Objective perimetry based on chromatic multifocal pupillometer for treatment follow-up and diagnosis in patients with retinal and macular dystrophies

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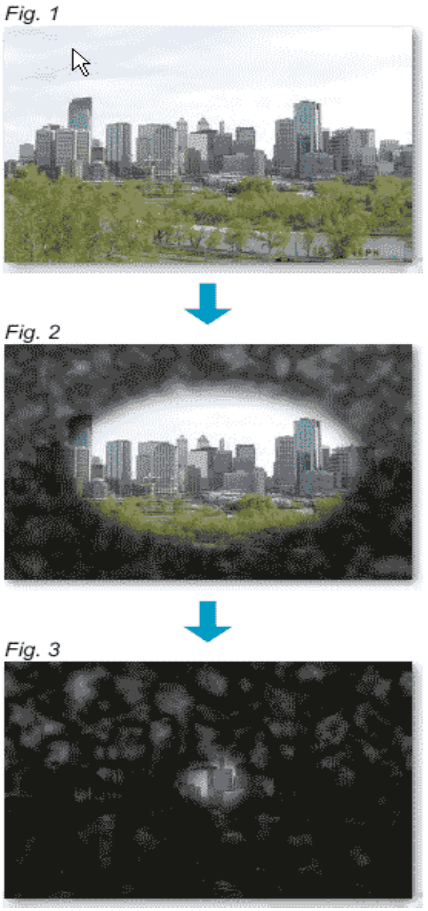
Accutome Inc.

Visual Feld constriction in optic nerve and retinal degeneration

Glaucoma- **>60M**

Photos: National Eye Institute, National Institutes of Health

Retinitis pigmentosa (RP) - **>1.5M**



Subjective perimetry and its limitations

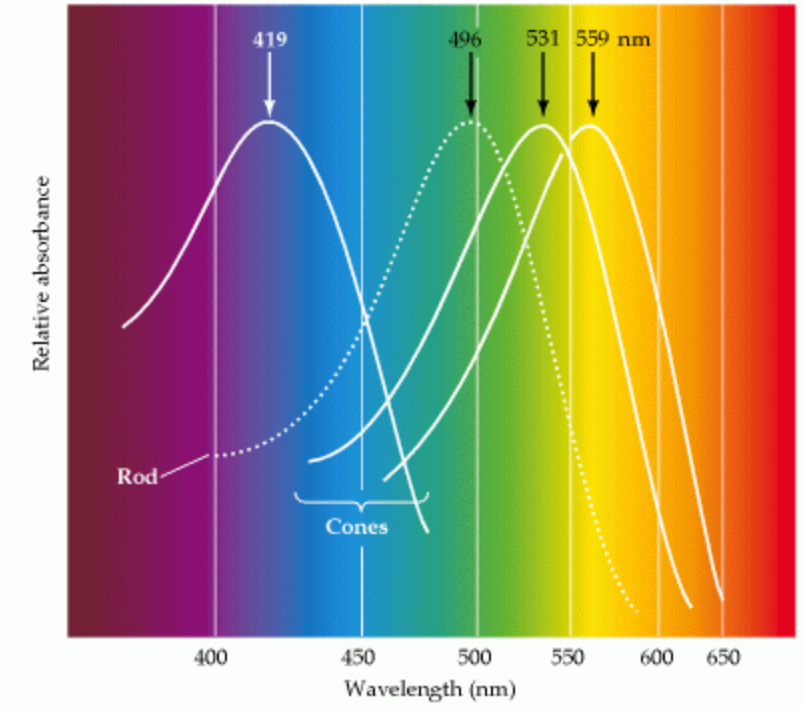
Goldmann

Humphrey

- Patients' cooperation is essential
- Prolonged and tiresome
- Qualified personnel
- The test can't distinguish between optic nerve vs. retina pathologies

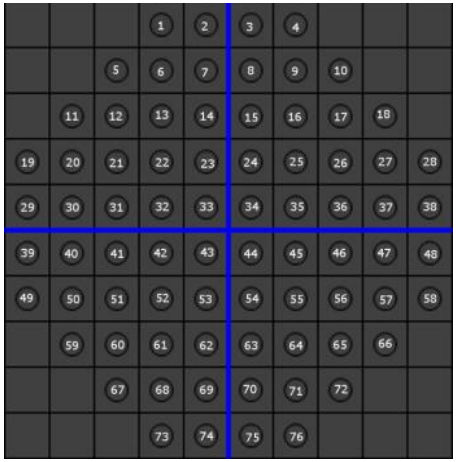
Perimetry based on Pupillary Light Reflex to multifocal chromatic stimuli

