Beacon Sensors & Telerehabilitation to Assess & Improve use of Devices for visual functioning (BeST-AID)

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Specific Aims: Indicate the purpose of the research, specifying the problems and/or hypotheses to be addressed.

Difficulty with reading is the chief complaint of most patients who present for low vision rehabilitation (LVR). Devices that provide magnification (i.e., hand-held or stand optical magnifiers, electronic magnifiers, or spectacle-based magnification as high adds) are commonly prescribed for this indication; however, about one in five patients will abandon their magnifier within three months. The successful application of magnification devices is predicated on their correct use while reading, which can require additional training sessions following the initial dispense of the device to further improve visual functioning. Many patients with low vision (LV) are unable to attend multiple training sessions in-office due to barriers related to transportation and/or co-morbidities. A promising solution to this problem is real-time videoconferencing to provide telerehabilitation, which involves remotely delivered LVR services by a LVR provider in-office to a patient at home. However, there are currently no publications on whether telerehabilitation can improve LV patient outcomes. We recently completed a small pilot study in which we showed that telerehabilitation for LV was feasible and acceptable by both patients and LVR providers. We next propose to further explore and develop our telerehabilitation protocol targeted at improving visual function outcomes in LV patients, so it can be evaluated in a phase III clinical trial in the future.

Specific Aims:
To assess the potential for telerehabilitation to enhance visual function by providing remotely-delivered LVR training to use magnification devices (i.e., hand-held or stand optical magnifiers, electronic magnifiers). Following basic LVR (i.e., one in-office training session) for new magnification device(s), we aim to determine if there is additional gain in visual functioning by randomizing subjects (2:1) to telerehabilitation or additional in-office LVR (active control). This will help provide estimates of effect size to plan a future larger-scale randomized controlled trial. We will compare visual function changes with the Activity Inventory questionnaire and validated reading tests in 60 LV patients with central vision loss due to any ocular disease recruited from 10 centers. Participants will be assessed before and after two consecutive periods: (1) no further training will be provided for one month after a single LVR training session (i.e., basic LVR), followed by (2) up to three LVR sessions over a three month period either via telerehabilitation (n=40) in the participants' homes with study loaner equipment (iPad/smartphone, stand, reading cards) via remote control assistance, or in-office LVR (active control; n=20). Multiple sessions will be conducted if the LVR provider deems the participant is not completely proficient with their magnification device. We will determine which patient characteristics and/or magnification devices are most likely to benefit from telerehabilitation, to be targeted in a future, larger-scale, phase III trial.

The primary goal of this proposal is to refine the methods and procedures for implementing these innovative technologies for LVR, in order to develop future protocols for randomized controlled trials. In the future, we envision that telerehabilitation could improve efficiency and patient outcomes by changing the method by which follow-up LVR services are provided. This is a high priority given the increasing prevalence of LV, paucity of LVR providers, and barriers related to transportation and geography.

Background and Significance: Provide a summary of the background for this study and explain how it will contribute to existing knowledge.

Low vision rehabilitation (LVR) can improve functional ability for individuals with low vision (LV), but effectiveness depends on and increases when rehabilitation techniques are applied over repeated training sessions to reinforce patient motivation, compliance, and skills in the correct use of magnification devices. The skills taught by LVR providers in-office may not translate when patients use their magnification devices at home, either because the lighting and ergonomics are not ideal, or they do not retain the specific instructions for using the device. Successful use of these devices requires the correct working distance, proper viewing angle, application to appropriate types of near tasks, use

with the better eye, eccentric viewing techniques and/or spectacle correction in some cases. Magnification devices are abandoned by LV patients when they are perceived as ineffective for the task, which is likely preventable by attending follow-up visits for additional LVR to maximize visual function with the device. The most common outpatient-based approach for delivering LVR training in-office has significant limitations since patients have difficulty returning due to geographic and/or transportation barriers. Roughly 70% are no longer able to drive. Access to LVR care in the developed world is estimated to be as low as 10 to 20%. As there is currently a paucity of LVR providers, access is particularly limited in rural areas of the United States. Physical disability and chronic illness prevalent in this population can prevent care utilization, as LVR may seem implausible due to patients' frailty or busy appointment schedules for comorbidities. Vision loss can lead to reduced quality of life, increased depression, anxiety, and/or emotional distress; these issues may persist after an initial LVR encounter if follow-up training is not given to best utilize patients' remaining vision by learning to correctly use magnification devices.

