Retinal Microperimetry as a Means to Assess Visual Field Expansion in Visual Restoration Therapy

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Objective:
Although several studies have reported that Visual Restoration Therapy (VRT) expands visual fields,[1] questions have been raised as to whether the results are explained by intermittent saccades or eccentric fixation into the "blind" field rather than restored vision in the previously non-seeing region. We used Micropermetry (MP-1) to test the hypothesis that expansion of visual field following VRT is independent of eye movements.

Background:
VRT is a computerized, home-based treatment for patients with homonymous visual field defects aimed at reducing the size of the defect through repetitive stimulation of the visual borderzone adjacent to the blind field. VRT targets the borderzone while central fixation is maintained through fixating on a central stimulus. Patient responds to either a central fixation stimulus color change or an eccentric stimulus appearing in the peripheral field.

MP-1 (Fig-1) has an automated tracking system that controls for eye movements. MP-1 has an infrared camera that uses the retinal vessel as a reference frame. With any shift or movement between this reference image and the real-time fundus image the stimulus position is corrected. The MP-1 also allows stimulus parameters, e.g. size, duration and luminance, to be chosen by the examiner to be similar to those used for VRT training and HRP visual field mapping.

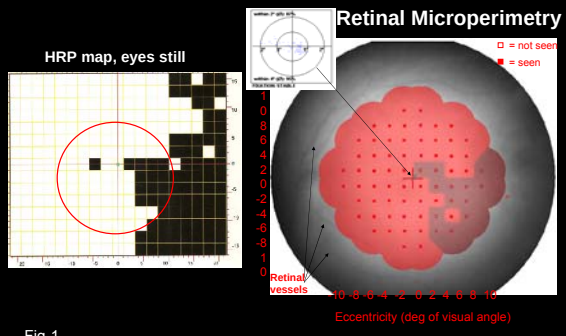


Fig-1

Methods:

Patients: Six patients (25-79) with retro-chiasmatic brain injury producing homonymous visual field defects underwent VRT >6 months following stroke.

Visual Restoration Therapy. Therapy was done at home twice-daily for 20-30 minutes, 6 days a week. VRT targets specific regions of the visual field while the patient maintains central fixation. With the chin supported on a frame 15 inches from an LCD screen, the patient fixates on a central stimulus (size=0.5deg) and presses a single mouse button when either the central fixation stimulus changes color or an eccentric stimulus appears in the peripheral field. The color change (yellow to green) was designed to be subtle enough to require foveal vision for discrimination, thus maximizing central fixation. During therapy, stimuli consisted of suprathreshold white squares 2 degrees in width which appeared sequentially along a horizontal path from a position in the seeing field 6 degrees from the border of the blind field, into the blind field 6 degrees, and then back into the seeing field. The luminance of the background was<1cd/m2, room lights off for the therapy. The interstimulus interval varied between 1000 and 1800 msec to minimize anticipation of the next stimulus. Eighty percent of the eccentric stimuli appeared in the visual borderzone; 20% appeared at random locations in the seeing and blind fields to reduce the predictability of target location..

Microperimetry (MP-1). The Nidek MP-1 (Nidek Technologies, Padova, Italy) uses a reference frame for stimulus presentation based on a photograph of the retinal vessels, adjusting the location of stimuli based on the referenced vessels. Precise stimulus presentation to known locations on the retina is therefore possible. Following pupil dilation (1% tropicamide and 2.5% phenylephrine hydrochloride) and adaptation to dim room illumination for 30 minutes the patient maintained fixation on a centrally placed red cross (2° in diameter) while responding to suprathreshold "white" test lights (stimulus size Goldman I, duration 200 msecs, 0 dB) presented on a dim "white" background (1.27 cd/m2). The non-tested eye was occluded throughout the procedure. Sixty-eight locations covering an area 20° in diameter were tested. Stimulus locations were spaced 2 degrees apart from each other and were centered around the fovea. The results of the microperimetry tests and the location of fixation during stimulus presentation were displayed on color digital photographs acquired by the MP-1 color camera.

Methods Cont'd
We defined relative-defect as cells where detection occurred 25% or 50% out of 4 trials at pre-treatment, whereas cells detected zero times were defined as absolute-defect. We excluded locations seen 3 out of 4 times to evaluate for improvement only in more severely affected resions.

We quantified performance within each cell and compared change over time for both relative and absolute zones among the six patients using a paired t-test. Furthermore, we translated the performance, stimulus detection rate, into a visual map using the following color code:

1) Black voxels represent all blind (absolute defect) fields (0) that did not improve.
2) Grey voxels represent blind field (0) that improved either to 1 or 2
3) Lime voxels represent relative defect zones (1,2) that improved.
4) Lavendor voxels represent relative defect zone (1,2) that worsened or did not improve.
5) White voxels represent normal detection (3, 4) at baseline.

Results:

For the group, there was improvement in stimuli detection at both absolute and relative defect zones ($P<0.038$). Improvement was seen in each patient, in contiguous cells along the borderzone and blind regions. Table 1 represents the stimulus detection rate at baseline and follow up including both absolute and relative defect cells.

