Use of a Novel, Objective Optokinetic Contrast Device to Determine Scotopic Range Visual Function and Discriminate between Patients with and Without Glaucoma

NCT02014597

Document Date: March 11, 2020

Compare

Institutional Review Board for Baylor College of Medicine and Affiliated Hospitals

Protocol Number: H-30109
Status: Approved
Initial Submit Date: 4/9/2012
Approval Period: 3/11/2020 - 3/10/2021

Section Aa: Title & PI

A1. Main Title

USE OF A NOVEL, OBJECTIVE OPTOKINETIC CONTRAST DEVICE TO DETERMINE SCOTOPIC RANGE VISUAL FUNCTION AND DISCRIMINATE BETWEEN PATIENTS WITH AND WITHOUT GLAUCOMA

A2. Principal Investigator

Name:	BENJAMIN FRANKFORT	Phone:	713-798-5952
Id:	038374	Fax:	713-798-4364
Department:	OPHTHALMOLOGY	Email:	frankfor@bcm.tmc.edu
Center:		Mail Stn:	NC205

A3. Administrative Contact

Name:	APRIL M LEGER	Phone:	713-798-4123
Id:	044552	Fax:	
		Email:	aharp@bcm.tmc.edu
		Mail Stn:	BCM633

A3a. Financial Conflict of Interest

Does any member of study personnel (Investigator (including investigator's spouse and/or dependent children)) that are involved in the design, conduct, or reporting of the research have a Significant Financial Interest (SFI) that would reasonably appear to be affected by the research for which funding is sought and/or associated with an entity/business that would reasonably appear to be affected by the research?

No

Section Ab: General Information

A4. Co-Investigators

Name:	SILVIA ORENGO-NANIA	Phone:	713-798-5055
Id:	011996	Fax:	713-798-4802
Department:	OPHTHALMOLOGY	Email:	silviao@bcm.tmc.edu
Center:		Mail Stn:	NC205
Name:	SAMUEL WU	Phone:	713-798-5966
Id:	017234	Fax:	713-798-6457
Department:	OPHTHALMOLOGY	Email:	swu@bcm.tmc.edu
Center:		Mail Stn:	NC205
Name:	PETER CHANG	Phone:	713-798-9165
Id:	130181	Fax:	
Department:	OPHTHALMOLOGY	Email:	ptchang@bcm.tmc.edu
Center:		Mail Stn:	NC205
Name:	MARGARET OLFSON	Phone:	713-798-4037

Id:	145118	Fax:	
Department:	OPHTHALMOLOGY	Email:	molfson@bcm.tmc.edu
Center:		Mail Stn:	BCM633
Name:	ROBERT SEILHEIMER	Phone:	713-798-4600
Id:	168183	Fax:	
Department:	STUDENT AFFAIRS	Email:	seilheim@bcm.tmc.edu
Center:		Mail Stn:	BCM368
Name:	MITCHELL WEIKERT	Phone:	713-798-4766
Id:	691429	Fax:	
Department:	OPHTHALMOLOGY	Email:	mweikert@bcm.tmc.edu
Center:		Mail Stn:	
Name:	YVONNE CHU	Phone:	713-798-5077
Id:	691699	Fax:	
Department:	OPHTHALMOLOGY	Email:	ychu@bcm.tmc.edu
Center:		Mail Stn:	NC205
Name:	CAMERON COWAN	Phone:	+41 61 69 78681
Id:	Non-Baylor	Fax:	+41 61 69 73976
Institution:	Friedrich Miescher Institute for Biomedical Research	Email:	Cameron.Cowan@gmail.com
Address:	Maulbeerstrasse 66 P.O. Box 3775 4002 Basel		

A5. Funding Source:

Baylor College of Medicine (Internal Funding Only)

A6a. Institution(s) where work will be performed:

Baylor College of Medicine -- Alkek Eye Center

A6b. Research conducted outside of the United States:

Country:
Facility/Institution:
Contact/Investigator:
Phone Number:

If documentation of assurances has not been sent to the Office of Research, please explain:

A7. Research Category:

A8. Therapeutic Intent

Does this trial have therapeutic intent?
No

A9. ClinicalTrails.gov Registration

Does this protocol/trial require registration on ClinicalTrials.gov due to it: meeting the definition of an Applicable Clinical Trial, being required under the terms and conditions of an award, or being proposed to be published in ICMJE journals?
Yes

Who will be responsible for registering and maintaining the registration of this Applicable Clinical Trial?
The BCM PI will register the trial because either:

- the trial is BCM PI-initiated,
- BCM is the lead site of this multicenter trial, or,
- the industry sponsor has instructed the BCM PI to register the trial, or,
- registration of this trail is required as a term and condition of the reward by the funding agency.

