An Exploratory Study on the Use of Hybrid Contact Lenses for Daily Wear Orthokeratology

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An Exploratory Study on the Use of Hybrid Contact Lenses for Daily Wear
Orthokeratology

Abstract
Purpose: This study investigated a novel method of delivering orthokeratology through a comfortable hybrid contact lens worn in the open eye for 4 hours, and compared the effects on the cornea to conventional RGP overnight orthokeratology lens data found in the literature.

Methods: Eight eyes of four subjects wore empirically ordered custom designed orthokeratology lenses in the Eyebrid hybrid lens material for 4 hours during the day while awake. Corneal topography, cornea OCT, and the appearance of the lens and cornea were recorded before and after 4 hours of lens wear. Subjects also gave subjective comfort scores from 0 (unable to tolerate) to 10 (perfect).

Results: Mean amount of corneal flattening was 2.09±1.02D with a mean treatment zone diameter of 1.98±1.01mm. 50% of the lenses were slightly decentered temporally. At least one eye in each subject had central epithelial punctate staining on the cornea after 4 hours of lens wear. Subjects reported a mean comfort rating of 7.25±0.7.

Conclusions: The amount of corneal flattening was comparable to conventional RGP ortho-K lenses, and comfort with the Eyebrid lens was rated as better than initial RGP comfort. This exploratory study may be one of the first to investigate hybrid orthokeratology lenses and its effects on the cornea. This provides the framework for future studies to assess whether orthokeratology can eventually transfer into this lens modality and decrease the number of patients sleeping in contact lenses.

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Committee Chair
Patrick Caroline

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Keywords
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MASTER'S THESIS APPROVAL FORM

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AN EXPLORATORY STUDY ON THE USE OF HYBRID CONTACT LENSES FOR DAILY WEAR
ORTHOKERATOLOGY

By
YUNO IWABUCHI

THESIS
Submitted in partial fulfillment of the requirements for the degree of Master of Science in Vision Science in the College of Optometry, Pacific University
October, 2017

FOREST GROVE, OREGON

MS Thesis Committee:

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AN EXPLORATORY STUDY ON THE USE OF HYBRID CONTACT LENSES FOR DAILY WEAR
ORTHOKERATOLOGY

YUNO IWABUCHI

MASTER OF SCIENCE IN VISION SCIENCE
PACIFIC UNIVERSITY, 2017

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orthokeratology can eventually transfer into this lens modality and decrease the number of
patients sleeping in contact lenses.
Keywords: orthokeratology, hybrid contact lens, myopia control
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INTRODUCTION

Orthokeratology and myopia control

Orthokeratology (ortho-K) is a contact lens method primarily used for correcting myopia, or nearsightedness. Traditionally, this is done using a corneal rigid gas permeable lens (RGP) that fits flat on the cornea to reshape the front surface of the cornea overnight as the patient sleeps in these lenses. The result is a flattened central cornea and a steeper peripheral cornea that takes the shape of a minus-powered lens (thinner in the center, thicker in the periphery), which is the required correction for those with myopia. The RGP is removed in the morning, and the minus-lens shaped cornea allows the patient’s myopia to be corrected for the remainder of the day until the cornea returns to its original shape again. Ortho-K designs have evolved over the years and the modern day ortho-K lens commonly uses a reverse geometry lens design. This consists of a lens with a flatter center, to provide applanation to the cornea, and steeper peripheral curves, to align the contact lens to the peripheral cornea. Since the introduction of reverse-geometry ortho-K lens designs in the 1960s and the FDA approval for overnight orthokeratology in 2002, research interest in orthokeratology has gained popularity.

Myopia is the most common “ocular condition” worldwide, prevalent in up to 90% of the population in some East Asian countries, and that number continues to increase.¹ Myopia is usually due to axial elongation, and while poor visual acuity attributed to myopia can be optically corrected with glasses or contact lenses, it can also pose a risk to ocular health. High myopia above 6 diopters is associated with increased risk factors for ocular pathologies potentially causing blindness, including myopic maculopathy, retinal detachment, posterior subcapsular cataract, and glaucoma.² The risks increase with high degrees of myopia and longer axial lengths.³
The most common application for ortho-K lenses is as the leading method for myopia control in children. It should be noted that the FDA does not currently approve ortho-K for myopia control it is used off-label. As the myopia epidemic continues to increase worldwide, myopia control has been employed to help slow the progression of myopia during childhood years with the goal of preventing children from having high myopia and its associated risks. As children are being diagnosed with myopia at an earlier age, they are predisposed to more severe side effects associated with myopia as they grow older. ³ It is not clearly understood how ortho-K slows myopia progression, but the current leading hypothesis involves the peripheral hyperopic shell and the prolate ocular shape of myopic eyes. ⁴ Myopic eyes have greater relative hyperopia in the periphery compared to the axial refractive error, indicating that the axial lengths of these eyes are longer than the equatorial diameter of the eye, creating a prolate shape. The growth of the eye is advanced by the hyperopic defocus that is created in the periphery. Orthokeratology induces an increase in “myopia” in the mid-peripheral zone of the cornea (steeper than prior to ortho-K), so that light passing through this part of the tissue is focused at a point in the periphery that is closer to the retina than the hyperopic shell. This decreases the relative peripheral hyperopia, and thus helps to eliminate the stimulus for the eye to grow and become more myopic. Studies have shown that eye growth can be slowed up to 55% with orthokeratology. ⁵, ⁶