Telerehabilitation is a potential solution to eliminate geographic and transportation barriers, which should allow LVR providers to maintain timely and effective communication with patients in their homes. Telerehabilitation involves using the Internet as a means to remotely deliver LVR services using a HIPAA compliant, secure videoconference platform and requisite hardware devices (i.e., cellular data enabled iPad tablet). Given the maturity of technology for the requisite hardware and videoconference services, as well as the near ubiquitous presence of cellular networks, the time is right for leveraging the power of this technology to provide LVR training on the proper use of magnifier devices to maintain optimal usage. A systematic review of 61 studies on telerehabilitation for any disability revealed that it has been widely and successfully applied in clinical practice for fields outside of LVR, e.g., cardiology and neurology.

Telerehabilitation allows LVR providers to deliver more personalized care since they can gain valuable insight into factors that are unique to patients' particular home environment or usual reading materials, which may affect visually difficult tasks. Telerehabilitation may help older adults to maintain independent living in their own home. Standardized near reading cards used during the session allow providers to assess if a significant visual decline has occurred due to possible ocular disease progression since the last office visit, which would prompt an in-person evaluation to provide timely treatment as needed. Telerehabilitation should enable more efficient system-wide resource allocation, which we anticipate will lead to improved vision-related outcomes.

A clinical model for LV telerehabilitation has already been implemented, in which the patient attends a video session at their local optometrist's office (not their home) with remotely located LVR providers at the Buffalo VA in NY. It is important to conduct research to document changes in patient outcomes following telerehabilitation, to provide evidence-based practice recommendations for this modality and future insurance reimbursement. Our eventual goal is to conduct a randomized controlled trial of telerehabilitation for LV compared to active in-office LVR (possibly an equivalence trial) to improve patients' visual function and reduce magnifier device abandonment. Given the projected dramatic increase in the expected number of people with LV over the next several decades, it is imperative to validate creative solutions to provide LVR to overcome economic and societal burdens caused by LV, and increase access to and quality of care for these individuals.

Premise:
There is a need for a clinical trial of telerehabilitation since the literature and a Cochrane systematic review completed by the PI and co-I, Dr. Yoshinaga, revealed that telerehabilitation has rarely been applied to LV and there are no published outcomes from studies (i.e., no evidence of efficacy). The rationale for telerehabilitation is supported by previous studies indicating that transportation, geography, patients' co-morbidities and the paucity of providers are barriers to receiving LVR in-office. It is premature to propose a large-scale, phase III randomized controlled trial (RCT) at this time since the following are yet unknown: effect size (i.e., possibility of visual function enhancement), which patients and/or magnification devices are most likely to benefit, appropriate number of telerehabilitation sessions for proficiency, and feasibility of in-office LVR as an active control; the current study will assess these factors and then design an RCT based on findings.

Innovation:
There are several innovative elements in the proposed research program:

Many barriers related to providing outpatient LVR follow-up training sessions in-office can be effectively eliminated with the option of remote delivery of services through telerehabilitation. It has the potential to enhance and change current clinical practice methods if future randomized controlled trials indicate support for its ability to improve LV patients' functional outcomes. In addition, it may be applied in research settings, for example, to provide training to new retinal prosthesis users. There is a high potential for capacity building since LV telerehabilitation portals can be used in the future to augment training programs for providers and students through group learning and observation both domestically and internationally. To facilitate telerehabilitation for patients who are not tech-savvy, we propose a creative solution: loaner equipment for the technology with remote access control.

