ANISEIKONIA AND STEREOACUITY: A BASELINE STUDY TO ASSESS ITS RELATIVE IMPACTS ON KERATOCONUS

A thesis presented to the graduate faculty of
New England College of Optometry in partial fulfillment
of the requirements for the degree of Master of Science.

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May 2024

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Abstract

ANISEIKONIA AND STEREOACUITY: A BASELINE STUDY TO ASSESS ITS RELATIVE IMPACTS ON KERATOCONUS

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New England College of Optometry, 2024

Purpose:

Optimal binocular vision relies on well-matched optics between the two eyes, which determine both the quality and relative size of retinal images. This study investigates the effect of inducing controlled levels of optical aniseikonia using image size altering lenses monocularly in healthy individuals, with a focus on measuring aniseikonia and stereoacuity utilizing custom psychophysical routines. The goal of this thesis is to obtain baseline data on the impact of relative interocular magnification on stereoacuity in controls as a first step before assessing its impact in keratoconus.

Methods:

Twenty-seven young adults (24.7± 1.9 years) healthy control subjects were recruited from the New England College of Optometry, Boston, MA, USA. The average spherical equivalent refractive error was - 2.57D, all subjects had anisometropia smaller than 0.75D. Higher order aberration measurements were acquired to ensure there was not mismatch optical quality measured as high order RMS (HORMS) between the two eyes. Size-altering afocal lenses of 1%, 3%, 6% and 9% were employed over one eye and custom psychophysical tests were used

to measure aniseikonia and stereoacuity first without the size lenses, then with each of the size lenses in a random order.

Results:

No interocular differences in refractive error or higher-order aberrations were noted. The average HORMS for all subjects was 0.11 ± 0.04 μm for the right eyes and 0.16 ± 0.18 μm for the left eyes, which are low values of HORMS and expected for eyes with regular corneas. The results from the aniseikonia measurement task did not show a predictable relationship with the interocular differences in image magnification and was overall unsuccessful in estimating aniseikonia. The correlation between the magnitude of afocal lenses and the point of subjective equality (PSE) in the aniseikonia task was low at 0.083. The PSE averages for the different afocal lens sizes, 1%, 3%, 6%, and 9%, were -0.66, -0.11, -0.07 and -0.21 respectively. Conversely, the results from the stereoacuity measurement task showed a greater reduction in stereoacuity corresponding to increases in interocular differences in image magnification.

Conclusion:

This thesis highlights the challenges encountered in measuring induced aniseikonia and outlines future directions for aniseikonia and stereoacuity research, particularly in the context of its relevance to future investigations in keratoconus.

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Abstract iii

Acknowledgements v

1 General Introduction 1

2 The Effects of Induced Aniseikonia on Stereoacuity Loss 12

3 Methods 16

4 Results 36

5 Discussion 45

6 Conclusions and Future Direction 56

References 58

Appendix 63

List of Figures

Figure 1 3
Figure 2 5
Figure 3 13
Figure 4 18
Figure 5 20
Figure 6 22
Figure 7 22
Figure 8 23
Figure 9 24
Figure 10 25
Figure 11 26
Figure 12 27
Figure 13 28
Figure 14 29
Figure 15 31
Figure 16 32
Figure 17 34
Figures 18 a-e 40
Figure 19 43
Figure 20 44

List of Tables

Table 1 36
Table 2 37
Table 3 39
Table 4 42
Table 5 42

List of Equations

Equation 1 4

1 General Introduction

1.1 Introduction to stereoacuity and prerequisites to stereoacuity

A sensitive indicator of binocular vision problems, stereoacuity, refers to the smallest depth detectable from disparity, which is the perspective difference between the two eyes' views. (1) Optimal binocular vision is dependent on well matched optics between the two eyes, both in terms of the quality of each individual retinal image, and in the relative sizes of those optical images. Clear and single binocular vision requires similar images falling on corresponding points on the two retinas and making reliable horizontal disparity information accessible to compute stereoscopic depth. Stereoscopic depth or 3-Dimensional (3D) vision is most sensitive when an object is at, or near the horopter (within the Panum's space), ensuring the object can be imaged on corresponding points in each retina and be fused into a single percept. (1,2) Fusion of the object into a single image can be impeded by mismatches between the two eyes' images, and outcomes can include double vision (diplopia), rivalry or suppression of one eye's retinal image; all these outcomes are associated with reduced or no stereo depth perception. Mismatches between the two eyes can broadly fall into two categories. The first reason for mismatches between the eyes is motor misalignment leading to different images on corresponding points generally due to strabismus, and the second reason for mismatches is optical, usually stemming from larger degrees of anisometropia that lead to differences between the quality of images falling on corresponding points. Optical mismatches could be due to image quality mismatches, such as differences in blur and contrast between the two eyes, or differences in magnification that are often caused by spectacle correction of anisometropia. Differences in optical image quality or magnification of the images between the two eyes can make binocular matching difficult and sensory fusion of the two monocular targets of each eye, to see a clear and single

binocular target challenging. (1,3) Stereoacuity deficits due to interocular optical mismatches, specifically, 1) differences in optical image quality, and in particular, 2) perceived magnification of the images between the two eyes (aniseikonia) with the goal of mapping these deficits in corneal ectasias will be the subject of this thesis. It is to be noted that while the introduction and discussion in this thesis is geared towards the goal of assessing the relative impact of aniseikonia on stereoacuity in keratoconus, studies in keratoconus subjects were not done, and will be the subject of a future investigation. A reduction of stereoacuity is associated with a decrease in performance of certain motor skills, leading to a host of self- reported problems that result in an overall reduction of quality of life, (4,5), and assessments of the relative roles of various optical factors in the stereoacuity losses in keratoconus is an important future goal.

1.2 Optical image quality

The first of the interocular optical mismatches described above, i.e., differences in monocular optical image quality, are caused by differences in lower and/or higher- order aberrations between the two eyes. When light or its wavefront encounters irregularities in the media, it results in aberrated wavefronts. (6,7) The shape of wavefronts of light can be described as mathematical functions, and in optometry, they are often described as a combination of several orders of Zernike Polynomials where individual polynomials describe different types of aberrations. The Zernike polynomials that are visually significant are the 2^{nd} through 4^{th} order aberrations. Second-order aberrations are known as lower-order aberrations (LOAs) and third-order and above are known as higher-order aberrations (HOAs). LOAs include oblique astigmatism, vertical astigmatism, and defocus. LOAs are the refractive errors that manifest as myopia, hyperopia, and astigmatism in the eye, commonly seen in the general population and

fully correctable by a spherocylindrical prescription of spectacles or contact lenses. HOAs are more complex in nature, and include aberration patterns such as coma, trefoil, and spherical aberration (depicted below in figure 1) and by definition, are not correctable with spectacle lenses. (8)

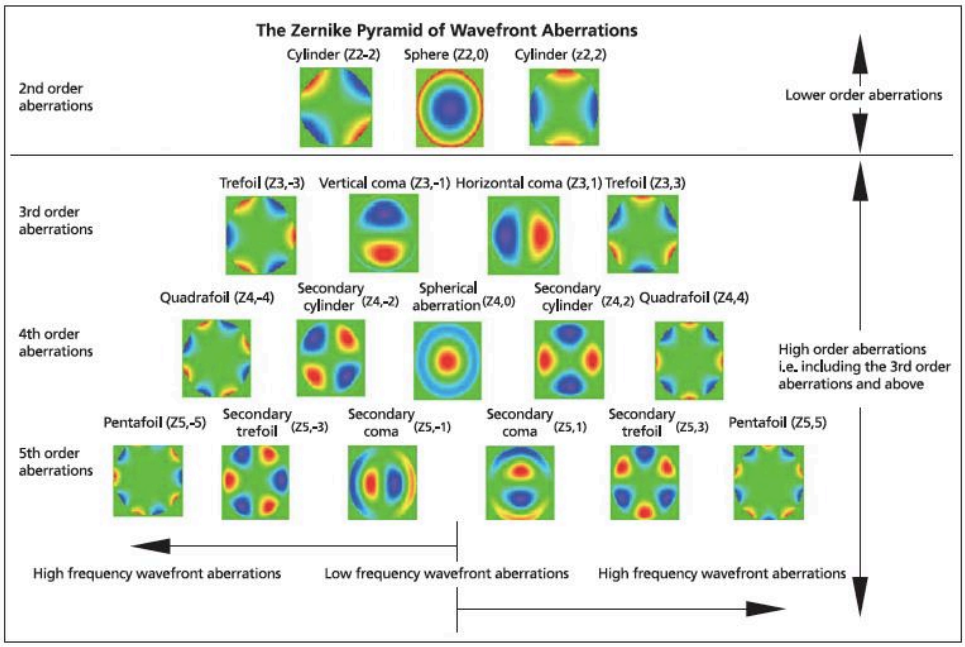


Figure 1

Zernike polynomials up to the 5th order. Red depicts positive aberration values, and blue depicts negative aberration values. Adapted from Jinabhai et al. 2009, figure 5. (7)

An increase in LOAs and HOAs reduces contrast of the retinal image and reduces the visual system's sensitivity to resolve a grating object. (1,9) Aberrations can also induce phase shifts, leading to a failure of preserving the spatial relations of the object faithfully in the image, and as such hamper the recognition of the object's shape (6,10) and overall, aberrations lead to a poorer visual experience. Aberration magnitudes can be measured with aberrometers up to several orders. Zernike polynomials or the root mean square (RMS) of several polynomials in a cornea without pathology, averages to about zero in most individuals (6,11), with decreasing

magnitudes as we go up in orders of HOAs. Corneas without pathology may have a very small slight positive value for spherical aberration, a fourth-order aberration, and given a 6mm diameter pupil this is a normal tendency. (6,12) This amount is about +0.14um, in the general population. (13) A study by Thibos et al. (2002) (11) provides a calculation (equation 1 below) to compute the equivalent defocus given RMS error.

$$M = 4\pi\sqrt{3}\frac{\text{RMS error}}{\text{pupil area}}$$

Equation 1

Equation from Thibos et al. (2002) used to calculate equivalent defocus. If RMS is in μm, then pupil area will be in mm, and M will output defocus in Diopters.

Collectively, the higher-order wavefront aberrations of a normal eye with no corneal pathology for a pupil size measuring 7.5mm cause blur equivalent to the blur caused by defocus of about a 0.25 D lens. (11) The RMS of several orders of HOAs (often the 3rd to 6th order, referred to higher-order RMS or HORMS), is used to quantify the amount of HOAs, and has been found to be significantly higher in corneas with keratoconus. Some studies show RMS values of up to almost 6μm. (14–16) Given the above formula by Thibos et al. (2002), assuming 6μm HORMS over a 6mm pupil, the blur experienced only due to the HOAs would be equivalent to approximately 1.5 D of defocus. (11) The degradation of visual quality with increased RMS values is not linear and often small values can significantly impair contrast sensitivity and resolution ability. (17) Figure 2 demonstrates the visual degradation of retinal images due to HOAs alone, following correction of LOAs with spectacles. Large amounts of HOAs often occur in corneal dystrophies, ectasias, or diseases due to the corneal shape changes of both the anterior and posterior corneal curvatures and also following laser refractive procedures. (7,11,13,18) In these instances, HOAs remain independent of refractive error. (19)

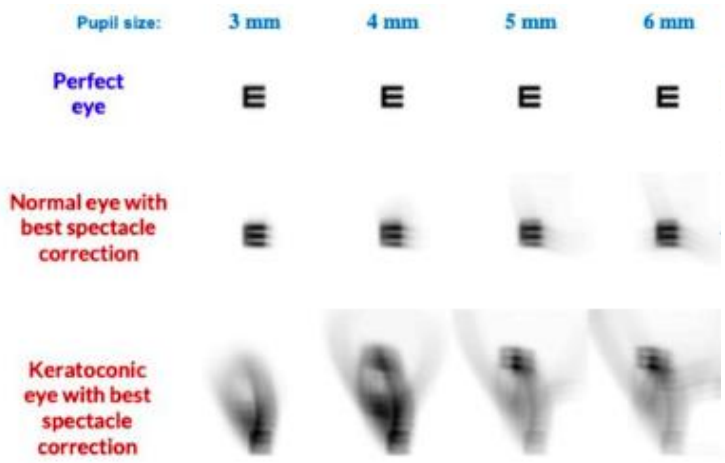


Figure 2

The visual effects of HOAs on keratoconic eyes, from Ovitz, 2019. (20)

Spherocylindrical correction in individuals with corneal pathologies, yields poor visual outcomes as it only corrects for LOAs and not HOAs. This is often seen in individuals with keratoconus, for example. These individuals may have visual acuities of 20/100 or worse through spectacles, but markedly improved visual acuity through rigid contact lenses. (21,22) Clinically, corneal, and scleral rigid gas-permeable (RGP) contact lenses minimize HOAs due to the creation of a complementary tear film between the irregular cornea and the contact lens but may not completely eliminate them. (19,23) The reason could be the complementary tear film, or lacrimal lens, complements the anterior curvature changes but the HOAs due to posterior curvature changes are left unaccounted for. (24) Correction of HOAs with adaptive optics systems that can only be used in laboratory settings has been shown to improve contrast sensitivity. (25) In recent years, wavefront guided correction has been added to more moderately to severely aberrated eyes. It has been shown that the added wavefront guided correction has further reduced HOAs when the corneal and scleral RGP lenses themselves are not adequate in eliminating subjective visual complaints or improving objective visual acuity. (26) Apart from

irregularities due to disease, many individuals who have undergone refractive surgery may unfortunately experience new symptoms following correction of their LOAs, such as glare, reduced contrast, starbursts, monocular polyopia and more, due to the induction of HOAs by the procedure altering the regularity of the anterior corneal layers. (27)

1.3 Optical image quality in the two eyes and stereoacuity

In the binocular realm, defocus and astigmatism blur from LOAs when present in equal magnitudes in the two eyes, has been well documented to decrease stereoacuity, especially when present in large amounts (28–32). Anisometropia refers to a difference in refractive error or axial length between the two eyes, or unequal amounts of blur, or LOAs, and is known to cause greater detriment to stereoacuity. Small amounts of anisometropia, as little as 0.5 diopter, have been shown to reduce clinically measured stereoacuity. (9,28) When large magnitudes of anisometropia are present, contrast is reduced unequally in the two eyes, which on its own is also known to affect stereoacuity. (33–36) Some studies suggest the reason for reduced stereoacuity in anisometropia is the lack of being able to fuse central details. (28,37) With as little as 1 diopter of anisometropia, peripheral fusion is affected. (37) While other studies suggest there may be foveal suppression in the eye with more LOAs and thus defocus, could be the reason for reduced stereoacuity (28,38)

Similar to losses of stereoacuity with blur and interocular mismatches of LOAs, blur and interocular mismatches of HOAs in keratoconus (39) and following refractive surgery has also been documented to reduce stereoacuity as it negatively affects disparity visibility in stereoacuity tasks, similarly to the way defocus affects contrast sensitivity. (40) HOAs are typically not present in amounts large enough to decrease visual acuity in the eyes of the normal population

even if they affect contrast sensitivity. They manifest in eyes with corneal disease or following refractive surgery in increased amounts and/or in asymmetric magnitudes between the two eyes; as such, an interest in exploring the role of HOAs on retinal image degradation and what that means for stereoacuity has evolved. (22)

1.4 Perceived interocular magnification differences (Aniseikonia) and Stereoacuity

Additional problems to binocularity may occur when anisometropia is corrected with spectacles, as differently powered spectacle lenses cause images to be magnified differently in the two eyes, resulting in optical aniseikonia. Since the plane of a spectacle lens is approximately 13mm from the cornea and that of a contact lens is at the cornea, correction of anisometropia with spectacle lenses, but not with contact lenses, induces size magnification differences of the retinal images between the two eyes, leading to optical aniseikonia. Optical aniseikonia is a difference in perceived image sizes on each retina and can proportionally reduce stereoacuity regardless of the image quality in each eye. (15,25,41–43) Apart from reducing stereoacuity, aniseikonia could cause dramatic distortions of three-dimensional spaces in disparity rich environments, and this is sometimes utilized in the measurement of aniseikonia using eikonometry. Generally, 1 diopter or anisometropia causes about 1 diopter of aniseikonia, but its effect on stereoacuity is not 1:1. (44) Each diopter of anisometropia that is corrected with spectacles can have the same effect on stereoacuity as 5-6% of optical aniseikonia. (9) This does not occur with contact lens correction of anisometropia. Clinically significant aniseikonia can manifest with only 3% aniseikonia, presenting with asthenopia, headaches, photophobia, and at 5% aniseikonia, will present with reduced stereoacuity. (42) It has been reported that anisometropia can affect up to 18% of the population, and issues of anisometropia and optical

aniseikonia can lead to issues of diplopia and amblyopia. (45,46) It has been suggested that induced aniseikonia in children, as a result of correcting refractive anisometropia, may limit the visual outcomes of children with refractive anisometropic amblyopia. (47) Elimination of optical aniseikonia can occur in 2 ways. One method is to use contact lenses that eliminate the issue of differential spectacle magnification in the two eyes, as contact lenses sit on the plane of the eye. (48) Another less commonly prescribed way but used in some clinics in the past to quantify aniseikonia, is with the use of afocal lenses. Afocal lenses, or size lenses, magnify the image using a positive front surface and a negative back surface, but without adjusting the focal length of the image, i.e., they do not induce any defocus. (49,50) Artificially induced aniseikonia can be achieved by size lenses of magnification of whole integers, 1% through 12%. Optical aniseikonia described above is sometimes referred to as static aniseikonia, and is different from dynamic aniseikonia, or anisophoria, which refers to the two eyes rotating by different amounts to gaze at the same point in space. This thesis only refers to static or optical aniseikonia.

1.5 Future investigation of stereoacuity deficits in keratoconus

Several of the optical mismatch issues discussed above may combine to degrade binocular vision and reduce stereoacuity in keratoconus, an ectatic degeneration of the cornea, affecting both the anterior and posterior curvatures of the cornea. Keratoconus typically starts in adolescence and progresses asymmetrically between the two eyes. One eye may manifest the condition earlier than the other, but both eyes will be affected. (51) Progressive thinning, and an eventual ‘cone-like’ protrusion of the cornea results in irregularity of the corneal surface. (23) A significant protrusion of the cornea or increased anterior and posterior corneal curvature may manifest as increased refractive myopia, and irregular corneal toricity may manifest as irregular

astigmatism. These are both abnormal increases of LOAs compared to the general population. Irregularities in the cornea due to corneal shape changes also lead to increased HOAs such as coma and spherical aberration compared to the normal population as described before. (52) Despite spherocylindrical correction of LOAs in keratoconus eyes, there can be contrast sensitivity reduction, ghosting and distortion effects, and significantly reduced visual acuity, due to the uncorrected HOAs. (7) The interocular asymmetry found in keratoconus makes it a great model to study the binocular consequences of optical mismatches between the eyes.

Early keratoconus individuals may have a refractive error that can be corrected to a clinically acceptable monocular visual acuity, but natural vision is binocular. The increased and asymmetric amounts of LOAs and HOAs in eyes with keratoconus compared to the normal population could cause greater problems with tasks involving stereo depth, as can correction of anisometropia seen in early keratoconus with spectacle lenses. Asymmetric LOAs may be corrected with spectacle lenses to yield clear optical images, but the perceived induced magnification effects also reduce stereopsis. When magnification effects occur in the optical images, they can not be overcome by any amount of vergence in the eye and such yield depth disparity information difficult to detect. (1) The use of RGP contact lens corrections use in keratoconus lead to an improvement in stereoacuity, but not to the levels of a subject with normal corneas, likely due to residual HOAs on the posterior corneal curvature. (22,39) Contact lenses correct LOAs, minimize HOAs and negate aniseikonia, but how much stereoacuity losses do each of these contributors account for in subjects with keratoconus? Aniseikonia in keratoconus remains largely unexplored.

In summary, reduction of stereoacuity in keratoconus could be due to three interocular optical mismatches: (i) lower- order aberrations (LOAs), (ii) higher- order aberrations (HOAs)

and (iii) spectacle magnification (optical aniseikonia). We wanted to assess their relative contributions, as this is unexplored. Our ultimate goal was to measure aniseikonia and stereoacuity in keratoconus subjects through different optical correction conditions when aniseikonia was present or minimized. We hypothesized that aniseikonia would contribute significantly to the stereoacuity losses seen in keratoconus in addition to the stereoacuity losses introduced by interocular mismatches of lower- and higher-order aberrations. Studying binocular vision in eyes with keratoconus may help provide a fundamental insight into the relative roles of these optical contributors to optimal binocular vision and help alleviate the problems faced by this population by optimizing their optics for better binocular performance. To this end, this thesis focuses on the baseline studies geared towards the first step of inducing known magnitudes of optical aniseikonia using size lenses in control subjects and measuring aniseikonia and stereoacuity with custom-written psychophysical routines.

1.6 Measuring aniseikonia

In general, there are several hindrances to aniseikonia measurements. Many researchers that have explored the effects aniseikonia in the past have reported aniseikonia by the percentage of afocal size lenses used to induce or correct it, and not the aniseikonia experienced or perceived by the subjects (9,53). Aniseikonia measurement tests available in the clinic either in book or software formats, often underestimate the presence of aniseikonia (53,54). The gold standard test for aniseikonia measurement, the Space Eikonometer, is a device that is no longer widely available. The Space Eikonometer requires subjects to have reasonable stereoacuity for an accurate measure. For this thesis, we built custom software that we hoped would alleviate some of these problems associated with aniseikonia measurement. Our goal was to confirm the amount of perceived aniseikonia after induction using size lenses in control subjects and move forward to

estimate aniseikonia in keratoconus. We hypothesized that aniseikonia would contribute significantly to the stereoacuity losses seen in keratoconus, in addition to the stereoacuity losses introduced by interocular mismatches of aberrations.

2 The Effects of Induced Aniseikonia on Stereoacuity Loss

We set out to assess the relative role of aniseikonia on stereoacuity in keratoconus; however, we began these explorations knowing that aniseikonia is notoriously difficult to measure. Many researchers that have explored the effects aniseikonia in the past have reported aniseikonia by the percentage of afocal size lenses used to induce or correct it, and not the aniseikonia experienced or perceived by the subjects. (9,53) The gold standard test for aniseikonia measurement, the Space Eikonometer (American Optical Corp., Southbridge, MA), is a device that makes precise measurements of aniseikonia using stereoscopic judgements. (55) Its manufacture has been discontinued, and it is no longer widely available. The Space Eikonometer requires subjects to have reasonable stereoacuity for an accurate measure. For this thesis that set out to measure aniseikonia in control and keratoconus subjects that typically experience stereoacuity losses, we could not use a device based on stereoscopic judgements. Aniseikonia measurement tests available in the clinic either in book or software formats often use a "direct comparison" method where the size of the target through the left and right eyes are compared while separating inputs to the two eyes using anaglyphs, and these underestimate the presence of aniseikonia. (53,54) Many clinicians do not routinely screen for aniseikonia as there is a lack of available aniseikonia tests. It could be that there is a lack of aniseikonia tests as the measurement of aniseikonia is not straightforward, and is influenced by several factors, including stereopsis. The tests that are currently available in the clinic do not measure aniseikonia accurately and are known to either underestimate or overestimate it compared to the gold standard.

The Eikonometer is a time-consuming test based on physiological optics and utilizes the 3D distortions caused by aniseikonia. (55) The visual target of the Space Eikonometer that the patient views are a red "X" or cross, with two vertical white lines behind the cross and two

vertical green lines in front of the cross. (50) The two green lines, the center X and the two white lines are each in three distinct planes, with the two objects of the same color appearing equidistant to a normal observer with no aniseikonia.

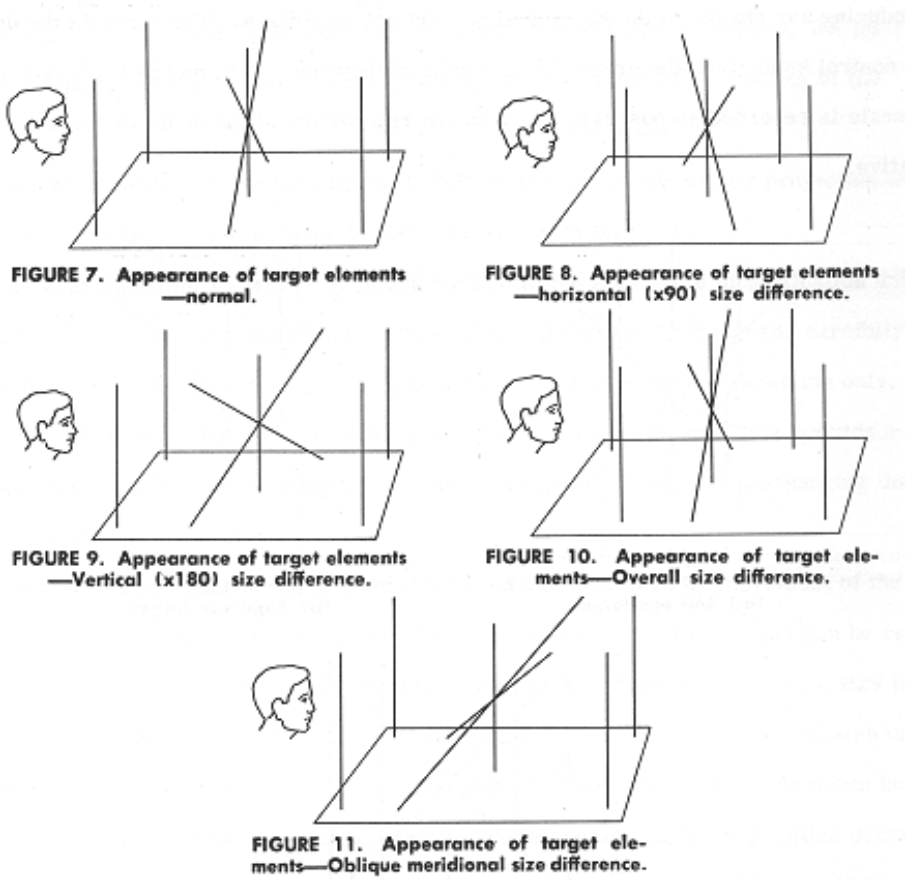


FIGURE 7. Appearance of target elements —normal.

FIGURE 8. Appearance of target elements —horizontal (x90) size difference.

FIGURE 9. Appearance of target elements —Vertical (x180) size difference.

FIGURE 10. Appearance of target elements—Overall size difference.

FIGURE 11. Appearance of target elements—Oblique meridional size difference.

Figure 3

Each of the different figures above demonstrates the different appearances of the Space Eikonometer to the subject with different size magnification differences. Adapted from the Space Eikonometer's user manual. The space eikonometer was manufactured by the American Optical Corporation (Southbridge, MA, USA).

Overall or meridional aniseikonia will have different impacts on the perception of the limbs of the cross and their relative distance, and on the distance of the vertical lines of each color. There are three controls the subject can adjust: 1) change the alignment of the vertical lines in the target until they appear to be in the same plane, 2) rotate the red cross around a vertical axis, and

3) rotate the cross around a horizontal axis until it appears to be in the same plane for both axes. (50,55) Tested in typical subjects, the Space Eikonometer accurately estimates the amount of aniseikonia (54).

