WAVEFRONT ABERRATIONS AND GLARE SENSITIVITY INFLUENCE ON VISION

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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June, 2021

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Abstract:

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New England College of Optometry, 2021

Introduction: Global population aging trends have increased the demand for treatment of presbyopia. Simultaneous vision correction modalities offer a solution, but depend on variables such as glare sensitivity and wavefront aberrations that can be uniquely individual. Wavefront aberrations and glare sensitivity are not typically studied together because of their independent mechanisms, but a connection between the two has not been ruled out. The purpose of this research is to explore this connection further in the context of visual acuity and to calculate the neural transfer function (NTF), a metric that accounts for the part of visual processing that occurs in the brain.

Methods: 46 healthy subjects aged 20 to 30 with best corrected visual acuity of at least 20/25 (+0.1 logMAR) were recruited and four data sets were collected on one randomized eye. Visual acuity was measured using a FrACT Landolt C eye chart on a computer monitor. Wavefront aberrations were measured with a Topcon KR-1W Wave-Front Analyzer. Contrast sensitively was measured in the presence and absence of glare with a Takagi-1000 Contrast Glare Tester. Intraocular straylight was measured with an Oculus C-Quant. Correlational analysis was performed between these data sets. The NTF was calculated as the ratio of the empirically measured contrast sensitivity function (CSF) and the modulation transfer function (MTF). The

MTF was calculated from the wavefront aberrations measured by the Topcon KR-1W Wave-Front Analyzer.

Results: There were no significant correlations between straylight and visual acuity or contrast sensitivity measured in the presence and absence of glare. There were no discernable trends between higher order wavefront aberrations and visual acuity, straylight, or contrast sensitivity. The NTF and the CSF were degraded by glare overall, but training effects limited the strength of this outcome.

Discussion: The lack of significant correlations between visual acuity, straylight, contrast sensitivity, and higher order aberrations may be due to a combination of different optical mechanisms, the independent actions of individual higher order aberrations, or our healthy and homogenous subject population. The NTF was not superior to the CSF overall, but the larger scale and intersubject variability suggest the NTF may be better for predicting individual preference.

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Chapter 1: General Introduction

The population of persons over 60 years of age is expected to double what it was in 2017 by the year 2050 and the population of persons over 80 is expected to triple (United Nations 2017). These global population aging trends have increased the demand for treatment of presbyopia, a consequence of aging which begins around age 40 (Łabuz et al. 2017). One solution is multifocal contact lenses. Multifocal contact lenses provide simultaneous vision allowing the user to view both distance and near targets through the same correction. The ideal lens design is still an active area of investigation because optimizing the performance of the multifocal contact lens depends on multiple factors including optics of the eye such as glare sensitivity and wavefront aberrations that can be unique to each user. This research focuses primarily on the application of glare sensitivity and wavefront aberration metrics to contact lenses, but it may also be applied in the context of intraocular lens selection prior to cataract surgery or when planning refractive surgery.

Glare Sensitivity. Glare sensitivity is caused by intraocular straylight interfering with the formation of a sharp image on the retina (Łabuz et al. 2017). There are two forms of light scatter, forward scatter and back scatter. Straylight is considered to be caused by forward scatter or the scatter of light toward the retina as opposed to back scatter which is the light that is reflected back out of the eye (van den Berg 2017). The scatter of light may be due to one of many causes such as cataracts, vitreous floaters, or corneal abnormalities (Rozema, van den Berg, Tassignon 2010). A previous study indicates that objectively measured levels of straylight do not correlate with clinically measured visual acuity (van den Berg 2017; van der Meulen et al. 2012). However, subjectively reported glare sensitivity can be debilitating even

when visual acuity is not quantitatively decreased (van der Meulen et al. 2012; Rozema, van den Berg, Tassignon 2010). Due to this disconnect, a better understanding of the effect of glare sensitivity on vision would be useful.

Wavefront Aberrations. It has been shown that visual acuity decreases exponentially with the increase in magnitude of defocus or astigmatism. Additionally, astigmatism axis precision becomes increasingly important as the magnitude of astigmatism increases (Villegas, Alcón, Artal 2014). When considering higher order aberrations, the effect on vision is still an active area of research because it is a more compound question. Large amounts of higher order aberrations can decrease vision (Villegas, Alcón, Artal 2008). However, it has also been shown that aberrations arranged correctly can mitigate each other, improving visual acuity even though the total amount of aberrations is larger (Applegate, Khemsara, Sarver 2001). This variability caused by interacting aberrations has been problematic in designing multi-focal contact lenses. In one study, it was shown that individual aberrations may prevent a multi-focal contact lens from providing simultaneous vision. The same study suggested a method to predict if the subject is a good candidate for multi-focal contact lenses bases on a measurement of their wave front aberrations (Martin, Roorda 2003). It would be beneficial to expand upon this work and be able to better predict a patient's visual acuity based on their wavefront aberrations.

Connection. Wavefront aberrations and glare sensitivity are not typically studied together because of their independent mechanisms (Artal 2014). However, a connection between the two has not been ruled out. For example, light scatter normally reduces contrast sensitivity. One study showed that when light scatter is combined with spherical aberrations the reduction

in contrast sensitivity decreased (Pérez, Manzanera, Artal 2009). We plan to investigate this connection further in the context of visual acuity. Ideally, this information will yield a metric that can be used to improve multifocal contact lens design or better select an intraocular lens implant or ablation pattern in refractive surgery.

Experimental Question: The purpose of this study is to determine the separate and combined impact of wavefront aberrations and glare sensitivity on vision and to develop a metric for predicting visual acuity using both.

- Objective I: Determine if there is a link between straylight measurements (C-Quant) and the contrast glare tester measurements (Takagi CGT) in predicting visual acuity.

- Objective II: Determine if there is a link between the results of the wavefront aberrometer (Topcon), straylight measurements (C-Quant), and the contrast glare tester measurements (Takagi CGT) in predicting visual acuity.

- Objective III: Derive a neural transfer function (NTF) from the results of the contrast glare tester (Takagi CGT) and aberrometer (Topcon).

Chapter 2: Design and Methods

Subject Participation. *46* subjects between 20 and 30 years of age with BCVA no worse than 20/25 (+0.1 logMAR) were enrolled. Subjects with media opacity such as cataract or who use orthokeratology contact lens correction were excluded from participation. Patients were screened with an anterior segment exam using a biomicroscope. Visual acuity was checked monocularly at 20 feet using a Landolt C chart on a computer monitor with FrACT software (Bach 2021). The light level in the room was kept the same for the duration of all screening steps and experimental measurements.

Measurements. Three measurements from three machines, detailed below, were performed on one, randomized eye of each subject for a total of nine measurements per subject. All measurements were taken without correction. All measurements are summarized in Table 1.

- Takagi-1000 Contrast Glare Tester: tests contrast sensitivity in the presence and absence of glare. Subjects were asked to press a hand-held button every time they saw a ring flash in the blue target circle. Stimuli were presented at six different spatial frequencies: 6.3, 4.0, 2.5, 1.6, 1.0, 0.7 (in degrees). The lowest level of contrast perceived by the subject for each stimulus size was recorded (Takagi 2000).
- Oculus C-Quant: measures the amount of straylight in the human eye. Subjects were asked to fixate on a center circle and to determine which half of the circle, the left or the right, appeared to be flashing, and press a corresponding button. The amount of straylight was determined by the threshold of detection in Log(s) (Oculus 2018).

- Topcon KR-1W Wave-Front Analyzer: a clinically used wavefront aberrometer traditionally used to predict refraction. We use it here to determine the magnitude of five different higher order aberrations (HOAs) in individual participants for a 4mm and 6mm pupil size: trefoil, coma, tetrafoil, secondary astigmatism, and spherical aberration. This was an objective measurement.

