TUMBLING E RESOLUTION PERIMETRY IN GLAUCOMA

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Abstract

Grating resolution has been shown to be sampling-limited in the periphery, in particular by the density of retinal ganglion cells. Laboratory-based experiments indicate that peripheral resolution is also sampling-limited for a tumbling E stimulus, meaning that this target can be used as a perimetric stimulus to measure localized ganglion cell density at different retinal locations. The authors have designed a tumbling E perimeter which measures peripheral resolution at 16 visual field locations using targets of four different orientations. The test has advantages over previous prototypes which employed gratings, in that it is more easily understood by the patient and allows a faster four-alternative forced choice (4AFC) psychophysical strategy. Resolution measurements in normal observers show good qualitative and quantitative agreement with the predicted resolution values based on anatomical counts of localized ganglion cell density. Preliminary measurements in glaucoma patients indicate patterns of visual field loss closely similar to those measured by Humphrey visual fields. This type of test has great potential to measure localized ganglion cell density, and thus detect early damage due to glaucoma.

Introduction

Previous studies have shown that, in peripheral vision, resolution acuity for high contrast grating targets is sampling-limited1-3; specifically, resolution acuity is limited by the coarsest array in the visual pathway, i.e., the retinal ganglion cells4,5. This means that measurement of resolution acuity under sampling-limited conditions gives a direct estimate of the density of the ganglion cell population responding. This is clinically relevant because, in glaucoma, the ganglion cells are predominantly affected.

Laboratory tests using gratings usually employ a target that contains at least six cycles, and this type of stimulus has been used successfully in assessing glaucoma patients6,7. However, grating targets are often difficult for untrained patients to comprehend, and test designs are usually restricted to a two-alternative forced choice

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(2AFC) paradigm. This typically requires a testing strategy of 3 up/1 down to limit the effects of the patient guessing correctly beyond their true resolution limit. This leads to a large number of target presentations being required, which in turn leads to a long test duration. For two reasons, our aim was to assess the usefulness of a tumbling E, as a replacement for the grating. Firstly, it is a more easily understood target and task for the patient; secondly, it allows a 4AFC paradigm which greatly reduces testing time.

However, the question is, does a tumbling E perform like a grating stimulus? In other words, is resolution of a tumbling E stimulus still sampling-limited, and hence will it give a direct estimate of ganglion cell density?

Some work has already been carried out on comparing the performance of gratings and the tumbling E. The E stimulus can be regarded as similar to a 2.5 cycle square-wave grating, and one study\(^8\) has shown that the difference amplitude spectrum for a horizontal and vertical grating is very similar to that for a ‘right’ and ‘up’ E (Fig. 1) and, as would be expected, resolution measurements at the fovea and out to 50° eccentricity are exactly the same for these two pairs of stimuli (Fig. 2). However, if a tumbling E target behaves like a 2.5 cycle square-wave grating, can we be confident that a stimulus which contains only 2.5 cycles behaves in a sampling-limited fashion?

The effect of the number of cycles on grating detection and resolution thresholds has also been assessed\(^3\), and although detection and resolution thresholds both deteriorate when there are fewer than six full cycles in the stimulus, there is still an aliasing zone present when there is only one full cycle. Hence, for a 2.5-cycle grating,

![Diagram](image-url)

*Fig. 1. Spatial frequency difference spectra for horizontal versus vertical 2.5-cycle square-wave grating and ‘right’ versus ‘up’ tumbling E.*
we still observe an aliasing zone indicating that resolution is still sampling-limited. We can therefore be reasonably confident that resolution for a tumbling E is also sampling-limited, and hence will give us a direct estimate of the ganglion cell density.

A final confirmation that the target behaves in a sampling-limited (rather than optically-limited) fashion would be that localized resolution performance values correspond to the expected values based on anatomical counts of ganglion cell density. Anatomical studies indicate that ganglion cell density is not the same in different retinal meridians. In particular, there exists a visual streak where, beyond the optic nerve head, ganglion cell density in the horizontal nasal retina is considerably higher than any other meridian, and cell density in the superior retina is significantly higher than in the inferior retina. This anatomical variation was confirmed psychophysically by Anderson et al. when they measured grating resolution at 25° using an interferometer in different retinal meridians. They found that resolution was higher in the nasal retina than in the temporal retina by a factor of two, and in the superior retina than in the temporal retina by 25%. We wished to confirm that this is also the case using a tumbling E stimulus.