Another aniseikonia measurement test that is available to be used in the clinic is the Aniseikonia Inspector (Optical Diagnostics, Culemborg, The Netherlands). Red-green anaglyphs are used to present a differently colored half-circle size target to each eye. Aniseikonia can be measured in steps of 0.5% in the vertical and horizontal meridians and 0.7% in the oblique meridian. Measurements are made twice in each meridian, averaged, and recorded as the amount of aniseikonia. (55) This test requires binocular visual alignment but does not require stereoacuity. The Aniseikonia Inspector underestimates the amount of aniseikonia in both vertical and horizontal meridians. (55) The New Aniseikonia Test, or NAT (Handaya, Tokyo, Japan) also exists for clinical use and it easy and quick to perform, as well as to interpret. The red-green anaglyph technique is used to directly compare two half-moon targets. When the half-moons are perceived to be the same size, that is the amount of aniseikonia present. But the NAT underestimates aniseikonia in normal subjects by a factor of up to 3.0 when known amounts of aniseikonia was induced in these subjects. (54,56)

We built custom software for aniseikonia measurement that was based on dichoptic direct size comparisons, and attempted to alleviate some of the issues might have occurred with clinical tests of aniseikonia. (54,57) While other researchers, e.g., Abdelzaher et al 2022 have written custom software, their goal was to closely mimic the Aniseikonia Inspector and they did not attempt to change any variables. (58) We set out to induce interocular magnification differences using specific afocal size lenses in control subjects and measure perceived aniseikonia, and stereoacuity losses introduced by this manipulation. Our goal from data acquired from these

experiments in normal subjects was to allow us to validate the custom psychophysical test for aniseikonia measurement, assess the impact of perceived aniseikonia on stereoacuity and have this serve as baseline data that would be used for comparisons with similar data obtained in subjects with keratoconus and anisometropia in future investigations.

We hypothesized that psychophysically measured aniseikonia thresholds would correlate strongly with the magnitude of size lenses used to induce it, and second, that stereoacuity would worsen with increasing magnitudes of induced aniseikonia.

3 Methods

The study described was approved by NECO's Institutional Review Board (IRB) and complied with the tenets of the Declaration of Helsinki.

3.1 Subjects

We recruited healthy pre-presbyopic male and female subjects aged 18- 40 years-old who were free of keratoconus or other eye diseases, amblyopia, or eye turns and did not undergo any ocular or laser refractive surgery procedures. Subjects who used hard contact lenses such as those who used orthokeratology, or those who wore daytime corneal or scleral RGP lenses were ineligible, while those wearing soft contact lenses were eligible to participate in our study. Our subjects were primarily recruited through emails sent out to Optometry students at the New England College of Optometry and were young subjects at varying stages of their Optometric studies. They were required have a recent spectacle and contact lens prescription, prescribed within the previous year as their habitual correction to be used for the study. They were correctable to a Snellen visual acuity of 20/20 or better and did not have anisometropia > 0.75 D, and spectacle Rx no greater than ± 9D and cylindrical power no greater than 2.50D was allowed.

3.2 Study Design

Each subject completed one 1.5-hour session of data collection that included a screening component, anterior segment examination, refraction, as well as aberrations, and psychophysical tasks for aniseikonia and stereoacuity measurements.

After obtaining informed written consent, an initial screening assessment occurred at the beginning of the session to ensure that eligibility criteria were met. First, subjects were asked a

series of questions that included basic demographic information, date of last eye exam, history of ocular disease, approximate age when prescribed glasses, personal history of refractive error, or surgery, if they had a valid contact lens prescription, and contact lens prescription. Following this, subjects' visual acuity was taken at both distance and year, pupils were confirmed to be equal, round, and both reactive to light. A clinical measure of stereoacuity, Randot 3S, was employed to ensure a minimum stereoacuity amount of 40 arcsec in all subjects.

Subjects were then asked to perform two experimental psychophysical tasks, an aniseikonia task and a stereoacuity task. Each task was performed with the subjects' habitual correction. first to ensure that the subjects understood the task. These tasks were then performed while the subjects wore one of a series of overall afocal magnifiers that magnified the images for the right or left eye. We randomized the size-lens-wearing eye to be right or left alternately for every consecutive subject and ensured that they performed all tasks while wearing a size lens over that chosen eye. The percent magnification induced by the size lenses were 1%, 3%, 6% and 9%. We used a randomized order suggested by MATLAB for the order in which the subjects performed their psychophysical tasks through these size lenses.

The subjects were given rest breaks as needed. Some subjects were brought back to a repeat visit, and for the second visit, we ensured that they had their original form of correction that was used at the first visit, to perform the psychophysical tasks wearing this correction.

3.3 Anterior Segment and Refraction

Subjects were screened in a shared lab space (figure 4), using a slit lamp to ensure they were free of any anterior segment pathology or opacities that would hinder the psychophysical measurements. Any corneal pathology, including previous scars, resulted in exclusion from the

study. All subjects were free of corneal pathology, and corneal opacities such as scars or other findings. No subjects had corneal haze, or any corneal striae.



Figure 4

Shared lab space at the New England College of Optometry where the screening, refraction, and slit lamp evaluation took place in.

Open- field autorefraction (figure 5 below) was performed while subjects looked at a target at 15m to ensure there was no anisometropic refractive error for both the sphere and cylindrical components. For subjects using contact lenses, it was also performed over their contact lens prescription, to ensure that there was no residual anisometropia through their contact lenses, as some subjects performed psychophysical tasks through their contact lens prescription.

Subjects then underwent a sphero-cylindrical subjective refraction using either the autorefractor or retinoscopy as the starting point to confirm accurate correction of the refractive errors. A full spectacle prescription was to be provided during the study if different from their habitual correction. This served as their best-corrected sphero-cylindrical prescription that was used for our psychophysical experiment. All the subjects were confirmed to be wearing a spectacle prescription that did not correct any anisometropia of more than 0.75D and our spherocylindrical refractions were similar to their current habitual spectacle correction. Current habitual contact lens prescriptions were acquired from the subjects Electronic Medical Record. Visual acuities for either correction modality, contact lenses and spectacle correction were 20/20 or better, in both eyes for all our subjects.



Figure 5

Open-field autorefractor used to the experiment, Grand Seiko Co, Ltd, Binocular Accommodation Auto Ref/Kerato meter Wam-5500, Hiroshima, Japan.

3.4 Wavefront aberration measurements

Control subjects wearing soft contact lenses as their habitual correction were asked to remove their contact lens habitual correction for the wavefront aberration measurements. No wash out period was necessary for the control subjects due to the nature of the soft contact lens material. Silicone hydrogel soft contact lens wear has negligible effects on cornea hysteresis, and minimal to no corneal edema or swelling with regular hours of daily wear. Keratocyte counts of contact lens wearers remain steady with continued contact lens wear and does not return to

baseline after stopping contact lens wear for any period of time, suggesting that any changes due to contact lens wear, can be deemed the patient's new baseline, and a washout period is not required (59,60). Wavefront aberrations of the eye were measured using the COAS™ aberrometer (Complete Ophthalmic Analysis System™, Wavefront Sciences Inc, Albuquerque, New Mexico) (figures 6,7). Subjects were asked to view a distant target equivalent of 20/100 placed that was 15 feet from the COAS. The target was placed directly in the line of sight of the subject with both eyes in real space to minimize the effects of accommodation while each eye is being measured. The aberrometer was set to measure over the widest possible pupil diameter of 8mm, in mesopic conditions, to ensure data was gathered over the fullest extent of the natural entrance pupil i.e., pupils were not pharmacologically dilated. Aberration snapshots were taken over 3 seconds and with a sampling resolution of 30Hz, and we collected ~90 aberration samples per eye. Wavefront aberration data was the average of these measurements collected for each eye for all subjects in both groups. See photos of the COAS™ instrument used below.



Figure 6

COAS Wavefront Analyzer in the Metlapally Lab, at the New England College of Optometry



Figure 7

COAS Wavefront Analyzer in the Metlapally Lab, at the New England College of Optometry, from the view of the data collector.

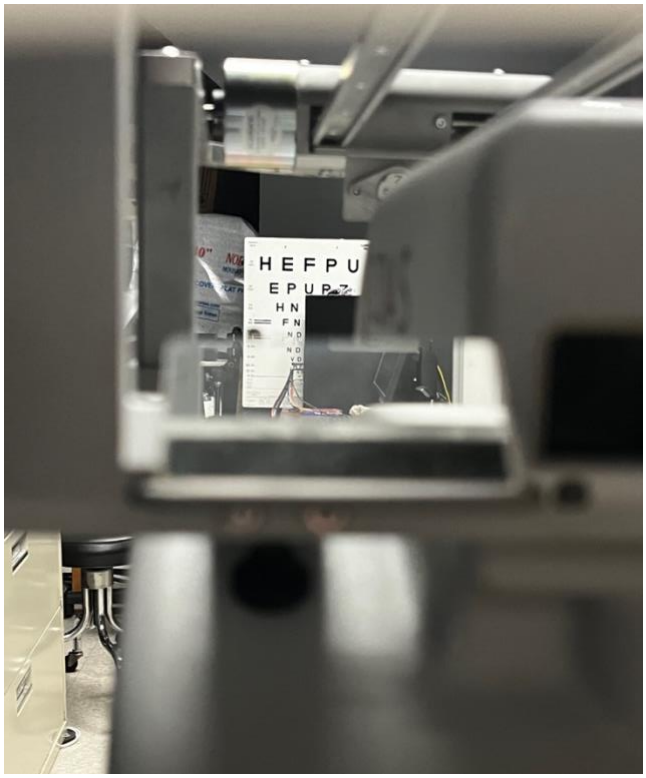


Figure 8

The view from the headrest in the COAS Wavefront Analyzer. The subject's head would be placed in the headrest. They were instructed to view a distance target, a letter on the top row of the Snellen chart.

3.5 Afocal/Size Lenses

In order to study the impacts of magnifying the image in one eye relative to the other in our experiment for our psychophysical tasks, i.e., stereoacuity and aniseikonia measurements, specific afocal lenses (also known as size lenses) were placed in front of one eye of our subjects. The afocal lenses we used magnified the overall image size. Size lenses have spherical front and back surfaces, where the front surface is positive and the back surface negative, to yield a magnification effect without changing the focal length, i.e., without the introduction of any refractive power. These lenses are much like a Galilean telescope system, where instead of a positive lens as an objective and negative lens as an ocular, they have positive front and negative

back surface curvatures built into a single lens. The lenses used in our experiment, were from Chadwick Optical (PA, USA), with a refractive index of 1.49, (CR-39) (figures 9, 10). We selected four size lenses that magnify by 1%, 3%, 6% and 9%. With increasing magnification, the thickness of the lens increases, but the magnification power is independent of the distance at which the lens is placed. The lenses have a uniform magnification power up to about 30 degrees of visual angle, and only when past 20 degrees of visual angle, do we have pincushion distortion. (50) Our screen was wider in both dimensions; however, no distortion would have occurred as the targets were presented close to the center of the screen.



Figure 9

Afocal/size lenses, by Chadwick Optical, sizes 1% through 5%.



Figure 10

Afocal/size lenses, by Chadwick Optical, sizes 6% through 10%.

3.6 Psychophysical Measurements

Psychophysical measurements of aniseikonia and stereoacuity were completed using custom designed software. The custom programmed aniseikonia and stereoacuity measurement tasks were created and deployed using MATLAB (Mathworks, Natick, MA) and Psychtoolbox and projected onto a 3D stimulus compatible rear-projection screen by VPixx (Montreal, Canada), (130.8cm x 73.6cm; visual angle of 36 x 20.85 degrees at the subject's eyes) using a VPixx Projector. The projector was 100cm from the screen and the subject was 200 cm from the screen. See figures 11 and 12 below.

Subjects performed distance and near visual acuity tasks during the refraction procedure to ensure their ability to see fine detail (20/20 or better visual acuity) both monocularly and binocularly, with their best-corrected sphero-cylindrical prescription and contact lenses, as described before. Subjects were then screened for stereoacuity using Randot 3S task to ensure

they had near stereoacuities of at least 40 seconds of arc to qualify to be control subjects. For the stereoacuity and aniseikonia measurements for our experiments, their self-reported most frequently used habitual correction was used.

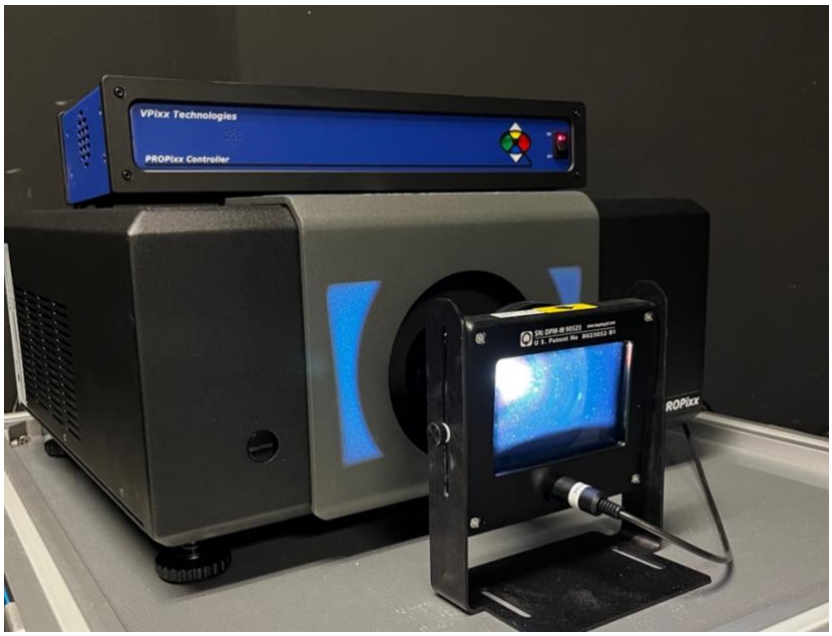


Figure 11

VPixx Technologies (Montreal, Canada) Projector and Controller used to display aniseikonia and stereoacuity stimuli onto a rear projection screen.



Figure 12

Photo of the arrangement to perform aniseikonia and stereoacuity tasks. On the left is the projector, which projects the polarized targets onto the screen, 100 cm away. The screen, 200cm from the subject, is then viewed by the subject sitting on the stool on the right. A chin and forehead rest helped center the subject in the apparatus and minimize head movements.

A short training session for each psychophysical task was provided before data was collected to ensure the subject understood the purpose of the test and how to complete it and how to pause the test for breaks if needed.

Optical aniseikonia was induced by magnifying the image in one eye using an afocal lens of 1%, 3%, 6% and 9%. The afocal lens was placed in front of the right eye for odd subject ID numbers, and over the left eye for even subject ID numbers. The order in which the afocal lenses of different magnifications were placed over the tested eye for aniseikonia and stereoacuity measurements was randomized using MATLAB prior to the subject visit. There is no evidence that eye dominance has a role in the perception of induced aniseikonia, and thus eye dominance was not considered when placing the afocal lens over the eye of the subject (61).

It is difficult to demonstrate the binocular effects and the 3D distortions caused by aniseikonia in a 2D presentation format. While the binocular system is vastly more complex, the photo of a 9% afocal lens (figure 13) over the left part of the field simply demonstrates the magnification difference between the two sides of the visual field of one eye.

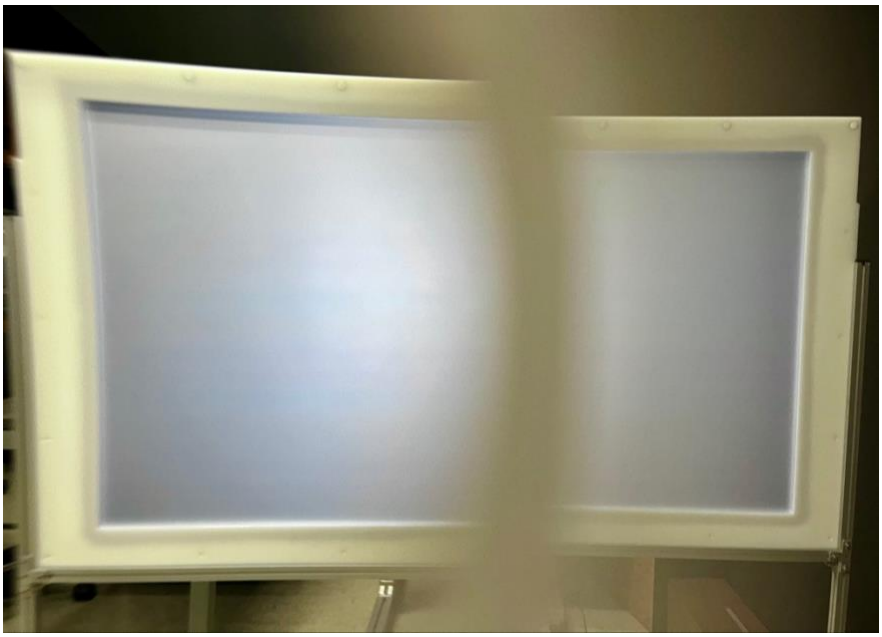


Figure 13

Facing the VPixx screen in the Metlapally lab at the New England College of Optometry, a 9% size lens is placed over the left side of the field magnifying only one side of the field.

3.6.1 Measurements of Aniseikonia

Two rectangular bar stimuli that were wider than they are high and of the same contrast and luminance were projected onto the screen, one above and the other below a fixation cross. The background was uniformly grey, had a vertical and a horizontal black line that bisected the screen horizontally or vertically to create a binocular fixation cross that extended to the edge of the screen, and the bars were bright in appearance as shown in the schematic (Figure 14). The bar stimuli were dichoptically presented using static circular 3D polarizers in front of each eye

that had been placed in a trial frame at 12 mm from the eyes. As a result, the top bar stimulus was seen only by the right eye and the bottom bar stimulus was seen only by the left eye of the subject. The subjects did not realize that they were viewing only one bar per eye as they were viewing the screen with both eyes open. The use of grey 3D polarizers allowed the use of polychromatic stimuli and eliminate size comparisons while the stimuli intended for the two eyes were colored differently in colors such as red, green blue or yellow. The two horizontal bars were parallel to each other and presented simultaneously in time one above the other, and centered on the vertical line that bisected the screen. Subjects were instructed to keep their eyes at the center of the screen, where the bisecting black lines intersected to form a binocular fixation cross at all times. We did no monitor eye movements, but the bars were flashed briefly for 150ms to prevent the subject from moving their eyes away from fixation, or make it so they don't move their eyes to each of the bars to make size comparisons.

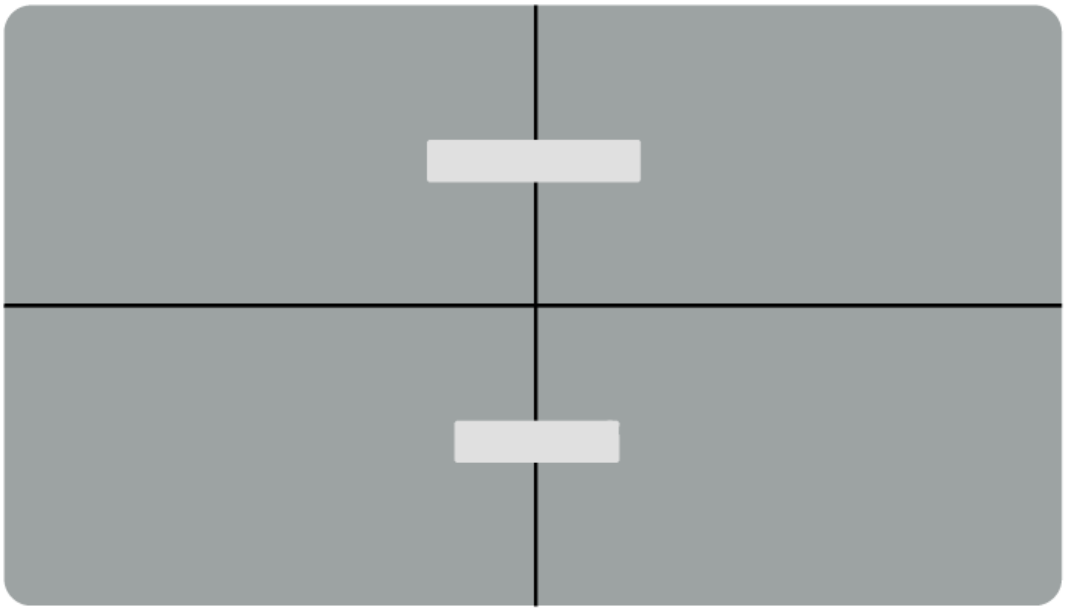


Figure 14

Schematic of the subject's view while performing the aniseikonia measurement task, with both eyes open. The grey area represents the uniform grey background or the full extent of the projector screen. The black fixation cross extends to the edges of the screen, while the subject was asked to fixate at the center. The bright bars represent the dichoptic stimuli (top bar seen by the right eye and the bottom bar seen by the left eye). The subject indicated whether the top or the bottom bar was wider using the response box.

The baseline width of the bar was 4 degrees in visual angle (2 degrees on either side of the vertical midline), about 14 cm at the 200 cm viewing distance. We performed all testing at a 200cm distance, as opposed to near or far to get around the resolution limitations of our set up. We used the method of constant stimuli (MCS) paradigm to present changes to the width of the bars throughout the experiment using MATLAB and Psychtoolbox. The size of the top bar that was seen by the right eye was made wider than the bottom bar by 0%, 1%, 3%, 6% or 9% for 25 trials each. The bottom bar that was seen by the left eye was made wider than the top bar by 1%, 3%, 6%, or 9%, also for 25 trials each. The pairs of bars with the specific relative changes of width as described above were presented randomly intermixed to minimize predictability, ultimately resulting in 225 size comparison trials for each size lens wearing condition. Other parameters of the bars that were left unchanged were their height (2.3cm), and its location on the screen (presented 6.5cm above or below the center of the fixation cross).

The subjects judged which bar was wider, the top or bottom, and indicated their choice using the top or bottom button on the gamer control in front of them (figure 15). With 0%, 1%, 3%, 6% or 9% afocal lens placed in front of one of their eyes, we expected optical aniseikonia to have a one-to-one relationship with the amount of relative magnification change we induced between the two subject's eyes. When data were plotted with the induced magnification on the abscissa and the response percentages for each optical condition along the ordinate, the recorded response data would be a "frequency of seeing the bottom bar as wider" graph that could be fitted with an appropriate sigmoid function, e.g., Weibull or logit. We could obtain information

about the point of subjective equality (PSE), the location along the X axis where the sigmoid function crosses the 50% chance level might indicate the overall aniseikonia experienced by the subject in each optical magnification condition. We expected optical aniseikonia to reveal itself as a rightward or leftward shift of the sigmoid psychometric function. For instance, when a 3% afocal size lens is placed in front of the right eye of a control subject, their responses when left eye's image (bottom bar) is magnified by 3% would be expected to be at chance level or 50% because they are equally likely to indicate that the top or the bottom bar is wider. With the afocal lens in front of their eye, they will be asked to indicate whether the top or bottom bar is wider than the other clicking on the controller. The amount of optical aniseikonia perceived by the subject as a shift in the psychometric function was expected to be a one-to-one relationship with the amount of optical aniseikonia induced in the subject's eyes.



Figure 15

RESPONSEPixx Controller created by VPixx Technologies, used in the study. Subjects made their responses on this controller. Top yellow, and bottom blue buttons are lit up during the aniseikonia measurement task for the subject to select top or bottom bar as larger.

3.6.2 Measurements of Stereoacuity

We used custom programmed stereoacuity measurement task that used random dot stimuli. For each optical magnification condition, or afocal lens percentage imposed in front of the chosen eye in a randomized order, the subject performed the stereoacuity task while viewing the display through static 3D circular polarizers as before. Each of the many trials of the stereoacuity task was a temporal two-alternative forced choice task with two square fields of bright random dots presented against a grey background with a central fixation square. Each presentation lasted 1500ms, with an inter-stimulus of 700ms with only the central fixation square showing on a grey background. Only one of these two intervals had a hidden stereo depth figure presented as an uncrossed disparity stimulus that was in the shape of a bowl, or a pit. The subject indicated whether the depth figure was in first or second interval of random dots by selecting the left button or the right button respectively using the gamer control in front of them (figure 16).



Figure 16

RESPONSEPixx Controller created by VPixx Technologies, used in the study. Subjects made their responses on this controller. Left green, and right red buttons are lit up during the stereoacuity

measurement task for the subject to select. If the depth was in presentation 1, they selected the left green button, or right red button if in the second presentation.

The subjects performed a pre-test that present standard disparities seen a stereo test performed at the clinic, descending from 400 arc seconds to 10 arc seconds. The pre-test had two goals; first, we wanted to use it as a screening test to determine an approximate threshold and it would also serve as a practice test for those that were performing our computerized stereo task for the first time. For the main test (figure 17), we implemented 0.1 log decrements from 400 arc seconds until a reversal occurred, after which both staircases were begun. We interleaved two staircases: i) a 1-up/ 3 down and ii) a 1 up/ 2 down staircase. The log decrements and increments were chosen as discrimination is poorer when stereoacuities are poorer, and the step sizes naturally got smaller as we tested finer disparities. If the program was unable to terminate based on the reversals, we specified an upper limit of 120 presentations (for both staircases combined).

The threshold/ stereoacuity was defined as the geometric means of the last 12 reversals. The reversals were calculated from the sequences of psychophysical responses and the threshold was extracted for each subject and size lens condition. Means and standard deviations were calculated for each size lens condition. ANOVA pairwise comparisons were done for each size lens conditions.

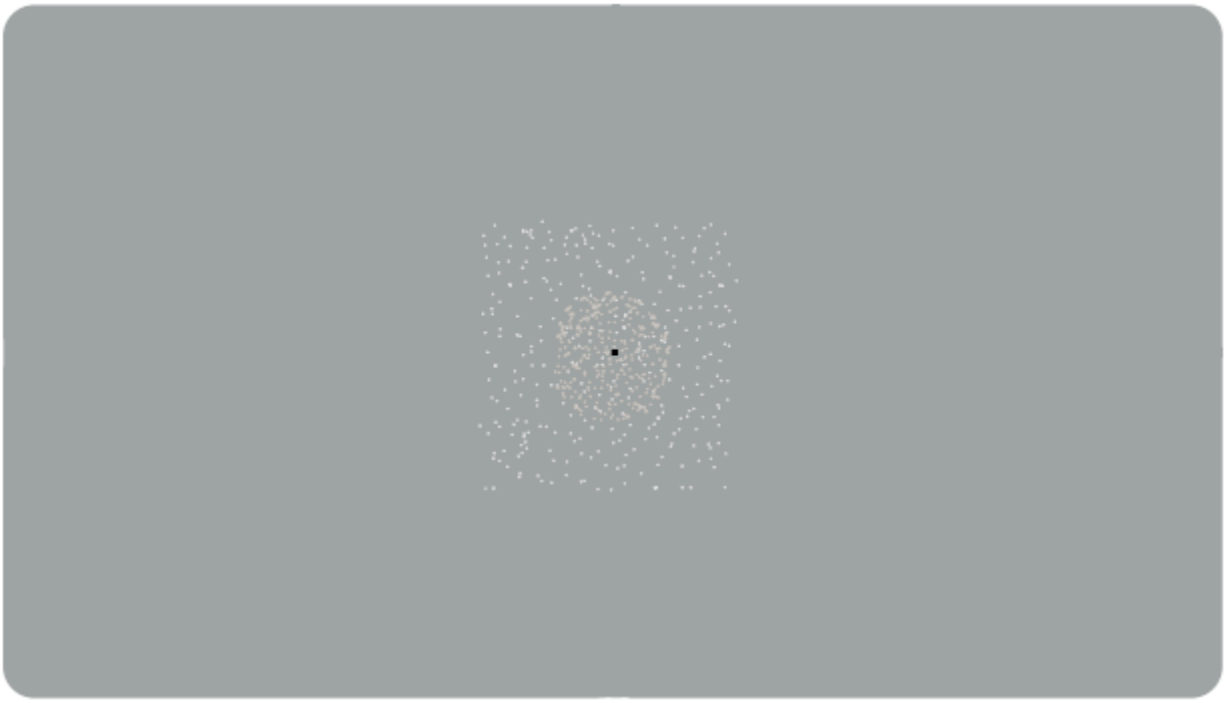


Figure 17

Depiction of randot stereogram stimuli that were presented in each trial. Two square fields of random dots were presented to the subject, 700 milliseconds apart, with only one field containing a depth figure. The grey area represents the projection screen. When there was a disparity figure or stereo-depth to be perceived, the inner circle of dots within the square depicts the boundary of the area within which the depth figure would have been presented.