As a method for myopia control, ortho-K is less invasive than topical atropine, and a better option for those children who are unable to keep their glasses on all day, whether they be single vision or bifocal lenses. The biggest advantage to ortho-K lenses compared to other myopia control methods is that the patient does not have to wear any correction while awake, and the optics needed to correct their myopia are present all day.
The mechanism by which ortho-K lenses achieve corneal flattening is due to the lens profile and the subsequent unequal fluid forces underneath the contact lens. This causes positive and negative pressure fluid forces on the tear film that push and pull on the cornea, respectively. The push force in the center of the cornea provides some applanation and central thinning, ideally leaving about only 5 microns of clearance in the center, but does not have any effect in the periphery. The pull force in the periphery “sucks” the epithelium into the steep reverse curve, but has no effect in the center. These two forces must be combined to achieve the desired ortho-K effect. This is why it is important to have a lens that minimizes fluid exchange. Choo et al. (2008) found there is epithelial cell compression centrally, rather than loss of epithelial cell layers, and elongation of cells in the mid-periphery. They have also proven that central changes are all in the epithelium but mid-peripheral thickening has both epithelial and stromal components.

Current issues with orthokeratology

The literature has shown that orthokeratology is a safe and effective method for delivering myopia control. However, there are issues with the current conventional method of ortho-K using RGP lenses that must be addressed.

The number one issue is that these lenses must be worn in a closed eye environment overnight. This is exacerbated by the fact that the majority of ortho-K patients are young children. Sleeping in contact lenses carries many risks, the most serious being increased opportunities for microbial keratitis. It is estimated that the incidence of microbial keratitis is approximately 7.7 per 10,000 patient-years, and the risk of microbial keratitis in patients that wear overnight orthokeratology is similar to other contact lens modalities worn overnight. Microbial keratitis tends to occur more in children than in adults, with the most common
offending pathogens being *Pseudomonas aeruginosa* and *Acanthamoeba*. 15-17 Watt and Swarbrick (2005) have reviewed the first 50 reports of microbial keratitis in overnight orthokeratology revealed that 60% of the patients affected were between 9 and 15 years old. 18 Watt and Swarbrick reviewed only the first 50 cases and only within the years 2001 to 2005. There are an alarming number of published reports of severe microbial keratitis due to overnight ortho-K, as well as some incidences that may not be published. 19

A retrospective study by Bullimore *et al.* (2013) found that previously mentioned incidence of microbial keratitis increases to 13.9 per 10,000 patient-years when isolated to just the children group. 20 They concluded that overnight wear in any contact lens modality is associated with higher risks for microbial keratitis and corneal infiltrates than daily use lenses. The major findings from their study were written up in patient information packets and package inserts for FDA-approved overnight ortho-K lenses, educating and informing patients of the possible risk for infections and vision loss. Although the incidence is relatively small, the severity of microbial keratitis as well as the target population for most ortho-K fits (children), need to be considered.

Other reports highlight several cases of bacterial corneal ulcers with overnight orthokeratology that eventually lead to corneal scarring and loss of best-corrected visual acuity. 21 Depending on the situation at home, children may be responsible for taking care of their own ortho-K lenses and often are not fully compliant in contact lens hygiene. Ortho-K also flattens the central cornea, thinning the cornea in that area and possibly making it more susceptible for infectious organisms. 14 Sleeping overnight also causes the lack of eye movements from blinking, which prevents the spread of bacterial glycocalyx and lysozymes normally found in the tear film to fight infections. 17 Optometrists are frequently educating their soft contact lens-
wearing patients not to sleep in their lenses, so why is it okay for us to put children to sleep in ortho-K lenses?

Another issue related to conventional RGP orthokeratology is discomfort. Although most practitioners disregard this issue because the patient is asleep in the lenses, there is still discomfort on insertion and lens removal. One study obtained comfort scores for overnight orthokeratology at lens insertion and removal and found that initial discomfort improved over the course of 5-7 days. However, this study included all subjects who were previous contact lens wearers so their data could be limited by previous contact lens experiences or lower corneal sensitivity, compared to children who have never worn contact lenses previously. Any lens discomfort could prevent the child from wearing their ortho-K lenses and hinder their myopia control.

As ortho-K popularity continues to increase, so will the incidences of related complications. For these reasons, practitioners should always be cautious and warn the patient about possible associated risks.

