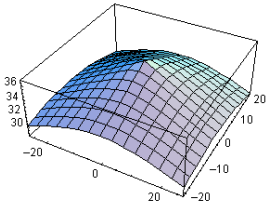
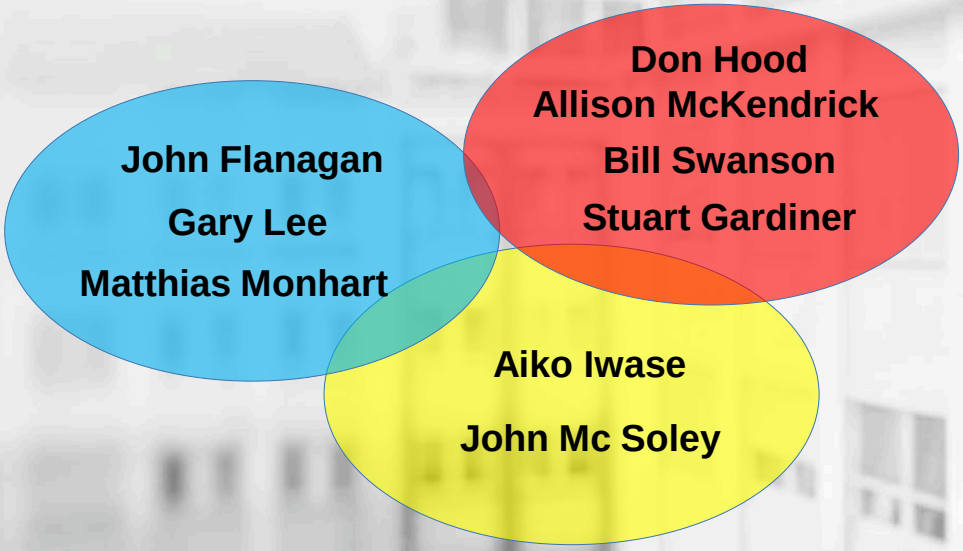
Challenges in creating a unified test pattern for the central 30° for Glaucoma (to start with) and potentially for general use



Glaucoma Progression Scholars 2015

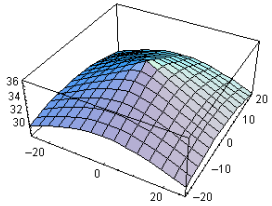


Matthias Monhart
ZEISS Glaucoma Group
October 30, 2015 / January 19, 2016

«The author has a financial interest in the subject matter» (E, Carl Zeiss AG)

GPS / NAPS presentation on New Test Pattern

GPS: Glaucoma Progression Scholars
NAPS: North American Perimetry Society



In the GPS / NAPS meeting the original test candidate and some modifications have been discussed. Most of the slides shown are in the «BACKUP» section at the end of this presentation.

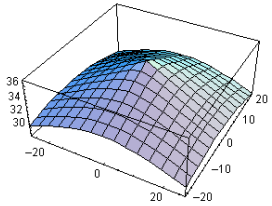
The fact that we work on a combined test pattern was seen positive.

We received the following input:

a) test location symmetry is not important in the macular area
b) following progression is more important than detection of abnormality
c) Other pathologies should not be included as they may have too different requirements
d) Nomdo Jansonius specifically asked to include the 4 central test locations (at +/-1° X and Y) for clinical and reference reasons

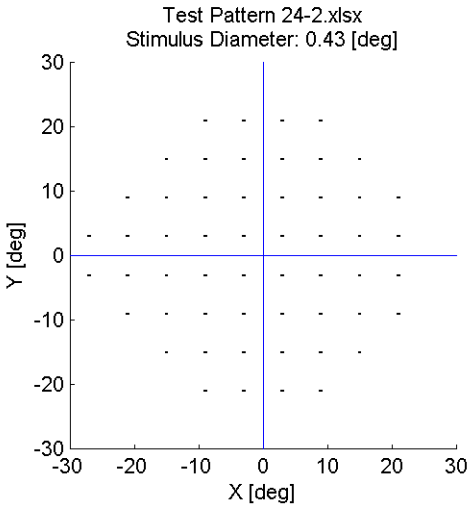
Comparison 24-2, Candidate Nov 10, 2014

Modified Test pattern: Jan 19, 2016

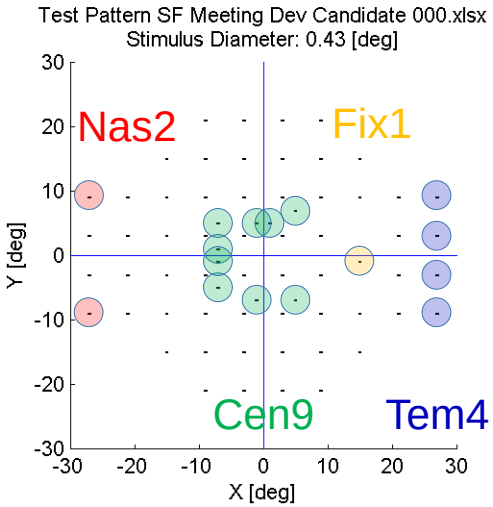


Based on input from GPS / NAPS 2015 and additional publications we suggested a slight modification to the test pattern candidate from Nov 10, 2014 as follows

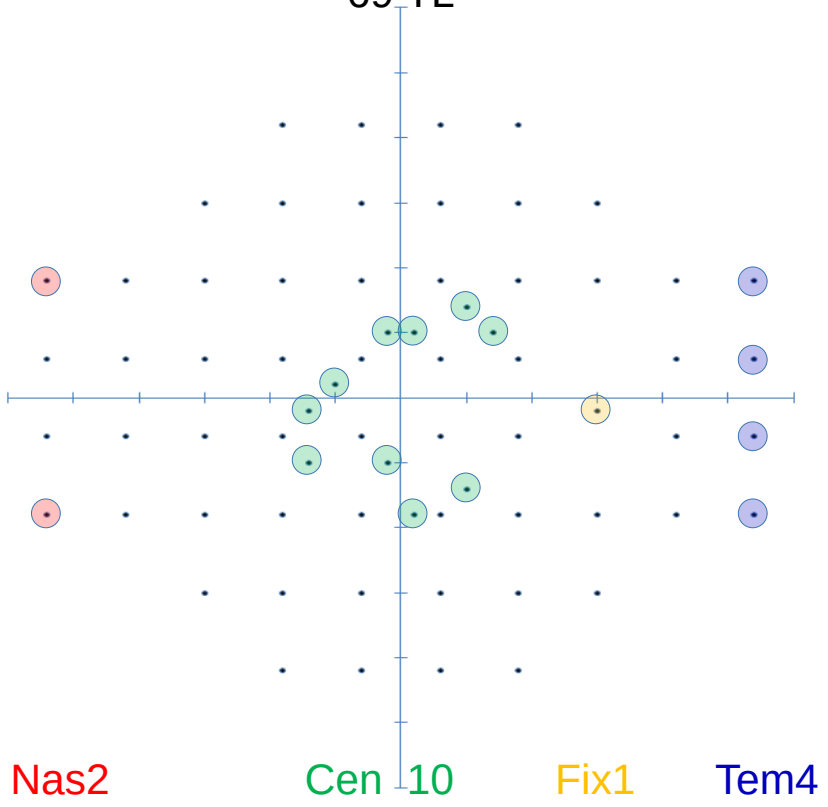
54 TL



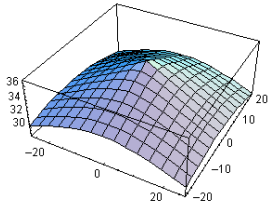
68 TL



69 TL



Test Pattern Evaluation



Re-Evaluation of the macular test point selection

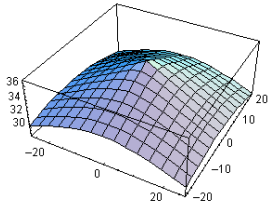
1. After GPS I reevaluated publications the test pattern group referred to and some additional resources with different focus

a) Locations with on average deep defects; to allow to look for progression
b) Locations that are frequently affected; to detect abnormality
c) Location pairs that most likely correlate with abnormal fields (Medmont data)
d) Locations which are flagged as abnormal in macular visual fields from Japanese normal tension glaucoma patients (with normal superior field and normal 24-2 results)

2. Based on the frequency of flagging in the different publications and case studies we identified most frequently affected locations and compared them with the originally designed test candidate how well either test candidate covers structurally relevant macular regions.

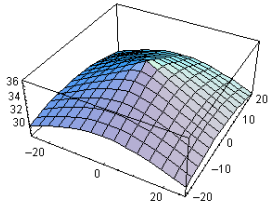
Re-Analysis of macular testing in 4 steps

Selection criteria to add test locations to the 24-2



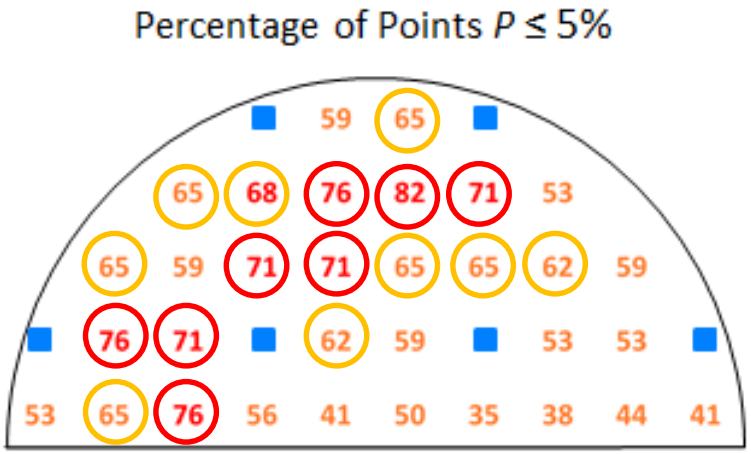
Superior Field

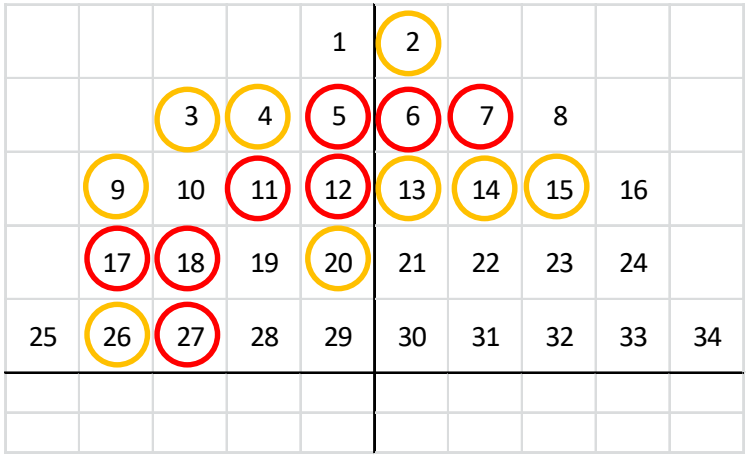
Selection criteria to add test locations to the 24-2



Input 1: Detection

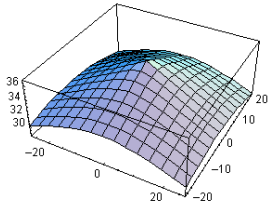
- Nr of tests with test locations with p≤5% in visual fields with MD better than -6dB





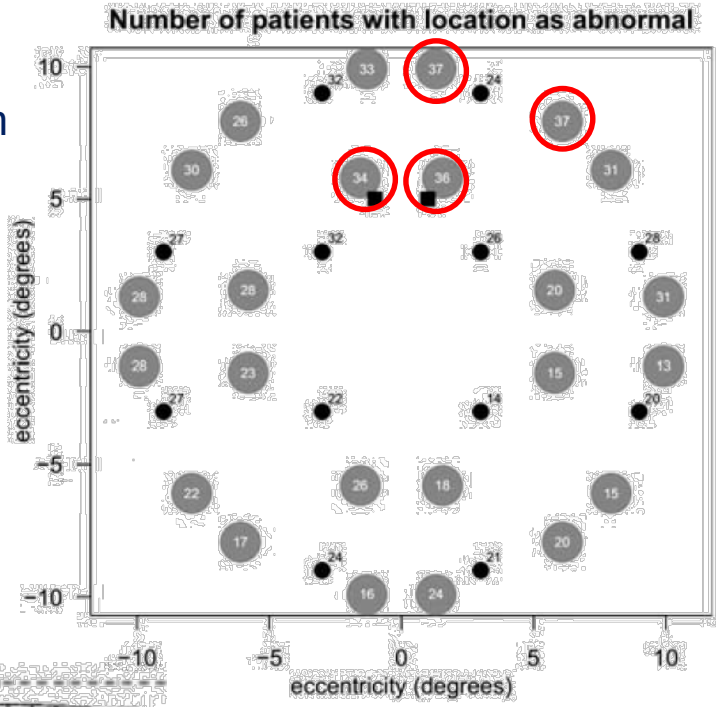
Ehrlich AC, Raza AS, Ritch R, Hood DC. Modifying the conventional visual field test pattern to improve the detection of early glaucomatous defects in the central 108. Tran Vis Sci Tech. 2014;3(6):6,