Pilot Study of Telerehabilitation for LV:
We recently completed a pilot study of telerehabilitation for low vision, in which our first goal was to perform the initial steps to develop, administer, refine, and evaluate components required to deliver follow-up low vision telerehabilitation services. Three low vision providers (Drs. Ross and Yoshinaga, and an OT) conducted telerehabilitation sessions from their office with ten visually-impaired older adults in their homes, who recently received a hand-held magnification device for reading and self-reported difficulty with returning for follow-up training at their provider's office. All except one participant had never used videoconferencing prior to our study, and three had never used the Internet. Participants and providers rated the use of loaner hardware devices (i.e., tablets, MiFi mobile hotspot) and HIPAA compliant, secure videoconference services during telerehabilitation sessions at which participants read MNread cards and received feedback on magnifier use. Drs. Ross and Yoshinaga reported little to no difficulty with evaluating participants' reading speed, reading accuracy and working distance with their magnifier. Both providers and participants rated both the audio and video quality as excellent to good with the iPad mini, which was noticeably better than the less expensive Android tablets we also evaluated. All participants agreed that they were satisfied and comfortable receiving telerehabilitation and evaluation via videoconferencing. Eight of 10 reported their magnifier use improved after telerehabilitation. All participants who had the session in their home reported they were very interested in receiving telerehabilitation services again if their visual needs change. Positive feedback from both participants and providers in this pilot study supports the feasibility, acceptability and potential value of LV telerehabilitation.

Surveys of LV patients' Interest in Telerehabilitation at our proposed sites:
Survey responses were collected over 1-2 months during November 2017 to January 2018 from LV patients seen for LVR and who received a magnification device at two of our proposed study centers. UNMC collected the following 62 survey responses over 2 months: mean age was 81 years (range 56-98), 42% were male, and 76% had age-related macular degeneration. About half of UNMC LV patients (52%) indicated that they were somewhat or very willing to have both a beacon sensor on their magnifier and a telerehabilitation session from their home if a community volunteer set up the loaner equipment for the session at no cost, with roughly a fifth (n=12; 19.4%) were very willing to do both. No experience with or no interest in computers was the primary reason for lack of willingness to try telerehabilitation in half of UNMC patients who declined telerehabilitation even after we offered the community volunteers. There were no significant differences in responses according to satellite location (site) or ocular diagnosis (all $P>0.05$), but older patients ($P=0.03$) and men ($P=0.009$) at UNMC were significantly less likely to be very willing to try both interventions. The site PI at SCCO had an unusually reduced LV clinic schedule and only five surveys were administered to eligible patients at SCCO over a month; however, 4 of 5 were somewhat or very willing to have both telerehabilitation and a beacon sensor, and one was very willing to do both, providing support for the feasibility to recruit at least one patient per month as per the plan for his site.

Research Design and Methods: Describe in detail the design and methodology of the study.

Research Plan and Methods:
We propose a minimal risk, phase 1/2 randomized controlled trial of telerehabilitation vs. in-office LVR (i.e., standard of care). The clinical trial in this proposal will include a run-in period to assess basic LVR (i.e., a single session in-office, which is part of standard of care, that all participants will receive) followed by randomization to one of two intervention groups (multiple telerehabilitation sessions with LVR provider vs. LVR in-office with the LVR provider). Our active control intervention for LVR in-office

will follow a standard protocol for the schedule of visits and number of sessions, but the intervention itself is considered standard of care. We considered using 'usual care' as a control but decided against it since there is no standard for the number of sessions and content delivered during the training, as much variability exists for the LVR practices of our providers; some do not tend to conduct multiple training sessions when new magnification devices are prescribed, while others will have one or more additional LVR session(s). Usual care comparator trials are also vulnerable to the Hawthorne effect in which practice may be influenced by the fact that providers are being studied. We are proposing the same standardized schedule of visits for both telerehabilitation and active controls in-office to keep the dosing of the interventions consistent in this parallel design trial. We anticipate that usual care will involve fewer LVR sessions and thus result in worse outcomes than a strict active control intervention, thus there is limited value to study usual care at this stage. Adding a third arm for usual care in the proposed trial would significantly increase the required sample size, which would be outside of the scope of this project. In the future, a much larger scale effectiveness trial can be designed to compare telerehabilitation to usual care practices.