Hybrid contact lenses

Hybrid contact lenses, a rigid lens surrounded by a soft lens skirt, were first introduced in 1983 as a contact lens that would carry the superior optical quality of a rigid lens with the comfort and centration of a soft lens. Soft lenses comprise of 95% of the total contact lens market, dominating due to a major factor over RGP lenses: comfort. Though initially piggyback contact lenses were used, where a soft lens was worn under an RGP lens, the inconvenience of carrying around two different lenses with their respective products became too cumbersome and lead to the development of hybrid lenses. Currently, hybrid lenses are most commonly used as a therapeutic lens and fit for irregular corneas, for example due to
keratoconus or post-surgical corneas. A study conducted by Nau (2008) in keratoconic patients found that an overwhelming majority of the subjects preferred the study hybrid lens to the RGP lens for comfort, and vision was comparable between the two lens modalities.  

**Purpose**

The purpose of this study was to explore a novel method for orthokeratology using a comfortable hybrid lens modality in an open eye environment. By closing off fluid escape to force changes in the cornea more rapidly, corneal modifications are accelerated and can take place without placing the patient to sleep in the contact lenses. To this date, no studies have been completed on hybrid lens orthokeratology. The hope is to have the necessary corneal changes take place fast enough so that patient is able to wear the lenses in an open eye environment for an hour. The ultimate goal is for children to either wear the lenses for about an hour in the evening before going to sleep, or in the morning as they get ready for school.

**METHODS**

**Subjects**

Seven subjects were recruited for this study from the Pacific University College of Optometry student population. Two subjects dropped out after the baseline visit because they moved away from the area and one subject was lost to follow-up after the baseline visit. Four subjects (all female) completed this study. Age ranged from 24 to 25 years. All subjects had less than 6.00 diopters of myopia and less than 1.75 diopters of astigmatism to meet the current FDA requirements for orthokeratology, and were all current soft contact lens wearers. Exclusion criteria included amblyopia, the presence of any corneal pathology, or any other contraindications to contact lens wear, including current ocular inflammations, microbial
infections, severe dry eye, allergies to contact lens products, and non-compliance of proper contact lens care. All participants gave informed consent and participation was voluntary.

Table 1: Overview of all subjects’ sex, age, OD and OS refractive errors.

<table>
<thead>
<tr>
<th>Subject</th>
<th>Sex</th>
<th>Age</th>
<th>OD refractive error</th>
<th>OS refractive error</th>
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<td>1</td>
<td>F</td>
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<td>-1.50-0.50x173</td>
<td>-1.75 DS</td>
</tr>
<tr>
<td>2</td>
<td>F</td>
<td>25</td>
<td>-4.00-0.75x006</td>
<td>-4.25-1.00x165</td>
</tr>
<tr>
<td>3</td>
<td>F</td>
<td>24</td>
<td>-1.75-0.25x138</td>
<td>-2.50 DS</td>
</tr>
<tr>
<td>4</td>
<td>F</td>
<td>24</td>
<td>-3.00-0.75x080</td>
<td>-3.00-0.75x110</td>
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</table>

**Eyebrid Lens**

The hybrid lens used in this study is the Eyebrid silicone hybrid contact lens (Caen, France), a rigid gas permeable (RGP) lens surrounded by a soft skirt. The center RGP material is made of fluoro-silicone-acrylate, with a Dk of 100, diameter 10.0mm, and center thickness 0.20mm. The soft skirt material is made of silicone hydrogel, with a Dk of 50 (water content 50%) and total diameter of 14.9mm. The skirt is available in three base curve radii: 8.9 (standard), 9.2 (flatter), and 8.6 (steeper). All study lenses were ordered in the standard skirt base curve. The two materials are bonded using a double-patented polymeric suture by Eyebrid. The Eyebrid lenses were manufactured for this study by No7 Contact Lens Laboratory (Hastings, UK) using the Chow 5.1 OrthoTool lens design for the RGP center (OrthoTool version 03.19.13). The lens design features a five-curve design, with an optical zone width of 5.2mm in the base curve, followed by a reverse curve width of 0.6mm, a second reverse curve width of 0.7mm, alignment curve width of 0.8mm, and a peripheral curve width of 0.3mm. At each zone, there is clearance of 5 microns at the apex, 77 microns at the first reverse curve, 20 microns at
the second reverse curve, touch at the alignment curve, and 34 microns at the peripheral curve, before joining with the soft skirt (Figure 1).

![Graph showing the lens profiles of the right (top) and left (bottom) RGP centers of the Eyebrid lens using the Chow 5.1 lens design in OrthoTool (version 03.19.13). The tear film volumes under the lens at each zone are also shown in mm.](image)

**Figure 1:**

**Procedure**

Baseline anterior ocular health was examined and corneal topography scans of 8 eyes of 4 subjects were taken with the Medmont E300 corneal topographer. Eyebrid lenses were then empirically ordered for all eyes using OrthoTool (version 03.19.13).