Table 1. Summary of Measurements

Measurement:	***Device:***	***Correction Modality:***
Visual acuity	FrACT software	Corrected
Wavefront aberrations	Topcon KR-1W	Uncorrected
Contrast sensitivity	Takagi 2000	Uncorrected
Straylight	Oculus C-Quant	Uncorrected

Statistical Analysis: MATLAB software was used for all data management and analysis (MathWorks 2021). Summary statistics can be found in Appendix 1 (Figures 11 and 12). Analysis for the three objectives was as follows.

- Objective I: The straylight measurements of the C-Quant were compared to the contrast sensitivity measurements of the Takagi CGT in the presence and absence of glare using a direct correlational analysis. Straylight measurements were also directly compared to visual acuity.
- Objective II: A correlational analysis was performed on the results of the aberrometer (Topcon) with the glare sensitivity measurements (C-Quant) and with the contrast sensitivity measurements (Takagi CGT) in the presence and absence of glare. The aberrometer results were also directly compared to visual acuity.

- Objective III: The neural transfer function (NTF) was calculated as the ratio of the contrast sensitivity function (CSF) and the modulation transfer function (MTF) (Michael et al. 2011, Campbell and Green 1965) (Figure 1). Contrast Sensitivity was measured by the Takagi CGT with and without glare. The CSF was calculated by interpolation of the contrast sensitivity measurements. The MTF was derived from the Topcon aberration measurements (Dai 2008). The NTF was calculated using the CSF with glare and then again using the CSF without glare. The results were compared to determine if there is an effect of glare on the NTF. A ratio greater than 1 indicates the NTF is improved by glare whereas a ratio less than 1 indicates the NTF is degraded by glare.

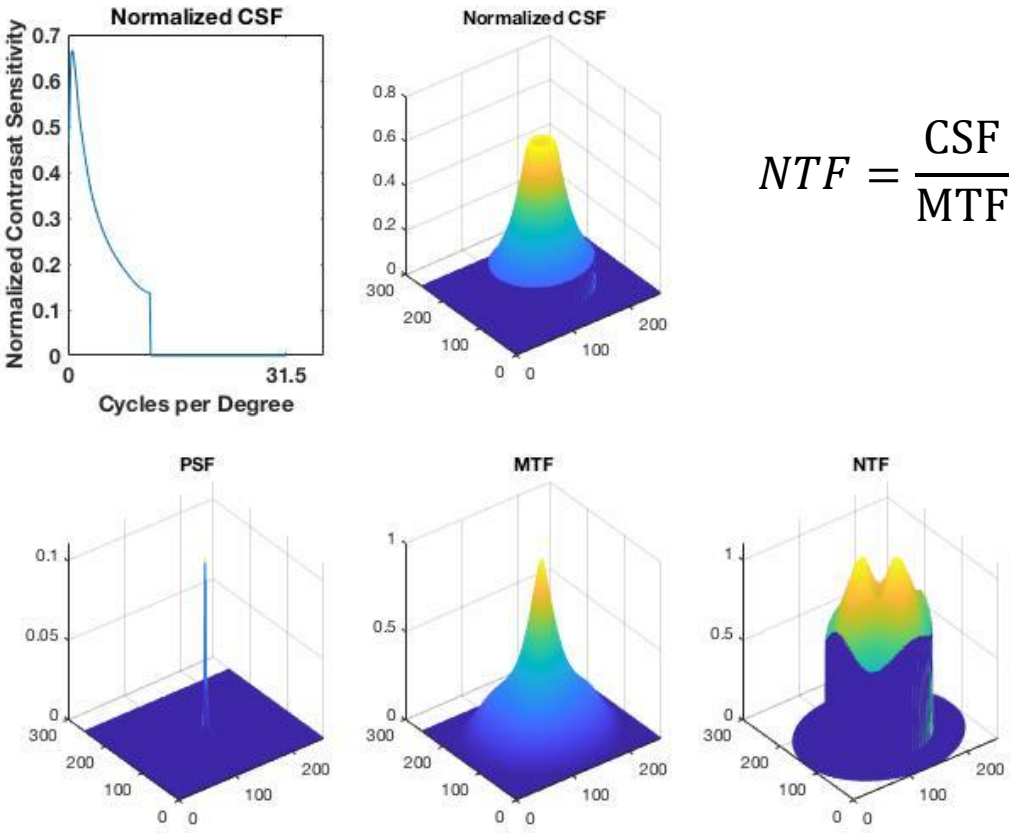


Figure 1. **An example of how the NTF ratio was calculated for one glare condition for one subject**. The Normalized CSF is measured, graphed, and interpolated (top left). The Normalized CSF is rotated 360°and extended over 256 units so it will be mathematically compatible with the MTF (top middle). 256 is a software standard number of sampling points. HOAs are measured and converted into Zernike coefficients. The PSF is calculated from the Zernike coefficients (bottom left). A Fourier transform is performed on the PSF to arrive at the OTF. The absolute value of the OTF is the MTF (bottom middle). The NTF was calculated by dividing the CSF by the MTF (bottom right). Edge effects were removed resulting in the base of the NTF being circular. This calculation was performed for the CSF measured with glare and without glare and repeated for all 46 subjects.

Chapter 3: Results

Objective I. A direct correlational analysis was used to compare straylight with contrast sensitivity measured in the presence and absence of glare and with visual acuity. A t-test was performed on each comparison to evaluate the correlation's level of statistical significance. The strongest correlation was between straylight and contrast sensitivity measured in the presence of glare (R = 0.1841), however this is a weak correlation and not statistically significant (P = 0.2207). Ultimately, there were no strong or significant correlations.

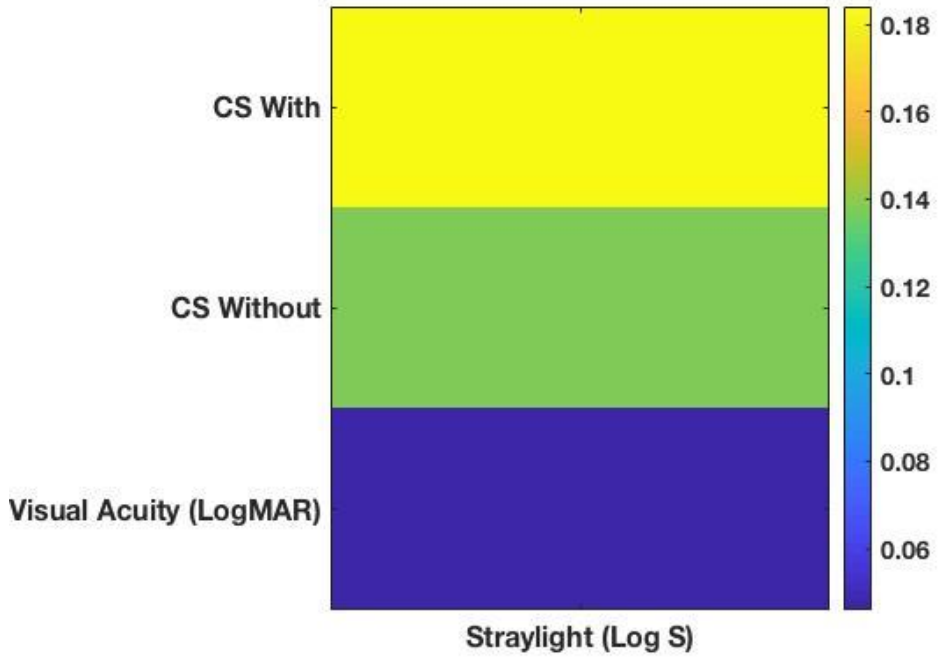


Figure 2. **A correlational analysis of straylight, contrast sensitivity with and without glare, and visual acuity**. Straylight is on the x axis and is measured in units of Log S. The condition to which the measured value of straylight is correlated is on the y axis. "CS With" is contrast sensitivity measured with glare present. "CS without" is contrast sensitivity measured without glare present. Corrected visual acuity was measured on a FrACT electronic chart in logMAR. The colored bar represents the correlation coefficient with yellow being the strongest positive correlation and blue being the weakest.

