Wilcoxon sign ranked test).

Discussion

The sensitivity function for corrugated sinusoidal gratings for stereoCT showed a peak at 1 cycle/deg, with a fall-off in sensitivity at both lower and higher spatial frequencies. These results are consistent with Tyler's[63] data and Rogers and Graham's[67] on the spatial limit of stereothresholds for disparity defined sinusoidal gratings. The optimal performance was found to be around 1 c/deg and efficiency deteriorates when the corrugation frequency is above 1c/deg or below 0.1cpd. Previous studies[37,118] have established that detection of a single step edge in depth is simpler than detection of a surface with numerous variations in depth. For a corrugated sinusoidal grating with constant dot density, increasing spatial frequency means introducing more variations in surface structure. As the spatial frequency increases, there are fewer dots that define each of these variations in depth. Introducing disparity noise to such surfaces increases difficulties in dot matching with neighboring dots whose disparities are different and also surface integration is disrupted.

4.4 Pilot Study 3: Effect of stimulus disparity on stereoCT

Introduction

Disparity processing has two resolution limits; the smallest disparity that can be detected and the largest disparity that can still convey a perception of depth[119] (more details in chapter 2, section 2.3, subsection 2.3.1). We measured the stereoCT at ranges of high and low stimulus disparities to find a stimulus disparity that had lowest thresholds and could be implemented in main experiments.

Methods

Participants for this pilot study were healthy volunteers with normal binocular vision. StereoCT were obtained on 20 participants. Stimulus presentation and psychophysical thresholds were obtained using a two alternative forced choice staircase as described in chapter 3, section 3.2, subsection 3.2.3. All stimulus parameters including dot density and dot size remained constant during the experiment. The maximum disparity amplitude of the sinusoidal gratings was manipulated in this experiment. Stereothresholds were tested with five different stimulus disparities 36, 72, 108, 144 and 216 seconds of arc. These disparity amplitudes were chosen to cover the range of low to high disparities of the sinusoidal gratings that could be presented on our

experimental screen. All the measurements were made in one session; the spatial frequency was presented in random order.

Results

The results are seen in Figure 7, where we have plotted the stereoCT as a function of five different disparities as a bar graph in the normal population sample. These results are normally distributed.

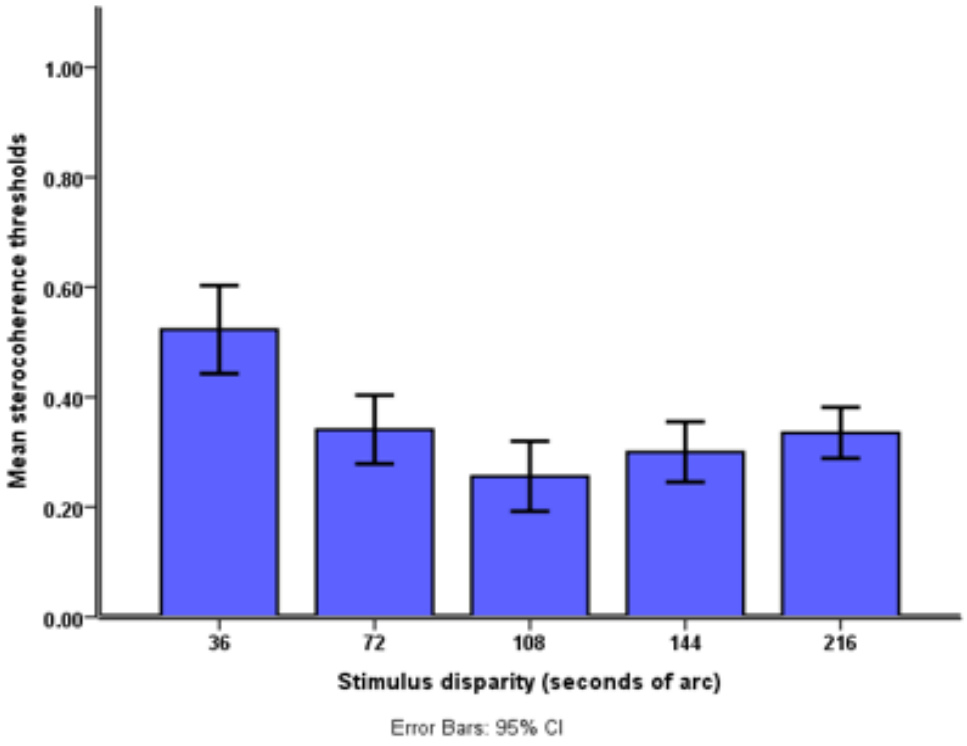

Figure 7: Mean stereoCT (proportion of signal dots) as a function of stimulus disparity (peak to trough) for RDS of corrugated sinusoidal gratings. Error bars represent 95% CI (n=20).

The stereoCT were lowest at 108 seconds of arc for this dot density and dot size. StereoCT were increased significantly for stimuli with higher and lower stimulus disparities when compared to thresholds at 108 seconds of arc ($p<0.05$, paired t-test) as shown in figure 7. We further did pair wise t-tests on all five groups. Table 3 shows significance values for paired t-tests at varying levels of disparity amplitude.

Table 3: Paired comparisons between RDS with different disparity amplitudes.

Disparity amplitude groups	t value	Sig. (p value, two tailed)
36 vs. 72 seconds of arc	4.68	0.00*
36 vs. 108 seconds of arc	7.83	0.00*
36 vs. 144 seconds of arc	5.74	0.00*
36 vs. 216 seconds of arc	5.11	0.00*
72 vs. 108 seconds of arc	3.33	0.00*
72 vs. 144 seconds of arc	1.50	0.15
72 vs. 216 seconds of arc	0.22	0.82
108 vs. 144 seconds of arc	-1.42	0.17
108 vs. 216 seconds of arc	-2.43	0.02*
144 vs. 216 seconds of arc	-2.05	0.05*

*Paired comparison of means using Tamhanee posthoc paired t test with Bonferroni correction.

The effect on stereoCT of disparity amplitude was significant F=11.6, p=<0.001, two-factor ANOVA. The lowest stereoCT threshold was found at 108 seconds of arc. StereoCT doubled to more than 50% coherence with the lowest disparity of 36 seconds of arc when compared to the mean threshold of 25% at 108 seconds of arc. StereoCT were significantly higher at lower

stimulus disparity of 72 and highest stimulus disparity of 216 seconds of arc when compared to the optimum disparity of 108 seconds of arc.

Discussion

StereoCT were elevated when the stimulus disparity of the sinusoidal RDS was too fine or too large. Thresholds were worse for the shallowest surface with a maximum depth of 36 seconds of arc than for deepest surface with a maximum depth of 216 seconds of arc. This might be due to the interaction of the sinusoidal grating with noise dots. At low stimulus disparities, the noise dots are densely packed within the peak and trough of the sinusoidal grating. This might lead to the disruption of the depth pattern due to crowding or possibly dot matching difficulty. At high stimulus disparities, the visual system is at its peak with regards to achieving maximum fusion to detect stereopsis. Adding noise dots might breakdown the smooth perception of background wave much easier and observers fail to integrate the information. The stereoCT might also have some additive effect with regards to the resolution of the background sinusoidal grating detection at different stimulus disparities.

4.5 Pilot Study 4: Test-retest repeatability of stereoCT

Introduction:

Any clinical test that is being used to diagnose or monitor disease progression should have its repeatability assessed to know correctly if the change in the measurement can be attributed to test-retest variability or demonstrates a clinically significant change.

Methods

To determine the repeatability of stereoCT, we measured test-retest repeatability of stereoCT. Test-retest repeatability was assessed using five different disparity amplitudes. Twenty normal participants took part in this study. All the measures of stereoCT were undertaken by the same examiner to minimize inter-examiner variability.

Results: The stereoCT of the first test is plotted against those of the retest in Figures 8a to Figure 8e.

Fig 8a

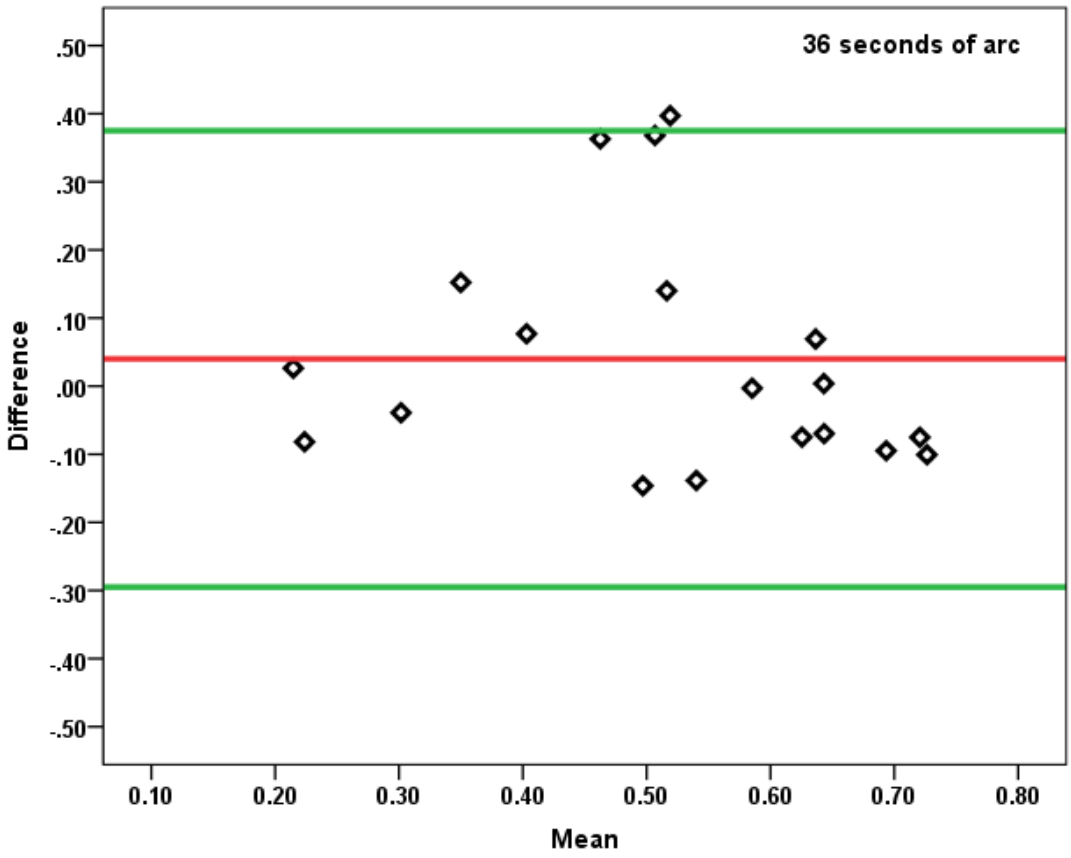
36 seconds of arc
Difference
.50
.40
.30
.20
.10
.00
-.10
-.20
-.30
-.40
-.50
0.10
0.20
0.30
0.40
0.50
0.60
0.70
0.80
Mean

