CHECK LIST FOR INVESTIGATOR'S SUBMITTING AN APPLICATION FOR THE INSTITUTIONAL REVIEW BOARD AND/OR THE RESEARCH RESOURCE COMMITTEE REVIEW

☐ *Face page complete*

☐ *Signatures*
- ☐ *Principal investigator*
- ☐ *Faculty mentor, if a Senior Research Project*
- ☐ *Associate Dean*
- ☐ *Assistant Dean for Research*
- ☐ *Service Chief(s), if research involves the Illinois Eye Institute or its patients*
- ☐ *Chief of Staff, if research involves the Illinois Eye Institute or its patients*
- ☐ *Senior Director of Student Development , if research involves students at ICO*
- ☐ *Assistant Dean of Didactic Education, if research takes place in the preclinic lab space*

☐ *Abstract*

☐ *Introduction/Literature Review*

☐ *Summary of Methods*
- ☐ *Description of subjects/study population*
- ☐ *Procedures*
- ☐ *Measurements*
- ☐ *Method of analysis*

☐ *Benefits*

☐ *Risks*

☐ *Alternative Forms of Treatment*

☐ *Consent Forms:*

☐ *Protocol*
- ☐ *1 original with signatures and 1 electronic submission to IRB chair*

For RRC only:

☐ *Pilot Information*

☐ *Budget*

☐ *Justification*

ILLINOIS COLLEGE OF OPTOMETRY
ILLINOIS EYE INSTITUTE
Institutional Review Board

APPLICATION FOR REVIEW AND APPROVAL OF CLINICAL RESEARCH AND INVESTIGATION INVOLVING HUMAN SUBJECTS

All investigators in studies involving human subjects must provide the following information to the Institutional Review Board. Please submit an original and an electronic copy via email of this completed application. The application must be signed by the Principal Investigator, the Associate Dean, the Director of Research, the Service Chief (if the research will take place in a service), the Chief of Staff (if the research is to be conducted in the Illinois Eye Institute (IEI) or use IEI patients, Dean of Student Affairs (if research involves students at ICO), and Chair of Clinical Education (if research takes place in the preclinic lab space). All material relating to the grant application, funding, research protocol and budget must be submitted as well. In addition, any recruitment materials (e-mails, fliers, etc), presentations, surveys, or questionnaires need to be submitted along with the protocol.

Please complete all applicable items. Do not indicate refer to attachment.

Principal/Student Investigator: Jennifer Harthan, Yi Pang

Co-Investigator(s)/Faculty Mentor (required for Senior Research Project): Valerie Kattouf, Janice Jurkus, Angela To
Department/ Service Where Research Will Take Place: Cornea Center for Clinical Excellence
Title of Protocol: Effectiveness of Orthokeratology in Myopia Control

Type of application: (Check ALL that apply)
- x☐ Faculty Development
- ☐ Resident Research Project
- ☐ Corporate Contract
- ☐ Senior Research Project
- ☐ Grant
- ☐ Other _____

Project Period Requested : Start Date: June 1, 2016 Ending Date: 6/1/ 2017
(Not to exceed one calendar year from date of IRB approval)

List All Sites Where Subjects Will Be Examined: Illinois Eye Institute

I certify that the protocol and method of obtaining informed consent as approved by the Institutional Review Board will be followed during the period covered by this research protocol. Any changes to the research protocol will be submitted to the IRB chair for review and approval prior to implementation. I accept responsibility for the ethical and scientific conduct of this research; and assure that all application regulations, by-law's, policies and procedures of the Illinois College of Optometry and the Illinois Eye Institute relative to the protection of human subjects involved in this research will be followed.

_____ _____
Principal/Student Investigator ***Date***

_____ _____
Faculty Mentor (required for Senior Research Project) ***Date***

I. Research Protocol Description:

A. Category of research activity
THE IRB HAS THE RIGHT TO CHANGE THE CATEGORY OF RESEARCH

x☐ **FULL REVIEW - RESEARCH PRESENTING RISK TO SUBJECTS.**

a. Collection of data from children. Exception to this rule is if it involves a file review only.

b. Instillation of anesthetic, dilating, or any other type of drugs into the eye(s).

c. Any procedure that touches the surface of the eye. Common examples of this include, but are not limited to gonioscopy, electroretinography, and contact lens placement.

d. Collection of biological samples in an invasive manner, such as blood samples by venipuncture.