- Objective
- More informative
- Applicable to all pathologies and patients

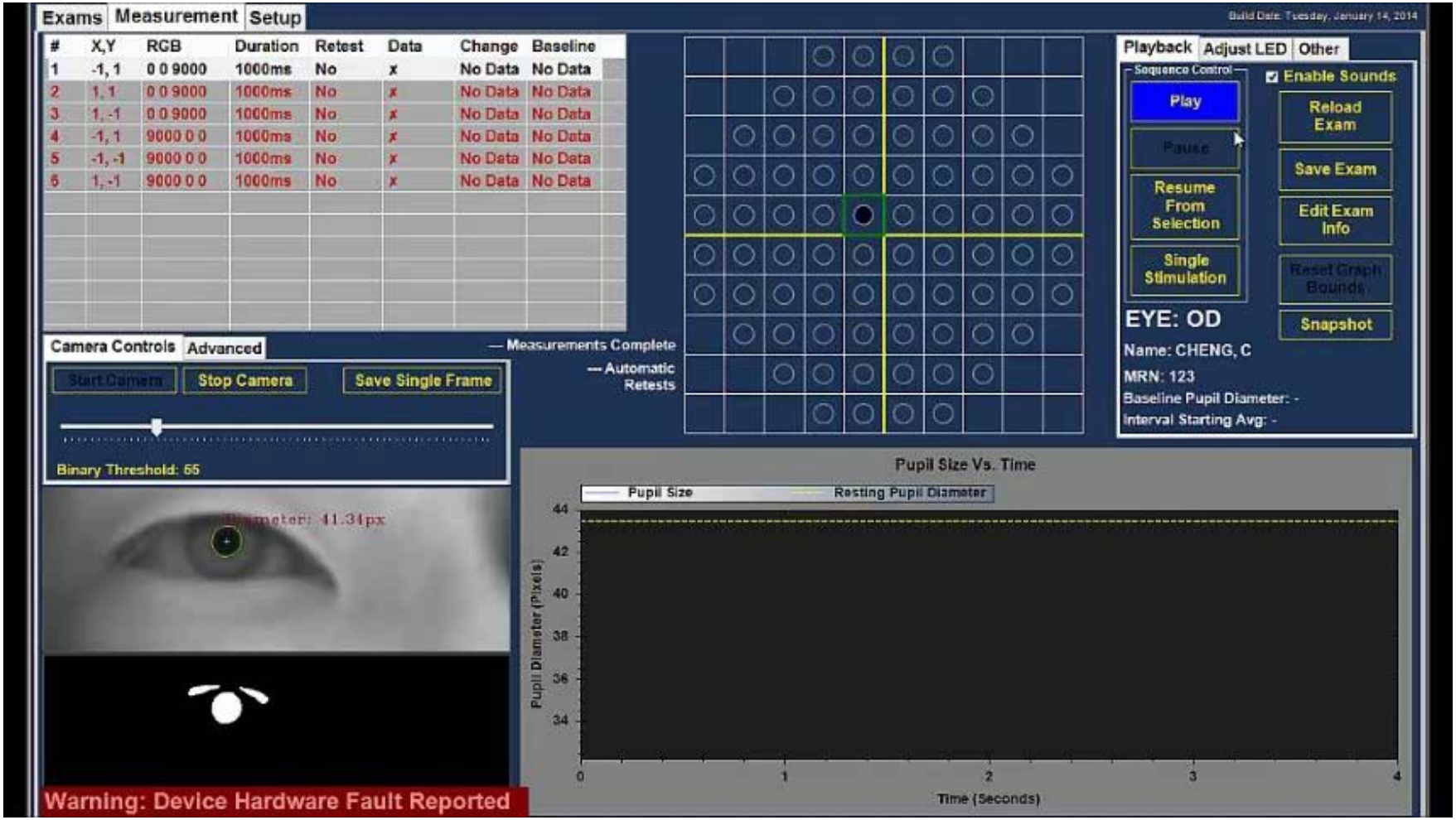


Cell Type	Stimulus
Cones	Low-intensity red (624nm)
Rods	Low-intensity blue (485 nm)
ipRGCs	**High intensity blue (485 nm)**

The Multifocal Chromatic Pupillometer - 76 Points (2mm)- 18° Visual Field



The multifocal chromatic pupillometer



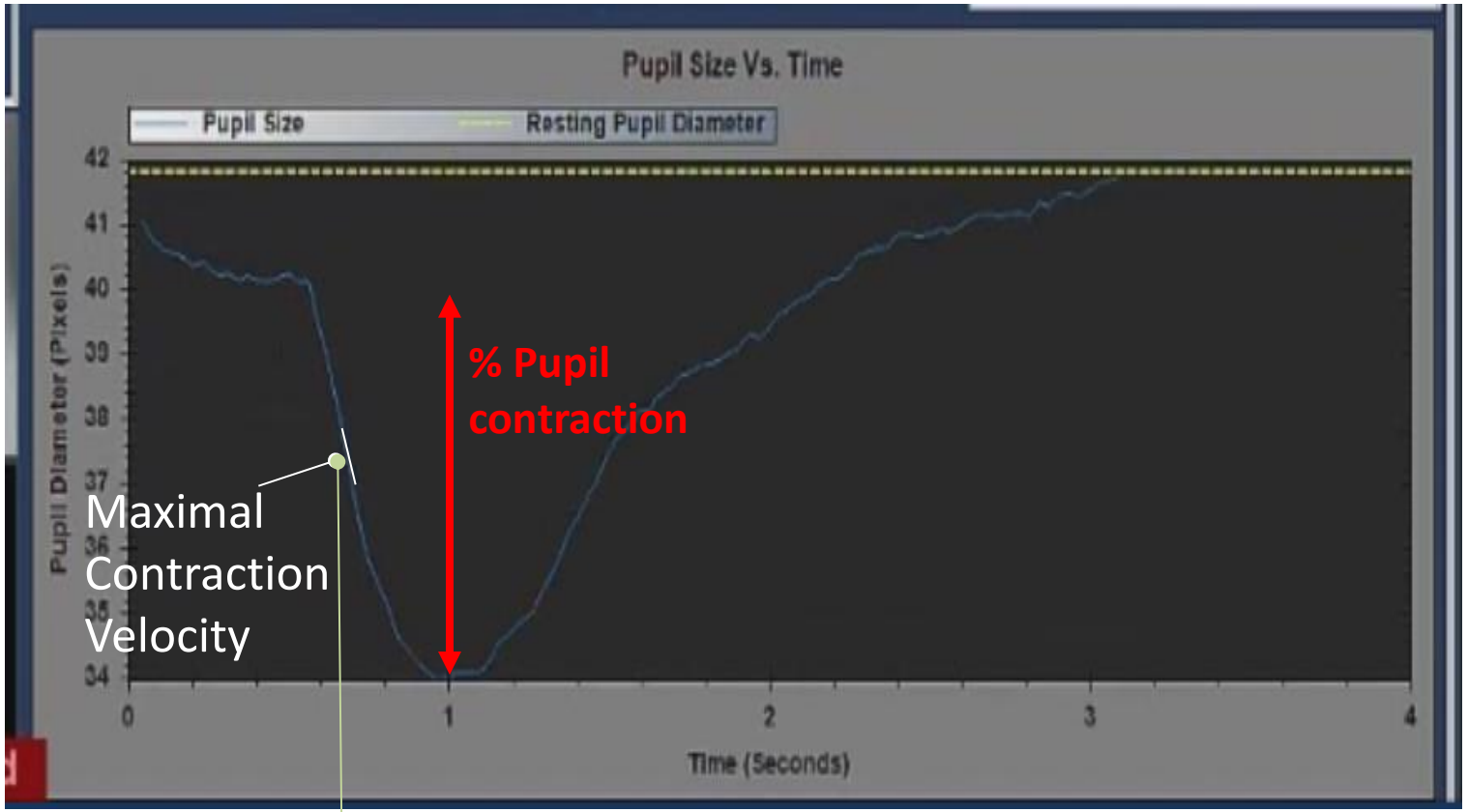
Study design:

- 13 retinitis pigmentosa (RP) patients
- 17 healthy age-matched volunteers
- In RP patients, the chromatic pupillometer recordings were compared with their dark-adapted Chromatic Goldmann

