Relationship between retinal INL, age and disease activity in progressive MS

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Retinal layer segmentation in multiple sclerosis: a systematic review and meta-analysis

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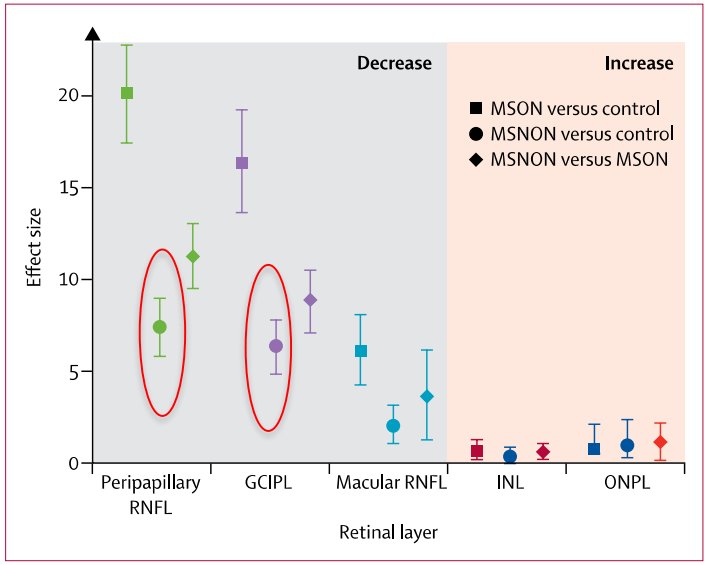
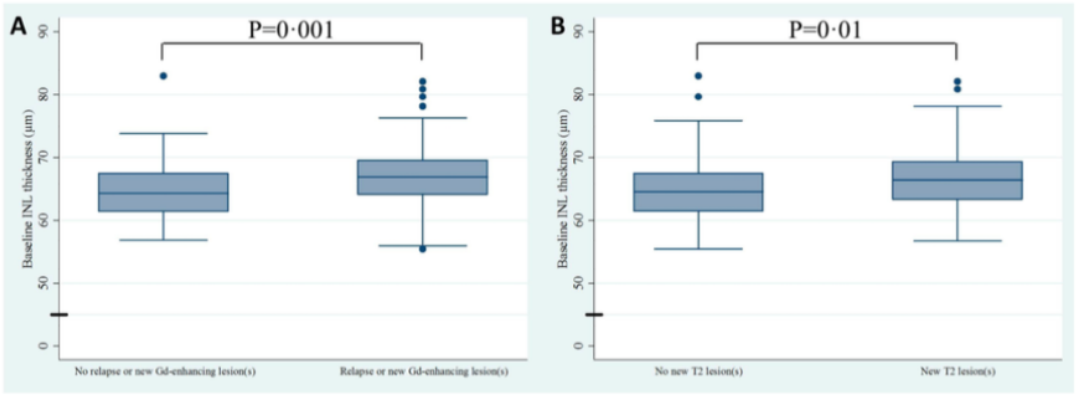


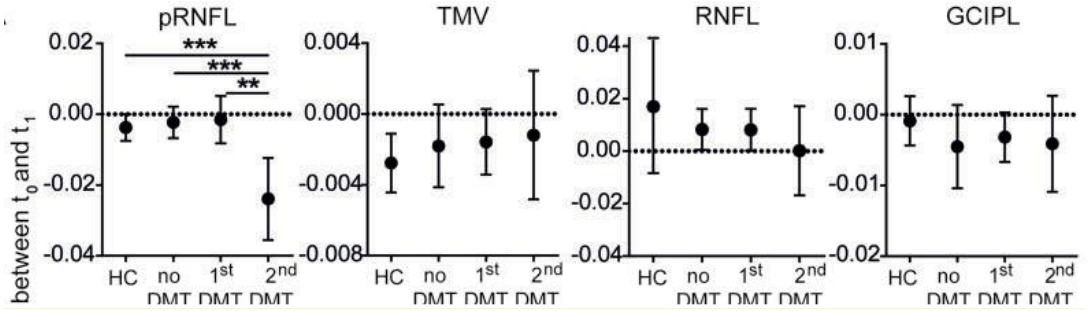
Petzold et al, Lancet Neurol 2017

- The largest and **most robust differences** between the eyes of people with multiple sclerosis and control eyes were found in the **peripapillary RNFL and macular GCIPL**.
- **pRNFL and GCIPL** thickness are considered **biomarkers of neurodegeneration in MS**

INL thickness correlates with ongoing and longitudinal disease activity in relapsing-remitting MS