Subjects and Magnification Devices:
Subject identification and recruitment will occur at all study sites. Adult participants will be recruited from the patients seen in the LVR service at four academic centers: (1) New England College of Optometry (NECO) in Boston, MA, (2) University of Nebraska Medical Center (UNMC) in Omaha, NE, (3) Southern California College of Optometry (SCCO) in Fullerton, CA and (4) University of California, Los Angeles (UCLA) and six private practices (Mid-Michigan Eye Care; Low Vision Services, PLC; See What You Miss Optometry; Frank Stein & Paul S. May Center for Low Vision Rehabilitation; Boston University Eye Associates, Inc.; Family Eyecare of Orange & Solinsky Eyecare LLC). Eligible patients will have newly received following types of magnification devices (multiple devices allowed): hand-held optical magnifiers, portable electronic video magnifiers, some stand magnifiers and CCTVs. Study screening, consent and enrollment procedures will only take place at UCLA and will only be conducted by the study team members at UCLA, which will include oral consent by phone.

Sex as a biological variable: We will recruit and enroll both genders, intending to have meaningful representation from both sexes, which should be achievable given our previous experience during our pilot study of telerehabilitation (4 of 10 subjects were men). About two-thirds of LV patients are women, and our survey data indicate women are more interested in our interventions; thus there may be a slightly greater proportion of women in our study. We will examine if gender affects outcomes, along with other potentially influential variables.

Telerehabilitation Methods:
All participants from our 10 clinical centers will use the study loaner devices to access the telerehabilitation session, rather than their own Internet-enabled device. Telerehabilitation sessions will be facilitated by a remotely located member of our study team at UCLA who will use remote access control provided by RescueAssist by LogMeIn to initiate/end the zoom videoconference session on the study loaner smartphone that they will receive in order to conduct the telerehabilitation session. This option would not require the participants to do anything on the smartphone to access the videoconference session (it can be completely set-up via our remote access control); all the participant would need to do at the scheduled time of the telerehab session is put the smartphone in the stand that will be provided to them when they join the study and orient the camera on the smartphone so the study team involved with the telerehabilitation session can see the participant using the magnifier. At the time of the scheduled telerehabilitation session, the UCLA study team member who will use Rescue Access remote control access will call the participant by phone to confirm their willingness to start the session prior to initiating the videoconferencing. We will print copies of the near reading card and MNread test cards, place them in a sealed envelope, provide it to the participant when they receive the study loaner smartphone, and the participant would open/use the reading card print-outs during the telerehabilitation session. We will continue to use secure and HIPAA compliant videoconference services from zoom.us (UCLA Health Zoom), which is accessible across Windows, Mac, iOS, Android, Blackberry, and Linux platforms on desktop, tablet, and mobile devices to enable our study team to use their device of preference. A private meeting code will be used to access the videoconference portal for the sessions. For security, the sessions will not be video-recorded, but a student research assistant will take notes. All sessions will take place in the subjects' home. Each session will last about an hour. LVR providers from all of our 10 clinical centers will administer the MNread test to their respective patients and will evaluate the participant's reading

technique (i.e., working distance, lighting) and reading fluency (i.e., speed, accuracy, print size) with their magnifier device. In addition, they will ask the participant to read or view their own materials of interest, while providing LVR training. If relevant, the providers will ask participants to demonstrate how to change the battery in the magnification device, or to walk around their home with the smartphone to show the illumination levels in places where they use their magnifier. We will continually assess the telerehabilitation survey responses we will collect from both the LVR providers from our clinical centers and participants, in order to resolve any reoccurring problems related to Internet connectivity, videoconference portal, hardware devices, or audio/visual quality.

Hypothesized Outcomes, Sample Size Calculation and Data Analyses
Our outcomes that are questionnaires or reading tests will be assessed by phone by a different UCLA research assistant at each evaluation. It is not possible to mask the participants or LVR providers. The outcomes assessors will be identically trained by the PI. We successfully administered reading tests by phone in a previous study by providing the materials in a sealed envelope that the subject opens only at the test exam time. Our two interventions (telerehabilitation versus additional in-office LVR) may have similar effects since the same LVR principles will be applied at the same planned schedule of sessions; however, it is possible that telerehabilitation may be more beneficial if compliance with scheduled sessions is better than in-office LVR and/or if home-based training is advantageous in the patient's own environment with relevant tasks of interest; on the other hand, there may be aspects of LVR training that work better in-person and in-office. In-office LVR or at-home LVR with a therapist in-person are currently considered standard of care. All participants will receive standard of care since they will all receive one in-office LVR training session prior to randomization.