Objective II. A direct correlational analysis was used to compare HOAs and glare sensitivity. HOA magnitude and HOA axis were analyzed separately. For HOA magnitude (Figure 3), the highest correlation coefficients were between 6mm Internal Spherical Aberration and Visual Acuity (R = 0.6056) and between 6mm Internal Secondary Astigmatism and Contrast Sensitivity measured with glare (R = 0.5308). There were no strong correlations between HOAs and straylight.

A Bonferroni corrected t-test was performed on each comparison (Antonisamy, Premkumar, Christopher 2017). A corrected P value of 0.00666 was used to account for the multiple comparisons. HOA magnitude and HOA axis were again analyzed separately. For HOA magnitude (Figure 4), the comparison of 6mm Internal Spherical Aberration and Visual Acuity (P = 0.0044) and between 6mm Internal Secondary Astigmatism and Contrast Sensitivity measured with glare (P = 0.0008) were significant.

The analysis was repeated for HOA axis measurements. The correlational analysis for HOA axis measurements (Figure 5) revealed low to moderate, negative correlations between Corneal Trefoil Axis and Straylight measured over both 4mm (R = -0.4583) and 6mm (R = -0.5110) pupil sizes. The Bonferroni corrected t-test for HOA axis measurements (Figure 6) revealed these comparisons to be significant (P = 0.0014 and P = 0.0005, respectively).

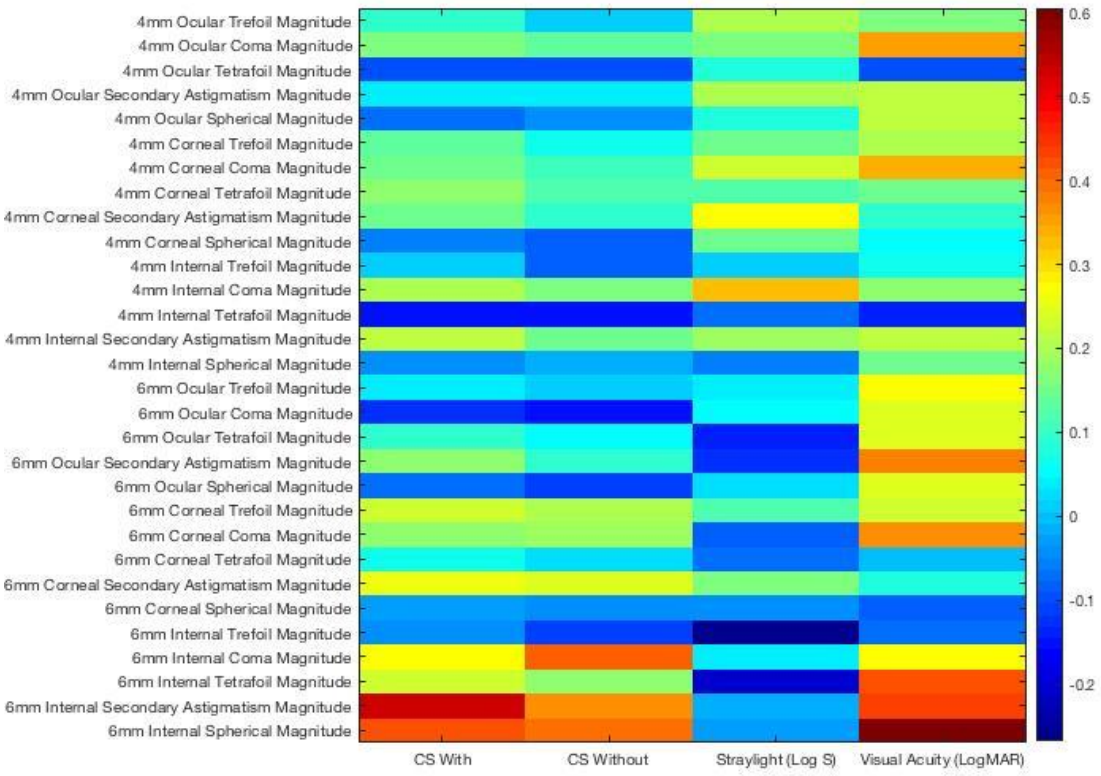


Figure 3. **A correlational analysis of HOA Magnitude, contrast sensitivity, straylight, and visual acuity**. The type of HOA is on the y axis. "Internal" is a measurement of HOAs contributed by the lens. "Corneal" is a measurement of HOAs contributed by the cornea. "Ocular" is the total amount HOAs. 4mm and 6mm are the pupil size over which the measurement was taken. The x axis is the condition to which the HOAs are correlated. "CS With" is contrast sensitivity measured with glare present. "CS without" is contrast sensitivity measured without glare present. Straylight is measured in units of Log S. Corrected visual acuity was measured on a FrACT electronic chart in logMAR. The colored bar represents the correlation coefficient with red being the strongest positive correlation and blue being a strongest negative correlation.



Figure 4. **A direct, Bonferroni corrected t-test between HOA Magnitude and contrast sensitivity, straylight, and visual acuity**. The type of HOA is on the y axis. "Internal" is a measurement of HOAs contributed by the lens. "Corneal" is a measurement of HOAs contributed by the cornea. "Ocular" is the total amount HOAs. 4mm and 6mm are the pupil size over which the measurement was taken. The x axis is the condition to which the HOAs are correlated. "CS With" is contrast sensitivity measured with glare present. "CS With" is contrast sensitivity measured with glare present. "CS without" is contrast sensitivity measured without glare present. Straylight is measured in units of Log S. Corrected visual acuity was measured on a FrACT electronic chart in logMAR. White boxes are < 0.00666 and considered significantly correlated. Black boxes are not significant.

