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HUMAN SUBJECTS RESEARCH PROTOCOL - RESEARCH SUMMARY (SUPP N)

DATE: 11/20/2018
TITLE OF PROJECT: External Eyelid Devices for Restoration of the Blink
PRINCIPAL INVESTIGATOR: Kevin Houston
FUNDING SOURCE: RPB U-grant

BACKGROUND

1) Discuss the following in paragraph format

- Discuss the importance of the topic (public health and/or clinical importance and impact on individuals/community; incidence, prevalence, mortality and morbidity)
- Critically appraise the relevant literature and discuss the state of current knowledge on the topic (including deficiencies in knowledge or gaps that make the study worth doing)
- Describe, in detail, your approach to address the research question
- Explain how your study will contribute to existing research and benefit other individuals or the wider community

RESPONSE: Two major types of eye lid movement disorders include lagophthalmos (incomplete closure of the eyelids) and blepharoptosis (incomplete opening of the eyelids). Both of these conditions occur because of a disruption in the normal agonist-antagonist neuro-muscular complex balance. Generally paralysis of the eyelid or facial muscles is responsible for the abnormality (the eyelids can close but not open, or open but not close). An external device, if able to generate an appropriately balanced force, could restore eyelid movement by performing the paralyzed function; for example, a ptotic (droopy) eyelid could be opened, and the functioning eyelid closure muscle could overcome the device's force (Conway, 1973; Barmettler et. al, 2014; Houston et. al, 2014).

Despite this seemingly straight-forward application, permanent magnets for eyelid movement disorders have not thus far become an available treatment. It is possible that earlier magnetic materials lacked the strength (at sizes which were acceptable to patients) to effectively restore the blink, or methods of implantation or external mounting were not effective. A newer class of permanent magnets made of alloys of neodymium (Nd), iron (Fe) and boron (B) might provide the technology needed to develop a feasible external magnetic device. They generate the strongest static magnetic fields yet possible, (1.3T compared to 0.4T of conventional ferrite magnets) (Cyrot, 2005) with exceptional uniaxial magnetocrystalline anisotropy, which makes them resistive to demagnetization (Chikazumui, 1997). The increased magnetic force at a fraction of the size has led to attempts for other medical applications including implantation for gastroesophageal reflux disease (Ganz, 2013), in dental prosthetics (Uribe, 2006), ocular reconstructive surgery (de Negreiros, 2012), and glaucoma (Paschalis et. al, 2013).

Problems with extended external non-surgical adhesion to the skin of the eyelid may be solved with hydrocolloid-based medical adhesives e.g. Tegaderm™ (Chen, 1997), already used for IV catheter securement, wound dressing, and as a protective eye covering (FDA, 1997). This material is extremely thin, transparent, and oxygen permeable with an established safety profile for days to weeks of wear. The hydrophyllic properties (FDA, 1997) may be beneficial to the eyelids, which are often moist.

In our prior work we established proof-of-concept data demonstrating safety and efficacy for temporary management ptosis up to 2 hour per day for 2 weeks. These participants were inpatient at Spaulding Rehab Hospital and so were under 24 hour supervision. This would be the first study to investigate the feasibility of sending a participant home with the device. We also have preliminary data suggesting similar safety for two participants with lagophthalmos. This study will expand on this preliminary work to examine longer wear times and feasibility for a wider range of eye lid disorders.

AIMS

2) Your aim(s) should arise from your literature review and state what the study hopes to accomplish.

RESPONSE: Aim 1: Determine the safety and feasibility of externally mounted magnetic devices for extended (> 1 week) home use for the management of early post-acute and chronic eyelid movement disorders. Aim 2: Collect preliminary data on the efficacy of external magnetic eye lid devices stemming from a variety of different pathologies.

OBJECTIVES

3) Your focused research question needs to be further refined into one or more study objectives. The study objective(s) should be single and quantifiable statement(s) that will allow you to answer your research question.