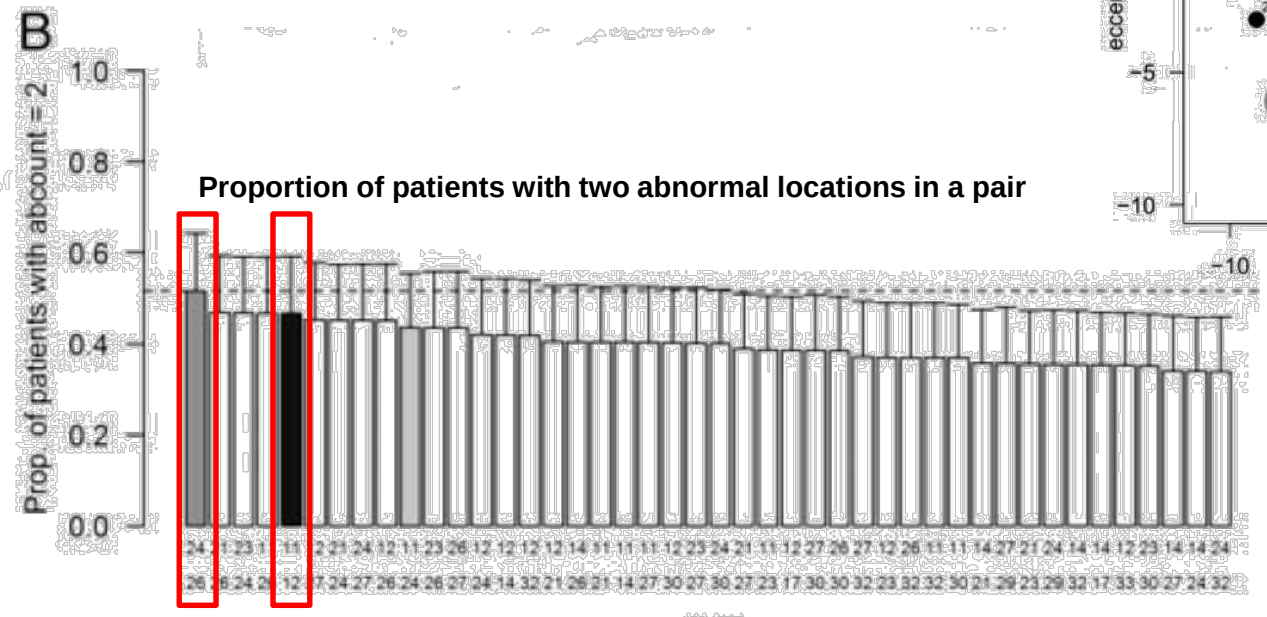
Selection criteria to add test locations to the 24-2



Input 2: Detection – Abnormal pairs – Superior Field

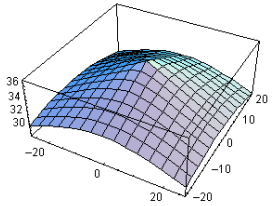
- Which 2 test locations are the most informative to to detect macular visual field loss
- Study on Medmont perimeter and different test pattern as validation and alternative to the HFA 10-2 as basis for test point selection





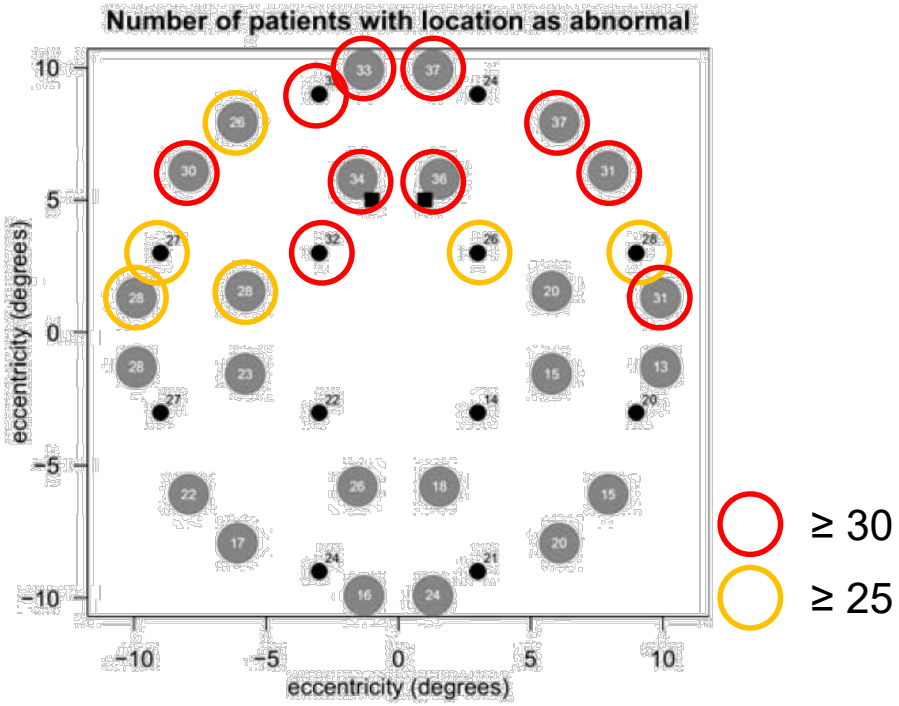
Chen S, McKendrick AM, Turpin A., Choosing two points to add to the 24-2 pattern to better describe macular visual field damage due to glaucoma., Br J Ophthalmol. 2015 Sep;99(9):1236-9. doi: 10.1136/bjophthalmol-2014-306431. Epub 2015 Mar 23.

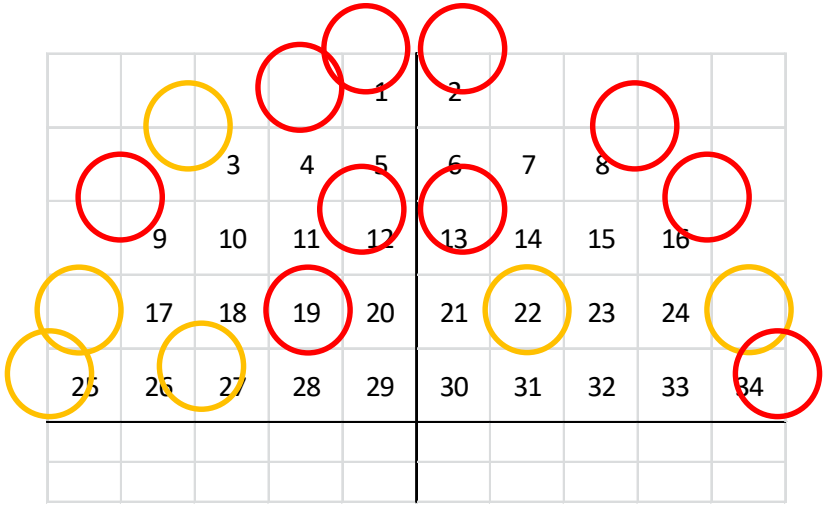
Selection criteria to add test locations to the 24-2



Input 2: Detection on different data set / perimeter

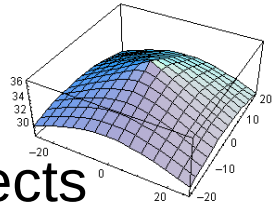
- Most frequently affected test locations in the inferior field
- Study on Medmont perimeter and different test pattern as validation and alternative to the HFA 10-2 as basis for test point selection





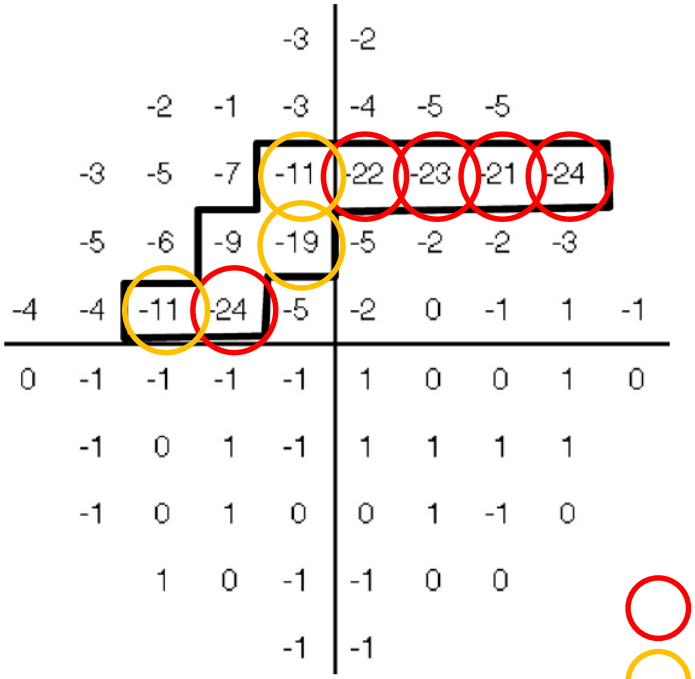
Chen S, McKendrick AM, Turpin A., Choosing two points to add to the 24-2 pattern to better describe macular visual field damage due to glaucoma., Br J Ophthalmol. 2015 Sep;99(9):1236-9. doi: 10.1136/bjophthalmol-2014-306431. Epub 2015 Mar 23.

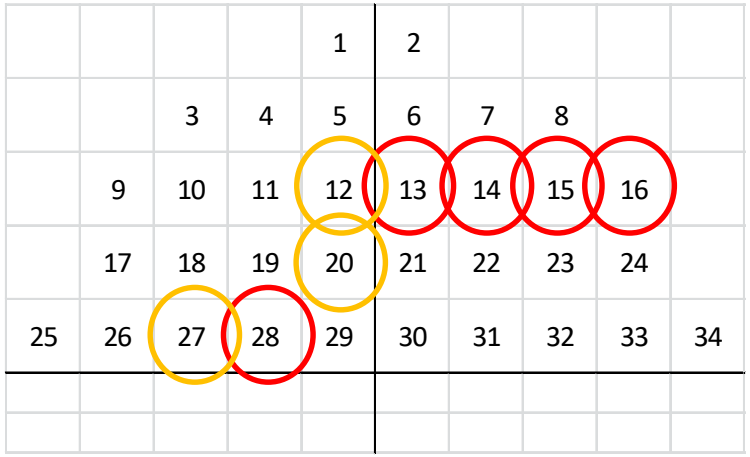
Selection criteria to add test locations to the 24-2



Input 3: Average defect depth in fields with superior defects

- Initial superior macular wedge defects



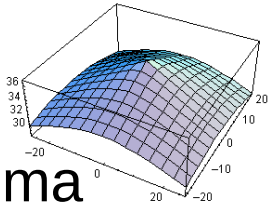


≤ -20dB

≤ -10dB

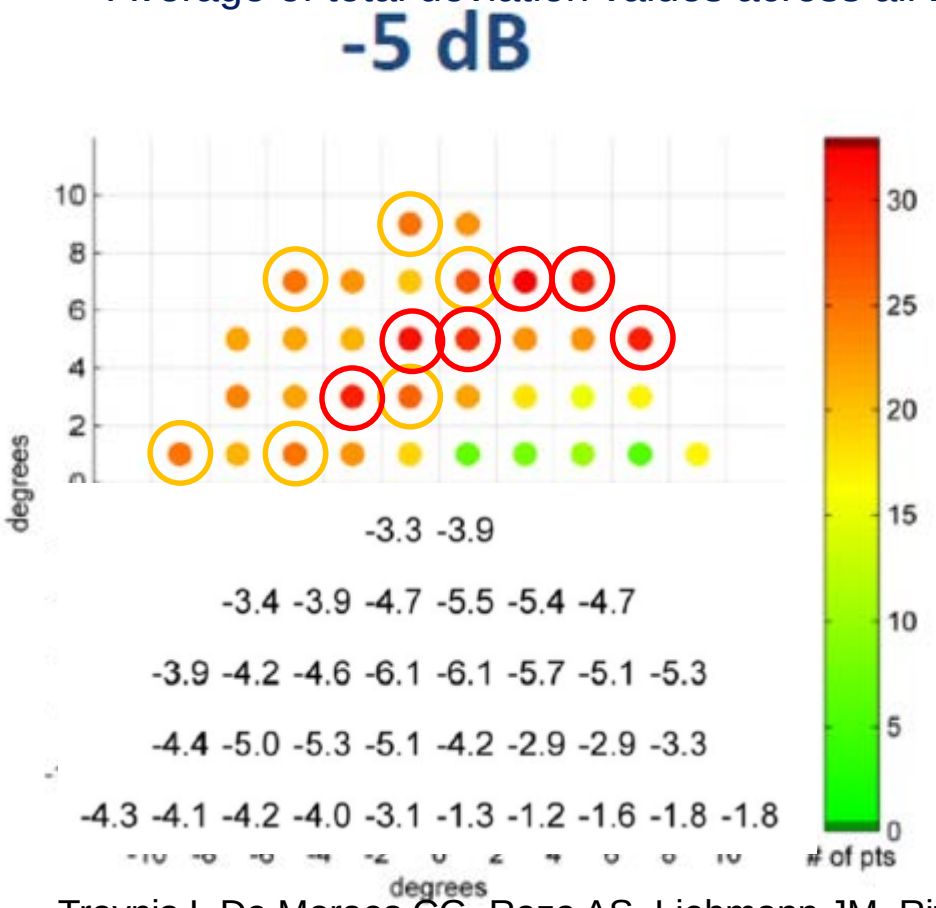
Hood DC, Raza AS, de Moraes CG, Odel JG, Greenstein VC, Liebmann JM, Ritch R., Initial arcuate defects within the central 10 degrees in glaucoma., Invest Ophthalmol Vis Sci. 2011 Feb 16;52(2):940-6. doi: 10.1167/iovs.10-5803. Print 2011 Feb.