ClinicalTrials.gov Identifier:
NCT02014597

Section B: Exempt Request

B. Exempt From IRB Review

Not Applicable

Section C: Background Information

Glaucoma is the second leading cause of blindness in the world, and estimates for 2010 hold that there are approximately 60.5 million people with either open angle glaucoma (OAG) or angle closure glaucoma (ACG). OAG makes up about 75% of disease and is the most common form encountered in the United States. In the U.S., OAG is a major cause of progressive, irreversible blindness, affecting approximately 2.22 million adults, including 700,000 aged 80 or greater. As the prevalence of OAG increases with age and the overall United States population is becoming older, the number of United States citizens expected to have OAG in 2020 is approximately 3.36 million. There are many known risk factors for glaucoma, but both disease onset and progression are most strongly associated with elevated intraocular pressure (IOP). Accordingly, all accepted treatment strategies center on IOP reduction, and this approach can be a successful management strategy even in cases where the IOP is initially measured in the normal range.

All forms of glaucoma lead to a common phenotypic endpoint of optic nerve cupping (thinning of the neuroretinal rim at the optic nerve head) and progressive functional deficit as measured by psychophysical testing such as perimetry (also known as visual field testing). Typical perimetric changes include an early and mild diffuse loss of retinal sensitivity and a later denser focal loss of retinal sensitivity in classic patterns. Contrast sensitivity is also decreased in early glaucoma, and there is evidence that it is decreased with ocular hypertension (elevated IOP without glaucomatous optic nerve changes) as well. Despite these mild changes in retinal sensitivity, central visual acuity is typically spared in the early and even moderate to advanced stages of the disease. Therefore, the early diagnosis of glaucoma is often circumstantial, based on suspicious appearance of the optic nerve head, and many patients present to an ophthalmologist with advanced disease. Furthermore, perimetry, or visual field testing, is subjective in nature and dependent on patient motor responses (such as clicking a button) in response to specific visual stimuli. In many patients, due to inattention, poor motor coordination, or the length of the test (typically 5-7 minutes of full attention per eye), the reliable and accurate assessment of visual function by perimetry is difficult.

Human disease is characterized by a loss of retinal ganglion cell (RGC) axons and their associated cell bodies in both human cadaveric and animal studies. Currently, it is not known if the observed decrease in retinal sensitivity is caused by RGC death, dysfunction, or both. Animal studies using both genetic and inducible models are similarly inconclusive and have largely focused on anatomic changes rather than functional studies. Details about RGC dysfunction in glaucoma are critical as RGCs represent the final cell type in the retinal signaling network, integrating the various signals from rod and cone photoreceptors via various interneurons including amacrine, horizontal, and bipolar cells. The distinct signaling pathways active under light (photopic) and dark (scotopic) conditions are well-understood. Cones dominate the photopic pathway and signal via cone bipolar cells directly to RGCs. Rods dominate the scotopic pathway and signal via rod bipolar cells to amacrine cells, which indirectly relay the rod-mediated signal to RGCs through cone bipolar cells. There is crosstalk between the two pathways at the level of both amacrine cells and RGCs. Thus, when RGCs are damaged by glaucomatous disease, it is very likely that both cone and rod information is lost.

Ophthalmologists are therefore presented with several challenges: increasing disease burden, the lack of objective assessments of visual function, and the need for improved early disease detection. We have developed a new device which has the potential to help meet all of these significant challenges. This device provides a rapid, automated, non-invasive and purely objective assessment of visual function (specifically contrast sensitivity) under both cone- and rod-dominated conditions. It is potentially able to not only track glaucoma progression over time, but also to detect glaucoma in its very earliest stages. Finally, it is portable, easy to use, and inexpensive. This proposal aims to optimize the testing parameters of this new device, and to determine contrast sensitivity levels under both scotopic and photopic conditions in a normal population and compare this population to patients at risk for glaucoma or with glaucoma as part of a pilot study.

Human studies of glaucoma have focused almost exclusively on photopic (cone) pathways and only very few published manuscripts address rod-mediated scotopic retinal function in patients with glaucoma. In animal models of glaucoma, however, several groups have reported abnormalities in amacrine cell numbers. We have studied single cell electrophysiology in a mouse model for elevated IOP and acute glaucoma. RGC and amacrine cell light sensitivity are both decreased within 1-2 weeks of elevation of IOP and RGC death occurs similarly to that seen in other animal models. Since amacrine cells are the critical relay station of rod cell signaling, these findings support the hypothesis that rod function is also abnormal in glaucoma. Importantly, these early abnormalities in light sensitivity precede overt evidence of RGC structural damage. In human glaucoma, central visual acuity is often preserved in even advanced disease, but many patients have decreased contrast sensitivity thresholds very early in the disease course. This reduction may provide an opportunity to identify patients with early disease. We hypothesize that a similar process occurs in both experimental and human glaucoma, and that patients will display decreased retinal sensitivity prior to large-scale damage to RGCs. Furthermore, we believe that it is possible to detect and measure these early changes in contrast sensitivity in patients at

risk for glaucoma or with very early disease.

