Improving Fixational Stability in Cases of Central Vision Loss

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Abstract: Poor fixation stability is one of the primary challenges to high-resolution in vivo imaging of human retina in cases of central vision loss. We tested the hypothesis that careful design of fixation targets may improve fixation stability. The ability to fixate on a visual target was measured by an eye-tracking camera. In participants without eye disease, target type, target-to-scotoma size ratio and presence or absence of an artificially generated scotoma were manipulated, and the effect on fixation was analysed. A significant interaction effect between target type and scotoma-to-target size ratio was seen in healthy participants, suggesting the optimal target type and size may be dependent on the degree of central vision loss. Data of Stargardt patients were difficult to obtain, paralleling difficulties in retinal imaging. Despite these difficulties, for the patient with least advanced disease, there were indications that instructions, target-type and practice with the task all contributed to improved stability. This has applications for allowing high-resolution imaging procedures to characterise disease progression in conditions of retinal degeneration.

1. INTRODUCTION

Stargardt disease is an inherited macular degeneration, commonly associated with an ABCA4 gene mutation\(^5\). The macula is a cone-rich region of the retina responsible for high-acuity central vision. Macular damage in Stargardt patients leads to a progressive loss of central vision, with a central scotoma that increases in size as the disease progresses. The condition is characterised by the accumulation of the lipid-rich pigment lipofuscin in the retinal pigment epithelium (RPE)\(^6\), and cell death. It is therefore expected that histological descriptions of the retinal cells may provide useful biomarkers as the disease develops over time. Advances in retinal imaging have recently made it possible to image individual photoreceptor cells non-invasively in vivo in the human eye. High-resolution imaging is achieved by using adaptive optics to compensate for aberrations caused by irregularities in the eye’s optics, as in an Adaptive Optics Scanning Laser Ophthalmoscope (AOSLO, Figure 1). This has great potential in clinical settings, potentially allowing disease progression to be characterised at a cellular level\(^\text{[3]}\text{[4]}\) and enhancing understanding of the underlying mechanisms of the disease.

However, AOSLO imaging requires a stable fixation of gaze to minimise distortions or blur in the image produced (Figure 1B). In healthy participants, this is achieved with instruction to look steadily at a stationary fixation target. However, the nature of the retinal damage in Stargardt patients can lead to difficulties in maintaining a stable fixation\(^\text{[5]}\text{[6]}\), and thus reduce the clarity of images produced. Different types and sizes of visual target have been shown to affect the extent to which participants are able to fixate on them\(^\text{[7]}\text{[8]}\). It is therefore possible that retinal imaging procedures in patients with Stargardt disease can be improved by incorporating a target type and size that enhances the ability of the patients to maintain a stable fixation. My project therefore aimed to test the suitability of different types and sizes of fixation targets in allowing patients with Stargardt disease to maintain a stable eye position. This was also tested in healthy participants through generating an artificial scotoma that mimicked the central vision loss seen in Stargardt disease.

2. METHOD

Healthy participants: I worked with other members of the lab to produce a system that simulated an artificial scotoma and measured fixation stability under these conditions. We used an infrared, video-based eyetracker (EyeLink1000) to continuously measure the participants eye-position at a rate of 2000 samples per second. Fixation targets were displayed on a computer screen in an otherwise dark room, and in half of the test sessions a central scotoma was simulated by inserting a uniform white field of limited spatial extent at the gaze position of the participant. The eyetracker and the visual display were controlled via custom-written MATLAB programs. Participants were required to fixate on one of six targets (a dot, a cross, a face, a four dot diamond, a Thaler target\(^\text{[9]}\) and a blank screen), shown in Figure 2. Each target was presented for four seconds, followed by a two-second break in which random binary noise was presented.

![Figure 1: AOSLO images of human retina. (A) Single frame (30 Hz refresh rate) with no eye movement; (B) Single frame with characteristic sheer patterns indicating an eye movement during image acquisition; (C) Average of 30 stabilised frames. Participant LKY.](Image)

The targets were displayed in five different size ratios (target of 0.5, 0.8, 1, 1.2 or 1.5 to scotoma size, with a scotoma size of either 2° or 5° of visual angle, corresponding to 119 and 299 pixels respectively at the viewing distance of 0.9 m). Participants viewed the stimuli in four blocks; two with an artificial scotoma (small in one block and large in the other), and two with no scotoma (one in which the target size assumed a small scotoma, and the other in which the target size assumed a large scotoma). Within each block, each of the six target types was presented five times each, at each of five different size ratios, assigned randomly without replacement. This generated 150 trials per each of the four blocks, giving an overall total of 600 trials.
**Stargardt patients**: Three patients with Stargardt disease were given a similar visual fixation task with no artificial scotoma. They were required to fixate on each of the five targets (excluding the plain white screen) while their eye movements were recorded. Each target was presented five times, giving a total of 25 trials per session. Accurate eye-tracking requires calibration to relate parameters of the video recording of the eye to screen coordinates. Due to calibration difficulties, data were obtained from only four sessions of the second patient (P07), and no eye-tracking data were obtained from the third patient (P08). Target size was 2° for the first patient (P05) and 5° for the second patient, adjusted according to scotoma size estimated from fundus images.

### 3. RESULTS

**Analysis**: We performed three analyses. Firstly, we calculated the proportion of the stimulus presentation that produced reliable tracking data. From the tracking data we then calculated two measures that are relevant to clinical retinal imaging: **stability** of fixation during stimulus presentation (which will affect image acquisition) and **reliability** of fixation location from one presentation to another (which will affect the ability to repeatedly image a particular retinal location). Stability was assessed using the root-mean-square (rms) deviation from the median location per trial. Reliability was assessed using the rms variability between the median locations of five repeated trials with the same target type.

**Proportion of time tracked**: This coarse measure confirmed marked differences between healthy participants and Stargardt patients: proportion of time tracked was lower for patients, decreasing with increases in scotoma size. The extent to which tracking failures reflected patients’ difficulties in maintaining a stable fixation on the target, or reflected failures in the eye-tracking calibration, is unclear. Future research with patients will optimise both the fixation targets and the calibration targets, relative to the patient’s scotoma. A novel finding was an improvement in tracking with practice. Figure 3A shows eye-movement traces from Patient 07, showing poor fixation stability compared to controls. Target 5 produces relatively good fixation performance, perhaps because it would have been possible for this patient to position a subset of dots outside his scotoma. With a fixation target of similar geometry we were able to obtain AOSLO images from this patient (Figure 3B).

**Figure 4**: Fixational stability and reliability in scotoma and no-scutoma conditions, for six target types. (A) RMS stability in relation to the median position per trial, for a scotoma-to-target ratio of 1.0; (B) RMS reliability between median fixation locations across five repeated trials.

### 4. CONCLUSION

Results from healthy participants with a simulated central scotoma indicate that the optimal fixation target is dependent on the relationship between the scotoma and the size and shape of the target, suggesting that, for patients, fixation targets should be designed based on the degree of retinal damage present. For Stargardt patient P07, the best fixation performance allowed AOSLO imaging in which cones were resolved at the edge of the damaged region.

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### 6. REFERENCES