Fig 8b

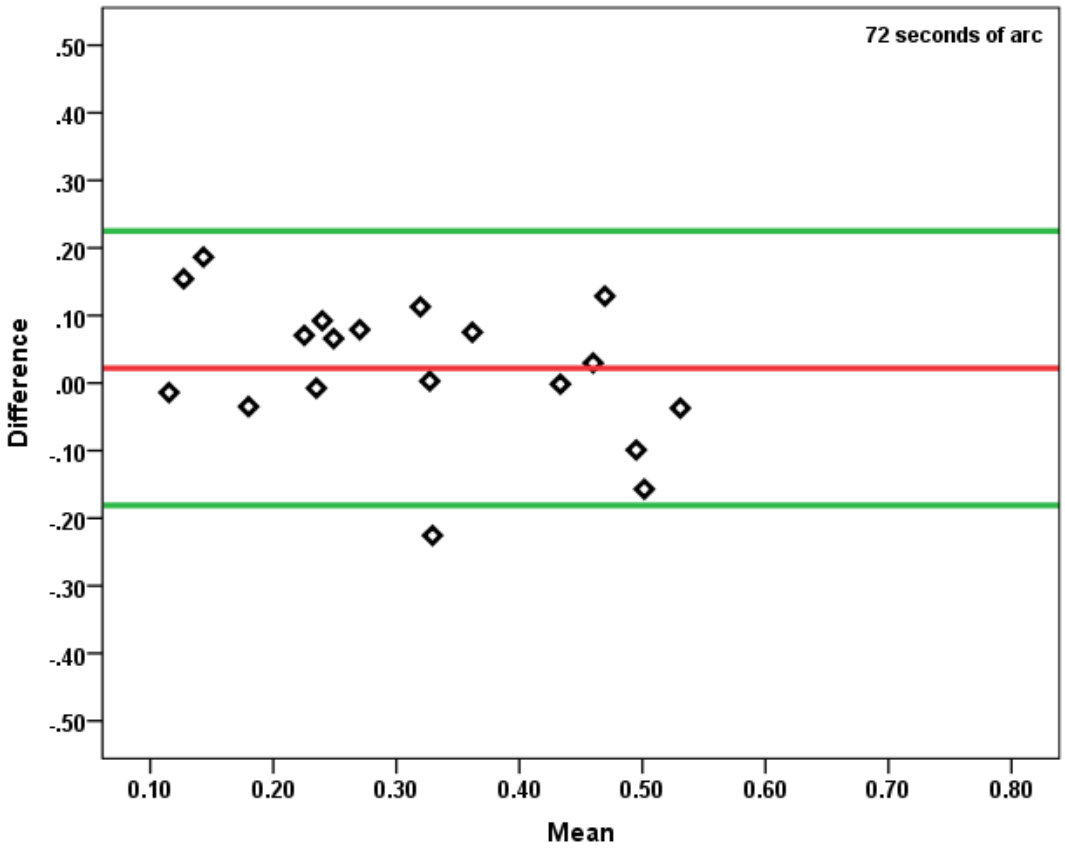
72 seconds of arc
Difference
.50
.40
.30
.20
.10
.00
-.10
-.20
-.30
-.40
-.50
0.10
0.20
0.30
0.40
0.50
0.60
0.70
0.80
Mean

Fig 8C

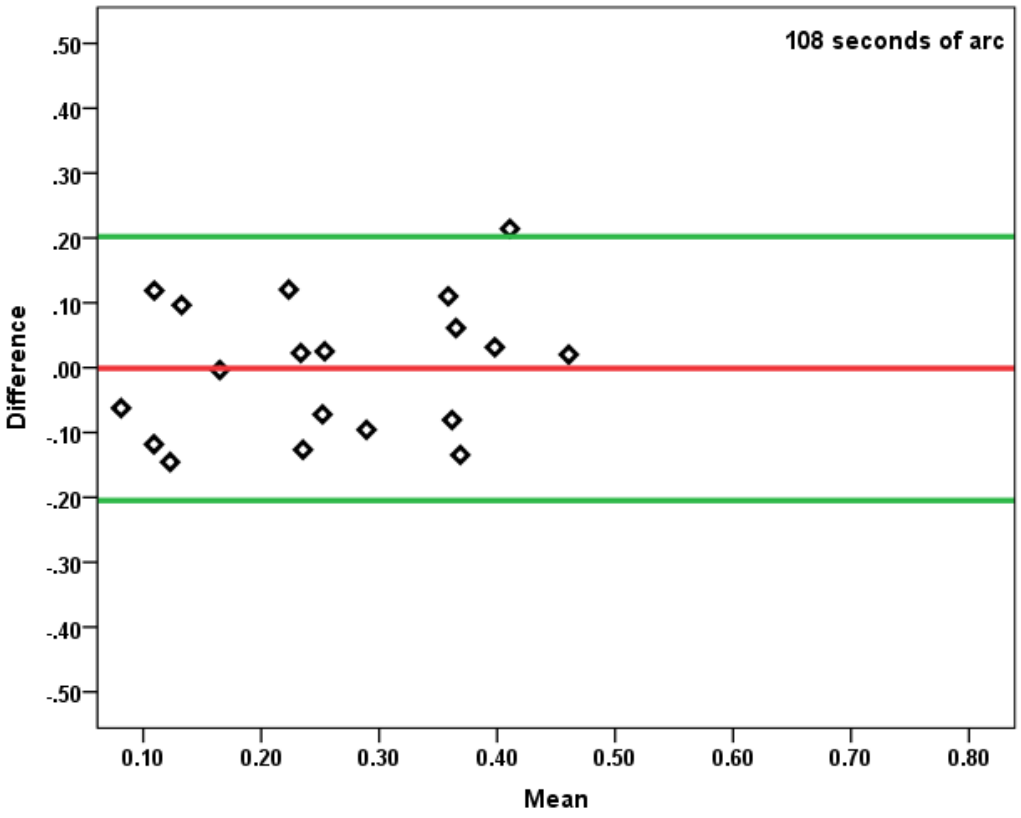
108 seconds of arc
Difference
.50
.40
.30
.20
.10
.00
-.10
-.20
-.30
-.40
-.50
0.10
0.20
0.30
0.40
0.50
0.60
0.70
0.80
Mean

Fig 8d

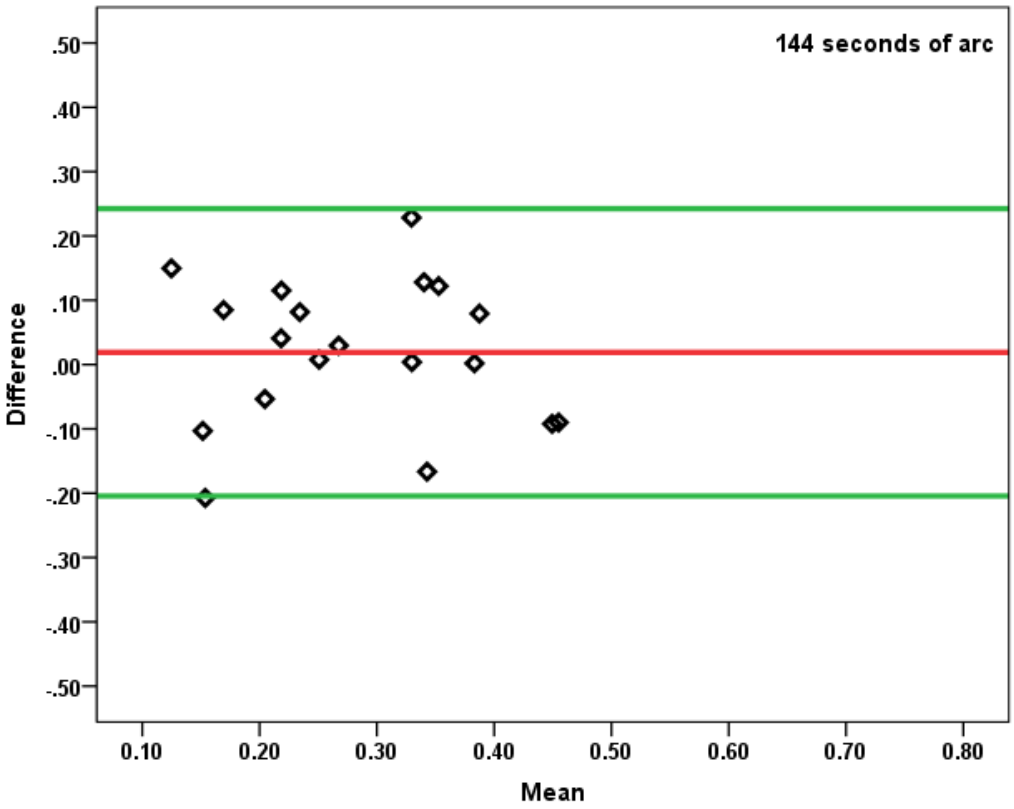
144 seconds of arc
Difference
.50
.40
.30
.20
.10
.00
-.10
-.20
-.30
-.40
-.50
0.10
0.20
0.30
0.40
0.50
0.60
0.70
0.80
Mean

Fig 8e

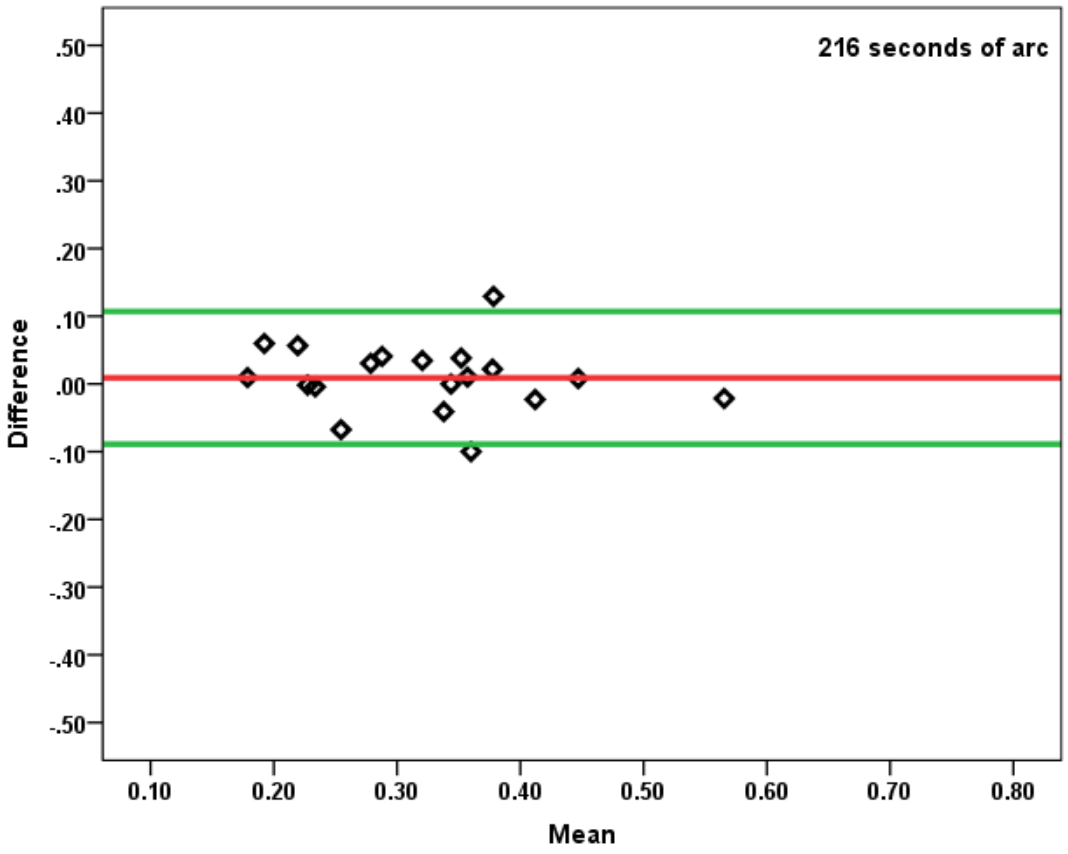

Figure 8: Bland-Altman plots of stereoCT measures at various maximal stimulus disparities (Fig 8a-36, Fig 8b-72, Fig 8c-108, Fig 8d-144 and Fig 8e-216 seconds of arc). Red line (middle) represents the mean difference and green line (above and below the red line) indicates lower and upper limit of agreement.

Table 4 Intraclass correlation coefficients on a two-tailed test.

Disparity Amplitude	Intraclass correlation coefficient
36 seconds of arc	0.70
72 seconds of arc	0.84
108 seconds of arc	0.80
144 seconds of arc	0.68
216 seconds of arc	0.93

The intraclass correlation coefficient was best at largest stimulus disparity (216 seconds of arc) and lower at finest stimulus disparity (36 seconds of arc) as shown in figure 8. Overall the stereoCT exhibited good test-retest repeatability at variable stimulus disparities.