The test protocol

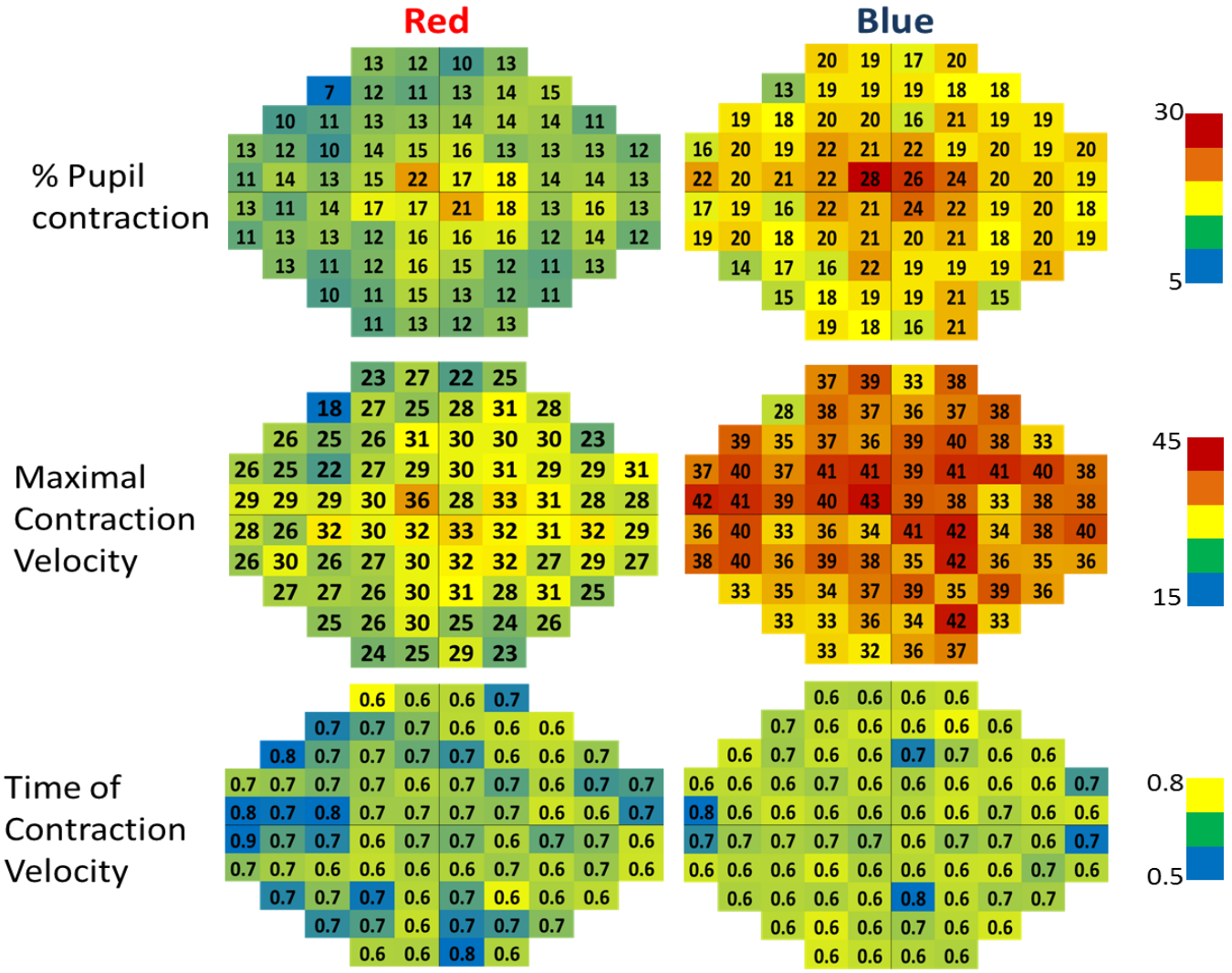
- Non-tested eye is covered by a patch
- Stimulus duration - 1 second
- Tracking of pupil size - 4 seconds
- Chromatic stimulus
  - Red (1000 cd/m², 624nm)
  - Blue (200 cd/m², 485nm)

Test Parameters:

