Probing Inflammatory Neurodegeneration in Multiple Sclerosis with Sector-to-Channel Correlation between mfVEP and OCT

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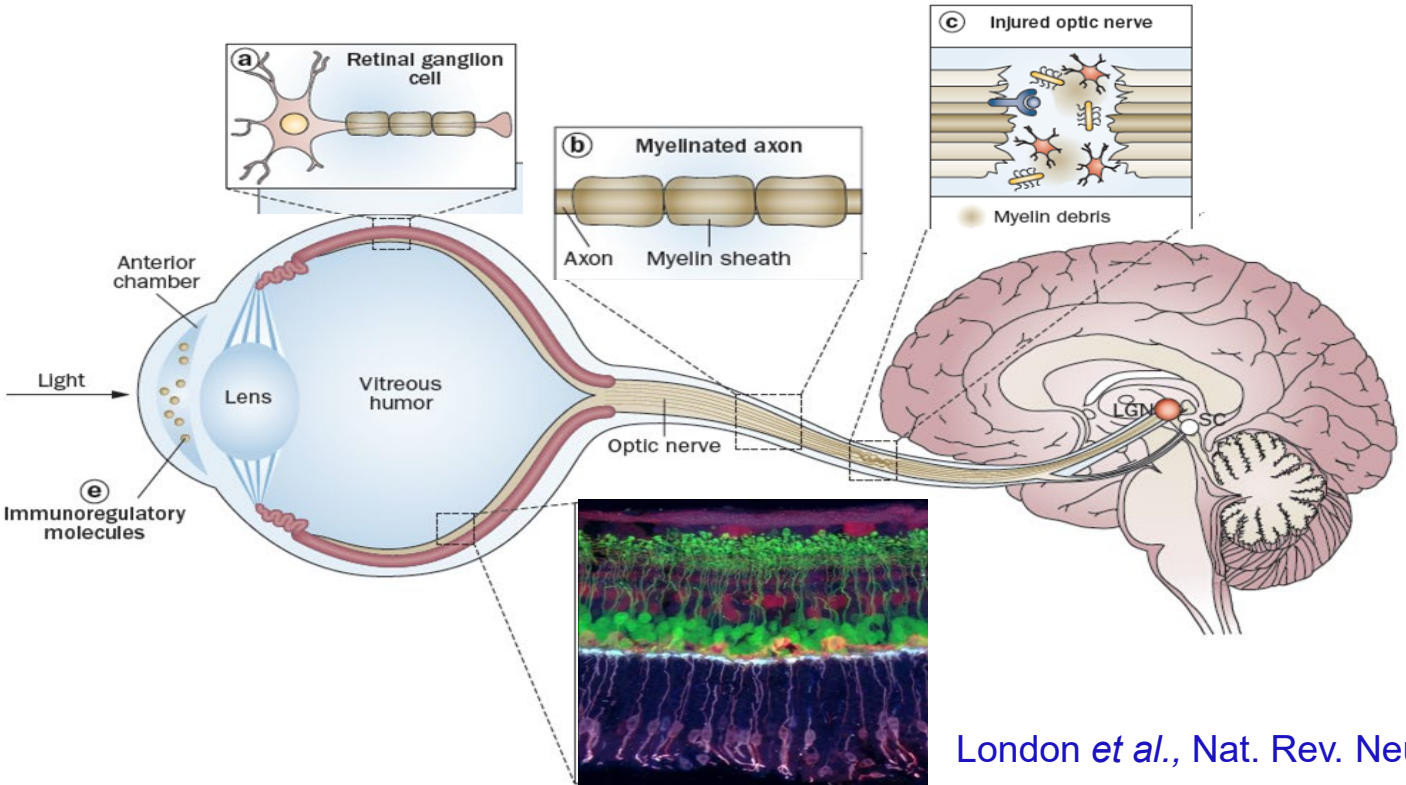
Retina: Window to the Brain

Retina: Most accessible CNS extension

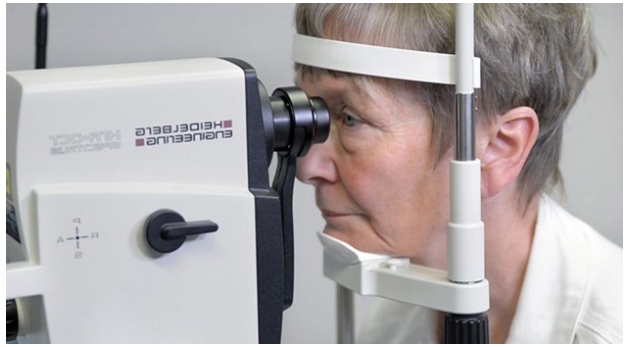
- *Similarities: anatomy, function, response to insult, immunology*
- Major neurodegenerative disorders reflected in the retina
- Technical advances in ocular imaging / function
- Convenient platform to study CNS diseases and therapies

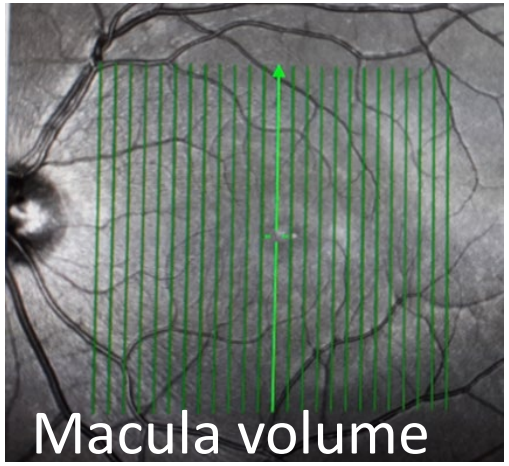


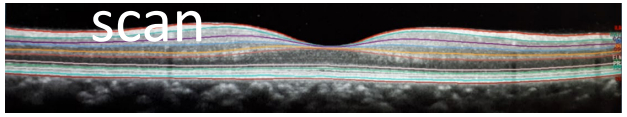
London *et al.*, Nat. Rev. Neurol. 9, 44-53 (2013)

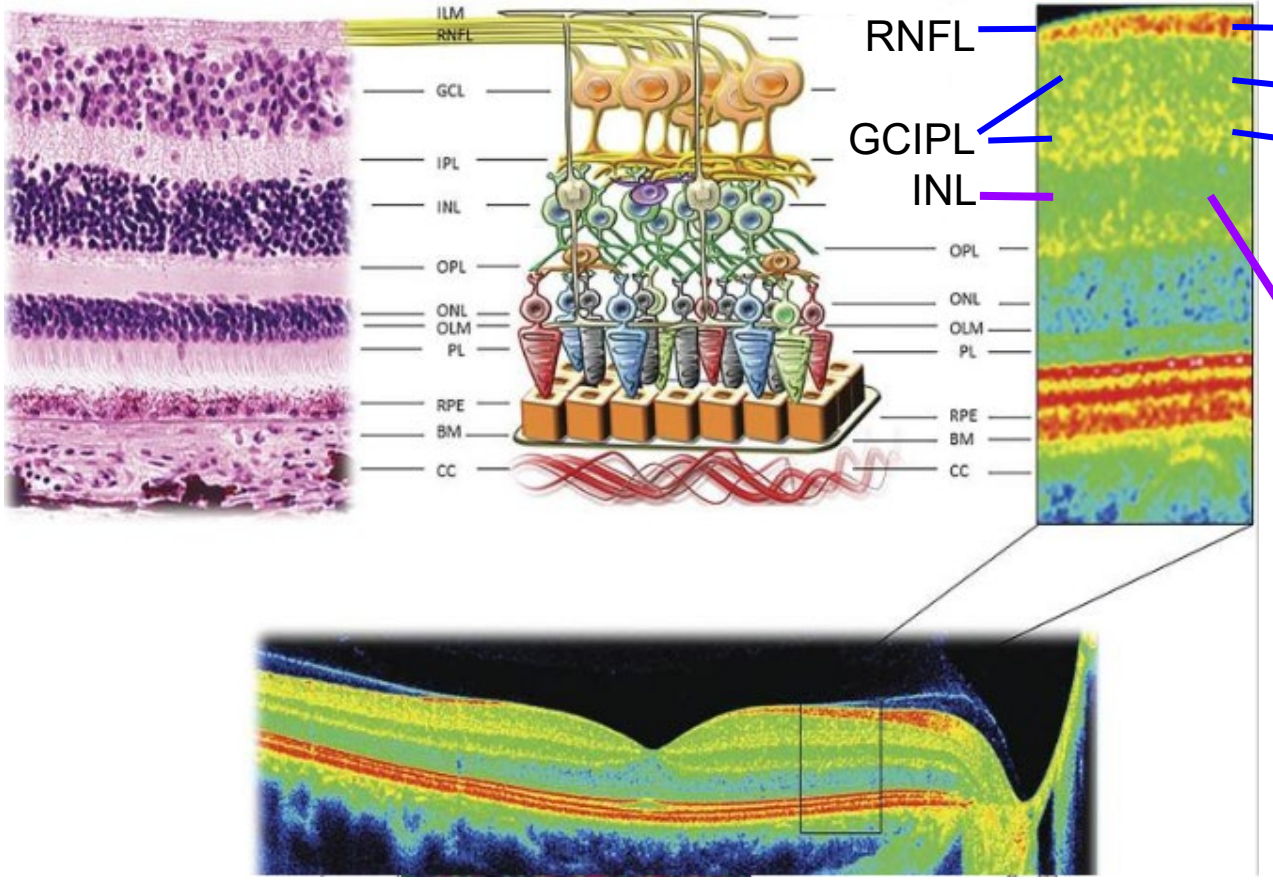
Optical Coherence Tomography

- Principle: equivelant to ultrasound.
- Thickness of the layers can be quantified as axonal/neuronal/dendritic loss









Petzold et al., 2017

Balk et al., 2019

RNFL = retinal nerve fiber layer; GCL = ganglion cell layer;
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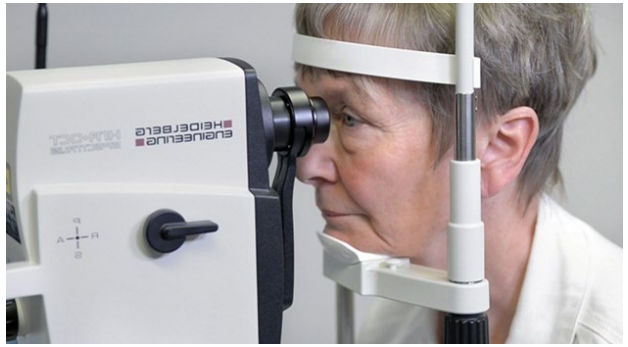

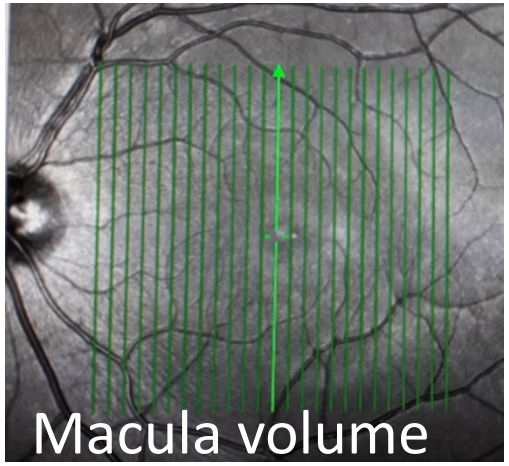

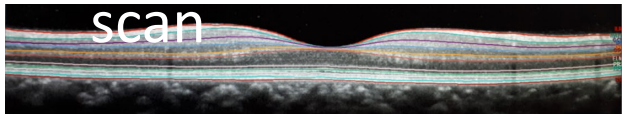

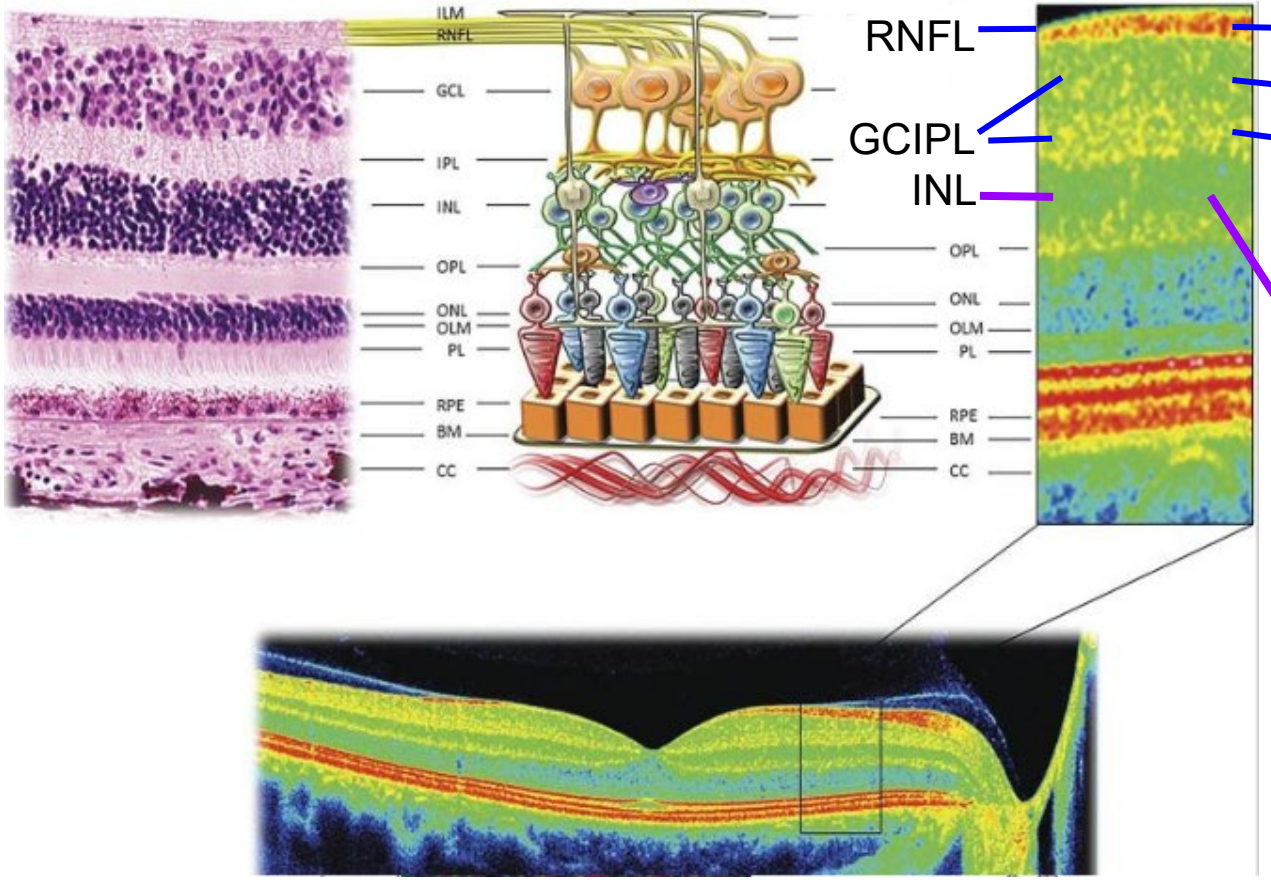

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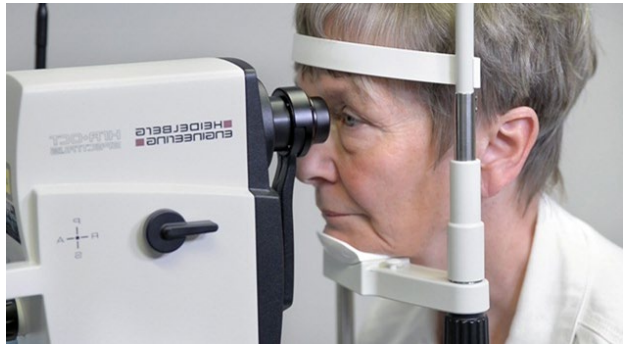