Discussion

The stereoCT showed good test-retest repeatability. The repeatability was best at largest disparity because of the cyclopean pattern in RDS was more easily discriminable as compared to fine stimulus disparity in normal observers. When noise is added to a large disparity sinusoidal grating, there might be some information of the wave pattern still preserved which might aid in the resolution of the pattern. In contrast, when the noise is added to fine disparities, there is a lot of crowding and dot matching constraints that make it more difficult to detect and additionally, there might be a total disruption of the stereoscopic surface with no residual information left to integrate. The stereothresholds obtained by conventional stereoacuity tests show evidence of wide variation between individual subjects and between stereo tests[51,120]. High test-retest variability of clinical stereoacuity tests has also been shown in patients with abnormal binocular vision[121]. We did not study repeatability of conventional stereoacuity thresholds because the resolution of our stimulus screen produced a floor effect for normal observers with a minimum available depth of 18 seconds of arc. In clinical tests, it has been reported that 89% of observers with normal binocular vision show floor effects for depths of less than 10 seconds of arc on the Frisby test and less than 40 seconds of arc on the widely used Titmus test[51,62]. The stereoCT did not reveal any floor effects because it is possible to display very low coherence levels, thus providing a below threshold stimulus for all observers.

4.6 General Conclusions from pilot studies

The objective of the pilot study was to find the spatial parameters which have lowest stereothresholds that can be used to design the test stimulus. Based on our findings, in normal participants, stereothresholds were lowest for dot density of 29% RDS densities. StereoCT showed better sensitivity at spatial frequency of 1cpd. StereoCT were also lowest when measured at mid-range disparity amplitudes of 72-108 seconds of arc. We used these parameters to design our test stimulus. In the main experiments all spatial parameters except for disparity amplitudes. In observers with disrupted binocular vision, we presented stimuli at higher disparities to improve repeatability and allow discrimination of the stereo target.

Chapter 5

Comparison of stereoCT with conventional disparity thresholds in normal and simulated abnormal vision

5.1 Introduction

The presence of degraded stereothresholds on clinical tests is commonly associated with reduced monocular or binocular visual functions such as visual acuity and contrast sensitivity. The associated dysfunctions typically result from various ocular conditions such as uncorrected refractive error, cataract, strabismus, anisometropia, and amblyopia[122]. Artificially degraded vision in one eye using optical blur, Bangerter filters and interocular luminance and contrast differences can impair stereovision (more details in chapter 2, section 2.3 and subsection 2.3.2). We evaluated the effect of using artificial disruption of binocular vision on disparity thresholds and stereoCT.

Chapter 5 includes two different experiments:

Study 1: Effect of interocular luminance and contrast differences on stereothresholds

The aim of this study was to determine the effect of varying interocular luminance and contrast on conventional disparity and stereoCT.

Study 2: Effect of induced uniocular optical blur and Bangerter filters on stereothresholds

This experiment was done to investigate the effects of artificially disrupting binocular vision using optical blur and Bangerter filters on conventional disparity and stereoCT.

The overall hypothesis was that stereoCT would show better sensitivity and less variability to different levels of induced deficit than conventional disparity thresholds.

5.2 Experiment 1: Effect of interocular luminance and contrast differences on stereothresholds

Introduction

Stereopsis is dependent on luminance and contrast. Differences in contrast and luminance between the two eyes disrupt binocular vision and lead to deterioration of stereopsis (more details in chapter 2, section 2.3, and subsection 2.3.2). In this study, we investigated the effects of interocular luminance and contrast differences on stereoCT and disparity thresholds.

Methods

Stereothresholds were obtained from10 participants for each experiment who had normal visual and stereoacuity determined on clinical tests (section 3.2.5). Participants in experiment measuring interocular contrast differences had a median age of 26 (range=19-34), six male and four female participants.Participants in experiment measuring interocular luminance differences had a mean age of 25 (range=19-33), four male and six female participants. Stimulus presentation and psychophysical thresholds were obtained as described in chapter 3, section 3.2 subsections 3.2.3. Dot density, dot size, contrast, luminance and stimulus disparity remained constant when measuring stereoCT (dot size 5.5 arcmin, dot density 183 dots/deg^2, stimulus disparity 108 seconds of arc, full contrast in both eyes). For disparity thresholds, all spatial parameters were similar to those for the stereoCT except for stimulus disparity which was measured using a staircase procedure. We manipulated the stimulus presented to one of the two eyes by changing contrast and luminance. The contrast was altered at four different left and right eye combinations. The contrast in one eye was always 50% (the maximum contrast between the grey background and white dots). The contrast in the other eye was 20%, 30%, 40% or 50% contrast. The stimulus contrast is expressed as Michelson contrast, which is defined as $C= (L_{max}-L_{min}/L_{max}+L_{min})$ where L_{max} and L_{min} are the maximum and minimum luminance of the stimulus respectively. The mean luminance seen in the non-dominant eye was manipulated by using neutral density (ND) filters placed in front of the eye. Four different ND filters were used 0.3, 0.6, 1.2 and 1.8 log units**.** All the measurements

were made in one session with the different contrast and luminance levels presented in random order.

Results:

The results are shown in Figure 9 where we have plotted the results of stereoCT and disparity thresholds as a function of interocular contrast and luminance differences. The results were normally distributed which were determined by performing Shapiro-Wilk test.

Fig 9a

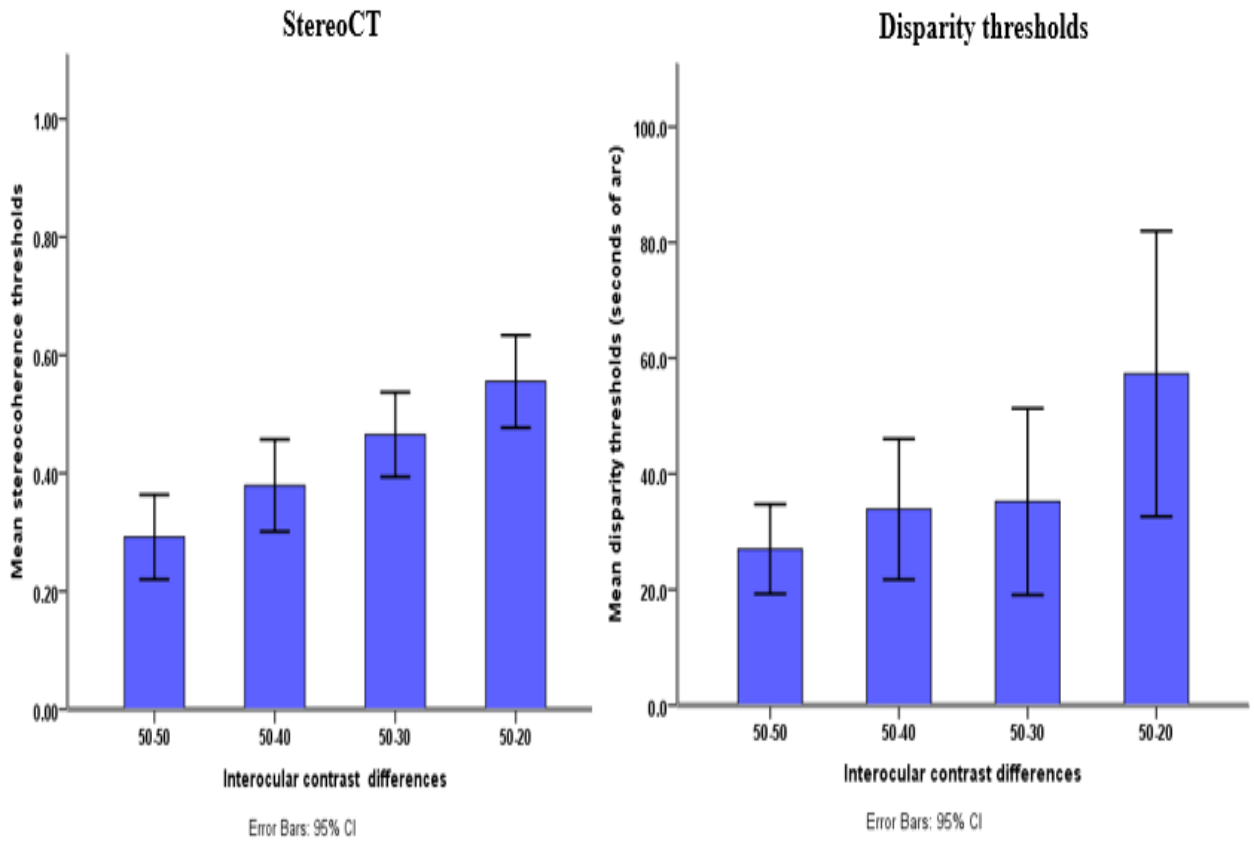
StereoCT
Mean stereocoherence thresholds
1.00
0.80
0.60
0.40
0.20
0.00
50-50
50-40
50-30
50-20
Interocular contrast differences
Error Bars: 95% CI
Disparity thresholds
Mean disparity thresholds (seconds of arc)
100.0
80.0
60.0
40.0
20.0
0.0
50-50
50-40
50-30
50-20
Interocular contrast differences
Error Bars: 95% CI

Fig9b

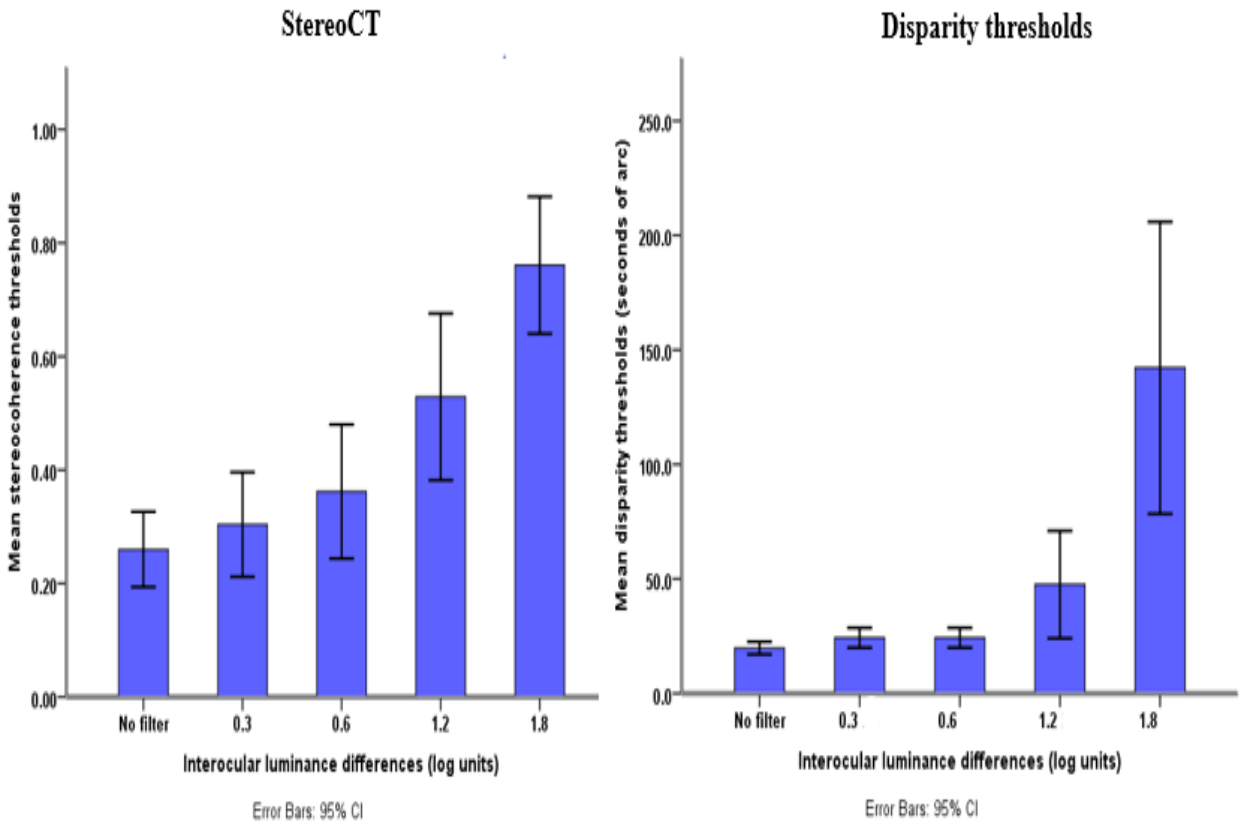

Figure **9a:** StereoCT (left) and disparity thresholds (right) plotted as a function of interocular contrast difference (n=10). Error bars represent 95% CI. The mean stereothresholds were measured at four different contrast levels: 10, 20, 30 and 50% contrast in one eye. The contrast in the other eye was always 50%**.**

Figure 9b: StereoCT (left) and disparity thresholds (right) plotted as a function of interocular luminance difference (n=10). Error bars represent 95% CI. Stereothresholds were measured at five different luminance levels: no filter, 0.3, 0.6, 1.2 and 1.8 log unit filter density. Filters were placed over only the non-dominant eye.