RESPONSE: Objective 1: Determine the safety and feasibility of externally mounted magnets for extended management of chronic eyelid movement disorders by measuring visual acuity and corneal and skin integrity and comfort over 8 weeks of wear.

HYPOTHESES

4a). Primary Hypothesis - Hypotheses are more specific than objectives and amenable to statistical evaluation. Your primary hypothesis is your statement of the hypothesized effect on the primary outcome measure. A hypothesis is worded very simply and written as 'testable' statements. Your experimental results will prove or disprove your hypothesis. Hypotheses are generally stated in the null form (H_o) as they have their basis in inferential statistics. Rejecting the null hypothesis increases our confidence, with a given level of probability, that there is a relationship between the variables being studied. However, a classic scientific hypothesis includes both a null and alternative (H_a) hypothesis.

**e.g. H_o: Asthma prevalence rates are not different among children from low and high socioeconomic groups in Istanbul. H_a: Asthma prevalence rates are different among children from low and high socioeconomic groups in Istanbul.*

RESPONSE: Hypothesis: Externally mounted magnet systems will have a good safety profile defined as a mean decrease in visual acuity 1 line or less, high-mag photo documented skin-integrity rating better

than 2 (FDA industry scale), and no more than a two grade (NEI/Industry Workshop scale (Lemp, 1995)) worsening in superficial punctate keratitis on high mag photo-documented analysis.

4b). Secondary Hypotheses - Although a study is usually based around a primary hypothesis, secondary hypotheses may also be pre-specified although based on outcomes of lesser importance or additional interest. As the primary hypothesis is usually the basis for statistical power calculations, secondary hypotheses with insufficient power will generally not lead to statistically robust conclusions.

RESPONSE: Externally mounted magnet systems will a) result in a significant improvement in the completeness of eye closure and opening as measured using image analysis of eye opening/closing with compared to without the device; b) will be comfortable to wear defined as a mean participant-reported comfort rating greater than or equal to 6/10 (or 60cm on a 100cm visual analog scale)

STUDY DESIGN

5) State the design of the research (e.g. randomized controlled study, cross-sectional survey, prospective or retrospective cohort/case-control).

**Whatever the study design, you need to ensure that you provide the reader with a clear statement and description of your proposed design. You may also explain why the particular study design has been chosen in preference to other possible designs (i.e. justification for choice of study design)*

RESPONSE: This is a prospective study. As the principal aim of this study is to determine safety and feasibility of extended home use, we will not attempt to randomize patients to a treatment and a placebo group nor will we have an age-matched control group. Participants will be made aware that a predicate device is commercially available and the magnet device is experimental.

ELIGIBILITY CRITERIA

6a). Inclusion Criteria - Inclusion criteria are the 'characteristics' that clearly describe the study population that are required for a subject to be included in the study. The criteria may be based on factors such as age, gender, the type and stage of a disease, previous treatment history, and co-morbid medical conditions. They may state appropriate criteria for admitting special 'at-risk' populations such as women of reproductive age, children or patients with disease states or organ impairment.

RESPONSE: Presence of an eyelid movement disorder for at least one eye, moderate cognitive function or better defined as greater than or equal to 18 out of 30 on a pre-screening of the Mini-Mental State Exam, age 5 or older

6b. Exclusion Criteria - Provide details of participants that will be considered ineligible to participate and justification for their exclusion. These criteria are not always clinical in nature, aiming principally to accommodate participants in a safe and ethical manner. Criteria may include circumstances that interfere with the participant's ability to give informed consent (diminished understanding or comprehension, or a language other than English spoken and an interpreter unavailable), contraindications to the study treatment(s)/procedure(s), taking certain concomitant medication(s), or conditions that interfere with a patient's ability to comply with all treatment(s)/procedure(s).

RESPONSE: Absence of an eyelid movement disorder or presence of a corneal ulcer. Those with a corneal ulcer are at risk for permanent loss of vision and should be managed with proven methods. Age less than 5, Severe Cognitive impairment defined as MMSE score <18, behaviors consistent with delirium (combinations of disorientation, hallucinations, delusions, and incoherent speech), or lethargy. These individuals must be excluded since participation requires competent self-care, reliable responses and cooperation during fitting of the devices.