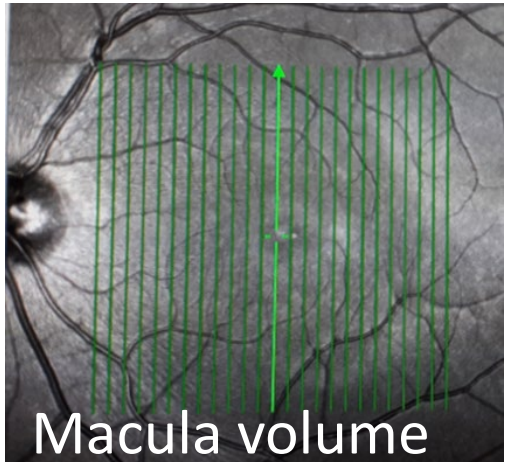

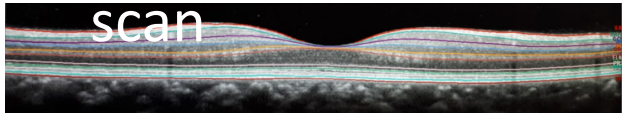

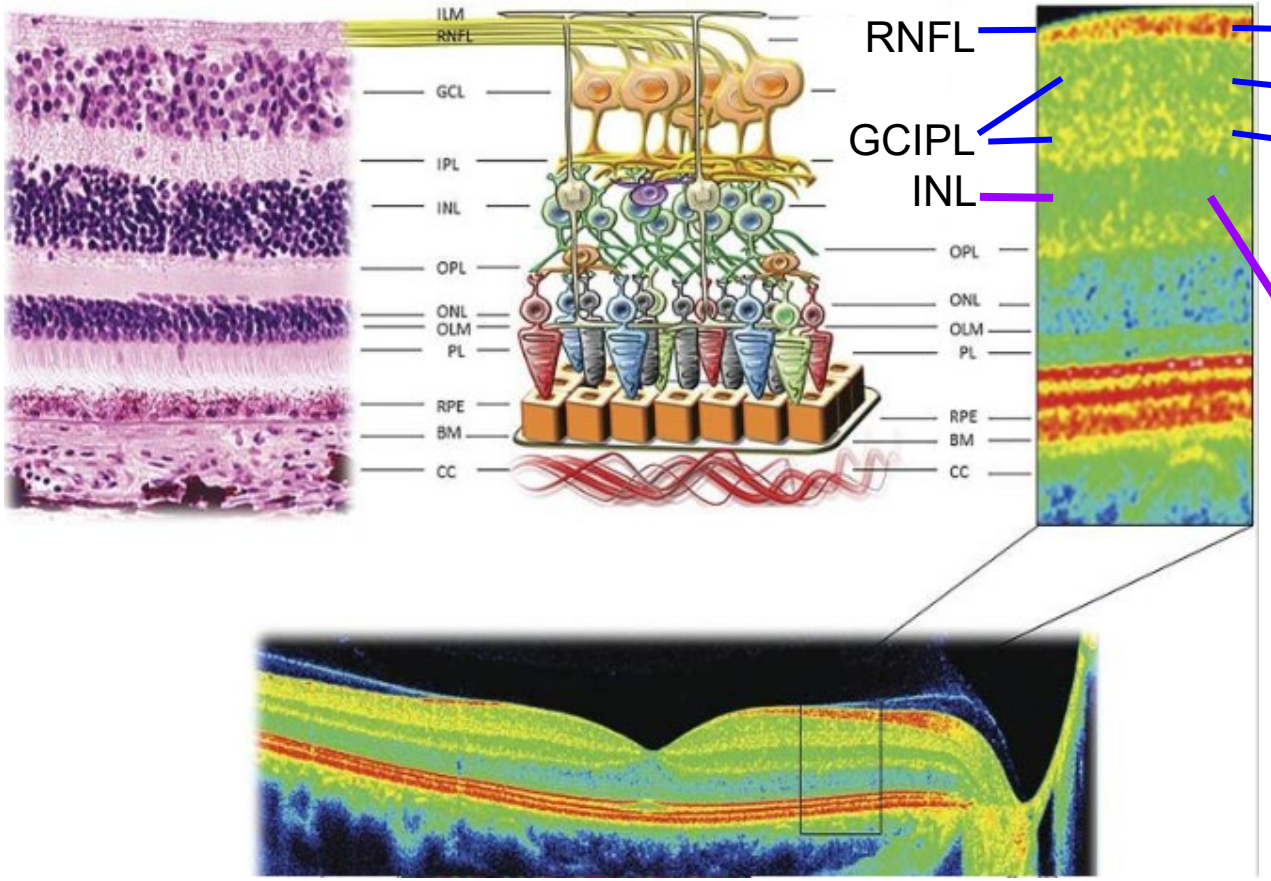

ganglion cell axon
ganglion cell body&
dendrite (synapses)

Thinning = Loss

Petzold et al., 2017

bipolar,horizontal, amacrine cells

Thickening = Inflammatory disease activity

Balk et al., 2019

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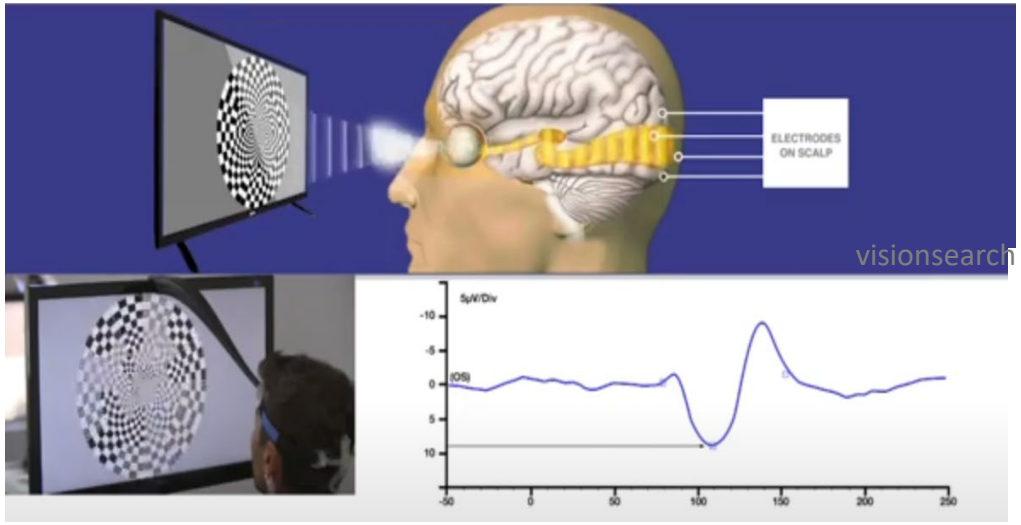
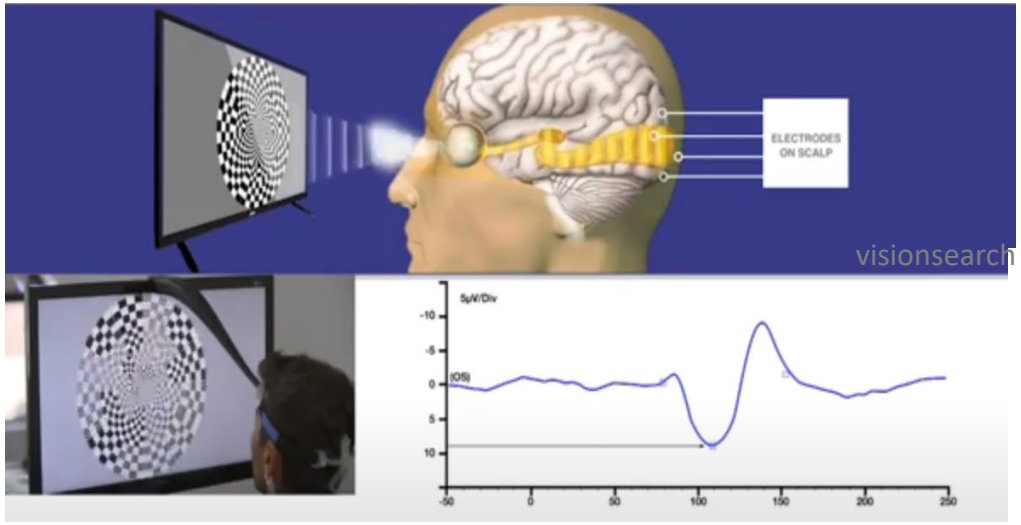
Galetta et al., 2015

Multi-focal Visual Evoked Potential & OCT



Functional Measure

Multi-focal Visual Evoked Potential & OCT



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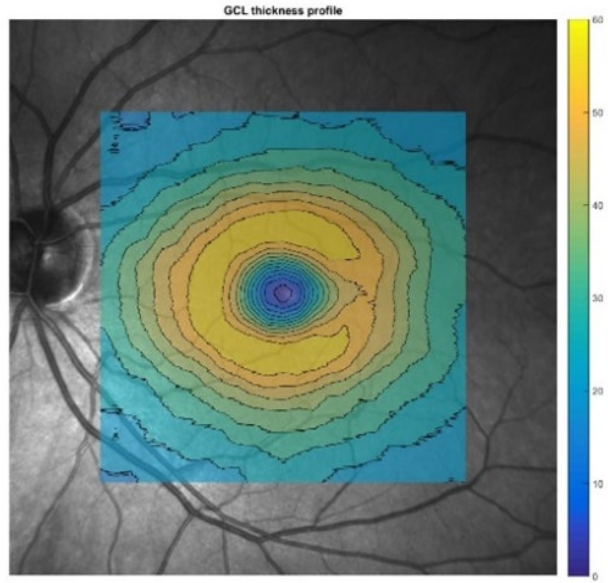

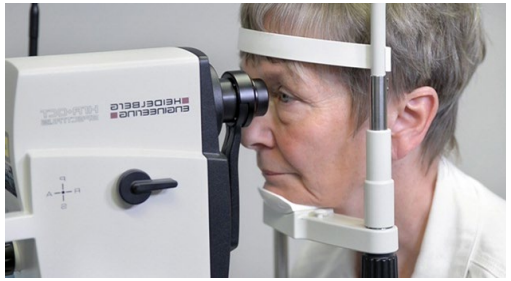

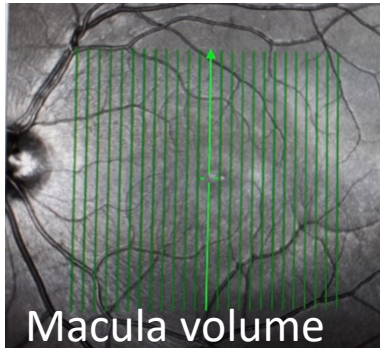

Structural Measure

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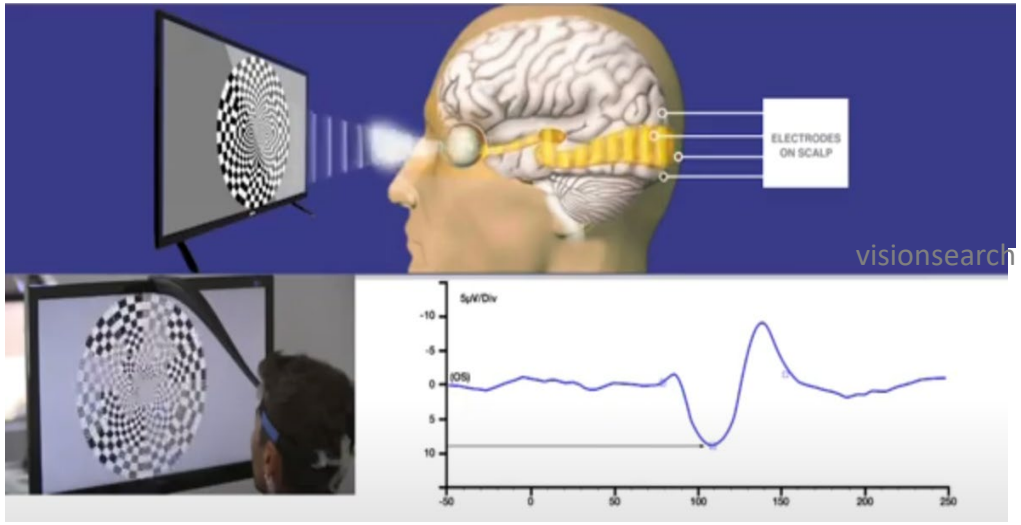