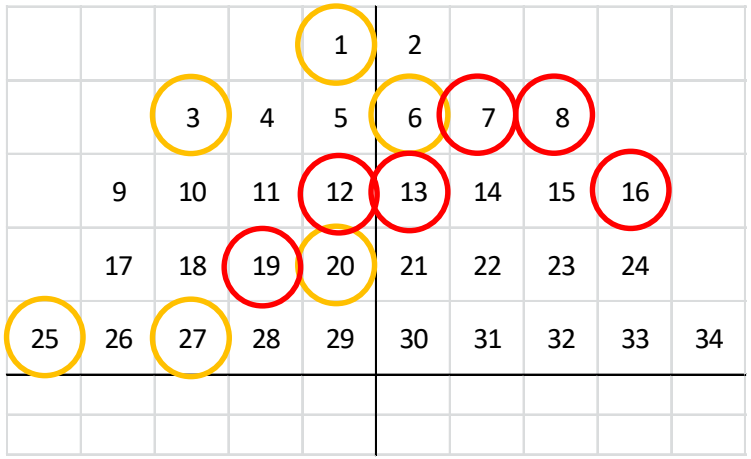
Selection criteria to add test locations to the 24-2



Input 4: Frequency&average defect depth in early glaucoma

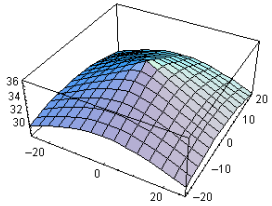
- Number of abnormal points (Ncrit) with TD values below a criterion (crit) level of −5dB was calculated
- Average of total deviation values across all 100 visual fields





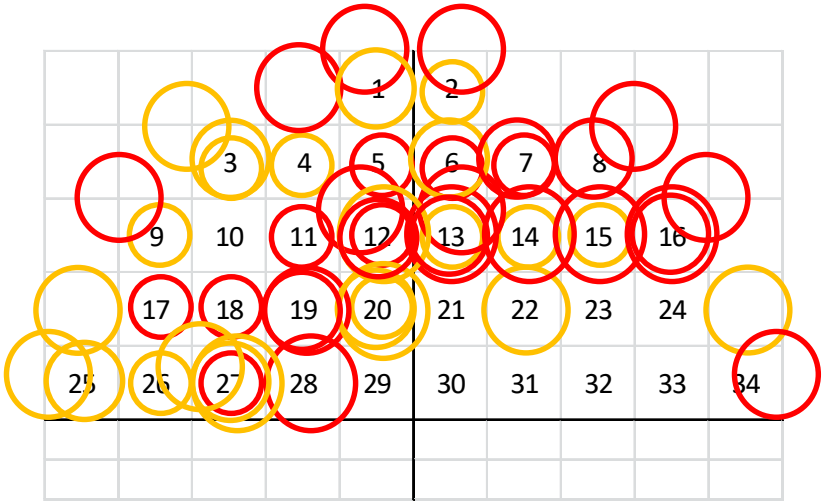
Traynis I, De Moraes CG, Raza AS, Liebmann JM, Ritch R, Hood DC. The Prevalence and Nature of Early Glaucomatous Defects in the Central 10° of the Visual Field. JAMA ophthalmology. 2014;132(3):291-297. doi:10.1001/jamaophthalmol.2013.7656.

Selection criteria to add test locations to the 24-2

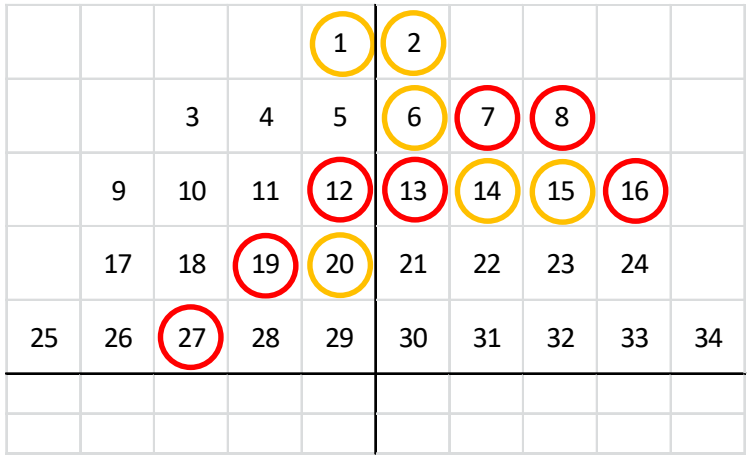


Superior field – Conclusions

- Input 1-4



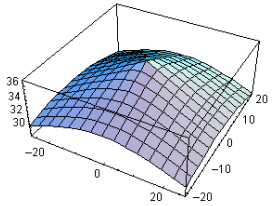
Red: 2 count; Yellow: 1 count



4 or more

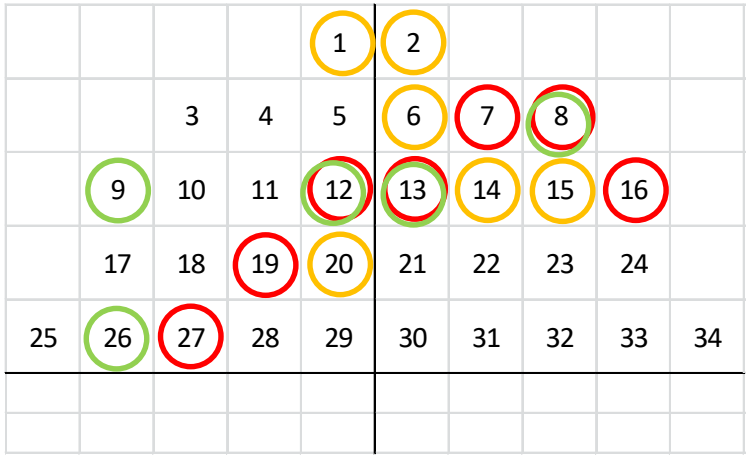
3 or more

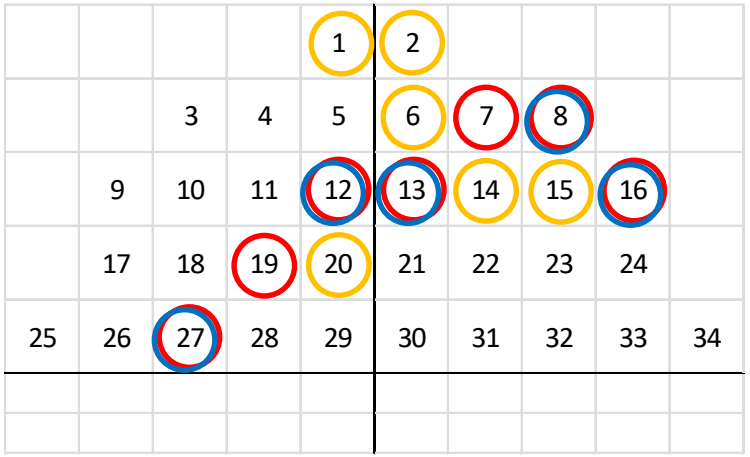
Selection criteria to add test locations to the 24-2



Superior field – Conclusions

- Input 1-4

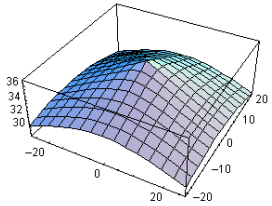




Comparison with test pattern group candidate

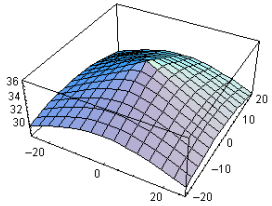
Blue – suggested modification

Selection criteria to add test locations to the 24-2



Inferior Field

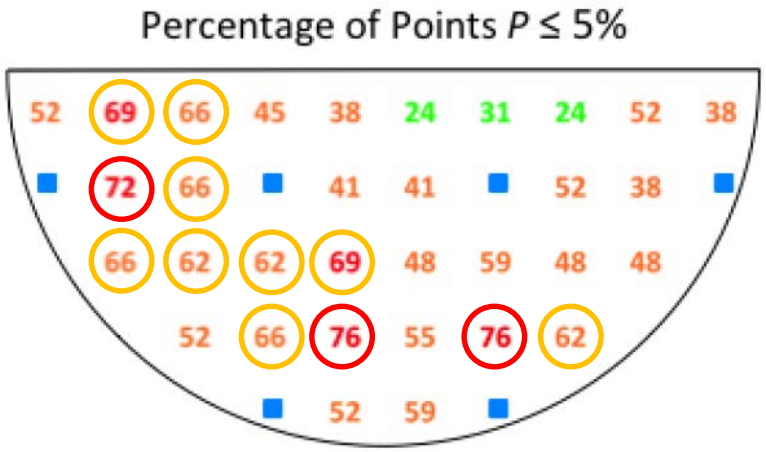
Selection criteria to add test locations to the 24-2



Input 1: Detection

- Nr of tests with test locations with p≤5% in visual fields with MD better than -6dB

35	36	37	38	39	40	41	42	43	44
	45	46	47	48	49	50	51	52	
	53	54	55	56	57	58	59	60	
		61	62	63	64	65	66		
				67	68				

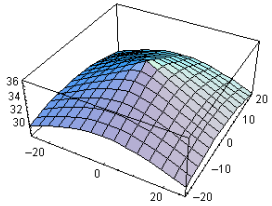


Red rings represent the highest rank and have a count of 2

Yellow rings represent the 2nd highest rank and have a count of 1

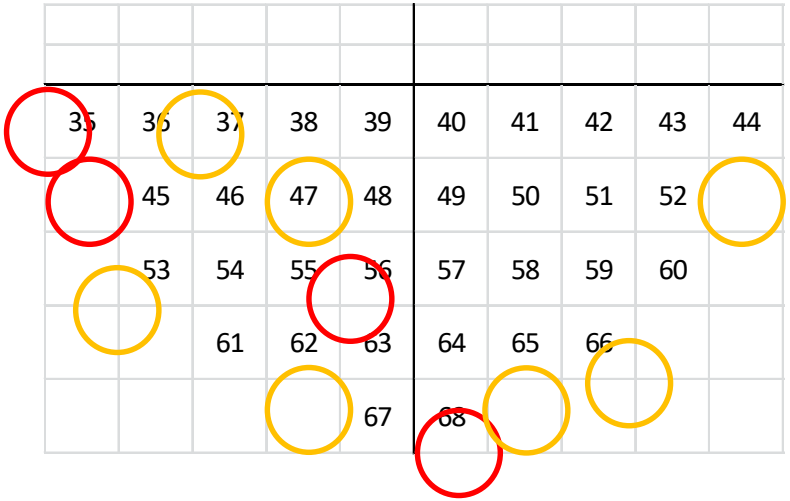
Ehrlich AC, Raza AS, Ritch R, Hood DC. Modifying the conventional visual field test pattern to improve the detection of early glaucomatous defects in the central 108. Tran Vis Sci Tech. 2014;3(6):6,