Fig-1 (a, b) illustrates one run of microperimetry tests at each of the time points (pre and post-VRT respectively) for patient 1.Location of fixation during stimulus presentation is also displayed on the color digital photographs acquired by the MP-1 color camera (cluster of blue dots), indicating consistent fixation within 1 degree of the central fixation spot. Fig-1 (C) summarizes the improvement in the visual field using the color code described above.

Figure 2 (a, b) illustrates one run of the Microperimetry at each of the time points for patient 2. Again consistent fixation is demonstrated. Figure 2 C is the constructed visual map demonstrating the visual field expansion for patient 2 2nd to VRT.

Using the same color code, Figures 3-6 display the expansion in the visual filed in contiguous cells along the border zone and the blind region for patients (3-6).

Table-1	T1	T2
Patient1	0.29	0.57
Patient2	0.33	0.50
Patient3	0.14	0.18
Patient4	0.30	0.45
Patient5	0.22	0.72
Patient6	0.23	0.60

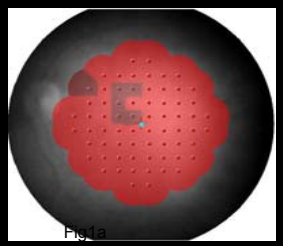


Fig1a

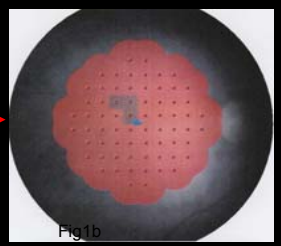


Fig1b

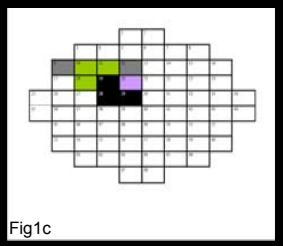


Fig1c

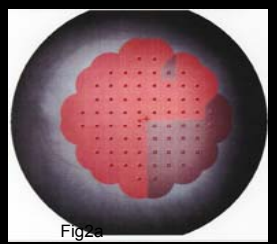
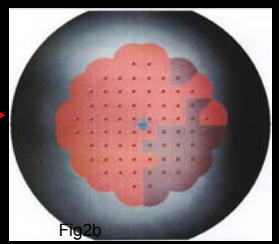


Fig2a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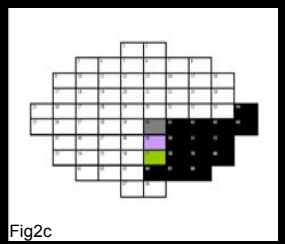


Fig2c

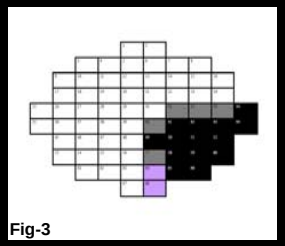
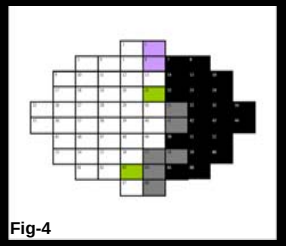


Fig-3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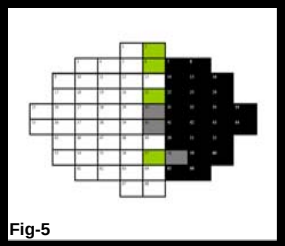
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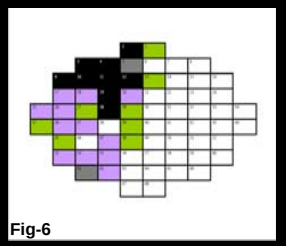
Fig-6

Conclusion:
- Using microperimetry we showed that visual field maps improved in 6 patients undergoing VRT. Our data suggest that with the use of microperimetry, visual field expansion can be demonstrated to be independent of eye movements.

- Although the mechanism of visual field expansion following visual field training with VRT is not addressed by this study, our findings of visual field expansion are consistent with animal models showing changes in cellular receptive fields after injury[2]. Other animal studies have shown that training of the visual system may result in plasticity at the cellular level[3]. In humans, we previously showed that 1 month of training by hemianopic stroke patients on the VRT program resulted in increases in the BOLD signal in regions related to visual processing, and these changes were specific to stimuli In the trained (borderzone) field compared with the untrained field[4]. The biological basis for the reassignment of new RFs to neurons within a previously silent cortical region is thought to be long-range horizontal connections in superficial layers of primary visual cortex[2].

References:

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2) Gilbert, C. D. & Wiesel, T. N. Receptive field dynamics in adult primary visual cortex. Nature 356, 150-2 (1992).
3) Yang T, Manusell JH. The effect of perceptual learning on neuronal responses in monkey visual area V4. J Neurosci 24, 1617-26 (2004)
4) Marshall RS, Ferrera JJ, Barnes A, Xian Zhang, O'Brien KA, Chmayssani M, Hirsch J, Lazar RM. Brain activity associated with stimulation therapy of the visual borderzone in hemianopic stroke patients. Neurorehabil Neural Repair. 2008 Mar-Apr;22(2):136-44. Epub 2007 Aug **14**.