Interocular contrast difference

The mean stereoCT is shown in figure 9a (left) and increased in a linear fashion as the interocular differences in contrast increased (ANOVA $F(3,40)=11.32$, $p<0.001$). Reducing unilateral contrast to 40% did not worsen stereoCT significantly (post hoc Tamhanee paired test $p>0.05$) shown in table 5. When the contrast in one eye was reduced to 30%, the thresholds rose significantly compared to the 50% contrast (baseline) condition (post hoc Tamhanee paired test $p<0.05$). Unilateral contrast reduction to 20% doubled the thresholds as compared to the 50% contrast condition. The mean disparity thresholds shown in figure 9a (right) revealed a main effect with change in contrast $F(3, 32) = 3.40$, $p=0.02$, one way ANOVA. Disparity thresholds remained stable for the 40 and 30% contrast conditions. At 20% contrast, the mean disparity thresholds also doubled when compared to full contrast conditions but the paired comparisons described in table 5did not reveal a statistically significant difference (post hoc Tamhanee paired test $p>0.05$). Analysis of the difference in variances is described below (Table 6)

Table 5: Effects of interocular contrast differences on stereoCT and disparity thresholds.

StereoCT				Disparity thresholds		
% Interocular contrast difference	Mean Difference	Std. Error	Sig. (p value) *	Mean Difference Arc seconds	Std. Error	Sig. (p value) *
50-40%	-0.08	0.04	0.40	-6.9	6.25	0.87
50-30%	-0.17	0.04	0.006	-8.2	7.75	0.89
50-20%	-0.26	0.04	0.000	-30.3	11.21	0.13
40-30%	-0.08	0.04	0.41	-1.3	8.75	1.00
40-20%	-0.17	0.04	0.01	-23.4	11.93	0.37
30-20%	0.09	0.04	0.36	-22.1	12.78	0.49

Posthoc paired comparison using Tamhanee paired test. *

Variance Analysis

The variance analysis was done separately for stereoCT and disparity thresholds. The variance between conditions was calculated at different contrast levels as described in table 6. For stereoCT, the variance between groups was not significantly different as the interocular differences in contrast increased (F test of variance, $p>0.05$). For disparity thresholds, as the interocular contrast was increased, significant differences in variance between conditions were

observed. At 40% contrast, the variance was not significantly different from the 50% contrast condition. At 30 and 20% contrast, variance was significantly larger than the 50% contrast condition.

Table 6: Analysis of variance (F-test) between conditions for interocular contrast differences. StereoCT and disparity threshold measures.

Contrast conditions	StereoCT P value	Disparity thresholds P value
50/40%	0.39	0.11
50/30%	0.49	0.02*
50/20%	0.39	0.001*
40% vs. 30% contrast in one eye	0.39	0.22
40% vs. 20% contrast in one eye	0.49	0.03*
30% vs. 20% contrast in one eye	0.39	0.12

*F test between conditions, p values <0.05 are significant.

Interocular luminance differences

The mean stereoCTs shown in figure 9b (left) increased in a linear fashion as the interocular differences in luminance increased $F=17$, $p<0.01$, ANOVA. Weak ND filters of 0.3 and 0.6 log units did not worsen the thresholds significantly ((post hoc Tamhanee paired test $p>0.05$) shown in table 7. As the ND filter strength increased to 1.2 log units, the thresholds rose significantly and almost doubled compared to no filter condition ((post hoc Tamhanee paired test $p<0.05$). Unilateral luminance reduction with the highest filter of 1.8 log units increased the stereoCT three-fold compared to no filter condition (paired t-test $p<0.001$). The mean disparity thresholds are shown in figure 9b (right). Significant increase in disparity thresholds were revealed only for the strongest filter with respect to the baseline condition (1.8 log units, post hoc Tamhanee paired test $p=0.01$) as described in table 7. Analysis of the difference in variances between groups is described below.

Table 7 Effects of interocular luminance differences on stereoCT and disparity thresholds.

StereoCT				Disparity thresholds		
ND filter strength	Mean difference	Std. Error	Sig. (p value)	Mean difference	Std. Error	Sig. (p value)
No filter-0.3 ND	-0.04	0.05	0.99	-4.5	2.26	0.49
No filter-0.6 ND	-0.10	0.05	0.69	-4.5	2.2	0.49
No filter-1.2 ND	-0.26	0.07	0.02*	-27.7	10.4	0.22
No filter-1.8 ND	-0.50	0.06	0.00*	-122.4	28.1	0.01*
0.3 ND vs 0.6 ND	-0.05	0.06	0.99	0.00	2.7	1.00
0.3 ND vs 1.2 ND	-0.22	0.07	0.09	-23.24	10.5	0.41
0.3 ND vs 1.8 ND	-0.45	0.06	0.00*	-117.9	28.2	0.02*
0.6 ND vs 1.2 ND	-0.16	0.08	0.46	-23.24	10.5	0.41
0.6 ND vs 1.8 ND	-0.39	0.07	0.00*	-117.9	28.2	0.02*
1.2 ND vs 1.8 ND	-0.23	0.08	0.12	-94.6	30.0	0.08

*Posthoc paired comparisons using Tamhanee paired test.

Variance Analysis

The variance analysis was conducted separately for stereoCT and disparity thresholds. The variance between groups was calculated at different interocular luminance differences as described in table 8. For stereoCT, the variance between groups was not significantly different at the low level of 0.3 log units compared with the no filter condition (F test of variance, $p>0.05$). StereoCT showed increased variance as the ND filter strength was increased until the highest filter density (1.8 log units, F test of variance, $p<0.05$). For disparity thresholds, as the interocular luminance differences were increased, significant differences in variance from baseline were observed only with higher filter strengths of 1.2 and 1.8 log units (F test of variance, $p<0.05$).

Table 8 P values for analysis of variance (F-test) between conditions for interocular luminance differences. StereoCT and disparity threshold measures.

ND filter density paired groups	StereoCT P value	Disparity thresholds P value
No filter vs. 0.3	0.17	0.08
No filter vs. 0.6	0.05*	0.08
No filter vs. 1.2	0.01*	<0.01*
No filter vs. 1.8	0.04*	<0.01*
0.3 filter vs. 0.6	0.23	0.5
0.3 filter vs. 1.2	0.09	<0.01*
0.3 filter vs. 1.8	0.21	<0.01*
0.6 filter vs. 1.2	0.26	<0.01*
0.6 filter vs. 1.8	0.4	<0.01*

* F test between conditions, p values <0.05 are significant.

Discussion

Interocular contrast differences

We first investigated the effect of interocular contrast differences on stereoCT and disparity thresholds. StereoCT was progressively degraded as contrast differences between the two eyes were increased. StereoCT were significantly degraded for all interocular contrast differences of 1.5 times contrast or greater and variances remained consistent. Disparity thresholds were not significantly different at any of the contrast levels tested from the baseline condition of 50% contrast in both eyes. However, interocular contrast differences increased the variances of disparity thresholds. The results imply that StereoCT is sensitive to smaller differences in contrast between the two eyes (interocular contrast differences ≥1.5 times than baseline) than conventional disparity thresholds (no differences in thresholds up to 2.5 times than that of baseline). Studies done in the past have implied that stereothresholds measured by conventional tests are affected by interocular contrast differences[68,85,123]. For example, Legge and Gu[85] measured the effect of interocular contrast difference on stereoacuity using sinusoidal gratings. Stereoacuity gradually deteriorated with interocular contrast differences of up to three fold with left/right eye ratio of 4:1 measured on a grating of 2.5 cpd. The average increase in threshold for two participants with 2:1 left/right eye contrast differences was greater than 400 seconds of arc for a grating of 0.5 cpd. In our study, average disparity thresholds increased to >60 seconds of arc with 2.5:1 interocular contrast differences from the baseline average threshold of 27 seconds of arc for a grating of 1 cpd but the differences was not significant in view of the high variances between participants. The

results from our study differ from those of Legge and Gu[85]. This might be because of the differences in stimulus design and field size etc. In the present study, variance analysis revealed no difference in variance between the baseline and disrupted binocular vision conditions for stereoCT. Differences were present for the disparity threshold data. This indicates that stereoCT is a particularly stable measure of stereoscopic function especially in conditions of abnormal binocular vision compared to conventional disparity threshold measures.

Interocular luminance differences

StereoCT and disparity thresholds progressively degraded as the interocular luminance difference was increased. The change in stereoCT with interocular luminance difference was progressive whereas disparity thresholds did not exhibit significant differences with low density filters and increased abruptly when a filter with higher ND (1.8 log units) was introduced over one eye. Studies done in the past have implied that stereothresholds measured by conventional tests are affected by interocular luminance differences[72,123,124]. Chang et al examined the effects of interocular differences in retinal luminance on stereoacuity by using neutral density filters. Stereoacuity was measured on Titmus test and Lang tests. On the Titmus test, stereoacuity began to decline significantly when the value of the ND filter was 1.4 log units with a mean stereoacuity of 92.8 seconds of arc. The results are consistent with our data on disparity threshold measures. Even though we did not measure thresholds at 1.4 log units, we found significant deterioration of stereothresholds for global stereopsis only for the 1.8 log units filter

with mean thresholds around 142 seconds of arc. StereoCT showed higher sensitivity with significant deterioration of thresholds at the 1.2 log unit filter level. Variance analysis revealed overall less variance differences between normal and disrupted binocular vision conditions for stereoCT. This indicates that stereoCT is more stable measure of stereoscopic function, especially in conditions of abnormal binocular vision compared to conventional disparity threshold measures

5.3 Experiment 2: Effects of induced uniocular optical blur and Bangerter filters on stereothresholds

Introduction

Degradation of the image in one eye leads to deterioration of stereopsis (more details in chapter 2, section 2.3 and subsection 2.3.2). In this study, we investigated the effects of induced optical blur and uniocular fogging with Bangerter filters on stereoCT and disparity thresholds.