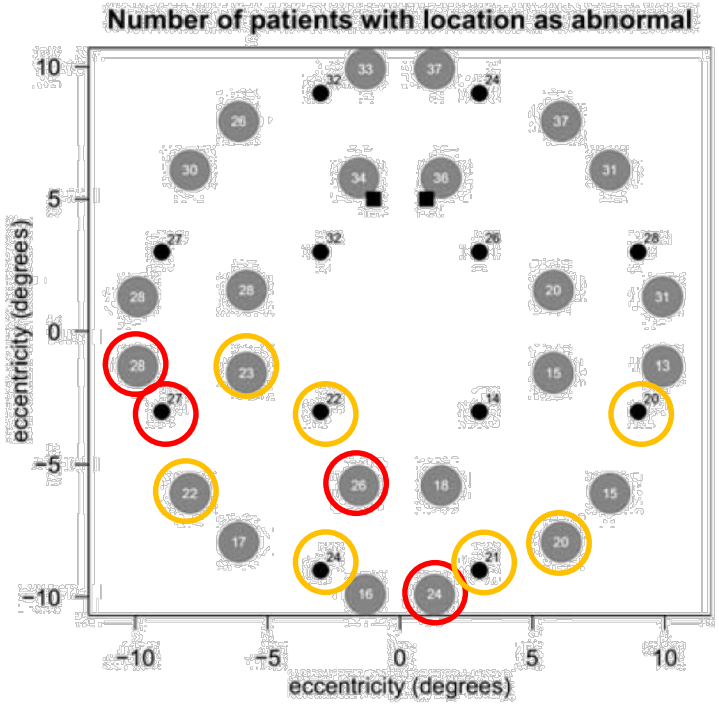
Selection criteria to add test locations to the 24-2



Input 2: Detection on different data set / perimeter

- Most frequently affected test locations in the inferior field
- Study on Medmont perimeter and different test pattern as validation and alternative to the HFA 10-2 as basis for test point selection





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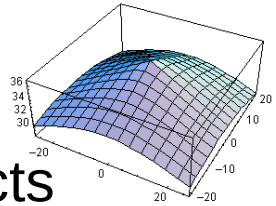
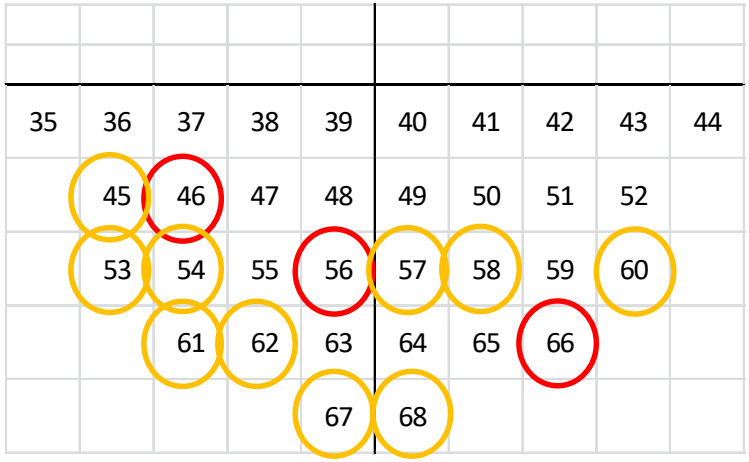
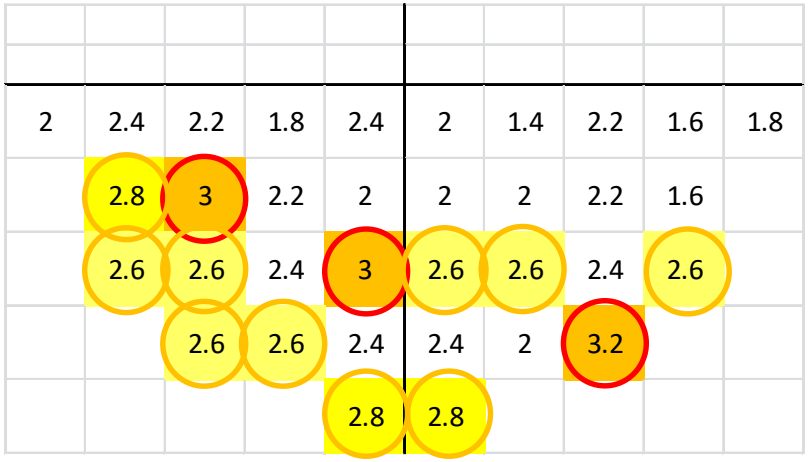
Selection criteria to add test locations to the 24-2



Input 3: Average defect depth in fields with inferior defects

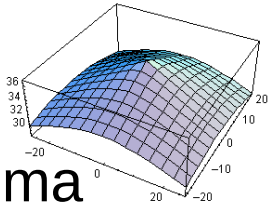
- Selection of visual fields with relevant defects (> 3 related test locations with 5% probability) in the Tajimi eye study
- Average of 5 visual fields who did not have any relevant superior loss AND did not have relevant loss in the corresponding 24-2 test at all.





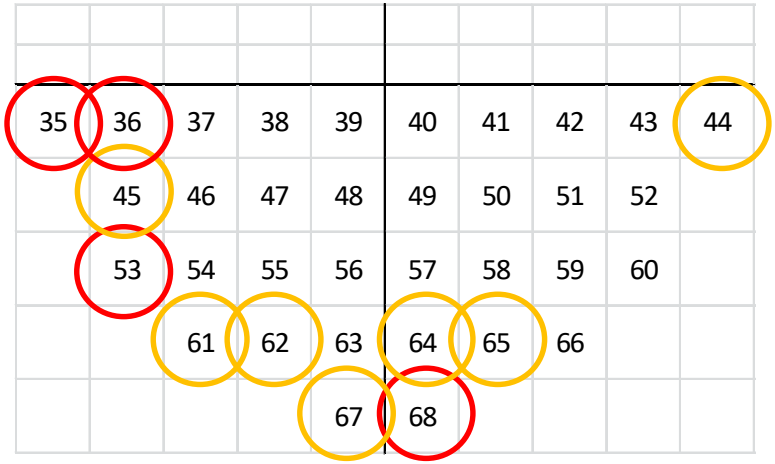
Anonymous cases contributed by Dr. Iwase on NTG from 3 different Japanese sites

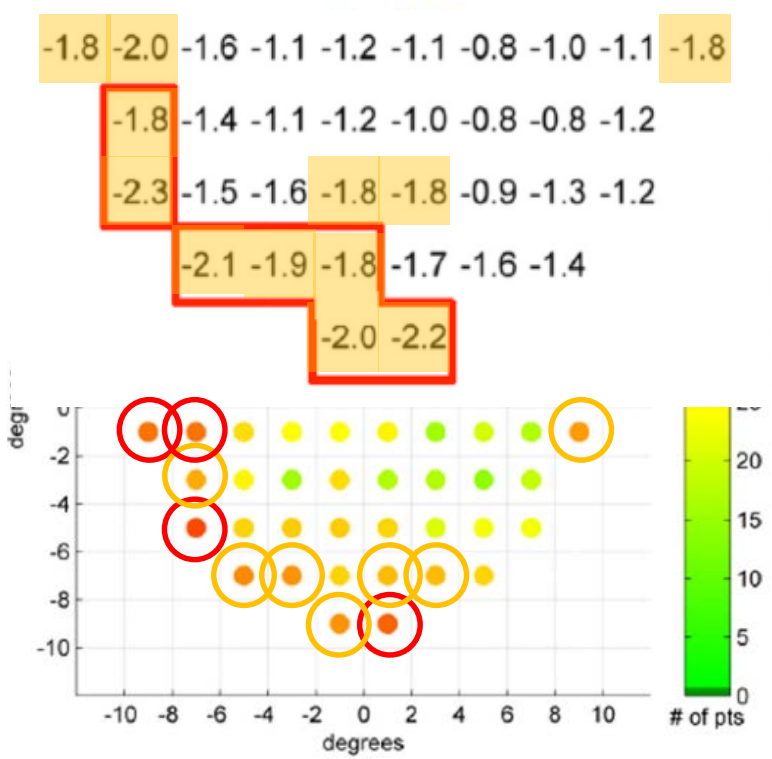
Selection criteria to add test locations to the 24-2



Input 4: Frequency&average defect depth in early glaucoma

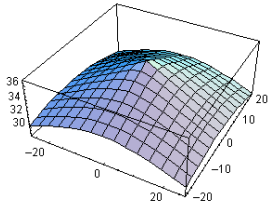
- Number of abnormal points (Ncrit) with TD values below a criterion (crit) level of −3dB was calculated
- Average of total deviation values across all 100 visual fields





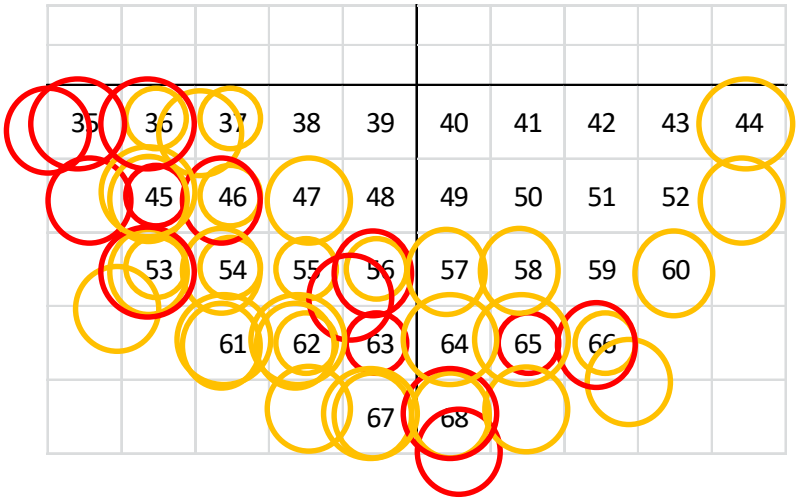
Traynis I, De Moraes CG, Raza AS, Liebmann JM, Ritch R, Hood DC. The Prevalence and Nature of Early Glaucomatous Defects in the Central 10° of the Visual Field. JAMA ophthalmology. 2014;132(3):291-297. doi:10.1001/jamaophthalmol.2013.7656.

Selection criteria to add test locations to the 24-2

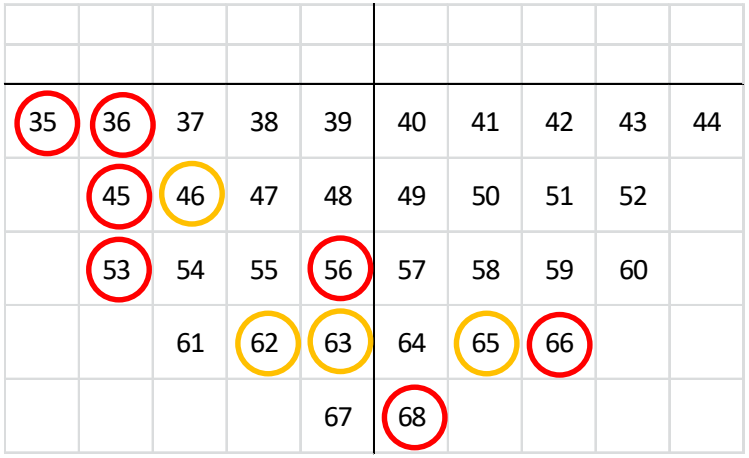


Inferior field – Conclusions

- Input 1-4



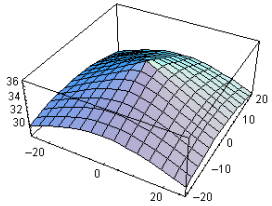
Red: 2 count; Yellow: 1 count



4 or more

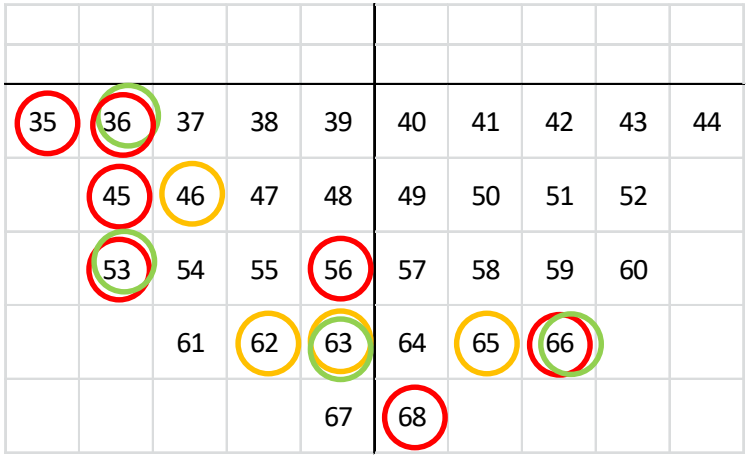
3 or more

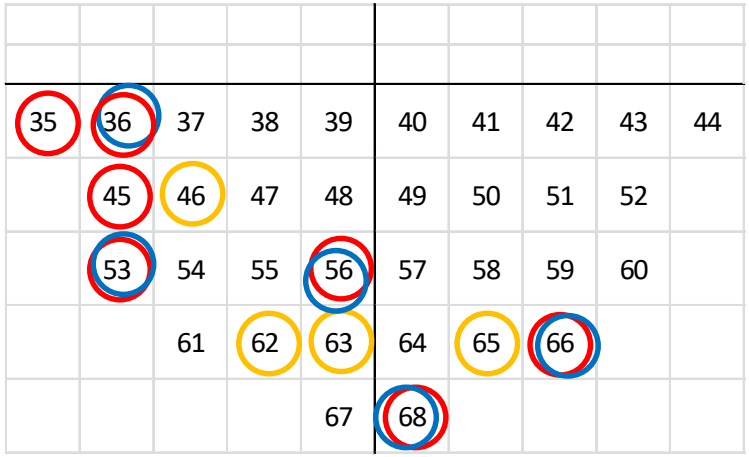
Selection criteria to add test locations to the 24-2