STUDY OUTCOMES

7a). Primary Outcome - The primary outcome should be the most important and clinically relevant outcome (e.g. clinical, psychological, economic, or other) of the study. This is the measure used to answer your study aim. However, it is also the outcome used to calculate study sample size and power and test the primary research hypothesis. Generally, no more than 1-2 primary outcome measures are pre-specified. Primary outcome measures may be measured in various ways such as: binary (e.g. caesarean/no caesarean, blood loss ≥500mL/blood loss <500mL); continuous (e.g. weight - kg, blood loss - mL); ordinal (e.g. pain - mild, moderate, severe); time to event (e.g. survival), and counts (e.g. number of infections, number of events occurring).

RESPONSE: Skin integrity scales, change in ocular surface staining rating, participant comfort and satisfaction rating, and change in visual acuity. Skin integrity will be analyzed by applying a likert-type rating system to a high-mag/high-resolution photo documented image of the subject's lid skin. The number of adverse events will also be reported, defined as incidents which require temporary or permanent suspension of the participant's involvement. These include any broken skin, decrease in visual acuity more than 2 lines, worsening of corneal rating of more than 1.5 points or other ocular surface ratings more than 2 points, and comfort rating lower than 5/10 (or 50cm on the 100cm visual analog scale).

7b). Secondary Outcome(s) - Secondary outcome(s) are measures of additional or less important research interest. They may include additional clinical, psychological, economic, or safety outcomes (e.g. treatment related side effects/adverse events). However, as these endpoints are not used to calculate study power and sample size it is often not possible to draw robust conclusions from the results.

RESPONSE: Video analysis of eyelid biomechanics to measure the completeness of eye closure and opening compared to 1) no device, 2) relative to the contralateral side (if normal), 3) relative to the ptosis crutch or external lid weights. The same paired comparisons will be performed for the clinician and participant rating scale data. 3) Cognitive score on the MoCA will be analyzed for relationship to length of time in the study and satisfaction rating scores).

STUDY PROCEDURES

8) In this section you need to clearly and comprehensively describe exactly what will happen to participants once they are enrolled in your study. Depending on the study it might include how potential participants will be approached, when they will be randomized, the frequency and duration of visits or whether they are expected to self-complete a daily diary at home, the duration of the study or follow-up, and any measurements taken at each visit (e.g. questionnaires, physical measurements, biological samples).

You should include precise details of the treatment(s)/intervention(s) intended for each group/participant. You should also provide details of any follow-up schedule (i.e. time between visits) and consider how you will monitor participants' adherence with the treatment schedule. You might also describe under which circumstances participants may be withdrawn and how this will occur. A schematic diagram or flow chart may be useful for this section.

RESPONSE: Twenty-five participants each with either paralytic ptosis or lagophthalmos will be enrolled for a total of 50 participants. The OCRO will assist in pre-identifying potential candidates targeting the practices of Dr.'s Joseph Rizzo, Michael Yoon, and Kevin Houston. They will mention the study to them/providing approved recruitment information (flyer and study description page). If OCRO pre-screening misses someone whom the Dr.'s think might be a candidate, they will mention the study and have their clinical staff provide the approved recruitment materials (a flyer and study brochure). A separate appointment will be arranged for the study candidate to return, if they are interested, to speak with the PI about the study and perform informed consent (conducted by the PI or other trained and experienced study personnel). Study visits may occur at MEEI in the Oculoplastics, Neuro-Ophthalmology, or Vision Rehabilitation Clinics, or at Schepens Eye Research Institute in the Lions Exam room booked with the online SERInet scheduling system. If seen at SERI, all data collected will be for research purposes (no clinical component); i.e. there will not be any overlap with their typical Ophthalmological care. If data is collected at MEEI, there may be, in the interest of efficiency, measurements taken clinically which can also be used for research to include visual acuity and slit lamp biomicroscopy. The PI will explain the study as detailed in the "consent" section and administer a pre-consent cognitive screening using the Mini-Mental State Exam (MMSE). If score is 18-23 (maximum of 30) representing mild cognitive impairment (Tomburgh et al 1992), candidates will be asked return with a caregiver (if one is not present). If score is <18, they will not be eligible. After the consent process, participants will complete the VFQ-25 (Mangione, 2001) and the MoCA (Montreal Cognitive Assessment, Nassreddine et. al 2012), have their visual acuity measured, anterior segment evaluation with NaFl and Lissamine Green, and a video recorded of their baseline eyelid function (capturing only the eyes).