**Part 1**

To examine this, we measured resolution for the tumbling E at 25° eccentricity in eight different meridians in the visual field in one subject who was also a subject in the study of Anderson et al. (RSA). Stimuli were high contrast (90%), computer generated tumbling E’s displayed on a high resolution monitor (Eizo) placed 0.3 m from the subject. The procedure was a 4AFC resolution task, where the subject viewed a central fixation cross and had to verbally indicate the orientation of the randomly presented target (right, up, left, down). Target presentation time was 0.5 seconds, and we still observe an aliasing zone indicating that resolution is still sampling-limited. We can therefore be reasonably confident that resolution for a tumbling E is also sampling-limited, and hence will give us a direct estimate of the ganglion cell density.

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resolution threshold was estimated using a 2 up/1 down reversal strategy where two correct responses resulted in a 10% decrease in stimulus size, and one incorrect response resulted in a 10% increase in stimulus size. Four reversals were recorded at each location, and the last two reversals were averaged to obtain threshold.

The results are shown in Figure 3. These results are qualitatively and quantitatively similar to those found in the previous study which used an interferometer, except that the resolution measurements are slightly lower, as would be expected with fewer cycles in the stimulus. This pattern of results reflects the visual streak which has been observed anatomically by Curcio and Allen. Hence, localized resolution acuity for the tumbling E stimulus reflects the distribution of retinal ganglion cells and provides further evidence that resolution for this stimulus is limited by the retinal ganglion cell density.

Part 2

We then designed a perimetric test, utilizing the tumbling E stimulus, for preliminary testing on a group of six confirmed glaucoma patients (mean 65 ± 6 years) and a group of six age-matched normal controls. All the glaucoma patients had established field defects using the 24-2 Program on the Humphrey perimeter. The test consisted of 16 field locations, eight in each of two concentric rings of 10 and 20° eccentricity (Fig. 4). Threshold was measured at each location, using the strategy described above. Appropriate foveal refractive correction was worn for all tests.

All points commenced at values determined to be suprathreshold for normal sub-

Fig. 3. Resolution acuity measurements (minutes of arc) at 25° eccentricity in different meridians for the tumbling E.
To reduce testing time on the glaucoma patients, recording stopped at any location where the target size increased to twice that of the starting level. This end-point was recorded as the test result for this location.

Figure 4 shows the results for a normal subject. The E is scaled relative to the

Fig. 4. Tumbling E plot for a normal subject showing relative threshold letter size.

Fig. 5. Mean of 16 resolution values for glaucoma patients and normals.

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Fig. 6. a. Tumbling E plot for glaucoma patient, and b. corresponding Humphrey 24-2 plot. Black E’s represent threshold sizes no more than 20% larger than the average age-matched normal value. Gray E’s represent the locations where the threshold letter size was more than 20% greater than for an age-matched normal.
threshold size. Resolution is much higher in the inferior field (superior retina) than in the superior field (inferior retina), agreeing with the anatomical data of Curcio and Allen. However, there was no noticeable difference in the nasal versus temporal field, probably because the eccentricity only goes out to 20°, and we did not include the horizontal meridians.

Figure 5 shows the mean resolution for both groups. Resolution for the glaucoma patients was significantly reduced compared to the normals ($p<0.01$).

Figure 6 shows the results for the tumbling E and the corresponding Humphrey plot for a glaucoma patient. Both tests were performed on the same day. On visual inspection of the plots, there is a reduction in resolution acuity in the areas corresponding to the Humphrey field plot defects, and there are also defects in resolution acuity in some areas of the field which are graded as normal on the Humphrey plot.

**Conclusions**

Early indications from using the tumbling E as a perimetric stimulus show that this stimulus is capable of identifying established field defects as found on the Humphrey Field Analyzer. Of more interest, however, is the possibility that it could highlight defective areas in the visual field which are classified as normal by standard perimetry. The implication is that, because of its sampling-limited nature, this test may afford a method of detecting areas of ganglion cell loss that are not severe enough to show up on standard perimetry tests. We are currently recruiting normal subjects of different ages to establish normative data and glaucoma patients and suspects in order to establish whether this method does in fact isolate areas of the visual field with reduced resolution acuity. If so, we want to determine whether this reduction in resolution acuity is a precursor to a measurable visual field defect using standard perimetric techniques.

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**References**