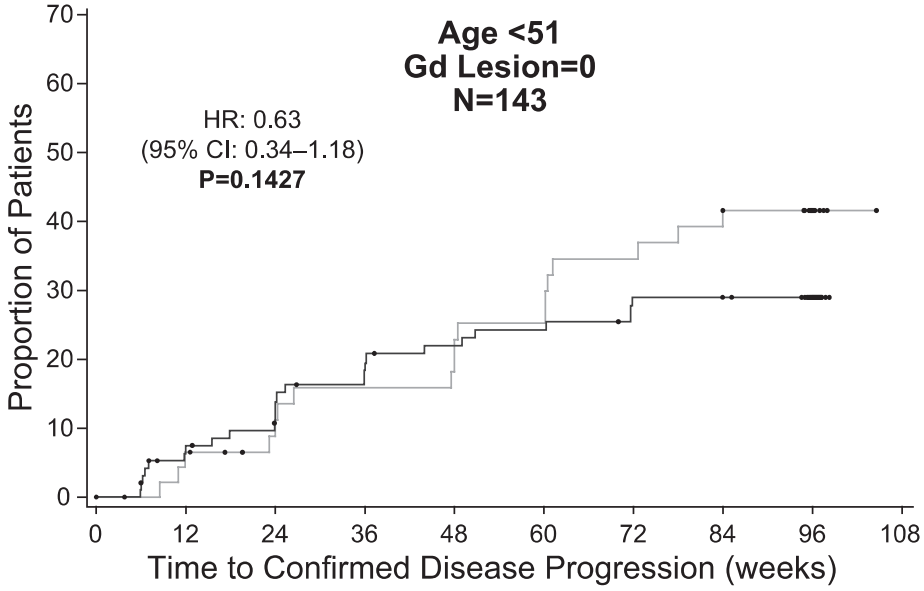


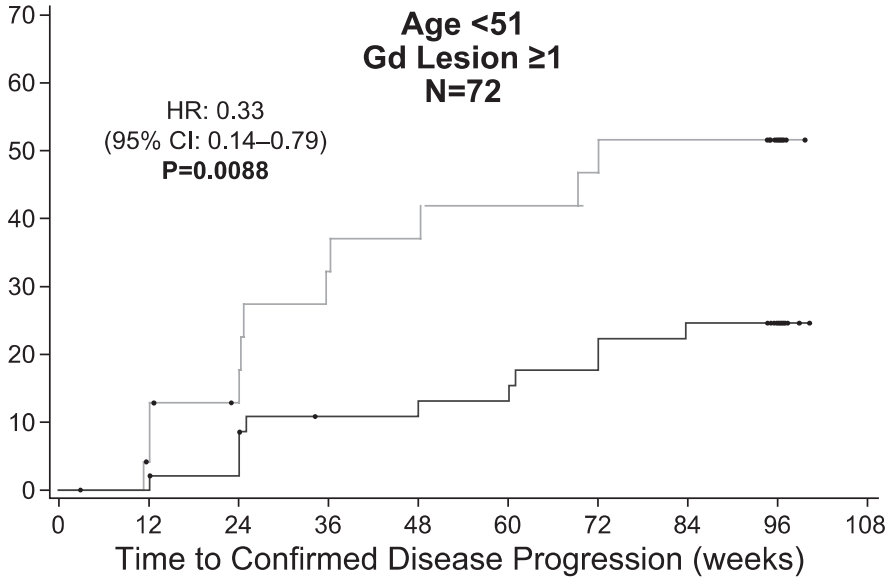
Saidha et at, Lancet Neurol 2012



Knier et al, Brain 2016

Younger age and MRI activity: biomarkers of treatment response in progressive multiple sclerosis





Hawker et al, Ann Neurol 2009

OBJECTIVES

1. **Compare PMS patients and controls in terms of INL thickness**

2. **Evaluate correlations between OCT metrics and T1/T2 lesion volume in PMS**

3. **Assess INL thickness differences in PMS patients stratified according to:**

   - **age** (< or > of 51 years)
   - **evidence of disease activity in the previous 12-months** , defined as presence of at least one of:

     a) occurrence of 1 or more relapses
     b) disease progression defined as 1 EDSS point increase or 0.5 if baseline EDSS$\geq$5.5
     c) MRI activity defined as new T2- and/or gadolinium-enhancing lesions

METHODS: study design

90 PMS patients
36 HC

- 6 examinations excluded due to poor OCT quality
- Eyes with previous ON excluded from the analysis

- **EDSS** score, **SD-OCT** and **MRI**
- Data regarding clinical **relapses/disease progression/MRI activity in the previous 12-months** collected retrospectively