Methods

Stereothresholds were obtained on 10 healthy participants for each experiment. The median age was 26 (range=21-41), eight participants were female and two male for interocular blur experiment.The median age of participants for interocular Bangerter filter experiments was 26.5 (range=22-41) with nine female and one male participant. Stimulus presentation and psychophysical thresholds were obtained as described in chapter 3, section 3.2, and subsection 3.2.3. Dot density, dot size, contrast, luminance and stimulus disparity remained constant when measuring stereoCT. For disparity thresholds, all spatial parameters were similar to stereoCT except for stimulus disparity which was measured using a staircase procedure. We manipulated the stimulus presented to one of the two eyes by inducing optical blur using plus lenses or Bangerter filters. We reduced vision using plus lenses to two visual acuity levels, 0.17 LogMAR

(6/9) and 0.30 LogMAR 6/12, for easier comparison between subjects. Bangerter filters are translucent occlusion filters consisting of a characteristic pattern of micro bubbles that cause visual degradation[125]. The filter label indicates the visual acuity in linear fraction predicted by the manufacturer when the filter is placed in front of eyes with normal visual acuity. Two Bangerter filter strengths of 0.8 and 0.6 were used over one eye to artificially degrade binocular vision. The stereoCT for blur and uniocular diffusion was obtained at a supra-threshold stimulus disparity of 270 seconds of arc. This is because the on the conventional disparity threshold, mean stereothresholds worsened to approximately 250 seconds of arc with induced blur and Bangerter filters. A supra-threshold stimulus disparity was used so that all observers could discriminate the equivalent depth pattern when binocular vision was disrupted and so that the inability to see stimulus disparity could not disrupt measured stereothresholds using the stereoCT. All the measurements were made in one session for either blur or Bangerter filters; the blur and Bangerter filter levels were presented in random order. Some participants did both the bur and Bangerter filter experiments in a single study.

Results

The results are shown in Figure 9 where we have plotted the results of stereoCT and disparity thresholds as a function of uniocular contrast and uniocular fogging. The results were normally distributed which were determined on Shapiro-Wilk test**.**

Fig 10a **Fig 10b**

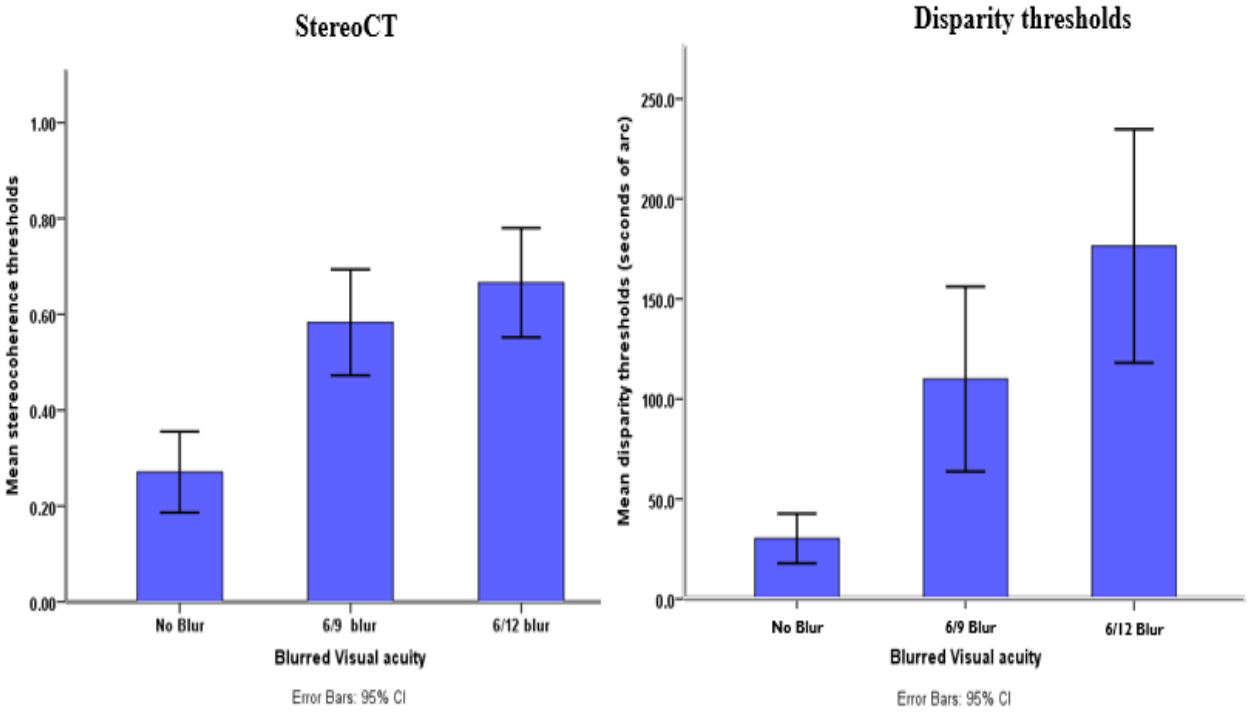

Figure **10** StereoCT (**10a**) and disparity thresholds (**10b**) plotted as a function of uniocular blurred acuity (n=10). Error bars represent 95% CI. Stereothresholds were measured for two levels of blurred visual acuity 6/9 and 6/12.

Fig 11a **Fig11b**

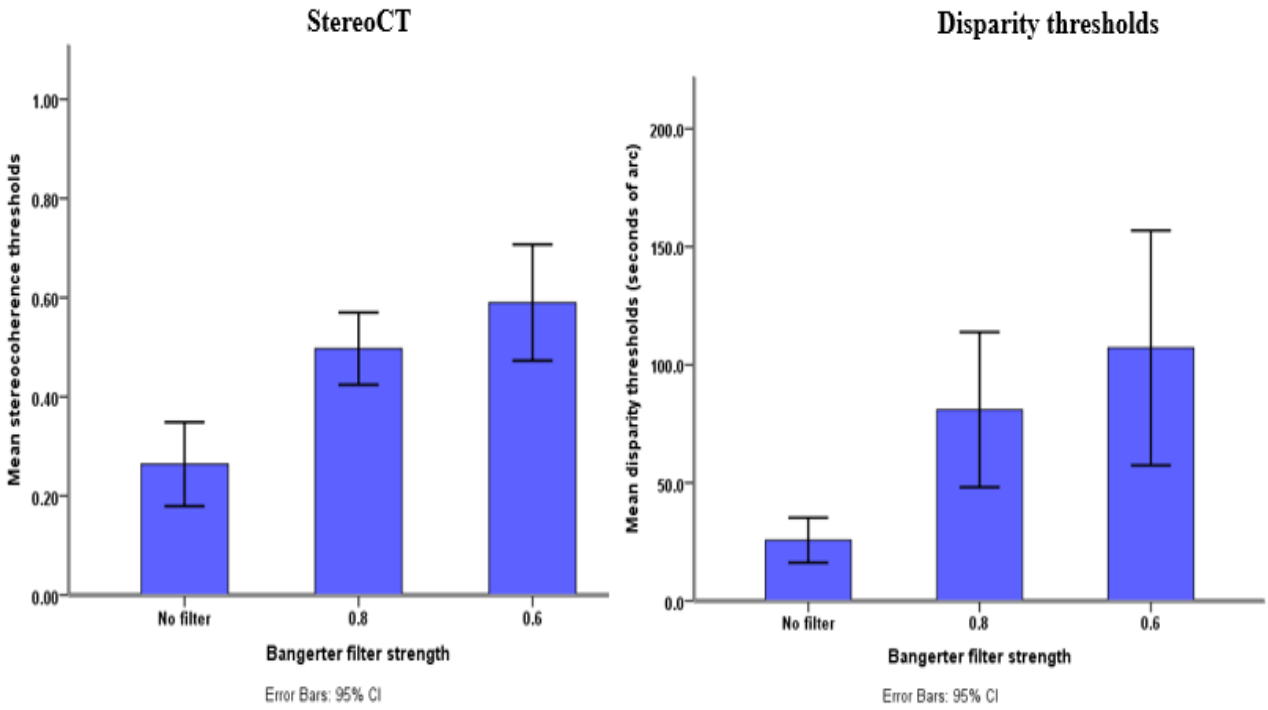

Figure 11: StereoCT (**11a**) and disparity thresholds (**11b)** plotted as a function of uniocular Bangerter filter strength. Error bars represent 95% CI. Stereothresholds were measured at two different Banger filter strengths, 0.8 and 0.6, over one eye, which reduced acuity to 6/12.1 and 6/16 on average as well as reducing uniocular contrast.

Effect on stereothresholds of uniocular blurring

The mean stereoCT shown in figure 10a (left) increased progressively as the blur levels increased $F=20$ $p<0.05$, one way ANOVA. Unilateral reduction of VA to 0.17 (6/9) almost doubled the stereoCT (Fig 10a). Degradation of stereoCT was significant for both blur levels used but the difference in stereoCT between the 6/9 and 6/12 blur levels was not significant (posthoc Tamhanee paired test $p>0.05$) (Table 9). The mean disparity thresholds are shown in figure 10b (right) which also shows that thresholds increased almost three-fold with blurred acuity to 6/9 (paired t-test $P<0.05$). Blurred acuity to 6/12 also revealed a significant deterioration of disparity thresholds (posthoc Tamhanee paired test $p<0.01$) but the differences observed between the 6/9 and 6/12 blurred levels were not significant (posthoc Tamhanee paired test $p>0.05$) as described in table 9. The error bars shown in figure 10a are less variable for stereoCT when compared to disparity thresholds. Analysis of the difference in variances is described below.

Table 9: Paired comparisons for stereoCT and disparity thresholds with uniocular blur

StereoCT				Disparity thresholds		
Interocular blur	Mean difference	Std. Error	P value	Mean difference	Std. Error	P value
No blur-6/9 blur	-0.31	0.06	0.00*	-79.7	21.1	0.01*
No blur-6/12 blur	-0.39	0.06	0.00*	-146.1	26.3	0.001*
6/9-6/12 blur	-0.08	0.06	0.42	-66.46	32.9	0.16

*Posthoc paired comparisons using Tamhanee paired test. $P<0.05$ is considered statistically significant.

Variance Analysis

The variance between groups was calculated at different blurred acuity levels as shown in table 10. For stereoCT, the variance between groups was not significantly different at either blurred acuity levels when compared to no blur condition (F test of variance, $p>0.05$). For disparity thresholds, as the blurred acuity deteriorated, there was a significant increase in variance between groups (F test of variance, $p<0.001$). Variance was not significantly different between two blurred acuity levels (F test of variance, $p>0.05$)

Table 10: Analysis of variance (F-test) between conditions for stereoCT and disparity thresholds with uniocular blur

Blurred acuity groups	StereoCT P value	Disparity thresholds P value
No blur vs. 6/9 blur	0.21	<0.001*
No blur vs. 6/12 blur	0.19	<0.001*
6/9 vs. 6/12 blur	0.46	0.24

*F test between conditions, p values <0.05 are significant.

Effect on stereothresholds of Uniocular fogging using Bangerter filters

Bangerter filters significantly deteriorated the visual acuity in all participants. The median LogMar visual acuity with 0.8 BF was 0.3 (6/12) range (0.16-0.48) and with 0.6 BF was 0.45 (6/16) range (0.25-0.63). The mean stereoCT is shown in figure 11 (left) increased progressively as the unilateral Bangerter filter strength was increased $F=16.5$, $p<0.05$, one way ANOVA. Inducing unilateral fogging using Bangerter filters even as low as 0.8 almost doubled the stereoCT (paired t-test $p>0.05$) as shown in table 11. There was no significant difference in stereoCT between the 0.8 and 0.6 strength Bangerter filters (paired t-test $p>0.05$). The mean disparity thresholds are shown in figure 11b (right) which also showed increased thresholds with both filters when compared with no filter condition (paired t-test $p<0.05$). There were no significant difference observed between the 0.8 and 0.6 Bangerter filter group (paired t-test $p>0.05$) as described in table 18. The error bars shown in figure 11b are less variable for stereoCT when compared to disparity thresholds. Analysis of the difference in variances is described below.

Table 11: Paired comparisons for stereoCT and disparity threshold measures with uniocular fogging (Bangerter filters).

StereoCT				Disparity thresholds		
Bangerter filter strength	Mean difference	Std. Error	P value	Mean difference	Std. Error	P value
No filter-0.8 BF	-0.23	0.04	0.001*	-55.2	15.1	0.01*
No filter-0.6 BF	-0.32	0.06	0.001*	-81.3	22.3	0.01*
0.8-0.6 BF	-0.09	0.06	0.38	-26.1	26.3	0.70

*Posthoc paired comparisons using Tamhanee paired test. $P<0.05$ is considered statistically significant.