Prior to wearing the study lenses, subjects were instructed to discontinue any contact lens wear for two days in order for the cornea to take its original shape (washout period). The Eyebrid lenses were placed on the unanesthetized eyes and anterior segment OCT scans were taken using the Cirrus OCT from Zeiss of the central 6mm of the cornea as well as the nasal and temporal edges of the lens (Figure 2). Upon dispensing, high molecular weight sodium fluorescein was placed in all eyes and images of the lens were taken with the Haag-Streit BX 900 slit lamp camera under cobalt blue lighting using a Wratten filter (Figure 3). Subjects then
wore the lenses for 4 consecutive hours while awake. After 4 hours, anterior segment OCT and images using the slit lamp were repeated. Subjects were also asked to subjectively rate the comfort of the lens each eye after 4 hours of wear on a scale from 0 (unable to tolerate) to 10 (perfect). The lenses were then removed using a DMV contact lens remover placed at 6 o’clock on the intersection of the two lens materials. After lens removal, corneal topography was taken again and compared with each eye’s baseline values to determine the overall difference in corneal power. Subjects were asked to wear the lenses for 10 consecutive days, returning to the lab on Day 10 to repeat all testing that occurred previously at lens insertion and after 4 hours of wear.

Figure 2: Central cornea 6mm (A), nasal (B), and temporal (C) anterior segment OCT scans taken on a right eye with the Cirrus OCT from Zeiss (Carl Zeiss, Germany) upon initial lens dispensing.

Figure 3: Image of the Eyebrid lens upon initial dispensing on a right eye using the Haag-Streit BX 900 slit lamp camera using cobalt blue and a Wratten filter. The eye is stained with high molecular weight sodium fluorescein.
RESULTS

Eight eyes of four subjects were available for analysis in this exploratory study. All subjects had normal anterior ocular health and showed no corneal staining at the beginning of the study.

Corneal topography and apical corneal power

The axial and tangential display difference maps on the Medmont Studio software for the topographer were used to analyze the corneal topography changes that occurred after four hours of lens wear. The axial display difference map shows the refractive changes that occurred, indicated by the blue treatment zone, which represents that the cornea was flattened between the pre- and post-lens wear maps (Figure 4A; figures from all eyes can be found in the Appendix). The tangential display difference maps indicate the centration of the orthokeratology effect on the cornea (Figure 4B). Of the eight eyes, 4 had orthokeratology effects that were decentered temporally, 3 were centered, and 1 was decentered superiorly. Treatment zones ranged from 0mm to 3.1mm (mean=1.98±1.01mm). Only one eye showed no visible topographic changes. Only one eye had a paracentral flattening effect with a 0.9mm diameter area of steepening in the center, creating a donut-like pattern (Figure 5). Five of the eight eyes showed areas of mid-peripheral steepening, but of those 5, only 2 eyes had a full circle of mid-peripheral steepening.
Figure 4: The axial display (A) and tangential display (B) difference maps on Medmont Studio showing the treatment zone size and amount of refraction change, and the centration of the orthokeratology effect, respectively.

Figure 5: The axial display difference map of an eye showing a paracentral flattening effect in the center of the treatment zone like a donut. The elevation change map on the bottom shows an area of steepening in the center of the “donut” of about 0.9mm.

All eight eyes achieved myopic reduction. The mean baseline corneal power was 44.68±1.47D measured at the apex of the corneas on the topographer. After 4 hours of wear of the Eyebrid lenses in an open eye, the mean apical corneal power flattened to 42.59±2.10D, resulting in a mean reduction of myopia 2.09±1.02D (range from 0.26D reduction to 3.23D reduction). Only one eye achieved less than 1D reduction in myopia.

Table 2 shows mean baseline and post ortho-K apical corneal powers for studies found in the literature that used RGP ortho-K lenses. These values were used as controls and
compared to the mean apical corneal powers found at baseline and after 4 hours of wearing the Eyebrid lens. Figures 6 and 7 show a visual representation of these comparisons. All control studies used a reverse geometry RGP ortho-K lens design. Figure 7 shows the Eyebrid lens performs better in terms of myopia reduction than a majority of the control values and for a shorter amount of wearing time.
Table 2: Mean±SD baseline, post ortho-K apical corneal powers, and mean reduction in myopia with duration and type of ortho-K lens for studies found in the literature.

<table>
<thead>
<tr>
<th>Study</th>
<th>Baseline apical corneal power (mean±SD)</th>
<th>Post ortho-K apical corneal power (mean±SD)</th>
<th>Mean myopia reduction (D)</th>
<th>Duration of ortho-K Wear schedule</th>
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<tr>
<td>Kang et al. 25</td>
<td>43.53±1.92</td>
<td>41.99±1.52</td>
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<td>6 weeks</td>
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<tr>
<td>Chan et al. 26</td>
<td>43.58±1.19</td>
<td>41.02±1.12</td>
<td>2.56</td>
<td>2 weeks</td>
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<td>60 minutes</td>
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<td>Rah et al. 28</td>
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<td>42.08±1.29</td>
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<td>Nichols et al. 29</td>
<td>44.73±1.86</td>
<td>43.90±2.04</td>
<td>0.83</td>
<td>60 days</td>
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<td>Kang et al. 30</td>
<td>43.13±1.30</td>
<td>41.19±1.55</td>
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<tr>
<td>Swarbrick et al. 7</td>
<td>43.08±1.39</td>
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Figure 6: Bland-Altman difference plot comparing baseline and post-lens wear apical corneal powers. Dashed lines indicate limits of agreement ±2SD. Y-axis is the difference in diopters. Negative numbers indicate flattening of the cornea from baseline to post-lens wear.

