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# Higher Resolution Pupillographic Multifocal Perimetry

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# Financial Disclosures.....

- Financial interests or relationships to disclose:
  - AC James, XL Goh and T Maddess are consultants to Seeing Machines Ltd
  - AC James and T Maddess have patents and patent applications under license to Seeing Machines Ltd
  - AC James and T Maddess have share options in Seeing Machines Ltd
  - M Kolic, CF Carle, none

# Motivations for present study...

- Automated perimeter test-retest variability is high
- ~10% of patients fail catch trials (fixation losses, false positive & negative rates), ~5% of normals
- This reduces sensitivity & specificity
- So objective perimetry would be nice but, mfERG, mfVEP poorly tolerated, and so far have been too slow
- The pupil is driven via the visual cortex and by Melanopsin containing ganglion cells

# Motivations ...continued

- Multifocal pupil perimetry has been demonstrated but low SNR, blinks, fixation losses have been a problem
- We have recently demonstrated that sparse multifocal stimuli give good SNR in mfVEPs providing reduced recording time
- New multifocal methods by AC James eliminate problems of blinks & fixation loss
- So let's try multifocal pupil perimetry!



# Methods

# Subjects

- All examined with: HFA achromatic, SWAP and Matrix 24-2 perimetry, Stratus OCT, and slit lamp (+ tonometry)
- no eye disease or surgery except ALT or SLT
- refractive error not greater than ( $\pm$ ) 9D or 2D of cylinder, acuity better than 6/12
- normals: no vertical cup to disk ratio  $> 0.6$  or between eye asymmetry  $> 0.2$
- normals: no 1<sup>st</sup>-order relatives with glaucoma
- 42 normal and 44 glaucoma subjects

# Subjects

	Age (yr) $\pm$ SD	males	females
Normal	59.4 $\pm$ 7.7	18	24
Glaucoma	63.7 $\pm$ 10.6	26	18

# Multifocal Pupillography

- we replace the electrode of ERGs or VEPs with infrared cameras measuring pupil contractions at 30 frames/s
- background luminance =  $10 \text{ cd/m}^2$ , maximum luminance  $290 \text{ cd/m}^2$
- 24 or 44 regions per eye within a 30 degree radius field
- each stimulus persisted for 33 ms
- the regions are stimulated concurrently but independently for both eyes (dichoptic)

# Methods

- Multifocal sparse stimulus made up of 8 segments of 30s duration, so the total stimulus duration is 4 minutes
- Up to 15% data loss from blinks, fixation losses permitted
- Relative pupil size measured
- Four experimental protocols
  - P44-1, 44 regions/eye, 1 presentation/s/region
  - P44-1/4, 44 reg/eye, ¼ pres/s/reg
  - P24-1, 24 reg/eye, 1 pres/s/reg
  - P24-4, 24 reg/eye, 4 pres/s/reg
- All subjects tested twice with all 4 protocols ~2 weeks apart,  $2 \times (44 + 42) \times 4 \times 2 = 1376$  eye tests

# Methods continued

- Visual field severities defined by HFA SITA or Matrix mean defects
  - Mild  $< 6$  dB
  - Moderate 6 db to  $< 12$  dB
  - Severe  $> 12$  dB
- Measures of field loss examined
  - N worst amplitudes (Amp), can be clusters
  - N worst delays ( $\Delta t$ )
  - linear combination of amplitude and delay (Amp+ $\Delta t$ )



# TrueField Analyser (TFA)

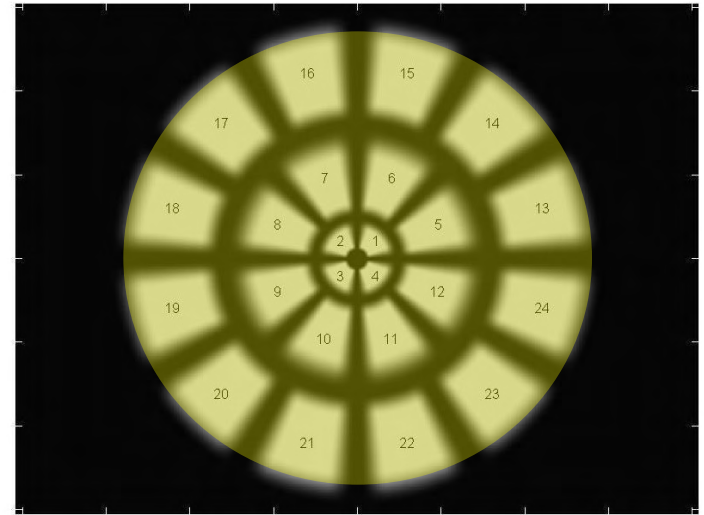
- Device is currently called the TrueField Analyser (TFA)
- Design by Seeing Machines Pty
- [www.truefield-analyzer.com](http://www.truefield-analyzer.com)