3.7 Statistical Analysis

Given the ultimate goal of performing this research in keratoconus subjects, we used effect size estimates for stereo acuity differences between keratoconus subjects wearing spectacle lenses and contact lenses and control subjects from a previous study. (62) We used a simulation of our design to calculate an n=12 to achieve a power of 80%. Because it was feasible to recruit n=27, we did so to further protect against Type II error.

All data were organized using Google spreadsheets (Alphabet Inc, Mountain View, CA USA), Microsoft® Excel (Microsoft Corp, Redmond, WA, USA) and analyzed using R (R Core Team (2021).

A Shapiro-Wilk test indicated that data were normally distributed. We performed parametric statistical analyses such as t-tests when two sets of data (such as from the right and left eyes of the subjects) were involved. Pearson's correlations were performed between the PSE values or the slope values of the psychometric functions, and induced aniseikonia. An ANOVA was performed when more than two groups were involved (such as when we compared the stereoacuities in the same subjects following the five different monocular magnification induction conditions), followed by ANOVA pairwise comparisons.

4 Results

4.1 Subjects

We collected data on subjects (n=27) of whom 23 were female, and 4 were males. Their age range was 22-32 years old, and the average age of our subject population was 24.7 years. Best-correction spherical equivalent refractive error ranged from -8.75D of myopia to +0.00 D (mean -2.57 ± 2.67 D). Nine subjects wore no spectacle or contact lens correction during the experimental tests, 11 wore spectacles, and six wore soft contact lenses during the experimental tests. Subjects' characteristics are shown in Table 1. Their right and left eyes were not different from each other, whether in their spectacle or contact lens corrections, and when confirmed with the autorefractor.

Table 1: Demographic and mean refractive error data of our subject population (n=27). Nine of our subjects were emmetropes, and of the 18 subjects with refractive error, all were myopic; we did not have any hyperopes in our population, and there were no significant differences between the subject's right and left eyes.

Demographic Data

	n	**Average Age**	**p**
Male	4	25.3	
Female	23	24.7	0.31

Refractive Error Means

	Right Eye	**Left Eye**	**p**
Spectacle Rx	-2.53 D	-2.62 D	0.455
Contact Lens Rx	-1.23 D	-1.19 D	0.471
Autorefractor Rx	-2.16 D	-2.16 D	0.497

4.2 Higher Order Aberration Data

Following the data collection of the aberration measurements, the Zernike coefficients for all the subjects were scaled down for a nominal diameter of 4mm, to ensure comparisons between the two eyes and across the different subjects, as pupil sizes have a significant impact on optical image quality. We calculated the higher order root mean squared (HORMS) for our subjects after recalculating Zernike coefficients over 4mm pupil diameter. One subject was excluded due to an error in the transferring and saving of their data from the COAS to our lab computer. The average HORMS for the right eyes for all subjects was 0.11 μm +/- 0.04 μm and for the left eyes was 0.16 μm +/- 0.18 μm. These values fall well within the norms reported for subjects with regular corneas in the literature. (11,63) Shapiro-Wilk test showed that the data withing our sample was normally distributed. Paired t-tests revealed no significant differences between the right and left eyes of the control subjects as we had expected.

Our analysis did not have had enough to analyze differences in HORMS between myopes and emmetropes, and this was not an important goal of the thesis. We expected similar amounts of spherical aberration between the two eyes of our subjects given we were analyzing eyes with regular corneas.

Table 2: Means and standard deviations of each eye's higher order aberration data for all the subjects (n=26). The p-value of the one tailed sample t-test indicates no significant difference between the eyes.

	Right eye	**Left eye**	**p- value**
HORMS (μm)	0.11 μm	0.16 μm	0.09
Standard Deviation	0.04	0.18	

4.3 Optical Aniseikonia

Below are the psychometric fits for a random, representative control subject, for each afocal size lens condition. Near the top left of each graph, there is the subject ID, followed by the percent afocal lens used, denoted as 1p, for 1% afocal lens, the eye in front of which the size lens was placed (OD or OS), and the PSE value. Each graph depicts the frequency of seeing the left eye's image (bottom bar) as wider. Increasing the percentage width of the bar stimulus presented to the right eye is depicted using positive numbers on the x-axis and increasing the percentage width of the bar stimulus presented to the left eye is presented using negative numbers on the x-. The y-axis depicts the percentage correct, and each data point is the response rate of judging the left bar as wider. We anticipated that PSE would be near zero when there was no size lens in place, and that the PSE would correspond to the size lens placed over the eye of the subject for the remaining magnification conditions as follows: increasing the magnification of the size lenses over the left eye would cause a rightward shift of the sigmoid function, with the PSE being positive numbers and vice versa, i.e., increasing the magnification of the size lenses over the right eye would cause a leftward shift of the sigmoid function, with the PSE corresponding to negative numbers. In other words, we expected the psychometric function to indicate the overall magnification to use to correct the interocular magnification imbalance. A positive number result in any subject would indicate that a magnifier of that magnitude was needed over the right eye, and vice versa.

The quality of the logit fits for our data were reasonable and PSE was tabulated for each optical condition for each subject. Point of subjective equality indicates when the subject was performing the psychophysical test at chance level of 50%. This is when they have difficulty judging differences between size percepts and will deem two percepts as the same size in this

task. The average PSE across all subjects for the optical condition when no size lens was worn was -0.55, which being zero seems like the task may be appropriately measuring the amount of induced aniseikonia. However, for the 1%, 3%, 6%, and 9% magnification conditions, the PSE averages were -0.66, -0.11, -0.07 and -0.21 respectively, which do not correlate with the size lens introduced in front of the eye and did not predictably increase when interocular magnifications were induced in increasing amounts. The correlation between the PSE averages and the magnitude of size lens was r= 0.08. The other parameter available for analysis, i.e., the slope of the psychometric function, also did not have any predictable relationship with the magnitude of induced aniseikonia in front of one eye. The correlation between the magnitude of the size lens and the slop of the psychometric function, was 0.07. Overall, these results suggest that the subject did not respond to the task as we expected, and that in its current format, the test does not allow us to predict the interocular magnification differences perceived by these subjects. We allowed subjects to wear whichever form of correction they typically use, between soft contact lenses and spectacle lenses, if required. We did not perform statistical analysis on any differences between aniseikonia measured between the different habitual correction methods as our we did not have enough statistical power for these comparisons.

Table 3 shows the means and standard deviations of the subjects' PSE that indicates measured aniseikonia for the condition when no size lens was used, and for each size lens condition that induced aniseikonia.

	0%	***1%***	***3%***	***6%***	***9%***
Mean	-0.55	-0.66	-0.11	-0.07	-0.21
Standard Deviation	1.11	1.16	0.88	1.19	0.92

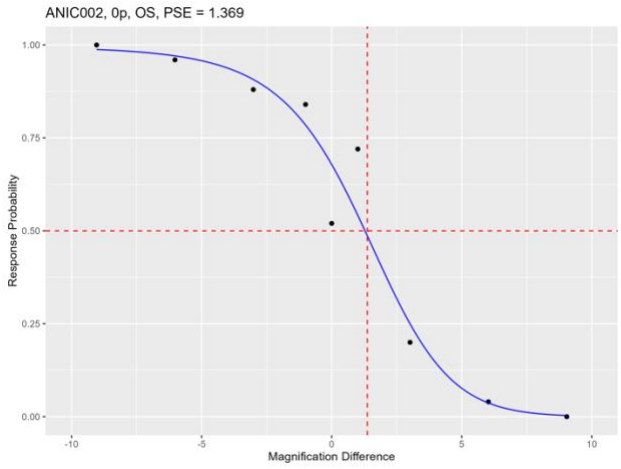


Figure 18 a

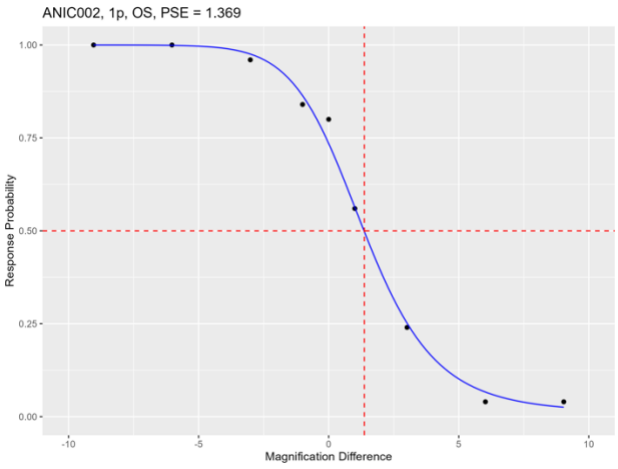


Figure 18 b

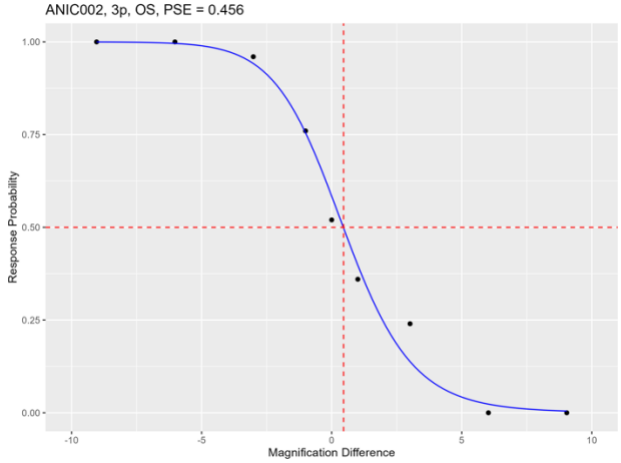


Figure 18 c

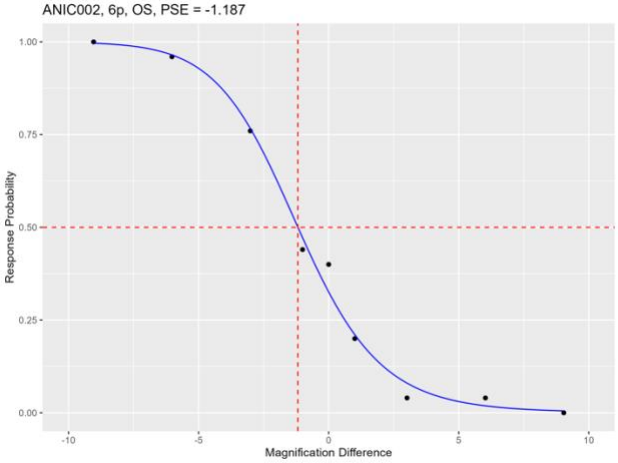


Figure 18 d

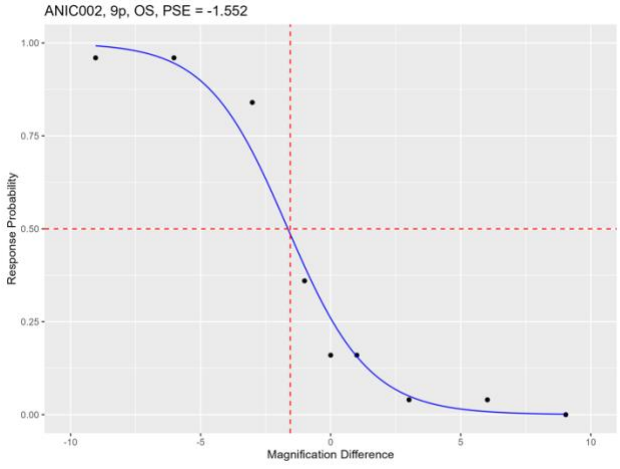


Figure 18 e

Figures 18 a-e

Psychometric functions showing the response probability of indicating the bottom bar (presented to the left eye) as wider for control subject 002, wearing (a) 0% (no size lens worn), (b) 1%, (c) 3%, (d) 6%, (e) 9%.
Positive numbers on the abscissa indicate presentations where the bar presented to the right eye (top bar) were objectively wider, and negative numbers on the abscissa indicate presentations where the bar presented to the left eye (bottom bar) were objectively wider. The logit fit is shown in blue, and the vertical red line coincides with the PSE. The subject ID, magnification induced in front of the eye, the eye tested and the PSE for each figure in the panel are indicated on the top left of the respective panel.

4.4 Stereoacuity changes with induced aniseikonia

Stereoacuity thresholds increased with increases in the magnitude of induced aniseikonia, as predicted. Figure 19 shows the data as a scatterplot, with a different colored line connecting the stereoacuity means for each subject across the different size lens conditions. In figure 20, the blue line and the grey shaded area, as well as the data in Table 4 show the means and standard deviations of the subjects' stereoacuities and standard deviations with no size lens (0%) and for each size lens condition, 1%, 3%, 6% and 9%. An increase in stereoacuity demonstrates a decrease in sensitivity and overall worse stereoacuity. In almost all the individual cases and when comparisons were made as a group, stereoacuity worsened with induced interocular differences in magnification.

Repeated measures ANOVA revealed that the stereoacuities were significantly different across the different size lens wearing conditions in controls ($p<0.05$). Pairwise comparisons (Table 5) indicate that all four size lenses tested decreased stereoacuity compared to not wearing size lenses. An interocular magnification difference of 9% decreased stereoacuity more than wearing any other size lens tested. All pairwise comparisons differences were significant except for those between the 1% and 3% and between the 3% and 6%. Our statistical analysis did not have enough power to make comparisons between emmetropes and myopes.

Table 4 Means and standard deviations for all the subjects stereoacuity thresholds for each magnification condition (0%, 1%, 3%, 6% and 9%).

	0%	*1%*	*3%*	*6%*	*9%*
Mean	64.10	88.01	93.61	109.72	136.01
Standard Deviation	27.84	39.12	46.66	57.84	44.25

Table 5 ANOVA pairwise comparisons of stereoacuity data, between the different size lens conditions that induced magnification differences in controls.

Size Lenses	*Difference in means*	*SE*	*df*	*t-ratio*	*p-value*
0 – 1 %	-23.90	7.6	84	-3.144	<0.05 *
0 – 3 %	-29.51	7.6	84	-3.882	<0.05*
0 – 6 %	-45.62	7.6	84	-6.001	<0.001***
0 – 9 %	-71.90	7.6	84	-9.459	<0.001***
1 – 3 %	-5.61	7.6	84	-0.738	0.9470
1 – 6 %	-21.72	7.6	84	-2.857	<0.05*
1 – 9 %	-21.72	7.6	84	-6.315	<0.001***
3 – 6 %	-48.00	7.6	84	-2.119	0.2218
3 – 9 %	-16.11	7.6	84	-5.577	<0.001***
6 – 9 %	-26.29	7.6	84	-3.458	<0.01 **

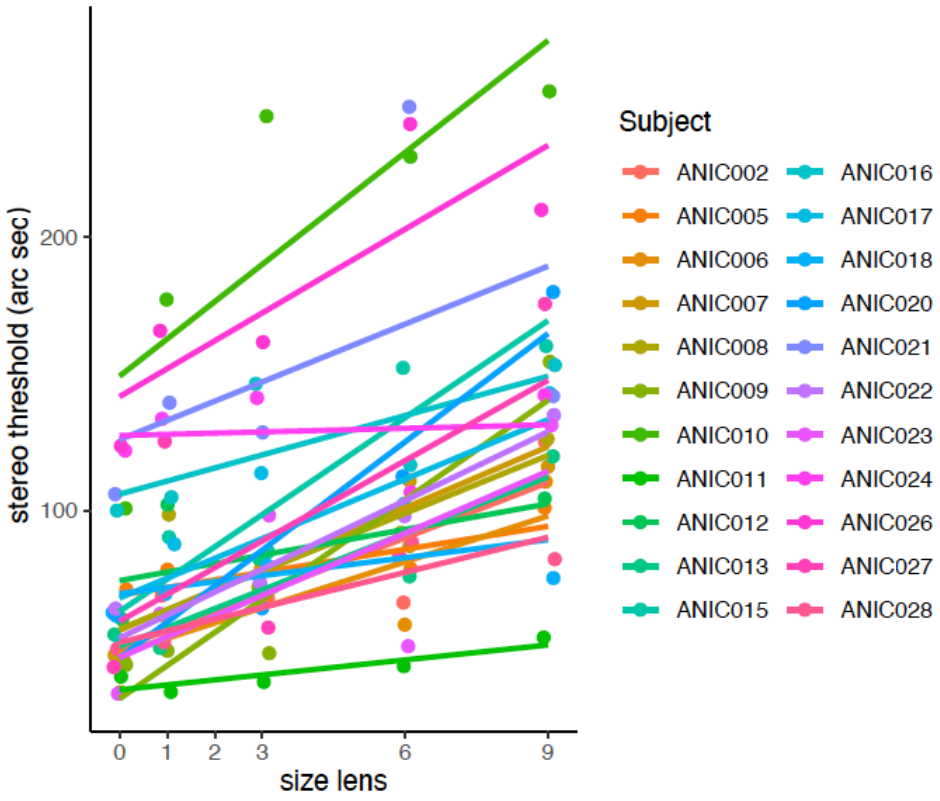


Figure 19

The stereoacuity thresholds obtained for each subject and when performing the stereoacuity task without a size lens (0%) and with a size lens 1%, 3%, 6% and 9%. The thresholds of each subject are connected by a colored line, the legend on the right indicates which subject is which colored line. Size lenses of increasing magnifications worsened the stereoacuity for all subjects as indicated by the positive slop of the colored lines, although significant individual variability was noted.

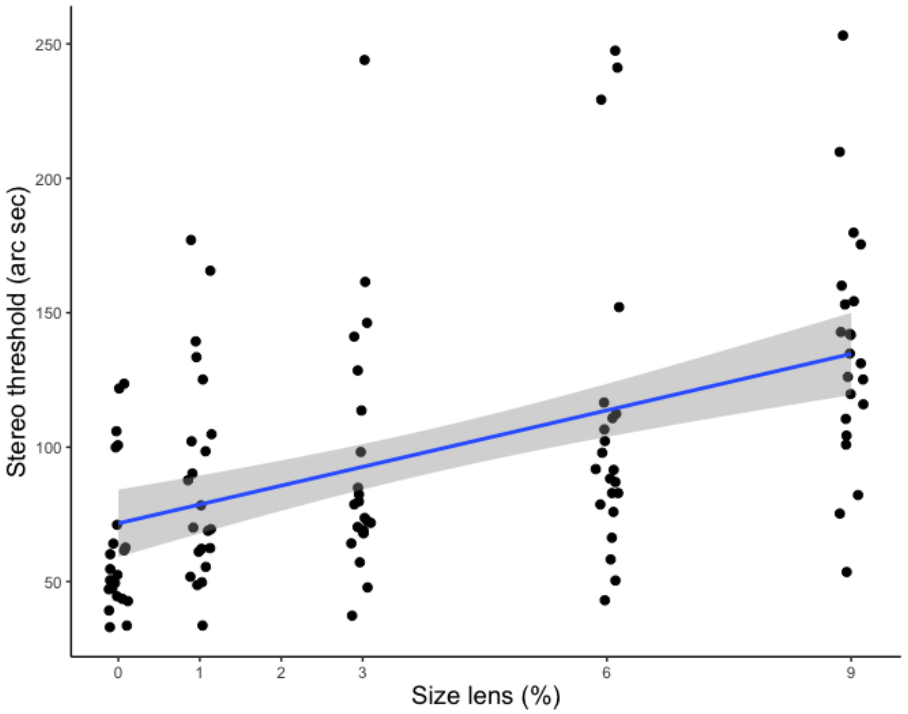


Figure 20

Stereoacuity thresholds obtained after each subject performed the stereoacuity task without a size lens (0%) and repeated the task while monocularly wearing the size lenses used in our experiment (1%, 3%, 6% and 9%). Size lenses of increasing magnifications worsened the stereoacuity overall, although significant individual variability was noted.

5 Discussion

This study investigated the effect of inducing controlled levels of optical aniseikonia using image size altering lenses in healthy individuals, with a focus on measuring aniseikonia and stereoacuity utilizing custom psychophysical routines. The goal of this thesis is to obtain baseline data on the impact of relative interocular magnification on stereoacuity in controls as a first step before assessing its impact in keratoconus.

5.1 Aniseikonia Measurements

Our results showed no change in the magnitude of aniseikonia measured psychophysically when 1%, 3%, 6% and 9% overall magnifying afocal lenses were used monocularly to induce interocular magnification differences in this group of subjects. We did not find correlation between induced and measured aniseikonia in the form of a relationship between the PSE with the induced aniseikonia, nor the slope of the function with the induced aniseikonia, and there were no predictable increases in the aniseikonia measured with increasing magnitudes of induced overall magnification in one eye.

The gold standard technique for aniseikonia measurement is the space eikonometer which is based on a stereoscopic assessment. The space eikonometer reliably estimates induced aniseikonia, and closely follows the 1:1 valid test criterion for induced vs measured aniseikonia. (54) Ogle's work from 1964 (50,64) demonstrated a strong correlation between a stereoscopic assessment of aniseikonia using the Space Eikonometer and the Direct Comparison technique using the Direct Comparison Eikonometer, yielding nearly a 1:1 relationship. They employed an eikonometer for (optical) distance viewing, with polaroid plates over each eye, which allowed each eye of the subject to view separate targets in each eye. Since Ogle's time, there have been

other Direct Comparison techniques such as the New Aniseikonia Test, Awaya and the computer based Aniseikonia Inspector. These techniques underestimated aniseikonia significantly and non-linearly with increasing magnifications, making estimations of this variable very difficult. Some previous studies thus report aniseikonia by amount of induced aniseikonia, rather than by the actual measured values. (9,29,30) We aimed to measure aniseikonia, first in control subjects with normal vision and normal optics, and then in subjects with keratoconus in order to deduce the impact of aniseikonia on stereoacuity.

For this purpose, we created a custom task to measure aniseikonia that uses the direct comparison technique described earlier. The subjects in our study were eligible for participation only if they had minimal to no anisometropia, as determined by sphero-cylindrical refractions smaller than 0.75D difference between the two eyes, in each principal meridian. Our goal was to use control data from subjects with normal vision to validate the software and subsequently conduct comparisons with subjects who have early keratoconus and are corrected with spectacle lenses. We had hypothesized that the psychophysically measured aniseikonia thresholds would coincide with the magnitude of size lenses used to induce it.

Our custom program software was designed to be a direct comparison test and after much thought put into alleviating the issues noted in previously used techniques that often underestimated true aniseikonia. The first problem we tried to overcome was avoiding the use of differently colored stimulus in each eye. Avoiding color hues such as red, green, yellow or blue, eliminates the phenomenon of size-color illusion, where the color hue can affect the perceived size of two identical objects. (57) Static 3D polarizers allowed us to present dichoptic stimuli without introducing color differences between the two eyes. Second, we ensure that the stimulus presentation was very short, 150ms, and the subject looked at the center of the binocular fixation

cross. We did not monitor the subjects' eye movements, and therefore the short stimulus time was designed to prevent the subjects from re-fixating and looking at each of the bars to make size comparisons. Third, we used a binocular fixation cross, rather than a dichoptic nonius stimulus was designed to negate effects of possible fixation disparity, which we did not measure in our subjects. (50,54,57) The fixation cross extended to the periphery of the relatively large screen that created an empty field in the periphery in efforts to minimize peripheral fusion textures that are thought to cause scaling effects that underestimate aniseikonia (54), which is important as the increasing number of size lenses were placed over the eyes. Finally, given that our test was computer based, with visual stimulus pairs that were presented in random order by the computer to minimize bias and predictability, combined with randomization of the order in which the different percentage size lenses were introduced and alternating between the right and left eye as the eye that received induced magnification for consecutive subjects, we minimized any procedural bias.

Subjects were asked to compare the size of two bars that subtended 4 degrees of our visual angle (baseline width), and had a vertical separation of 3 degrees, 1.5 degrees above or below from the midline. They were asked to fixate on a central cross that extended all the way to the periphery to allow for peripheral masking. Despite a carefully design experiment and stimuli, we were not able to reliably estimate the amount of induced aniseikonia, even though we found its impact on stereoacuity (see next section). There are three reasons that could possibly have led to this unexpected result. First, the length of time of the bar stimuli were presented for may have been too brief. This, in conjunction with where they were presented in visual space (about 3 to 4 degrees superiorly and inferiorly), may have limited the subject's ability to compare the sizes as at those eccentricities the magnocellular pathway prevails. Allowing for foveal refixation has

shown to underestimate the amount of aniseikonia induced, as shown in the New Aniseikonia Test. The macula is more sensitive to edges and patterns, than flickers, and our presentation may have resembled a flash or flicker. This may have impaired our subjects' ability to directly compare the size of the bars. (65)

Another possibility for the lack of correlation with induced and measured aniseikonia is that when there is monocular magnification, there is a recalibration of retinal disparity and visual direction which restricts subjects from partaking in a direct comparison test, such as the one created in the lab. (66) It has been well documented that regardless the length of time for which an afocal size lens is worn, the subject will adapt to the size lens over one eye. (50) This phenomenon forms the basis of the clinical pearl of anticipating patients to be able to adapt to changes in spectacle prescription within a few weeks, and how prior to prescribing prism, we check for prism adaptation. Early work by Ames (1945), demonstrated that subjects with aniseikonia, who had adapted to their environment, an environment with many monocular cues, when placed in a disparity rich environment (no monocular cues), experienced distortion due to the aniseikonia. (67) An example of a disparity rich environment is the leaf room. In this environment, when aniseikonia is induced, monocular cues are in disagreement with binocular cues. There seems to be evidence that when subjects no longer perceive induced aniseikonia, the environment is rich in monocular cues and these override, and binocular cues are downweighed. (67,68) In our experiment, the periphery of our subjects' view, perhaps provided had monocular cues available, such as the screen border that was some distance away from the target, and the rectangular wall they were facing. It is likely that monocular cues were weighted over binocular cues when aniseikonia was induced. It is possible our subjects quickly adapted to the aniseikonia or did not perceive the induced aniseikonia over their one eye. To further our experiment, the

adapted subjects could have been brought into a room with only binocular cues, such as a leaf room, to see if when monocular cues were eliminated, they could perceive the aniseikonic distortions.