Figure 7: Scatter plot comparing the mean myopic reduction values from each control study vs. duration of wear in log days.
**Slit lamp findings**

The fluorescein fitting pattern on initial fit, under the cobalt blue filter with a Wratten filter, showed a “bull’s eye” fitting pattern with adequate apical clearance, midperipheral fluorescein pooling, and acceptable peripheral alignment (Figure 8A; figures from all eyes can be found in the Appendix). The Eyebrid lenses after 4 hours of wear showed adequate centration and movement of the lenses. Compared to the images taken at dispense, there was increased central bearing and reduced tear film volume under the reverse curves. Additionally, five out of the eight eyes also showed punctate epithelial staining in the central cornea after 4 hours of wear, ranging in diameter from 1-2mm (Figure 8B). This occurred on at least one eye per subject, and the staining was all subjectively rated as grade 2. Due to this unexpected adverse event, it was decided to discontinue lens wear for all subjects after one day.

![Figure 8: Slit lamp images of the Eyebrid lens on a right eye at dispense (A) and after 4 hours of wear (B). B shows more apical touch with central epithelial punctate staining and less fluorescein pooling in the reverse curve zone.](image-url)
**OCT findings**

Some changes in the lens-cornea fitting relationship were noted on the OCT of the cornea after four hours of wear. On initial lens application, there is a slight bump seen on the posterior surface of the lens near the GP lens-soft skirt junction, which elevates the entire GP portion of the lens away from the underlying cornea (Figure 9; figures from all eyes can be found in the Appendix). Eventually, with blinking and pressure from the upper lid, this bump settles into the corneal epithelium in proper position for orthokeratology to take place. This was seen in the OCT images taken after four hours of wear (Figure 10). All eight eyes showed this change in the lens-cornea fitting relationship over four hours.

![Bump on posterior surface of the lens](image)

**Figure 9:** Anterior segment OCT of the temporal cornea of a left eye at initial lens dispense. The bump is seen on the posterior surface of the Eyebrid lens near the GP-soft skirt junction, elevating the GP portion of the lens off the cornea.

![Bump on posterior surface of the lens](image)

**Figure 10:** Anterior segment OCT of the temporal cornea of a left eye after four hours of lens wear (same eye as Figure 7). The bump is still visible on the posterior surface of the Eyebrid lens but the GP portion of the lens has settled onto the corneal epithelium.
**Comfort**

Comfort ratings ranged from 6 to 8 (mean=7.25±0.7). All but one subject subjectively rated their comfort as symmetrical between the two eyes (Table 3). A study by González-Meijome *et al.* (2011) measuring subjective comfort scores at insertion and removal of conventional RGP ortho-K lenses at 1 day and 1 month found that comfort increased throughout the month for both insertion and removal. They also used a subjective scale from 0 to 10, and found mean comfort scores at insertion of 5.33±2.42 on the first day and 8.02±2.01 at 1 month. Mean comfort scores at lens removal was 6.72±2.79 on the first day and 9.12±0.87 at 1 month.

Table 3: Subjects’ comfort ratings for each eye with the presence or absence of epithelial punctate staining after wearing the Eyebrid lens for 4 hours.

<table>
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<th>Subject</th>
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<th>Left eye</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Comfort (out of 10)</td>
<td>Punctate staining</td>
</tr>
<tr>
<td>1</td>
<td>8</td>
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<tr>
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<td>7</td>
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</tr>
<tr>
<td>3</td>
<td>7</td>
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<tr>
<td>4</td>
<td>8</td>
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**DISCUSSION**

The main purpose of this study was to investigate a new method for delivering orthokeratology through hybrid contact lenses. The goal is to make these lenses comfortable for the patient, while at the same time rapidly changing the cornea profile so that the patient is
able to wear these lenses while awake. Currently, no studies exist in the literature on hybrid orthokeratology lenses.

Though the eventual goal is to have children wear these lenses for only an hour and there is data supporting that corneal changes can take place within 10 minutes\(^{27}\), four hours of wear time was decided for this study.

As mentioned previously, subjects were to wear the lenses for 10 consecutive days, but lens wear for all subjects was discontinued after one day due to grade 2 punctate staining on at least one eye in each subject.

**Corneal topography and apical corneal power**

The corneal topographer showed that 50% of the eyes had treatment zones that were decentered slightly temporally, while 37.5% of the eyes had centered treatment zones. It has been noted in other studies in the literature that ortho-K lenses have a tendency to decenter slightly temporal due to topographical differences in the nasal and temporal cornea.\(^{19}\) It has also been suggested that the variability in eyelid tension while the eye is closed may be related, but does not apply to this study as lenses were worn while awake.

The lack of mid-peripheral thickening of the cornea may affect the desired result for myopia control. Increased plus power in the periphery creates the optical defocus for maximum myopia control effects. As a method for myopia control, enough mid-peripheral steepening did not occur in this study. The lens may have to be worn for a longer amount of time in order to achieve the desired effect, or the lens design may need to be changed.