The optokinetic reflex (OKR) requires both visual function and cortical function. When presented with a drifting image of sinusoidally modulated gratings, the eye will reflexively track the stimulus (slow phase). At a certain point, the eyes will rapidly re-fixate in the opposite direction (fast phase) and then begin to track again. By adjusting the characteristics of the drifting image, contrast sensitivity thresholds can be measured. Others have attempted to use the OKR under photopic conditions to assess contrast sensitivity thresholds differences between normal patients and patients with glaucoma. These data suggest that it is possible to use contrast sensitivity to distinguish between these groups, but the investigators were restricted by the technologies available at the time and the cumbersome techniques used to track and record OKR-induced eye movements. Our new device takes advantage of a high resolution monitor, real time infrared light eye tracking, and intelligent software that adjusts the monitor-presented sinusoidally modulated gratings in response to patient eye movements to rapidly determine contrast sensitivity levels in 3-5 minutes per eye.

Section D: Purpose and Objectives

This proposal has the potential to define a novel and clinically relevant testing strategy for the diagnosis and monitoring of glaucoma. The strategy is based on the assessment of contrast sensitivity and is objective, rapid, automated, and simple. It has potential utility as a testing strategy to establish a diagnosis of glaucoma very early in the disease process, as well as an alternative testing strategy for those unable to perform standard perimetry. This device can potentially be used to uncover some of the most basic concepts of glaucoma disease by assessing visual function in dark-adapted patients, and to integrate these findings into a comprehensive testing strategy. Furthermore, this device will allow us to explore the limits of human scotopic contrast detection - a topic that has not been previously addressed. Lastly, development of this device as an objective and automated assessment of visual function has many potential benefits beyond the initial scope of this protocol, including: detection of visual function in pre-verbal children, detection of visual function in poorer functioning adults, detection of visual function in stroke victims, and detection of visual function in paralyzed individuals. These just scratch the surface and many situations where the device is useful can easily be imagined.

Section E: Protocol Risks/Subjects

E1. Risk Category

Category 1: Research not involving greater than minimum risk.

E2. Subjects

Gender:
Both

Age:
Adult (18-64 yrs), Geriatric (65+ yrs)

Ethnicity:
All Ethnicities

Primary Language:
English

Groups to be recruited will include:
Both patients and healthy, non-patient, normals

Which if any of the following vulnerable populations will be recruited as subjects?
Employees or lab personnel, Students

Vulnerable populations require special protections. How will you obtain informed consent, protect subject confidentiality, and prevent undue coercion?

In some cases, for the first study of the protocol, lab or clinic staff may be asked to participate or request to participate. All participation will be completely voluntary and there will be no penalties for not participating. There will be no coercion at any point and there will be no benefit, real or implied, in participation.

In some cases, medical or graduate students may be asked to participate or request to participate. All participation will be completely voluntary and there will be no penalties for not participating. There will be no coercion at any point and there will be no benefit, real or implied, in participation.

E3. Pregnant woman/fetus

Will pregnant women and/or fetuses (as described in 45 CFR 46 Subpart B) be enrolled in the research?
No

E4. Neonates

Will neonates of uncertain viability or nonviable neonates (as described in 45 CFR 46 Subpart B) be enrolled in the research?

No

E5. Children

Will children be enrolled in the research?

No

Section F: Design/Procedure

F1. Design

Select one category that most adequately describes your research:

i) Device, Phase I, Single Center

Discuss the research design including but not limited to such issues as: probability of group assignment, potential for subject to be randomized to placebo group, use of control subjects, etc.

This protocol is divided into 2 studies. Study 1 involves the optimization of the device parameters. Study 1 will test adult subjects with no history of ocular disease (Study 1A) to assess the limits of human contrast sensitivity and subjects with definite glaucoma (Study 1B) by gathering preliminary data for comparison. These two pilot sub-studies intend to provide rapid data in regard to the device testing results to support the study hypothesis. This strategy will help rule out false negatives and false positives so that any adjustments can be made prior to the start of Study 2 for longitudinal data collection. Study 2 involves determination of baseline population parameters for an older population more likely to be age-matched with patients with glaucoma, as well as performance of patients with various levels of glaucoma severity.

Enrollment of participants in Study 1B will begin after the first 5 participants have been enrolled and tested in Study 1A. Study 2 will begin after Study 1A and B are complete.