# TrueField Analyser (TFA)



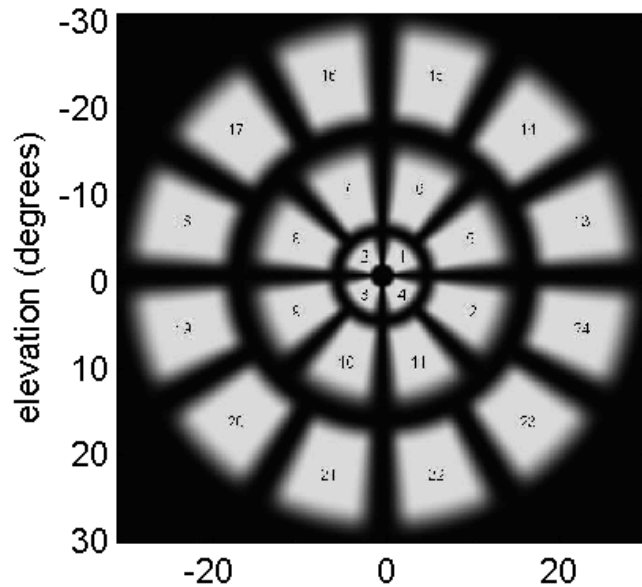
# TFA stimuli

- T30-24 stimulus pattern, shown as if all regions were on
- deliberately blurred to provide tolerance to mis-refraction
- regions and background were yellow