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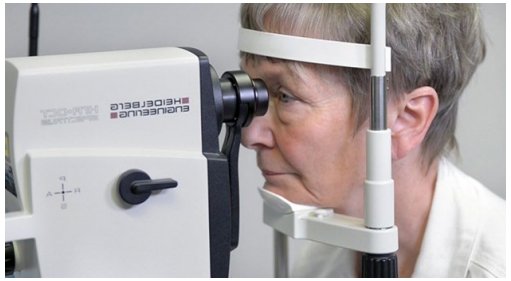
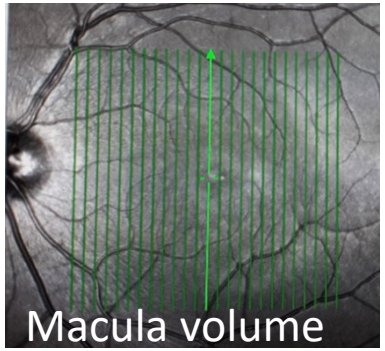
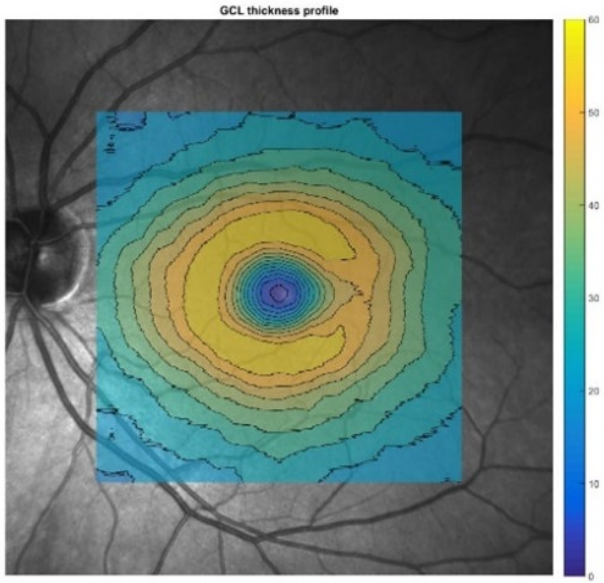




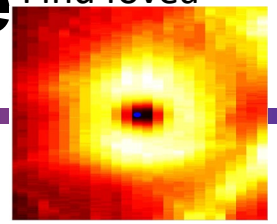
Structural Measure

Voxel-Based Morphometry



Sector-to-channel correlation

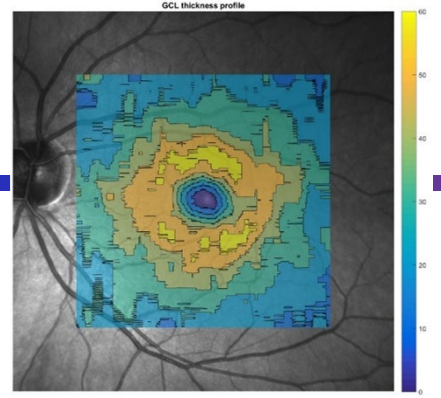
VBM pipeline



Find fovea

fovea alignment

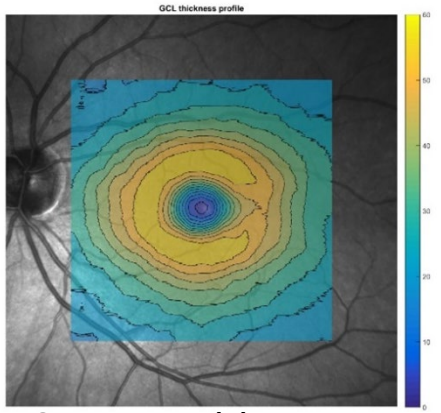
Affine transform to target space



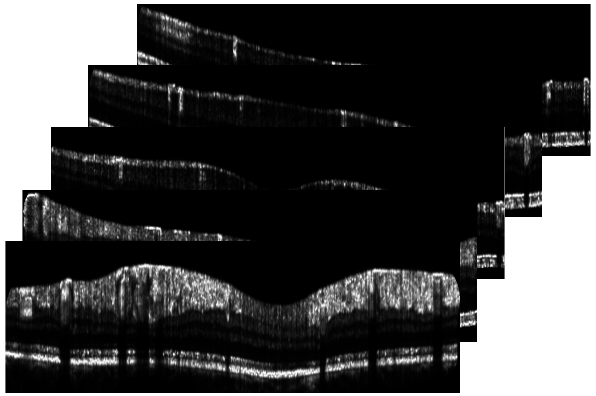
Individual healthy map

Average

Apply the transformation matrix to each **thickness map**



Group Healthy map

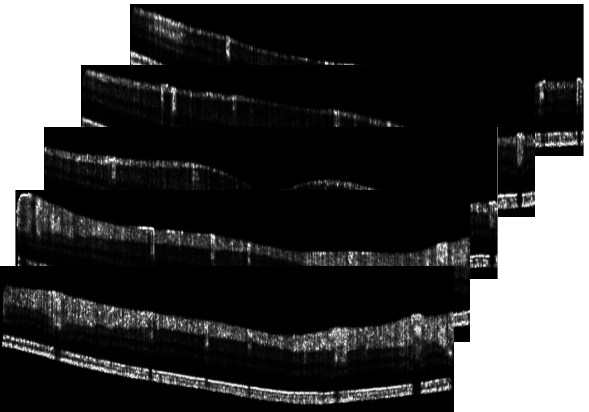


Healthy OCT

Voxel-wise t-est of every map

Reconstruct full-field view

patient OCT



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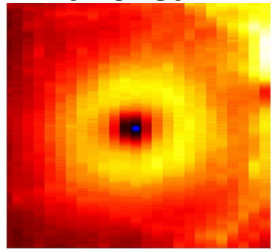

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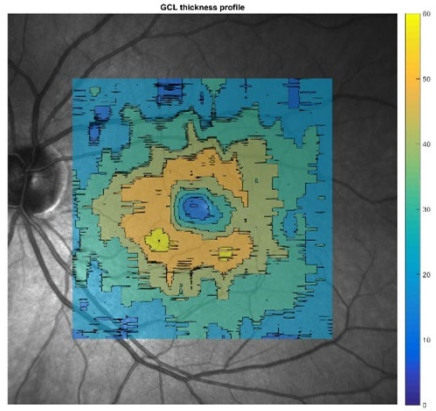
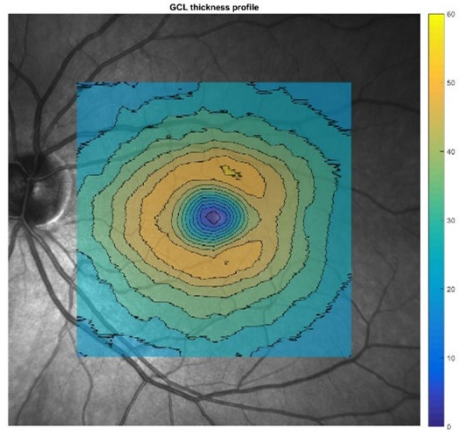


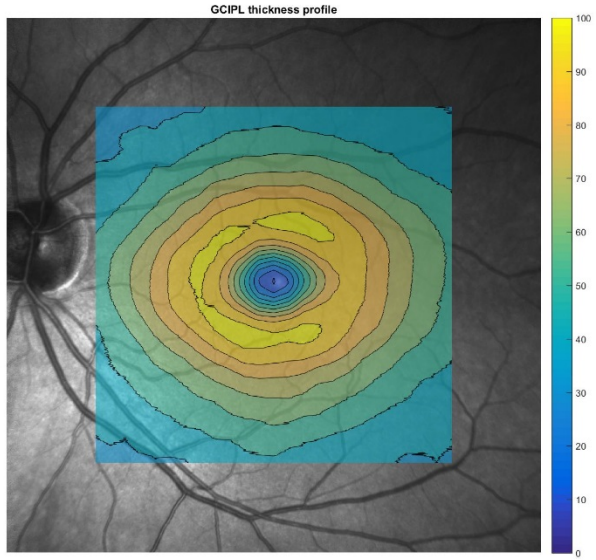
Individual patient map

Average

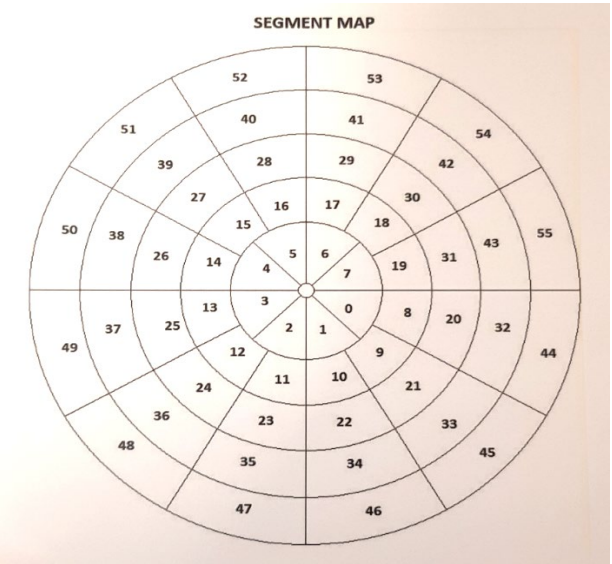


Group patient map

OCT Sector to mfVEP Channel correlation



Central 32 channels



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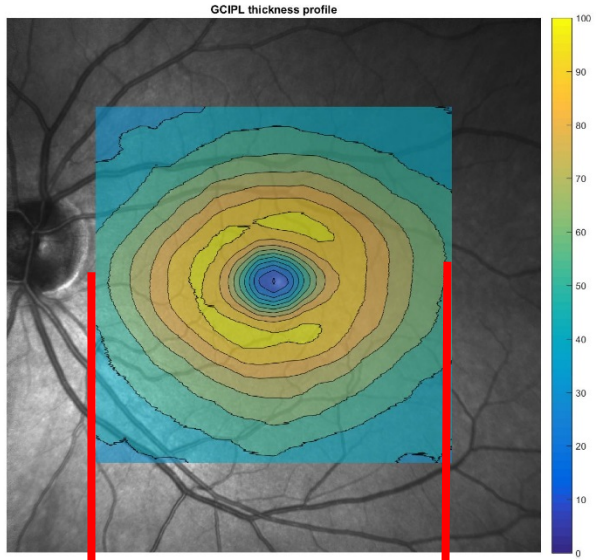

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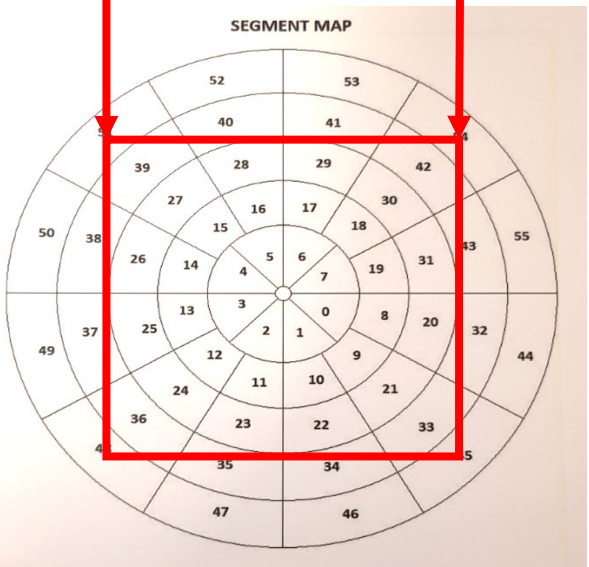
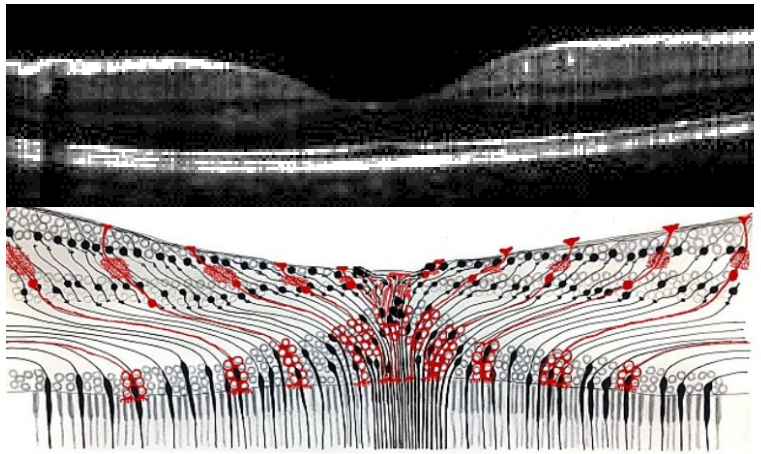
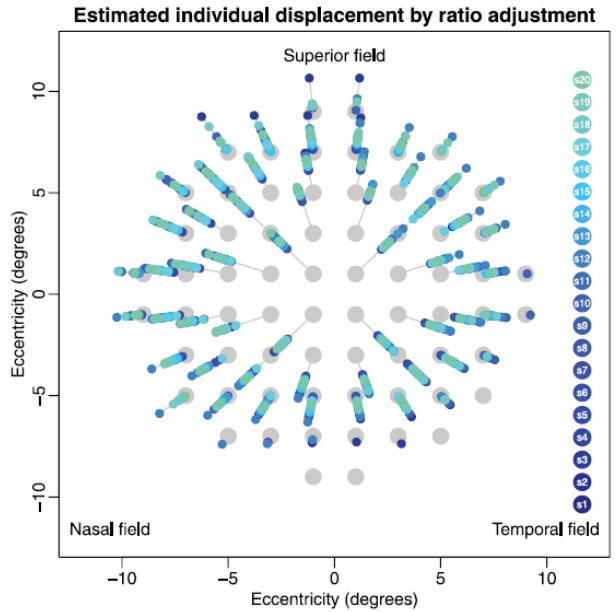