Inferior field – Conclusions

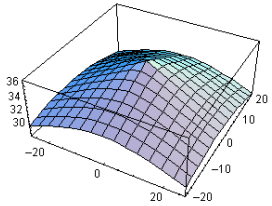
- Input 1-4





Comparison with test pattern group candidate Blue – suggested modification

Selection criteria to add test locations to the 24-2



Suggested changes

				1	2				
		3	4	5	6	7	8		
	9	10	11	12	13	14	15	16	
	17	18	19	20	21	22	23	24	
25	26	27	28	29	30	31	32	33	34
35	36	37	38	39	40	41	42	43	44
	45	46	47	48	49	50	51	52	
	53	54	55	56	57	58	59	60	
		61	62	63	64	65	66		
				67	68				

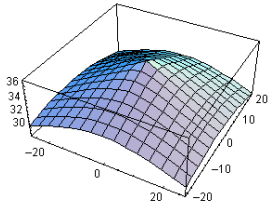
Original Candidate

				1	2				
		3	4	5	6	7	8		
	9	10	11	12	13	14	15	16	
	17	18	19	20	21	22	23	24	
25	26	27	28	29	30	31	32	33	34
35	36	37	38	39	40	41	42	43	44
	45	46	47	48	49	50	51	52	
	53	54	55	56	57	58	59	60	
		61	62	63	64	65	66		
				67	68				

Modified Candidate

Comparison with test pattern group candidate Blue – suggested modification

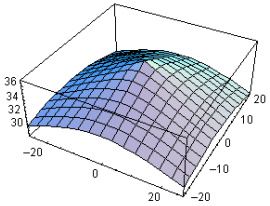
Selection criteria to add test locations to the 24-2

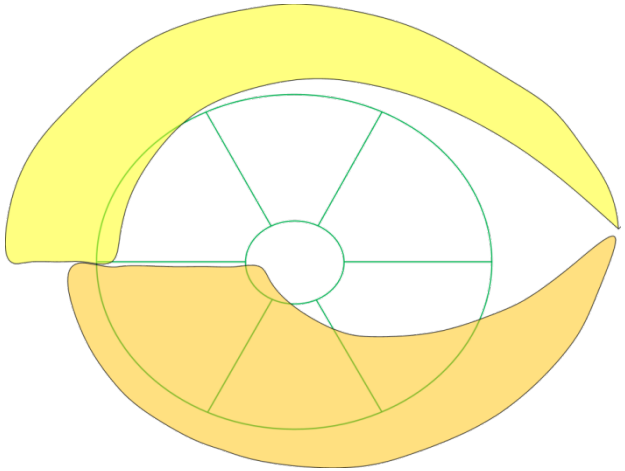


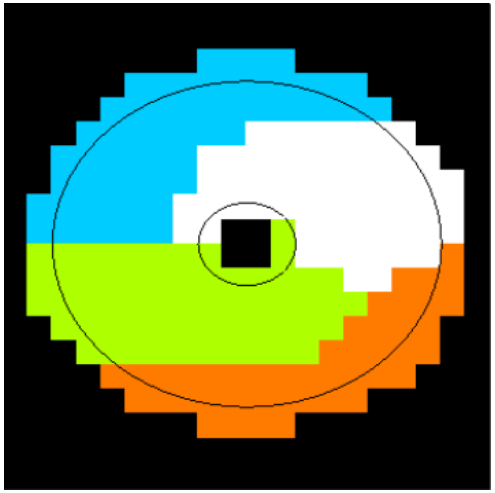
Discussion

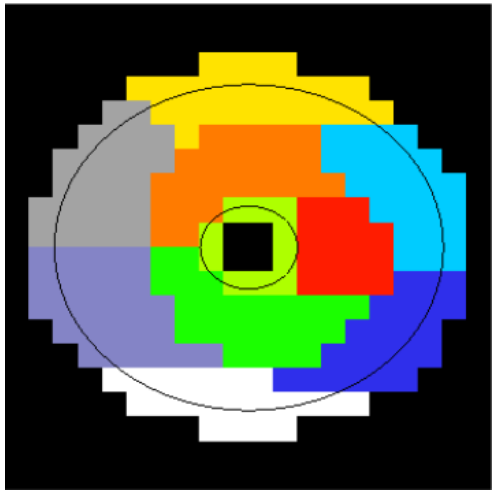
S-F Locations compared to GCA Analysis

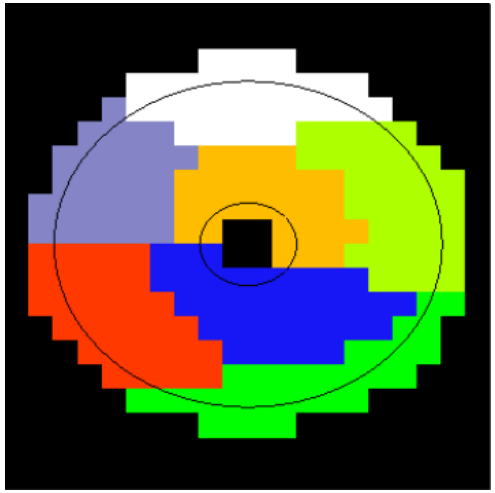
- missing reference
- Gerd Klose; GCA cluster analysis, 2015 (Data Dr. Suzuki)





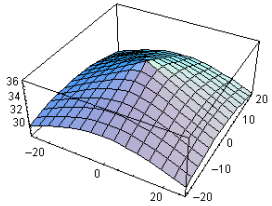






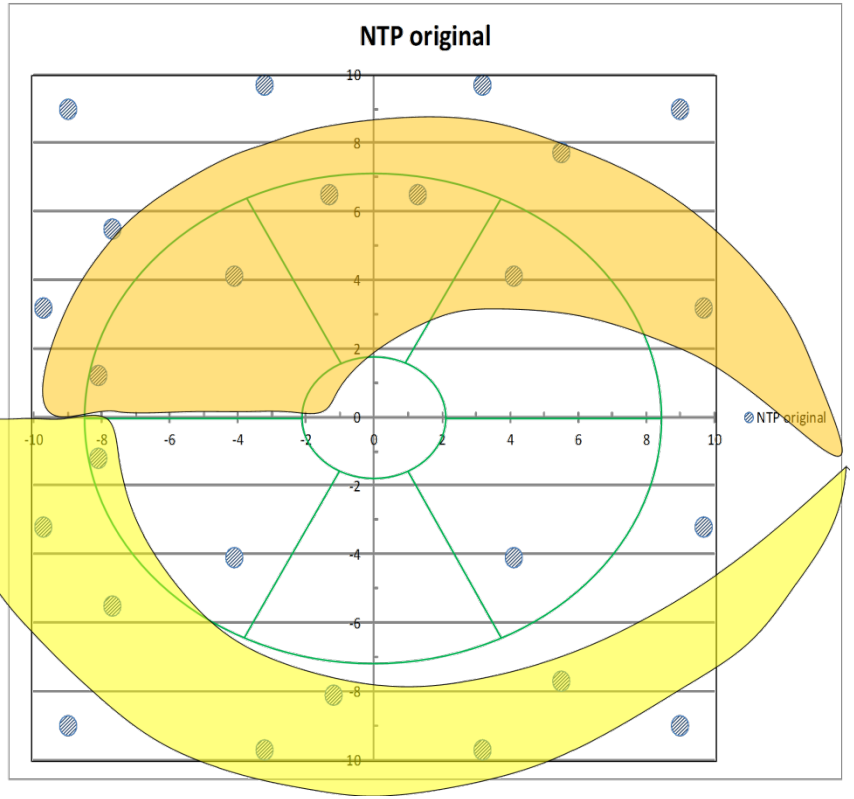
4, 7 and 10 GCA auto-correlated sectors based on deviation from the norm

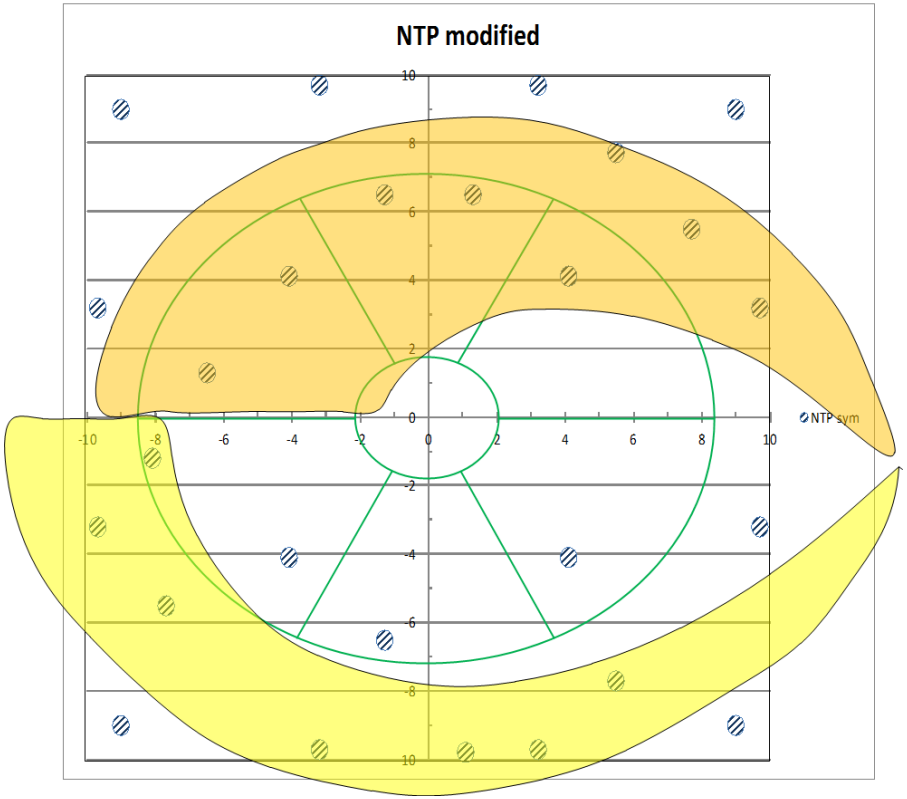
Screening example Orig



S-F Locations compared to structurally affected sectors

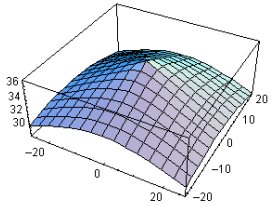
The positions of the test locations are corrected for the length of the Henle fibers according to work of Don Hood et al.