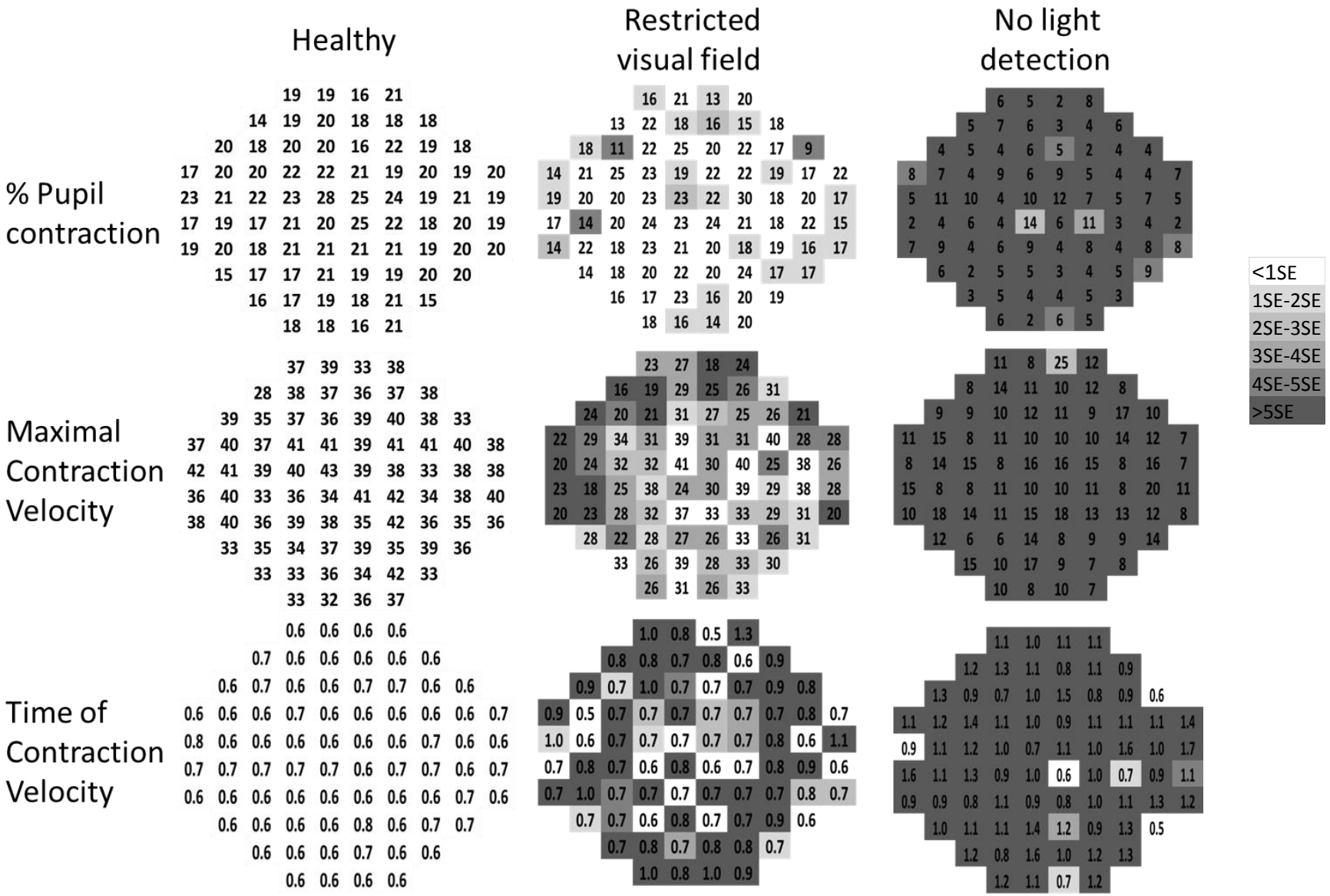


Time of Maximal Contraction Velocity

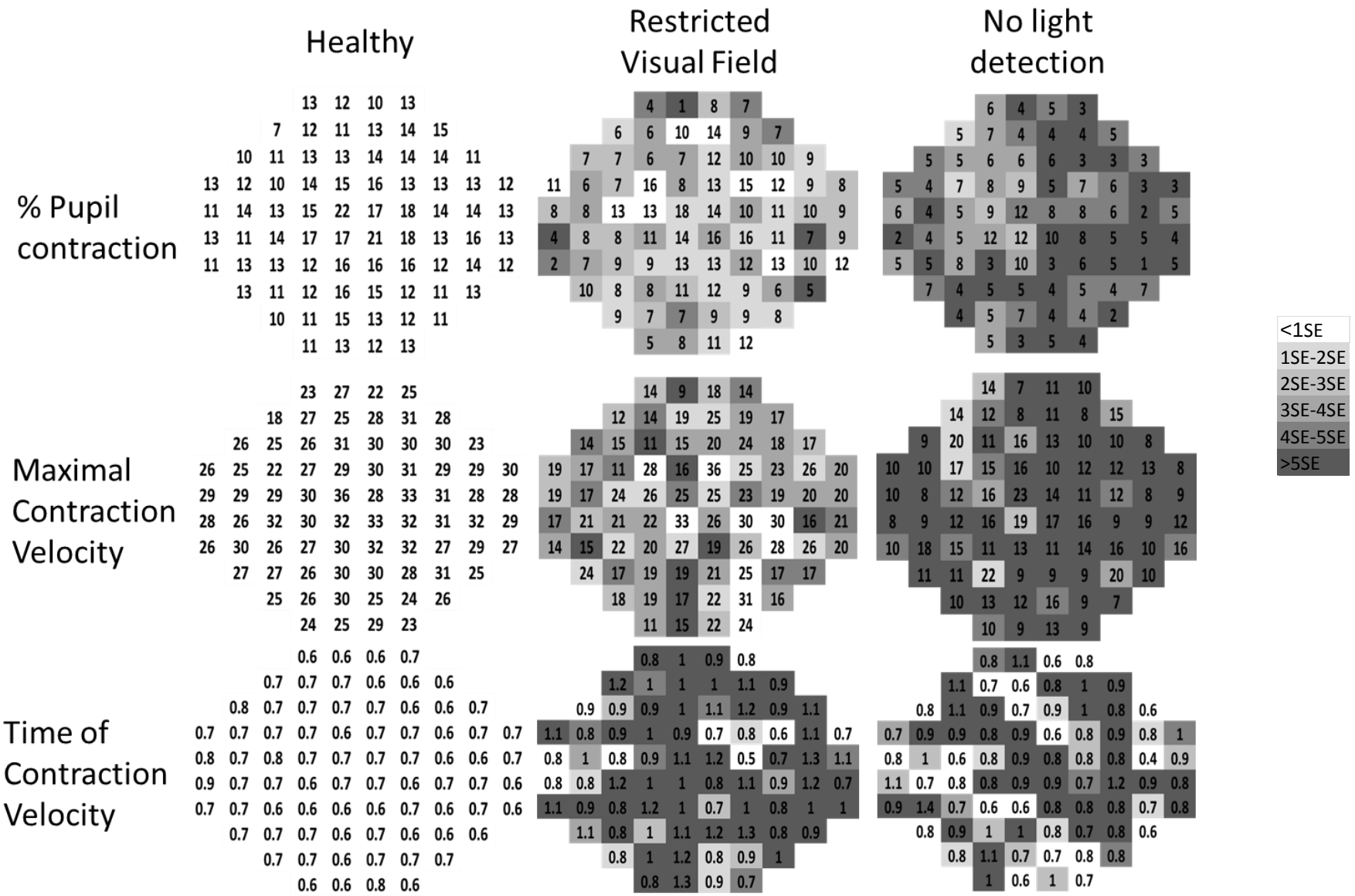
In healthy subjects: PLR to blue and central light stimuli are stronger than to red and peripheral stimuli



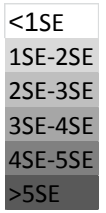
RP patients: reduced response to blue light, correlating with VF restriction severity

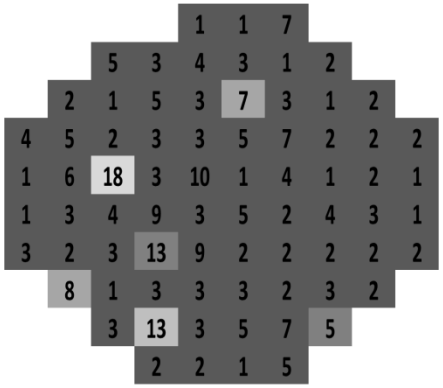
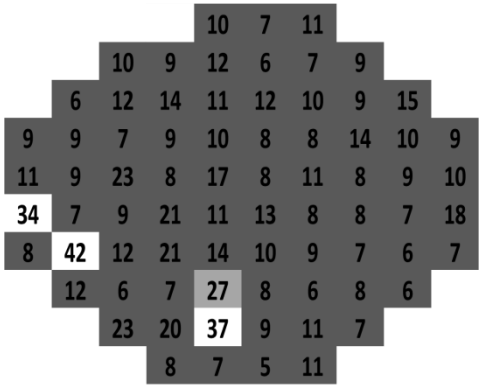
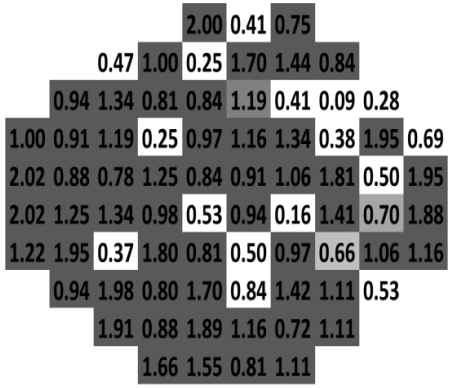
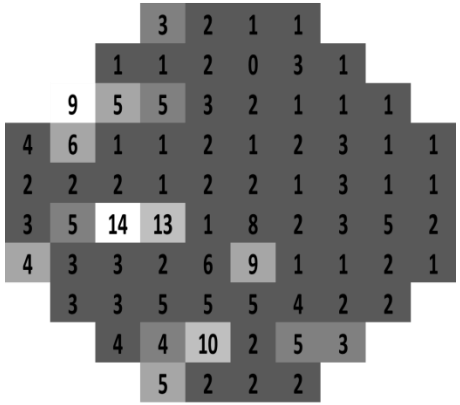
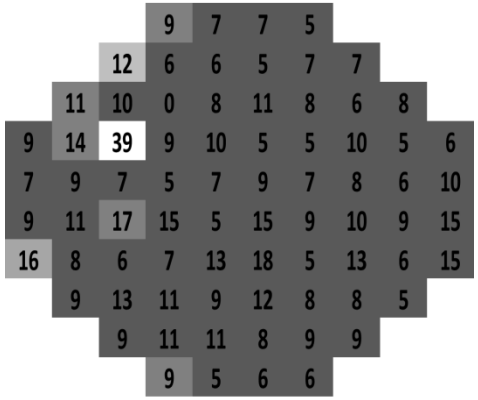
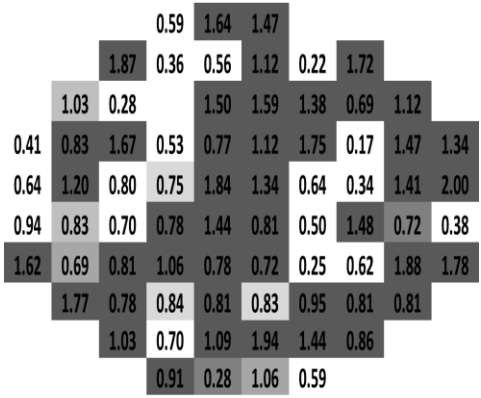


RP patients: milder reduction in PLR to red light



Case I – patient with no light detection



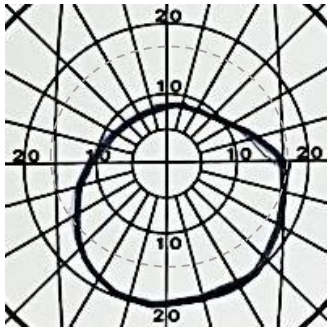
DA-GVF	PPC	MCV	LMCV
Blue No light detection			
Red No light detection			