Outcome measures
Our primary outcome measure, the Activity Inventory questionnaire, and the secondary outcome measure, the Sustained Silent Reading test by Ramulu et al., will be administered by phone by a UCLA research assistant at baseline (time of study entry), one month following receipt of the new magnification device, and four months after receipt of the magnification device (at time of study completion). The SF-36 general health questionnaire, Telephone Interview for Cognitive Status (TICS), Geriatric Depression Scale, and Hospital Anxiety Depression Scale questionnaires will be administered by phone by a UCLA research assistant at baseline (time of study entry), and four months after receipt of the magnification device (at time of study completion). The MNread test will be administered by the OD/OT provider at each in-office visit and/or during telerehabilitation sessions. Within 24 hours of each telerehabilitation session or in-office rehabilitation session, the UCLA research assistant will administer a satisfaction survey by phone. To characterize participants' baseline level of visual impairment, we will gather information from a medical record review from each our sites, in which we will record the results from validated visual acuity and contrast sensitivity tests at the initial in-office visit. These vision tests are used as part of standard of care.

The PI will be responsible for training the research assistants in basic interview skills and instructions for administering the survey instruments, as well as internal quality assurance measures. To help assure the quality and consistency of responses from participants for our primary and secondary outcomes, the PI will instruct the research assistants involved in data collection to adopt a neutral demeanor and interviewing style when administering the questionnaire (i.e., avoid directing, guessing responses; suspend judgment, but not standoff-ish). The PI will periodically observe about 10% of the survey administrations throughout the study to confirm they are being conducted consistently and according to instructions. The research assistants will be trained to respond to possible depression or suicidality by connecting the at-risk participants to someone by phone by either calling 911 or someone at the National Suicide Prevention Lifeline. If a subject indicates suicidal ideation and indicates that they have means and intent to accomplish this, the study team will keep the subject on the telephone while asking another study team member in the participant's local area to telephone 911 for immediate intervention. If the study team encounters a subject who expresses suicidal ideation or suicidal intent, they will keep the subject on the phone call until they are able to transfer the subject to speak to a specialist at the National Suicide Prevention Lifeline. In the case of severe depression or anxiety, we will refer them to see their internist or general physician so they can find appropriate care locally. The cut-off scores that will trigger referral are <=38 for the SF-36 mental component summary, >=12 for the Geriatric Depression Scale, and >=11 for the Hospital Anxiety Depression Scale (HADS-D). These three questionnaires will be scored while the subject is still on the telephone and study personnel will let the subject know that they will be making the referral for

follow-up evaluation with their primary care provider.

Procedures at each study site
- Marshall B Ketchum University, Southern California College of Optometry: subject identification, recruitment, conduct of vision rehabilitation training sessions in-office or via telerehabilitation, and data collection procedures from in-office visits
- New England College of Optometry: subject identification, recruitment, conduct of vision rehabilitation training sessions in-office or via telerehabilitation, and data collection procedures from in-office visits
- University of Nebraska, Medical Center: subject identification, recruitment, conduct of vision rehabilitation training sessions in-office or via telerehabilitation, and data collection procedures from in-office visits
- UCLA: subject identification, recruitment, written consent from patients seen at UCLA, conduct of vision rehabilitation training sessions in-office or via telerehabilitation, data collection procedures from in-office visits, the coordinating site involved in obtaining consent and administering study phone questionnaires (data collection) to participants at other sites, as well as all study data analyses.
- Boston University Eye Associates, Inc.: subject identification, recruitment, conduct of vision rehabilitation training sessions in-office or via telerehabilitation, and data collection procedures from in-office visits.
- Frank Stein & Paul S. May Center for Low Vision Rehabilitation at The Eye Institute: subject identification, recruitment, conduct of vision rehabilitation training sessions in-office or via telerehabilitation, and data collection procedures from in-office visits.
- See What You Miss Optometry: subject identification, recruitment, conduct of vision rehabilitation training sessions in-office or via telerehabilitation, and data collection procedures from in-office visits.
- Low Vision Services, PLC: Low Vision Learning Center: subject identification, recruitment, conduct of vision rehabilitation training sessions in-office or via telerehabilitation, and data collection procedures from in-office visits.
- Mid-Michigan Eye Care: subject identification, recruitment, conduct of vision rehabilitation training sessions in-office or via telerehabilitation, and data collection procedures from in-office visits.
- Family Eyecare of Orange & Solinsky Eyecare LLC: subject identification, recruitment, conduct of vision rehabilitation training sessions in-office or via telerehabilitation, and data collection procedures from in-office visits.