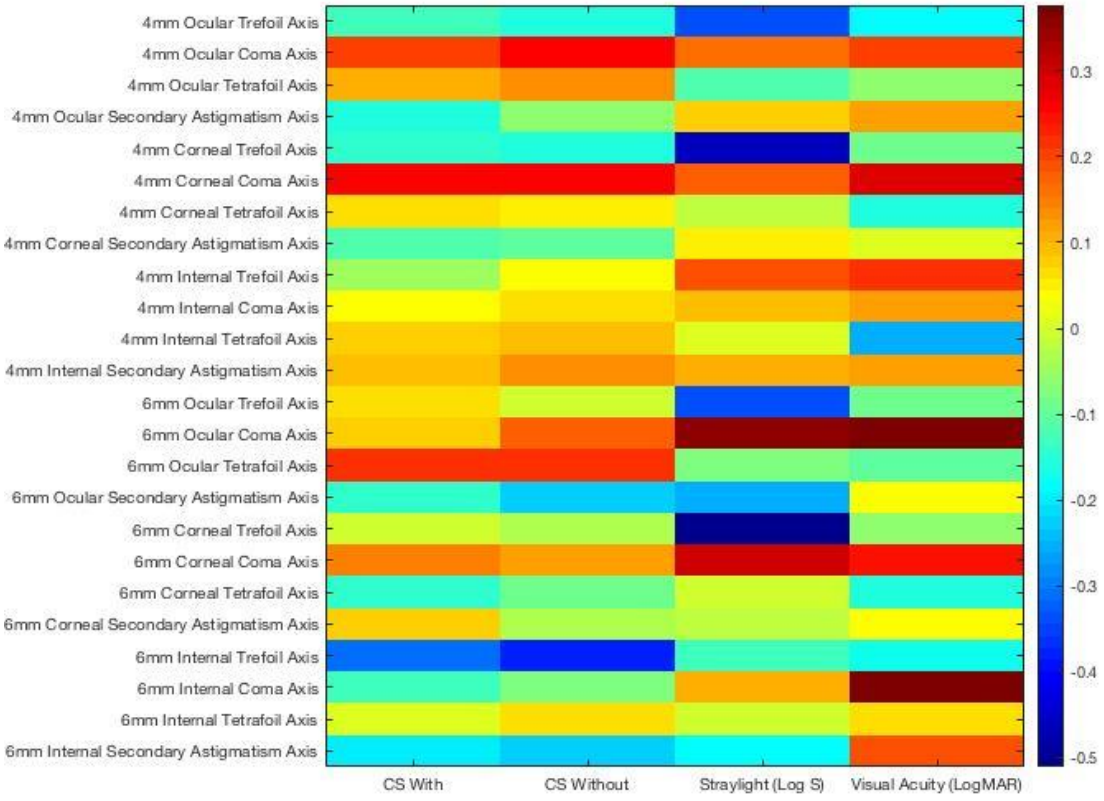


Figure 5. **A correlational analysis of HOA Axis, contrast sensitivity, straylight, and visual acuity**. The type of HOA is on the y axis. "Internal" is a measurement of HOAs contributed by the lens. "Corneal" is a measurement of HOAs contributed by the cornea. "Ocular" is the total amount HOAs. 4mm and 6mm are the pupil size over which the measurement was taken. Note that spherical aberration has been excluded from axis analysis. The x axis is the condition to which the HOAs are correlated. "CS With" is contrast sensitivity measured with glare present. "CS without" is contrast sensitivity measured without glare present. Straylight is measured in units of Log S. Corrected visual acuity was measured on a FrACT electronic chart in logMAR. The colored bar represents the correlation coefficient with red being the strongest positive correlation and blue being a strongest negative correlation.

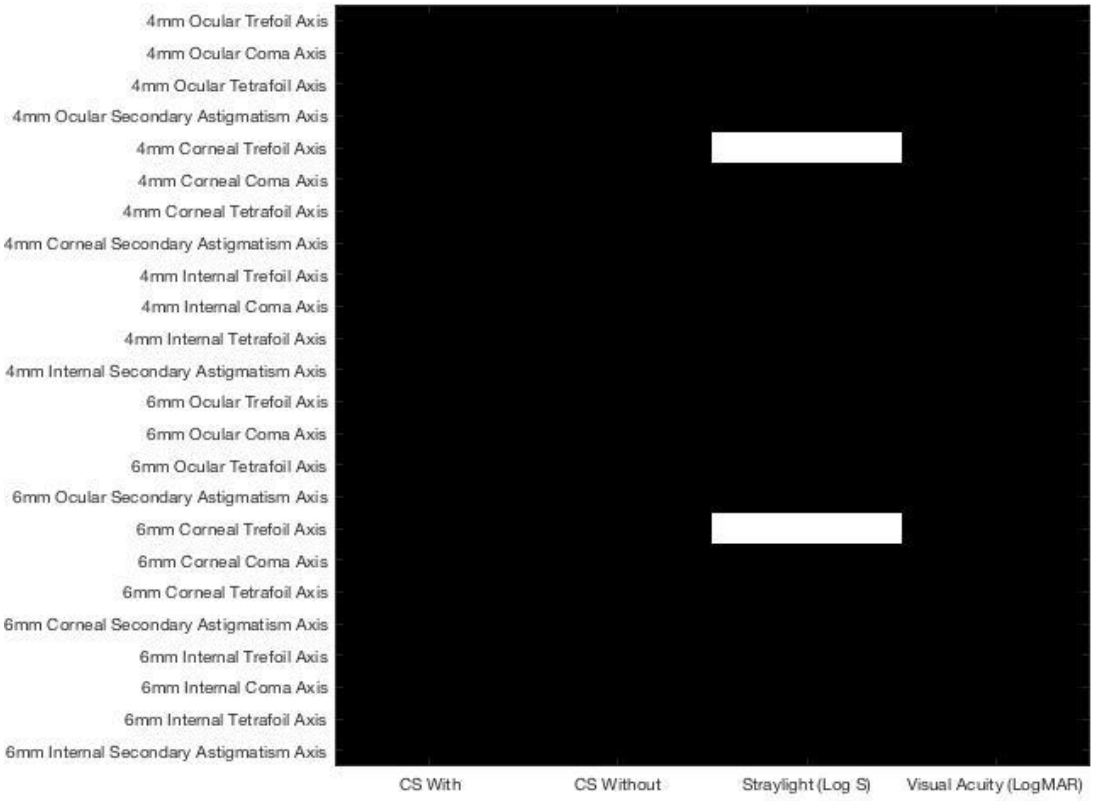


Figure 6. **A direct, Bonferroni corrected t-test between HOA Axis and contrast sensitivity, straylight, and visual acuity**. The type of HOA is on the y axis. "Internal" is a measurement of HOAs contributed by the lens. "Corneal" is a measurement of HOAs contributed by the cornea. "Ocular" is the total amount HOAs. 4mm and 6mm are the pupil size over which the measurement was taken. Note that spherical aberration has been excluded from axis analysis. The x axis is the condition to which the HOAs are correlated. "CS With" is contrast sensitivity measured with glare present. "CS without" is contrast sensitivity measured without glare present. Straylight is measured in units of Log S. Corrected visual acuity was measured on a FrACT electronic chart in logMAR. White boxes are < 0.00666 and considered significantly correlated. Black boxes are not significant.

Objective III. The NTF was calculated as explained in Figure 1 for all 46 subjects. A ratio of the integral of the NTF with glare versus the integral of the NTF without glare was then computed (Equation 1). 29 subjects showed an NTF integral ratio less than 1, indicating the NTF is degraded by glare, as we expected. The other 17 subjects showed an NTF integral ratio greater than 1, indicating the NTF was improved in the presence of glare. The ratio of CSF integrals with and without glare was also computed (Equation 2). This CSF integral ratio was less than 1 for 26 subjects. The results of these calculations are plotted in Figure 7.

$$(1)\ NTF\ Integral\ Ratio = \frac{Integral\ of\ NTF\ with\ glare}{Integral\ of\ NTF\ without\ glare}$$

$$(2)\ CSF\ Integral\ Ratio = \frac{Integral\ of\ CSF\ with\ glare}{Integral\ of\ CSF\ without\ glare}$$

To determine the benefit of including the MTF, a direct correlational analysis was performed on the NTF and CSF integral ratios (Figure 8). There was a strong, significant correlation ($R = 0.9654$, $P = 0.000$).

To rule out an effect of uncorrected refractive error, the NTF integral ratio and the CSF integral ratio were each compared to the spherical equivalent refractive error (Figure 9). The analysis revealed that there was no strong correlation between uncorrected refractive error and the NTF integral ratio ($R = -0.0344$, $P = 0.8204$) or between uncorrected refractive error and the CSF integral ratio ($R = -0.0984$, $P = 0.5154$).

