Title: Multiplexing Prism Fitting for Field Expansion of Monocular Vision

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Study Site: Schepens Eye Research Institute, Massachusetts Eye and Ear Infirmary

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Clinical Trial Protocol and Statistical Analysis Plan

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Background:

- It has been reported that about 50,000 people develop acquired monocular vision (AMV) in the United States each year because of trauma, ocular injury, or ocular diseases. The incidence of enucleation (removal of an eye) is 4.3 per 100,000 people (Erie et al., 1992). Multiple studies have shown the impact of AMV on spatial vision, depth perception, and motion perception (Brady, 1994; Ihrig & Schaefer, 2007; Kraut & Lopez-Fernandez, 2002).
- The binocular field of view decreases from 190 to ~155 degrees when one eye is lost. As a result, when looking straight ahead, an individual with AMV will lose 35 degrees (temporal crescent) visual field. Typically, it takes about a year to adapt to the deficit with a personal strategy (Coday et al., 2002).
- Previously, we prototyped multiplexing prism (MxP) as an assistive device for field expansion in AMV (Jung & Peli 2018). The MxP provides true field expansion (measured by perimetry), allowing the observer to simultaneously see the physical world through the prism and the "expanded/shifted view" from the non-seeing side (Peli & Jung 2017, Jung & Peli 2018).
- In this pilot study (Jung & Peli 2018) we expanded the nasal visual field of the seeing eye from ~55 to 80 degrees in simulated monocular vision.
- However, the previous MxP was constantly mounted on a 3D-printed holder attached to a spectacle frame. It was difficult to detach the prism from the glasses. In addition, it requires custom fitting with multiple iterations, and severely limited the frames that could be used.
- This study aims to improve the design of the MxP, develop a simple fitting guideline, and determine the field expansion.

Specific Aims:

- To develop, fit, and test the MxP as a field expansion device for patients with AMV. The fitting of the MxP is based on a simple self-confrontation test.

General Description of the Study:

- We will first develop a magnetic clip-on multiplexing prism. A fitting method (to identify the tilt angle needed for each patient) based on self-confrontation test will be established to simplify and expedite the process. An adjustment screw added to the MxP provides continuous tilt angles for wide field expansion.
- A set of MxP trial pieces will be designed to expedite the fitting process.
- In this prospective study, we will recruit patients with AMV and identify the suitable prism tilt angle with the self-confrontation test. The study will include 2 visits. In the first visit, the patients will undergo baseline vision test screening, refractive error, Goldmann perimetry to determine the baseline visual field. The patients will select a suitable spectacle frame. The lab will order a pair of glasses with the prescription. The patient will come for the second visit to pick up the glasses. During the 2nd visit, the examiner will fit the MxP based on the self-confrontation test. Goldmann perimetry will again be performed to measure the field expansion with the new prisms as the outcome measure. There will be no masking involved. Each study visit will last 2.5-3 hours.

Statistical Analysis

- Paired t-test (within subjects) of the nasal visual field between the two conditions (with and without MxP)
- We will record all the feedback and comments from the patients about the protocol.
- Sample size estimate: Based on the previous result with 3 AMV subjects, for a repeated measure (matched-pairs) 2 tail t-test of alpha 0.01, power 0.9, effect size of 6.4 (25.3º effect with 3.9º standard deviation), a total sample size of 4 is required. However, this effect was based on different prismatic power. In addition, the field expansion obtained in

the previous study was based on multiple iterations to maximize the visual field. In this study, we prescribe the MxP based on subjective response, and we expect the standard deviation to be larger. Besides, we would like to test if the magnetic clip-on MxP will give consistent results across participants with different ocular, facial features, and multiple types of frames. For conservative estimation for 3x standard deviations, the adjusted effect size is 2.1 (25.3º effect with 12º standard deviation), and the sample size is 7. To account for a 20% drop-out rate, we will recruit at least 9 subjects.

Inclusion criteria - Common

- At least 16- years of age
- In sufficiently good health to be able to complete sessions lasting 2-3 hours
- Able to understand English
- Able to give voluntary and informed consent
- No medical health issues such as seizures, motor movements problem

Inclusion criteria – subjects with acquired monocular vision

- Loss of vision in one eye for >1 year
- Better than 20/32 visual acuity in the seeing eye with correction
- No visual field defect in the seeing eye (nasal field of at least >45degree)

Exclusion criteria

- Patients with any physical or mental disabilities, including cognitive dysfunction, balance problems, or other deficits that could impair their ability to respond to the stimuli presented in this study will be excluded
- Any person with motor movement problems (e.g., unable to use extremities)

Subject Recruitment:

We will recruit participants from our database who have previously participated in other studies in our lab and have consented to be contacted about future studies. We will place advertisements about the study within Schepens Eye Research Institute. Interested volunteers who qualify can complete a permission-to-be-contact form and send it to the research assistant mentioned in the advertisement. We will contact patients using the Research Patient Data Registry (RPDR), Rally, and those referred to us by outpatient clinics and primary physicians. Information about the study will be posted on social media such as Facebook groups and other outlets. Study information will also be printed on flyers and posters distributed in and around the greater Boston area. We will contact Mass Eye and Ear Infirmary's Low Vision / Oculoplasty departments and request referrals.