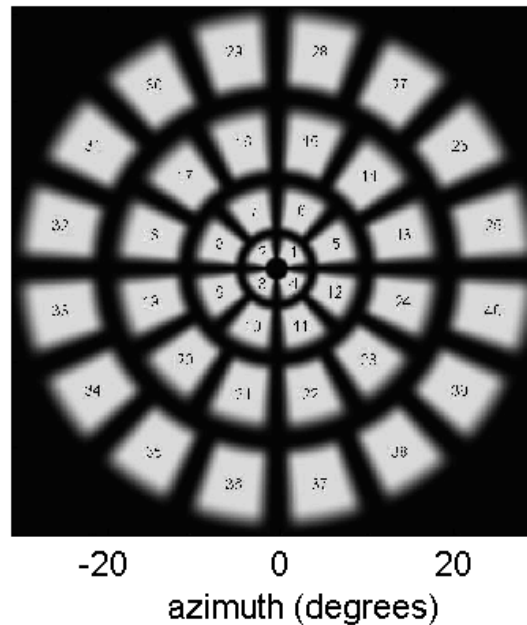


# Gaps a problem?

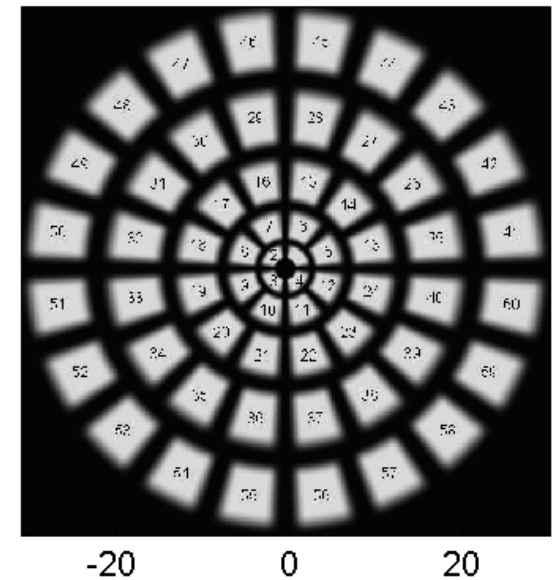
T30-24



T30-40

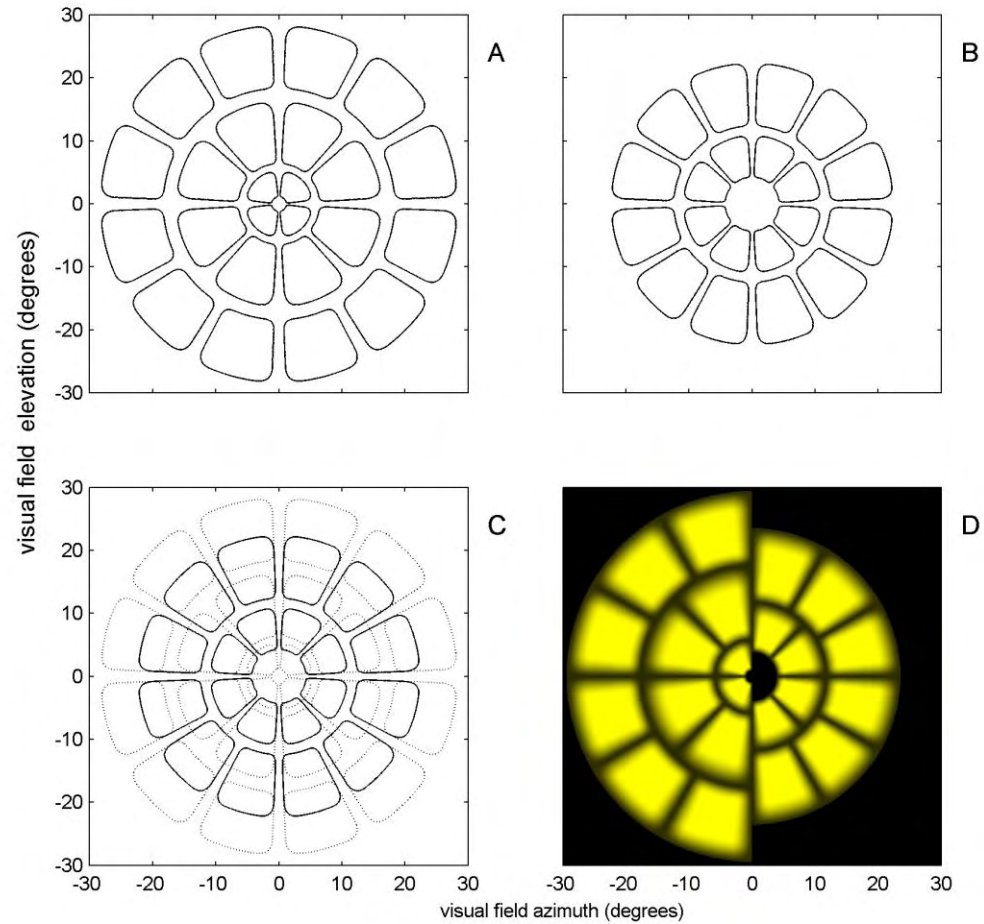


T30-60