All aniseikonia tests, apart from the Space Eikonometer, either dissociate the eyes, are present targets in a way such that they do not overlap (56) and we did the same. Our custom aniseikonia measurement software also showed targets that do not overlap. Our stimuli were uniform-colored grey blocks that did not show differing colors to each eye. Color has been shown during direct comparison tests to affect the perception of apparent size when different colors are the same hue and can simulate aniseikonia. (69) Using monochromatic shades of grey eliminates this issue and should be used in any further versions of our own custom software.

5.2 Stereoacuity Experiment

Stereoacuity measurements revealed a linear relationship between the degradation of stereo with increased magnification (size of the lens presented over one of the eyes). The aim of our experiment was to create a custom program software that accurately measured perceived aniseikonia by the subject and confirm that it was 1:1 with the size lens percentage that was placed in front of the subject eye. Our hope was to use measured or perceived aniseikonia, as opposed to induced aniseikonia, in the interpretation of our stereopsis results. However, due to the negative results on the amount of perceived aniseikonia, we resorted to using induced aniseikonia when describing our stereoacuity results. Aniseikonia was induced and we are confident that it was affecting the visual system, even if we are not able to measure it, because for equal size lens conditions, stereoacuity was reduced incrementally with increasing magnification. In our experiment, we did not use a technique for aligning the two eyes such as

using a dichoptic nonius fixation cross. (50) The dichoptic nonius fixation cross would have brought to light any fixation disparity or vergence errors of our subjects that might have made size comparisons difficult. This can occur in patients with normal binocular vision, but enough of a vergence error to make Panum's area smaller than in a subject without fixation disparity. (50,70) We chose this path as we wanted the fixation cross to be the same for our controls and future keratoconus subjects and because there were no stimulus presentations for the subjects to compare that was outside of the fixation plane. Stereoacuity thresholds are lowest at the fixation plane (71) subjects are most sensitive to disparities presented within 11 arcminutes from fixation. (72) Numerous people have a fixation disparity. It is reported that for each fixation disparity curve type 1, 2, 3, 4 the prevalence is 60%, 25%, 10% and 5%. (64) This would mean among our recruited subjects, many of them would have one of these curve types, rendering the measuring of stereoacuity a long and complicated task, and particularly challenging among our subjects with keratoconus.

The thickness of the lenses, related to their size, may slightly reduce retinal illumination in the tested eye compared to the eye without sized lens. But this reduction in illumination would be very small amount, and compared to the 0% size condition, but stereoacuity is thought to be only reduced as a function of monocular retinal illumination, when transmission nears 5% in one eye. (73) We do not think the difference thickness of the size lenses used in the study would have impacted our stereoacuity results significantly.

5.3 Future study of the relative contributions to stereo deficits in Keratoconus

It was our hope to use a validated custom program software to measure aniseikonia, in our keratoconus population. There are naturally occurring interocular differences of LOAs,

HOAs and aniseikonia, between the eyes of keratoconus. We were hoping to compare the stereoacuity of keratoconus subjects under three optical correction conditions: i) spectacles, where only LOAs are corrected, ii) spectacles and afocal size lenses, where LOAs and aniseikonia are corrected, leaving the effects of uncorrected HOAs, and iii) RGP Contact Lenses, where LOAs are corrected, and HOAs and aniseikonia are minimized. Our aniseikonia task was not able to accurately measure perceived aniseikonia, and thus we were unable to move forward with aniseikonia measurements in keratoconus.

Further, our aim was to use the comparisons between the three optical correction groups described above to identify the relative contributions of residual HOAs and aniseikonia to the reduced stereoacuity measured in these subjects. We had hoped to compare these results to the data gathered in control subjects, the earlier part of my thesis, where we expected mismatches in LOAs, but not in HOAs. The control group would have helped us elucidate any impacts of neural adaptations to aniseikonia (e.g., anisometropes habitually wearing spectacles) and neural adaptations to HOAs (e.g., stable keratoconus subjects who have likely adapted to their own increased HOAs).

We had hypothesized that aniseikonia will contribute significantly to stereoacuity losses seen in keratoconus in addition to stereoacuity losses introduced by interocular mismatches of HOAs. However, since our aniseikonia task was not able to accurately measure perceived aniseikonia, we were unable to move forward with using it for aniseikonia or stereoacuity measurements in keratoconus.

5.4 Trouble shooting and limitations of the study

While creating our custom program software to measure stereoacuity and aniseikonia, we initially ran into several difficulties with programming the sizes of the bars, and programming the randot stereograms in relation to the number of pixels they required to display these stimuli. We also explored programming software that measured reaction times, but concluded that this was too broad, and not specific enough for the purposes of our experiments.

Our custom software to measure stereo was initially set up to use a QUEST psychophysical routine. The QUEST method uses two pieces of information, the first being any prior information about the threshold. The second set of information used is the set of trials collected at any point, which becomes the posterior probability density function. QUEST uses this information to guide the placement of trials, by placing it where the algorithm finds the most probable estimate of the threshold. It does so by placing the next trial at the mode of the posterior density. QUEST methodology is an alternative to the staircase method, and more quickly and more accurately achieves the threshold of interest. But unfortunately, our stereoacuity measurements with the QUEST parameter employed were displaying stereoacuities of sub 20 seconds of arc, despite our lab team trialing the stereoacuity program with a 6% magnifier over one eye. We then switched from the QUEST parameter to a staircase method. A total of 27 subjects were asked to return to the lab to recollect this data, which slowed down our data collection and analysis. Some subjects were not available to return, mostly due to change in clinical rotations for the 4th year students, leaving us with data from 22 subjects available for analysis.

We had recruited one pilot subject with keratoconus in efforts to understand any other difficulties that our set up may pose for a future study on these subjects. We concluded that the

QUEST parameter was unable to estimate the correct stereoacuity threshold when this subject with asymmetric keratoconus with 20/100 vision in one eye (20/20 in the other) through his spectacles, was measured to have 12 arcseconds of stereoacuity. All our control subjects therefore required a second visit due to needing to recollect stereoacuity data using a different psychophysical procedure. Visual acuity was confirmed to still be 20/20 with each mode of correction, but there were no other tasks were performed at this visit. Subjects brought back to a repeat visit, were instructed to ensure they had their original form of correction, that was used at the first visit, as to perform the stereoacuity task wearing this correction. Visual acuity was confirmed to still be 20/20 at this second visit, no other screening tests were performed at the second visit.

The 0% aniseikonia condition differed from the other conditions, in that the trial frame did not have any lens, in addition to their spectacle prescription if present, while the 1, 3, 6, 9 % size conditions each had a size lens on top of their spectacle prescription. The 0% size condition was also always done first while the other size lens conditions were randomized. This was done in order to allow subjects to familiarize themselves with the task without additional hindrances. While not having a clunky lens by itself could have caused the stereo threshold to be more sensitive, we could also argue that this was the condition where the subjects had least practiced the task, and still produced the most optimal thresholds across all condition. There is a possibility that the addition of extra lenses for the other size conditions may have also created an unconscious bias, and reduced stereoacuity for each condition. However, given that there were incremental decreases in stereo thresholds despite randomization, we know that unconscious bias could not have accounted for all of our unexpected results.

Axial length measurements were not acquired in our study. It was confirmed for the three habitual corrections, i.e., spectacles, contact lenses and autorefractor data that there was no more than 0.75D of anisometropia either in the sphere or in either meridian. Sample t-tests confirmed no differences in the means between the eyes of the subjects, and that there was no difference between the spectacle and autorefractor refractive correction of each eye. It is possible that in a given subject there may have been axial anisometropia that was countered by the refractive power in that eye, to yield an isoametropic prescription between the two eyes of that given subject. Stretching of the retina in the longer or shorter eye may have influenced the perception of size or aniseikonia but given the small differences in refractive errors, these differences are unlikely. Retinal morphology has shown to have effects on the quantification of aniseikonia by subjects, due to its role in adaptation. (74) Additionally, our study was comprised of all myopes, the most plus prescription was plano. Although no axial measurements were taken, most myopes are axial myopes, and likely had some amount of retinal stretching. (75) This may have altered our subjects' sensitivity to our aniseikonia presentations, but not differentially between the two eyes. Some studies have shown increased peripheral flicker thresholds in myopes, which may result in altered sensitivity in psychophysical perception, (76) but again, given our focus was mapping interocular magnification differences and measuring stereoacuities which are most sensitive when there are differences between the two eyes, it is unlikely to have affected our results.

We did not to record eye movement in these experiments. Although eye movement recordings would have offered the exact knowledge of where the subjects were fixating and not just assuming fixation, (77) we limited the presentation time of our aniseikonia task to avoid refixation. Our stereoacuity task needed longer presentation times as stereo perception takes

longer to process, but we were reliant on subjects keeping their eyes on the fixation dot and making judgements without moving their eyes.

6 Conclusions and Future Direction

In this thesis, the goal was to create and validate a custom program software for the measurement of aniseikonia, and further, to use this software in a group of subjects with keratoconus to determine and quantify the largest contributor of their stereoacuity losses. Although this could not be achieved, the results of this thesis did raise many questions of the measurement of aniseikonia and its challenges. While we were not able to estimate aniseikonia, we found in fact that it affects our perception of depth seen psychophysically as a deterioration of stereoacuity. We were able to create and validate a custom program software of the measurement of stereoacuity and measure the impacts of induced magnification differences on stereoacuity. The results of the stereoacuity experiment align well with previous literature; (9,30) demonstrating that stereoacuity losses occur when aniseikonia is induced, and proportionally lost when aniseikonia increases. The big question that remains is why there is such difficulty measuring perceived aniseikonia using direct comparison tests. It may be a "catch-22" problem where a stereoscopic technique that nulls the distortions caused by aniseikonia results in the most precise measurements; however, if stereo-depth perception is a requirement, how do we estimate this variable of aniseikonia, or glean its relative importance when stereo-depth is altered due to a combination of issues that affect it.

Some future steps may be to perform experiments in an environment rich in disparity cues such as the constructed leaf room used by Ogle. (50) The leaf room has a disparity-rich environment and has only stereoscopic cues. Perhaps using the leaf room to quantify the effects of aniseikonia, rather than just for qualitative determinations as used in the past by Ogle, Ames and their team may help us elucidate the relative effects of aniseikonia on the visual system. If

not conducted in a leaf room, intentionally eliminating peripheral cues can also be something else that is done to ensure proper measurement of aniseikonia induced.

Other future directions that can be taken are to carefully map presentation times of stimuli to explore what presentation times subjects are most sensitive to when making size comparison judgments. Additionally, other parameters that can be carefully mapped include, altering the visual angle of visual stimuli and where in the periphery from the fovea, they are mapped. Different stimuli shapes can also be explored to see what shapes subjects are more able to help make size judgements.

Aniseikonia, although difficult to measure clinically, is a relevant measure, both clinically and in terms of quality of life. It may be the reason for the stereoacuity deficits in children with refractive amblyopia after refractive errors are corrected and visual acuity is improved, and in keratoconus where there may be multiple factors causing stereoacuity losses. It is a worthwhile future pursuit to find a way to estimate this variable reliably and accurately.

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Appendix

8.1 Data Collection Forms for controls

Data Collection Form- Control

Subject ID:_____ **Today's Date:**_____

Visit Number:_____ **Start Time:**_____

A: Patient history/Screening for inclusion

When was their last eye exam (month/day/year)? _____

What was the reason for their last exam? _____

_____

Any ocular problems or diseases or allergies (CL solutions):_____

_____

_____

Any other notes:_____

_____

What methods of correction do they currently use or own?

- ☐ Spectacles
- ☐ Soft/Hybrid CLs
- ☐ GPs- specify type:_____
- ☐ Bifocal or readers
- ☐ None

What method of correction do they use the most? _____

Age of current Rx: Spectacle:_____ **CLs:** _____

B: Preliminary Screening Exam

ii) Entrance Testing

Habitual correction (circle): Spectacles / Soft CLs / RGPs / none

logMAR OD:

logMAR OS:

Pupil size (OD/OS):

Far:

1

Subject ID:_____

Near:

CL Over- Refraction if applicable:

OD	**CL Type:**		
	Sph		
	BCVA at distance:		

OS	**CL Type:**		
	Sph		
	BCVA at distance:		

IOP (mmHg):

Method:

OD:

OS:

Randot 3 Stereoacuity (arcsec)

Habitual correction (circle): Spectacles / Soft CLs / RGPs / none

Arc Seconds:

Slit Lamp Examination- Anterior Segment/Screening:

Structure	**OD**	**OS**
Lids/Adnexa		
Conjunctiva		

Subject ID:_____

Cornea/Tear Film		
Iris		
Lens		

C: Refractive Error Information

i) Autorefractor

Interpupillary distance (per auto-refractor):_____mm

OD	**Autorefractor**		
	Sph	**Cyl**	**Axis**
	K values (put meridian closest to 180 first)		
	@	@	

OS	**Autorefractor**		
	Sph	**Cyl**	**Axis**
	K values (put meridian closest to 180 first)		
	@	@	

ii) Spectacles Rx

Spectacle Rx: YES / NO (circle one)

Starting point: Retinoscopy / Autorefractor (circle one)

Subject ID:_____

OD	Spectacle Rx/Latest Sphero-cyl refraction		
	Sph	**Cyl**	**Axis**
	Any pertinent recommendations made for Rx:		
	BCVA at distance:		

OS	Spectacle Rx/Latest Sphero-cyl refraction		
	Sph	**Cyl**	**Axis**
	Any pertinent recommendations made for Rx:		
	BCVA at distance:		

Dominance test (circle one): OD / OS

Subject screening (circle one)? Pass / Fail
Reason/Comments(s):_____

D: Wavefront Aberration Information

i) Wavefront Aberration Information

COAS: (circle as appropriate. No Rx/ spectacle Rx/ CL Rx;
Database/ File(s) saved as: _____

(leave blank if not used)

Right eye: Distance [ ]
Left eye: Distance [ ]

Subject ID:_____

E: Psychophysical Measurements

i) Stereoacuity

Habitual correction (circle): Spectacles / Soft CLs / RGPs / none

	1st measurement	2nd measurement	3rd measurement
Stereoacuity (arcsec)			

ii) Aniseikonia Measurements

Inducing aniseikonia using size lenses

Magnification over (circle): OD / OS

Random order in which size lenses should be imposed: [____; ____; ____; ____]

Overall aniseikonia (%) using Psychophysical test:

Size lenses used	0%	1%	3%	6%	9%
Measured aniseikonia (%)					
Stereoacuity (indicate units)					

Any qualitative comments about the subject and their performance: _____

_____

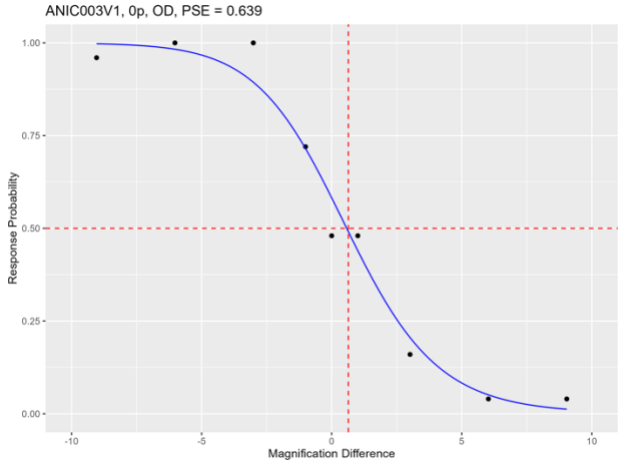
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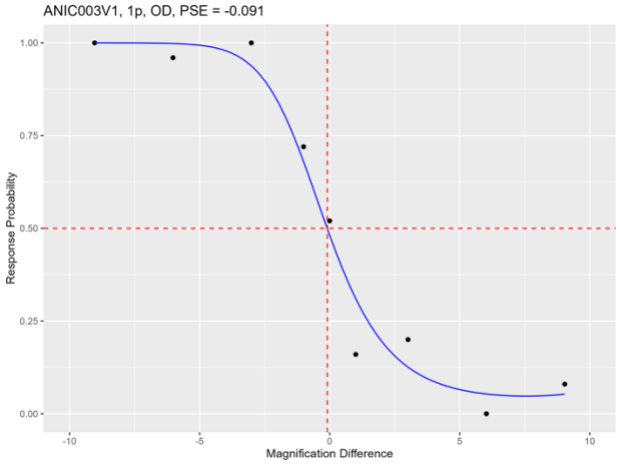
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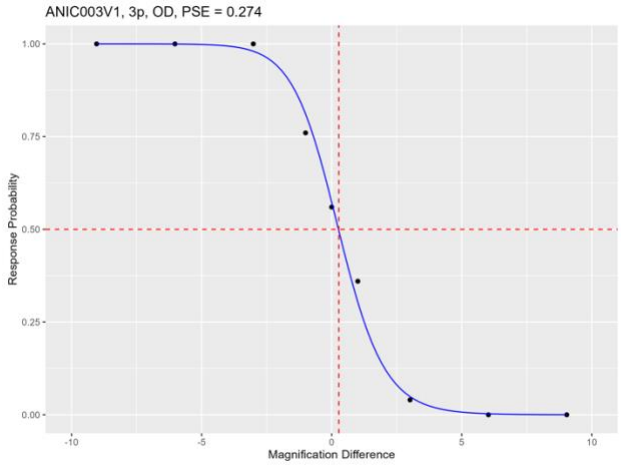
End time:_____

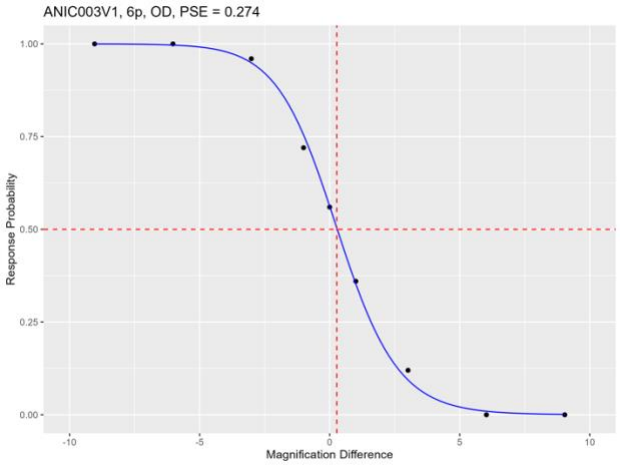
8.2 Additional aniseikonia plots of all our subjects and size lens conditions

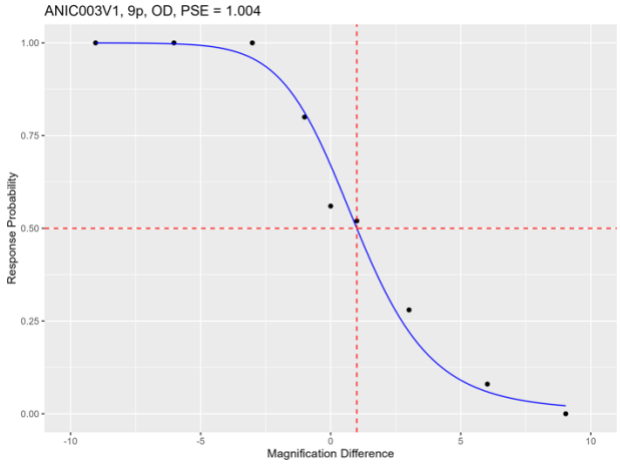
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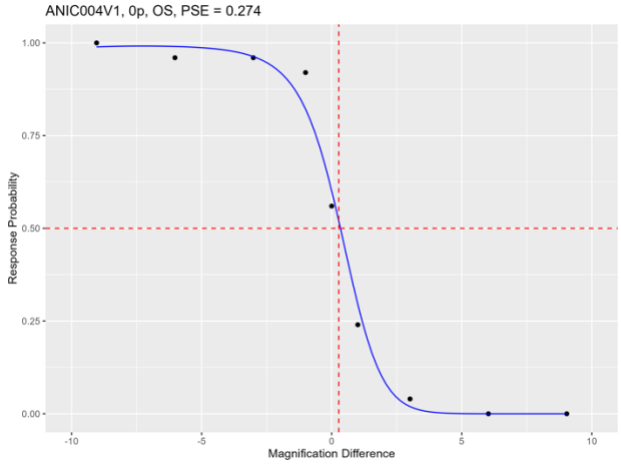


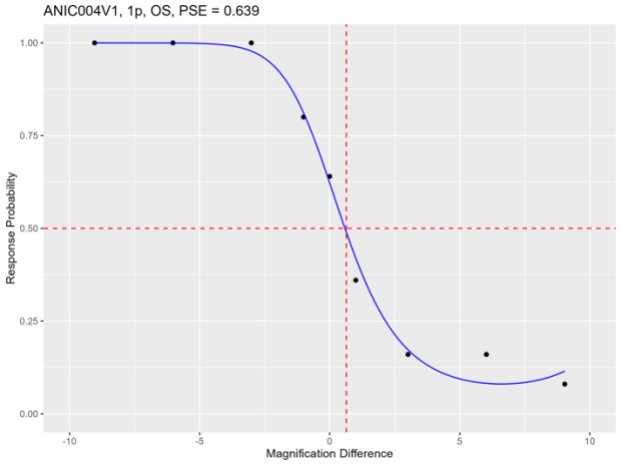


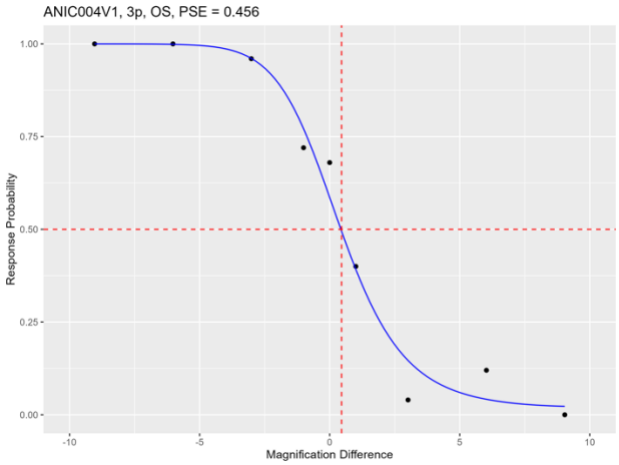


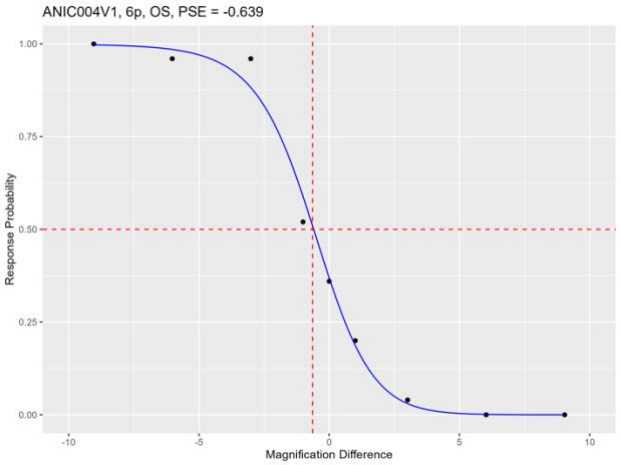


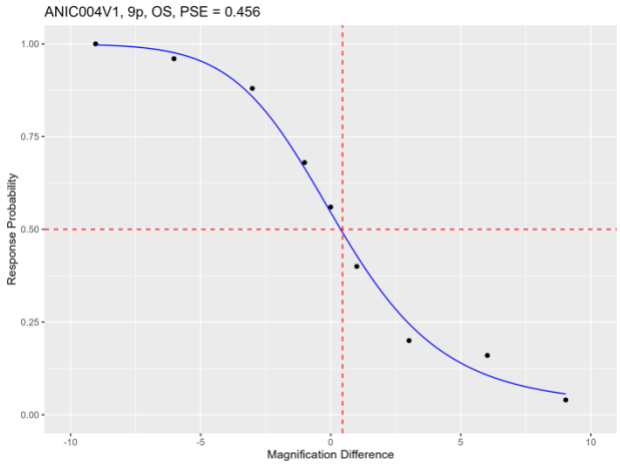
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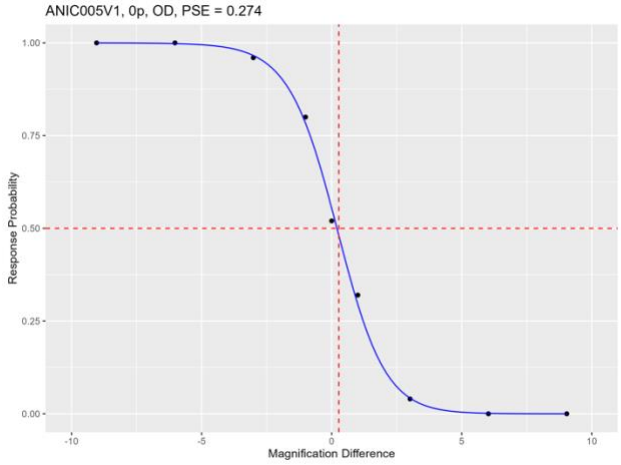