Stratification according to **age cut off of 51 years (n=84 patients)**

Stratification according to **disease activity in the previous 12-months (n=77)**

METHODS: acquisition and post processing

SD-OCT (Spectralis, Heidelberg Engineering, Germany):

- **pRNFL**: was obtained with a 360° RNFL-B circle scan located at 3.4 cm from the center of the optic nerve head. Peripapillary measurements were *averaged from 100 images* and macular estimations *from 15 ART*
- *Macular volumetric scans* consisting of at least *25 single horizontal axial B-scans* were acquired in a rectangular section centered over the macula. Segmented automatically into different layers using the *Heidelberg Eye Explorer mapping software version 6.0.9.0*. Segmented layers were checked and manually corrected, if necessary. **GCIPL and INL** thickness were measured

MRI:

- Aquired at 1.5T (n=27) and 3T MRI (n=57)
- Axial spin echo *2D T2-weighted* (3-mm-thick continuous slices covering the entire brain) and *3D T1-weighted* (1 mm^3 isotropic) images standardized between the two centers
- **T2LV and T1LV** were measured (Jim version 7.0; XInapse Systems Ltd, UK)

RESULTS (I)

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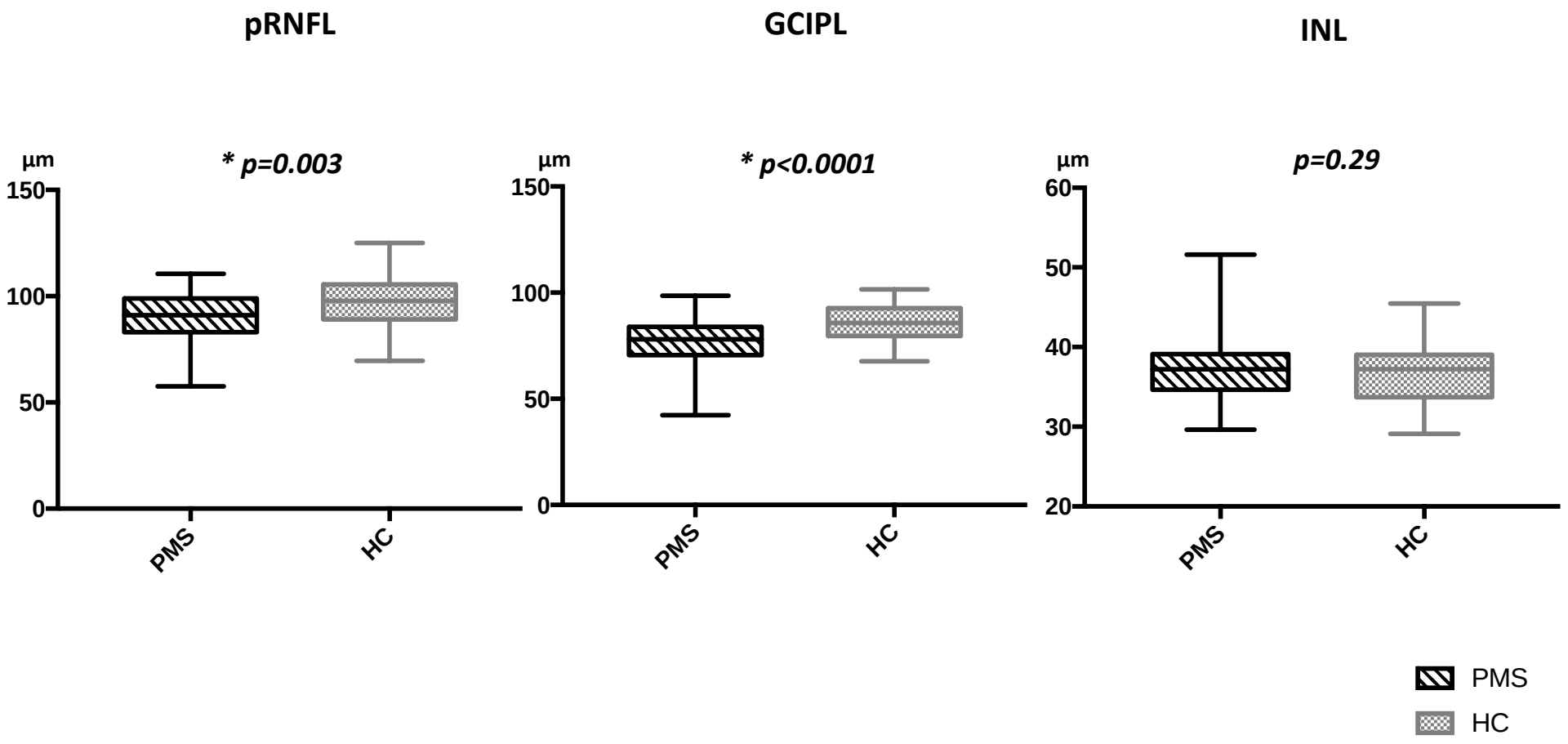
Demographics characteristics