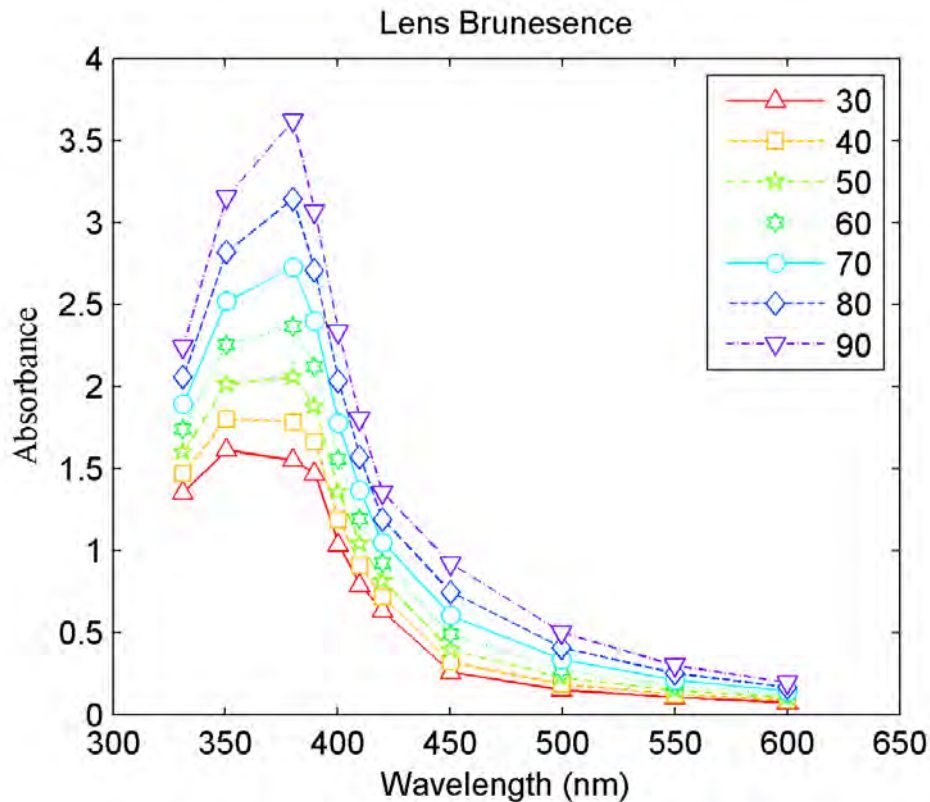


# O30-44 stimulus

Overlapping Polar Stimulus Ensemble



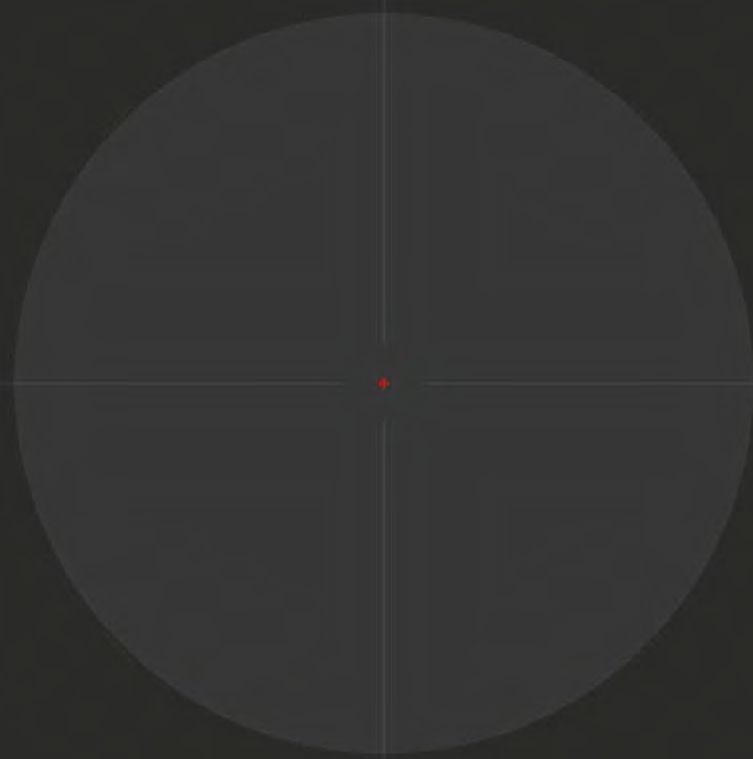
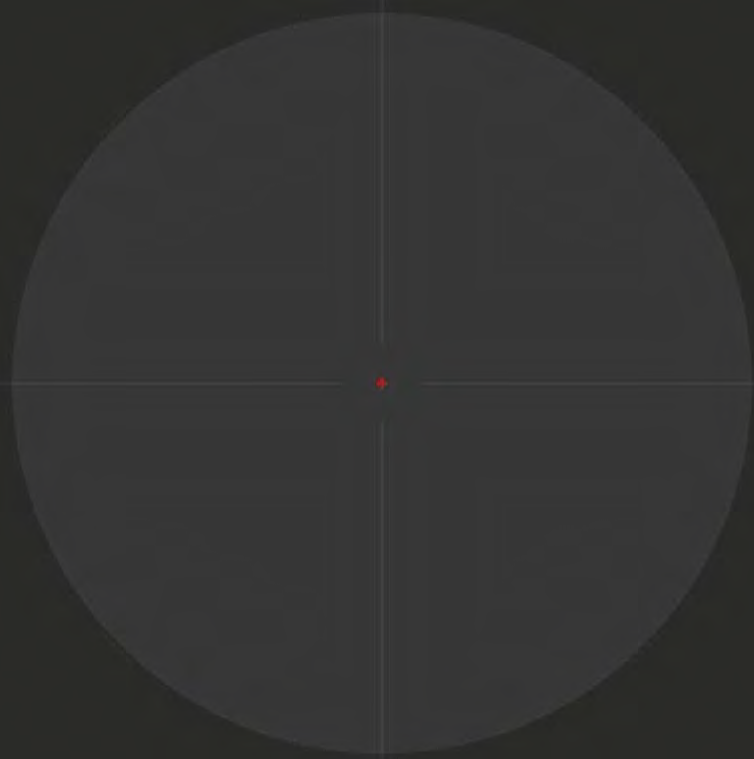
# Lens Brunescence