Correction for visual field displacement



Kolb et al., 1995



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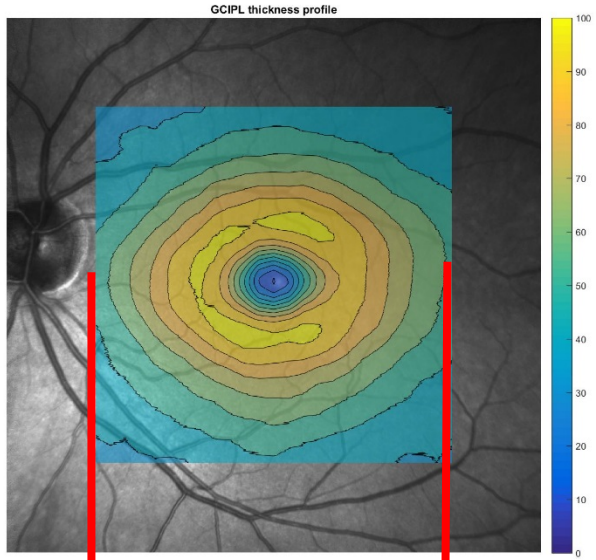

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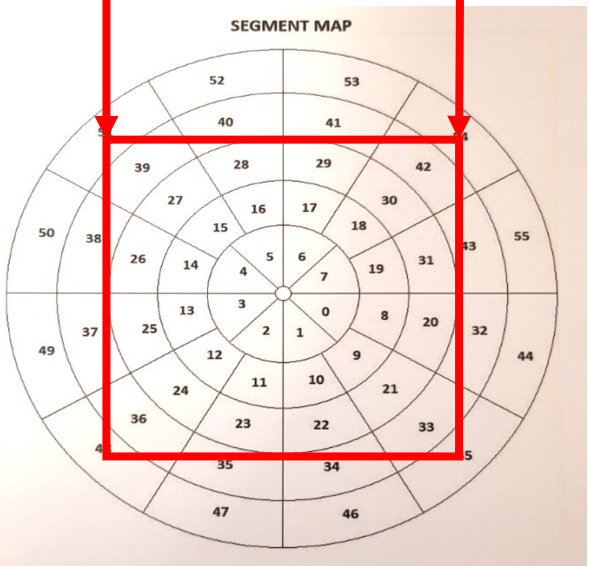

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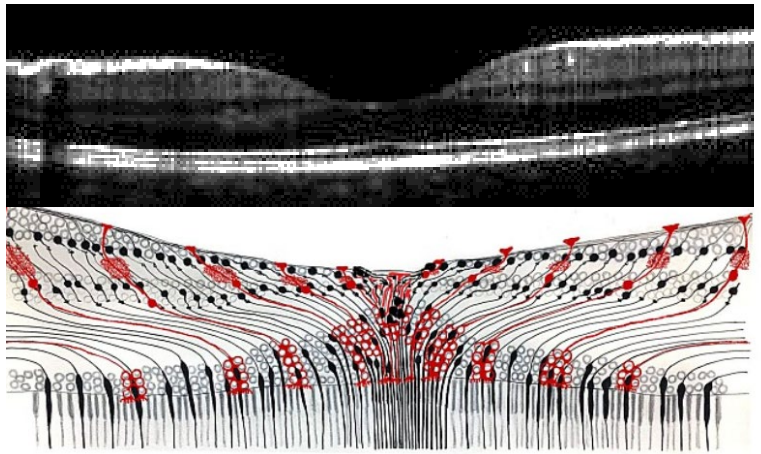

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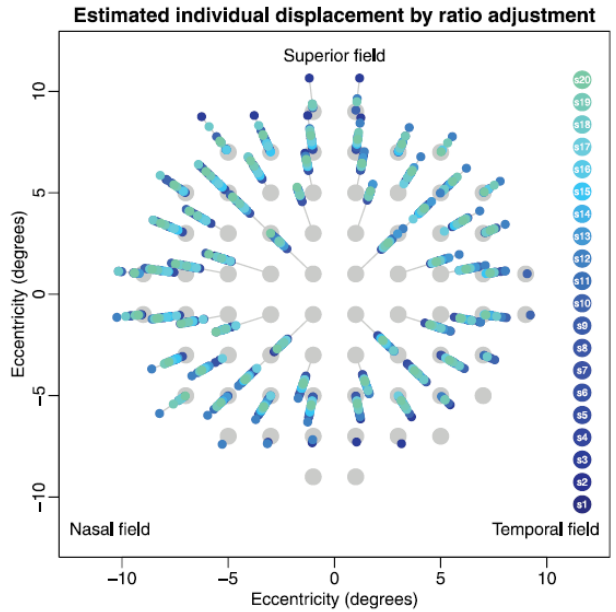

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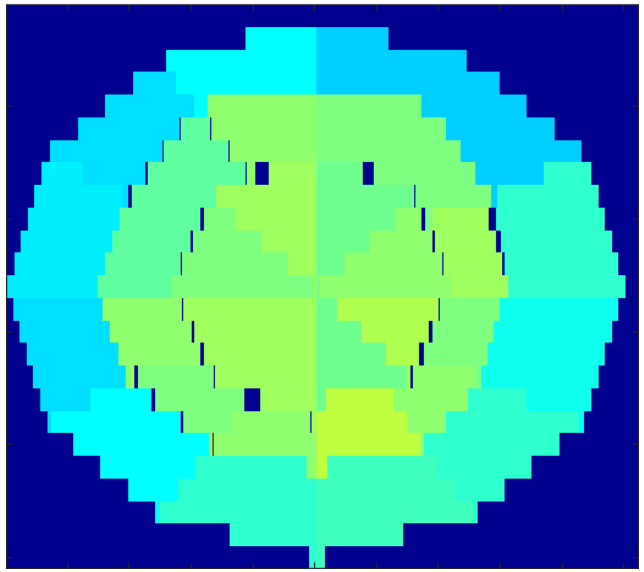
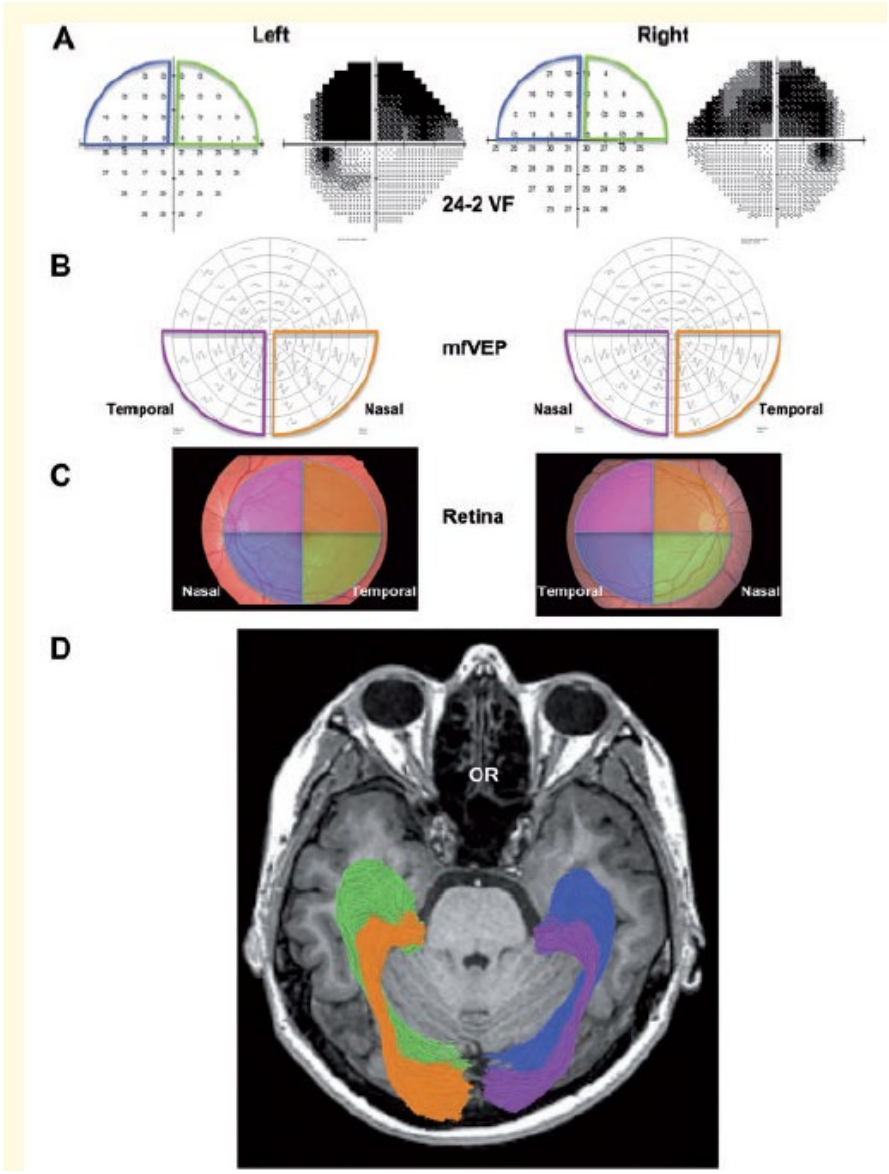
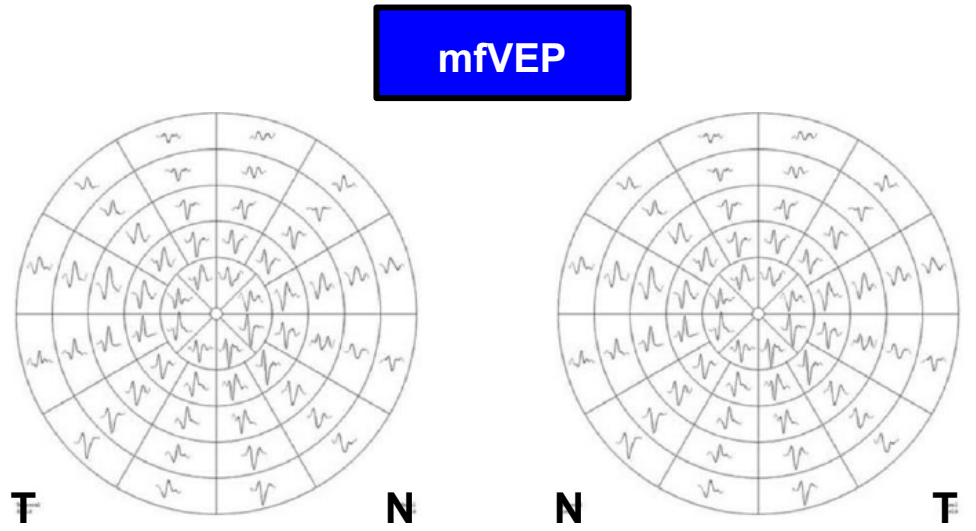
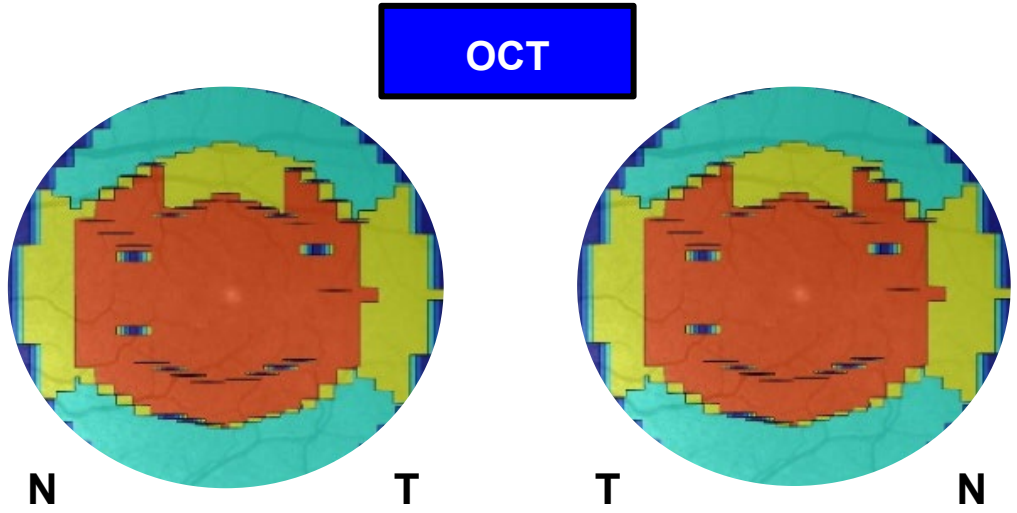
Macula segmented into sectors that are corresponding mfVEP channels