Variance Analysis

The variance between groups was calculated at different uniocular Bangerter filter strength as described in table 12. For stereoCT, the variance between groups was not significantly different at

either BF levels when compared to no filter condition (F test of variance, $p>0.05$). For disparity thresholds, as the Bangerter filter strength increased, there was a significant increase in variance between groups (F test of variance, $p<0.001$) compared to no filter condition. Variance was not significantly different between 0.8 and 0.6 levels (F test of variance, $p>0.05$)

Table 12: Analysis of variance (F-test) between conditions for Bangerter filters, stereoCT and disparity threshold measures.

Uniocular fogging groups	StereoCT P value	Disparity thresholds P value
No filter vs. 0.8 BF	0.33	<0.001*
No filter vs. 0.6 BF	0.17	<0.001*
0.8 vs. 0.6 BF	0.08	0.11

*F test between conditions, p values <0.05 is significant

Discussion

Thresholds progressively degraded as optotype visual acuity was degraded in one eye using Bangerter filters or optical blur for disparity and stereoCT. Previous studies have examined the effects of induced optotype acuity deficits on disparity thresholds using either optical blur or diffusing filters[73,126]. The increase in an optical blur in one eye caused proportional loss in stereoacuity assessed by the Titmus test[127] that is proportional to Snellen acuity. Odell et al[73] examined the effects of fogging induced by Bangerter filters on stereoacuity measured using real depth and random dot tests. Their study reported that the degradation of fine stereoacuity of 60 seconds of arc or better on the preschool Randot test was observed with visual acuity 0.1 LogMar or worse. Coarse to nil stereoacuity of >200 seconds of arc was observed with 0.8 LogMar visual acuity or worse. More than 85% of the participants had stereoacuity >200 seconds of arc on distance Randot test with fogging to 0.8 LogMar. Stereoacuity was found to be more easily degraded when using random dot tests compared to real depth tests. We found median disparity thresholds to be 67.5 seconds of arc (range=18-162) with 0.8 BF which reduced the LogMar visual acuity to 0.3 and 94.5 seconds of arc (range=18-252) with 0.6 BF which reduced the LogMar visual acuity to 0.45. According to Odell et al[73] with visual acuity reduction using Bangerter filters to 0.3 and 0.4 more than 50% of participants were able to detect fine stereoacuity of better than 60 seconds of arc. In our study however, 50% participants had stereoacuity better than 60 seconds of arc with 0.3 LogMar visual acuity reduction using uniocular Bangerter. This percentage reduced to 30% when the acuity was reduced to 0.45 LogMar.The degradation of

stereothresholds measured with Bangerter filters is the cumulative effect of reductions in both optotype visual acuity and contrast sensitivity[128]. Our findings are consistent with Li et al[74] who found a linear reduction in stereothresholds measured on the Randot preschool test for normal observers. Their study concluded that Bangerter filters significantly disrupt binocular vision more than monocular defocus. Bangerter filters had significant and pronounced effects on stereopsis when compared with monocular acuity. StereoCT showed better sensitivity to unilateral blur using defocus or Bangerter filters than conventional disparity thresholds. Stereothresholds have been shown to exhibit a great deal of variability in responses, especially in disrupted binocular vision conditions[129,130]. We found that the variability in stereopsis associated with disrupted binocular vision from optical blur and Bangerter filters was limited to the conventional disparity thresholds. Variability for stereoCT did not increase with uniocular blur or fogging. Improved sensitivity and reduced variability of stereoCT indicate that it may be a useful test for assessing stereopsis, especially in conditions of abnormal binocular vision such as strabismus and amblyopia.

Chapter 6

Disparity and stereoCT in amblyopia: a feasibility study on a small sample

Introduction

Abnormal binocular vision in amblyopia is a result of abnormal visual input early in life and is associated with deficits in a spatial vision such as impaired visual acuity, contrast sensitivity, and perception of depth. According to Weber and Wood[131], impaired stereopsis is the most common deficit associated with amblyopia under binocular viewing conditions. Studies in the past have provided evidence that degrading the vision in one eye in the normal population by blurring[129,132,126], filtering[128], reducing contrast[85] and luminance[69,133] results in reduced stereoacuity. One developing approach to treatment in amblyopia is focused on rebalancing binocular vision by manipulating the contrast between the two eyes. Contrast is gradually reduced in the fellow fixing eye (FFE) to balance it with the amblyopic eye (AE). Previous studies have provided evidence of improvements in visual functions based on binocular balancing by manipulating contrast between the two eyes[91,93–95] (more details in chapter 2, section 2.4).

Clinically, stereoacuity is one of the visual functions used to monitor amblyopia. Accurate measurement and quantification of stereoacuity are highly important. The current clinical tests used to measure stereoacuity have limitations in design when applied to patients with amblyopia. The clinical stereoacuity tests have a cap on the largest disparity that can be presented based on

the test design (chapter 2, section 2.3). Subjects who initially fail to detect the maximum disparity are labelled as having no measurable depth perception (nil stereopsis). This has a major disadvantage as the clinician cannot quantify or report improvements in people with nil stereopsis. Stereoacuity tests used in clinics also exhibit poor repeatability and high variability in people with abnormal binocular vision[134135]. Redesign of clinical stereoacuity tests could therefore provide a more accurate estimate of stereopsis for the diagnosis and monitoring of abnormal binocular vision.

The objective of the study was to investigate the use of stereoCT to quantify stereopsis in patients with amblyopia and to study the effect of contrast balancing on stereothresholds. The hypothesis was that stereoCT would improve with an optimum contrast reduction in the FFE. This improvement might be greater and/or more easily quantified than that found with conventional disparity thresholds.

Methods

Participants

StereoCT and disparity thresholds were obtained from four participants with amblyopia. The participants had strabismic amblyopia or a mix of strabismic and anisometropic amblyopia. A complete clinical examination was performed based on the screening and clinical tests described in section 3.2.4. Amblyopia was defined as a 2 line (0.2 LogMar) or greater interocular difference in best-corrected visual acuity associated with strabismus or anisometropia. Anisometropic amblyopia was defined as amblyopia in the presence of a difference in refractive error between both eyes of ≥1 diopter (D) of spherical or cylindrical power[136]. Two out of four patients had undertaken previous patching therapy but still met the criteria for amblyopia. Two patients had no measurable stereoacuity on the stereo fly test. All measurements were made after providing best-corrected vision through glasses or contact lenses.

Table 13: Demographic data of control and amblyopia group

	Control group (n=11)	Amblyopia group (n=4)
Median Age	26 (range 19-34)	33 (range 23-50)
Median VA LogMar	-0.14 (range 0.26-0.04)	AE= 0.66 (range 0.56-0.9) FFE= -0.01 (range 0.14-0.08)

Table 14 Clinical details of the amblyopic observers.

Participant	Age	Amblyopia type	Refractive error	Affected Eye	Stereoacuity(seconds of arc)	Motor evaluation
JP	50	Strabismic	RE=-0.75/-2.00 LE=-0.75/-1.50	LE	400	4PD ET for distance near
DA	23	Mixed	RE=+6.50 DS LE=-1.50 DS	RE	Not measurable on stereo fly test	10PD XT at near
CW	39	Aniso	RE=+3.50 DS/-1CYL LE=plano	RE	40	8PD XP at near
GJ	27	Aniso	RE=+3.50 DS/-0.25 LE=Plano	RE	Not measurable on stereo fly test	

The following abbreviations have been used in Table 14: aniso for anisometropia, mixed for mixed strabismic–anisometropic. Motor evaluation: ET for esotropia, XT for exotropia, XP for exophoria and PD for prism diopters. Refractive error (RE): DS for diopter sphere, RE for the right eye and LE for the left eye.

Experimental design

Stimulus presentation and psychophysical thresholds were obtained as described in section 3.2.3. Dot density, dot size, and spatial frequency remained constant during the experiment. With full refractive correction in place, we manipulated the stimulus presented to the FFE by manipulating the contrast (interocular contrast ratio). The amblyopic or the non-dominant eye (AE) eye always was presented with full contrast (50% contrast between dots and background) and the contrast in the FFE was presented at full contrast (50%), 40, 30, 20, 10 and 1% contrast (interocular contrast ratios of 1, 0.8, 0.6,0.4,0.2 and 0.02).The stimulus contrast is expressed as Michelson contrast, which is defined as $C=(L_{max}-L_{min}/L_{max}+L_{min})$ where Lmax and Lmin are the maximum and minimum luminance of the stimulus respectively. StereoCT were obtained at supra-threshold stimulus disparities that were subject-specific and above their own disparity thresholds. A supra-threshold stimulus disparity was used so that observers could accurately discriminate the disparity defined grating stimuli before noise was added for the measurement of stereoCTs.

Control group:

Stereothresholds were obtained on 10 participants. Control group data was obtained from chapter 5; section 5.2 investigating the effects of interocular contrast differences on stereothresholds in normal participants. The contrast in one eye was always 50% (the maximum contrast between the gray background and white dots). The contrast in the other eye was manipulated at different

levels; full contrast (50%), 40%, 30% and 20% contrast levels (interocular contrast ratio 1, 0.8, 0.6 and 0.4). Sinusoidal gratings in the control experiment were presented with a maximum disparity of108 seconds of arc. Dot density, dot size, and spatial frequency were matched between the control and the amblyopia experiments.

Results:

Five participants were screened for the study. One participant was excluded due to failure in detecting the highest disparity presented in the disparity threshold test (500 seconds of arc). Four participants with amblyopia had sufficient stereopsis to achieve disparity threshold measures. The disparity thresholds for the four participants were 90, 306, 396 and 405 seconds of arc. Based on the disparity thresholds, the suprathreshold stimulus was chosen randomly between 10 to 30 arc seconds higher than the threshold based on the available disparities and the participant's ability to see the presented stereo target. The suprathreshold levels used were 108, 324, 405 and 432 seconds of arc. Disparity and stereoCT measured with equal contrast in each eye and with contrast reductions in the dominant eye for the individual participants with amblyopia are shown in figures 12-15.

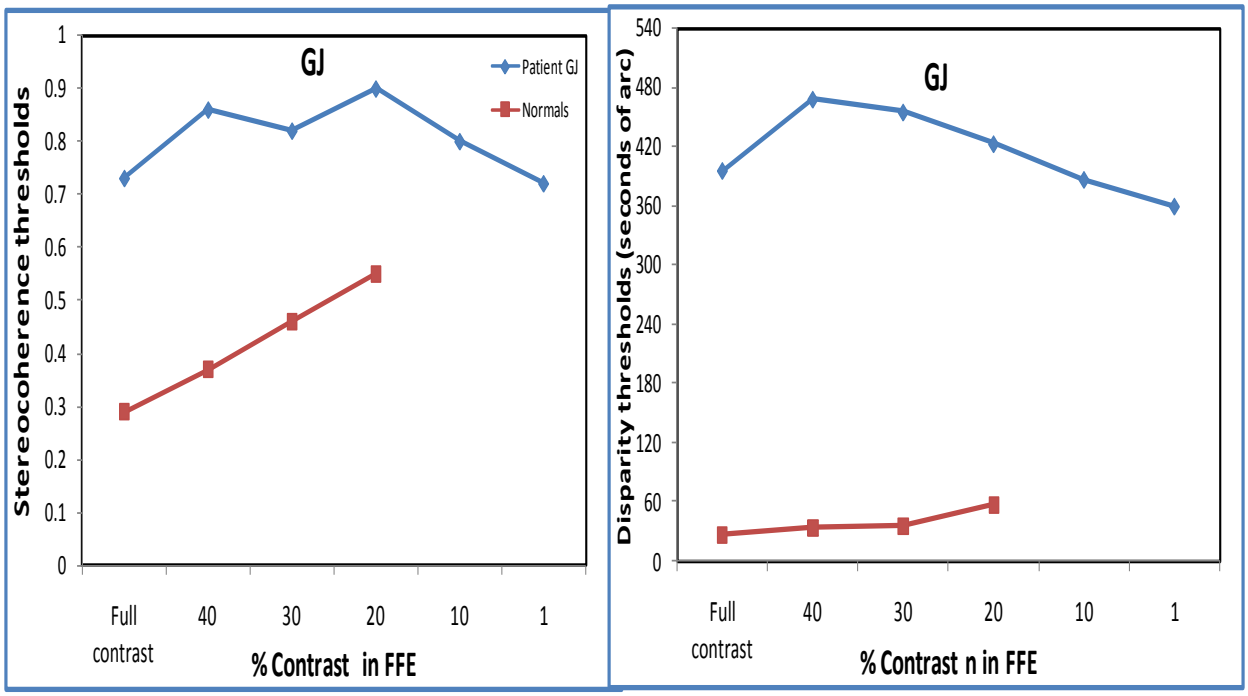

Figure 12 Stereothresholds for participant GJ. The blue line (diamonds) represents patient's data while the red line (squares) represents mean threshold data from the normal population (n=11). Figure 11 (left) stereoCT is plotted on the x-axis and % contrast reduction in the FFE is plotted on the y-axis. A suprathreshold stimulus disparity of 405 seconds of arc was used to measure stereoCT. Figure 11 (right) Disparity plotted as a function of contrast reduction.