For each of the non-UCLA sites, consent for the non-UCLA subjects at those sites will be obtained by phone by the UCLA research assistants.

Indicate how much time will be required of the subjects, per visit or contact, and in total for the study.

Per study visit/session to receive telerehabilitation or training in-office = approx. one hour

Per study telerehabilitation session to complete follow-up survey = approx. 15-30 minutes

Per study session to complete questionnaire outcome measures by phone = approx. 2-3 hours

Total anticipated time commitment per subject = approx. 8-15 hours over 4 months

Statistics and Data Analysis: Describe the proposed statistical procedures or descriptive analyses for the study. If applicable, indicate how the sample size was determined.

Data analyses: Data management will be an ongoing task for the PI.
Descriptive statistics will used to summarize the study data and findings, We will determine the effect sizes for basic LVR (one session in-office as part of standard of care), additional in-office LVR (active control), and telerehabilitation for changes in the Activity Inventory and reading outcomes by comparing the scores at each follow-up to baseline (pre-LVR). For the Activity Inventory questionnaire, we anticipate that the reading domain may have the largest magnitude of change since magnification devices are most often used for reading tasks, which is the chief complaint of most LV

patients. For the MNread test, we will primarily focus our analyses on reading acuity and maximum reading speed. Separate analyses (sub-groups) for all outcomes will be used to compare outcomes for participants with hand-held or stand-based magnifiers (optical or electronic) versus spectacle-based high add power magnification (hands-free).
Multiple regression analyses will assess if effect sizes for the telerehabilitation and in-office LVR control group (i.e., changes in the outcomes: Activity Inventory score, reading speed) are related to the number of telerehabilitation sessions, patient demographics, visual acuity, contrast sensitivity, diagnosis, or scores on the SF36, Telephone Interview for Cognitive Status (TICS), Geriatric Depression Scale, or Hospital Anxiety Depression Scale questionnaires. We will apply advanced statistical methods (e.g., multilevel models) for missing data. We will perform a Rasch analysis of our Activity Inventory data in comparison to a very large database of LV patients (several thousand) who have completed the Activity Inventory. Goals and activities have their item measures, and the fit properties of the Activity Inventory from the database of previous responses can be used to convert raw scores into person measures. In the event of non-normally distributed data, we will use a binary outcome (proportion of subjects with improvement greater than 0.14 logits) to compare changes between telerehabilitation and in-office LVR for the Activity Inventory domains using chi-square tests and logistic regressions.

Sample Size calculation: We plan to enroll and compare findings for two equal sized groups based on visual acuity (VA); i.e., those better or worse than 20/63. A sample size calculation for matched pairs t-test revealed that 18 subjects in each of the 2 groups would detect a within-subject mean improvement of 0.14 logits on the Activity Inventory (primary outcome) following telerehabilitation (equivalent to 1-line or 0.1 logMAR VA), when considering a standard deviation of 0.17 logits for the differences, power of 0.80 and 0.05 type I error probability. We will aim to enroll a total of ~40 subjects randomized to telerehabilitation (given our 2:1 randomization plan), and aim to have a total of ~20 active controls randomized to receive in-office LVR. We will determine the effect sizes for basic LVR (one session in-office as part of standard of care), telerehabilitation and additional in-office LVR for changes in the Activity Inventory and reading outcomes.