☐ **EXPEDITED REVIEW - RESEARCH PRESENTING MINIMAL RISK TO SUBJECTS.**

a. Collection of biological samples, if non-invasive or if patient care indicates a need for removal or collection.

b. Recording of data from human subjects 18 years or older using noninvasive procedures routinely employed in clinical practice

c. Voice recording made for research purposes such as investigations of speech defects.

d. Moderate exercise by healthy volunteers.

e. Study of existing data, documents, records, pathological specimens or diagnostic specimens.

f. Research on individual or group behavior or characteristics of individuals such as perception studies, cognition, game theory or test development where the investigator does not manipulate subjects and will not involve significant stress to subjects.

g. Research conducted in established or commonly accepted educational settings, normal educational practices, e.g. i) research on regular and special education strategies or ii) research on the effectiveness of or the comparison among instructional techniques, curricula or classroom management techniques.

h. Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behavior unless: i) information obtained is recorded in such a manner that subjects can be identified, either directly or through identifiers linked to the subject, or ii) any disclosure of subject's responses outside the research could reasonably place the subject at risk of criminal or civil liability or be damaging to the subjects financial standing, employability or reputation.

B. Does this research involve the use of Investigational New Drugs(s)? x☐ No ☐ Yes
If yes, Drug Name: Company:
IND Number:
Phase: ☐ I ☐ II ☐ III ☐ IV

C. Does this research involve the use of an Investigational Medical Device? x☐ No
☐ Yes

If yes, Device Name:
Company:
IDE Number:

D. Human subjects from the following population will be involved in this study (Check all that apply):

x☐	Minors (under the age of 18 years)	☐	Pregnant Women
☐	Individuals with mental illness	☐	Prisoners
☐	Individuals with intellectual disability	☐	The Unborn

E. Will a student conduct the research? x☐ No
☐ Yes
If yes, What is student's previous experience?

What is the additional training provided by the faculty mentor, if needed?

Will the student be supervised during invasive procedures? ☐ No ☐ Yes
If no, please provide a detailed explanation as to why.

II. Abstract - Brief (200 words or less) description of purpose, methods, and expectation.

The high prevalence of myopia – especially in Asian countries – is well documented, as are the sight-threatening complications of high or degenerative myopia. Retinal detachment, glaucoma, vitreal degeneration and focal retinal changes may occur secondary to the progressive axial elongation of the eye with age. Specialty rigid lenses have long been shown to lessen this progression in the pediatric population; orthokeratology (ortho-k) lenses are worn at night and change the corneal topography to correct low to moderate amounts of myopia. Most of the studies on orthokeratology were conducted on Asian children. To the best of our knowledge, no study has been done on African American (AA) children. Our project seeks to investigate the efficacy of ortho-k in slowing axial elongation and myopic progression in AA children compared to that in other races.

III. Introduction/literature review: Please describe the research rationale, aim, and hypothesis with relevant background (citing published studies). Also, provide a list of pertinent references.

Orthokeratology (ortho-k), when used for partial or full correction of myopia, has been shown to slow myopic progression in children by 36-56% as compared to their spectacle or contact-lens wearing peers.[1] This effect is achieved by limiting the axial elongation of the eye,[1, 2,3, 4] which is of particular concern in high myopes (>6.00D) and children, where myopic progression has been shown to proceed at a faster rate than average.[1] As early intervention is considered beneficial if not essential, Ortho-k as a treatment modality for diminishing myopic progression has, to our knowledge, been studied mostly in Asian children.