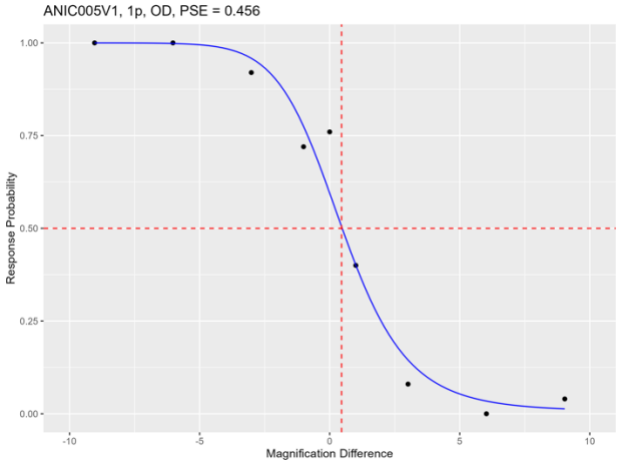


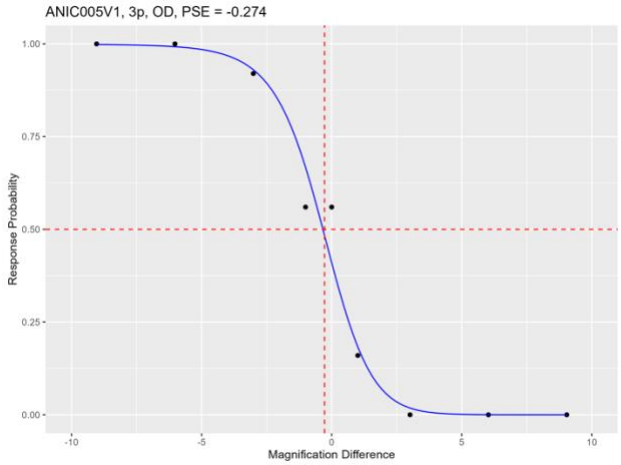


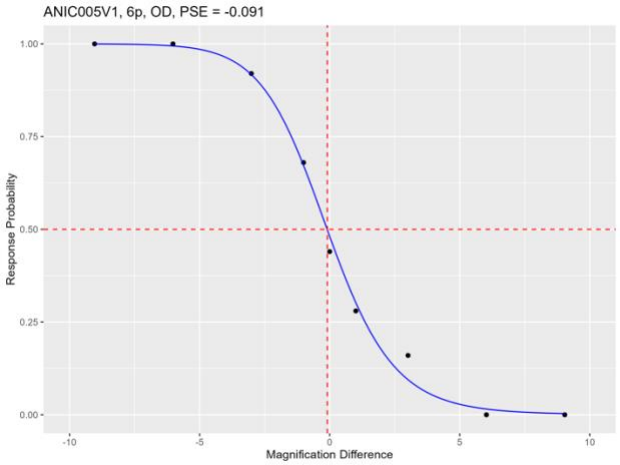


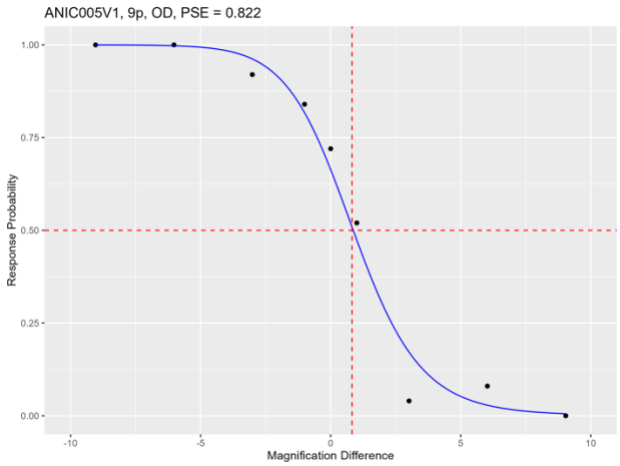
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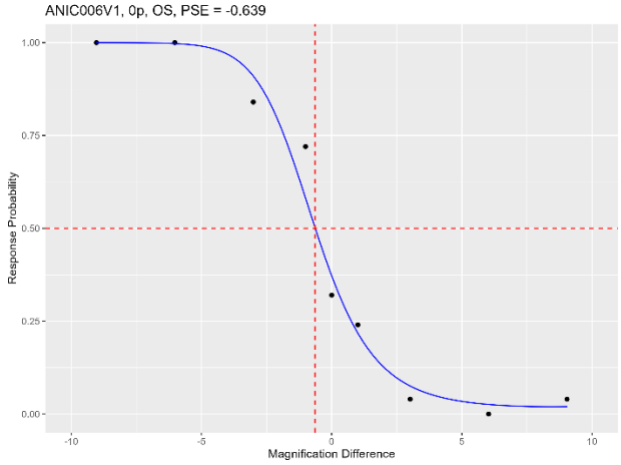


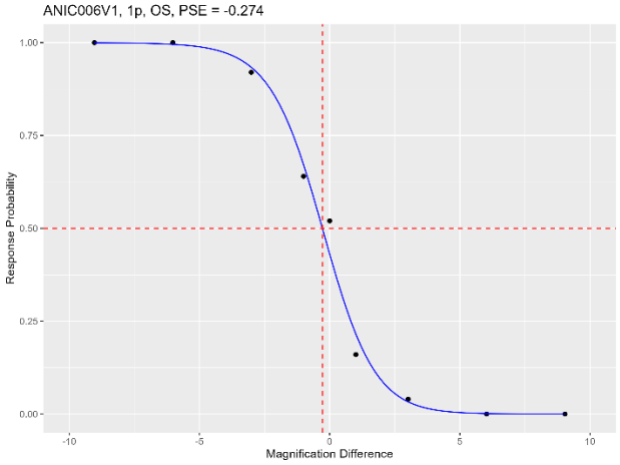


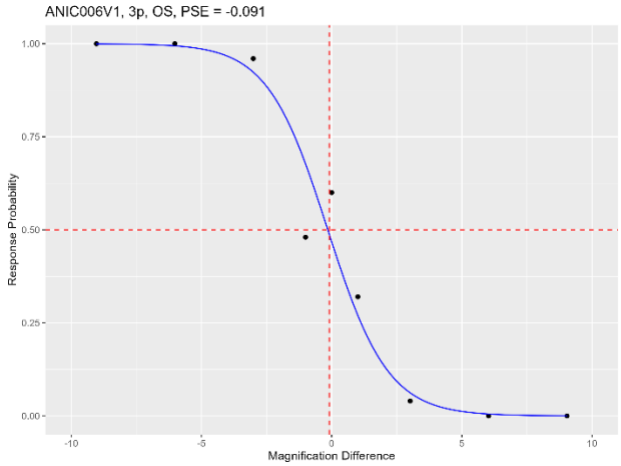


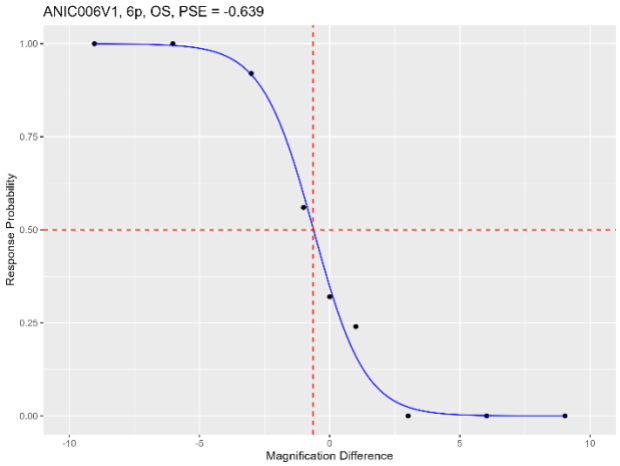


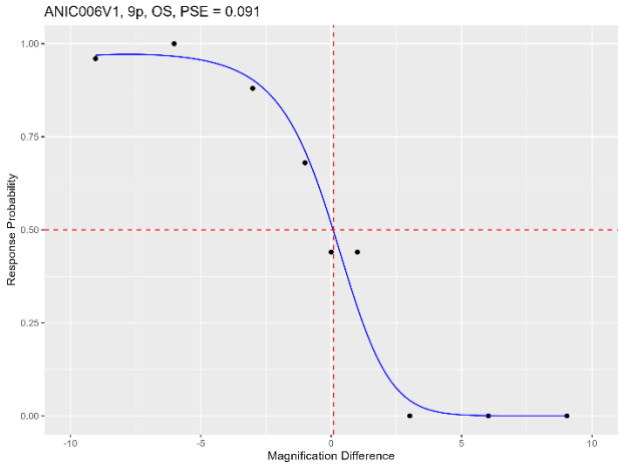
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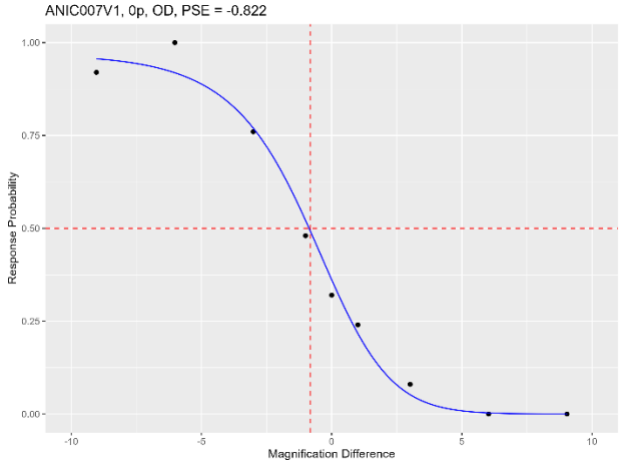


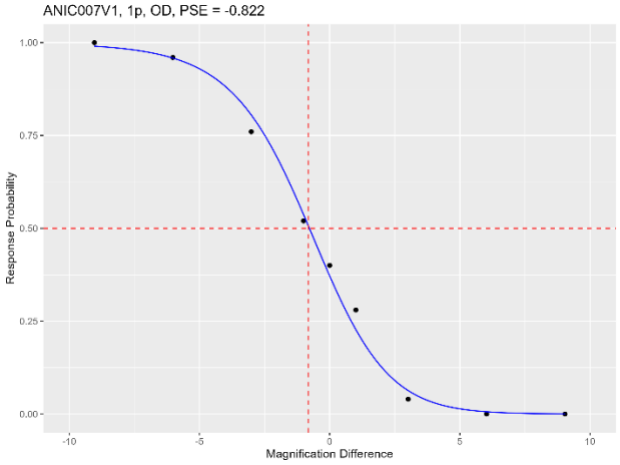


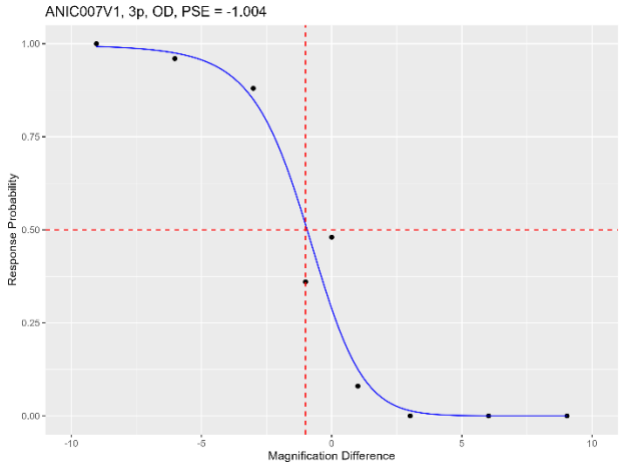


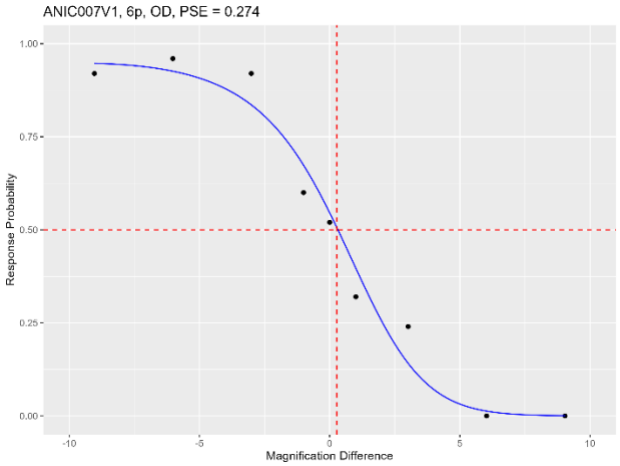


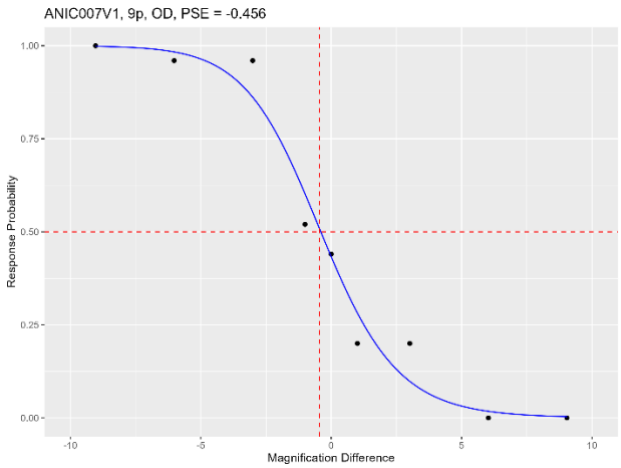
Subject ID: ANIC007, psychometric functions of each size lens condition: 0%, 1%, 3%, 6%, 9%.



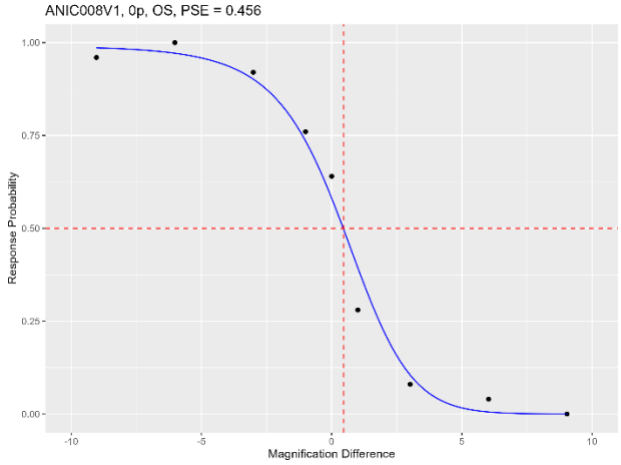


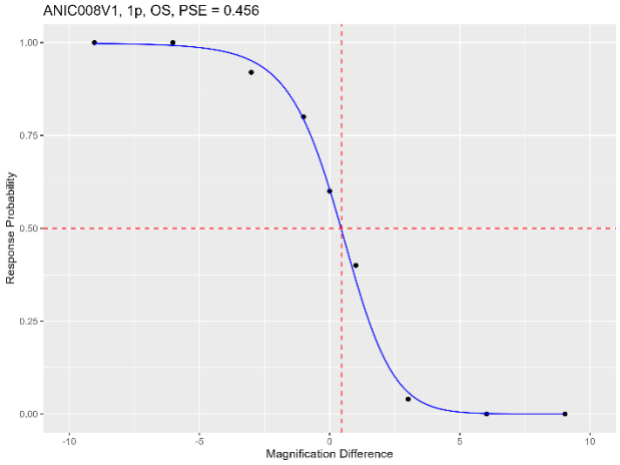


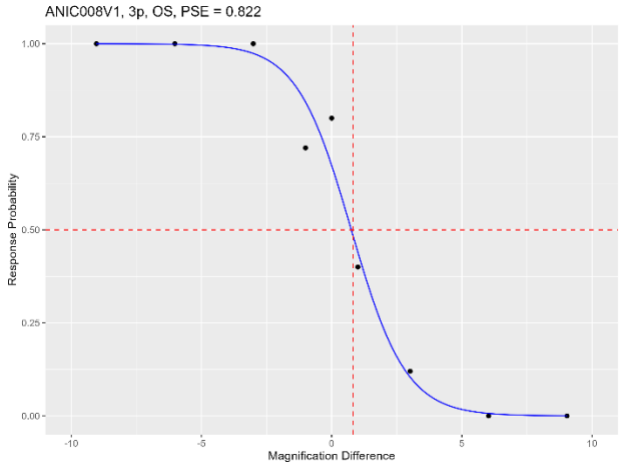


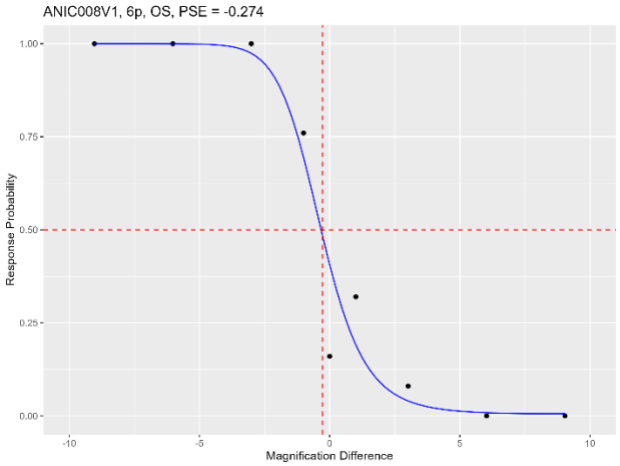


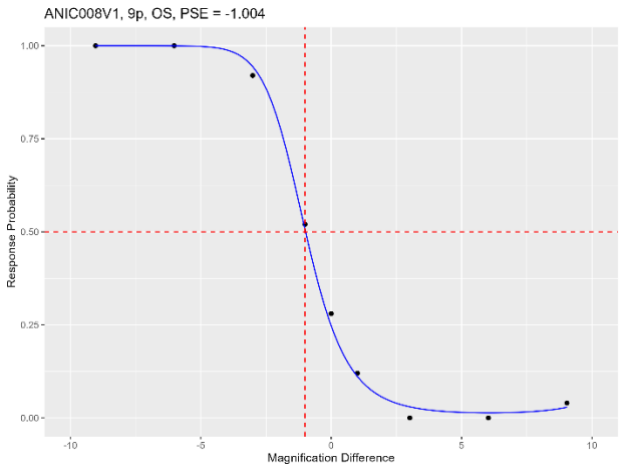
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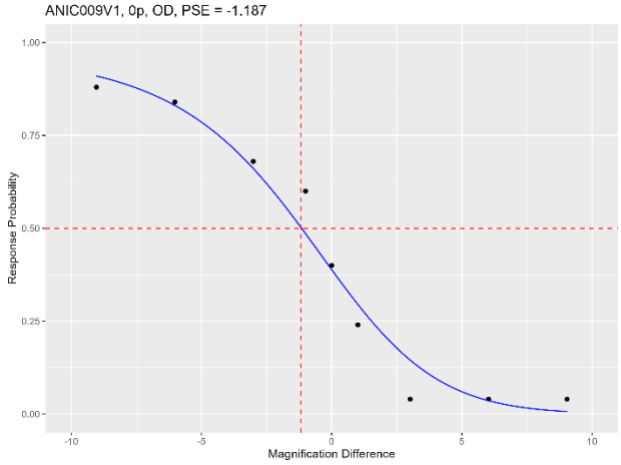


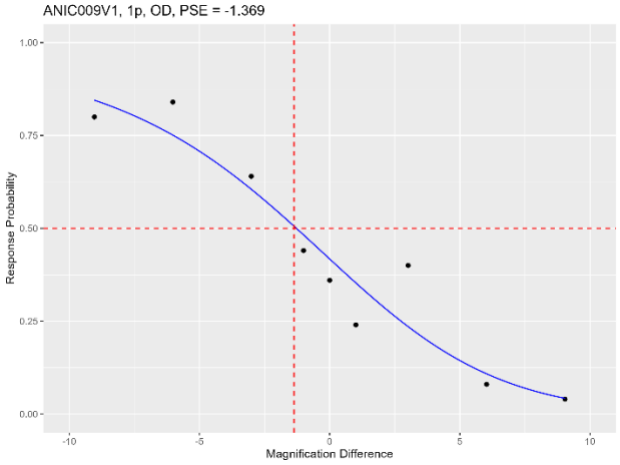


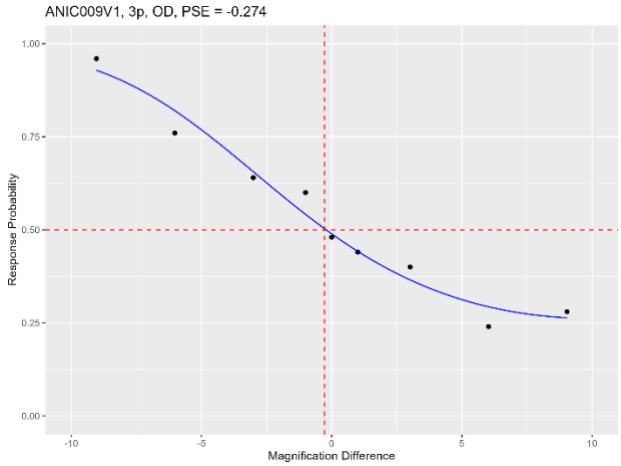


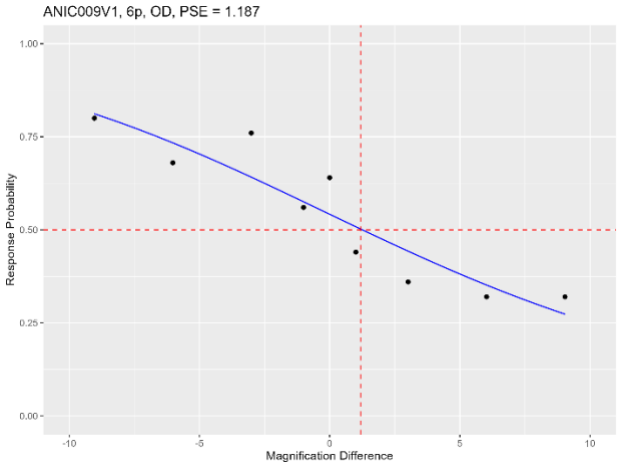


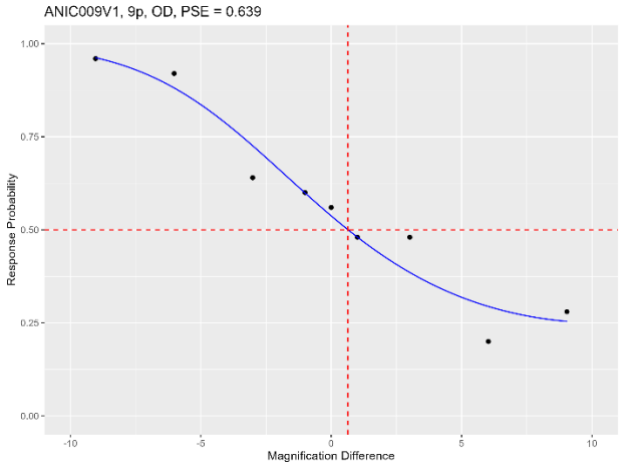
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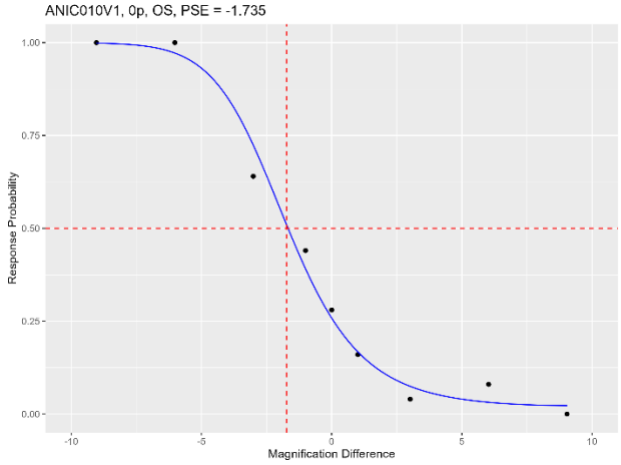


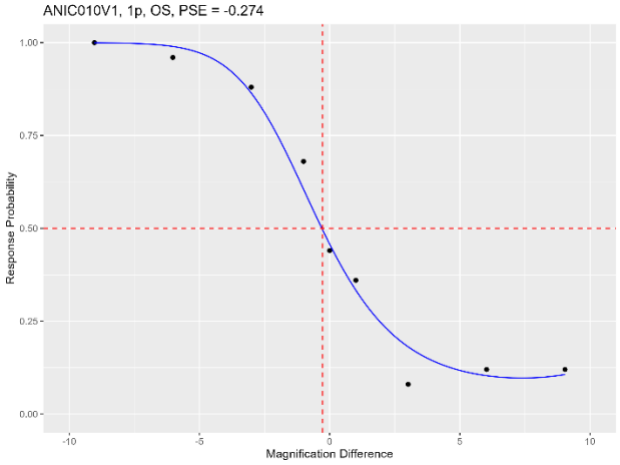


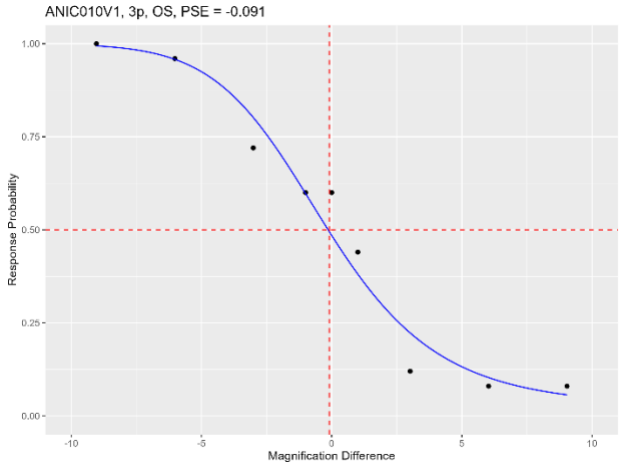


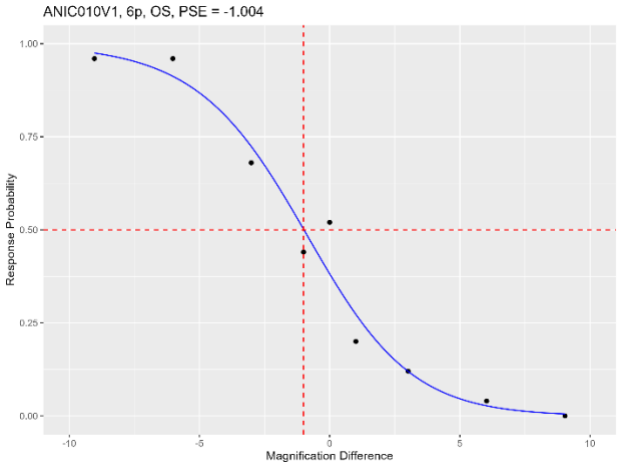


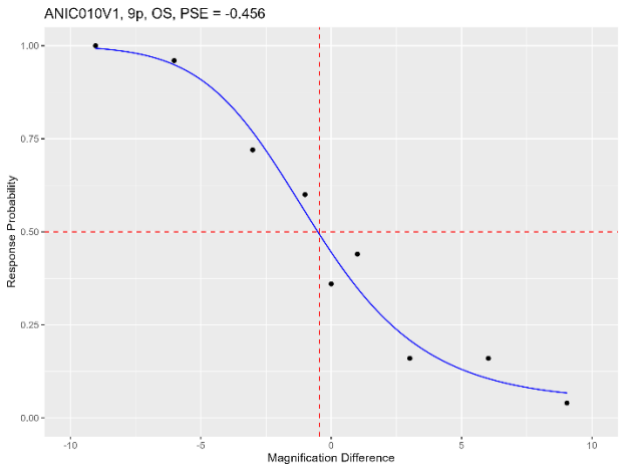
Subject ID: ANIC010, psychometric functions of each size lens condition: 0%, 1%, 3%, 6%, 9%.