To ensure the ratio is not masking a trend related to uncorrected refractive error, correlational analysis with uncorrected refractive error was also performed on individual ratio components (Figure 10). There was a significant, borderline strong correlation when spherical equivalent refractive error was compared to the integral of the CSF with glare ($R = 0.5600$, $P = 0.0001$) and the integral of the CSF without glare ($R = 0.4668$, $P = 0.0011$). There was no significant correlation when spherical equivalent refractive error was compared to the integral of the NTF with glare ($R = 0.1208$, $P = 0.4238$) or to the integral of the NTF without glare ($R = 0.1242$, $P = 0.4109$).

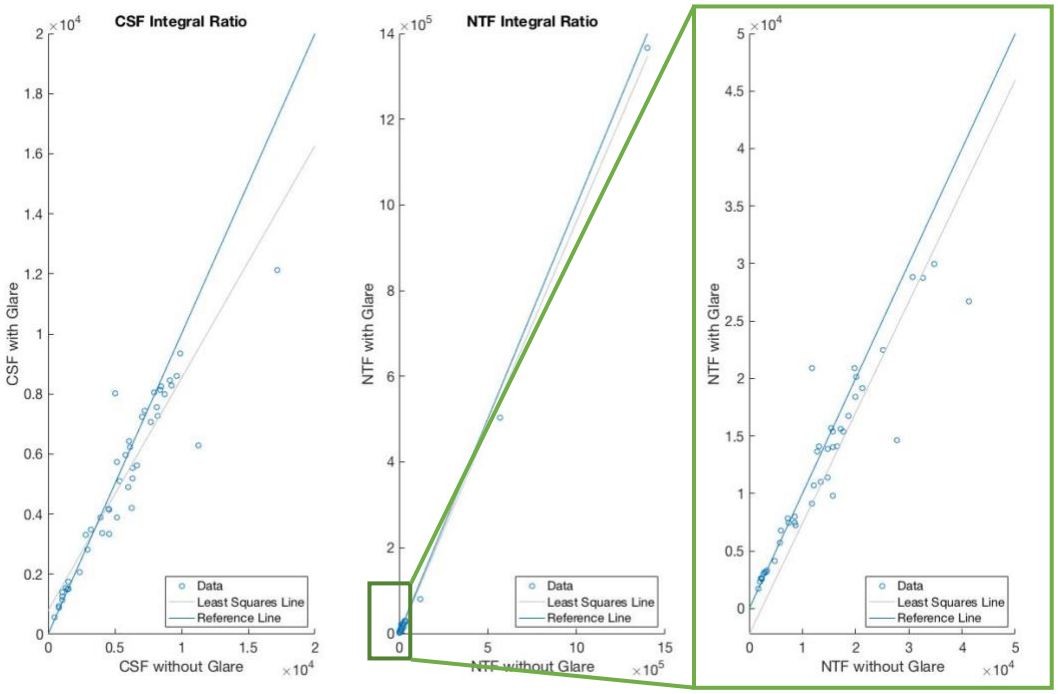


Figure 7. CSF Integral Ratio and NTF Integral Ratio. The left panel is the integral of the contrast sensitivity function (CSF) measured without glare compared to the integral of the CSF measured with glare for all 46 subjects. The middle panel is the integral of the neutral transfer function (NTF) measured without glare compared to the integral of the NTF measured with glare for all 46 subjects. The right panel is an enlarged area of the middle panel (NTF) outlined by the green box. In all panels, each blue dot represents a different subject, the grey line is a least squares regression line, and the blue line is a reference line with a slope of 1 and y-intercept at 0.

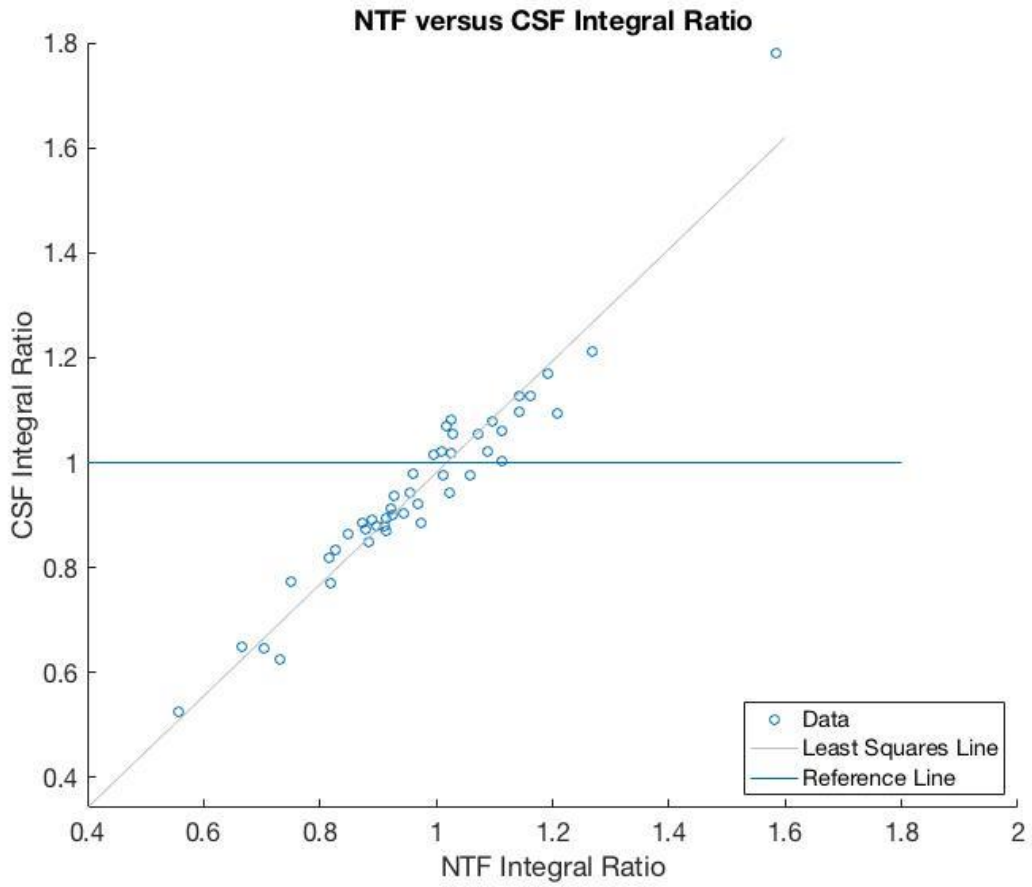


Figure 8. **A correlational analysis of CSF Integral Ratio and NTF Integral Ratio.** The neutral transfer function (NTF) integral ratio compared to the contrast sensitivity function (CSF) integral ratio for all 46 subjects. Each blue dot represents a different subject, the grey line is a least squares regression line, and the blue line is a reference line for the ratio of 1:1.