Study 1: 20 adult subjects with no history of ocular disease and 20 adults subjects with definite glaucoma will be recruited to assist with optimization of device parameters. Study 1A: The individuals will not be patients of the co-investigators but rather volunteers who are recruited by word of mouth (co-employees, residents, research staff, etc.) and are willing to volunteer their time to assist in the development of the project. No coercion or implied benefits will be applied to recruit participants (see section E2). Volunteers can be of any age >18, male or female, and must be of self-reported excellent ocular health. Best spectacle corrected visual acuity of 20/40 or better is required (verified by Snellen acuity testing on the day of participation) and the participant must have no reported history of glaucoma, retinal disease, amblyopia, ocular trauma, or ocular surgery of any kind with the exception of refractive surgery (LASIK, PRK, or equivalent). Study 1B: These individuals will be recruited from the Alkek Eye Center patient population with confirmed diagnosis of glaucoma and of any age > 18.

Study 2: Potential subjects will be recruited from the Alkek Eye Center of the Department of Ophthalmology at Baylor College of Medicine and their families we will recruit 100 patients for this study in the following distribution:

1) 20 normal controls age 50 or older

2) 20 patients age 50 or older with ocular hypertension

3) 20 patients age 50 or older who are glaucoma suspects

4) 20 patients age 50 or older with early to moderate glaucoma

5) 20 patients age 50 or older with moderate to advanced glaucoma

Inclusion Criteria:

Normals for Study 1

1. Male or Female

2. age 18 or older

3. Corrected visual acuity 20/40 or better in both eyes.

Normal Controls for Study 2

1. Male or Female

2. age 50 or older

3. IOP 21 or less in both eyes

4. Corrected visual acuity 20/40 or better in both eyes.

Subjects with ocular hypertension

1. Male or Female

2. Age 50 or older

3. Defined as IOP> 21 without medication on two or more clinic visits in one or both eyes

4. Corrected visual acuity 20/40 or better

5. Normal optic nerves

6. Normal automated perimetry in both eyes

Subjects who are glaucoma suspects

1. Male or Female

2. Age 50 or over

3. Increased optic nerve cupping in one or both eyes regardless of IOP

4. Corrected visual acuity 20/40 or better

5. Normal automated perimetry in both eyes

Subjects with early to moderate glaucoma

1. Male or female

2. Age 50 or over

3. Increased optic nerve cupping regardless of IOP in one or both eyes

4. Corrected visual acuity 20/40 or better in both eyes

5. Early to moderate perimetric changes defined as a mean deviation (MD) no less than -7.5 and a pattern standard deviation (PSD) no greater than +7.5 in the worse eye.

Subjects with moderate to advanced glaucoma

1. Male of Female

2. Age 50 or older

3. Increased optic nerve cupping regardless of IOP in one or both eyes

4. Grossly abnormal automated perimetry (MD less than -7.5 or PSD greater than +7.5 in the worse eye)

5. Best-corrected visual acuity of 20/40 or better in both eyes

Exclusion Criteria:

Normal Controls:

1. glaucoma or glaucoma suspicion in either eye

2. IOP > 21 in either eye

3. History of use of IOP-reducing drops in either eye except temporarily following cataract extraction

4. History of any ocular surgery except cataract extraction or refactive surgery (LASIK, ORK, or equivalent) in either eye

5. Retinal disease in either eye

6. Abnormal measured automated perimetry in either eye

7. Abnormal measured contrast sensitivity in either eye

F2. Procedure

The protocol is divided into two studies that will have two separate consent forms (Study 1A and B, and Study 2).

All participants requiring spectacle correction will will use their own glasses or contact lenses or a pair of provided trial glasses (if needed) during the research study.

Study 1: Subjects participating in this portion of the study will attend one single visit:

1) Informed consent will be obtained and inclusion/exclusion criteria will be confirmed. Demographic information, ocular history, refraction, and visual acuity information will be collected for all patients. Additional clinical data will also be collected for Study 1B participants only. Information to be collected will include name, date of birth, ethnicity, gender, ocular history (surgery, etc), type of glaucoma (study 1B), current visual acuity, refraction, central corneal thickness (study 1B), intraocular pressure (study 1B), recent slit lamp exam including lens status (study 1B), recent dilated exam including optic nerve appearance (study 1B), and recent automated perimetry results (Humphrey visual field, study 1B)

2) Snellen visual acuity will be measured while wearing current spectacle correction to ensure acuity of 20/40 or better. The current spectacle correction (refraction) and acuity will be recorded.

3) OKR-based contrast testing will be performed with the OCD - optokinetic contrast device (the device in study with this protocol). Subjects will be shown a brief demonstration of the OCD under infrared light (to begin dark adaptation) to familiarize themselves with the device and the expected testing strategy.