Optic Radiation and Visual Field







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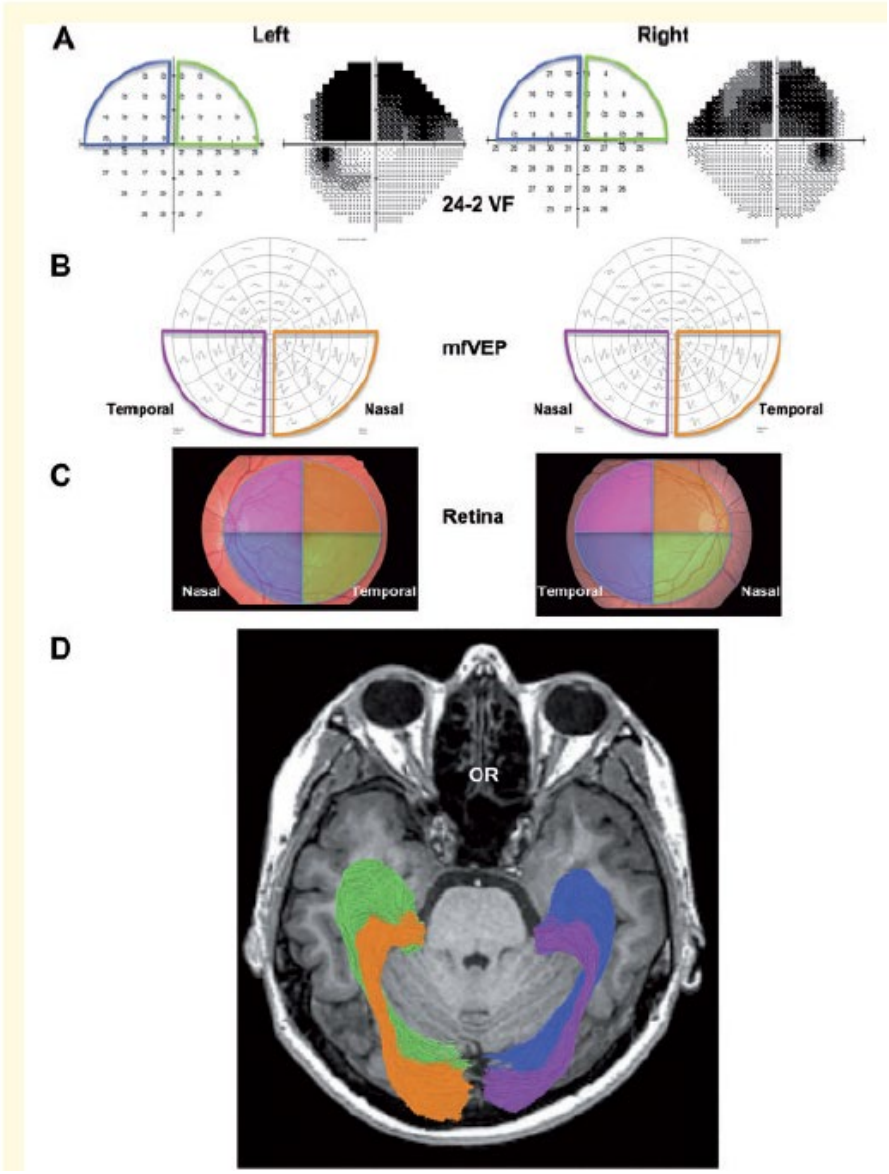

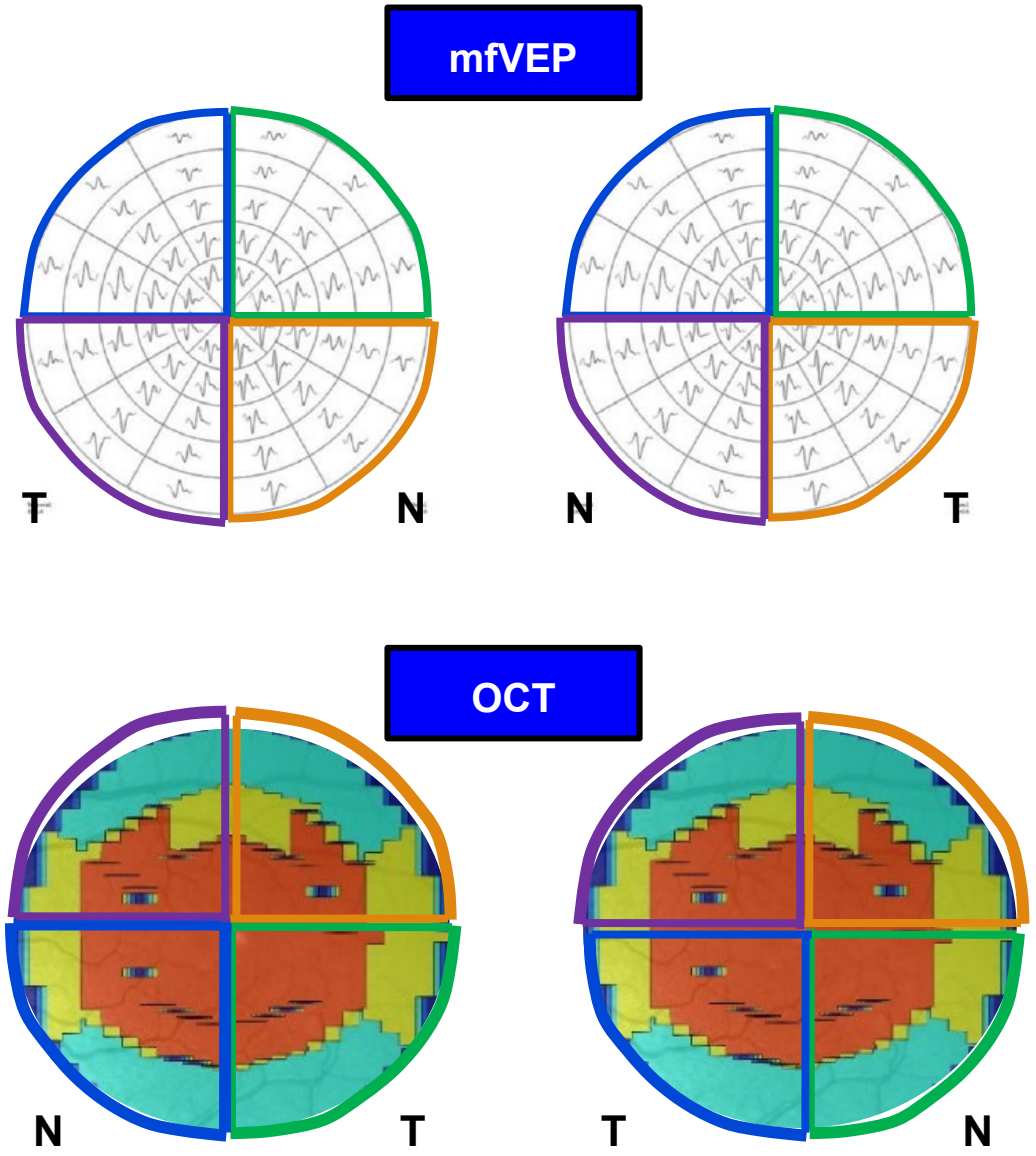

Subject Demographic

	Healthy (N = 30)	PPMS (N = 17)	SPMS (N = 20)
Gender (M/F)	9/21	13/4	8/12
Age (y)	32,2 ± 9,8	45,6 ± 11,1	47,5 ± 7,2
Disease Duration (y)	-	2,7 ± 1,0	14,0 ± 8,8
Progression duration (y)	-	2,7 ± 1,0	1,7 ± 1,4
EDSS	-	4,6 ± 0,9	5,3 ± 1,3
Eyes with ON (N))	-	5	10
Global pRNFL thickness(µm)	98,7 ± 9,1	94,4 ± 10,1	90,2 ± 8,4

- people with **newly-confirmed** progressive MS consecutively enrolled from fall 2015 to summer 2018 (PPMS: primary progressive MS; SPMS: secondary progressive MS)
- Left and right eyes were averaged (in case of no history of ON in both eyes)
- Only Eyes **without history of optic neuritis** (ON) and **with normal global peripapillary RNFL** (pRNFL) thickness were used.

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Disease Duration (y)	-	2,7 ± 1,0	14,0 ± 8,8
Progression duration (y)	-	**2,7 ± 1,0**	**1,7 ± 1,4**
EDSS	-	4,6 ± 0,9	5,3 ± 1,3
Eyes with ON (N))	-	5	10
Global pRNFL thickness(µm)	**98,7 ± 9,1**	**94,4 ± 10,1**	**90,2 ± 8,4**

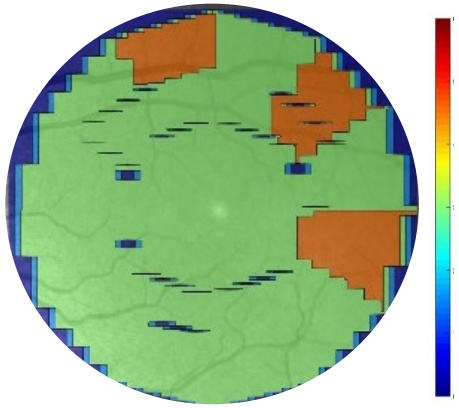
- people with **newly-confirmed** progressive MS consecutively enrolled from fall 2015 to summer 2018 (PPMS: primary progressive MS; SPMS: secondary progressive MS)
- Left and right eyes were averaged (in case of no history of ON in both eyes)
- Only Eyes **without history of optic neuritis** (ON) and **with normal global peripapillary RNFL** (pRNFL) thickness were used.

Group comparison: mfVEP parameters

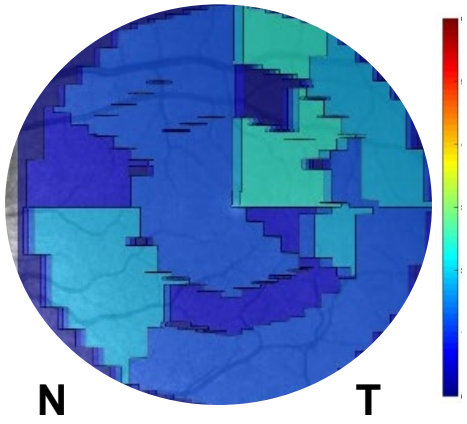
- Amplitude and relative latency of every channel were quantified. *Malmqvist et al., 2016*

Healthy

Amplitude



relative Latency



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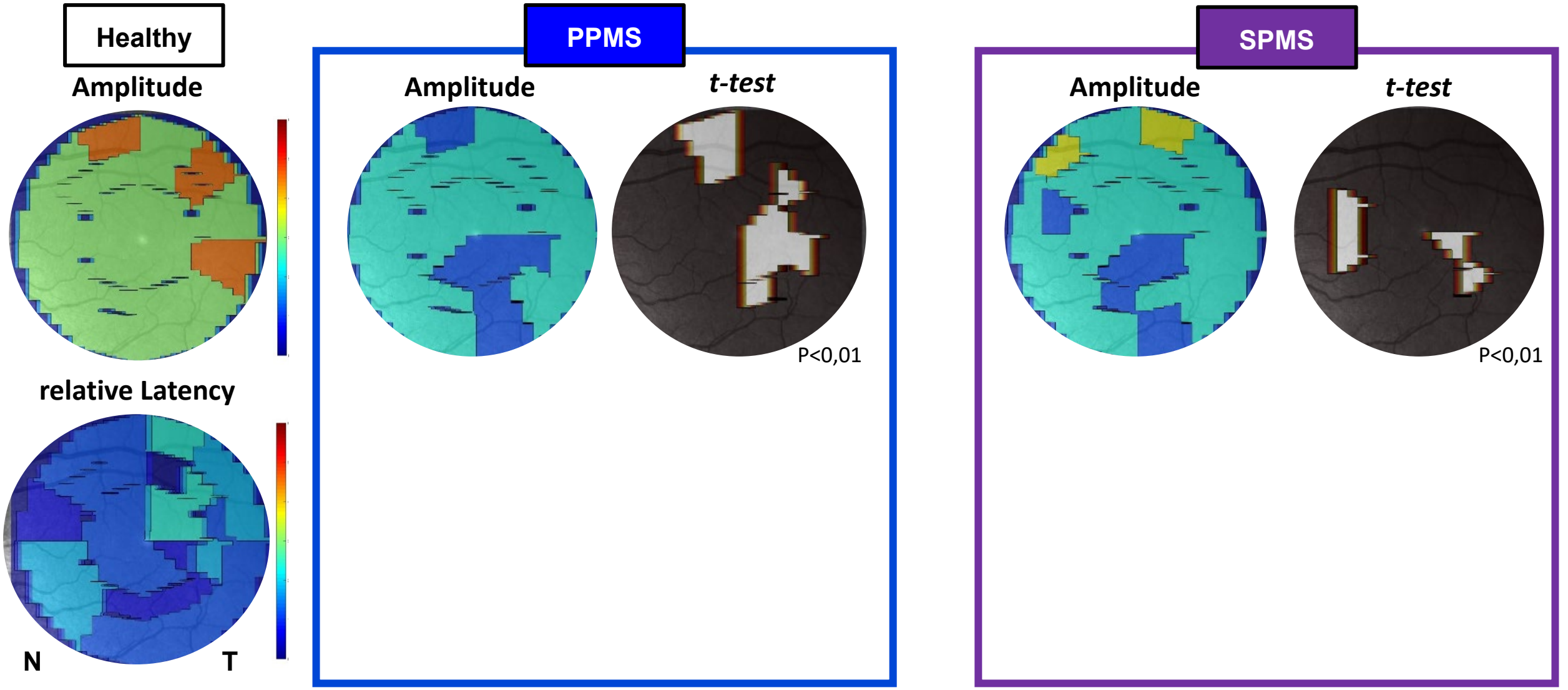