Only one eye did not show any visible topographic changes on the difference display maps. The central flattening in this eye was measured at the apex as 0.26D. On initial insertion, there was a small 0.5mm bubble present on this eye in the mid-periphery at the 11 o’clock
position. The OCT after 4 hours of Eyebrid wear shows some clearance on the central cornea between the posterior surface of the lens and the corneal epithelium, meaning the lens did not settle into the epithelium. The nasal and temporal OCT scans show the lens has settled into the epithelium in these areas. The lack of myopia reduction in this eye can most likely be attributed to an erroneous fit and the small bubble. This may have prevented the lens from settling into the corneal epithelium and creating orthokeratology changes. This lens should have been removed and reapplied. Subjects at home may be able to view a bubble in their lens without sodium fluorescein depending on its size.

One eye showed a flattening effect, but with an area in the very center that did not flatten as much, which could be classified as a “central island” (Figure 5). This can most likely be attributed to a lens that was fitting slightly too steep to induce total changes across the entire central cornea. These lenses were ordered empirically using baseline measurements, which may not always fit ideally. A cause of this could be an error or failure in the initial baseline topography that the lenses were ordered off of. This area of tissue could just be resistant to change, as it is still flatter than the original cornea but only slightly steeper than the surrounding tissue. These effects usually disappear within a week.

Figures 6 and 7 show that the corneal flattening induced by Eyebrid lenses versus conventional RGP ortho-K lenses is comparable. Figure 6 visually illustrates that the Eyebrid lens performs above average in comparison to literature values for reducing myopia, with one Eyebrid lens data point even being higher than the upper limit of agreement. Figure 7 shows that the mean myopia reduction after wearing the Eyebrid lenses for 4 hours in an open eye environment was better than all but one of the control values, and in a shorter wearing time. The lenses in this study were only worn once. However, it is known through several studies that corneal and refractive changes continue occurring and increasing until reaching stability.
after 7 to 10 nights of wear.\textsuperscript{19} The Eyebrid lenses may further increase myopia reduction with consistent wear, potentially giving those with moderate-high myopia an opportunity to benefit from orthokeratology as well.

**Slit lamp findings**

The changes in the fluorescein pattern seen between initial lens wear and post-4 hours of wear can be attributed to the settling of the lenses into the corneal epithelium. The appearance of a flat-fitting lens after 4 hours of wear is expected as the effects of orthokeratology take place due to flattening of the cornea, leaving only a few microns of clearance between the cornea and the lens.

The finding of the punctate epithelial staining was unexpected. At least one eye in each subject showed staining. Only one subject rated the comfort lower on the eye with staining, otherwise it did not affect comfort. Corneal staining is a common finding reported in patients wearing ortho-K.\textsuperscript{14} If corneal staining is persistent, the ortho-K fit is likely suboptimal and can also be associated with lens adherence to the corneal surface. Subjects only wore the Eyebrid lenses for one day, but the next round of the Eyebrid lens study should have the subjects wear the lenses for multiple days to see if these staining effects recur. Liu and Xie (2016) suggests that corneal staining worse than a Grade 2 necessitates discontinuation of lens wear temporarily to avoid more serious complications such as deep corneal abrasions and ulcers.\textsuperscript{14} Due to this adverse event, our study was discontinued after only one day of lens wear and subjects were sent home with artificial tears. Subjects at home are unable to determine if their cornea is staining without being examined under the slit lamp biomicroscope with cobalt blue and fluorescein.
After corneal staining was found to have occurred on 63% of the eyes, at least one eye on each subject, we drilled three fenestrations into the reverse curve at 3, 6, and 9 o’clock with the hope that increased fluid exchange through the fenestrations would prevent the staining from occurring. 2 of the subjects wore the Eyebrid lenses again for 4 hours with the fenestrations. The fenestrations did not help to eliminate any of the staining after 4 hours of wear so no further data from this trial was obtained. Fenestrations have been used in the past to facilitate fluid exchange to improve issues associated with lens binding. In their study, Cho et al. (2012) found that fenestrations did not affect the ortho-K treatment, nor do they lead to less incidences of lens binding, but less severe incidences of lens binding did occur.

Physiologically, the corneal change taking place that create the ortho-K effect with the Eyebrid lens is most likely due to physical mechanical pushing of the epithelium. This hypothesis would explain the central staining that is present, meaning there is physical touch between the lens and epithelium, rather than 5 microns of clearance that is present with traditional RGP ortho-K lenses, creating a break in the epithelium. It also may be how the corneal apical power can be reduced in a shortened amount of time. The brute force of the lens on the epithelium allows the cornea to be flattened in the center within a matter of hours instead of overnight, but does not create the negative pull force that is required for the mid-peripheral corneal steepening. This is important, as the mid-peripheral effect is the main mechanism behind ortho-K for myopia control.