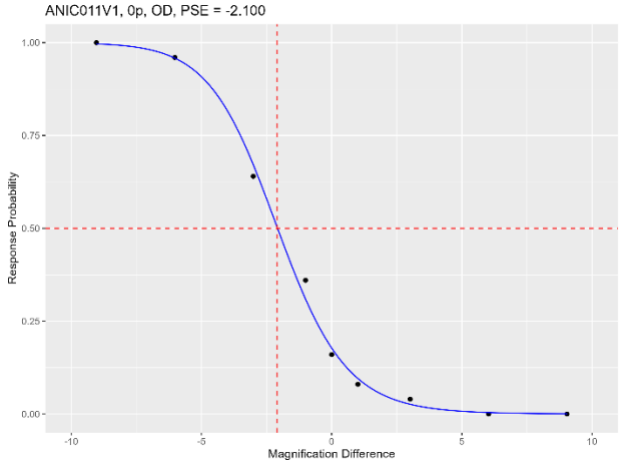


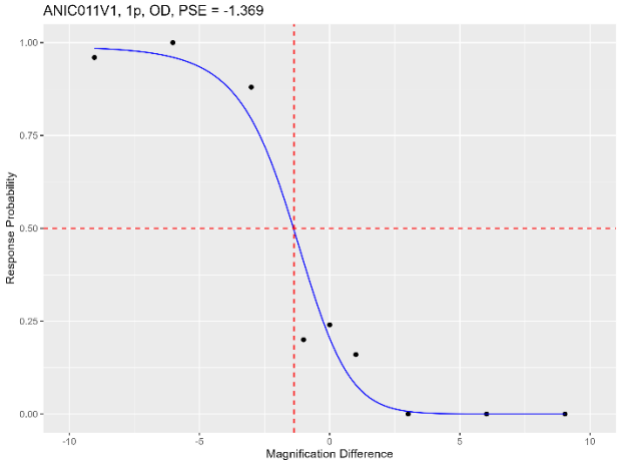


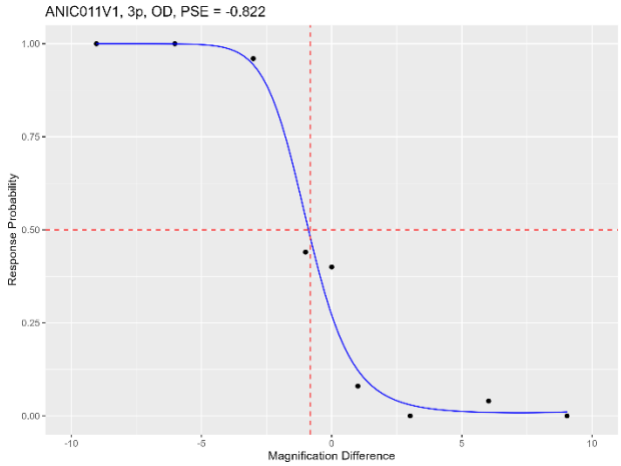


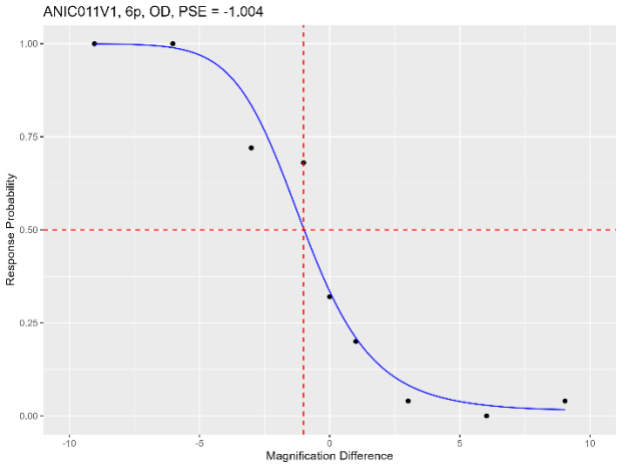


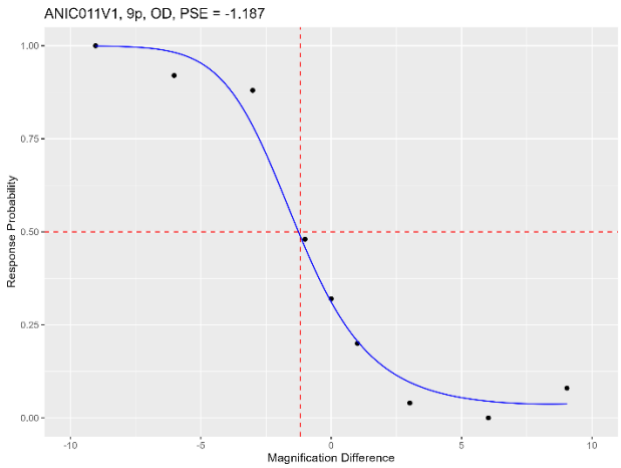
Subject ID: ANIC011, psychometric functions of each size lens condition: 0%, 1%, 3%, 6%, 9%.



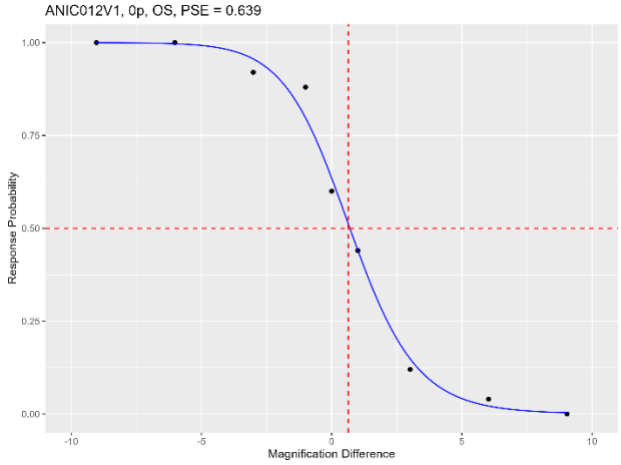


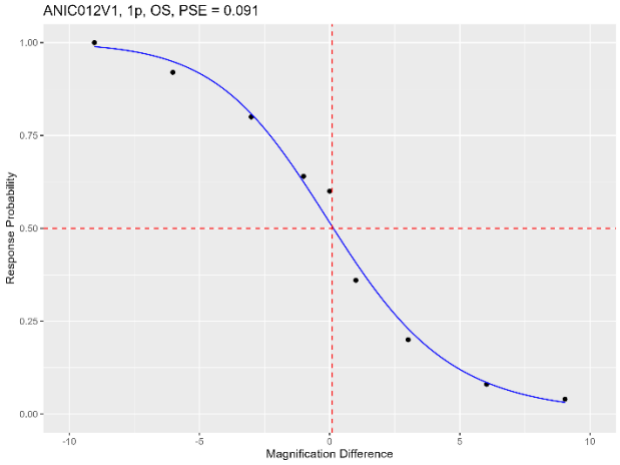


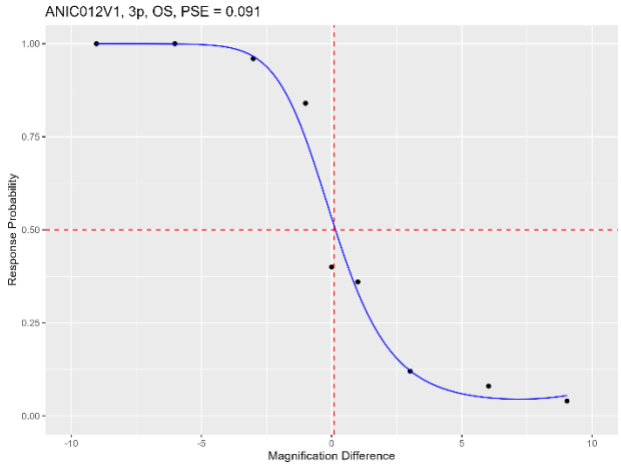


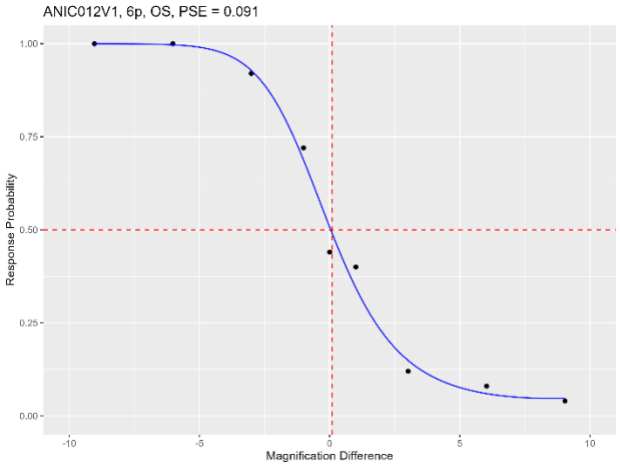


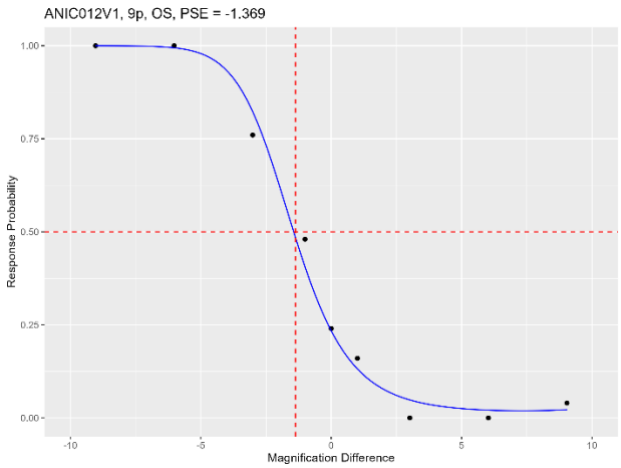
Subject ID: ANIC012, psychometric functions of each size lens condition: 0%, 1%, 3%, 6%, 9%.



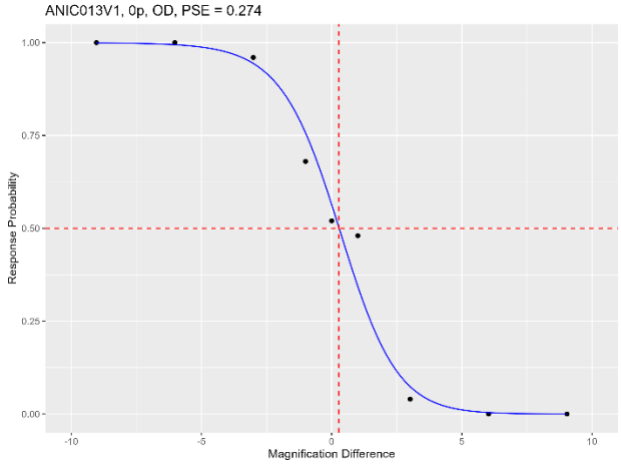


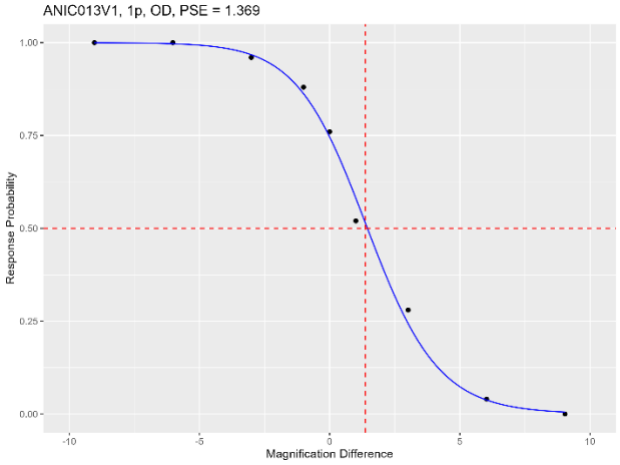


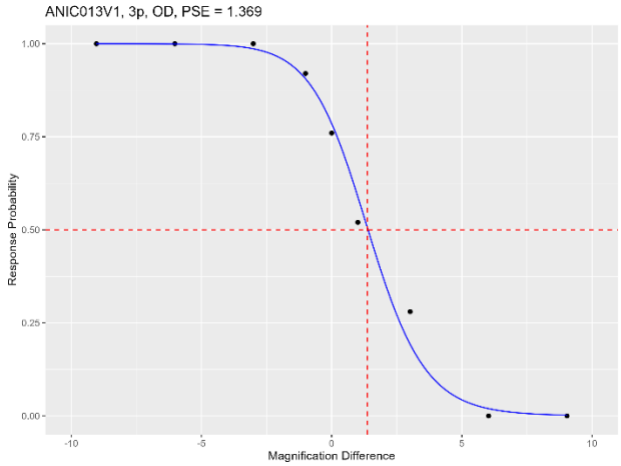


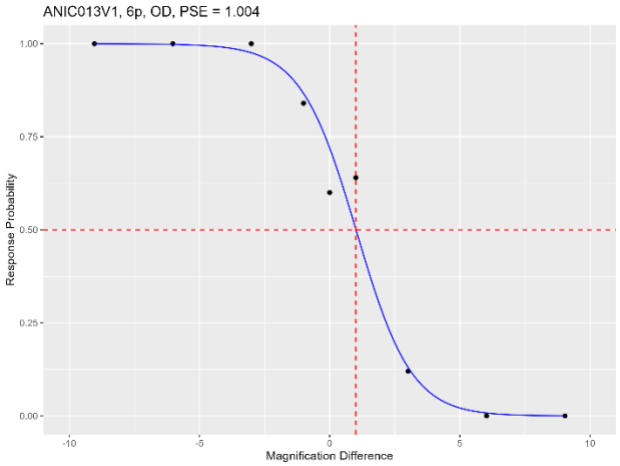


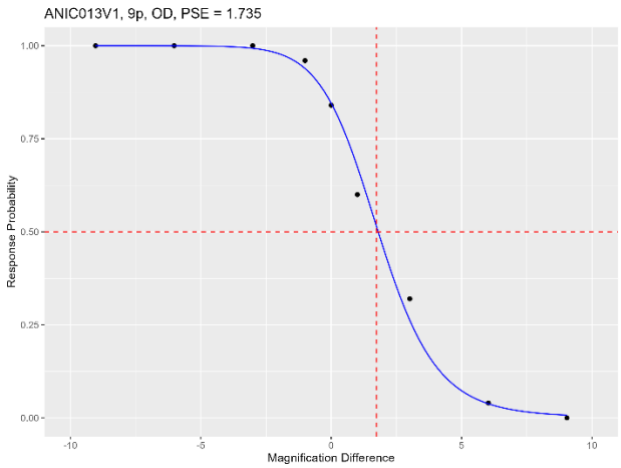
Subject ID: ANIC013, psychometric functions of each size lens condition: 0%, 1%, 3%, 6%, 9%.



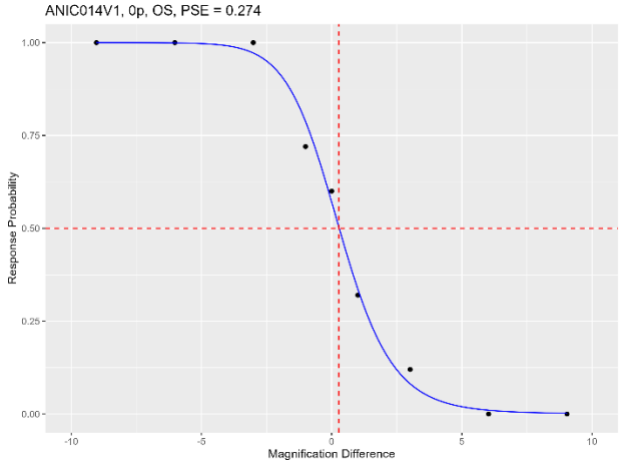


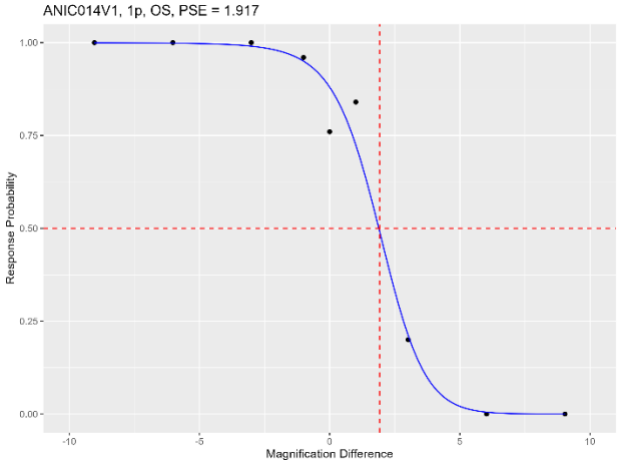


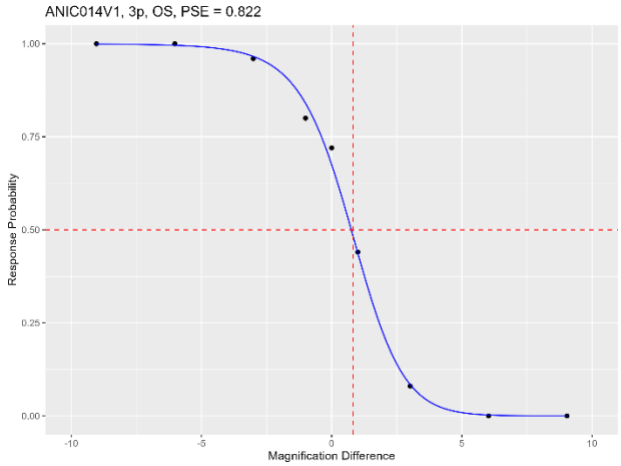


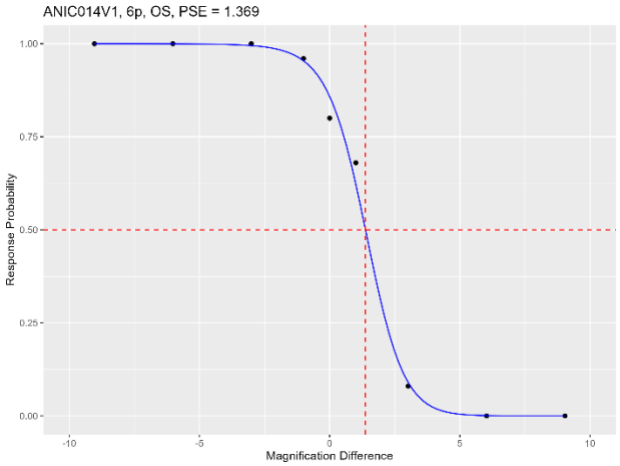


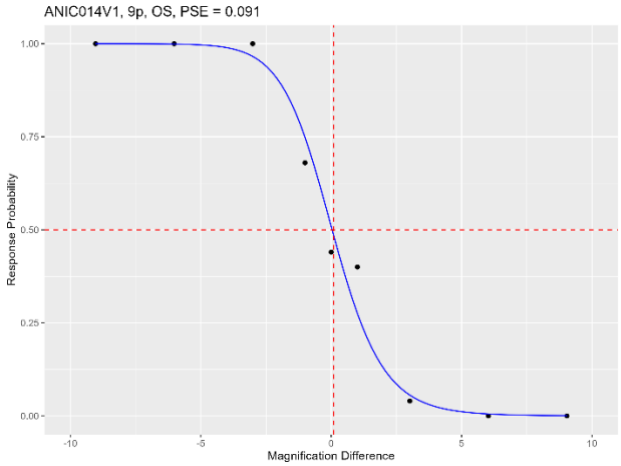
Subject ID: ANIC014, psychometric functions of each size lens condition: 0%, 1%, 3%, 6%, 9%.



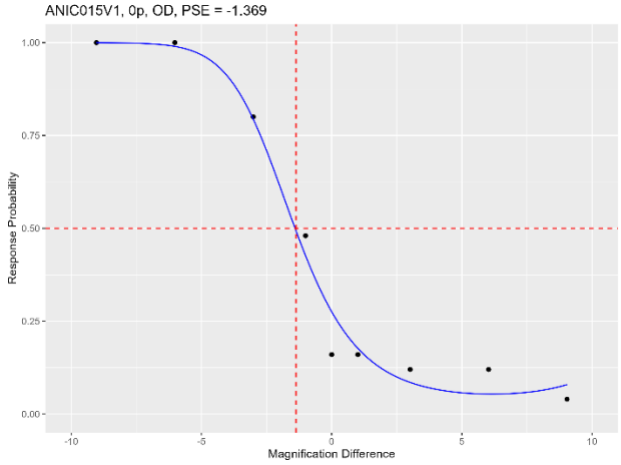


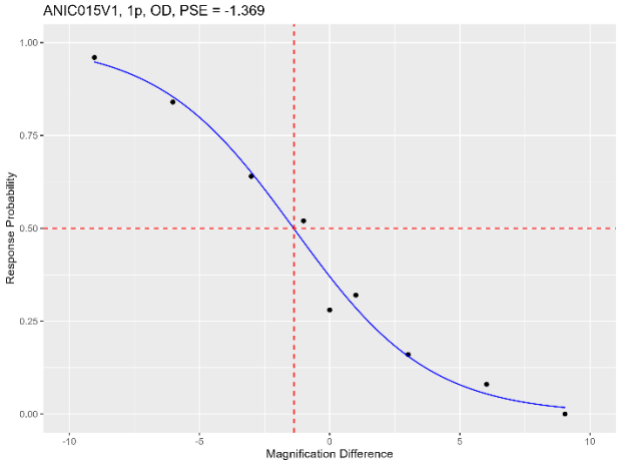


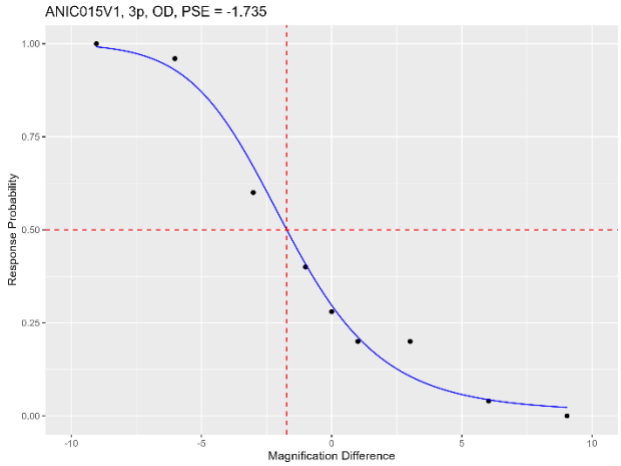


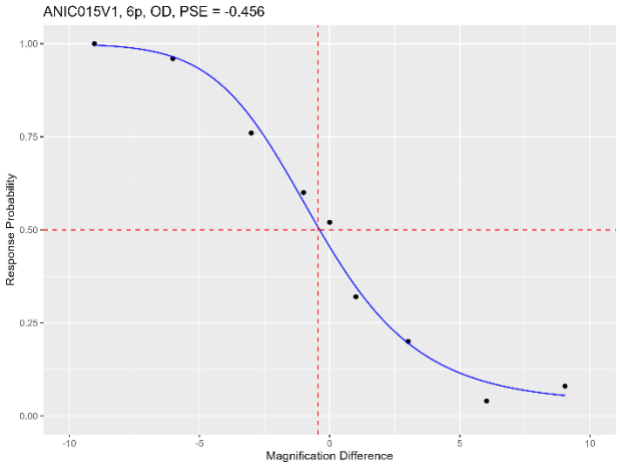


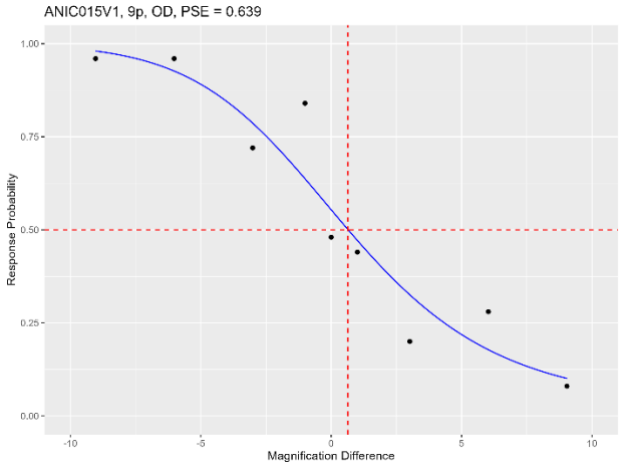
Subject ID: ANIC015, psychometric functions of each size lens condition: 0%, 1%, 3%, 6%, 9%.



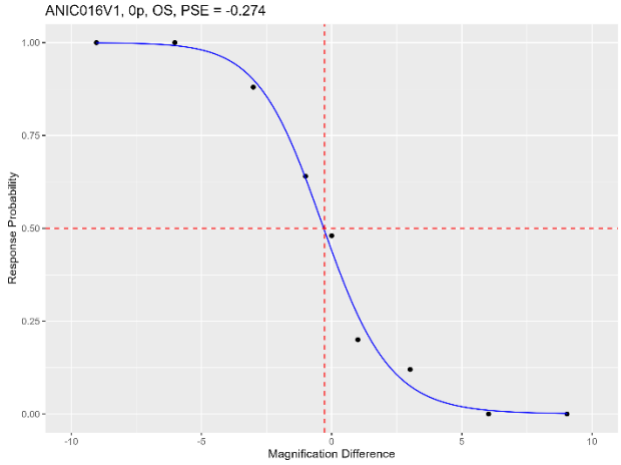


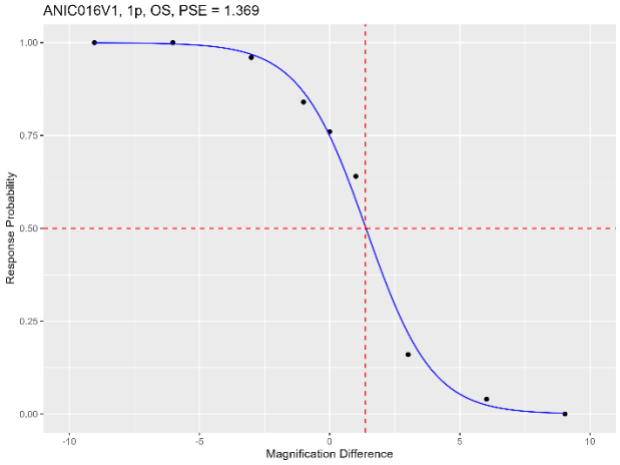


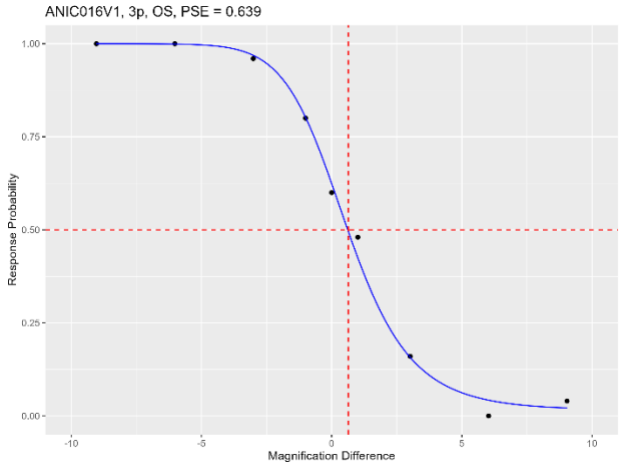


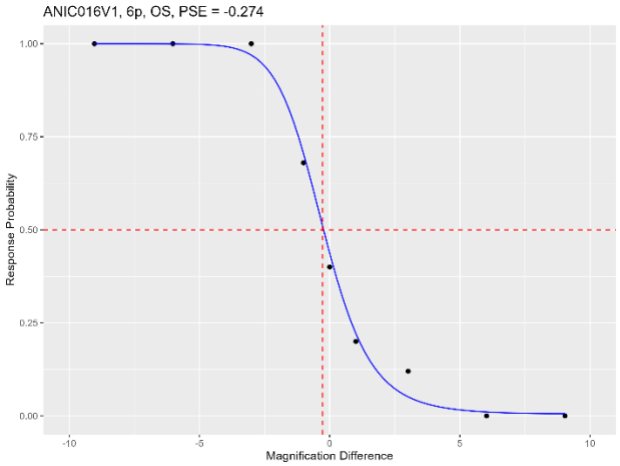


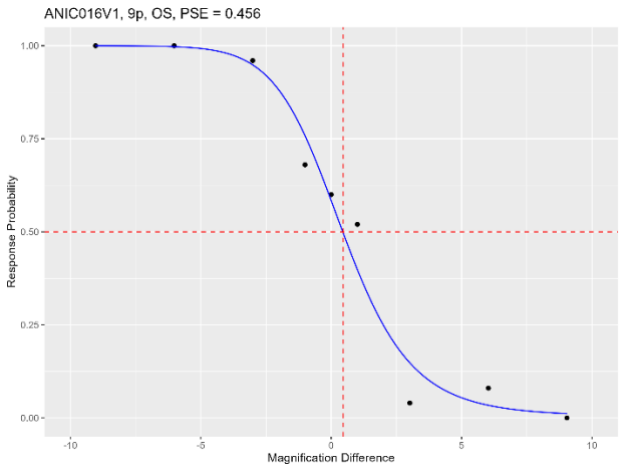
Subject ID: ANIC016, psychometric functions of each size lens condition: 0%, 1%, 3%, 6%, 9%.