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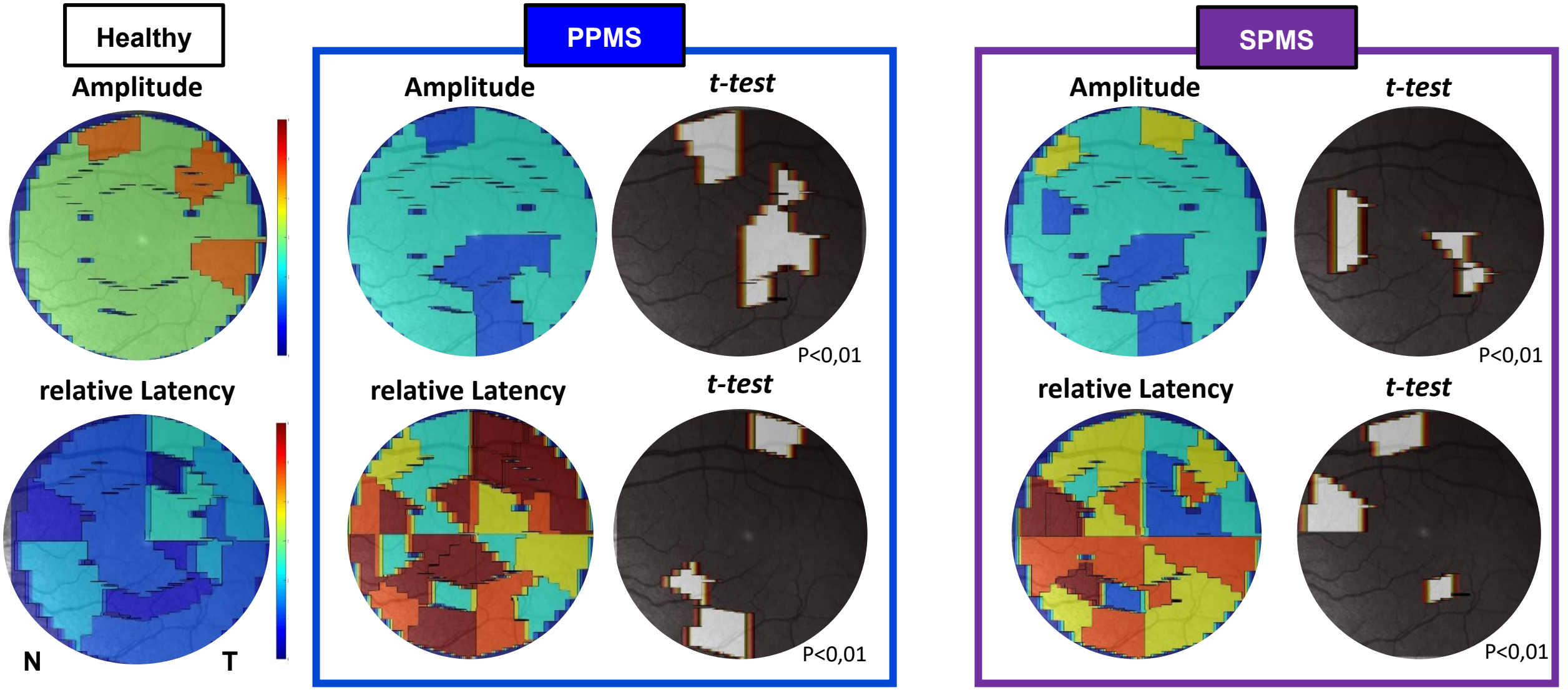
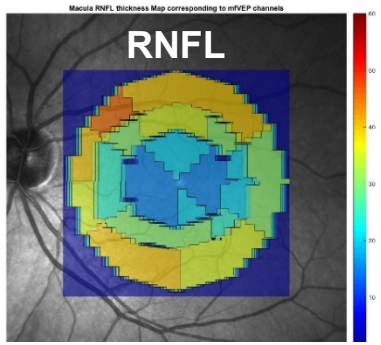
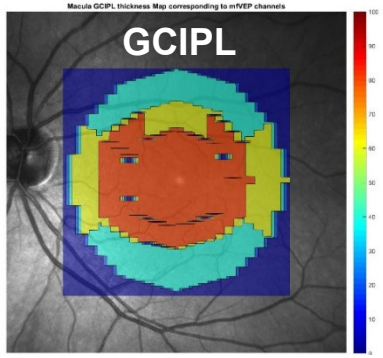
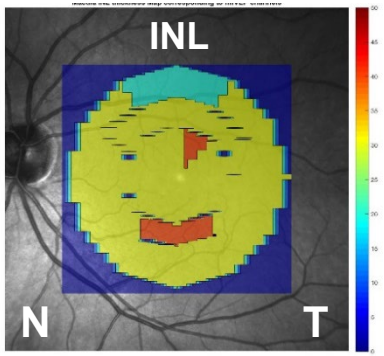