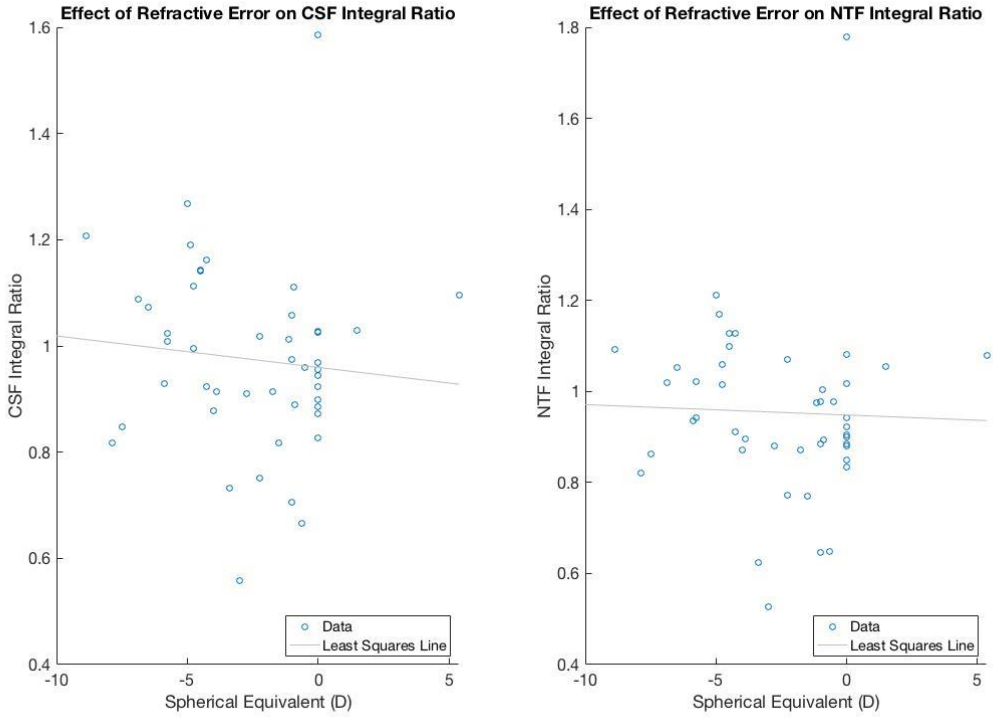


Figure 9. The effect of Refractive Error on CSF and NTF Integral Ratios. The left panel is the contrast sensitivity function (CSF) integral ratio compared to spherical equivalent refractive error in diopters for all 46 subjects. The right panel is the neural transfer function (NTF) integral ratio compared to spherical equivalent refractive error in diopters for all 46 subjects. In both panels, each blue dot represents a different subject and the grey line is a least squares regression line.

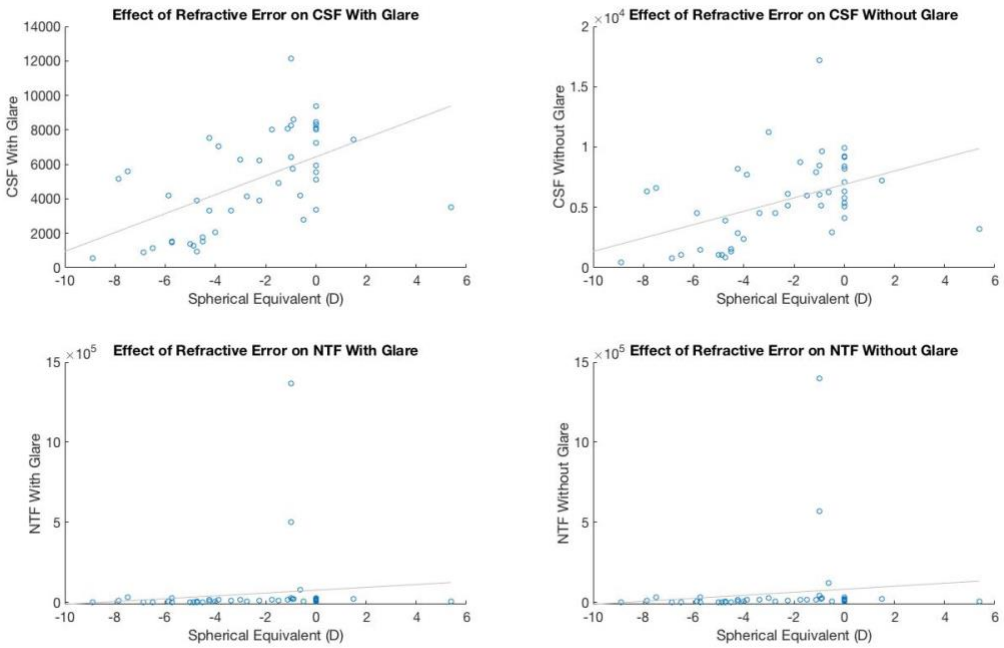


Figure 10. **The effect of Refractive Error on individual glare conditions for NTF and CSF calculations.** The top row of panels is a comparison between the contrast sensitivity function (CSF) integral and spherical equivalent refractive error for 46 subjects. The bottom row of panels is a comparison between the neural transfer function (NTF) integral and spherical equivalent refractive error for 46 subjects. The left column of panels are conditions measured with glare. The right column of panels are conditions without glare. In all panels, each blue dot represents a different subject and the grey line is a least squares regression line.

Chapter 4: Discussion and Conclusions

Objective I. The correlational analysis revealed there was no strong correlation between straylight and visual acuity. This finding is consistent with previous research published in the field (van den Berg 2017, van der Meulen et al. 2012). The proposed mechanism behind this lack of correlation is that forward scatter (responsible for straylight) affects the periphery rather than the center and so does not degrade visual acuity (van den Berg 2017).

It has been reported that straylight can subjectively decrease contrast (van den Berg 2017), but our correlational analysis revealed no strong correlation between straylight and contrast sensitivity measured with or without glare. This suggests that straylight and contrast sensitivity contribute independently to the perception of glare. The literature is mixed on this topic. A 2011 study also found no correlation between straylight and contrast sensitivity measured in subjects after undergoing refractive surgery (Lorente-Velázquez et al. 2011) but a 2018 study did report a correlation in both subjects with cataracts and a reference group with subjects of a similar profile to ours (aged 25-30 years) (Paz-Filgueira and Colombo 2018). The trend in recent publications has been to report both straylight and contrast sensitivity separately as metrics of visual quality (Koh et al. 2017, Casares-López et al. 2020).

Objective II. The correlational analysis revealed a few significant correlations between HOA magnitude and axis and straylight, visual acuity, and contrast sensitivity, but there was no discernable pattern that supported previously reported trends.

It has been reported that straylight and aberrations interact (Artal 2014), but this body of work used adaptive optics to induce only spherical aberration (Pérez, Manzanera, Artal 2009) as opposed to our study which examined the connection between a subject's full spectrum of habitual aberrations and straylight. It may be that these interactions are more nuanced and the role of higher order aberrations must be studied on an individual basis (Applegate, Khemsara, Sarver 2001).

A study showed that reducing spherical aberration in intraocular lenses reduces subjective glare and improves contrast sensitivity in patients who have undergone cataract surgery (Casprini et al. 2005). Studies also show that the increase in higher order aberrations after laser in situ keratomileusis (LASIK) and orthokeratology are accompanied by a decrease in contrast sensitivity (Yamane et al. 2004, Hiraoka et al. 2007). In normal eyes like with our study population, Oshika et al. found a significant correlation between contrast sensitivity and coma, but reports a low R^2 value which lead them to conclude that contrast sensitivity is multifactorial. We did not find a connection between coma and contrast sensitivity, but our conclusion is largely the same given the sporadic nature of the correlations we did identify (Oshika et al. 2006).

Regarding aberrations and visual acuity, it has been established that increasing the overall amount of aberrations degrades visual acuity (Applegate et al. 2003). It has also been shown that subjects with normal VA have a normal amount, but varied type of aberrations (Villegas, Alcón, Artal 2008). This could explain why there was little correlation between aberrations

and visual acuity in our study because we had a homogenous subject population who were all correctable to at least 20/25 (+0.1 logMAR). Neural adaptation to individual aberration patterns has also been proposed as an explanation for why varied aberrations can yield different levels of visual acuity which we attempted to assess by calculating the NTF (Artal 2014).

