Study Title: Neurolens and Contact Lens Discomfort

Study Site: The Southern California College of Optometry at Marshall B. Ketchum University
Ketchum Health: 5460 E La Palma Ave, Anaheim, CA 92807

PROTOCOL & CLINICAL TRIAL OUTLINE: Neurolens and Contact Lens Discomfort
NCT05801991
Principal Investigator: Erin Rueff, OD, PhD
Document Date: 3/10/2025

Background & Rationale

Discomfort is the primary reason for contact lens dissatisfaction and discontinuation.[1-3] Symptoms of contact lens discomfort are often attributed to dryness; however, severity of dry eye and discomfort symptoms is not correlated with clinical dry eye severity.[4, 5] When clinical signs of contact lens discomfort and dryness misalign with symptom severity, the possibility of an under-recognized etiology must be considered.

Symptoms associated with contact lens discomfort are similar to symptoms reported with binocular vision disorders and accommodative and vergence strain.[6] Eyestrain, fatigue, and increased/more frequent end-of-day symptoms are noted by patients in both groups of conditions.[6] It has been reported that uncomfortable contact lens wearers have an unusually high prevalence of binocular vision disorders and clinical signs.[6] Basic optical calculations show that myopes must converge and accommodate more when corrected with contact lenses versus spectacles,[7] so it is reasonable to hypothesize that a myopic contact lens wearer may experience eyestrain and discomfort associated with vergence fatigue while wearing contact lenses, but not while wearing single vision spectacles.

neurolens® is a type of spectacle lens that uses contoured prism to alleviate vergence demands and fatigue at near and, therefore, encourages comfortable vision.[8] This spectacle design uses the neurolens® Measurement Device (nMD) to measure eye alignment and determine the spectacle lenses that are uniquely designed for each wearer.[8] Acknowledging that some amount of contact lens discomfort may be caused by vergence fatigue, it is possible that uncomfortable contact lens wearers who wear neurolens® over their contact lenses will achieve discomfort relief.

Objective & Hypothesis

The objective of this study is to determine how neurolens® influences contact lens discomfort in uncomfortable myopic soft contact lenses wearers. We hypothesize that uncomfortable soft contact lens wearers are experiencing some level of discomfort associated with increased vergence demand when looking at near targets and will experience discomfort relief when wearing neurolens® over their habitual soft contact lenses. Uncomfortable, myopic soft contact lens wearers will be recruited. Each participant will be masked and randomly assigned a placebo pair of spectacles or a neurolens® spectacle pair for approximately one month.

Study Design

A prospective, randomized clinical trial will be performed. Participants and investigators will be masked to the treatment.

Sample Size

This is the first study to explore the relationship between contact lens discomfort and neurolens® correction. The nature of this study is, therefore, exploratory and the data and results collected will be pilot in nature. A reasonable sample size goal has been determined to be 30-60 total participants (15-30 per treatment group).

Primary Outcome Variable

The primary outcome variable will be change in contact lens discomfort, as measured by the Contact Lens Dry Eye Questionnaire-8 (CLDEQ-8).[9, 10]

Secondary Outcome Variables:

Secondary outcome variables will be change in symptoms scores measured on the Convergence Insufficiency Treatment Trial (CISS), Headache Impact Test (HIT-6), and the Standard Patient Evaluation of Eye Dryness (SPEED).[11-13]

Inclusion Criteria & Study Procedures:

Table 1 lists all study inclusion and exclusion criteria. Figure 1 outlines the general flow of the study design.

Study Materials

The neurolens® Measurement Device (nMD2; neurolens, Inc. Costa Mesa, CA) and the neurolens spectacle lenses are Class 1 Medical Devices (exempt).

The nMD2 is a desktop diagnostic instrument. The following is the description provided in the manufacturer's nMD2 Users Manual:

> The nMD2 is a microprocessor-controlled system used to measure eye misalignment at distance and near. Eye misalignment is measured through a dissociative test where the eyes are shown independent non-fusible targets, and direction of gaze is measured. This measurement is combined with an associative test where peripheral fusion is attained, and central alignment is measured. Effectively this measurement of eye alignment is an objective measurement of the angle of strabismus, and/or an evaluation of binocular vision.
>
> The nMD2 uses an eye tracking system along with a stereoscopic display to measure eye alignment at distance and at near. From this information, a nMD2 number is calculated which is to be used along with other clinical assessments in the diagnosis and management of visual disorders.