Group comparison: OCT parameters

Healthy

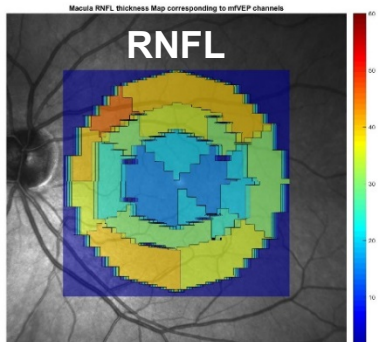


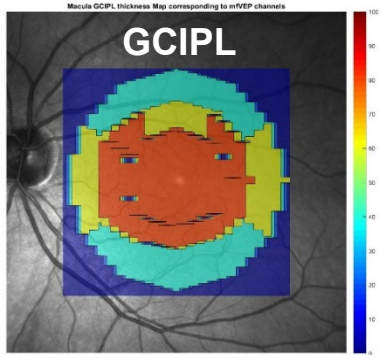


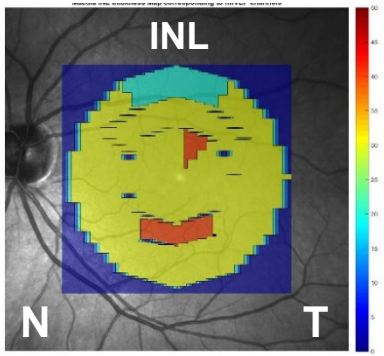


Group comparison: OCT parameters

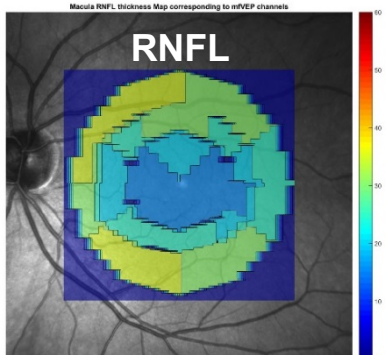
Healthy

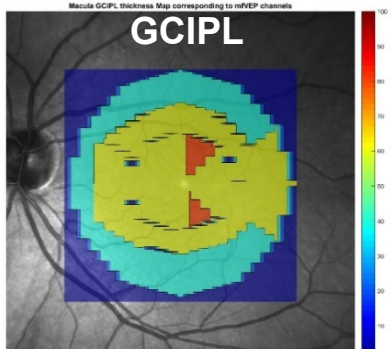


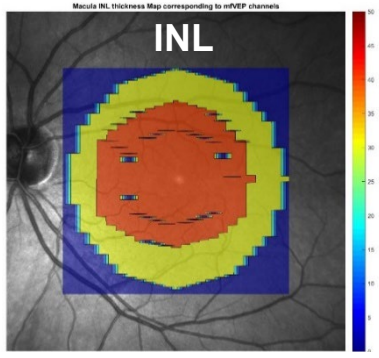




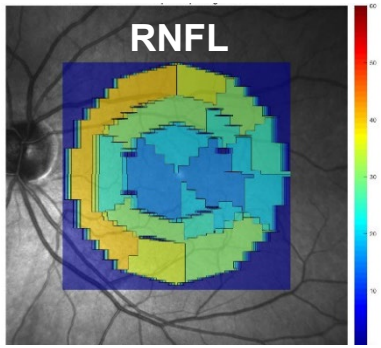
PPMS

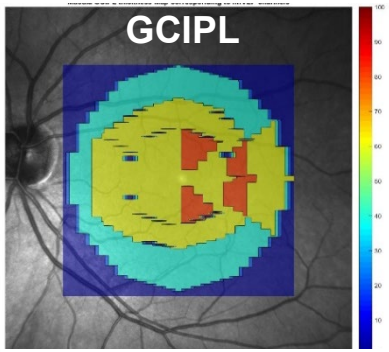


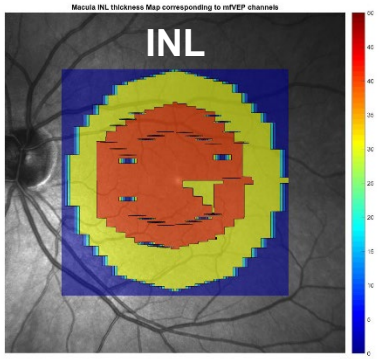




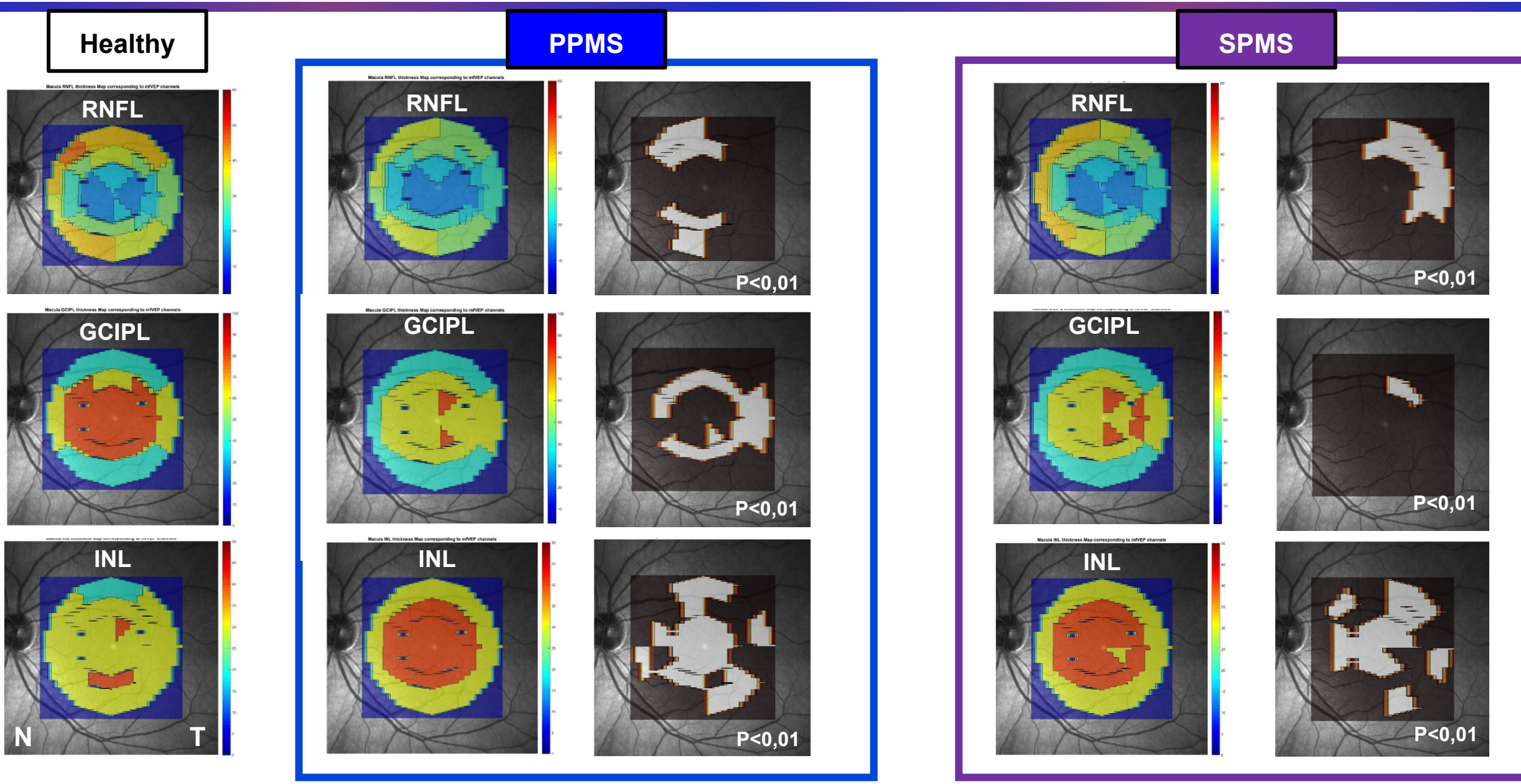
SPMS





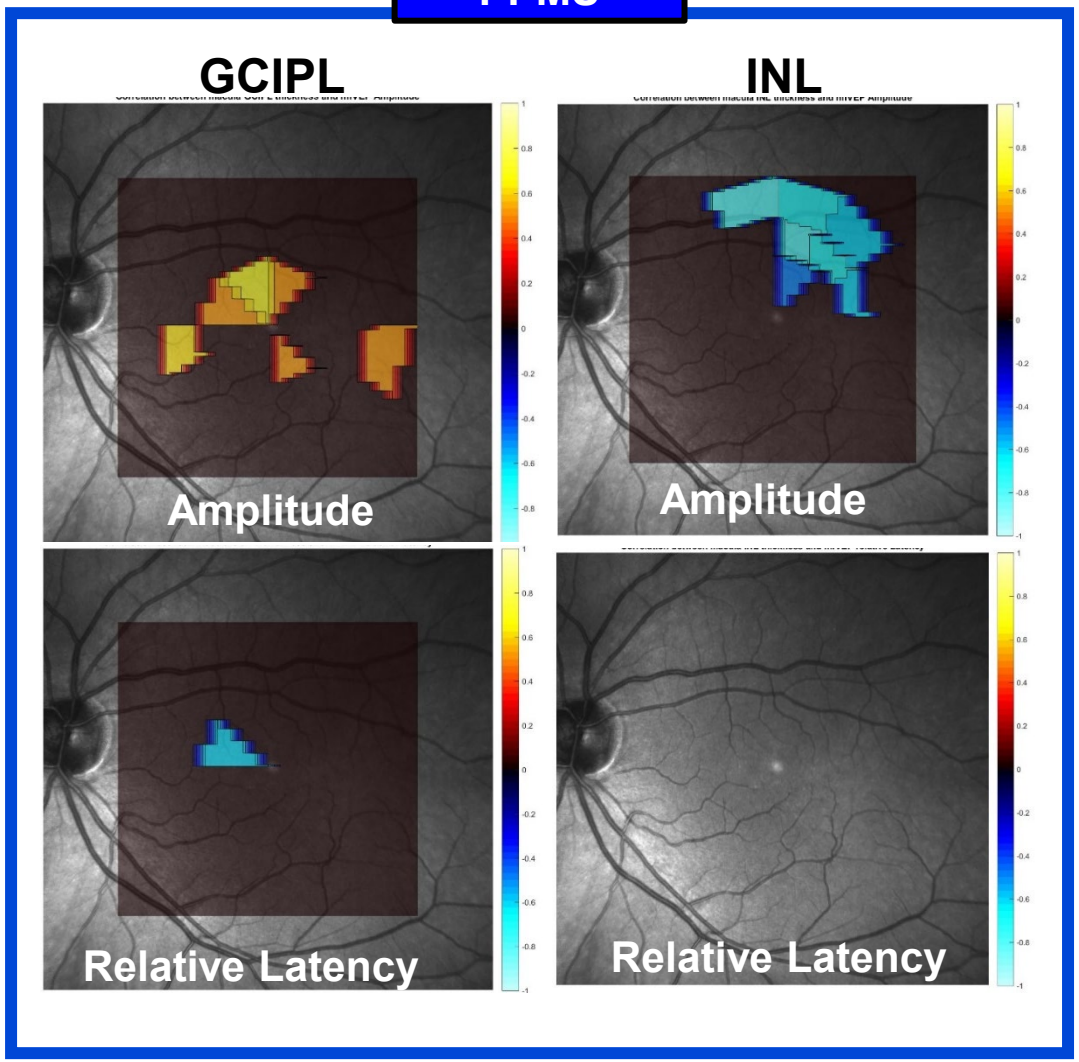


Group comparison: OCT parameters



Sector-to-Channel Correlation

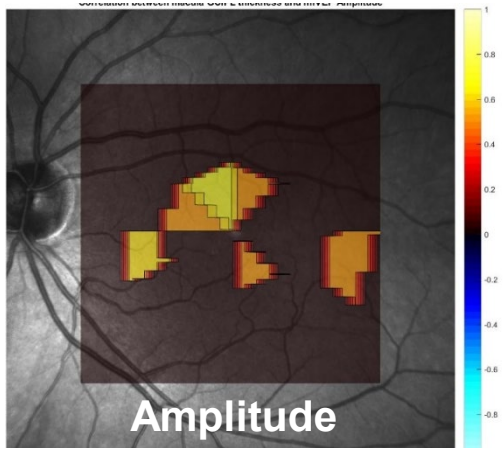
PPMS

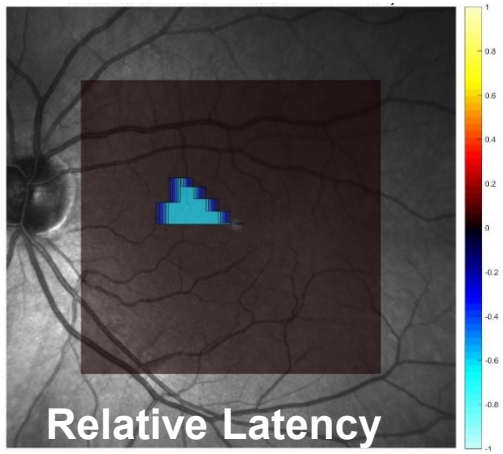


Sector-to-Channel Correlation

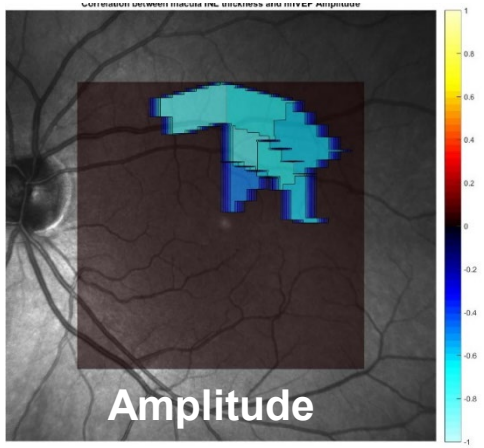
PPMS

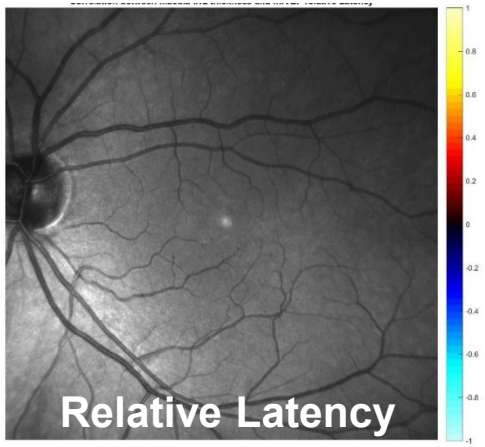
GCIPL





INL





SPMS

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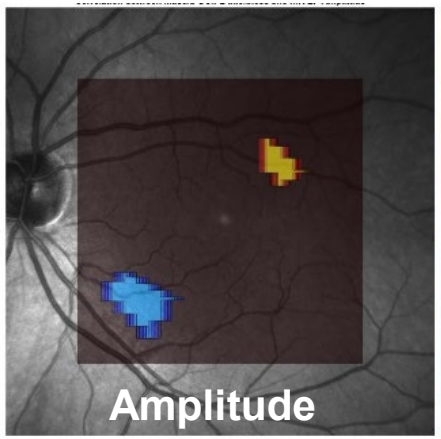

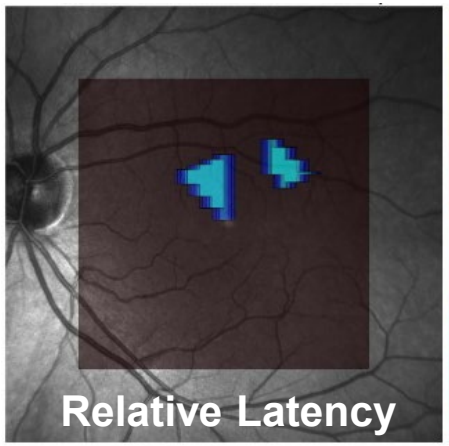

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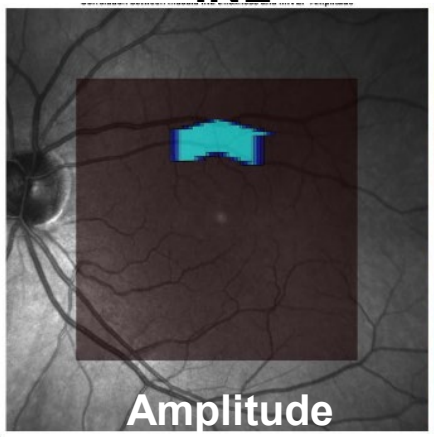
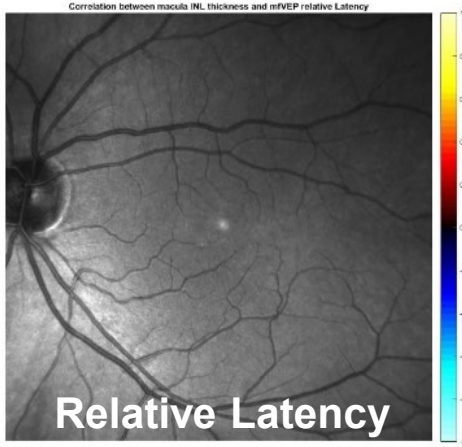
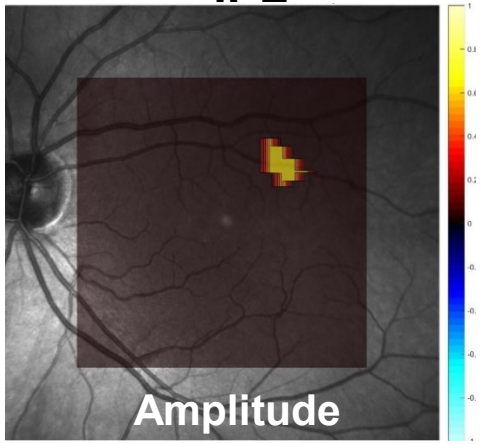
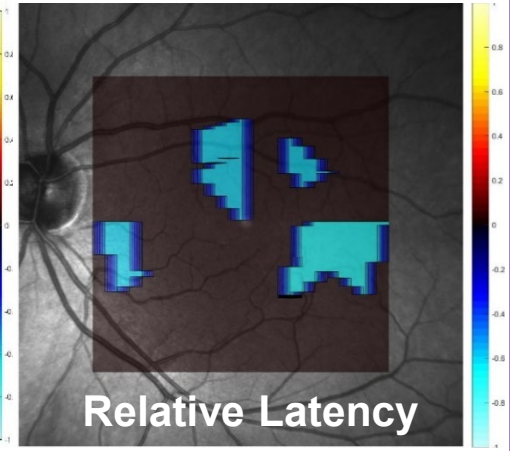




IPL





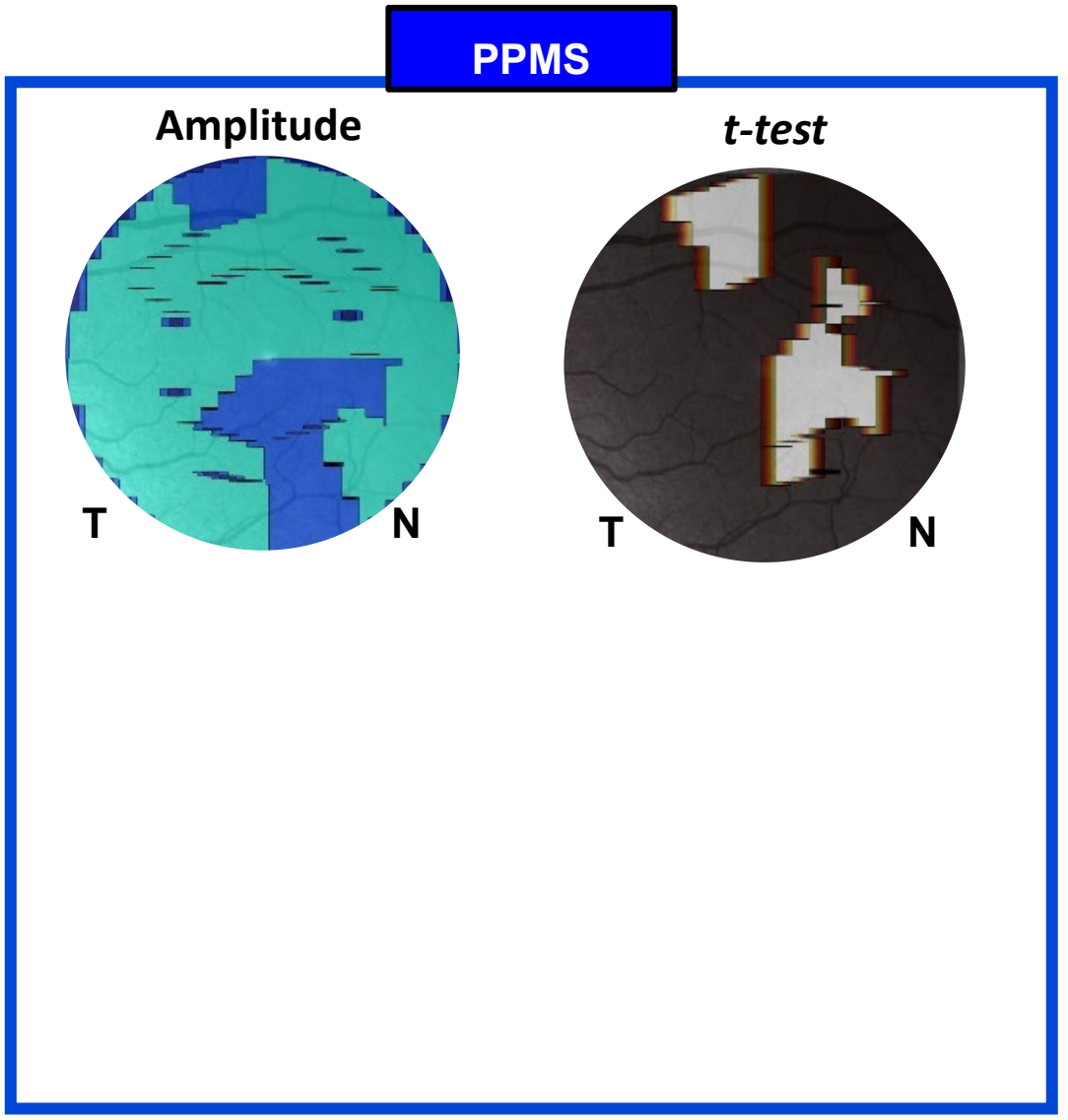
Discussion

- In PPMS, the amplitude was correlated with:
  - Positive correlation with GCIPL
  - Negative correlation with INL

- Smaller amplitude: more axonal loss
- Thinnr GCIPL: more neuronal/dendritic loss
- Thicker INL: higher inflammation

- The results suggest that the integrity of axons within the optic radiation is correlated with the neuronal/dendritic loss and inflammatory in the retina

Trans-synaptic retrograde degeneration?