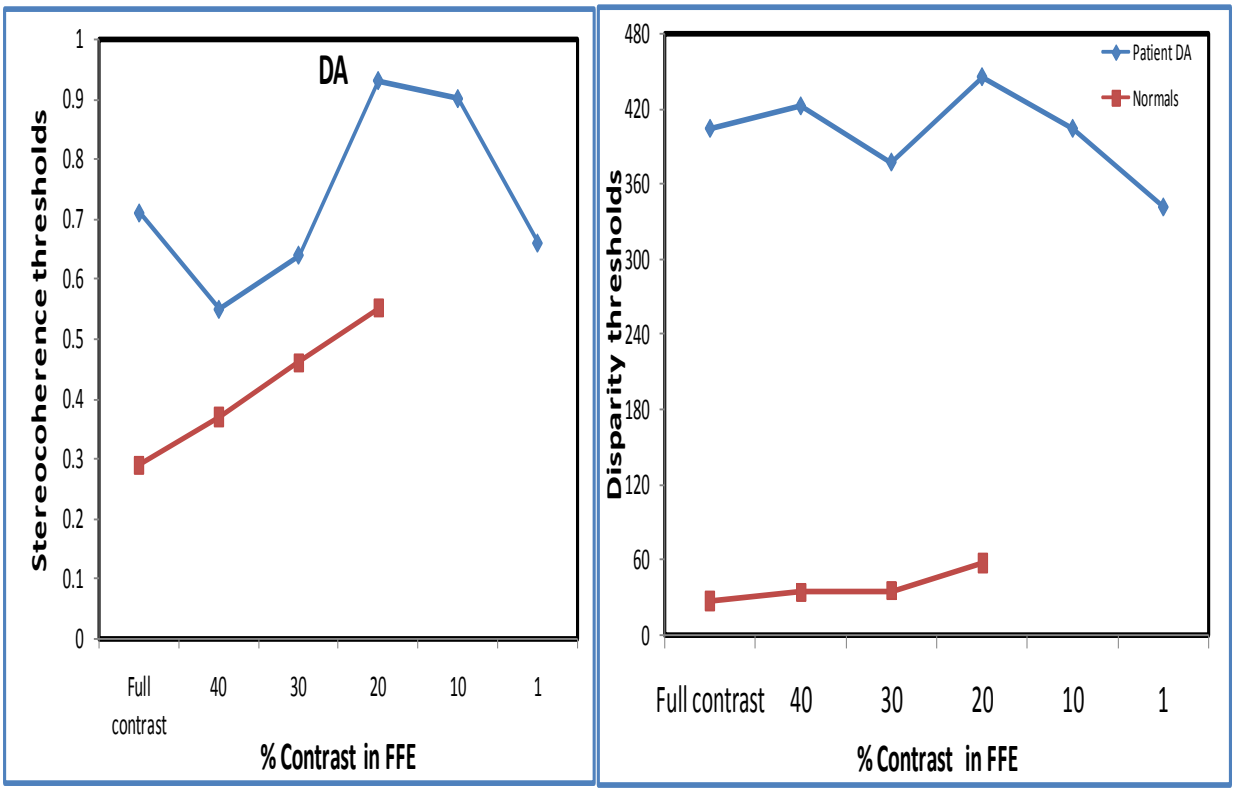

Figure 13 Stereothresholds for participant DA. Data plotted as in Figure 12. A suprathreshold stimulus disparity of 432 seconds of arc was used to measure stereoCT.

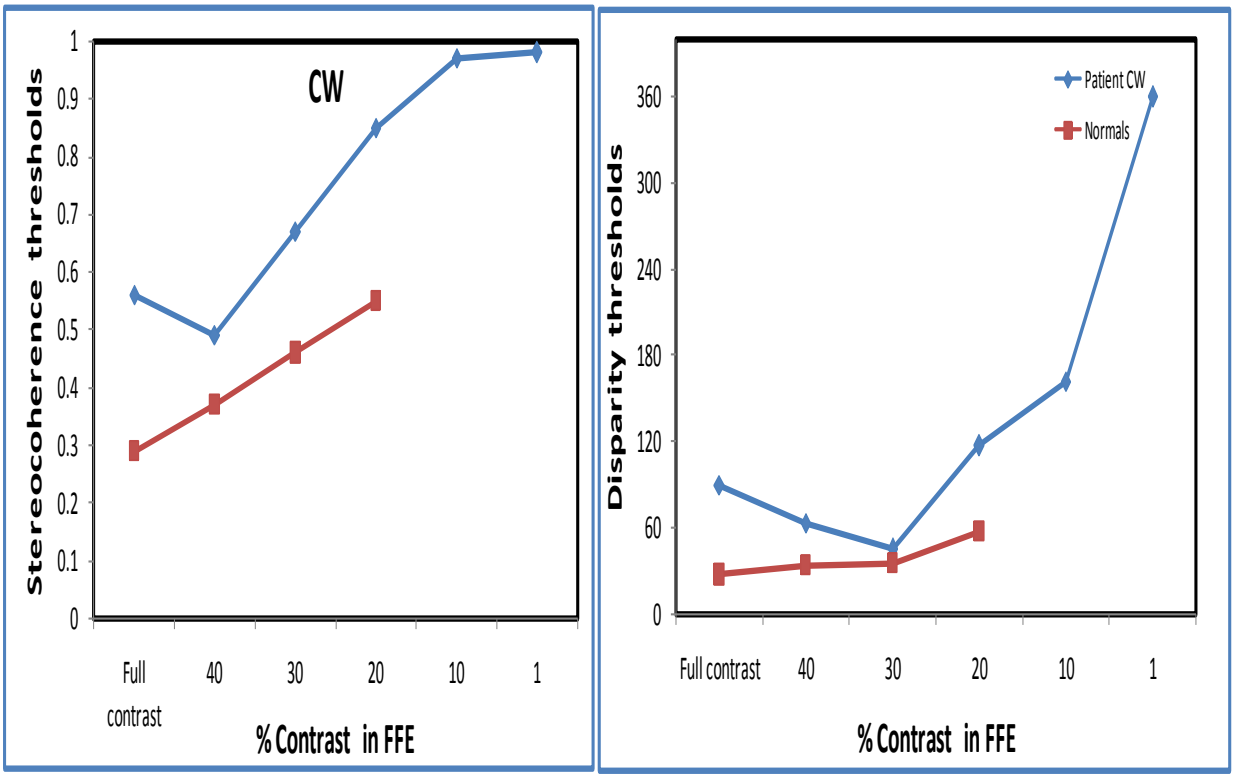

Figure 14 Stereothresholds for participant CW. Data plotted as in Figure 12. A suprathreshold stimulus disparity of 108 seconds of arc equal to that of control group was used to measure stereoCT.

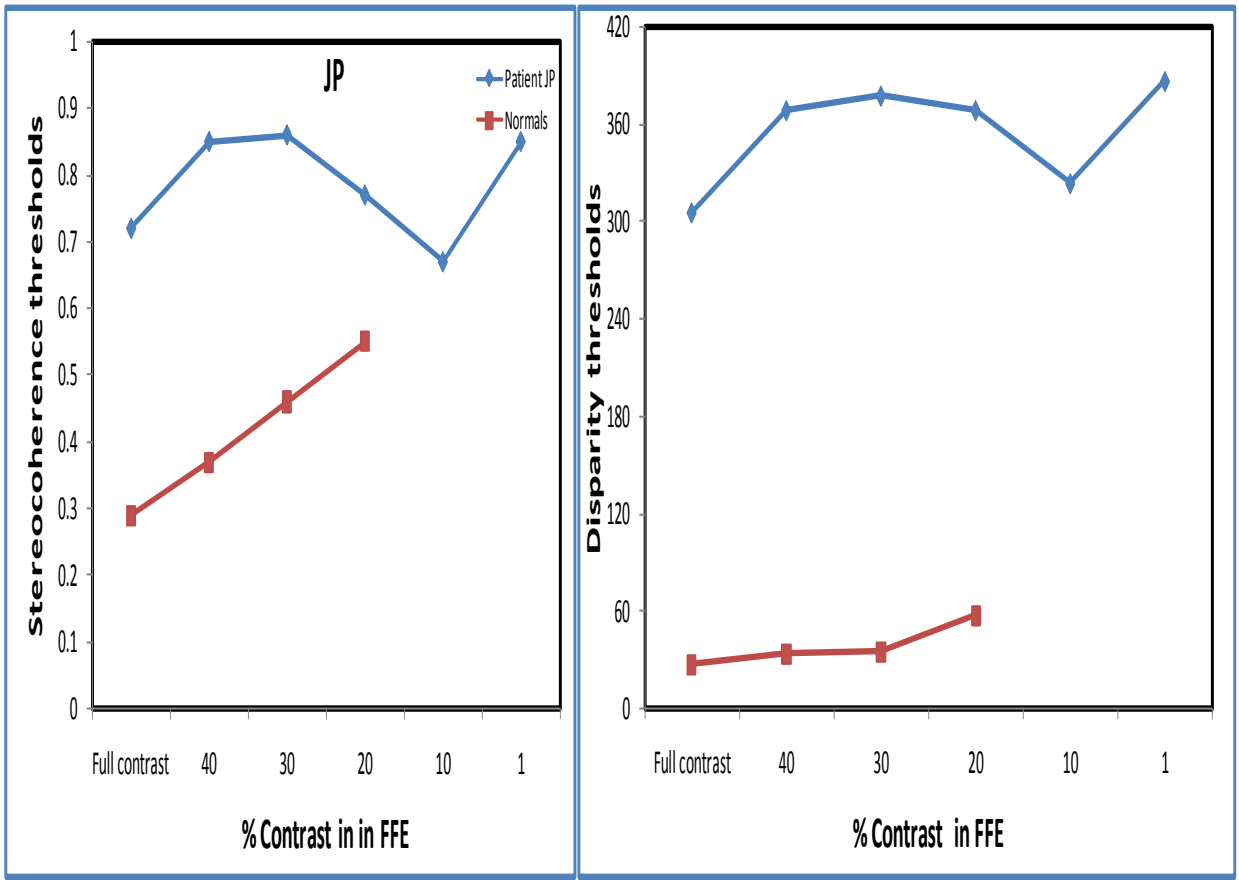

Figure 15 (left) Stereothresholds for participant JP. Data plotted as in Figure 12. A suprathreshold stimulus disparity of 324 seconds of arc was used to measure stereoCT.

Results

Improvement in stereothresholds was observed in three participants (CW, DA and JP). For participant CW, on conventional disparity thresholds, the improvement in contrast was twofold when the contrast was reduced to 30% in the FFE when compared to full contrast condition.