The neurolens spectacle lenses include a proprietary contour prism design that provides the patient with increasing prism from the distance to near portion of the lens. The prism value used in this study will be determined using the nMD2 device. No significant adverse events/risks are anticipated for any participant who is examined with the nMD2 device.

All other study materials and instrumentation are those that are used in a normal eye examination, including anterior segment slit lamp assessment with sodium fluorescein staining and Schirmer tear volume assessment. No significant adverse events/risks are anticipated for any participant who participates in the study and/or undergoes any study procedures.

Table 1: Inclusion/Exclusion criteria

- Uncomfortable soft contact lens wearers (CLDEQ-8 ≥ 17 points)[10]
- Adult, pre-presbyopic age range (18 – 35 years)
- Visual acuity of 20/25 or better in each eye with habitual contact lenses
- Soft, spherical, single vision soft contact lens wearer:
  *Habitual contact lens sphere power -0.75 D or more myopic
  *Habitual contact lens are spherical design
  *Habitual soft contact lenses are single vision design
  *Valid contact lens prescription at the date of the baseline
- No significant subjective over-refraction in either eye with habitual soft contact lenses
  *Sphere: ≤ 0.50 D myopia, ≤ 0.50 D hyperopia
  *Cylinder: ≤ 0.75 D
- No history of ocular surgery
- No history of ocular disease, amblyopia, strabismus, or vision therapy
- No history of neurolens or prism spectacle correction
- No history of significant vertical phoria or vertical phoria correction
- No current ocular medication use
- No significant signs of dry eye in any eye:
  *≤ Grade 1 ocular surface staining[14]
  *Schirmer score ≥ 7 mm[15]
  *Tear break-up time ≥ 7 seconds[15]
- Appropriate fit and surface of habitual soft contact lenses:
  *Sufficient movement, centration, and coverage
  *No significant lens deposits
  *No signs of corneal or conjunctival contact-lens related complications
- Valid measurement on the neurolens® Measurement Device (nMD2)
  *A numerical neurolens value
  *Acceptable Measurement Quality Index (MQI)
  *No low MQI (<0.8) or convergence excess

Participant Screening

Potential participants in the MBKU community will be contacted via email and print advertisements. Participants will contact an investigator by phone, email, or QR code (contact information will be included in the email/flyer) to determine if they may qualify based on basic inclusion criteria including the CLDEQ-8 survey. The intended population that will be recruited are members of the MBKU community (students, faculty, staff) via MBKU email addresses (anyone with email address). Please see the Protocol for more details on recruitment. Interested participants will be instructed via printed and emailed advertisements to contact study coordinators via email, phone, and/or QR code as described below:

If potential participants contact study coordinators by email, study coordinators will call the interested participant and perform screening over the phone. The CLDEQ-8 will be administered verbally to determine initial eligibility, and then all other inclusion criteria that can be verified verbally will be confirmed over the phone. If the participant meets this inclusion criteria screening, they will be invited for a baseline examination.

If potential participants contact study coordinators over the phone, The CLDEQ-8 will be administered verbally to determine initial eligibility, and then all other inclusion criteria that can be verified verbally will be confirmed over the phone. If the participant meets this inclusion criteria screening, they will be invited for a baseline examination.

If potential participants utilize the QR code included on the advertisement, the QR code will lead them to an online version of the CLDEQ-8 that the potential participant will complete. If their score qualifies them for the study, they will be instructed to contact study coordinators via phone or email. The study coordinators will then complete screening as described above.

The score obtained on the pre-screening CLDEQ-8 will not be used in the study.

Baseline Examination, Participant Enrollment, & Randomization

The baseline and enrollment examination is expected to last approximately one hour. At the baseline examination, all inclusion criteria will be confirmed again. Informed consent and HIPAA forms will be distributed to and signed by each participant. Participants will be asked to bring a copy of their current contact lens prescription and/or the boxes/blister packages of their current contact lenses to confirm prescription information.

Visual acuity will be measured monocularly with the habitual soft contact lenses at distance (approximately 6 meters) with a high contrast Snellen chart. Subjective over-refraction will be performed using a phoropter. These measurements will not influence eligibility for study inclusion. The CLDEQ-8, CISS, HIT-6, and SPEED questionnaires will be administered on an iPad.