4) Subjects will then be dark adapted for 20-30 minutes. During this time they will be sitting in a darkened room. If the room is not dark enough a loose blindfold may be used. Music options will be available to help pass the time and ease potential discomfort.

5) After 20-30 minutes, the blindfold will be removed (if used) and patient will have monocular dark-adapted (scotopic) testing done with the OCD, left eye followed by right eye. The non-tested eye may be covered during testing. After scotopic testing, the light of the OCD will be increased and light-adapted (photopic) testing will be performed in the same manner.

6) Debriefing. Subjective assessments of the testing modality and dark adaptation process will be collected.

This visit should take approximately 60 minutes to complete.

****

Study 2:

Study subjects participating in this portion of the study will require two study visits.

Potential participants will be approached by the PI to ask if they are willing to participate in this study. If the subject agrees to participate, during their next scheduled clinic visit, the PI will also do a slit lamp examination including lens status using the AREDS 2008 Clinical Lens Opacity Grading Standards in addition to their standard of care clinic eye visit. The slit lamp examination including lens status using the AREDS 2008 Clinical Lens Opacity Grading Standards is the only research related activity in this clinic visit. Potential participants who are the "normals" for Study 2 will be recruited from one of the co-investigator's clinic who is their treating physician. If interested, their physician (co-investigator) will contact the research coordinator to meet or call the patient and explain the study. If he/she agrees to participate, the PI will do a slit lamp examination at their next scheduled visit in the same manner as the other Study 2 participants, except the central corneal thickness will also be determined by ultrasonic pachymetry (standard testing for patients with glaucoma but not normal controls). Data from these clinic visits will be used as baseline information for the study. The baseline clinical and demographic data to be collected in the study will be:

1. Date of Birth 2. Ethnicity 3. Gender 4. Ocular History (surgery, etc) 5. Type of Glaucoma 6. Current visual acuity 7. Refraction 8. Central corneal thickness 9. Intraocular Pressure 10. Slit lamp examination including lens status by methods above 11. Dilated examination including optic nerve appearance 12. Recent automated perimetery results (Humphrey visual field)

Research Study Visit 1 (within 2 months of clinic visit from which clinical data is obtained):

1) Humphrey standard automated perimetry (visual field testing). This is a form of static perimetry used to assess retinal function and sensitivity. It is a commonly used photopic testing modality for the diagnosis and status of glaucoma and used frequently throughout ophthalmology and many ophthalmologic clinical studies. We hypothesize that there will be similarities in performance between Humphrey automated perimetry and OKR testing which will help validate our testing strategy. For patients with glaucoma, for whom visual field testing is frequently performed, this test will not be performed if a high-quality visual field test has been obtained within the last 6 months. For such patients, the visual field test from the

clinical record will be used in the study.

2) OKR-based contrast testing will be performed with the OCD - optokinetic contrast device (the device in study with this protocol). Subjects will be shown a brief demonstration of the OCD under infrared light (to begin dark adaptation) to familiarize themselves with the device and the expected testing strategy.

3) Subjects will then be dark adapted for 20-30 minutes. During this time they may be blindfolded (depending on darkness of the room) and sitting in a dark room. Music options will be available to help pass the time and ease potential discomfort.

4) After 20-30 minutes, the blindfold will be removed (if used) and patient will have monocular dark-adapted (scotopic) testing done with the OCD, left eye followed by right eye. The non-tested eye may be covered during testing.

5) After scotopic testing, the light of the OCD will be increased and light-adapted (photopic) testing will be performed in the same manner.

This visit should take approximately 90 minutes to complete.

Second Research Visit (approximately 1 month after the first research visit):

1) Pelli-Robson Contrast Sensitivity Testing. This is a form of stationary central vision contrast sensitivity that is a commonly used testing modality for photopic contrast in many ophthalmologic clinical studies. We hypothesize that there will be similarities in contrast performance between Pelli-Robson and OKR testing which will help validate our testing strategy.

2) OKR-based contrast testing. This will be performed as in the second visit described above except that the testing order will be the right eye first, followed by the left eye.

3) Debriefing. Subjective assessments of the testing modality and dark adaptation process will be collected.

This visit should take approximately 90 minutes to complete.

For those participating in Study 2, participants will be asked if they will allow the study staff to review their medical records to track clinical outcomes for 5 years. Participants will be asked to allow review of their medical records related to their developing or not developing glaucoma or other eye conditions to collect longitudinal data. This is an optional portion of the test for which they can opt out.