Objective III. A large intersubject variability was observed in NTF ratio in response to glare. The majority of subjects demonstrated a degraded performance as measured by the NTF ratio in the presence of glare, but not all. To ensure this was not an effect from having the subjects perform the experiments uncorrected, additional analysis was performed between the NTF and CSF integral ratios. There was an effect on the CSF from the uncorrected refractive error, but there was no effect of uncorrected refractive error on the NTF. This suggests the improved ratios in the NTF and CSF integral ratios were likely due to a training effect in the subjects. The Takagi CGT always presents the "without glare" condition before the "with glare" condition for all three trials. The software does not allow for randomized trials.

In a direct comparison of NTF integral ratio and CSF integral ratio, the two data sets were highly correlated suggesting there is not a strong benefit of using the NTF over the CSF as a metric of visual quality in general. The NTF may be better at separating out individual differences between subjects because of the larger scale and may be a better metric to help predict individual preference.

A limitation of this study is that patients were uncorrected during all measurements, but the visual acuities to which the measurements were compared was the best corrected visual acuity. This choice was made to avoid introducing uncontrolled variables in the form of patient's habitual correction (contacts and glasses of unknown material, index, and coatings) which could have biased the measurements of contrast sensitivity and glare sensitivity. This means the lower order aberrations which tend to be larger in the age range of our study population were corrected for the visual acuity measurements, but not for contrast sensitivity, straylight, or higher order aberration measurements, confounding analysis. It is possible more trends would emerge if we compared uncorrected acuity or lower order aberrations with contrast sensitivity and straylight in this age group, but more analysis is needed to test this hypothesis.

A second limitation is that all of the subjects were correctable to at least 20/25 and the subjects in general were a homogenous group. It was important for us to first establish these methods in normal subjects, but it would be interesting to repeat this analysis with more diverse groups. Recently, one study reported that luminance affects both optical and neural metrics and that factoring in a neural component improved accuracy of predicting visual acuity in older patients (Hastings et al. 2020). In the future, we propose examining how the correlations discussed here change when comparing this first data set to presbyopic subjects, normal subjects in varied luminance levels, or subjects known to have a higher level of aberrations as with keratoconus. Given the bias introduced by the training effect on the CSF measurements, we did not try to correlate our NTF calculations with visual acuity. This would be interesting to do in a new study with a randomized order of CSF measurements.

Chapter 5: Bibliography

Antonisamy B, Premkumar PS, Christopher S. Principles and practice of biostatistics. New Delhi: Elsevier; 2017.

Applegate R, Khemsara V, Sarver E. Are All Aberrations Equal? Optometry and Vision Science. 2001 Dec;78(Supplement):234.

Applegate R, Ballentine C, Gross H, Sarver EJ, Sarver CA. Visual Acuity as a Function of Zernike Mode and Level of Root Mean Square Error. Optometry and Vision Science. 2003;80(2):97-105.

Artal P. Optics of the eye and its impact in vision: a tutorial. Advances in Optics and Photonics. 2014 Sep 30;6(3):340.

Bach M. Freiburg Visual Acuity & Contrast Test – Homepage [Internet]. Home. [cited 2021May20]. Available from: https://michaelbach.de/fract/

Campbell FW, Green DG. Optical and retinal factors affecting visual resolution. The Journal of Physiology. 1965 Dec 1;181(3):576-93.

Casares-López, M., Castro-Torres, J.J., Martino, F. *et al.* Contrast sensitivity and retinal straylight after alcohol consumption: effects on driving performance. Sci Rep. 2020; 10: 13599.

Casprini F, Balestrazzi A, Tosi GM, Miracco F, Martone G, Cevenini G, Caporossi A. Glare disability and spherical aberration with five foldable intraocular lenses: a prospective randomized study. Acta Ophthalmol Scand. 2005 Feb;83(1):20-5.

Dai G-ming. Wavefront optics for vision correction: Guang-ming Dai. Berlingham, Wash: SPIE; 2008.

Hastings GD, Marsack JD, Thibos LN, Applegate RA. Combining optical and neural components in physiological visual image quality metrics as functions of luminance and age. J Vis. 2020 Jul 1;20(7):20.

Hiraoka T, Okamoto C, Ishii Y, Kakita T, Oshika T. Contrast sensitivity function and ocular higher-order aberrations following overnight orthokeratology. Invest Ophthalmol Vis Sci. 2007 Feb;48(2):550-6.

Koh S, Maeda N, Ikeda C, Asonuma S, Ogawa M, Hiraoka T, Oshika T, Nishida K. The Effect of Ocular Surface Regularity on Contrast Sensitivity and Straylight in Dry Eye. Invest Ophthalmol Vis Sci. 2017 May 1;58(5):2647-2651.

Łabuz G, López-Gil N, van den Berg TJTP, Vargas-Martín F. Ocular Straylight with Different Multifocal Contact Lenses: Optometry and Vision Science. 2017 Apr;94(4):496–504.

Lorente-Velázquez A, Nieto-Bona A, Collar CV, Mesa AG; Straylight and Contrast Sensitivity After Corneal Refractive Therapy, Ophthalmol. Vis. Sci. 2011;88(10):1245-1251.

Martin JA, Roorda A. Predicting and Assessing Visual Performance with Multizone Bifocal Contact Lenses: Optometry and Vision Science. 2003 Dec;80(12):812–9.

MathWorks [Internet]. Reference List - MATLAB & Simulink. [cited 2021May20]. Available from: https://www.mathworks.com/help/referencelist.html?type=function

Michael R, Guevara O, de la Paz M, Alvarez de Toledo J, Barraquer RI. Neural contrast sensitivity calculated from measured total contrast sensitivity and modulation transfer function. Acta Ophthalmologica. 2011 May;89(3):278–83.

OCULUS, Inc. (2018). C-Quant: Instruction Manual. Arlington, WA.

Oshika T, Okamoto C, Samejima T, Tokunaga T, Miyata K. Contrast sensitivity function and ocular higher-order wavefront aberrations in normal human eyes. Ophthalmology. 2006 Oct;113(10):1807-12.

Paz-Filgueira C, Colombo EM. Quantifying the effect of straylight on photopic contrast sensitivity. J. Opt. Soc. Am. A 2018; 35(7):1124-1130.

Pérez GM, Manzanera S, Artal P. Impact of scattering and spherical aberration in contrast sensitivity. Journal of Vision. 2009 Mar 1;9(3):19–19.

Rozema JJ, van den Berg TJTP, Tassignon M-J. Retinal Straylight as a Function of Age and Ocular Biometry in Healthy Eyes. Investigative Ophthalmology & Visual Science. 2010 May 1;51(5):2795.

Takagi Seiko Co.,LTD. (2000). CGT-1000: Instruction Manual. Japan

Thibos LN, Hong X, Bradley A, Applegate RA. Accuracy and precision of objective refraction from wavefront aberrations. Journal of Vision. 2004 Apr 23;4(4):9.

United Nations Department of Economic and Social Affairs, Population Division. World Population Ageing, 1950-2050. New York: United Nations; 2017.

van den Berg TJTP. The (lack of) relation between straylight and visual acuity. Two domains of the point-spread-function. Ophthalmic and Physiological Optics. 2017 May;37(3):333–41.

van der Meulen IJE, Gjertsen J, Kruijt B, Witmer JP, Rulo A, Schlingemann RO, et al. Straylight measurements as an indication for cataract surgery. Journal of Cataract & Refractive Surgery. 2012 May;38(5):840–8.

Villegas EA, Alcón E, Artal P. Minimum amount of astigmatism that should be corrected. Journal of cataract and refractive surgery. 2014 Jan 31;40:13–9.

Villegas EA, Alcón E, Artal P. Optical Quality of the Eye in Subjects with Normal and Excellent Visual Acuity. Invest Ophthalmol Vis Sci. 2008 Oct 1;49(10):4688–96.