Case II – patient with VF restriction

<1SE
1SE-2SE
2SE-3SE
3SE-4SE
4SE-5SE
>5SE

DA-GVF | PPC | MCV | LMCV

Blue

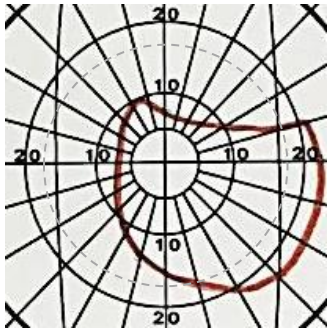


			32	38	25	30			
		11	36	28	18	2	26		
	24	16	38	31	40	35	25	4	
9	29	40	36	30	35	31	34	31	34
29	37	36	36	34	45	45		37	
27	22	27	37	36	32	32	27	37	27
5	30	33	27	37	33	33	28	28	35
	24	30	27	30	31	29	34	35	
		30	27	33	33	30	33		
			24	29	27	32			

				8	13	17				
			17	15	36	13	7	34		
		23	20	21	56		26	30	10	
	9	13	41	33	73	43	49	70	40	
	14	17	46	51	43	45	49		45	
	11	20	38	39	41	46	63	47	54	53
	11	16	49	48	40	38	54	43	51	28
		33	32	39	43	14	45	35	55	
			41		61	46	45	51		
				39	51	34	46			

				1.00	0.72	0.28				
			0.75	0.63	0.69	0.72	0.67	0.69		
		0.62	0.95	0.66	0.59		0.63	0.70	0.75	
	0.86	0.41	0.66	0.64	0.62	0.66	0.59	0.70	0.66	0.66
	0.69	0.91	0.62	0.59	0.66	0.69	0.61		0.59	
	0.66	0.95	0.64	0.56	0.59	0.59	0.69	0.62	0.62	0.62
	0.69	0.81	0.66	0.61	0.62	0.63	0.58	0.63	0.58	0.61
		0.67	0.66	0.62	0.67	0.75	0.59	0.66	0.56	
			0.66		0.59	0.70	0.62	0.66		
				0.73	0.69	0.66	0.59			

Red

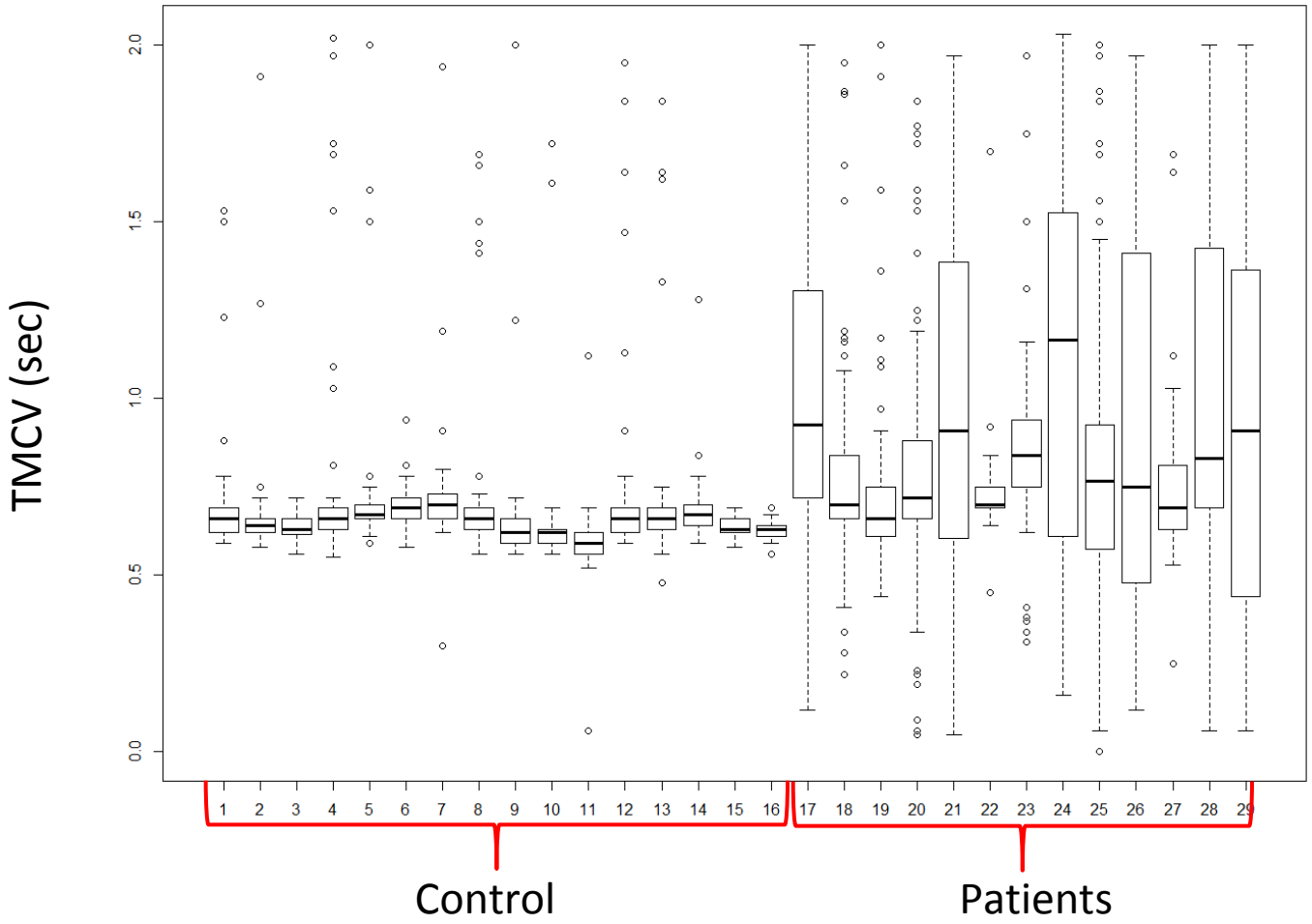


			3			13				
		11	7	24	17	24	8			
	20	9		18	27	19	23	5		
22	8	15	28		29	26	32	25	22	
7		26	23	37	25		31	22	21	
	14		27	26	28	26	32		31	
2	9	20	21	32	26	29	24	29	30	
	22	15	21	34	26	22	15	12		
		21	6		22	23	19			
			10	25	25	20				