The fit of the habitual soft contact lenses will be assessed with a slit lamp. The lenses will be removed and the patients will wait approximately ten minutes to allow the tear film to equilibrate. The neurolens® Measurement Device will then be used to obtain objective binocular vision measurements while the contact lenses have been removed, the tear film has equilibrated, and before topical fluorescein has been instilled. Topical fluorescein will be instilled to measure ocular surface staining and tear break-up time. General corneal, conjunctival, and anterior segment health will be assessed in the slit lamp. Schirmer

strips will be instilled in the lower temporal canthus of the right eye for five minutes to determine Schirmer score.

Once all inclusion criteria have been confirmed, participants will be enrolled and assigned to a treatment group. Participants who do not meet all inclusion criteria will be excused from the study and compensated for their time ($50). Participants who meet all inclusion criteria will be informed that they will receive their study compensation ($100) upon completion of the study at the final visit.

Randomization to treatment group will be achieved using an online random number generator to determine the order of allocation (1:1) before subject enrollment. Participants will be enrolled and assigned to a treatment group in the order they qualify for enrollment at the baseline examination.

Enrolled participants will be provided with a $100 credit card cash gift card to offset the cost of spectacle frames that can be purchased at the Ketchum Health University Eye Center Optical, or they can provide their own spectacle frame. Once a frame has been identified, it will be sent to the neurolens® lab for fabrication and placement of lenses depending on treatment group assignment. Participants in the placebo group will receive single vision plano lenses. Participants in the neurolens® group will receive lenses based on the measurements made by the neurolens® Measurement Device.

Participants will be contacted when their completed spectacles have arrived. At pick-up, each participant will be instructed to wear the spectacles full time over their habitual contact lenses. At this time, they will schedule the final study visit 35 ± 5 days after spectacle pick-up.

Final Examination

The final examination is anticipated to last approximately 30 minutes. At the final examination, participants will be instructed to return wearing their habitual soft contact lenses and the spectacles dispensed at the last visit. Visual acuity will be measured monocularly with the habitual soft contact lenses and study spectacles at distance (approximately 6 meters) with a high contrast Snellen chart. The spectacles will be removed and repeat measurements will be taken using the neurolens® Measurement Device. Participants will complete the CLDEQ-8, CISS, HIT-6 and SPEED surveys. Participants will be asked to report approximately how many hours per day and days per week they wore their contact lenses, and the same parameters for their time wearing the contact lenses with the study spectacles over the last 35 ± 5 days.

After all measurements and surveys have been completed for all subjects, participants will be unmasked to the treatment group they are in. Both groups will be able to keep the spectacle lenses dispensed in the study, will be compensated for their time at both visits ($100), and will be dismissed from the study.