Yamane N, Miyata K, Samejima T, Hiraoka T, Kiuchi T, Okamoto F, Hirohara Y, Mihashi T, Oshika T. Ocular higher-order aberrations and contrast sensitivity after conventional laser in situ keratomileusis. Invest Ophthalmol Vis Sci. 2004 Nov;45(11):3986-90.

Appendix I: Summary Statistics

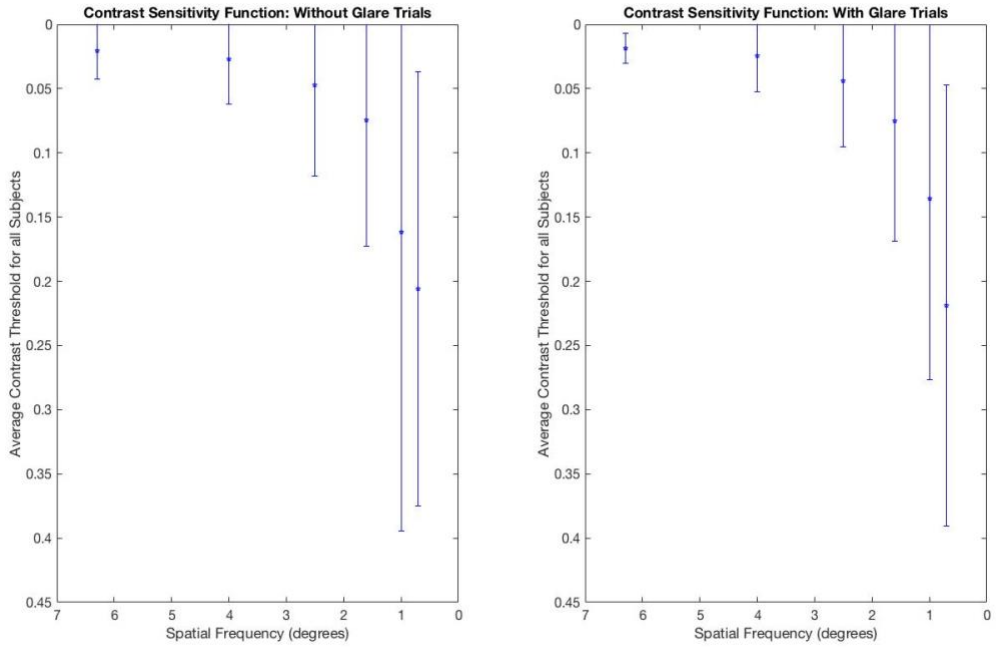


Figure 11. Average of all subject contrast sensitivity functions. The left panel is the average contrast sensitivity function of all 46 subjects measured in the absence of glare. The right panel is the average contrast sensitivity function of all 46 subjects measured in the presence of glare. In both panels, spatial frequency, in degrees, is on the x axis and the average contrast threshold is on the y axis. Error bars represent the large inter-subject variability.

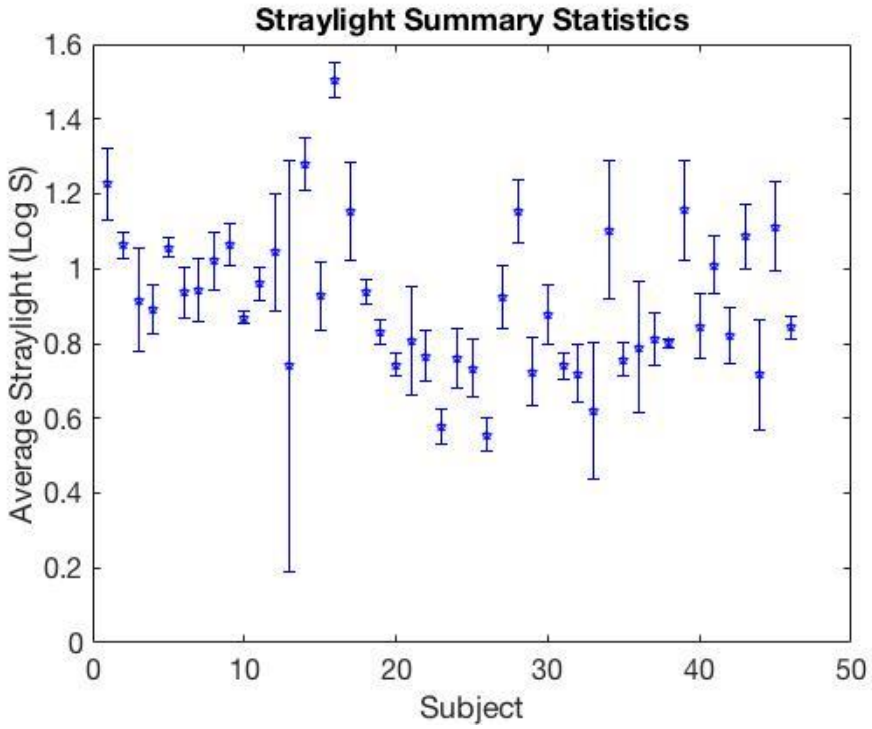


Figure 12. Straylight summary statistics. Subject number is on the x axis. Average straylight value of the three trials for each subject is on the y axis in Log(s). Error bars illustrate intra-subject variability. A small error bar indicates the subject's straylight values were repeatable. A large error bar indicates variability among the here trials.

Appendix II: Final Notes

For completeness, a direct comparison between contrast sensitivity and visual acuity is included here. There was a significant correlation between contrast sensitivity measured with glare and corrected visual acuity (P=0.03), but it was a weak correlation (R=0.32). This is consistent with previous literature in which visual acuity is weakly correlated with contrast sensitivity. The subjective perception of visual quality is often worse than what is objectively measured by visual acuity when glare is introduced.

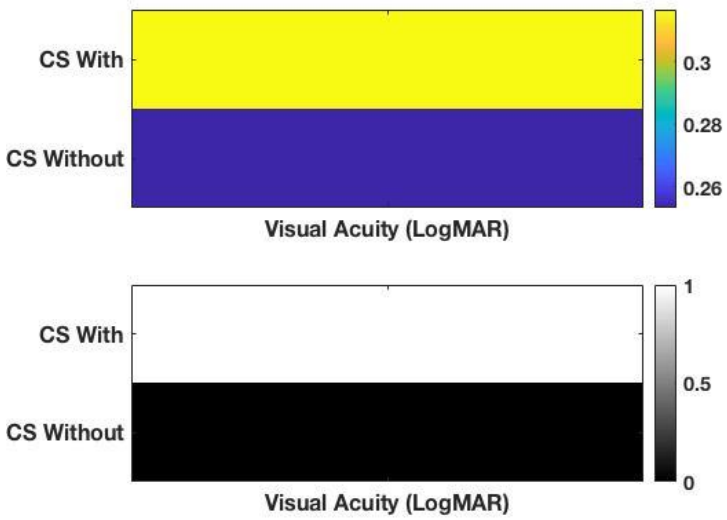


Figure 13. A comparison between visual acuity and contrast sensitivity with and without glare. The top box is a correlational analysis of visual acuity and contrast sensitivity with and without glare. Corrected visual acuity is on the x axis and was measured on a FrACT electronic chart in logMAR. The condition to which the measured visual acuity is correlated is on the y axis. "CS With" is contrast sensitivity measured with glare present. "CS without" is contrast sensitivity measured without glare present. The colored bar represents the correlation coefficient with yellow being the strongest positive correlation and blue being the weakest. The bottom box represents the p value from a t test between visual acuity and contrast sensitivity. White boxes are < 0.05 and considered significantly correlated. Black boxes are not significant.