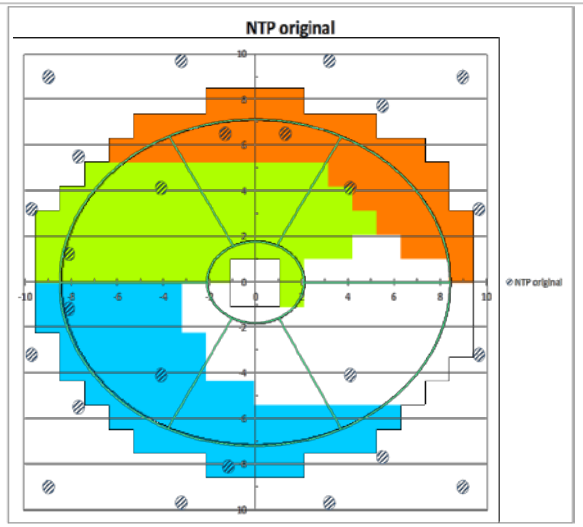


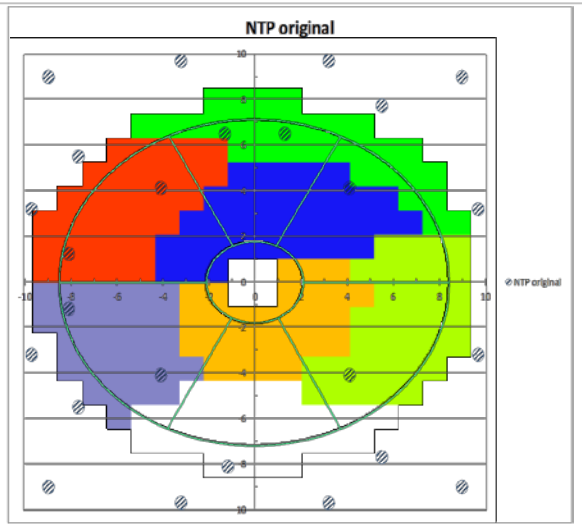


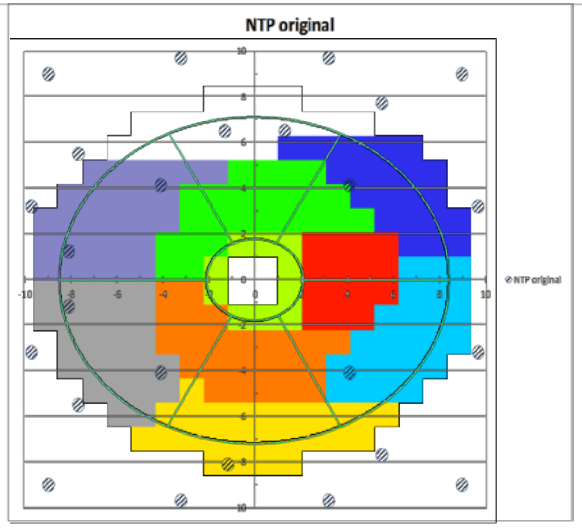
- Missing Reference

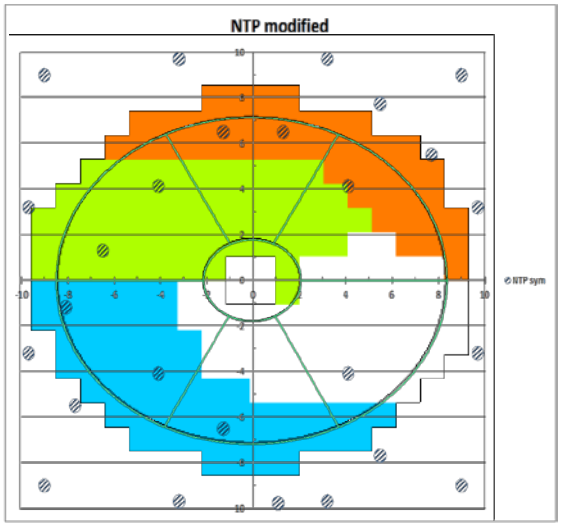
S-F Locations compared to GCA Analysis
Coverage of auto-correlated GCA clusters
Gerd Klose; GCA cluster analysis, 2015

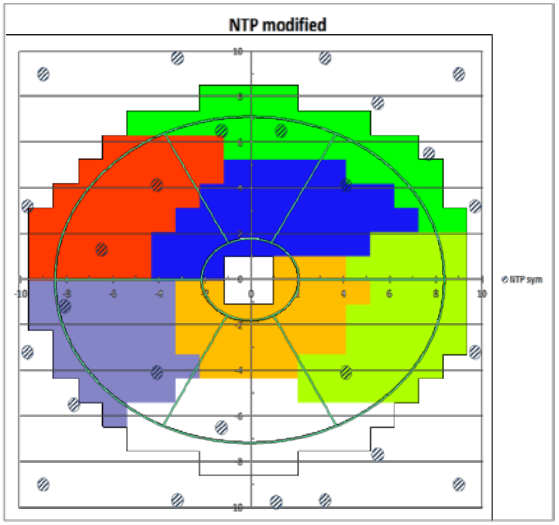


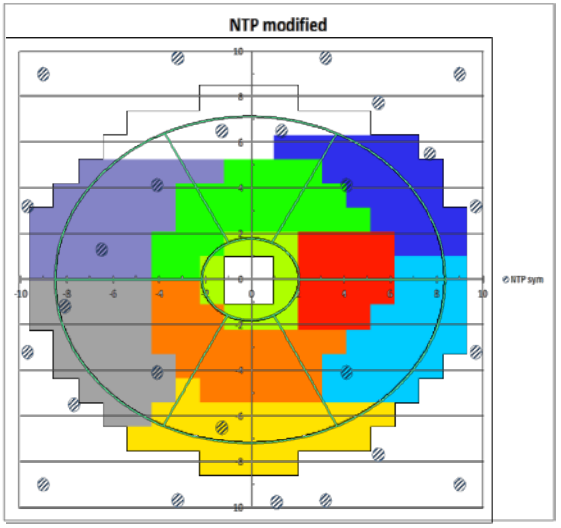




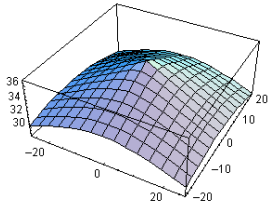








Selection criteria to add test locations to the 24-2



Clusters in glaucoma

- Test locations with similar behaviour (OS orientation)

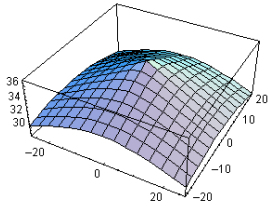
Author's comments:

Sectors 10, 11 and 12 are probably a consequence of VF change in advanced glaucoma patients, similarly to clusters in the central inferior VF area.

However, some sectors, such as 11, 12, 21, 28, 37, 54 and 55, were not stable.

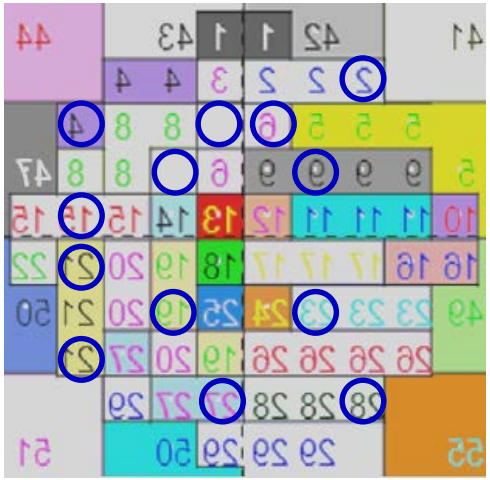
Asaoka R., Mapping glaucoma patients' 30-2 and 10-2 visual fields reveals clusters of test points damaged in the 10-2 grid that are not sampled in the sparse 30-2 grid., PLoS One. 2014 Jun 20;9(6):e98525. doi: 10.1371/journal.pone.0098525. eCollection 2014.

Discussion

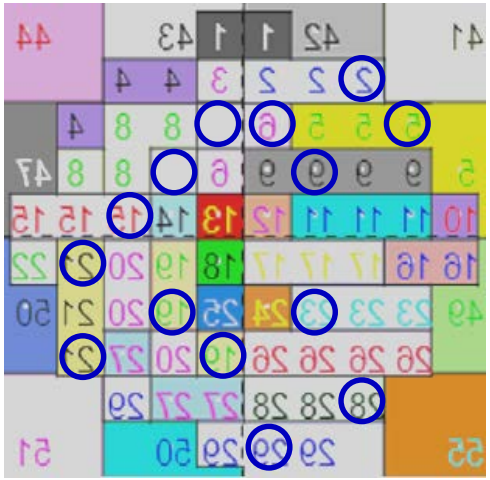


Detection – Initial wedge defects OD orientation

Original



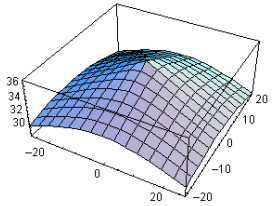
Modified



No clear conclusion can be drawn due to the high number of identified clusters

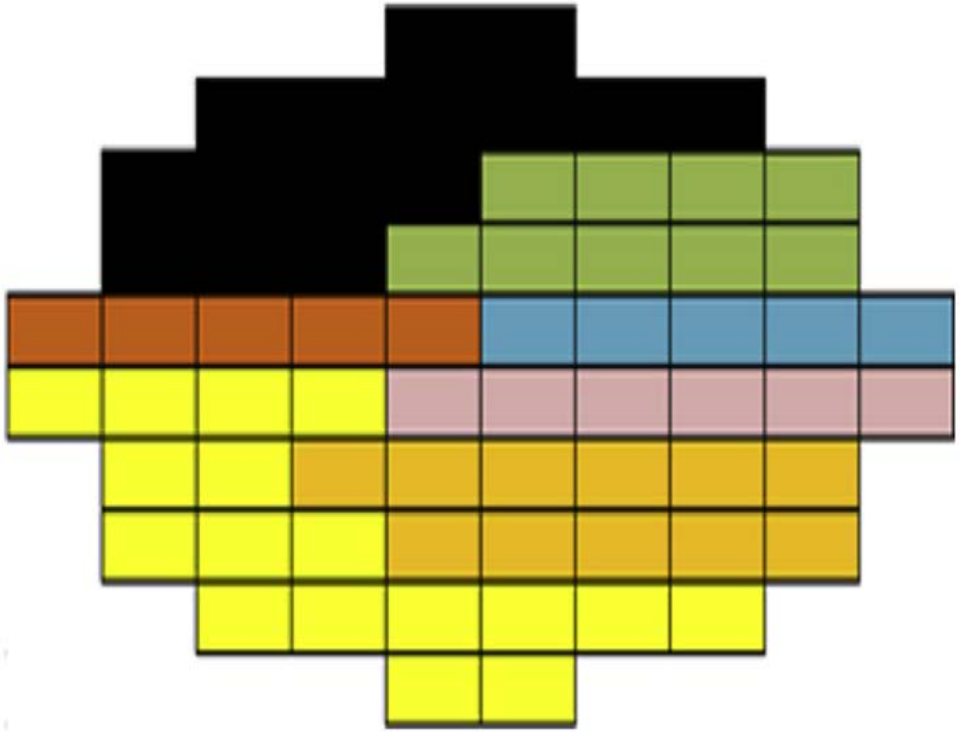
Asaoka R., Mapping glaucoma patients' 30-2 and 10-2 visual fields reveals clusters of test points damaged in the 10-2 grid that are not sampled in the sparse 30-2 grid., PLoS One. 2014 Jun 20;9(6):e98525. doi: 10.1371/journal.pone.0098525. eCollection 2014.

Selection criteria to add test locations to the 24-2



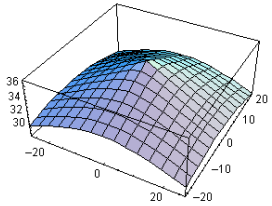
Progression

- Correlating progression clusters (OS orientation according table 2 in the publication, mirrored here)



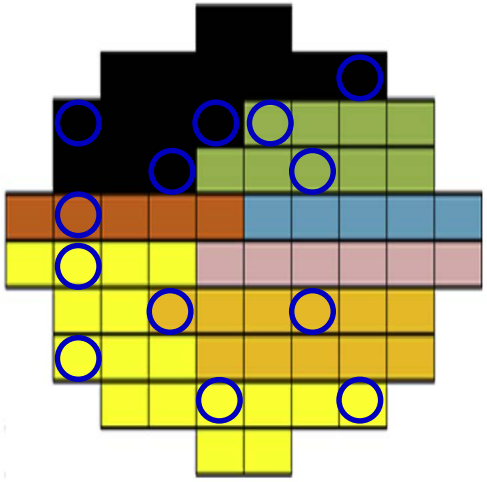
de Moraes CG, Song C, Liebmann JM, Simonson JL, Furlanetto RL, Ritch R., Defining 10-2 visual field progression criteria: exploratory and confirmatory factor analysis using pointwise linear regression., Ophthalmology. 2014 Mar;121(3):741-9. doi: 10.1016/j.ophtha.2013.10.018. Epub 2013 Nov 28.

Discussion

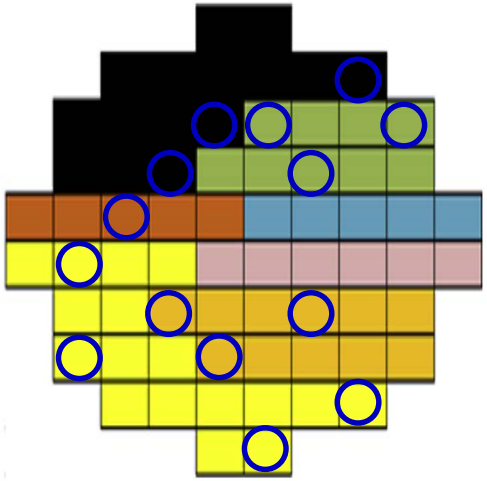


Which progression clusters need coverage?

Original



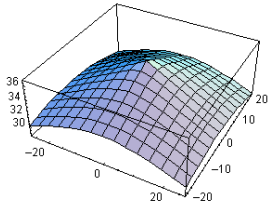
Modified



Similar coverage of progression clusters, but slightly better distribution in modified pattern, covering 4 of the main clusters with 3-4 test locations each vs 2 clusters in the original pattern.

de Moraes CG, Song C, Liebmann JM, Simonson JL, Furlanetto RL, Ritch R., Defining 10-2 visual field progression criteria: exploratory and confirmatory factor analysis using pointwise linear regression., Ophthalmology. 2014 Mar;121(3):741-9. doi: 10.1016/j.ophtha.2013.10.018. Epub 2013 Nov 28.