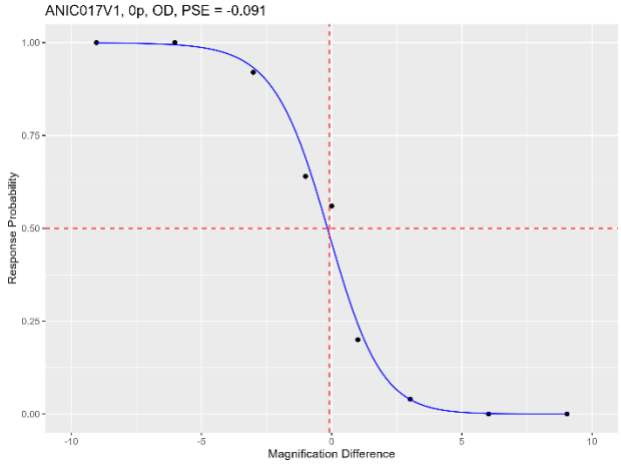


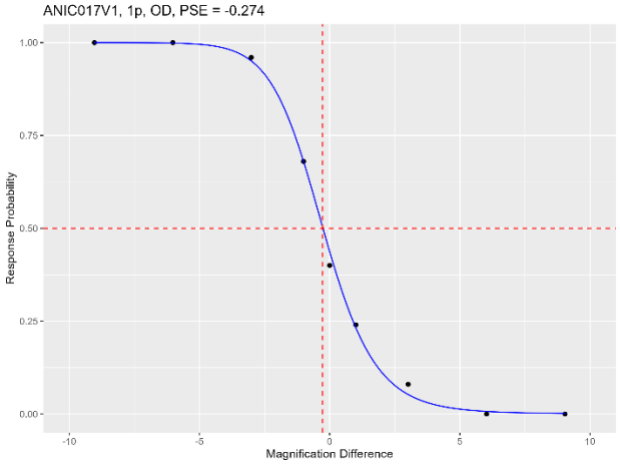


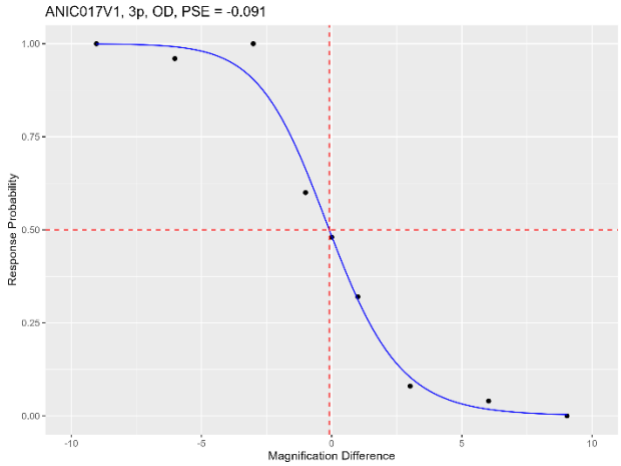


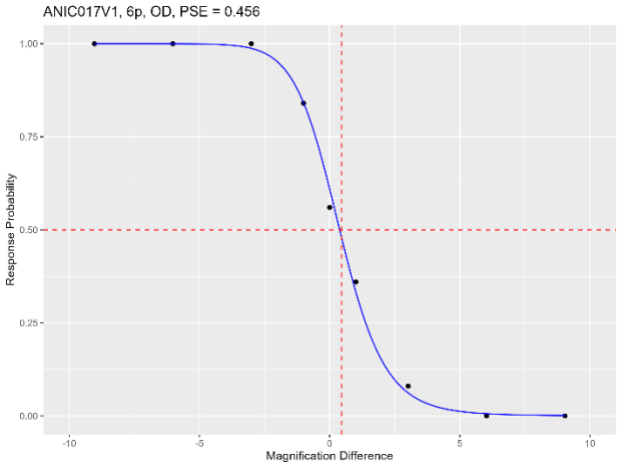


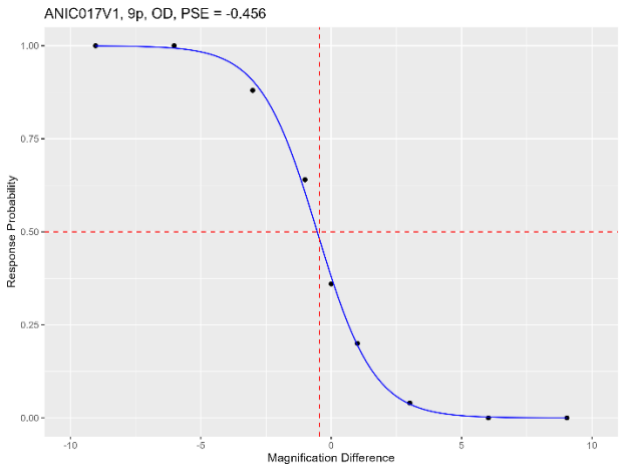
Subject ID: ANIC017, psychometric functions of each size lens condition: 0%, 1%, 3%, 6%, 9%.



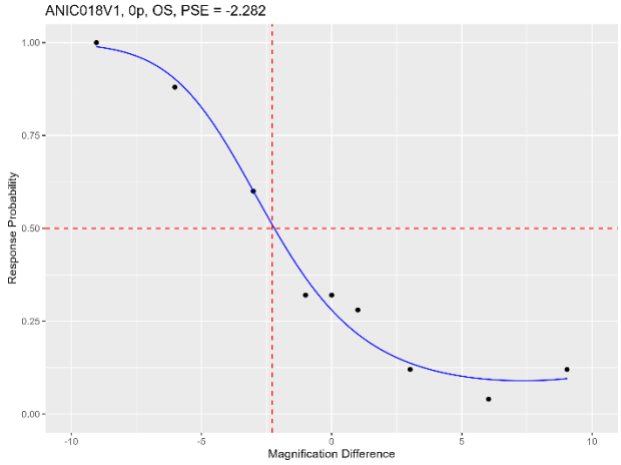


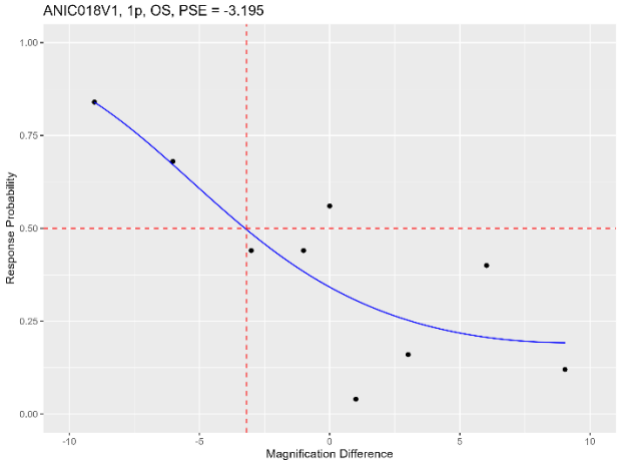


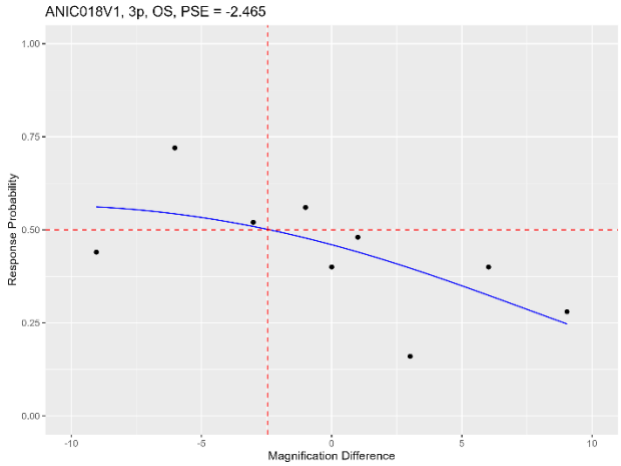


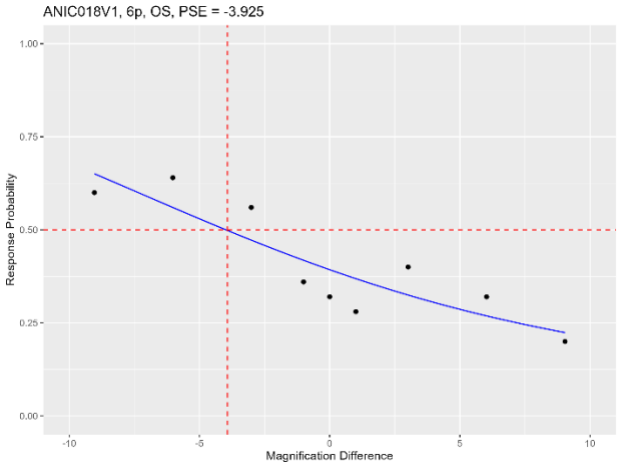


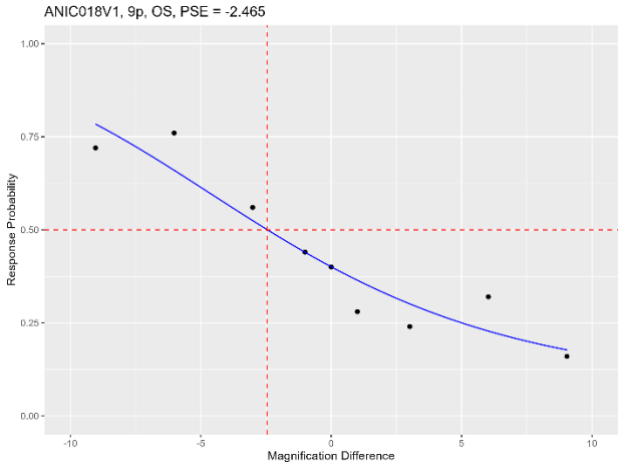
Subject ID: ANIC018, psychometric functions of each size lens condition: 0%, 1%, 3%, 6%, 9%.



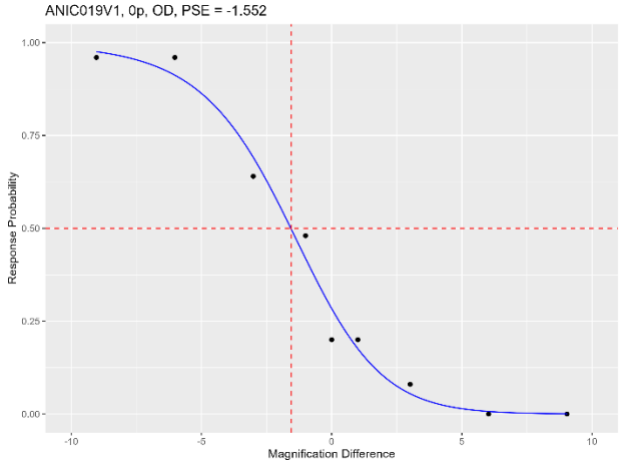


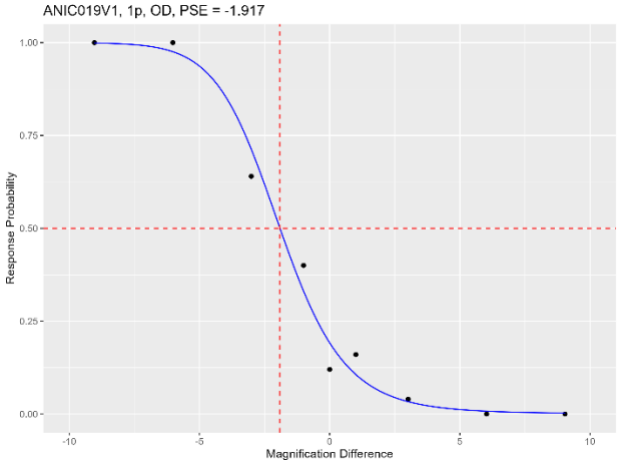


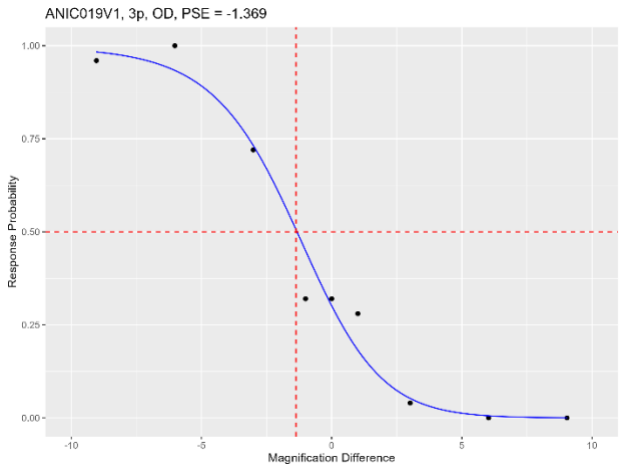


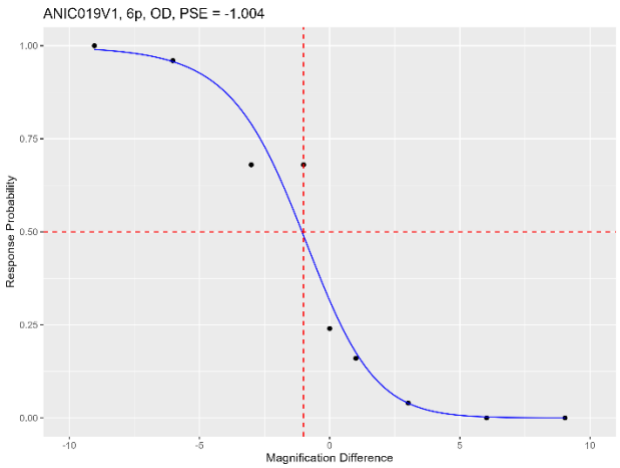


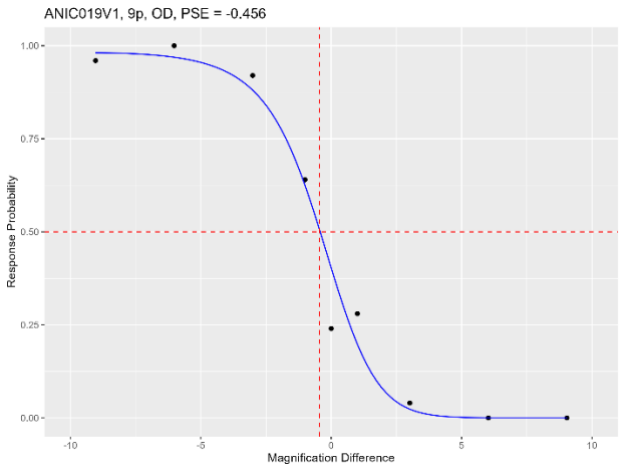
Subject ID: ANIC019, psychometric functions of each size lens condition: 0%, 1%, 3%, 6%, 9%.



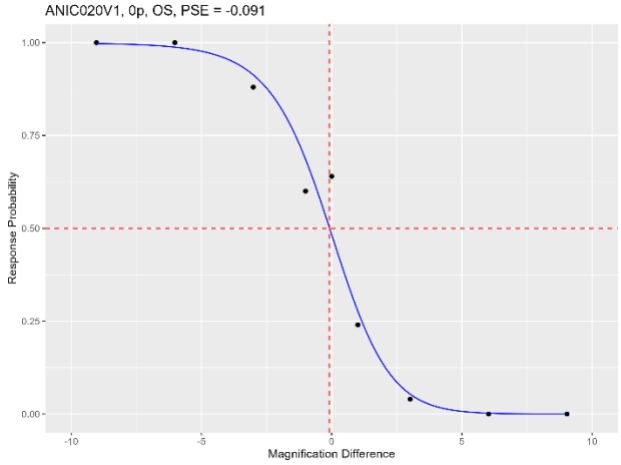


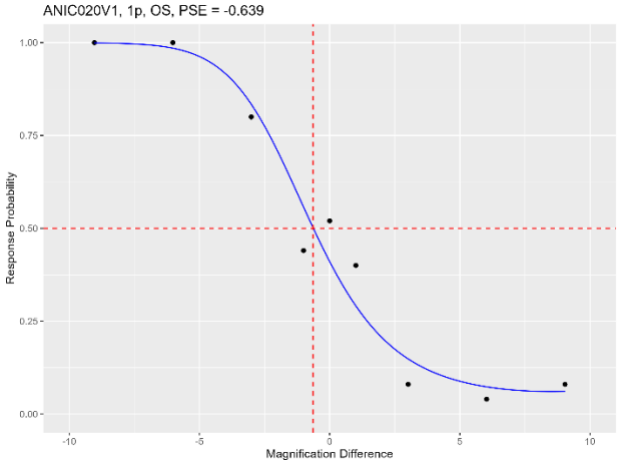


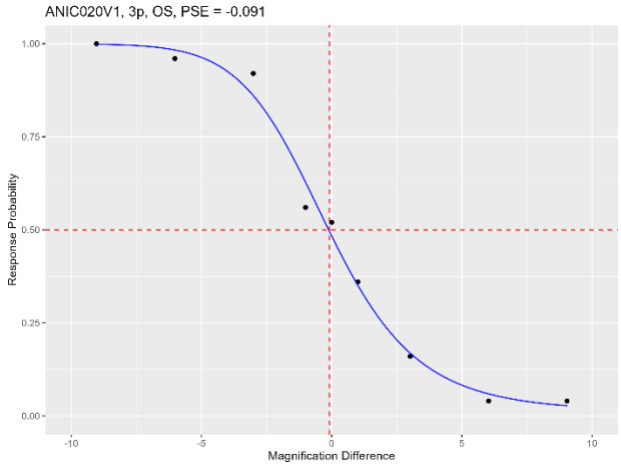


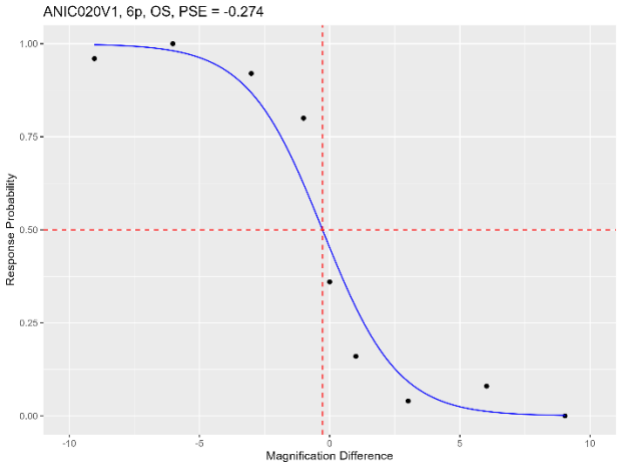


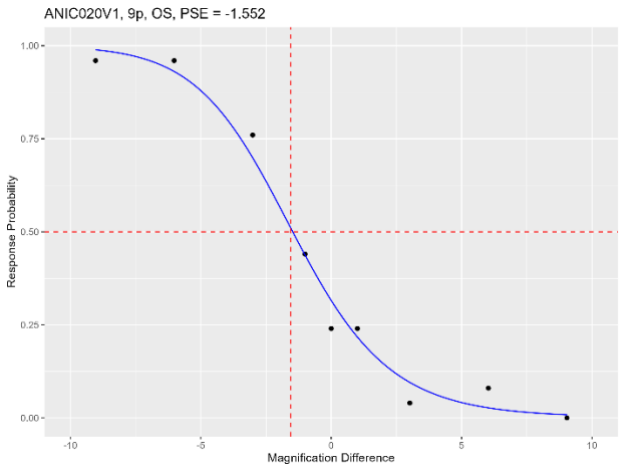
Subject ID: ANIC020, psychometric functions of each size lens condition: 0%, 1%, 3%, 6%, 9%.



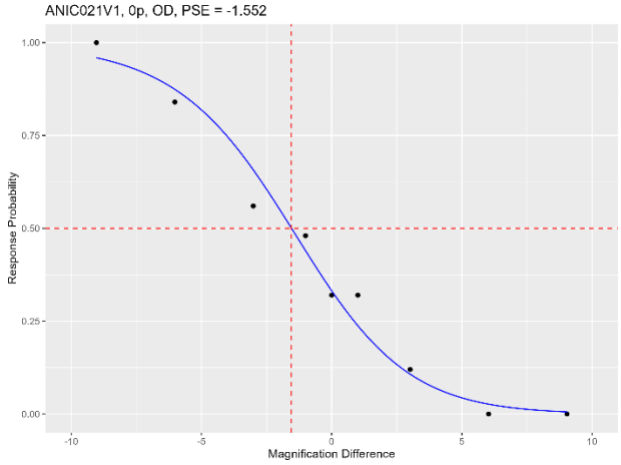


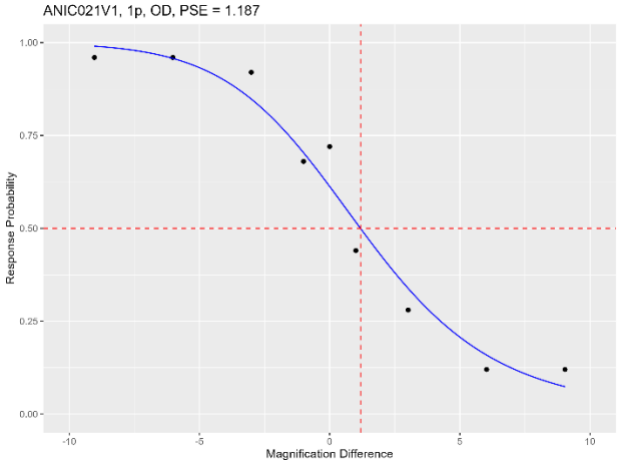


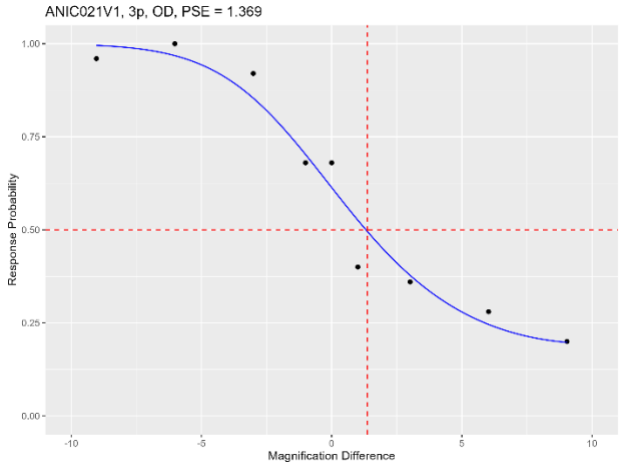


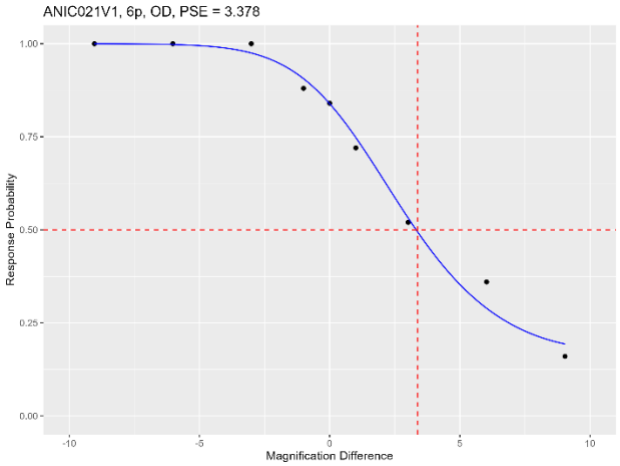


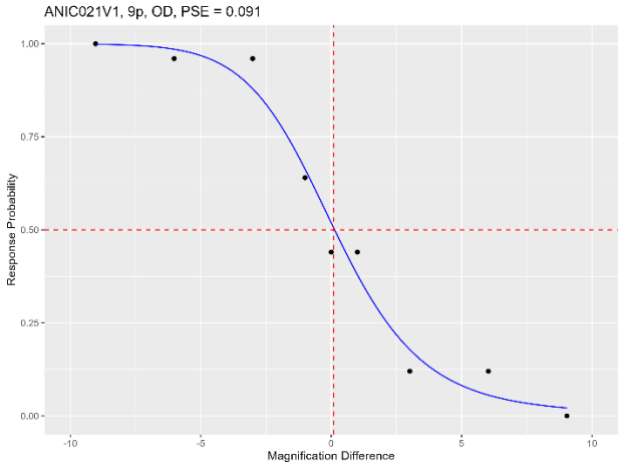
Subject ID: ANIC021, psychometric functions of each size lens condition: 0%, 1%, 3%, 6%, 9%.