For the potential application of these lenses being worn in the evening while the ortho-K effect remains overnight and throughout the next day, it is unknown whether the effect will last under a closed lid as the patient is sleeping. Potential interferences include the pressure of the lid on the cornea, as well as the swelling that takes place as the cornea becomes hypoxic.
**OCT findings**

The bump seen on the posterior surface of the lens at the GP lens-soft skirt junction is something that was purposely designed into the traditional Eyebrid lens design, for use in normal myopia/hyperopia/astigmatism, where significant clearance between the posterior lens and the central cornea is desired. The presence of the bump, and therefore the clearance created, means that ortho-K changes on the corneal epithelium cannot take place until the lens settles into the epithelium. This may potentially limit the duration of wear required for a therapeutic effect. It is unknown how fast the Eyebrid lens settles into the cornea, but after four hours of wear, a reduction in clearance can be appreciated in all eight eyes. Only one eye was left with visible clearance after four hours of wear, in which ortho-K changes did not take place in that matter of time, likely due to a bubble leading to an undesired fit.

**Comfort**

One subject rated their subjective comfort asymmetrically between the two eyes, giving a lower rating to the eye that showed epithelial staining on the cornea. All other subjects perceived equal comfort between both of the eyes, even with epithelial staining present on one eye, indicating that the staining did not change the comfort of the lens in a majority of the patients. One subject had epithelial staining on both eyes, yet rated the comfort as 7 out of 10, indicating the patient was not too bothered by it. The ratings are subjective, so it is difficult to compare between subjects, as each subject has a different perception of comfort. Compared to comfort ratings found by Gonzalez-Meijome et al. (2011) for conventional RGP ortho-K lenses on insertion and removal, the Eyebrid lens comfort was better than the conventional lenses on the first day. These comfort ratings improved after 1 month of wear. This trend could indicate that the comfort ratings of the Eyebrid lens would only improve with repeated wear over time.
as well. If initial comfort on Day 1 is higher than in conventional RGP lenses, it could lead to successful wear in more ortho-K patients and less dropout due to discomfort.

**Limitations**

This exploratory study gives us the first insight on how hybrid contact lenses can be applied to deliver orthokeratology treatment. However, there are still many questions left to be answered.

The study had a very small sample size of 4 subjects. This limited proper data analysis to determine whether there was any significance in the comparison versus the control studies.

Rather than using control studies to compare myopic reduction and comfort scores, more subjects need to be recruited to create a control group that wear overnight ortho-K lenses to allow a more reliable comparison with the same instruments being used by the same researcher.

In addition, this study should have had subjects wear the lenses for more than one day as originally planned. If the lenses were worn for at least 7 consecutive days, more data would be available on the time needed for the ortho-K changes to stabilize like the conventional ortho-K lenses do. This would also give a better insight on whether comfort improves with longer wear.

The eventual application for these lenses will be for myopia control in children. However, adults were used in this pilot study to determine if the lenses would have any effect at all. The subjects do not represent the target audience for myopia control.

A useful measurement to conduct in this study would have been a manifest refraction. It has been shown that apical corneal power underestimates the change in the manifest
refraction. Although we know the amount that the cornea was flattened, a manifest refraction would allow us to know how much of the subjects’ refractive error was actually corrected.

Finally, this study did not measure how long the ortho-K effects lasted on the cornea. This would be useful data to have, as a potential application of these lenses is to have patients insert the lens for a few hours of wear in the evening and then remove the lenses before sleeping, correcting their myopia until the following evening.

The lenses for this study had to be designed and manufactured specifically for this purpose. The manufacturer is located overseas in England, but we also had to coordinate with the creator of the lens design software in Australia, as well as the maker of the Eyebrid lens material in France. Once the manufacturer was able to input this new lens design into their computer, they had to obtain the buttons, cut the lenses, and then ship them internationally. This process took longer than anticipated resulting in the dropout of 2 of the subjects.

**Future Studies**

The questions still left unanswered are:

1. How can we eliminate the corneal staining?
2. How fast do the ortho-K effects take place? Can the lenses be worn for less than 4 hours and achieve the same effect?
3. How long does the effect last?
4. How can we achieve mid-peripheral steepening so these lenses are effective for myopia control?

To answer the first question, a second arm of the study is already being planned with an updated lens design. Changes set to take place include fenestrations closer to the center of the lens to eliminate the corneal staining, as well as the removal of the bump on the posterior
surface of the lens so that ortho-K treatment can take effect immediately. In order to adequately compare the Eyebrid lens to traditional RGP ortho-K lenses, the next study should have at least 20 eligible subjects enrolled. Each subject will be randomized to wear the Eyebrid lens in one eye and a conventional RGP ortho-K lens in the other eye for 10 consecutive days. At the baseline examination, topography, slit lamp evaluation, and manifest refraction with best-corrected visual acuity should be completed. On the night prior to Day 1, subjects will wear the RGP in one eye at night and sleep overnight. On the morning of Day 1, the Eyebrid lens should be placed in the other eye for 1 hour in the morning. After one hour of wear of the Eyebrid lens, both lenses are removed at the same time in the morning. On Days 1 and 10, the subjects should come in for testing in the morning to take OCT images of the lenses on the eyes, and then remove both lenses in the lab. Immediately afterwards, corneal topography, manifest refraction, and visual acuity measurements will be taken. On Days 1 and 10, subjects will also come back to the lab 8 hours after the morning measurements to repeat the same tests in order to determine how much regression has occurred during the day. Subjects will also be given a survey to subjectively rate their vision and comfort on a scale of 0 to 10 in each of the lenses for Days 1 and 10. Surveys will be administered 4 times: morning of Day 1 immediately after removing lenses from both eyes, afternoon of Day 1 eight hours after lens removal, morning of Day 10 immediately after removing lenses from both eyes, and afternoon of Day 10 eight hours after lens removal.