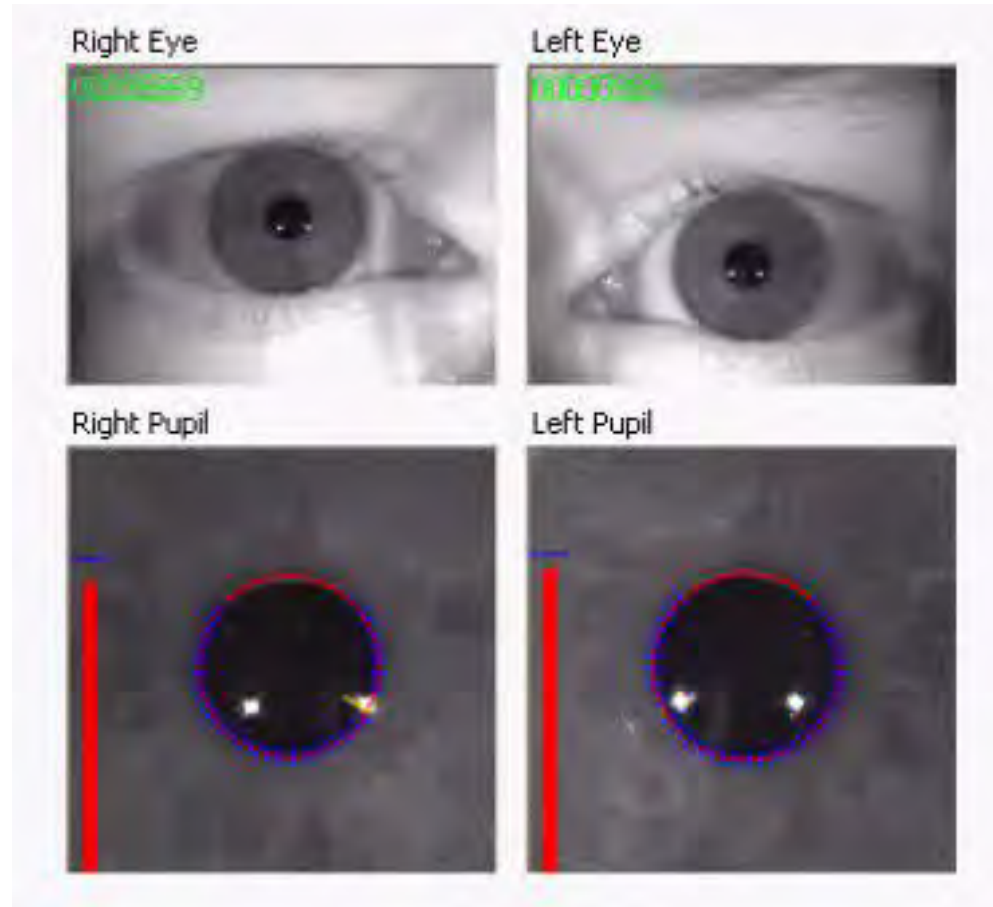
Weale RA (1988)  
J Physiol 395:577-587

**Fortune B, Johnson CA (2002)** Decline of photopic multifocal electroretinogram responses with age is due primarily to preretinal optical factors.  
J Opt Soc Am A Opt Image Sci Vis **19**:173-184.

Independent binocular ***sparse*** stimuli.....