This will be followed by fitting of the experimental magnetic device. A video is recorded for approximately 1 minute to document device performance and a rating instrument (visual analog scale for participant measures and a likert-type 10-pt scale for the examiner) is administered to capture subjective comfort and opinion of efficacy (see rating scales attached). DEVICE FITTING DETAILS-THE IMMEDIATE TRIAL: FOR PTOSIS, In order to best fit the MLP we will measure 1) the force (i.e. magnet size) needed to elevate the paralyzed lid; 2) the thickness of the coating on the spectacle magnet needed to allow adequate blinking; 3) the best orientation of the magnets (thru height or thru thickness). Force measurement to open or close the eye lid may be taken by attaching a low force transducer (miniature strain gauge) to the lid(s) with a small piece of IV 3000 medical tape, a 2-3 minute procedure.

Next, a lid attached magnet array (see photos in manuscript attached) is painlessly applied to the upper lid with the participant's eye closed by placing a small swatch of Tegaderm medical adhesive (3M, St. Paul MN, Smith and Nephew, Canton MA) over the top of the micro-magnet array (a 1-minute procedure). For ptosis the array is only attached to the upper lid and a set of fit-over frames with a larger magnet embedded within the upper eye wire (spectacle magnet), which can be worn over the participants own glasses if needed, will be placed on and adjusted to the appropriate position. This secondary spectacle mounted magnet activates the ptosis system, providing the force to lift the lid. The spectacle magnet must be encased in plastic, and if the coating is too thin, the patient will not be able to blink properly. To determine the best coating thickness we will test 10 different coating thicknesses, done with 1mm plastic inserts which can be stacked. The video is recorded and rating instruments completed. This process is then repeated for lid magnets having a slightly modified polarity (thru height compared to the standard thru thickness). We will also test 4 different orientations of the spectacle magnet to determine the best fitting. FOR LAGOPHTHALMOS (failure of eye closure, e.g. facial palsy) the participant will first be fitted with a predicate device, an external lid weight, applied with double-sided "blink-eze" adhesive (supplied by the distributer with the product) and the video recording and rating instruments completed. Then this will be removed and lid magnet arrays identical (or very similar) to those described for ptosis will be applied to the upper and lower lids. The weight of the upper magnet will pull the eyelid down in a similar manner as the gold lid weight. (Townsend, 1992) The magnet on the lower lid will promote a more complete blink as the two magnet arrays draw towards one-another. A secondary