To answer the second question, in order to find the most efficient wearing time, at least 10 subjects for three different groups should be recruited. The groups will vary in wearing time: one hour, two hours, and three hours. The data collected should be the same as this pilot study, including topography, OCT, and slit lamp imaging at dispense and removal. The results
can be compared to determine if a wear time of less than 4 hours achieves the same effect on
the cornea.

To answer the third question for determining how long the ortho-K effect lasts, at least
10 subjects should wear the Eyebrid lens for the wearing time determined most efficient. After lens removal, corneal topography should be repeated every hour to determine how fast or slow regression takes place. A second part to this study should include the same subjects wearing the lenses for the specified amount of time in the evening, then returning in the morning to determine the amount of regression that has taken place overnight to determine if lid interference hinders the ortho-K effect during sleep.

In regards to the fourth question, at its current state, the Eyebrid lens for ortho-K is just an effective method for correcting a myopic refractive error in those who do not want to wear glasses or contact lenses during the day, but without any mid-peripheral steepening, does not stand to be useful for myopia control. The current hypothesis is that the ortho-K changes take place due to a physical push on the cornea by the lens, rather than hydraulic push and pull forces at play. It was shown in this pilot study that the Eyebrid lenses in the current design do induce some mid-peripheral steepening, but not to the extent that occurs with traditional ortho-K lenses. To try to answer this question, a proposed change to the lens design would be to use the steeper base curve on the soft skirt in order to tighten the fit of the Eyebrid lens, hopefully closing off fluid exchange even more to achieve the same hydraulic force mechanism as traditional lenses.

Answering the above questions will start to lay the foundation for advancing hybrid ortho-K lens designs and its potential application.
CONCLUSION

This study was conducted to investigate whether orthokeratology could be made more comfortable and rapid to prevent patients from sleeping in contact lenses. The amount of corneal flattening was comparable to conventional RGP ortho-K lenses, and comfort with the Eyebrid lens was rated as better than initial RGP comfort. This study showed that hybrid ortho-K lenses can be designed and successfully worn in an open eye for a few hours with similar results to overnight orthokeratology. However, further research is needed to confirm these findings. This exploratory study may be one of the first to investigate hybrid orthokeratology lenses and its effects on the cornea. This provides the framework for future studies to assess whether orthokeratology can eventually transfer into this lens modality and decrease the number of patients sleeping in contact lenses.

REFERENCES


## APPENDIX A: Results of all 8 eyes

**Corneal topography difference maps**

<table>
<thead>
<tr>
<th>Subject 1 right eye</th>
<th>Axial display</th>
<th>Remarks</th>
<th>Tangential display</th>
<th>Remarks</th>
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</table>
|                     | ![Axial Display](image1) | -2.72D change  
Treatment zone = 2.4mm  
No mid-peripheral steepening | ![Tangential Display](image2) | Decentered superiorly |
| Subject 1 left eye  | ![Axial Display](image3) | -3.23D change  
Treatment zone = 2.1mm  
No mid-peripheral steepening | ![Tangential Display](image4) | Centered |
| Subject 2 right eye | ![Axial Display](image5) | -2.05D change  
Treatment zone = 3.0mm  
Full mid-peripheral steepening | ![Tangential Display](image6) | Centered |
<p>| Subject 2 left eye | -1.16D change Paracentral flattening Treatment zone = 3.1mm Full mid-peripheral steepening | Decentered temporally |
| Subject 3 right eye | -2.77D change Treatment zone = 2.0mm Slight mid-peripheral steepening | Decentered temporally |
| Subject 3 left eye | -1.58D change Treatment zone = 1.1mm Slight mid-peripheral steepening | Decentered temporally |</p>
<table>
<thead>
<tr>
<th>Subject 4</th>
<th>Subject 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>right eye</td>
<td>left eye</td>
</tr>
</tbody>
</table>

- **Subject 4 right eye**
  - Change: -0.26D change
  - Treatment zone = 0mm
  - No mid-peripheral steepening
  - Centered

- **Subject 4 left eye**
  - Change: -2.91D change
  - Treatment zone = 2.1mm
  - Slight mid-peripheral steepening
  - Decentered temporally
### Slit lamp examination

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<thead>
<tr>
<th>Subject 1 right eye</th>
<th>At dispense</th>
<th>Remarks</th>
<th>Post-lens wear</th>
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Nasal:

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