# Camera view of pupil tracking...



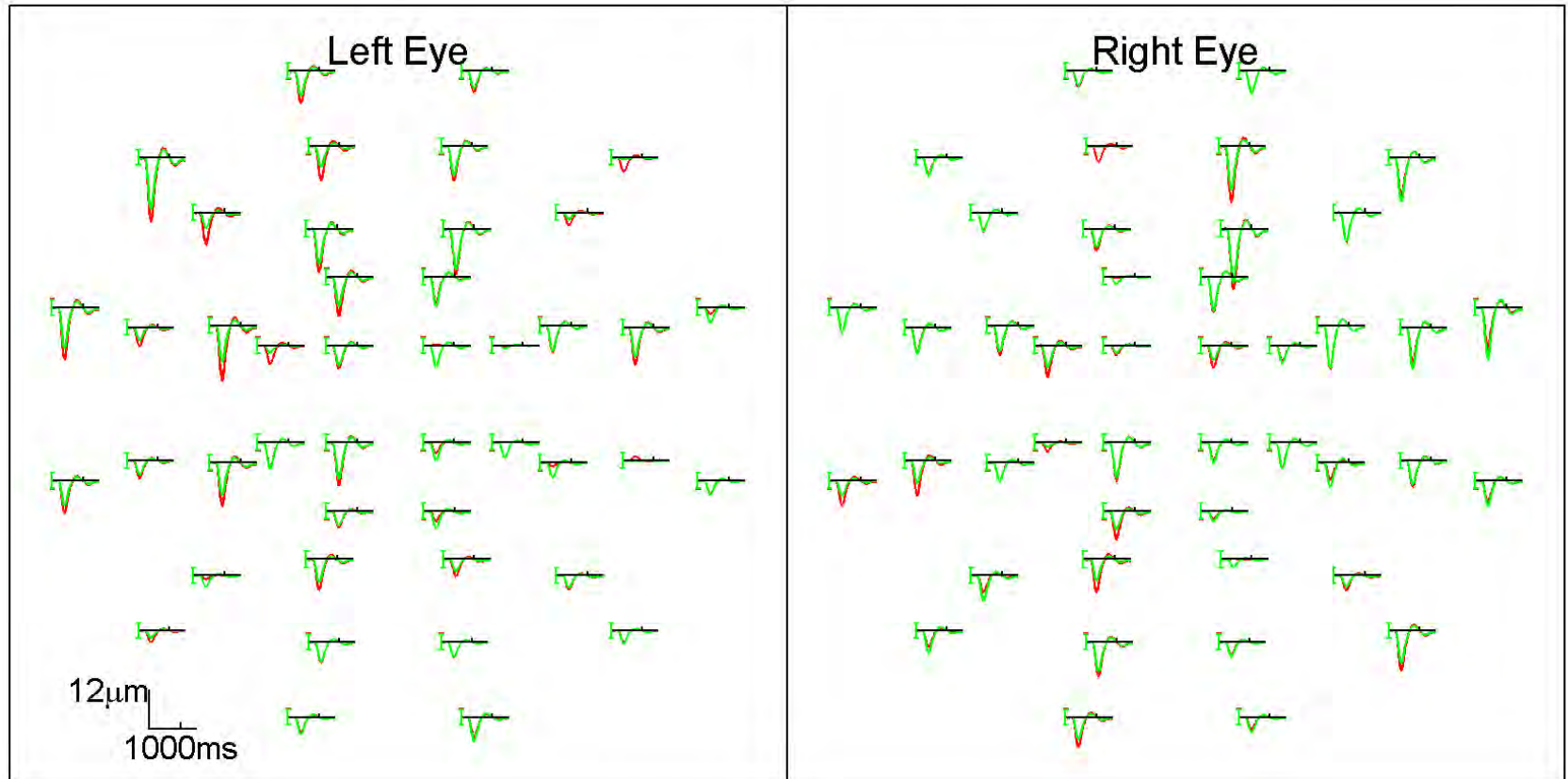


# Results

# Basic results

- **24 regions/eye**, giving 48 responses/eye = **96** amplitudes & delays obtained from each test
- **44 regions/eye**, giving 88 responses/eye = **176** amplitudes & delays obtained from each test
- compare with **54** thresholds for 24-2
- most of the diagnostic effect is in the response amplitudes

O30-44, Subject= 971



— LeftPupil  
— RightPupil




# **LINEAR MODELS**

# P44-1

	Constriction ( $\mu\text{m}$ )	SE ( $\mu\text{m}$ )	p-value
Const	9.31	0.199	0
female	-0.764	0.042	1.63E-73
consensual	-0.487	0.041	4.14E-32
glaucoma	-0.792	0.043	1.92E-76
repeat	0.111	0.041	7.38E-03
age ( $\mu\text{m}/\text{yr}$ )	-0.033	0.002	3.79E-47