The following information will be re-reviewed: 1. Date of Birth 2. Ethnicity 3. Gender 4. Ocular History (surgery, etc) 5. Type of Glaucoma 6. Visual acuity 7. Refraction 8. Central corneal thickness 9. Intraocular Pressure 10. Slit lamp examinations including lens status 11. Dilated examinations including optic nerve appearance 12. Automated perimetery results (Humphrey visual field)

Section G: Sample Size/Data Analysis

G1. Sample Size

How many subjects (or specimens, or charts) will be used in this study?

Local: 140 Worldwide: 140

Please indicate why you chose the sample size proposed:

Study 1: 20 healthy non-patients and 20 patients with definite glaucoma will offer a very large sample size to optimize testing parameters and provide information about scotopic and photopic range constrast sensitivity in healthy adults. Because of the speed of testing, a moderate sample size is desirable. It is difficult to predict the sample size required since this is a new device and the range of results are unknown. In smaller studies in the laboratory, similar contrast ranges were seen among most test subjects (all of whom were believed to be normal) so a very large normative database is unlikely to be required. As a point of reference, previous studies of optokinetic-based contrast have showed a rather tight range of human performance and have published peer-reviewed studies with fewer than 10 participants. 5 healthy non-patients will be enrolled before the 15 remaining healthy non-patients and the 20 glaucoma patients are enrolled to ensure appropriate procedures are used and to identify any issues yet to be identified. Study 1 subjects may be retested if technical problems are identified with the device.

20 normal patients and 20 participants with definite glaucoma should provide enough of a baseline for the 4 disease groups as the number of participants in each of the disease groups is of relatively large size.

Study 2: 20 participants will be enrolled in each of the five groups described in the Section F2 Procedures section (N=100). If the study team is able to establish intrasubject reliability of testing, the number of subjects needed in Study 2 may be decreased with a future amendment submission.

G2. Data Analysis

Provide a description of your plan for data analysis. State the types of comparisons you plan (e.g. comparison of means, comparison of proportions, regressions, analysis of variance). Which is the PRIMARY comparison/analysis? How will the analyses proposed relate to the primary purposes of your study?

Study 1 and 2: Statistical comparison of the study groups will be performed using a combination of pairwise and multivariate analyses. A sample size estimate is not possible at this time as the ranges of contrast sensitivity are not yet determined due to uncertainty of the testing parameters. The normative database will be critical for the design of larger scale future studies.

The primary expected comparisons are as follows:

Intra-patient:

1) Comparison of scotopic constrast between the two eyes

2) Comparison of photopic contrast between the two eyes

3) Comparison of scotopic to photopic contrast within each eye

4) Comparison of intraocular scotopic to photopic contrast ratio (3 above) between the two eyes

5) Comparison of 1-4 to automated perimetry testing (Study 2 only)

6) Comparison of 1-4 to Pelli-Robson testing (Study 2 only)

Interpatient:

Comparison of 1-6 above among all patients and groups.

For subjects in Study 2, longitudinal data will be collected for 5 years after participation to track clinical progression of glaucoma where present.

Interim analysis will be performed after the first 5 patients of Study 1A have been enrolled to ensure that the device hardware and software are properly functioning.

Interim analysis will be performed after the first 10 patients for both Study 1A and Study 1B have been enrolled to ensure that the device hardware and software are properly functioning .

Interim analysis will be performed after the completion of Study 1 to determine if the study sample size of Study 2 is appropriate.

Section H: Potential Risks/Discomforts

H1. Potential Risks/Discomforts

Describe and assess any potential risks/discomforts; (physical, psychological, social, legal, or other) and assess the likelihood and seriousness of such risks:

Only minimal risk is present as there is a small chance of loss of confidentiality as with any study. Study personnel attempt to minimize this risk.

The only contact the participant has with the device is via the chin rest and forehead rest, which are standard equipment purchased from an ophthalmic device supplier. There is no other contact with the device required.

There is no risk associated with the small infrared (IR) light used in this protocol, A dim LED-generated infrared (IR) light source is used during examination. The amount of light, power and thermal levels emitted from the device used in this study is less than international standards (IEC 60825-1) set for this type of light (IR exempt).

The use of a blindfold during dark-adaptation is potentially uncomfortable. This will be positioned very gently and the ambient light dark as well with music of the participant's choice playing to minimize discomfort. It may be possible to use a patch instead of a blindfold for participants who are particularly uncomfortable, but this will slow the process down slightly.

H2. Data and safety monitoring plan

Do the study activities impart greater than minimal risk to subjects?

No

H3. Coordination of information among sites for multi-site research

Is the BCM Principal Investigator acting as the SPONSOR-INVESTIGATOR for this multi-site research?

No or Not Applicable

Is BCM the COORDINATING CENTER for this multi-site research?
No or Not Applicable

Section I: Potential Benefits

Describe potential benefit(s) to be gained by the individual subject as a result of participating in the planned work.
There is no direct benefit to subjects for their participation in the study.