The safety and efficacy of ortho-k as a means of decreasing myopic progression was well established by the Children's Overnight Orthokeratology Investigation (COOKI), who evaluated refractive error, visual changes and ocular health over a period of 6 months in myopic children.[7] The Longitudinal Orthokeratology Research in Children (LORIC) study looked at axial elongation in children as old as 12 years, and found that ortho-k decreased axial elongation by approximately 50% compared to be-spectacled controls.[2] They also noted, however, high variability amongst the children that limits the clinician's ability to predict the outcome of the intervention.[2] The Corneal Reshaping and Yearly Observation of Myopia (CRAYON) study confirmed that patients fit with ortho-k lenses showed less change in axial length and vitreous chamber depth when compared to subjects wearing soft contact lenses.[3] Other more recent studies by Santodomingo-Rubido et al, [7] Kakita et al[4] and Charm et al[1] confirm this decrease in axial elongation using IOL Master measurements.

The most commonly accepted theory on how orthokeratology decreases axial elongation relies on the peripheral defocus created on the retina by the corneal changes made by the rigid lens.[9] Hoogerheide et

al showed that those at greatest risk for myopic progression were those whose peripheral refraction was hypermetropic[10] – that is, they had a hyperopic peripheral 'defocus'. A number of studies have since suggested that treatment approaches to myopia correction should address this peripheral refraction as a means of slowing further axial elongation.[9] When looking at subjects treated with ortho k, we see that the lenses do in fact introduce a peripheral myopic defocus while leaving the central refraction more or less emmetropic.[9] With this study, we hope to expand potential application of orthokeratology to a novel population, AA children.

References

1. Charm, J, Cho P. High Myopia - Partial Reduction Ortho-k: A 2-Year Randomized Study. Optom Vis Sci. 90.6 (2013): 530-539.
2. Cho P, Cheung SW, Edwards M. The Longitudinal Orthokeratology Research in Children (LORIC) in Hong King: A Pilot Study on Refractive Changes and Myopic Control. Curr Eye Res. 30. (2005): 71-80.
3. Walline JJ, Jones LA, Sinnott LT. Corneal Reshaping and Myopia Progression. Br J Ophthalmol 1993. (2009): 1181-1185.
4. Kakita T, Hiraoka T, Oshika T. Influence of Overnight Orthokeratology on Axial Elongation in Childhood Myopia. Invest Ophthalmol Vis Sci. 2011 Apr 6;52(5):2170-4.
5. Loman J, Quinn GE, Kamoun L, Ying GS et al. Darkness and Near Work: Myopia and its Progression in Third-Year Law Students. Ophthalmology. 2002 May;109(5):1032-8.
6. Kinge B, Midelfart A. Refractive Changes Among Norwegian University Students--A Three-Year Longitudinal Study. Acta Ophthalmol Scand. 1999 Jun;77(3):302-5.
7. Walline JJ, Rah MJ, Jones LA. Children's Overnight Orthokeratology Investigation (COOKI) Pilot Study. Optom Vis Sci. 2004 Jun;81(6):407-13.
8. Santodomingo-Rubido J, Villa-Collar C, Gilmartin B, Gutiérrez-Ortega R. Myopia Control with OrthokeratologyContact Lenses in Spain: Refractive and Biometric Changes. Invest Ophthalmol Vis Sci. 2012 Jul 31;53(8):5060-5.
9. Charman WN, Mountford J, Atchison DA, Markwell EL. Peripheral Refraction in Orthokeratology Patients. Optom Vis Sci. 2006 Sep;83(9):641-8.
10. Hoogerheide J, Rempt F, Hoogenboom WP.Acquired Myopia in Young Pilots. Ophthalmologica. 1971;163(4):209-15.

IV. Summary of methods: describe study design by including:
- A. Description of subjects:
  1. number of participants
  2. selection process
  3. inclusion/exclusion criteria
- B. Procedures
- C. Measurements
- D. Method of analysis of data

The study will be a randomized control study using a single-masked design to investigate axial elongation and myopic progression in children wearing ortho-k lenses (study group) versus single-vision spectacles or soft contact lenses (control group) for a period of 24 months. A minimum of 40 and a maximum of 60 subjects will be recruited from patients at Illinois Eye Institute. Once eligibility has been determined by an unmasked observer, patients will be randomly assigned to either the orthokeratology group or the single-vision contact lens /spectacle group.

Patient recruitment: Both research alert and chart review in E.H.R. will be used to help us recruit patients.