spectacle mounted magnet may also be used for lagophthalmos (mounted within the inferior eye-wire to pull the upper lid down). In this scenario there is no lower lid array. 20 MINUTE TRIAL: For both the ptosis and lagophthalmos magnet devices: If experimenter likert-type scale score is greater than or equal to 6 on the blink mechanics and efficacy and better than 8 on the skin integrity and the participant rated comfort is greater than or equal to5/10 on likert-type or 50mm or better on a 100mm Visual Analog Scale and they express a desire to continue wearing the device, they will be offered participation in an extended 20 minute trial. This is followed by a repeat of the visual acuity, slit lamp exam, video and rating scale data collection. EXTENDED 1-WEEK TRIAL: Participants who have a successful 20 minute magnet device trial defined as an Examiner Rating Scale score of greater than or equal to 6 on the blink mechanics and efficacy, better than 8 on the skin integrity, participant rated comfort greater than or equal to 5/10 (or 50mm on a 100mm Visual Analog Scale), and express a desire to continue wearing the device will be offered participation in an extended 1-week trial. These cut-offs were based on observations during the pilot study at Spaulding (see manuscript attached) where patients who reported a desire to wear the device typically rated their comfort and satisfaction at this level or better. The PI or other trained study staff supervised by the PI will train the patient how to apply and remove the lid magnet; similar to what is done for insertion removal of contact lenses. They will be trained how to place on the secondary magnet spectacles to sit in the correct position on their face. If the participant is able to successfully demonstrate the ability to do this, only then will the magnet device be dispensed home with the patient (see exception* below). During each 1-week during the extended trial, the participant will be advised (instructional sheet sent with the participant) to wear the device as much as they would like up to 8 hours per day in the case of ptosis and 24 hours per day for lagophthalmos so long as comfort remains 5 or better (see participant instructions). Participants will be asked to document their wear time and assess their comfort on a 10-pt scale (10 being best) on a regular (min. daily) basis. For lagophthalmos, the device ideally will be worn 24 hours/day. For ptosis, the magnet glasses will be removed at night, and the lid magnet will remain attached to the eyelid. The participant may shower/wash face with the lid magnet on as the Tegaderm is not critically bothered by water and the magnet is encased in PDMS. They will be advised not to submerge the device (i.e. swim with the device on). Lid magnets will be removed and applied as they start to become detached (typically 2-3 days). If self-assessed comfort is worse than 5/10 or if the intervention fails (eg. stops working of falls off and cannot be reapplied) the participant will be instructed to contact the PI directly. The PI will advise if the device should be removed, and will come to MEEI or Schepens within 24 hours of the complication to evaluate the problem. If there is a problem requiring immediate attention, the participant will be advised to seek attention in the MEEI EW. AT A 1-WEEK FOLLOW-UP study appointment we will repeat visual acuity, slit lamp, rating instruments and video recording. SAFETY CUTOFFS: The participant's study status will change to suspended and an adverse event reported to the IRB with any of the following findings at the follow-up or any emergency visit: Any broken skin, decrease in visual acuity more than 2 lines, worsening of corneal rating of more than 1.5 points or other ocular surface ratings more than 2 points, and comfort rating lower than 5/10 (or 50cm on the 100cm visual analog scale). The extended trial of the magnet device may be renewed 3 times (for a total of 1 month with weekly visits) as long as the above mentioned criteria continue to be met. If still safe/effective at 1 month, the participant will be given the option to take the device home for an additional 1 month The device trial/study ends after 8-weeks (4 weekly trials followed by a 1-month trial) or with failure/complication or voluntary withdrawal. If the device is successful over the duration of the study and the participant would like to continue wearing it, a clinical decision will be made as to if and for how long per day it should be worn. This is justified when there appears to be no other equivalent treatments which may be substituted. It would not be ethical to retract the device from a participant if it is working and there is no other comparable option. In such cases, the participant will return 1 month later for an additional follow-up evaluation prior to turning the maintenance of their care over to the neuro-ophthalmology, oculoplastics, or vision rehabilitation service. Their specialist will continue to monitor for complications after the study if the patient keeps the device. The study will end when 25 participants in each group have completed the study (~2yrs). EXECPTION* TO TRAINING REQUIREMENT: If the participant is unable to apply and remove the device themselves (physical or cognitive limitations) and/or they have cognitive impairment (MMSE 20-23), they may still participate in an extended 1-week trial if the following criteria are met: 1) a caregiver is able to be trained to apply/remove the device, 2) The primary caregiver assures 24-hour supervision (see form on the last page of the "instructions for use document"), 3) The cognitively impaired participant (or participant who cannot apply the device themselves) agrees to attend daily study visits for the first

week of the extended trial. If there are no complications after 1-week, a clinical decision may be made by the PI to decrease the visit frequency to the standard protocol.