Describe potential benefit(s) to society of the planned work.
As the OCD is a fully automated and objective device, it may provide a significant improvement in our ability to monitor and diagnose glaucoma. It is also likely to be very helpful in the monitoring of patients with retinal disease, especially in situations where visual acuity is diminished, although this is not being directly assesed in the current proposal. It also may provide an opportunity to assess visual performance in various individuals who are unable to effectively communicate with examiners (children, extreme elderly, stroke victims, ICU patients), although this is not being directly assessed in the current proposal.

Do anticipated benefits outweigh potential risks? Discuss the risk-to-benefit ratio.
There is huge potential benefit with no appreciable risk.

Section J: Consent Procedures

J1. Waiver of Consent

Will any portion of this research require a waiver of consent and authorization?
No

J1a. Waiver of requirement for written documentation of Consent

Will this research require a waiver of the requirement for written documentation of informed consent?
No

J2. Consent Procedures

Who will recruit subjects for this study?
PI
PI's staff

Describe how research population will be identified, recruitment procedures, any waiting period between informing the prospective participant and obtaining consent, steps taken to minimize the possibility of coercion or undue influence and consent procedures in detail.
Study 1: Participants will be recruited from volunteers among the co-PIs clinical and research staff, associates, etc. without any coercion, according to the inclusion criteria previously delineated. There will be no professional benefit, real or implied, to participation in the study and this will be made very clear. Once identified, informed consent will be obtained. The minimal risk associated with maintaining a research file and infrared light used will be discussed. The minimal discomfort associated with dark-adaptation (sitting in dark for 20-30 minutes) will be addressed. The non-contact nature of the device will be explained. Subjects may be retested if technical problems occur with the device or software.

Study 2: Patients will be identified by the PI and the co-PIs and recruited to the study. It will be made clear that there is no financial or medical benefit to participation in the study, real or implied. If the patient agrees to participate then they will be scheduled for the initial visit which will include informed consent. The minimal risk associated with maintaining a research file and infrared light used will be discussed. The minimal discomfort associated with dark-adaptation (sitting in dark for 20-30 minutes) will be addressed. The non-contact nature of the device will be explained.

Are foreign language consent forms required for this protocol?
No

J3. Privacy and Intrusiveness

Will the research involve observation or intrusion in situations where the subjects would normally have an expectation of privacy?
No

J4. Children

Will children be enrolled in the research?
No

J5. Neonates

Will non-viable neonates or neonates of uncertain viability be involved in research?
No

J6. Consent Capacity - Adults who lack capacity

Will Adult subjects who lack the capacity to give informed consent be enrolled in the research?
No

J7. Prisoners

Will Prisoners be enrolled in the research?
No

Section K: Research Related Health Information and Confidentiality

Will research data include identifiable subject information?
Yes

Information from health records such as diagnoses, progress notes, medications, lab or radiology findings, etc.
Yes

Specific information concerning alcohol abuse:
No

Specific information concerning drug abuse:
No

Specific information concerning sickle cell anemia:
No

Specific information concerning HIV:
No

Specific information concerning psychiatry notes:
No

Demographic information (name, D.O.B., age, gender, race, etc.):
Yes

Full Social Security #:
No

Partial Social Security # (Last four digits):
No

Billing or financial records:
No

Photographs, videotapes, and/or audiotapes of you:
No

Other:
No

At what institution will the physical research data be kept?
Physical PHI data will be kept at Baylor College of Medicine.

How will such physical research data be secured?
Physical PHI data will be kept in locked cabinets at all times in a Research suite that is closely monitored during business hours and locked at all other times.

At what institution will the electronic research data be kept?
Electronic PHI data will be kept at Baylor College of Medicine.

Such electronic research data will be secured via BCM IT Services- provided secured network storage of electronic research data (Non-Portable devices only):

Yes

Such electronic research data will be secured via Other:

Yes, (describe below):
Electronic PHI data will be secured via password-protected files, encrypted devices, secure servers identified by institution/owner, and restricted shared drive permissions

Will there be anyone besides the PI, the study staff, the IRB and the sponsor, who will have access to identifiable research data?

No

Please describe the methods of transmission of any research data (including PHI, sensitive, and non-sensitive data) to sponsors and/or collaborators.

Transmission of PHI to collaborators will be via secure/encrypted e-mail and SSL encrypted web portals.

Will you obtain a Certificate of Confidentiality for this study?

No

Please further discuss any potential confidentiality issues related to this study.

We do not forsee any potential confidentiality issues related to this study.

Section L: Cost/Payment

Delineate clinical procedures from research procedures. Will subject's insurance (or subject) be responsible for research related costs? If so state for which items subject's insurance (or subject) will be responsible (surgery, device, drugs, etc). If appropriate, discuss the availability of financial counseling.