# P24-1

	Constriction ( $\mu\text{m}$ )	SE ( $\mu\text{m}$ )	p-value
Const	8.94	0.299	1.34E-191
female	-0.69	0.071	2.94E-22
consensual	-0.664	0.07	1.97E-21
glaucoma	-0.764	0.072	4.22E-26
repeat	-0.033	0.07	6.34E-01
age ( $\mu\text{m}/\text{yr}$ )	-0.042	0.004	4.79E-27



Amp +  $\Delta t$

# AREAS UNDER ROC CURVES

# % AUC – field severity by Matrix

	Experimental Protocol			
Field severity	P44-1	P44-1/4	P24-1	P24-4
Mild	<b>68.2</b>	59.5	65	64.4
Moderate	<b>87.7</b>	81.7	86.9	87.1
Severe	<b>95.8</b>	85.1	90.3	90.5

# % AUC – field severity by SITA

	Experimental Protocol			
Field severity	P44-1	P44-1/4	P24-1	P24-4
Mild	<b>72.4</b>	64.1	70.7	65.5
Moderate	<b>80.4</b>	71.2	72.6	77
Severe	<b>97.1</b>	90.6	89.1	95.8

# % AUC – means for P44-1

Field severity	Field Severity Method		
	Matrix	SITA	Mean
Mild	68.2	72.4	<b>70.3</b>
Moderate	87.7	80.4	<b>84.1</b>
Severe	95.8	97.1	<b>96.5</b>

# % AUC – means for 3 trials

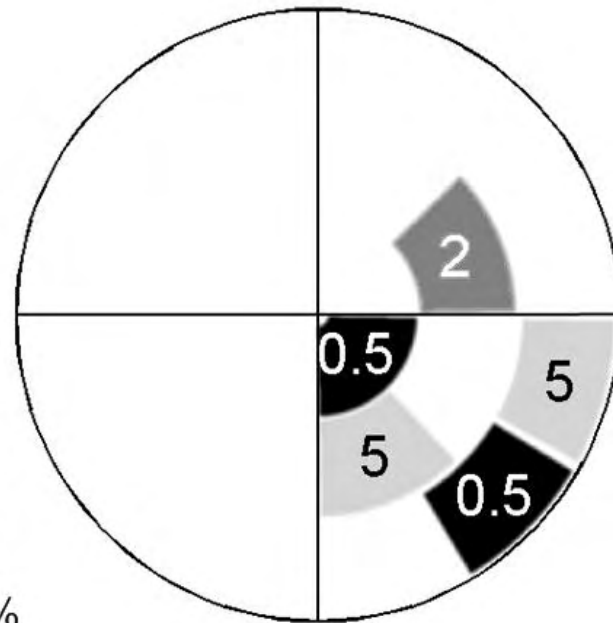
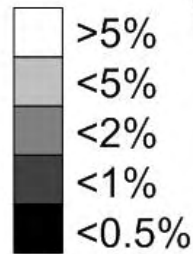
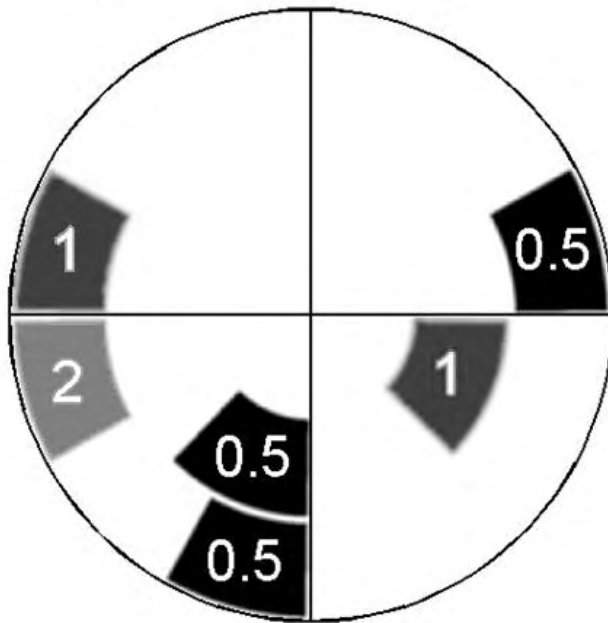
	Trial Name (N fields)		
Field severity	P44-1	T17	T22
Mild	70.3 <sub>(107)</sub>	82.2 <sub>(26)</sub>	75.4 <sub>(28)</sub>
Moderate	84.1 <sub>(38)</sub>	98.3 <sub>(8)</sub>	94.3 <sub>(9)</sub>
Severe	96.5 <sub>(23)</sub>	100 <sub>(6)</sub>	97.5 <sub>(5)</sub>