Eligible participants will be informed of the benefits and risks of the study both verbally and in writing. Ethics approval will be obtained from the Institutional Review Board at the Illinois College of Optometry. Inclusion criteria include: the subjects, aged from 6 to 13 yeares, must have yearly myopia progression ≤>-1.00 D , with a myopic prescription between -1.00D and -6.00D in at least one eye with refractive astigmatism <1.50D. Visual acuity must be at least logMAR 0.10 (Snellen 20/25) or better at baseline examination in both eyes through best corrected manifest refraction. Ocular examination must not reveal any strabismus,

ocular pathology or contraindications for orthokeratology lens wear, and no ocular trauma history. Subjects must be in good general health with no systemic conditions that might impact their ocular health or refractive error. They must be willing to sleep a minimum of six hours per night. Finally, subjects must be willing and able to present to clinic for all necessary follow-up care. Subjects will be excluded if their prescription falls outside the refractive guidelines, have a history of any type of trauma or ocular surgery, have a history of prior experience with myopia control treatment, are amblyopic or if they are current gas permeable lens wearers. They will be discontinued from the study if they are non-compliant with the treatment protocol or do not achieve a desirable subjective result.

Baseline examination will include measurement of logMAR acuity (monocular and binocular), subjective manifest refraction and auto-refraction (with cycloplegia) with measurement of peripheral refraction, anterior segment evaluation, corneal topography (tangential map recordings, including pupil measurement), IOL Master measurement of axial length and ultrasound pachymetry. Refractions will be performed with a maximum-plus endpoint which gives maximum vision. Objective measurements (including IOL Master, autorefractor and pachymetry) will be taken in triplicate and averaged at both baseline examination and 6-month examination. Cycloplegic measurements will be taken at the baseline, 6-month evaluations, 12-month evaluations, and 24-month evaluations. Measurements will be taken approximately 30 minutes after instillation of drops, in this order; Proparacaine 0.5%, Tropicamide 1%, and Cyclopentolate 1%.

After baseline examination, specialty orthokeratology (Euclid) lenses will be ordered for those assigned to the treatment arm based on topography, non-cycloplegic refraction, pupil size, and horizontal visible iris diameter. Subjects will have a dispensing appointment as well as after-care appointments at 1-day (+/- 1 day), 1-week (+/-3 days), 1-month (+/-1 week), 6-month (+/-15 days), 12-month (+/-15 days), 18-month (+/-15 days), and 24-month (+/-15 days). Lenses and solutions will be provided at no cost to the subject by examiners.

The subjects wearing spectacles will have a baseline examination, and follow up appointment at 6-month, 12-month, 18-month, and 24-month. New spectacle lenses will be provided at no cost to the subject if their current lenses differ from their spectacle prescription (as determined by the examiner) by more than 0.50D in either sphere or cylinder power. Throughout the study, spectacles will also be updated at no cost for every 0.50D change in either the sphere or cylinder measurement. If spectacles are lost or broken, the investigators will cover 50% of the cost of replacement. The same protocol applies for those subjects wearing soft contact lenses.

The principal investigator, co-investigator and supervisor, who will act as unmasked examiners, will collect all examination data except axial length. Masked observers (up to a maximum of 3) will be trained by the principal investigator in the use of the IOL Master and will perform all measurements with the instrument. Objective measurements will be repeated three times and averaged to minimize inter-operator differences. Refractions will be performed at each examination and will follow a specific protocol to generate a balanced, maximum-plus endpoint. All subjects will be required to wear the prescribed treatment every day for the 6-month period under investigation.

Repeated measure ANOVA will be performed to determine if change of refractive error and axial length is different comparing subjects in the ortho-K group vs. ones in the control groups.

V. Describe the potential scientific benefit(s) of the study.

Those with myopia would most immediately benefit from this research. Subjects who were not treated with ortho-k at a young age would benefit from evidence that the lenses are effective in an older population. Another beneficiary would be the segment of the population at highest risk for degenerative changes: those who have high (>6.00 diopters (D)) myopic refractive errors or those whose axial length elongates at a faster rate than average. These subjects would be most poised to benefit from this research, as axial length has been directly linked to increased risk of ocular pathology.