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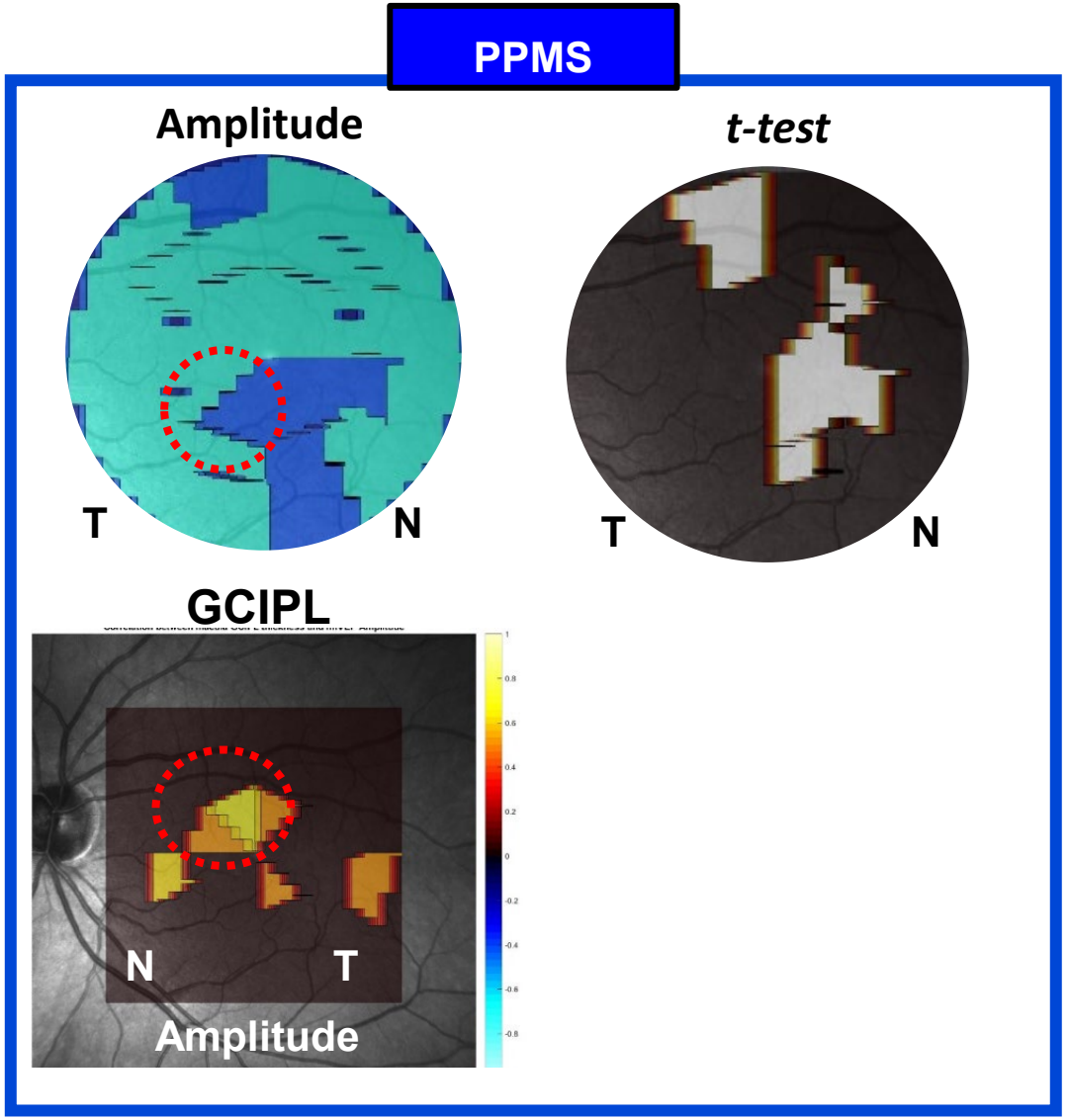

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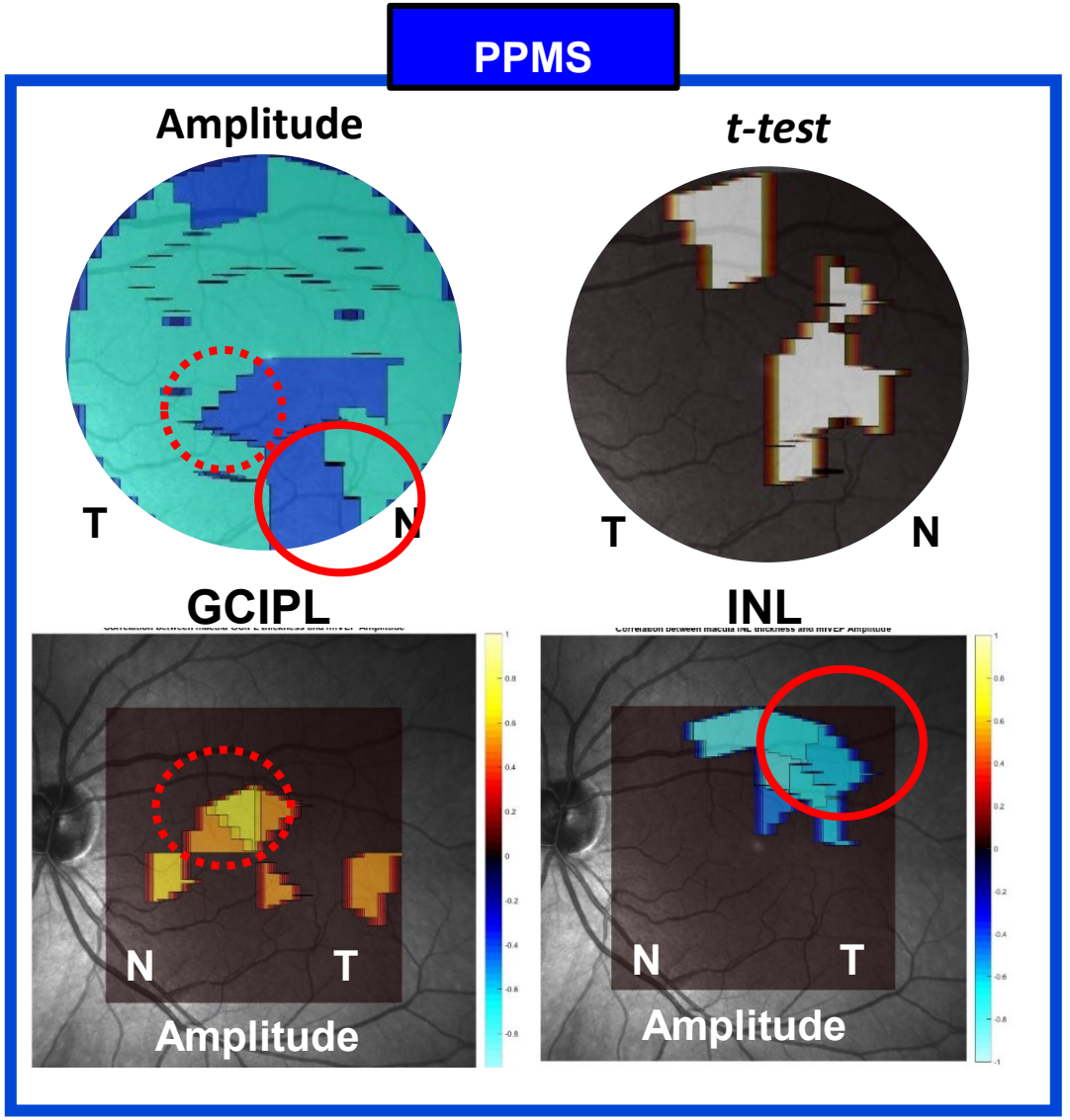
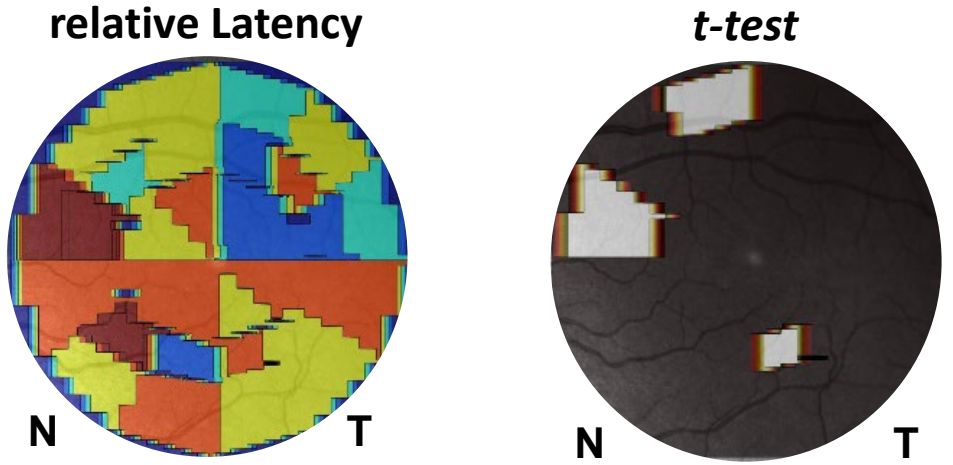


Discussion

- In SPMS, the latency was negatively correlated with GCIPL thickness, especially the IPL thickness, while almost no significant GCIPL atrophy was found.
- Longer latency, which reflects demyelination, has been reported to be an early sign of neurodegeneration. *You et al., 2019*
- IPL thinning suggests dendritic atrophy, which is also an early sign of neuronal death. *Merten et al., 2020*
- This correlation may be an sign of the trans-synaptic degeneration among the visual pathway

SPMS



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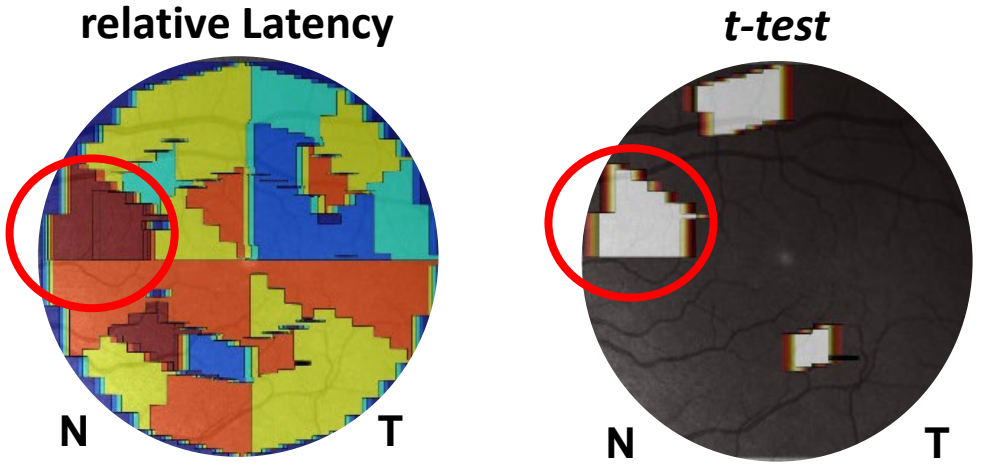

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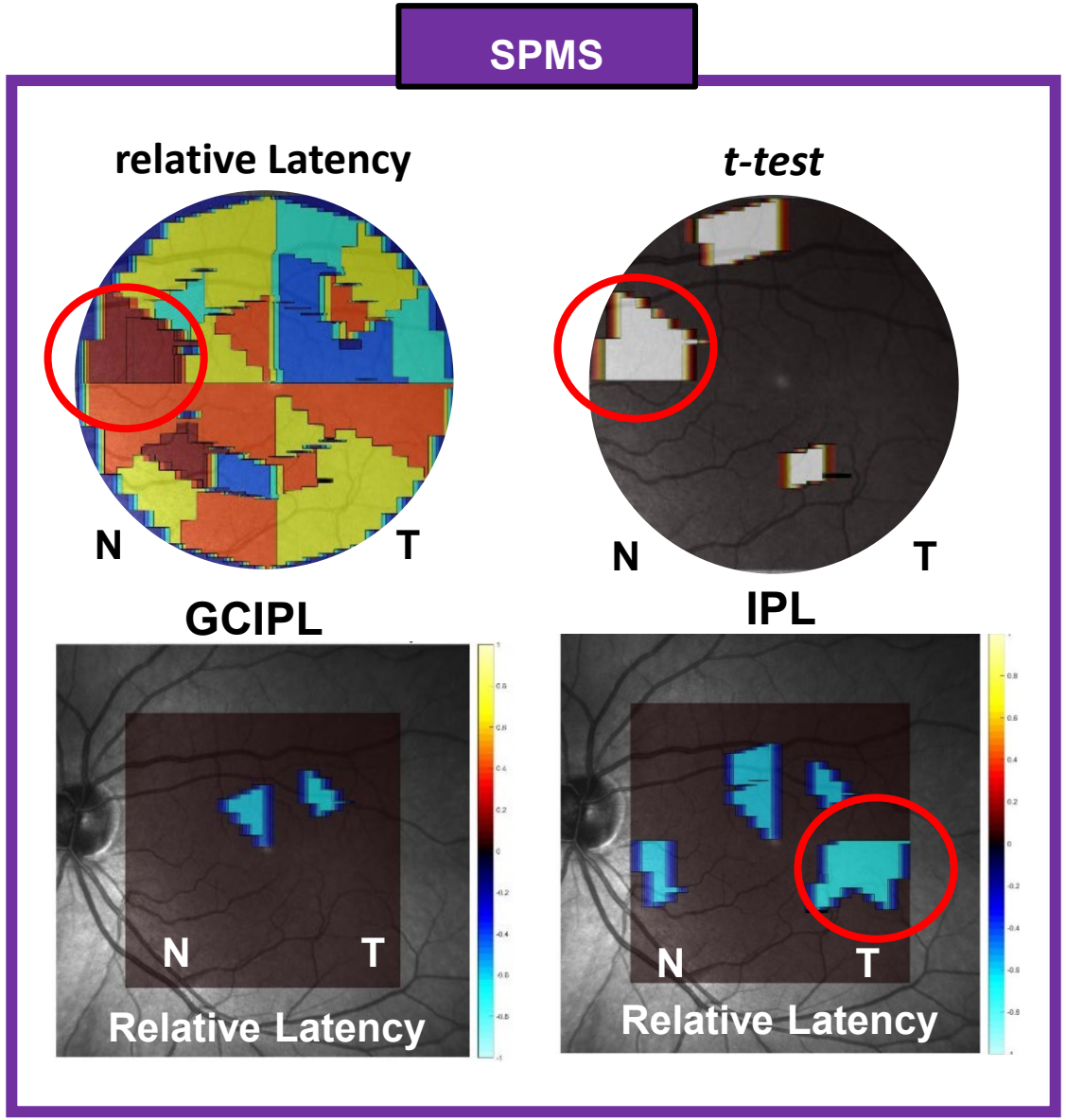

Conclusion

- The sector-to-channel correlation between OCT and mfVEP provides a tool to study the relationship and propagation of inflammation/demyelination and neurodegeneration *in vivo*.
  - In PPMS, correlation was found between mfVEP amplitude and OCT parameters(GCIPL and INL). A hint of ongoing inflammation in optic radiation resulted in retrograde degeneration in the retina?
  - In SPMS, IPL seems to be the early responder to the process of trans-synaptic neurodegeneration
- Future direction
  - Bigger sample size to confirm the current observation
  - Correlate with other modalities and clinical features to better explain the results
    - MRI
    - Cognitive state
    - EDSS
    - Visual function
    - Motor function
    - Biopsy/post-mortem study