# TFA report: deviation probabilities

Left Eye / OS

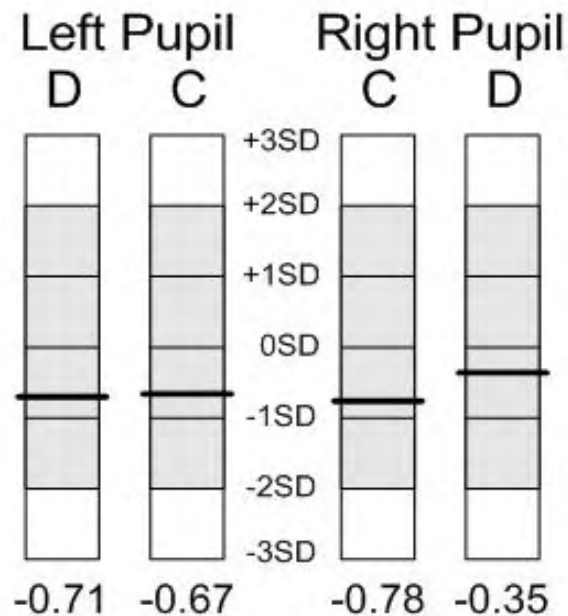
Right Eye / OD

Deviation Probabilities [%]



# TFA report: pupil response

## Pupil Responses



<u>Left</u>	<u>Pupil Data</u>	<u>Right</u>
3.0 mm	Baseline Ø	3.0 mm
98%	Valid Data	98%
5.9 µm	M.Contraction	6.2 µm
482 ms	Median Delay	474 ms
3.0	Median SNR	3.0



# FDA approval (510k)

- August 2007
- Substantially equivalent to the HFA2
- See you at AAO!



# Conclusions

# Conclusions

- both visual fields consistently within 5 minutes practical ( ~2.5 min/eye )
- problems of blinks and fixation losses eliminated
- reasonable reproducibility
- sensitivity and specificity approaching usable levels
- independent efferent and afferent pupil defect data at each field location

# Thank you for listening!

*Thankyou to Gaby Moreland, Wendy Holland, Bronwyn Jennings and staff at C.E.H for ongoing support ...*



**Research School of Biological Sciences at the ANU**

**Seeing Machines Ltd: TrueField Team**

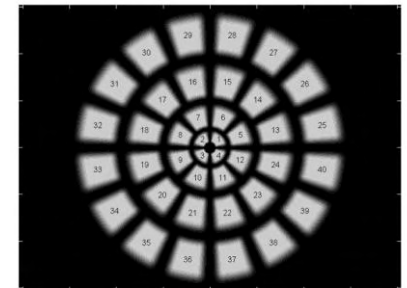
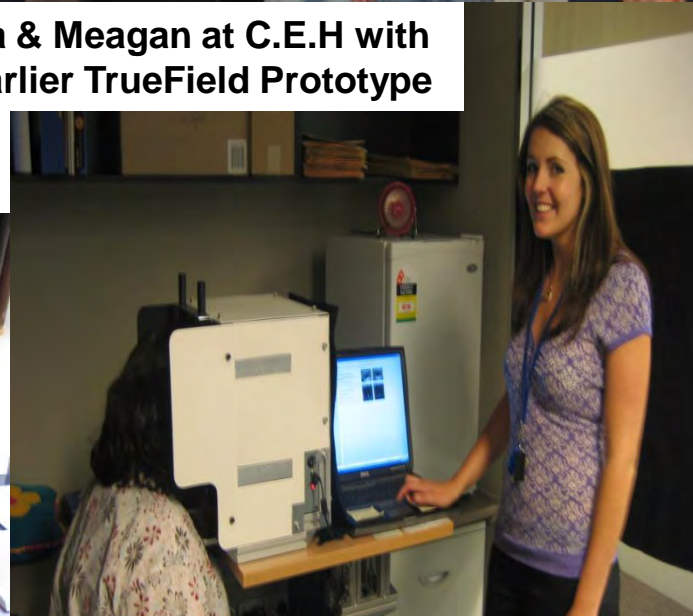


**Canberra Eye Hospital**



**Ted Maddess**

**Maria & Meagan at C.E.H with an earlier TrueField Prototype**



**Andrew James**