

# CONCURRENT BINOCULAR MULTIFOCAL PUPILLOGRAPHIC FIELD TESTING

EVIDENCE LEVEL II

ORIGINAL



A.C. James, T. Maddess.  
ARC Centre of Excellence in Vision Science,  
Australian National University, Canberra, Australia.



## ABSTRACT

**PURPOSE:** This study was a preliminary investigation of a means of concurrently assessing the visual fields of both eyes by recording the responses of both pupils to independent stereoscopically presented multifocal stimuli, to investigate the sensitivity and specificity of this as a method for objective perimetry for glaucoma.

**DESIGN:** Experimental design.

**PARTICIPANTS:** The 20 normal subjects were given a thorough eye exam including HFA achromatic 24-2 fields (SITA) and fundus photography assessed by a single skilled observer. The 26 open angle glaucoma patients had stable, moderate to severe, HFA fields. Subjects were age and sex matched. All subjects gave written consent in accordance with the Helsinki Declaration and ANU Human Ethics Protocol 238/04.

**METHODS:** Dichoptic stimulation was provided via a pair of stereoscopically arranged LCD displays. The subject thus saw a single cyclopean stimulus. Each display presented a circular dart-board-like array of 24 stimulus regions extending to 30 deg eccentricity. Each region in each eye received independent stimulus presentations at a mean rate of 1/s. Four stimulus presentation conditions were tested: each stimulus region containing either a single or a 2x2 array of patches, being presented either steady for 133ms or flickered half-on half-off at 15 Hz for 266ms. For each of the 4 tests the recording duration was 4 minutes, divided into 8 segments, or 2 minutes per eye.

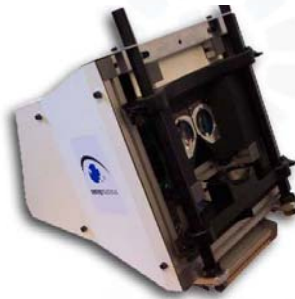
**MAIN OUTCOME MEASURES:** Sensitivities and specificities for each of the 4 stimulus protocols as obtained from receiver operator plots.

**RESULTS:** Both pupils were recorded with 24 regions mapped in each eye, giving a total of 96 responses/subject from each 4 minute record. The regressive analysis method meant that about 10% of each record could be lost due to blinks etc. without affecting accuracy, e.g.[11,12]. The median peak contraction amplitudes expressed as z-scores for the 4 conditions were 4.1, 3.3, 3.2 and 2.3. The best diagnostic performance was obtained by taking the mean of the 10 worst deviations from the normal profile across the visual field regions, providing a joint sensitivity and specificity of 85% for the flickered single patch condition.

**CONCLUSIONS:** The pupillographic multifocal method provided diagnostic accuracy that approached that of standard perimetry even though the raw test time was equivalent to 2 min per eye. Measuring the visual fields of the two eyes concurrently has statistical advantages for comparing the two eyes. Unlike perimetry the method provides both sensitivity and temporal dynamics for each visual field region. Unlike evoked potential based multifocal methods pupillography requires no additional setup time for electrode placement. Further experiments also presented at this meeting indicate that with modification of the stimulus parameters can improve sensitivity and specificity.

## INTRODUCTION

- Automated perimeter test-retest variability is high<sup>[1-3]</sup>
- ~10% fail catch trials (reducing sensitivity & specificity)<sup>[4,5]</sup>
- So objective perimetry would be nice but, mfERG, mfVEP poorly tolerated, and so far have been too slow<sup>[6,7]</sup>
- Recent work shows the human pupil is partly driven by visual cortex and therefore by the optic nerve<sup>[8]</sup>
- Multifocal pupil perimetry has been demonstrated but low SNR, blinks, fixation losses a problem<sup>[9,10]</sup>
- We have recently demonstrated that sparse multifocal stimuli improve can so reduce recording time, possibly making pupillographic multifocal perimetry possible<sup>[11-13]</sup>
- Multiple regression methods for estimating the multifocal responses mean we can eliminate the effects of data losses due to fixation losses, blinks etc. <sup>[11-13]</sup>
- Can test both eyes concurrently, with consensual responses obtain 4 visual fields at once



So, let's try multifocal pupillography to assess visual fields in glaucoma.

FIGURE 1:

The P2 prototype dichoptic stimulator and infrared pupillography device used in these experiments.