VI. Outline the risks to the subjects and precautions that will be taken to minimize them. Note: risks may extend beyond physical risk and may include psychological, social, and/or financial risk(s)

While orthokeratology is considered to be a safe and effective procedure by the American Academy of Ophthalmology, potential risks include: mild lens binding upon awakening, corneal staining, solution allergy, fluctuating vision, irritation, redness, and in rare cases, corneal infection. To minimize risks, patients will be well educated on proper lens wear and care and will be provided with the appropriate solutions at no cost. Patients will also be given written instructions. Patients will also be seen for frequent follow-up care and will have the 24 hour emergency contact information for the Urgent Care Service at the Illinois Eye Institute.

VII. Describe the methods to be used to insure confidentiality of data.

In order to ensure confidentiality, each subject will be randomly assigned a unique study number. Therefore, all data will be tracked by number rather than by an IEI chart number, name, or initials. Only the researchers will have access to that information. All data throughout the study will be coded using this ID number. The randomized numbers will be kept separate from the data collected.

VIII. All research requires that the subject be aware of the fact that they are participating in a research project. This is accomplished using an Informed Consent Process that includes a verbal and written description of the project and other relevant information. The Consent Form is used for adults (individuals over the age of 18) and children or individuals who are not their own legal guardian (to obtain assent). The form must be written at an eighth grade (or lower) level and fully explained to the research subject. It must also be signed by the research subject, a legal guardian, if necessary, and a witness. Please refer to Handbook For Investigator for specific guidelines to be followed.

A. Consent forms should be attached.
B. Describe the process that will be used to obtain consent, including information on who will obtain the consent, and where and when will it be obtained.

Investigators will consent the parents and children in either pediatric clinic or contact lens clinic.

IX. Please provide additional information that will be beneficial to the IRB.

The following apply to proposals that are being submitted for review by the Research Resource Committee only:

Pilot Study

Certain studies are meant to obtain preliminary information in order to determine if a larger more involved study would be worthwhile. Such studies are considered pilot studies. Sometimes these studies require a minimum budget other times the budget may be quite extensive. The research allocation committee may look at your request in a different manner if your request for funding involves a pilot study. Many of the projects funded are considered to be pilot studies.

X. Budget

In writing research budgets for ICO funding the following factors should be considered.

1. The total faculty research budget is limited. The amount can vary with the academic year. Funding for large projects (generally over $5000) is usually not a possibility. The Research Resource Committee will do its best to support faculty requests on a first come first supported basis. The fiscal year ends on June 30th. Requests for funds should be submitted as early as possible during the academic year. Include all itemized costs for funding. Approved funds not spent by July 1st (end of the academic year) are deposited back to the general fund. A new request will need to be submitted.

2. Certain budget items will not be funded. These include money allocated for salary, travel, long term support for experimental animals or services that could be provided by ICO support or secretarial staff. Payment of human subjects for research projects will be considered on a case by case basis.

Justification

The Research Resource Committee may look at a research project on the basis of its interaction with other ongoing or upcoming faculty projects. Please indicate whether a portion of your budget for items or equipment can be reused for other faculty projects. This may include a project that may be a continuation of the first project or a new project by another faculty member. It is not a requirement that faculty justify their request for funding on the basis of other future research projects. The committee would request that justification be provided for any high priced items and any items listed in the miscellaneous categories.

This study is supported by Wessley Foundation, Euclid, and Bausch & Lomb. Euclid will supply the ortho K lenses. Bausch & Lomb will supply the contact lens solution.

INSTITUTIONAL ENDORSEMENTS

Your endorsement is required to assure the Institutional Review Board (IRB) that you have reviewed this research protocol and approve it for submission, and that this protocol will be supported by your service(s) if approved by the IRB.

_____ _____

Service Chief (if needed) ***Date***

_____ _____

Chief of Staff (if needed) ***Date***

_____ _____

Assistant Dean for Research (required) ***Date***

_____ _____

Associate Dean (required) ***Date***

_____ _____

Sr. Director of Student Dev. (if needed) ***Date***

_____ _____

Asst. Dean of Didactic Education (if needed) ***Date***