9) Randomization (if applicable)
Include the method (including any software) used to generate the random allocation sequence. Describe type of randomization performed, ratio of assignment to groups, block size permutation and stratification if applicable. Explain the methods used to conceal group allocation until assignment. Also, include information on who will generate the allocation sequence and who will assign participants into their groups.

This section should also discuss if participants, the investigator, and those assessing/analyzing the outcome(s) will be blind (or masked) to group assignment or if the study will be an open-label study (investigators and subjects know their assigned group).

RESPONSE: There is no randomization counterbalancing will be used given the small sample size.

10) Study Specific Procedures: List all procedures (interventions, tests, surveys, etc.) to be performed ONLY for research purposes

RESPONSE: Specific to the study are the high magnification photo analyses of skin integrity, participant comfort and satisfaction ratings (visual analog scales), video analyses of the eyelid movements to measure the change in the amount of eye-opening and closing (volitional and reflexive opening and closing) with the magnetic devices compared to no device, comparisons of the amount of opening and closing with the magnetic devices compared to with the ptosis crutch or external lid weights, and efficacy ratings by both the clinician and participant.

11) Standard of Care Procedures: Clearly list all standard of care (standard therapy) procedures (interventions, tests, etc.) to be performed regardless of the subject's enrollment in the study, but that will be included in the research assessment.

RESPONSE: NA

MEASUREMENT TOOLS

12) It is essential to state how the data will be collected to assess the primary and secondary outcome(s) of the study (e.g. patient questionnaire, medical charts, routinely collected hospital/research database, biological specimens). Describe at what point(s) of the study data collection will occur. You should make statements that justify the validity of the study measure/instrument. If not, you will have to verify how you will ensure the validity and quality of data being collected. Also, mention here if you are going to have one or more assessors to collect data, their level of training/experience (or how they will be trained), and if you are planning to assess inter-rater reliability (if applicable).

RESPONSE: Cognitive tests and the visual function test used in the study are validated. The Mini-Mental State Exam is being used as a pre-screening to enter the study. Scores on the MMSE represent no

impairment (24-30), Mild (18-23), and severe 0-17) (Tomburgh et. al 1992). Once in the study, the Montreal Cognitive Assessment MoCA will be administered, which is a slightly longer and more sensitive test battery for detecting and quantifying cognitive impairment (see http://www.mocatest.org/normative_data.asp). Any study staff administering the cognitive tests will be trained and practiced in using the standardized instructions (attached). The Visual functioning questionnaire (VFQ-25) is a validated survey and will be self-administered by the participant. Visual acuity will be collected using eye charts available in the services involved in a calibrated exam lane with controlled lighting. Participants will be tested on the same chart at every visit. IMAGE CAPTURE: All devices will be registered with MEEI. Video data collection may be done with the PI's iPhone (which is registered with MEEI and password protected) or a high resolution video recording device (yet to be purchased) and a digital SLR camera. The PI will personally collect this data. Any such device will be registered and compliant with MEEI safe computing policies. All data will be immediately transferred and removed from the image acquisition device. Use of USB drives will be avoided, but if necessary will be encrypted/protected consistent with MEEI policies. All effort will be made to only capture the eyes in a manner which would prevent identification of the participant from the images. RATING SCALES: We are using the ocular surface quantification method endorsed by the NEI (NEI/Industry Workshop scale (Lemp, 1995)). We are aware of no validated instruments for the other subjective measurements needed (skin integrity, comfort and efficacy of devices). We will use a well-accepted method of subjective rating (Likert-type rating scales), scored on a 10-point scale. Skin integrity will be rated by the clinician at the time of the study visit, and later by an independent rater (prior to publication) using the photos/video using a likert-type scale. Additionally we will evaluate the use of a visual analog-type rating scales (not used in our previous work). The visual analog scale method allows a continuous measure of subjective response which simplifies analysis. Study staff will read the rating scale instructions word for word (see recording forms, attached).