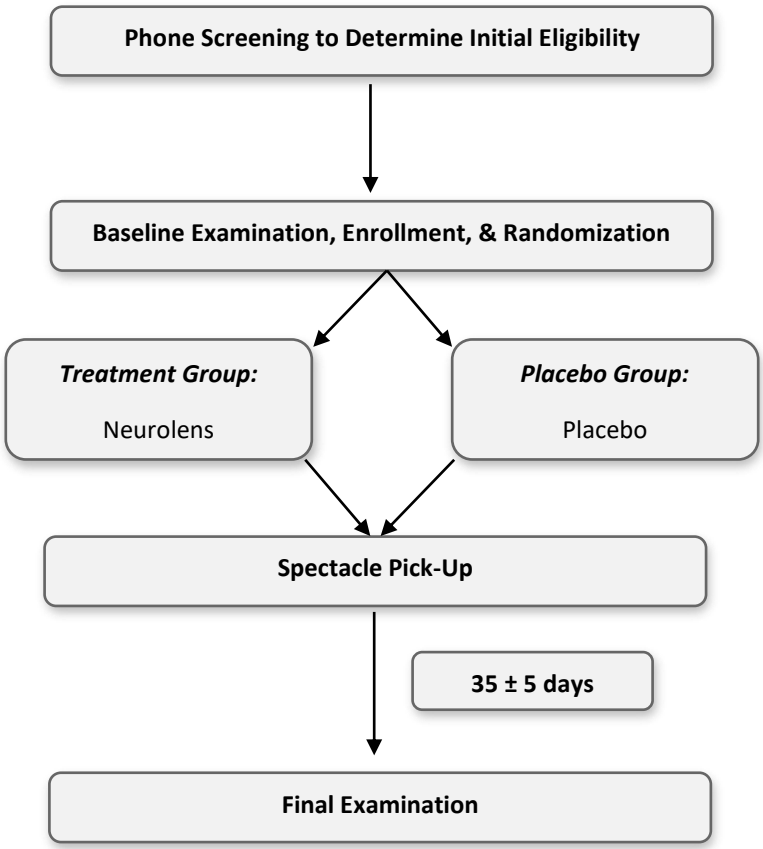

Figure 1: Flow chart of study procedures

Informed Consent and Patient Privacy

Upon arriving at the baseline examination visit, all participants will sign an informed consent form. The form will explain the purpose of the study, any anticipated risks/benefits, and the rights the participant has. Each participant will be able to ask investigators questions and keep a copy of the informed consent form. As well, all participants will sign a Health Insurance Portability and Accountability Act (HIPAA) explaining that their health information is private and any personal health identifiers collected in the study will not be used in association with their identity and/or for any other purpose. Additionally, all participants will read and sign the MBKU COVID research consent document.

Statistical Analyses

Statistical analyses will be performed to compare the survey scores of the two treatment groups before and after treatment. ANOVA and/or Wilcoxon Rank testing will be used depending on the distribution of the data according to Shapiro statistics. Additional analyses will also be performed to determine if particular demographic information (gender, age, etc.) and/or clinical data (refractive error, wear time, etc.) influenced symptom changes as measured by the four surveys administered.

References:

1. Pritchard N, Fonn D, Brazeau D. Discontinuation of Contact Lens Wear: A Survey. Int Contact Lens Clin 1999;26:157-62.
2. Richdale K, Sinnott LT, Skadahl E, Nichols JJ. Frequency of and Factors Associated with Contact Lens Dissatisfaction and Discontinuation. Cornea 2007;26:168-74.
3. Young G, Veys J, Pritchard N, Coleman S. A Multi-Centre Study of Lapsed Contact Lens Wearers. Ophthalmic Physiol Opt 2002;22:516-27.
4. Nichols KK, Nichols JJ, Mitchell GL. The Lack of Association between Signs and Symptoms in Patients with Dry Eye Disease. Cornea 2004;23:762-70.
5. Young G, Chalmers R, Napier L, et al. Soft Contact Lens-Related Dryness with and without Clinical Signs. Optom Vis Sci 2012;89:1125-32.
6. Rueff EM, King-Smith PE, Bailey MD. Can Binocular Vision Disorders Contribute to Contact Lens Discomfort? Optom Vis Sci 2015;92:e214-21.
7. Alpern M. Accommodation and Convergence with Contact Lenses. Am J Optom Arch Am Acad Optom 1949;26:379-87.
8. Neurolens: Technology. http://www.neurolenses.com/technology.
9. Chalmers RL, Begley CG, Moody K, Hickson-Curran SB. Contact Lens Dry Eye Questionnaire-8 (Cldeq-8) and Opinion of Contact Lens Performance. Optom Vis Sci 2012;89:1435-42.
10. Chalmers RL, Keay L, Hickson-Curran SB, Gleason WJ. Cutoff Score and Responsiveness of the 8-Item Contact Lens Dry Eye Questionnaire (Cldeq-8) in a Large Daily Disposable Contact Lens Registry. Cont Lens Anterior Eye 2016;39:342-52.
11. Rouse MW, Borsting EJ, Mitchell GL, et al. Validity and Reliability of the Revised Convergence Insufficiency Symptom Survey in Adults. Ophthalmic Physiol Opt 2004;24:384-90.
12. Yang M, Rendas-Baum R, Varon SF, Kosinski M. Validation of the Headache Impact Test (Hit-6) across Episodic and Chronic Migraine. Cephalalgia 2011;31:357-67.
13. Asiedu K, Kyei S, Mensah SN, et al. Ocular Surface Disease Index (Osdi) Versus the Standard Patient Evaluation of Eye Dryness (Speed): A Study of a Nonclinical Sample. Cornea 2016;35:175-80.
14. Bron AJ, Evans VE, Smith JA. Grading of Corneal and Conjunctival Staining in the Context of Other Dry Eye Tests. Cornea 2003;22:640-50.
15. Sullivan BD, Whitmer D, Nichols KK, et al. An Objective Approach to Dry Eye Disease Severity. Invest Ophthalmol Vis Sci 2010;51:6125-30.