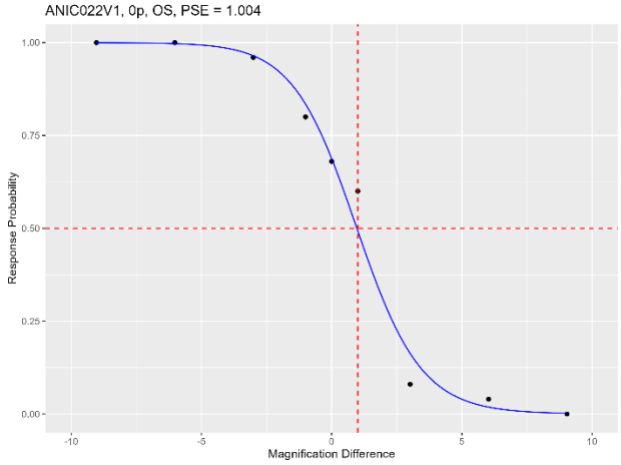


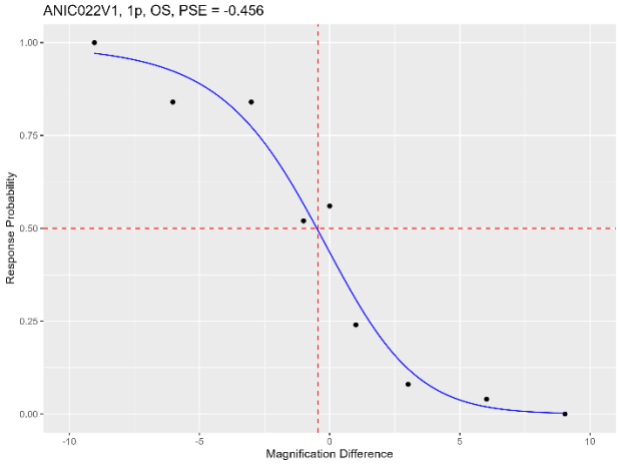


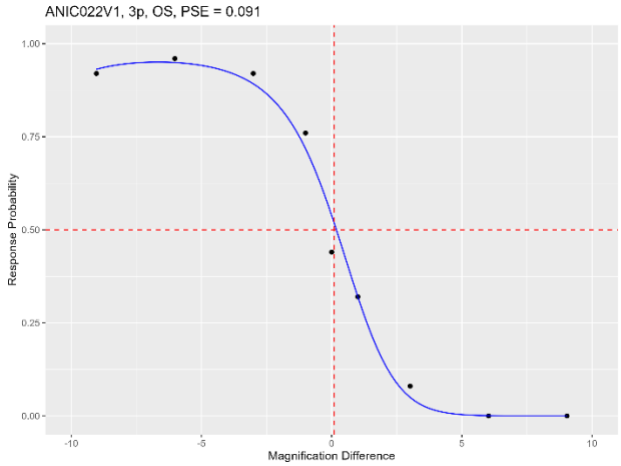


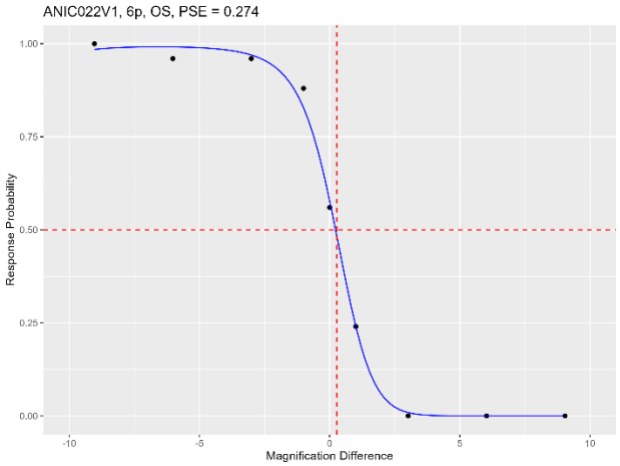


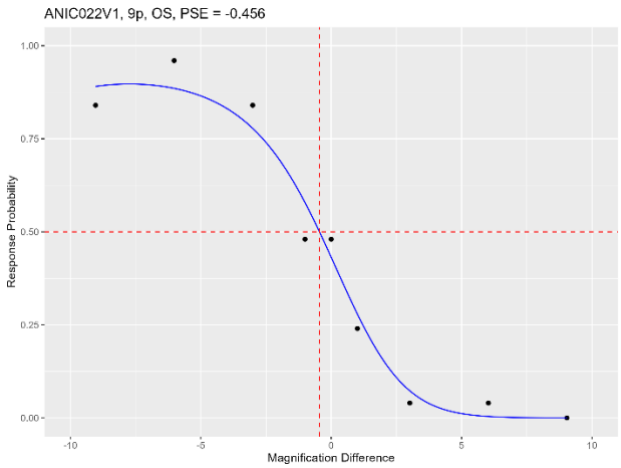
Subject ID: ANIC022, psychometric functions of each size lens condition: 0%, 1%, 3%, 6%, 9%.



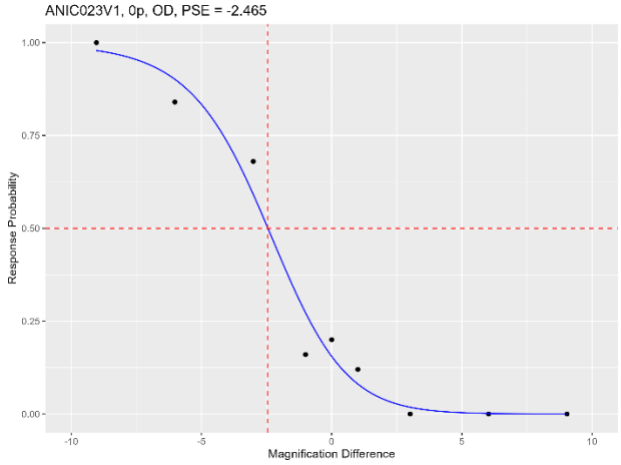


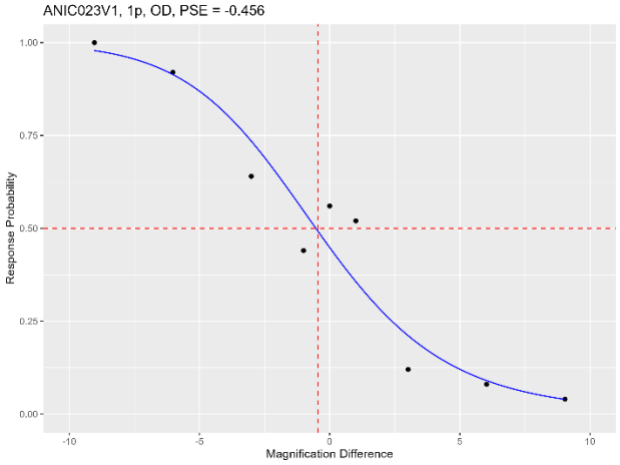


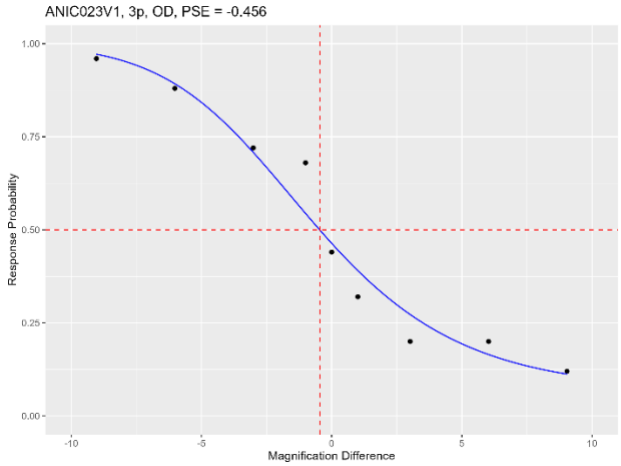


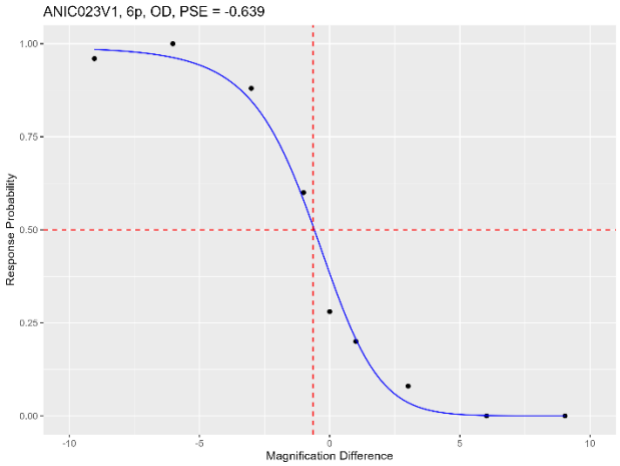


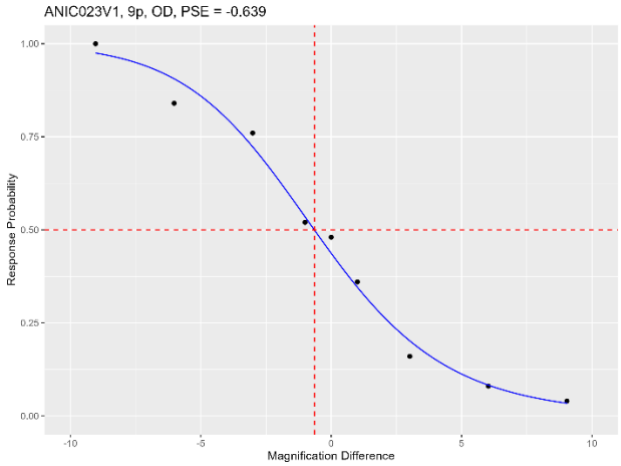
Subject ID: ANIC023, psychometric functions of each size lens condition: 0%, 1%, 3%, 6%, 9%.



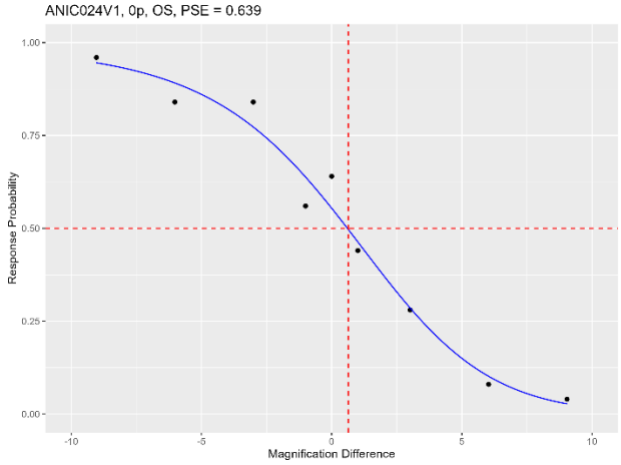


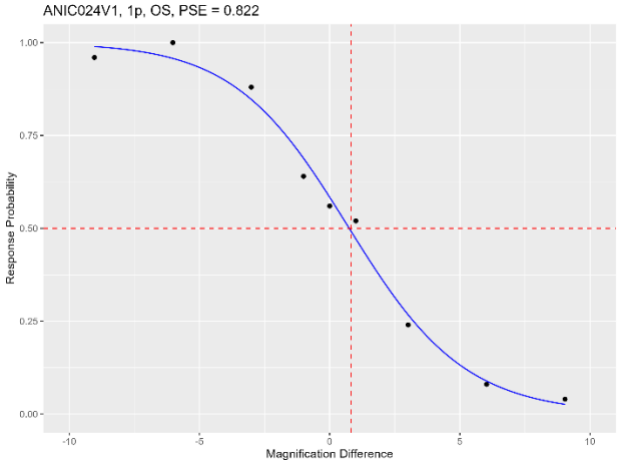


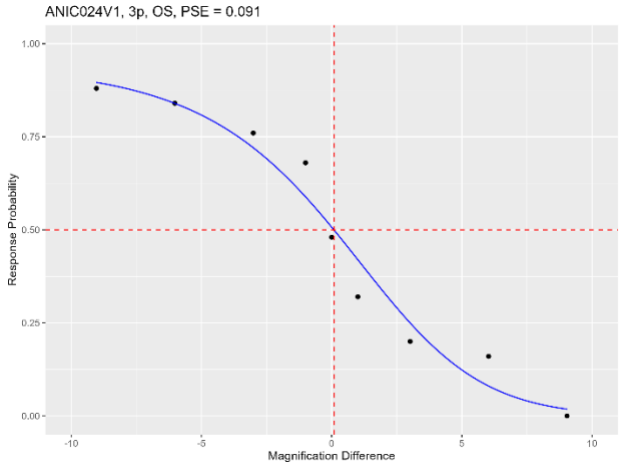


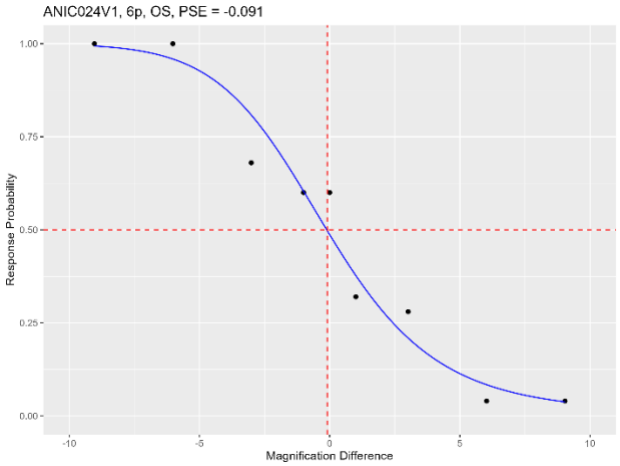


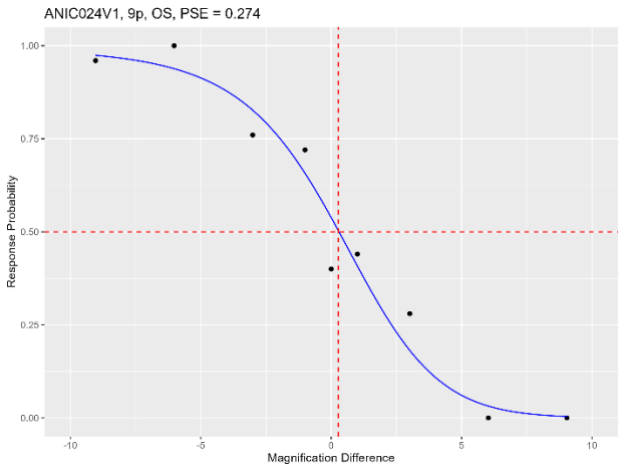
Subject ID: ANIC024, psychometric functions of each size lens condition: 0%, 1%, 3%, 6%, 9%.



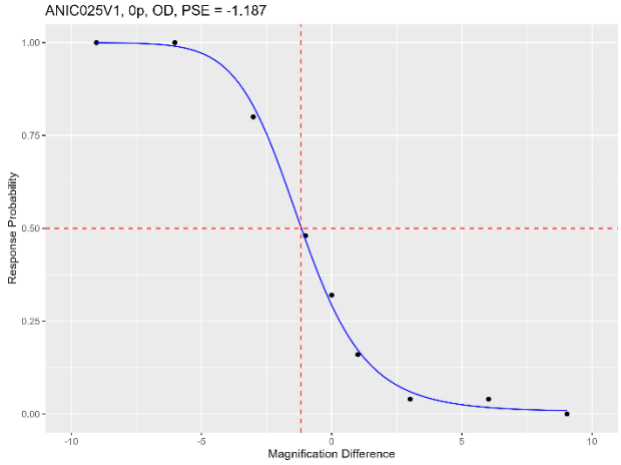


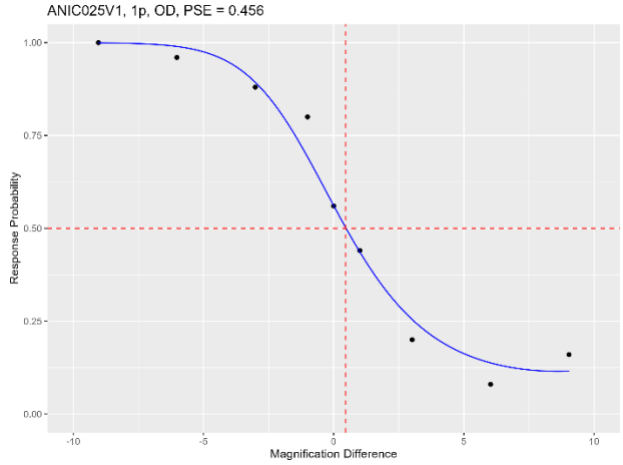


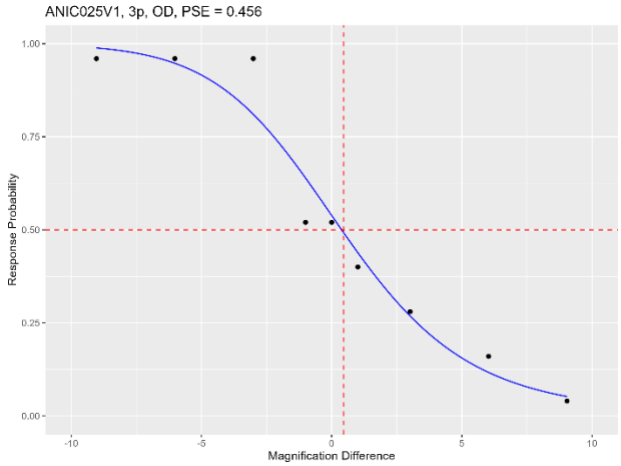


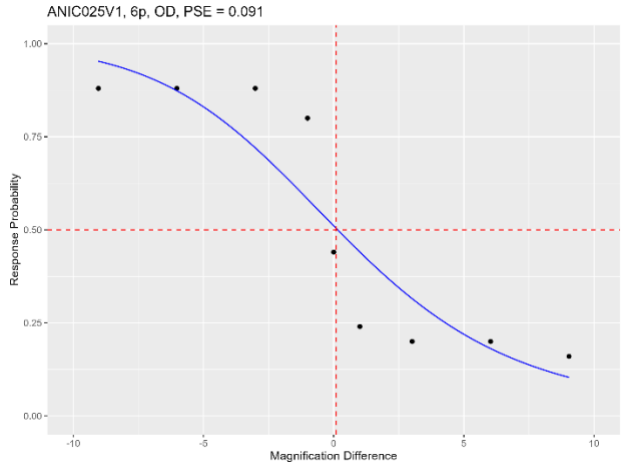


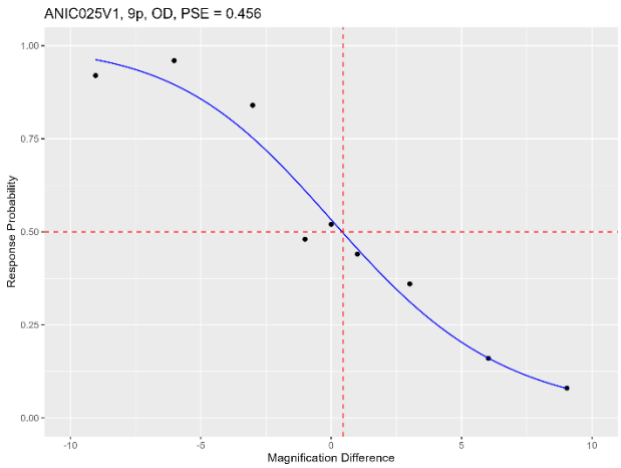
Subject ID: ANIC025, psychometric functions of each size lens condition: 0%, 1%, 3%, 6%, 9%.



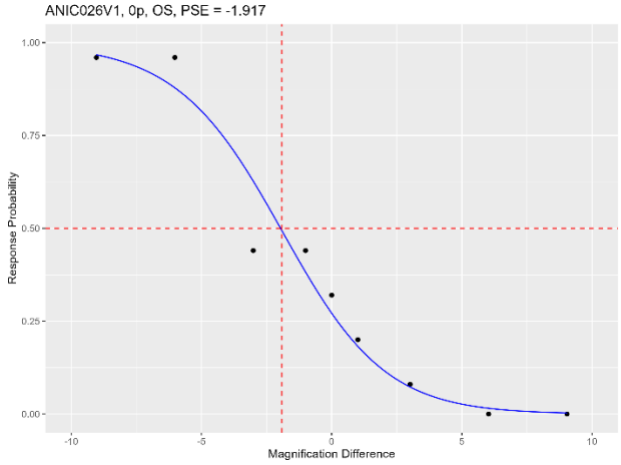


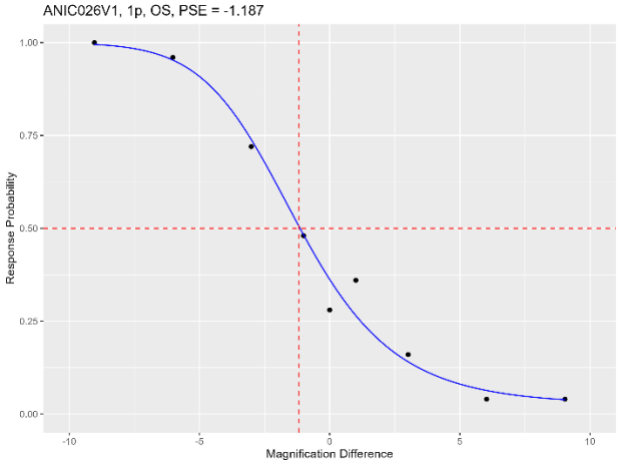


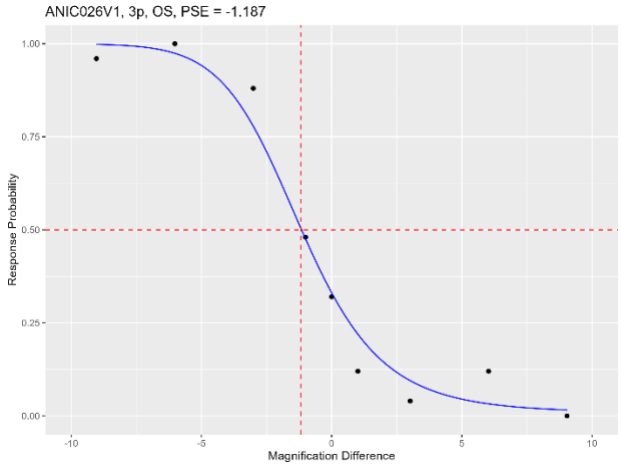


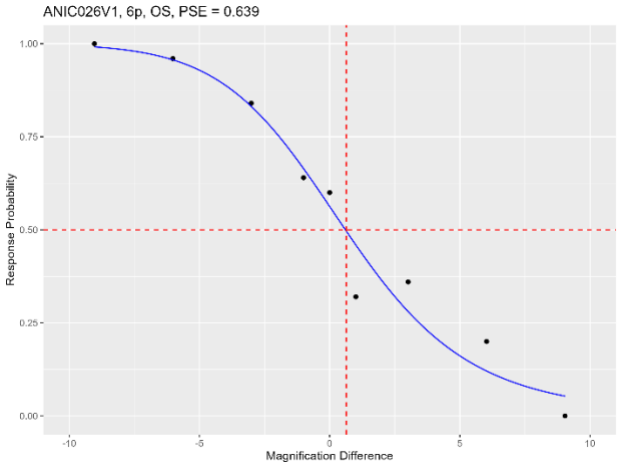


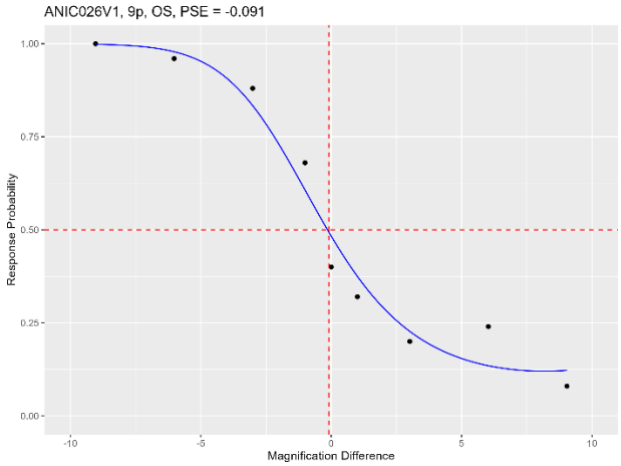
Subject ID: ANIC026, psychometric functions of each size lens condition: 0%, 1%, 3%, 6%, 9%.



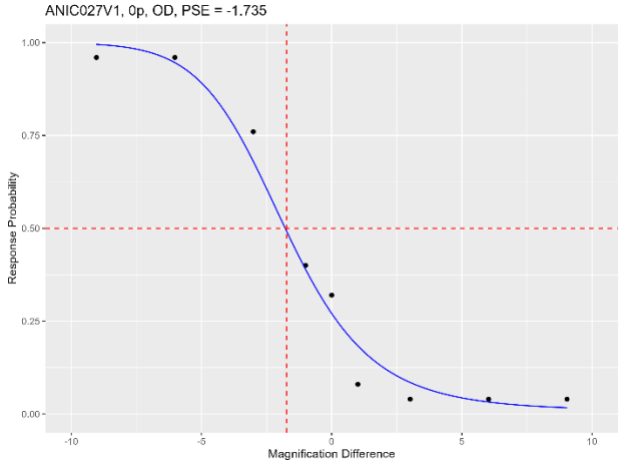


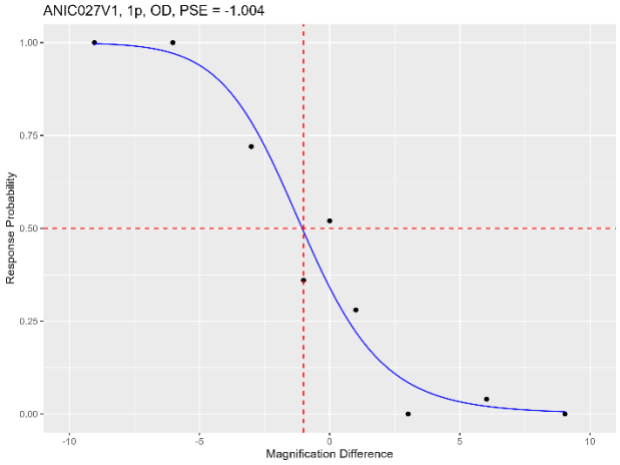


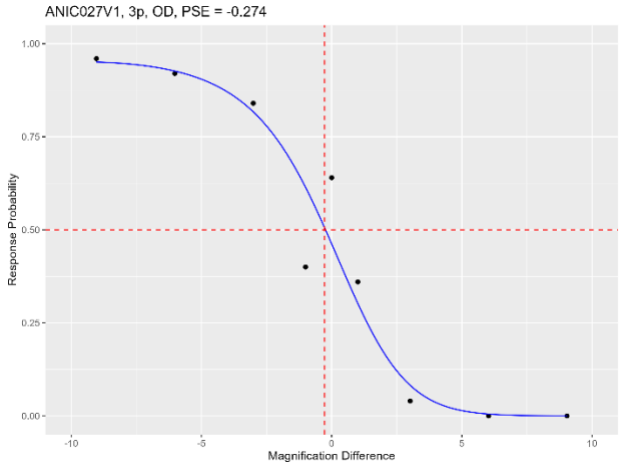


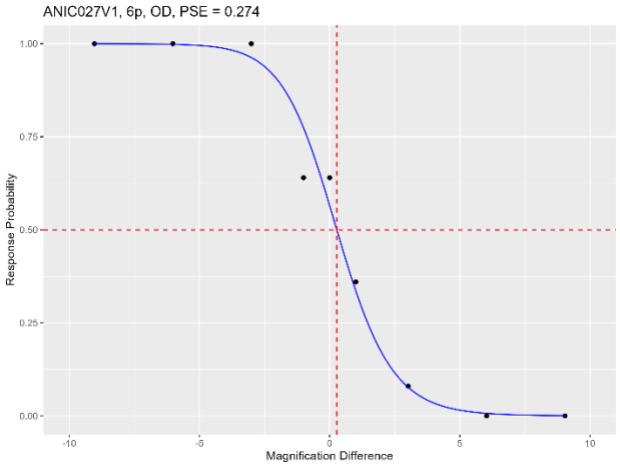


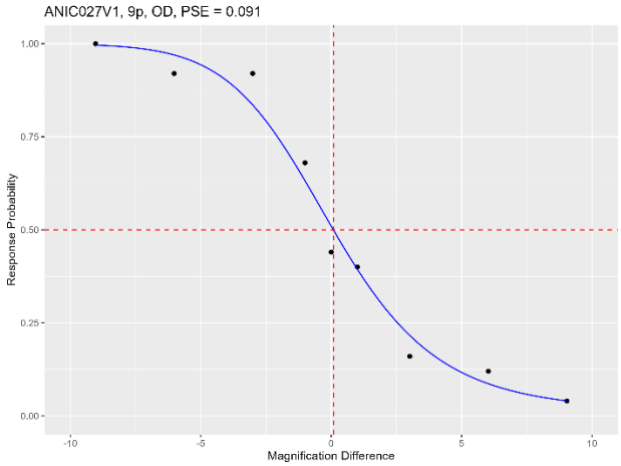
Subject ID: ANIC027, psychometric functions of each size lens condition: 0%, 1%, 3%, 6%, 9%.











Subject ID: ANIC028, psychometric functions of each size lens condition: 0%, 1%, 3%, 6%, 9%.