## METHODS

### SUBJECTS

- 6/12 or better acuity
  - no distance refraction of more than  $\pm 5$  D
  - exclude more than 2D cylinder
  - HFA, SITA 24-2
  - optic disc photography
  - pupil size greater than 2.5 mm in test room
- N = 20

### NORMAL SUBJECTS

- no chronic ocular disease
- vertical cup to disc ratios of less than 0.6
- cup to disc asymmetry between eyes of less than 0.2
- IOP < 22 mmHg
- no family history of glaucoma (self reported)

### GLAUCOMA PATIENTS

- 12 to 36 points depressed at 5% or below,
  - or 8 to 19 pts depressed at below 1%
  - (4 worse, 4 better)
  - No total loss in central 5°
  - No adjacent pairs of points in one hemifield within the central 5 degrees that are depressed by 15 dB or more
- N = 26

### STIMULI

- 24 regions, 30° radius, 48 responses/eye
- 12 to 180 cd/m<sup>2</sup>
- 8 x 30s segments = 4 min. for both eyes
- blinking permitted, & no fixate = no data
- mean interval per region 1/s
- 133 ms on (On) or 266 ms 15 Hz (Fl)
- 1 large check or 2x2 checks hence the stimulus names:
  - On1, On2, Fl1, Fl2

## RESULTS

Main effects – normal subjects referenced to the On1 stimulus

Effect	Estimate dB	SE dB	Anti -log	t-value	P(> t )
Left Pupil	10.48	0.200	11.17 $\mu$ m	52.39	< 2e-16
Right Pupil	10.58	0.199	11.43 $\mu$ m	53.10	< 2e-16
Consensual	-0.153	0.065	$\times 0.965$	-2.33	0.020
Fl1	0.54	0.280	$\times 1.132$	1.95	0.051
On2	-1.192	0.300	$\times 0.760$	-3.98	6.99e-05
Fl2	-1.543	0.305	$\times 0.701$	-5.06	4.30e-07

\*efficiency gain = 1.281x

### ROC analysis

- 96 responses/subject/protocol
- calculate RMS  $\mu$ m 0.25 to 0.75s
- take larger of 2 pupil responses/region (48)
- compute deviations from median normal field profile
- mean of 10 worst deviations (up to 20 same), hence a patient-wise diagnosis
- no contrast between eyes as yet (but did measure both eyes concurrently)

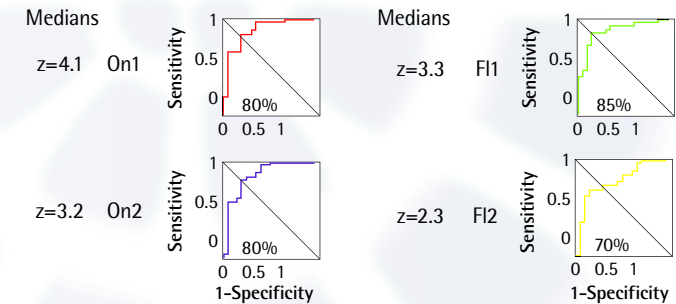


FIGURE 2:

Receiver Operator Characteristic (ROC) plots for diagnosis of glaucoma versus normal subjects. The Fl1 protocol was the best performing at 85% sensitivity and specificity. The median Z-scores (across regions and subjects) for each protocol is given at left.

## CONCLUSIONS

- We stimulate both retinas
- Record both pupils (which each respond to both retinas)
- Hence there are same-eye and consensual-eye responses for both retinas
- So 2 measures of 24 visual field points of each retina (hence 96 responses / person)
- Fl1 approached the diagnostic performance of automated perimeters at 85% sensitivity and specificity
- 4 visual fields in about 2 min. recording / eye
- Only one pupil needs to work but...
- brimonidine, diabetes, rheumatic diseases

## REFERENCES

- Artes P, et al. 2002, *Invest Ophthalmol Vis Sci* 43:2654-2659
- Heijl A, et al. 1989, *Am J Ophthalmol* 108:130-135
- Plittz J, et al. 1989, *Am J Ophthalmol* 108:109
- Bickler-Bluth M, et al. 1989, *Ophthalmology* 96:616-9
- Birt CM, et al. 1997, *Ophthalmology* 104:1126-30
- Fortune B, et al. 2001, *Optom Vis Sci* 78:206-14
- Goldberg I, et al. 2002, *Am J Ophthalmol* Jan; 133:29-39
- Kardon R, et al. 1996, *Invest Ophthalmol Vis Sci* 37:S159
- Tan L, et al. 2001, *Vision Res* 41:1073-84
- Wilhelm H, et al. 2000, *Invest Ophthalmol Vis Sci* 41:1229-38
- James AC 2003, *Invest Ophthalmol Vis Sci* 44:879-90
- James AC, et al. 2005, *Vis Neurosci* 22:45-54
- Maddess T, et al. 2006, *Visual Neurosci* 23:703-712