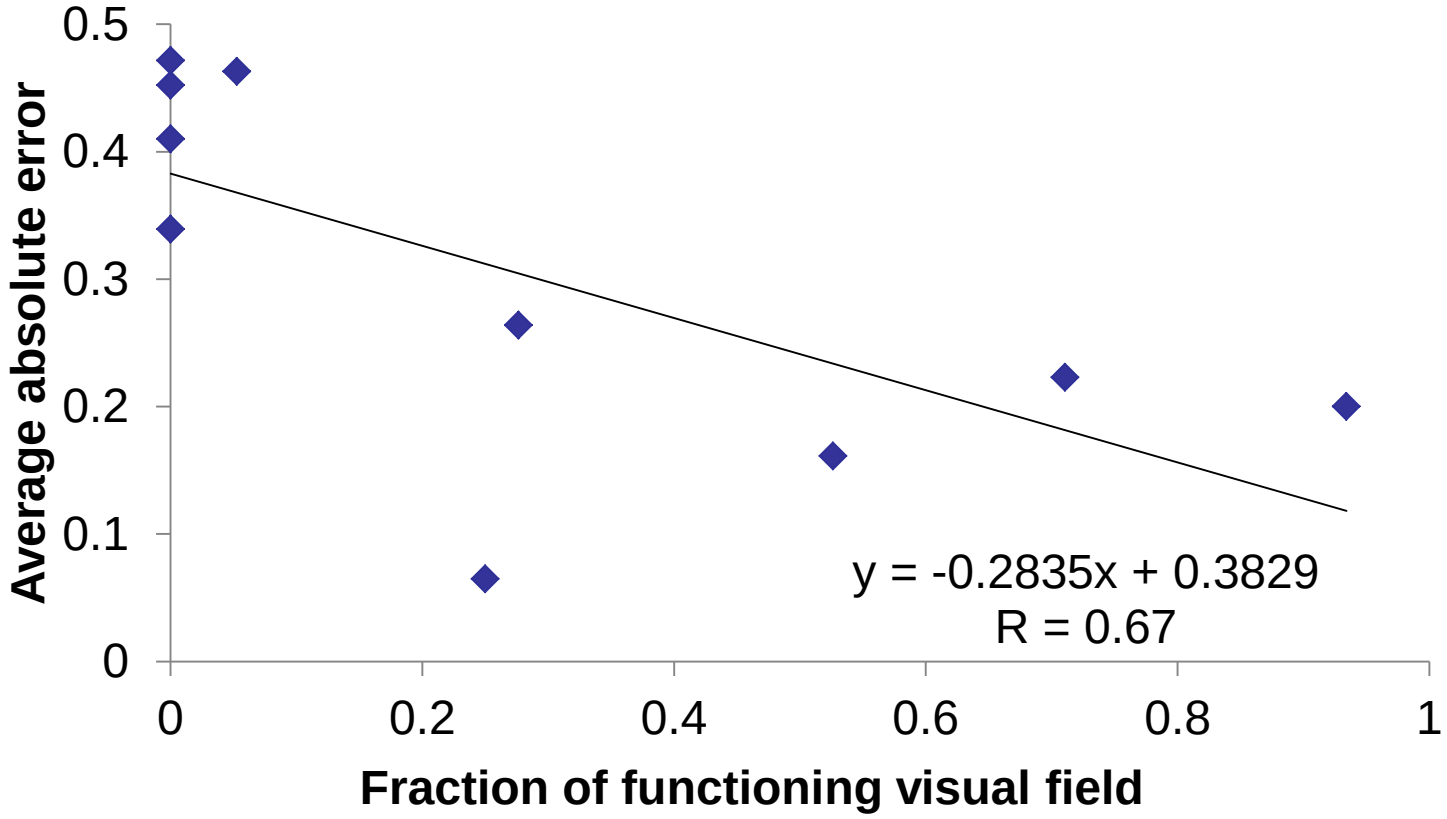
				19			21			
			14	16	27	25	36	22		
		25	11		26	34	26	20	12	
	21	13	22	40		53	37	50	41	28
	10		46	45	42	42		44	32	40
		43		45	59	39	51	51		53
	18	20	43	34	52	23	57	41	49	48
		29	26	42	41	34	50	38	30	
			30	18		33	41	28		
				20	24	37	33			

				0.72			0.78			
			1.36	0.62	0.66	0.97	0.63	0.84		
		0.78	2.00		0.69	0.70	0.75	0.72	0.44	
	0.78	0.75	0.75	0.66		0.59	0.61	0.59	0.62	0.61
	1.17		0.66	0.58	0.59	0.69		0.61	0.59	0.66
		0.72		0.63	0.56	0.64	0.64	0.59		0.59
	1.09	1.91	0.62	0.66	0.75	0.78	0.64	0.66	0.63	0.59
		0.66	0.66	0.62	0.62	0.78	0.66	0.62	0.59	
			0.81	1.11		0.61	0.66	0.62		
				1.59	0.84	0.69	0.62			

Variability in the time to maximal velocity of contraction was significantly higher in RP patients compared with controls (p<0.0001, AUC=0.97)

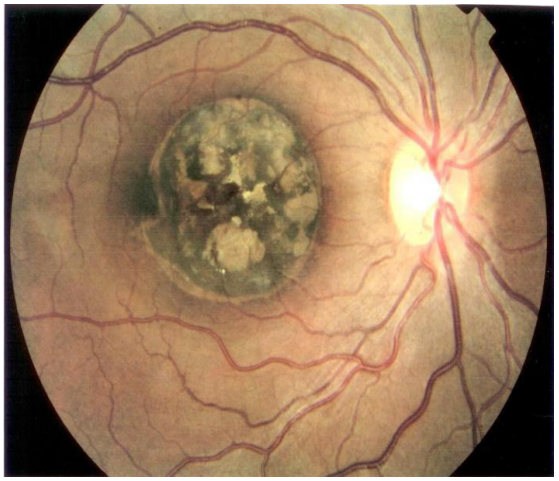


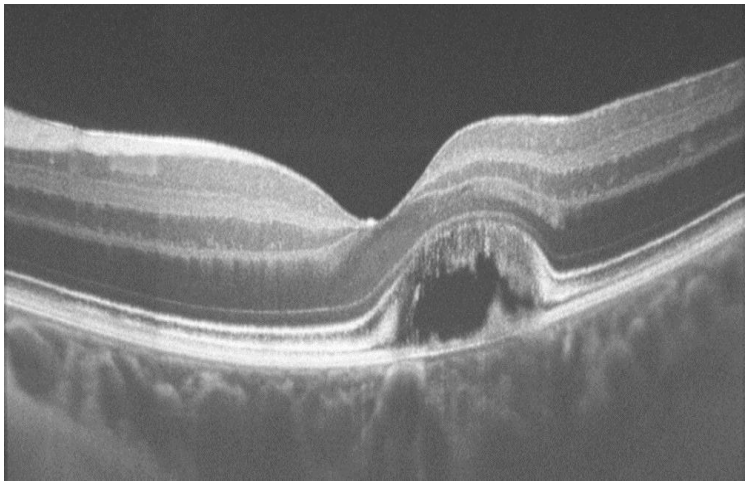
Linear neagtive correlation between the subjective VF (chromatic Goldmann) and the variability in the time parameter



Best disease - Vitelliform macular dystrophy

- Autosomal dominant disease that affects the retinal pigment epithelium (RPE) at a very young age.
- Characterized by lipofuscin accumulation in the RPE.
- In these patients an eccentric preferred retinal locus is taking over, leading to a discrepancy between retinal damage and Humphrey's perimetry.