Detail information about Methods and procedures:

- <u>Visit 1 – Screening procedures and baseline:</u> After the informed consent process, the subjects will complete a series of screening tests procedures to ensure that they meet the study criteria. The preliminary procedures include a brief history of ocular and systemic diseases, screening of baseline visual functions such as near and distance visual acuity (with computer logMAR chart), refraction & lensometer (if needed), visual field testing (with Goldmann perimeter). Questions about mobility and quality of life will also be asked. Refraction will be performed if the distance visual acuity is worse than 20/32 in the seeing eye.

- For Goldmann perimetry, the patient will place their chin on a chinrest and fixate at a center target. A spot of light will appear at different locations of the subject's visual field as

controlled by the examiner, and the subject will be asked to press a buzzer when they detect the light target while fixating at the center.

- The patient will then select a spectacle frame from the available collection. The examiner will measure a few ocular parameters, such as interpupillary distance, back vertex distance, pantoscopic tilt, and wrap angle. The experimenter will place an order for the prescription with the selected frame at the end of the first visit. This visit is estimated to last between 2.5-3 hours.

- Visit 2: MxP fitting and assessment of field expansion: In the second visit, the subject will wear the new spectacles, and adjustments will be made to ensure comfort and good fitting. Goldmann perimetry will be performed with the fitted spectacles as a baseline measure.

- Next, the examiner will fit the magnetic MxP based on the self-confrontation test. The examiner will explain to the subject that this procedure measures the extent of their field of view and creates awareness of how far into the side they can see without moving their eyes and head.

- After the fitting, the patient will repeat the Goldmann perimetry with the prism. The spectacles and magnetic MxP will be dispensed to the patients at the end of the study.

Outcome Measures:

a) Primary Outcome: The amount of field expansion with the MxP (in degrees). Field expansion is calculated based on the difference between with and without (baseline) the MxP. If the nasal field with MxP is larger than without a prism, there is a gain in field expansion.
b) Secondary Outcome: The farthest nasal field of view with MxP (in degrees).

Details about interventions:

The magnetic MxP do not come under FDA oversight as medical devices or therapeutic intervention. This is not a study exploring therapeutic intervention. There is no dose/time of intervention applicable to the participant interaction. The MxP is just a clip-on prism that can be attached/removed easily from the glasses that will show immediate effect.

Risk and adverse effect:

We do not anticipate any serious adverse effects for the study as all the procedures are also performed during regular eye examinations. There will be no dilation or eye drops used during the visits. All procedures in this study are minimal risk and are otherwise regularly performed in the clinic or a task of daily living that study participants would otherwise perform anyway. Screening is composed of standard clinical procedures (visual acuity, visual field), which will be carried out in a stationary sitting and pose a minimum risk for patients. Testing for prisms will also be conducted in seating position and will only involve the patient to move their arms from side to side posing no risks. There is minor discomfort for being seated or paying attention for prolonged periods. However, each procedure will be split into sub-components to allow the subject to take frequent breaks and study visits will be flexible so that subjects may choose to come back to complete the study. Any discomforts are expected to be naturally dissipated quickly. Patients may need a few days to adapt to the prescription from the spectacles. The MxP may cause a small area of peripheral monocular diplopia far in the periphery that not be noticed easily. The MxP can be attached/ removed easily from the spectacles. All adverse events and unanticipated problems will be reported to MGB IRB as per the MGB IRB policy.

Data Analysis:
All the results will be written on the recording sheet. Visual field limits (nasal with and without MxP) will be stored in a spreadsheet. The mean and standard deviation of the nasal field (with and without MxP) across the subjects will be computed. Statistical analysis as mentioned above, will be performed at the end of the study.

Data Monitoring:
The PI will be responsible for monitoring the integrity of the data. The research assistant will ensure the accuracy and completeness of data records and informed consent. Research staff will enter data into study spreadsheets in a timely fashion. Summaries of data for each subject will be reviewed and discussed by the study team at weekly project meetings. After each subject has completed study participation, the research assistant will prepare a brief report summarizing the data and findings. The PI will review it, and it may be presented and discussed with the rest of the project team at a weekly project meeting. The data reviewed will include the participant's informal feedback about the experiment and the experimenter's notes about the study visit. The PI will determine whether the research should be altered or stopped. Research data will be coded using a subject identification number that does not include the subject's initials and is not derived from the subject's identifiable information.

The document linking the code to personal information will be stored on a secure password-protected database of the local MEEI network that only authorized study staff can access. Any paper files with subject-identifiable information (such as the consent form) will be kept in locked file cabinets at SERI and accessible only to laboratory personnel in a locked office. Any paper data collection sheets that do not contain subject-identifiable information will be physically stored in a binder in the lab at SERI in a locked office that only authorized staff can access. Electronic data will be stored on secure password-protected computers and network drives. All study staff will complete all training required by MGB IRB and Mass Eye and Ear related to the confidentiality of data.

Payment for participation:
Subjects will be reimbursed up to $50 per visit for transportation. Subjects will be reimbursed at $20/visit ($40 for 2 visits) for their time. The subject will be allowed to keep the spectacles and magnetic MxP at the end of the study.

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