Disparity thresholds gradually worsened when the interocular contrast differences increased beyond this level. StereoCT also exhibited improvements with contrast balancing. Participant JP showed improvements in stereoCT with contrast reduced to 10% in the FFE, whereas disparity thresholds did not improve on contrast balancing when compared to full contrast conditions. For participant DA, performance improved on disparity thresholds when the contrast was reduced to 30% and 1%. StereoCT showed corresponding improvements with contrast reduction of 40% to 30% and with 1% reduction of contrast in FFE. Participant GJ did not reveal any advantage in either disparity or stereoCT with contrast reduction. Thresholds worsened with contrast reduction in FFE between 40-10% ranges. Stereothresholds improved when the contrast was reduced to 1% but was similar to threshold values on the full contrast condition. Overall, the thresholds were higher and more variable for the patients compared to the controls.

Discussion:

A binocular approach to improving stereopsis in patients with amblyopia can be attempted by interocular contrast balancing of stereo thresholds. The effects of reducing suppression on stereoacuity by presenting contrast balanced images between two eyes in patients with amblyopia have been studied in the past. Significant improvements in stereo sensitivity were observed as a consequence of a combination of perceptual learning and anti-suppression treatment[91,93,137], [138]. To our knowledge, the effect of acute contrast balancing on stereoscopic resolution has not been reported before. We did not find a consistent pattern of improved thresholds of either stereoCT or

disparity thresholds with five levels of contrast reduction in the fellow eye relative to the amblyopic eye in our four participants.

Under normal binocular viewing conditions, the weak signals coming from the amblyopic eye do not allow for optimal local matching between the two eyes, which is crucial for stereoscopic perception. Global integration of stereoscopic images relies on the successful resolution of local matches between the two eyes. Since local matching is impaired in amblyopia, the global integration of stereoscopic images measured using stereoCT also shows impaired thresholds. The balancing contrast of the images between the two eyes may reduce suppression and allow for local matching and global integration to occur at optimum contrast as demonstrated in our study for one participant. Participant CW who had best initial stereopsis showed the expected pattern of improved thresholds when the balance point was reached with contrast reduction in the FFE. Our findings show that quantitative measures of binocular interactions for global stereopsis in patients with amblyopia can be assessed using the stereoCT measure. For some patients with coarse stereopsis, the limitation of no measurable stereothresholds on clinical tests can be overcome by measuring stereoCT on suprathreshold disparity defined targets. We also addressed the limitation of smaller dot sizes on clinical tests. Clinical RDS test designs are made up of smaller dot sizes which may contribute to the decrease in stereothresholds in amblyopic participants. Accurate and reliable measurements of stereoscopic deficits may improve the treatment of amblyopia.

Our study also has implications the use of contrast-balanced stereo targets between two eyes for perceptual learning experiments. Although, our participants showed some benefit of using interocular contrast balancing, the effects were not consistent. Future studies might be needed to study the effect of using contrast balanced targets on stereoresolution. Also, more detailed investigation of the benefits of using contrast balanced targets in different types of amblyopic patients is also required.

Chapter 7

General discussion and conclusion

The objective of our study was to develop a new clinical measure of global stereopsis that was complimentary to the presently used clinical tests. Stereopsis tests presently used in clinics exhibit limitations in test design such as floor and ceiling effects, which affects measurement reliability. We developed a new measure of stereothreshold called as stereoCT. The stimulus used to measure stereoCT is based on a signal in noise test. Coherence thresholds were obtained for disparity defined form (sinusoidal grating) that was degraded by assigning random disparity to a subset of noise dots in a random dot stereogram. We also measured conventional disparity thresholds by introducing positional differences between two images. Both stereoCT and disparity thresholds were measured psychophysically using an adaptive staircase.

The first aim of the study was to investigate spatial parameters which would reveal low stereoCT and can be used to design stimuli which would be used for the main experiments. We investigated the effects of dot density, dot size, disparity amplitude and spatial frequency on stereoCT. In normal participants, we found that best stereoCT were encountered around the dot density of 29% and the dot size of 5.5 min of arc. StereoCT also was most sensitivity at spatial frequency of 1cpd and significantly elevated for 4 and 8cpd gratings. StereoCT were significantly lower for gratings with maximal depth of 108 and 144 seconds of arc. We used these parameters to design our test stimulus.

The second aim of the study was to see the performance of stereoCT in artificially degraded binocular vision conditions. We measured these effects by inducing abnormal vision using interocular contrast differences, interocular luminance differences, unilateral defocus and unilateral fogging using Bangerter filters. StereoCT was a worse with each level of disrupted binocular vision. We related this reduction in performance to reduction of conventional disparity threshold measures. Disparity thresholds were also worse but only for much larger interocular differences compared to the stereoCT. The decline in thresholds was more abrupt for disparity thresholds in contrast to a gradual decrease in performance on stereoCT. We also measured the variance between each level of disrupted binocular vision on both stereoCT and disparity thresholds. The performance on stereoCT was less variable between control participants with different levels of degraded binocular vision compared with conventional disparity thresholds. Disparity thresholds had different variances between conditions even with low level of degradation. We conclude from these findings that stereoCT might be a better measure of stereoscopic performance especially in conditions of abnormal binocular vision such as in amblyopia. Lower variances allow more sensitive detection of abnormality and of change.

Finally, we conducted a feasibility study on a small set of amblyopic participants. We used the interocular contrast balancing method on stereo targets measuring both stereoCT and disparity thresholds. Step-wise contrast reduction in FFE was introduced and the stereoscopic performance was measured. Stereo thresholds are reported for four amblyopic participants. We found the expected systematic benefit of acute contrast reduction in the FFE on stereoscopic performance in

one participant with good initial level of stereoacuity. In others, the effects of contrast reduction were inconsistent. Our findings show that quantitative assessment of binocular interactions for global stereopsis in patients with amblyopia can be assessed using the stereoCT measure. The limitation of no measurable stereothresholds on clinical tests can be overcome in some ambyopes by measuring stereoCT on suprathreshold disparity defined targets.

Our study has some limitations. We examined parameters within ranges where we expected good thresholds but did not evaluate all the combination of parameters. Some parameters such as field size were not assessed. Our stereoCT is dependent on the successful resolution of the disparity defined sinusoidal grating since it measures global stereopsis. If stereoCT is to be implemented as a new clinical test, either designing a test with step by step detection of first disparity thresholds followed by stereoCT or measuring disparity thresholds on conventionally used clinical tests and presenting a suprathreshold stimulus disparity to measure stereoCT might be required. We have reported stereoCT for a corrugated sinusoidal grating; future work might focus on stereoCT for a square wave and other simple stereo targets in order to create a clinical test that does not require patients to complete psychophysical staircase testing.

StereoCT is a new measure of stereopsis which targets the second stage of stereoscopic processing where global integration of the 3D image occurs from local matching between two eyes. The global integration of stereopsis measured by stereoCT might involve higher and more complex level of neuronal processing.

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Appendix A

Information and consent Letter

INFORMATION LETTER/CONSENT FORM

Title: Binocular interactions in Amblyopia-electrophysiology and psychophysical study

Faculty Supervisor

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2Ms. Dania Abuleil BSc

(Co-investigator)

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Study procedure:

Screening

1. **Ocular Health History:**You will be asked to answer questions regarding the history of your eyes health*(E.g.*: history of reduced vision, history of patching, previous ocular surgeries etc.)

2. **Visual acuity:**This is to determine how well your eyes see separately and together. You will be asked to read the vision chart with different sized alphabets.

3. **Cover test:** This is to determine the amount of eye turn (strabismus) using special lenses called prisms. You will be asked to look at the given target while the examiner neutralizes your eye turn using prisms.

4. **Sensory status:**This is to determine how well your eyes work together. This procedure involves two steps.

- Participant will be asked to wear 3D glasses and look at images with depth information for recording depth perception.

- Worth four dot tests is used where participant will be shown a torch with four dots and asked to wear red green goggles and specify number of dots seen. This test helps in identifying patients with amblyopia

Psychophysical tests

Participant will be asked to first wear 3D glasses and look at images on a computer monitor. Sets of dots will be presented with motion or depth information. Participants have to respond the direction of the coherent dots in a field of randomly moving dots for motion coherence thresholds and to the orientation of a pattern defined by depth for stereopsis threshold.

Your participation in the study is voluntary. You may decide to withdraw from this study or may refuse to complete any of the experimental tasks or other tasks in whole or in part, at any time for any reason by advising the researcher, and may do so without any penalty or loss of participation To do so, please do inform Ms. Viquar Unnisa Begum or Ms. Dania Abuleil.

CONSENT FORM

I have read the information presented in the information letter about a study being conducted by **Ms. Viquar** Unnisa under the supervision of **Dr. Ben Thompson and Dr. Daphne McCulloch** of the Department of **Optometry** at the University of Waterloo.I have made this decision based on the information I have read in the Information letter. All the procedures, any risks and benefits have been explained to me. I have had the opportunity to ask any questions and to receive any additional details I wanted about the study.I am aware that I may withdraw from the study without penalty at any time by advising the researchers of this decision

I understand that this project has been reviewed by, and received ethics clearance through a University of Waterloo Research Ethics Committee. I was informed that if I have any comments or concerns resulting from my participation in this study, I may contact the Director, Office of Research Ethics at (519) 888-4567 ext. 36005.

By signing this consent form, I am not waiving my legal rights or releasing the investigator(s) or involved institution(s) from their legal and professional responsibilities.

With full knowledge of all foregoing, I agree, of my own free will, to participate in this study.

Print Participant Name: _____

Participant Signature: _____

Witness Name and Signature: _____

Dated At Waterloo, Ontario: _____

UNIVERSITY OF WATERLOO

OFFICE OF RESEARCH ETHICS

Notification of Ethics Clearance of Application to Conduct Research with Human Participants

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Faculty Supervisor: Benjamin Thompson	**Department:** Optometry, School of
Faculty Supervisor: Daphne McCulloch	**Department:** Optometry, School of
Student Investigator: Viquar Unnisa Begum	**Department:** Optometry, School of
Student Investigator: Dania Abuleil	**Department:** Optometry, School of

ORE File #: 20955

Project Title: Binocular interactions in adult Amblyopia-electrophysiology and psychophysical study

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This certificate provides confirmation the above project has been reviewed in accordance with the University of Waterloo's Guidelines for Research with Human Participants and the Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans. This project has received ethics clearance through a University of Waterloo Research Ethics Committee.

***Note 1**: This ethics clearance is valid for one year from the date shown on the certificate and is renewable annually. Renewal is through completion and ethics clearance of the Annual Progress Report for Continuing Research (ORE Form 105).*

***Note 2**: This project must be conducted according to the application description and revised materials for which ethics clearance has been granted. All subsequent modifications to the project also must receive prior ethics clearance (i.e., Request for Ethics Clearance of a Modification, ORE Form 104) through a University of Waterloo Research Ethics Committee and must not begin until notification has been received by the investigators.*

***Note 3**: Researchers must submit a Progress Report on Continuing Human Research Projects (ORE Form 105) annually for all ongoing research projects or on the completion of the project. The Office of Research Ethics sends the ORE Form 105 for a project to the Principal Investigator or Faculty Supervisor for completion. If ethics clearance of an ongoing project is not renewed and consequently expires, the Office of Research Ethics may be obliged to notify Research Finance for their action in accordance with university and funding agency regulations.*

***Note 4**: Any unanticipated event involving a participant that adversely affected the participant(s) must be reported immediately (i.e., within 1 business day of becoming aware of the event) to the ORE using ORE Form 106. Any unanticipated or unintentional changes which may impact the research protocol must be reported within seven days of the deviation to the ORE using ORE form 107.*

Maureen Nummelin, PhD
Chief Ethics Officer

Oct. 23/15
Date

OR
Julie Joza, MPH
Senior Manager, Research Ethics