Decision to go on with the modified test pattern



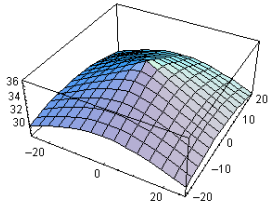
Reasoning

Covering areas typically affected by structural changes:
When comparing the original vs the modified test pattern with structural data we did not include in the selection process, the modified test pattern appears to cover predominantly defective areas better.

«Validating» with publications on defect and progression clusters not considered in the selection process:
The modified test pattern shows a slightly better adaptation to identify progressive clusters as compared to the original test pattern candidate

Decision to choose the modified test pattern based on performance with structural and progression data not used in the test location selection process.

Decision not to add the central +/-1° test locations



Reasoning

«Foveal» testing

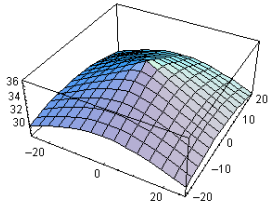
We did not add the 4 central test locations to the test because

a) All other new central test locations lie between existing 24-2 test locations and their age matched sensitivity and probability levels can be interpolated using the coherent 24-2 (30-2) normal value data set. This would not hold true for +/-1° test locations

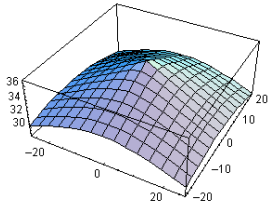
b) Adding 4 more points would have prolonged the test beyond a critical limit: The goal is to keep 24-3 SITA Faster test times below 24-2 SITA Fast test times which would be at risk with 73 test locations

c) Testing foveal threshold at 0/0 can always be included by the operator as with any other standard test pattern

Selection criteria to add test locations to the 24-2



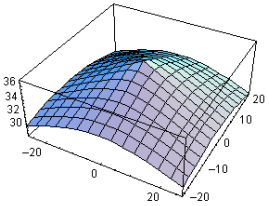
END



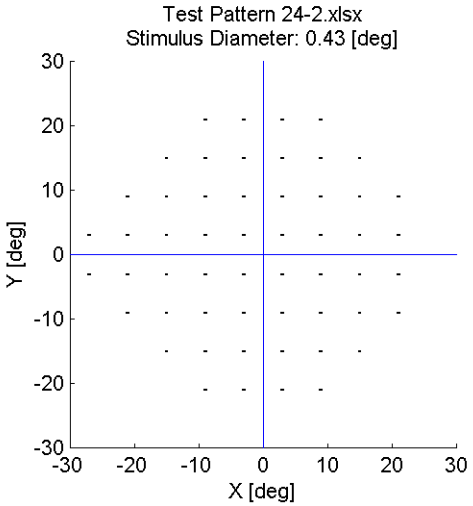
Backup Slides

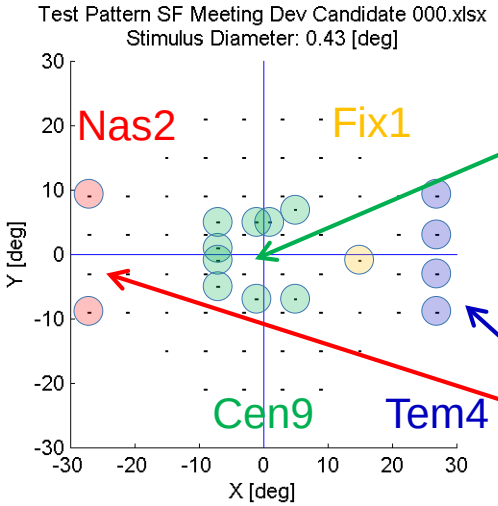
From the GPS / NAPS presentation

Structure-Function Test Pattern
Candidate Pattern



- **Enhanced pattern based on 24-2**



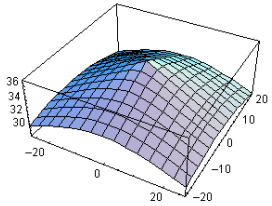


IMPROVED DIAGNOSIS
Based on various empirical 10-2 data and discussions

BETTER S-F
Based on RNFL bundle tracing and discussions

- **Short term – Maintain compatibility with 24-2**
  - Additions/Changes to the 24-2 field
    - Added 9 Central points (Cen9) from 10-2 pattern
    - Added 2 Nasal points (Nas2) and 4 Temporal points (Tem4) in the periphery
    - Replaced 2 points near blind spot with 1 point (Fix1) to represent disc
- **Long Term – All possibilities open**

Glaucoma Fields
% Fields with TD flagged at *P* < 5%



All Glaucoma

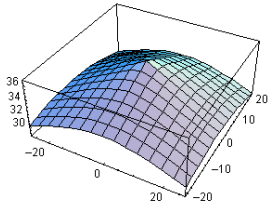
			48	46	49	47			
		57	53	53	54	50	42		
	62	60	61	60	62	51	45	42	
62	64	64	59	62	63	62	55	37	34
64	72	68	64	54	43	53	0	41	33
52	60	58	54	44	33	41	0	42	29
50	54	58	53	57	50	47	51	39	40
	49	51	58	58	55	46	42	45	
		50	52	54	50	46	45		
			43	44	41	48			

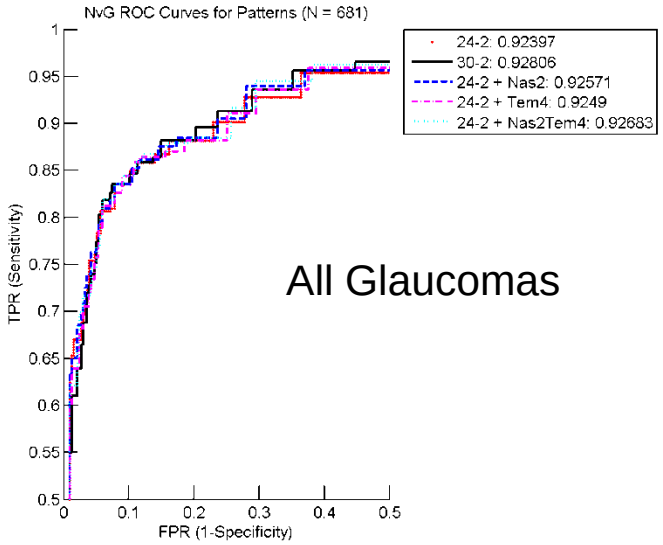
Early Glaucoma

			26	23	26	24			
		33	26	28	29	26	19		
	39	37	40	35	38	24	22	18	
37	41	38	36	39	38	38	32	14	16
39	52	47	43	29	18	28	0	25	14
29	37	36	29	22	14	20	0	23	10
27	29	35	30	35	26	25	26	16	22
	24	28	39	38	34	21	18	25	
		29	30	33	28	22	23		
			21	23	19	24			

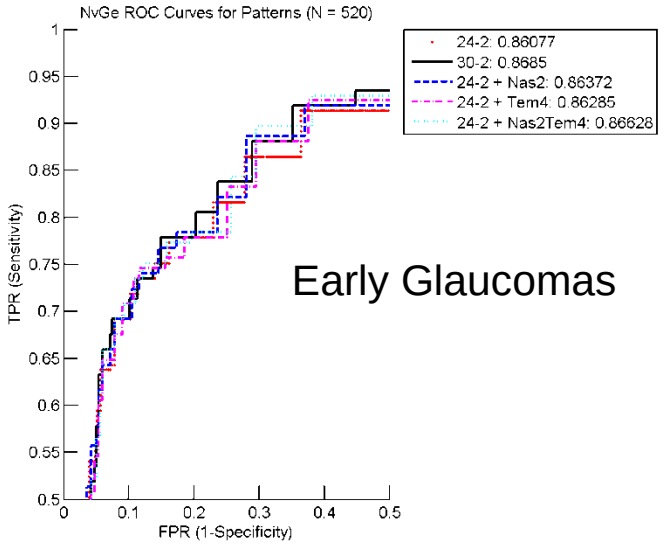
- Each test point is showing the % of the glaucoma fields that were flagged as abnormal
- New nasal points tend to be flagged as abnormal more often than the new temporal points

ROC Curves
#TD points *P* < 5%





All Glaucomas



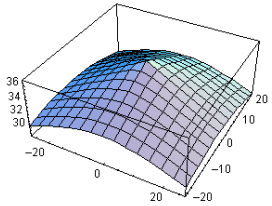
Early Glaucomas

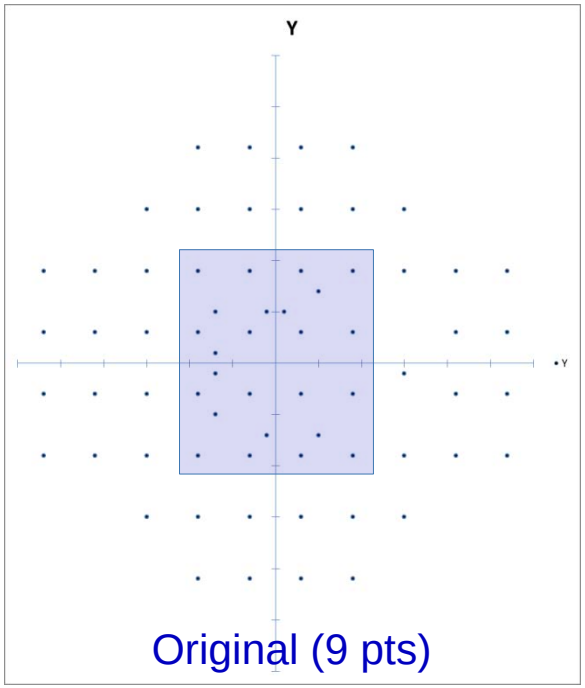
ROC1	ROC2	dAROC	SE	Pvalue
24-2	30-2	-0.0041	0.0023	0.074797
24-2	24-2 + Nas2	-0.00174	0.000637	0.00622
24-2	24-2 + Tem4	-0.00093	0.001355	0.491786
24-2	24-2 + Nas2Tem4	-0.00286	0.001446	0.047578

ROC1	ROC2	dAROC	SE	Pvalue
24-2	30-2	-0.00773	0.004171	0.063907
24-2	24-2 + Nas2	-0.00295	0.001164	0.011206
24-2	24-2 + Tem4	-0.00208	0.002517	0.408325
24-2	24-2 + Nas2Tem4	-0.00552	0.002681	0.039591

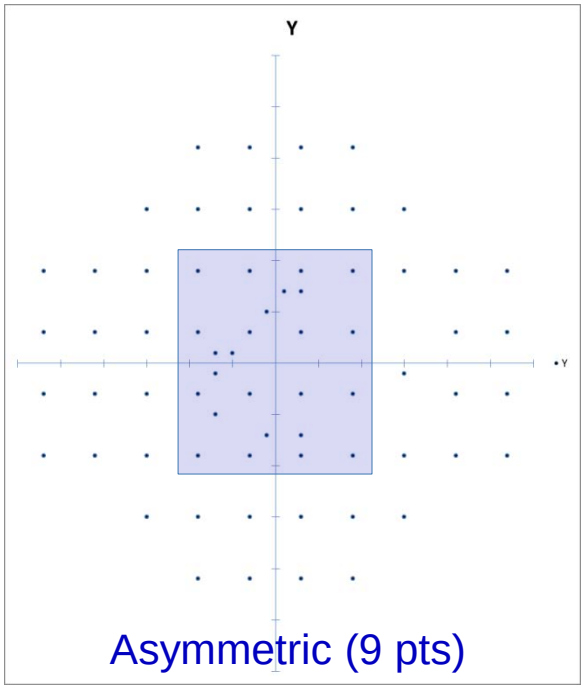
- ROC curves based on the # of TD points flagged at *P* < 5%
- **24-2 + Nas2Tem4** had statistically higher AROC than **24-2** alone
  - Magnitude is not high and *Pvalue* only ~.05 … clinically significant?