13) Sample size and statistical power - A sample size or power calculation should be performed. This calculation is used to estimate the number of subjects required to answer your primary study hypothesis with an accepted power. Conversely, it also allows you to estimate what power can be achieved with a limited number of participants. This number is calculated by specifying the magnitude of the effects that are expected (i.e. informed and clinically significant), variability of the measurements and the acceptable degree of type I and II errors. You need to specify the assumptions made for the calculation. It is recommended that you consult with a statistician for this section. Also keep in mind the estimated recruitment rate and whether you need to adjust for anticipated non-responders and losses to follow up.

RESPONSE: The primary hypothesis is that externally mounted magnet systems will have a good safety profile and will be feasible for home use therefore we will report the proportion of participants who have a safety issue and complete the trial. As this outcome is based on summary statistics and not comparisons between groups, a power calculation is not appropriate. Sample size was selected based on providing an as-broad-as-possible but feasible (within the time of the study) assessment of safety and feasibility. The sample size calculation for the secondary within subject comparison between devices is estimated at 10 for the ptosis group, using preliminary unpublished data for cranial nerve III palsy at Spaulding (n=7; efficacy for opening (mm) magnet vs. crutch was borderline with 7 participants p=0.08, and comfort had reached significance, p=0.05). A power calculation is not possible for the lagophthalmos group as preliminary data are only available for 3 participants. Power calculations for the secondary analysis will be re-evaluated during data collection.

14) Statistical methods - The statistical methods used for the study objectives/hypotheses (e.g. t-test, chi-squared, multivariate modeling) must be sufficiently detailed. If conducting a randomized controlled study, you should state whether methods will include an "intention to treat" (ITT) analysis, per protocol analysis, or both. An ITT analysis is preferred as it compares all subjects in the

groups to which they were originally randomly assigned (despite withdrawal, treatment failure or cross-over). Consultation with a statistician is strongly recommended. See Harvard Catalyst Statistical Consulting for more information.

RESPONSE: Descriptive statistics will be calculated including a mean rating scale value for skin, corneal integrity, and visual acuity (logmar). A repeated-measures ANOVA will be used to determine if there is any change across visits/measurements. The completeness of opening and closing with and without the magnet and with the other devices will be compared using paired t-tests. As this is not a randomized design, ITT will not be used.

DATA SAFETY MONITORING PLAN (DSMP)

Complete question 15 **OR** 16 depending on the risk of the study. If your study is submitted as minimal risk and determined by the HSC to be more than minimal risk you will be asked to complete question 16 during the review process.

15) If the research is **no more than minimal risk**, please describe any provisions in place to ensure the safety of participants and the validity and integrity of data. If safety monitoring will occur a safety monitoring plan may include elements such as: parameters for safety review, the frequency in which safety review will occur, the person(s) responsible for safety review, and the plan (including the person(s) responsible) for reporting adverse events, protocol deviations, or noncompliance to the HSC and others (where applicable). Data monitoring may include the specific elements that will be reviewed (e.g., informed consent documentation, verification of the accuracy of data), the frequency of data monitoring, and the person(s) responsible.

RESPONSE: On-site monitoring of participant safety will be utilized by the PI or other study personnel. This is appropriate since problems can be immediately detected and addressed by research staff experienced in examination of the eye. A monitoring log of expected and unexpected events will be kept. Events will be documented on paper and sent to the PI (if he is not the one examining the participant) who will place a follow-up call to the participant that day and the next day as needed. Paper documentation will be kept in the study binder and then transferred to a worksheet in the study master spreadsheet. Unexpected events will be reported to the IRB ASAP. Expected events will be reported at continuing review. Non-compliance with protocol (e.g. failure to use the study checklist or properly document or report in a timely manner adverse events) will be documented. Once identified, minor issues will be addressed by the PI by special meeting or at quarterly study meetings. Special meetings will be called depending on the seriousness of the issue. Repeated offenses will result in removal of that study staff from the protocol.

16) If the research is **more than minimal risk**, a more detailed data and safety monitoring plan is required. Please detail the plan for this study below:

The study is minimal risk and there will not be a more detailed data and safety monitoring plan.

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