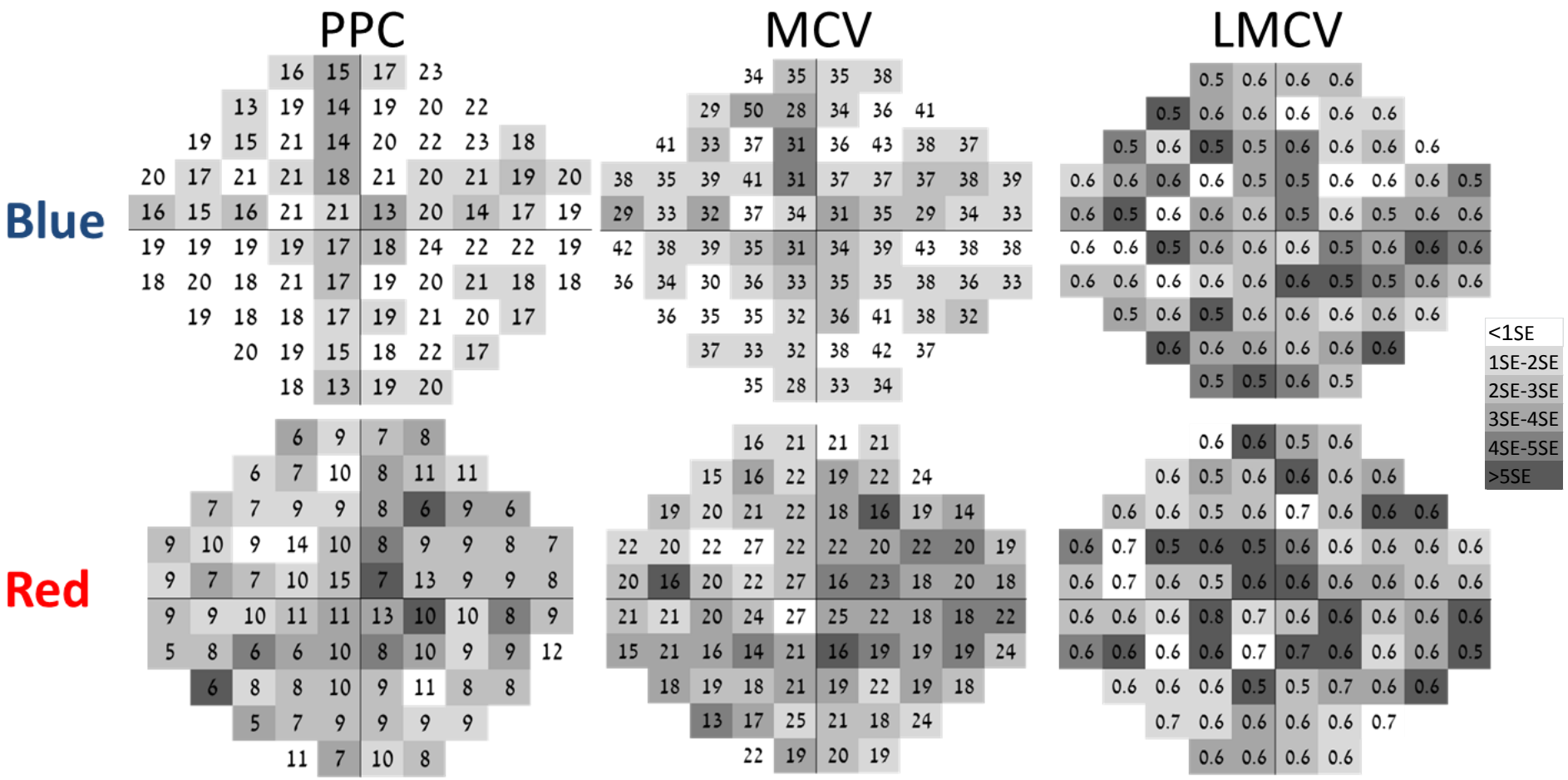




Study design

- 5 Best patients
- 17 healthy individuals
- The pupillary responses of Best patients were compared with the pupillary responses obtained from normal control subjects and with their findings on Humphrey's 24-2 perimetry and OCT.

Best's patients: reduced PLR to red light



Best patient #1 – correlation with OCT and Humphrey 24-2 perimetry

A

Red

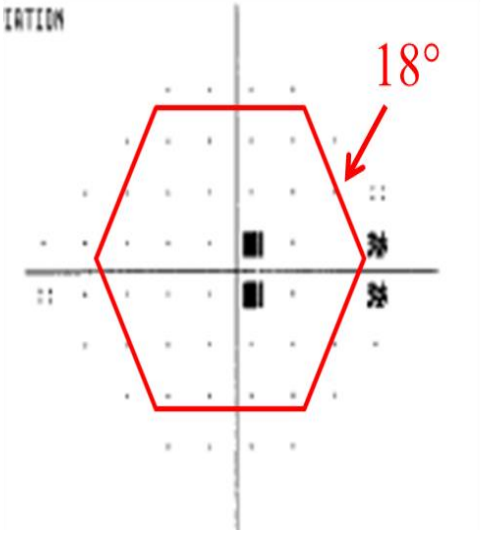
			8	8	2	7			
		9	8	7	3	9	10		
	8	5	5	11	7	ND	8	4	
8	10	7	11	6	5	4	8	8	4
8	6	5	8	11	8	5	5	6	5
6	6	9	ND	6	9	11	6	9	7
4	4	3	3	7	4	6	7	4	4
	2	7	5	7	6	17	4	0	
		ND	5	4	6	10	10		
			6	6	11	4			

B

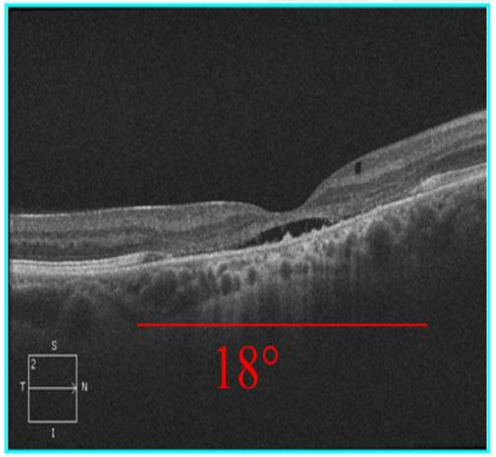
Blue

			18	18	23	22			
		16	ND	15	18	26	21		
	21	22	25	16	24	25	25	20	
19	19	21	19	15	23	22	26	26	24
15	ND	15	20	15	13	17	7	17	18
19	18	22	20	11	ND	26	22	27	14
14	20	18	26	18	12	20	20	ND	24
	23	17	26	17	20	16	20	18	
		25	21	15	ND	23	13		
			ND	12	17	16			

C



D



Conclusions

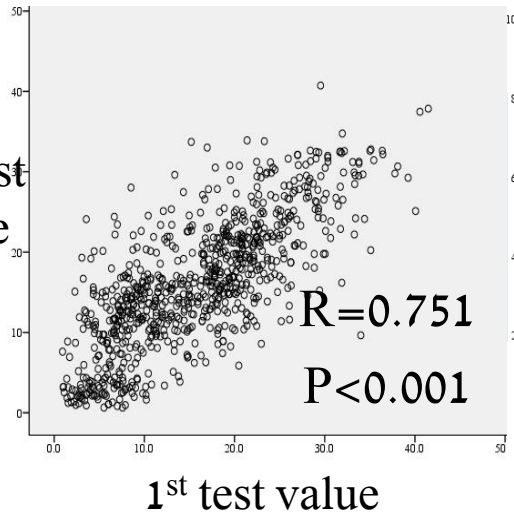
- The chromatic multifocal pupillometer enables non invasive objective diagnosis of macular and peripheral defects
- Significant rod deficit was demonstrated in RP patients, correlating with their subjective VF detected
- Significant cone deficit was demonstrated in Best patients, correlating with their OCT findings while subjective VF detected a smaller defect.