Structure-Function Test Pattern
Candidate Pattern Variations

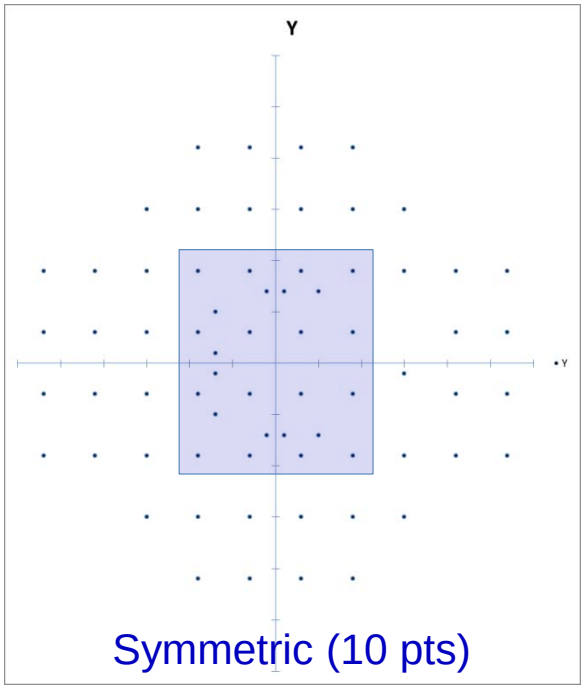




Original (9 pts)



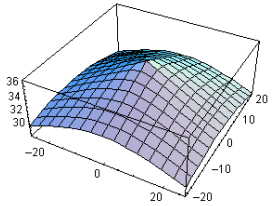
Asymmetric (9 pts)



Symmetric (10 pts)

- Original (9) – Initial Candidate Test pattern
- Asymmetric (9) – Original adjusted for empirical data
- Symmetric (10) – Original adjusted for empirical data and symmetry considerations
- ***Test patterns can be optimized for specific disease, empirical data, symmetry, etc***

ROC of 3 different candidates

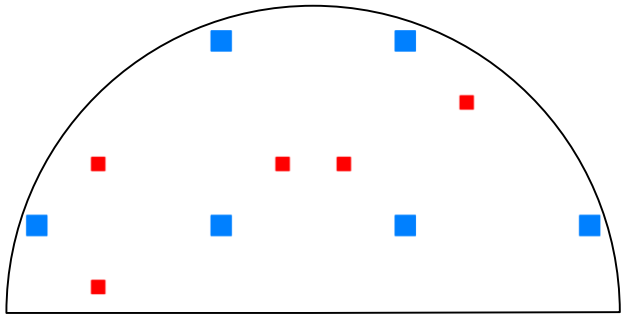


“Original” test pattern candidate

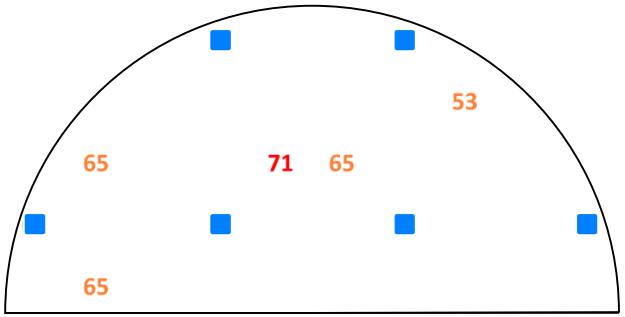
A.

Zeiss 24-2 +9 Original (Upper VF)

Test Pattern



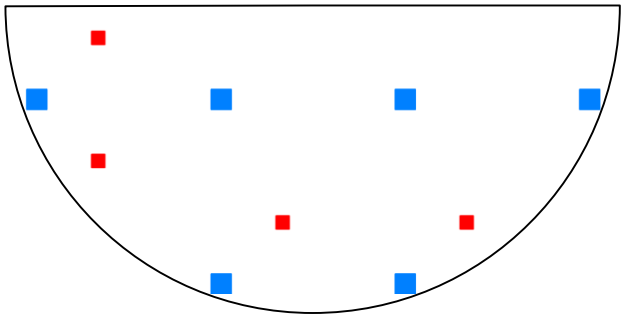
Percentage of Points $P \leq 5\%$



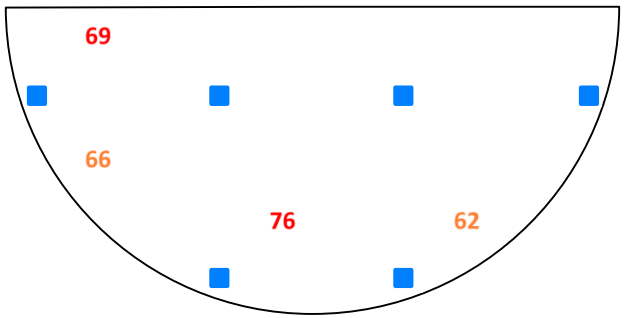
B.

Zeiss 24-2 +9 Original (Lower VF)

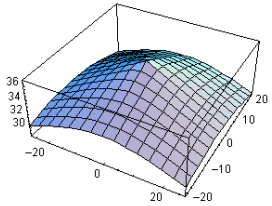
Test Pattern



Percentage of Points $P \leq 5\%$



ROC of 3 different candidates

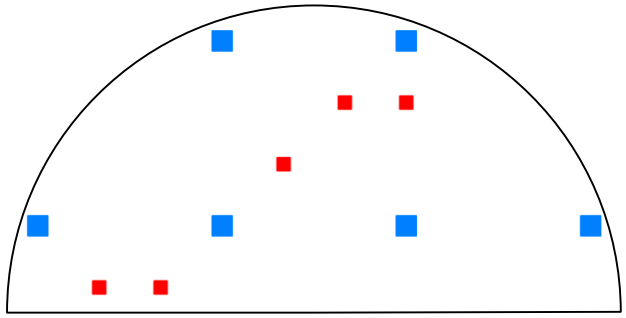


“Asymmetric” test pattern candidate

A.

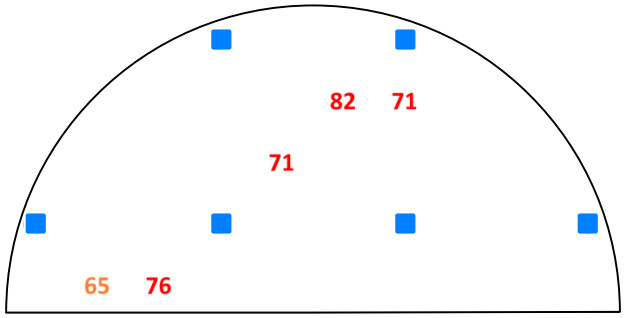
Zeiss 24-2 +9 Asymmetric (Upper VF)

Test Pattern



±10°

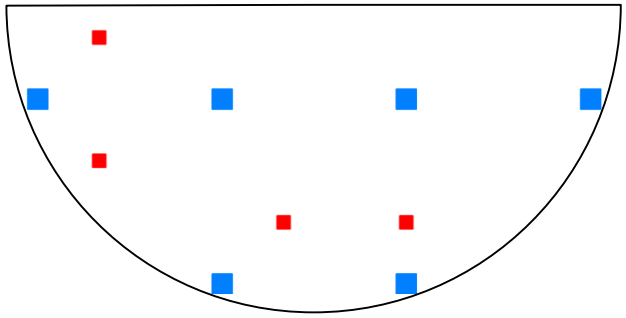
Percentage of Points $P \leq 5\%$



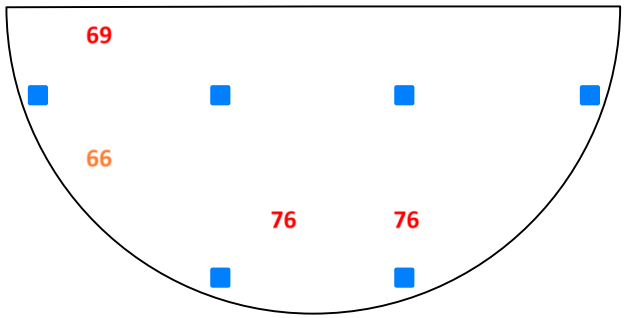
B.

Zeiss 24-2 +9 Asymmetric (Lower VF)

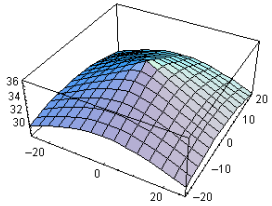
Test Pattern



Percentage of Points $P \leq 5\%$



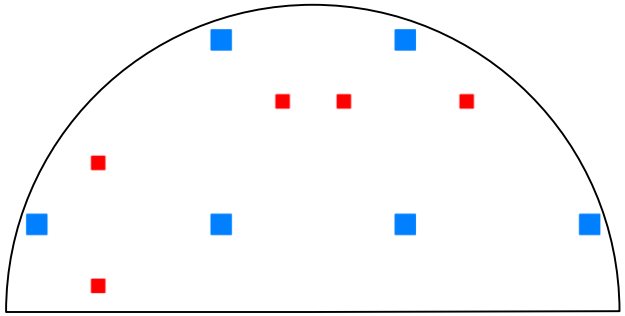
ROC of 3 different candidates



“Symmetric” test pattern candidate

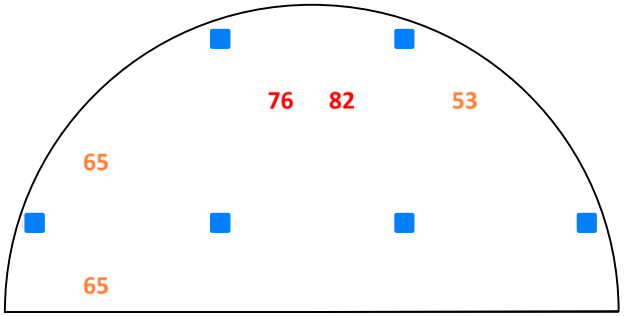
Zeiss 24-2 +10 Symmetric (Upper VF)

Test Pattern



±10°

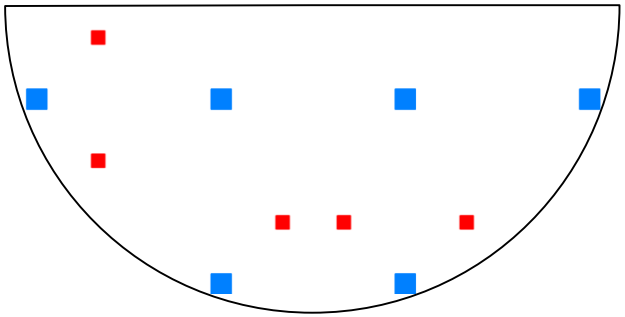
Percentage of Points $P \leq 5\%$



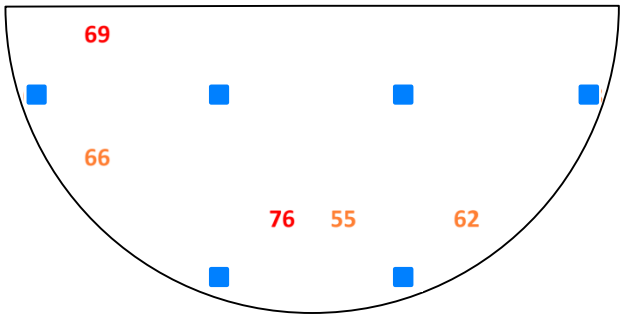
B.

Zeiss 24-2 +10 Symmetric (Lower VF)

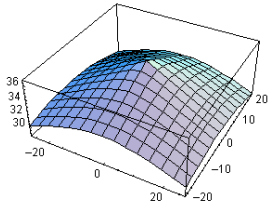
Test Pattern



Percentage of Points $P \leq 5\%$

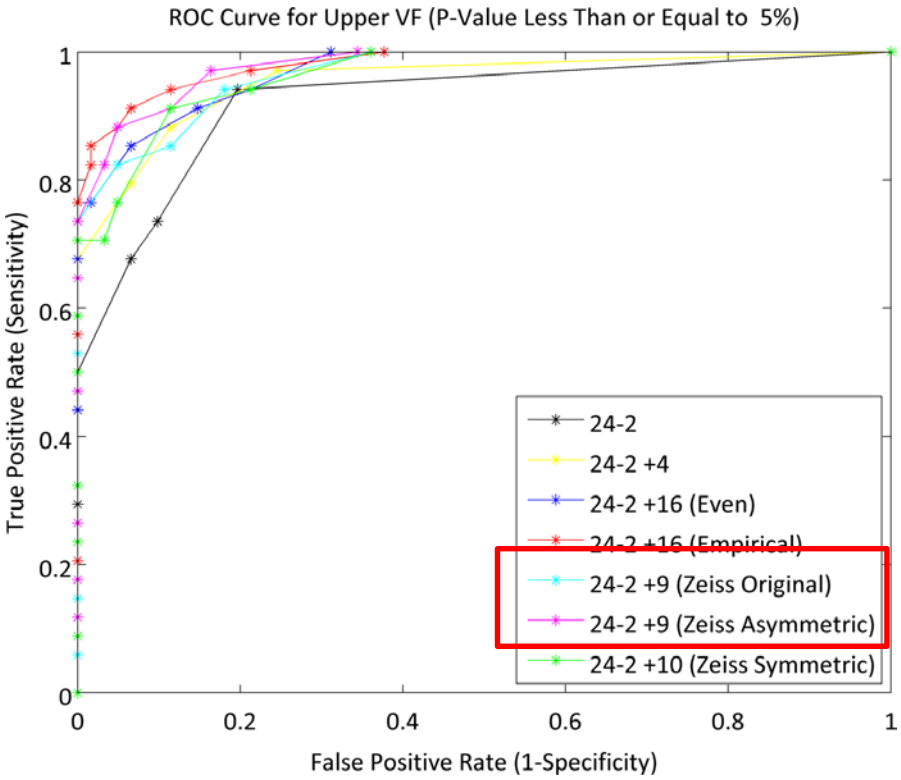


ROC of 3 different candidates



"Asymmetric" test pattern candidate

A.



B.