Participants will not be charged for any research related activities. Participants and/or their insurance carrier will be responsible for the Study 2 clinic visit as this is standard of care and not being done for research purposes. All other activities are research related and will not be charged to the participant.

If subjects will be paid (money, gift certificates, coupons, etc.) to participate in this research project, please note the total dollar amount (or dollar value amount) and distribution plan (one payment, pro-rated payment, paid upon completion, etc) of the payment.

Dollar Amount:

30

Distribution Plan:

Participants in Study 1B will receive a total parking disbursement of up to $15 for the single visit. Participants in Study 2 of the protocol will receive a total parking disbursement of up to $30 for up to 2 visits.

Section M: Genetics

How would you classify your genetic study?

Discuss the potential for psychological, social, and/or physical harm subsequent to participation in this research. Please discuss, considering the following areas: risks to privacy, confidentiality, insurability, employability, immigration status, paternity status, educational opportunities, or social stigma.

Will subjects be offered any type of genetic education or counseling, and if so, who will provide the education or counseling and under what conditions will it be provided? If there is the possibility that a family's pedigree will be presented or published, please describe how you will protect family member's confidentiality?

Section N: Sample Collection

None

Section O: Drug Studies

Does the research involve the use of ANY drug* or biologic? (*A drug is defined as any substance that is used to elicit a

pharmacologic or physiologic response whether it is for treatment or diagnostic purposes)
No

Does the research involve the use of ANY gene transfer agent for human gene transfer research?
No

O1. Current Drugs

Is this study placebo-controlled?
No

Will the research involve a radioactive drug?
No

Section P: Device Studies

Does this research study involve the use of ANY device?
Yes

Device 1: Optokinetic Contrast Detector (OCD)

Name of Device (Including HDE # if applicable):
Optokinetic Contrast Detector (OCD)

FDA intended use of the device in use
Not applicable at this time

Actual use of the device in this clinical trial
Objective determination of human contrast sensitivity

Manufacturer of the device :
One of a kind, conceived and constructed at BCM

FDA number for the device (IDE for investigational device, HDE #, or 510K #) :
Not applicable

Method of proof of the validity of this IDE, HDE, or 510K (check all that apply):

Sponsor Investigator

Is the BCM investigator serving as sponsor/investigator for this study?
No

Device Risk

This is a non-significant risk device and will fulfill all of the abbreviated requirements of an IDE found in 21 CFR 812.2(b)
Please enter a brief explanation of why the device is not a significant risk device below:
This device qualifies as a non-significant device for several reasons in accordance with 812.2: A) It is not a significant risk device. Study participants will only have contact with a chin and forehead rest and eye movements recorded with a camera in response to a stimulus on a screen about 1 meter away. The device consists of the following: A computer monitor (old CRT), a camera to observe the eye, an infrared (IR) lighting source, a chin rest (from an old ophthalmic slit lamp), a screen to block one of the eyes, and an adjustable table (from an ophthalmic retailer). This IR source is a series of readily available low intensity IR LEDs that are mounted together and powered in unison. A commercially available ground glass diffuser sits in front of the LEDs to spread the light. There is no opportunity for pain, discomfort, or damage to the eyes in any way. The device is investigational and will not be used to make a clinical diagnosis. It is one of a kind and not currently meant for distribution. There is no more than minimal risk to subject. B) The device will be labeling in accordance with 812.5, stating: "CAUTION--Investigational device. Limited by Federal (or United States) law to investigational use." C) Informed consent will state clearly that this is an investigational device only. D) Investigators will comply with the requirements of 812.46 with respect to monitoring investigations and notify the IRB immediately of any unexpected finding or realization that the device may represent more than minimal risk. E) The study coordinator will maintains the records required under 812.140(b) (4) and (5) - The name and intended use of the device and the objectives of the investigation; - A brief explanation of why the device is not a significant risk device: - The name and address of each investigator: - The name and address of each IRB

that has reviewed the investigation: - A statement of the extent to which the good manufacturing practice regulation in part 820 will be followed in manufacturing the device; and - Any other information required by FDA. - Records concerning adverse device effects (whether anticipated or unanticipated) and complaints and will make the reports required under 812.150(b) (1) through (3) and (5) through (10); F) The study coordinator and investigators will ensure that participating investigators maintain the records required by 812.140(a)(3)(i) and make the reports required under 812.150(a) (1), (2), (5), and (7);

Control, storage, and use of the device

How does the PI plan to store, control, and use the device?

Storage, control and use under supervision of the Principal Investigator

Section Q: Consent Form(s)

Study 1A and 1B

Study 2

Section R: Advertisements

None