Objective
Differential diagnosis

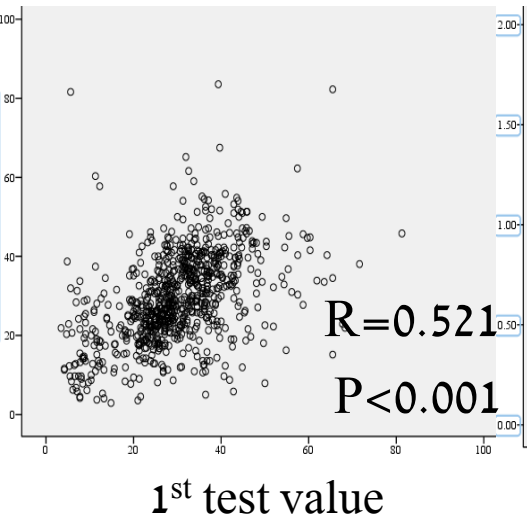
	Best	Retinitis Pigmentosa
Stimulus more affected	Red	Blue
Parameter more affected	Time- Shorter	Time Longer /Velocity
Variability in time	Same as normal	High
% constriction		
Blue	Reduced very mild	Reduced moderate
Red	Reduced mild	Reduced mild moderate
Maximal velocity		
Blue	Reduced mild	Reduced Severe
Red	Reduced mild moderate	Reduced moderate
Time to max velocity		
Blue	Shorter moderate	Longer Severe
Red	Shorter moderate	Longer moderate severe

Response consistency in serial testing of normal subjects Red & Blue

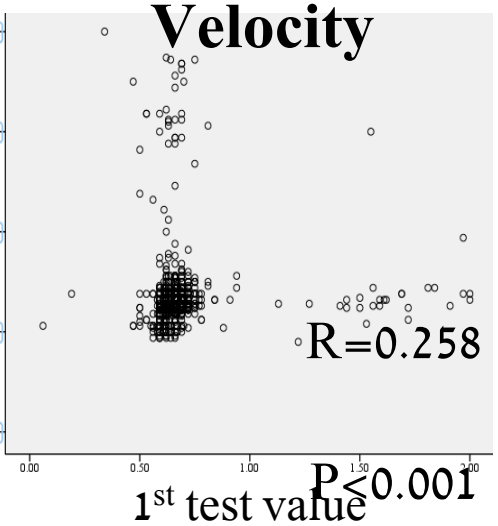
% contraction



Max Velocity



Time of Max Velocity



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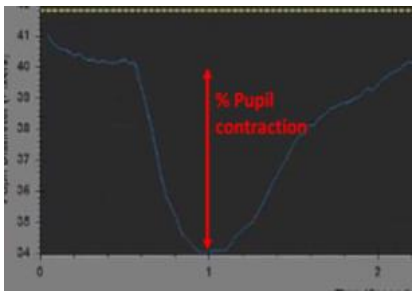
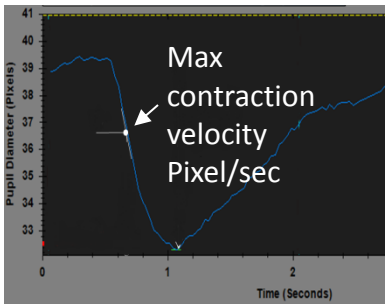
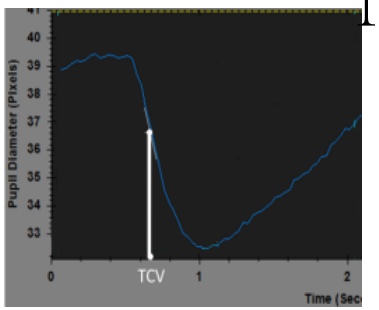






New large clinical trial

Objective perimetry based on chromatic multifocal pupillometer 30 degree visual field

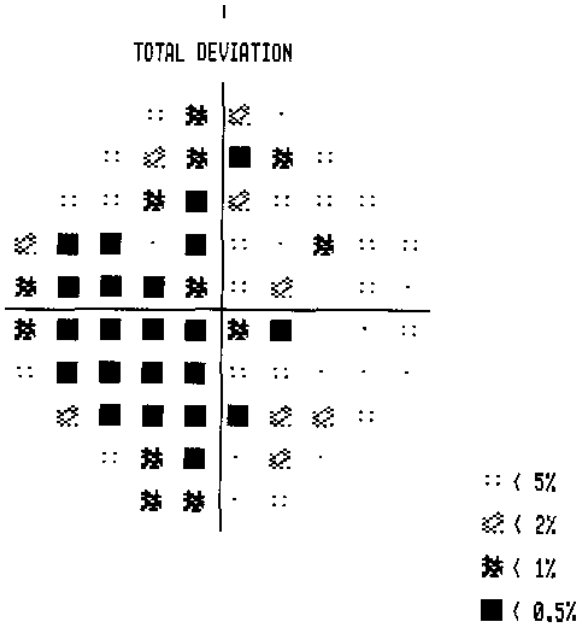
Glaucoma, Retinitis Pigmentosa, AMD, Diabetic Retinopathy

Clinical trial design – 30 degree VF

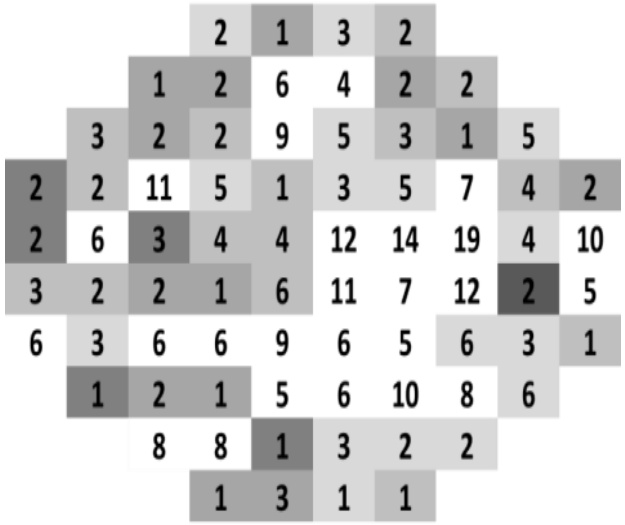
- Study population
  - 90 healthy control subjects, 40 Retinitis Pigmentosa patients, 40 Glaucoma patient, 40 diabetic retinopathy, 40 Adult macular degeneration patients
- Chromatic stimulus
  - Red (1000 cd/m², 624nm)
  - Blue (170 cd/m², 485nm)
- Stimuli will be presented by 76 LEDs in a **30**-degree visual field.
- The pupillary responses of the patients will be compared with control group
- All subject will also be tested in: 1) Humphrey perimetry, 2) OCT, 3) Optometrist exam, 4) Color vision test.

Preliminary results- Glaucoma patient #1

Humphreys



PPC-red



The pupilometer maybe used for early diagnosis of :

- Traumatic Brain Injury (TBI)
- Alzheimer disease
- Parkinson disease

Studies are currently underway

Acknowledgements

Current Team

- **Dr. Ifat Sher**
- **Dr. Mohamad Mhajna**
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- Inesa Kelner
- Ravit Getenuo

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- Dr. Kinori Michael
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- Prof. Arnon Nagler : Tel Hashomer, Israel
- Dr. Avi Treves: Tel Hashomer, Israel
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- Prof. Nathali Savion: Tel Aviv University, Israel
- Prof. Abraham Zangen : BGU, Israel
- Prof. Michal Schwartz: Weizmann Institute
- Prof. Michael Eisenbach: Weizmann Institute
- Prof. Shlomo Margel: Bar Ilan University