	MS (n=84)	HC (n=36)	p-values
Demographics			
Mean (SD) age, y	50.3 (10.9)	51.1 (14.7)	0.77
Female, no (%)	42 (50%)	18 (50%)	0.57
Mean (SD) disease duration, y	12.3 (8.7)	-	-
PPMS, no (%)	62 (74%)	-	-
Treated patients, no (%)	51 (61%)	-	-
Median (range) baseline EDSS score	5.5 (2-7.5)	-	-

Reduced pRNFL and GCIPL thickness in PMS compared to controls



ANCOVA adjusted for gender, age

RESULTS (II)

1. **Compare PMS patients and controls in terms of INL thickness**

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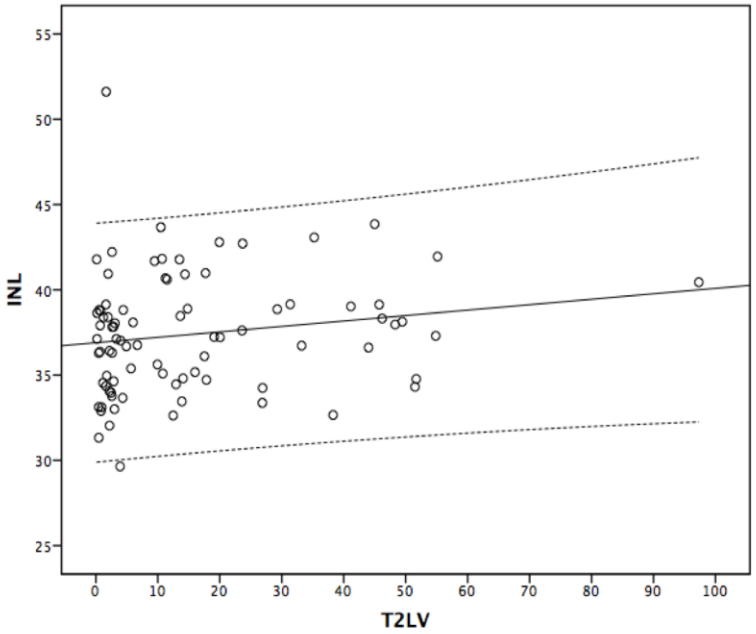
Correlations between OCT and MRI metrics

INL and T2LV

**** r=0.2, p=0.04***

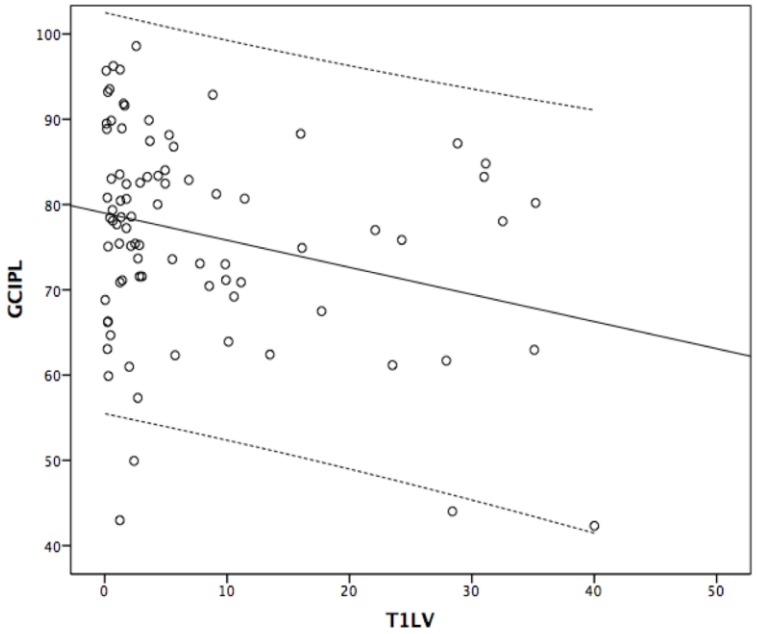
a)



GCIPL and T1LV

**** r= - 0.2; p=0.03***

b)



Spearman correlation modoels adjusted for gender, age, treatment, MRI scanner

RESULTS (III)

1. Compare PMS patients and controls in terms of INL thickness

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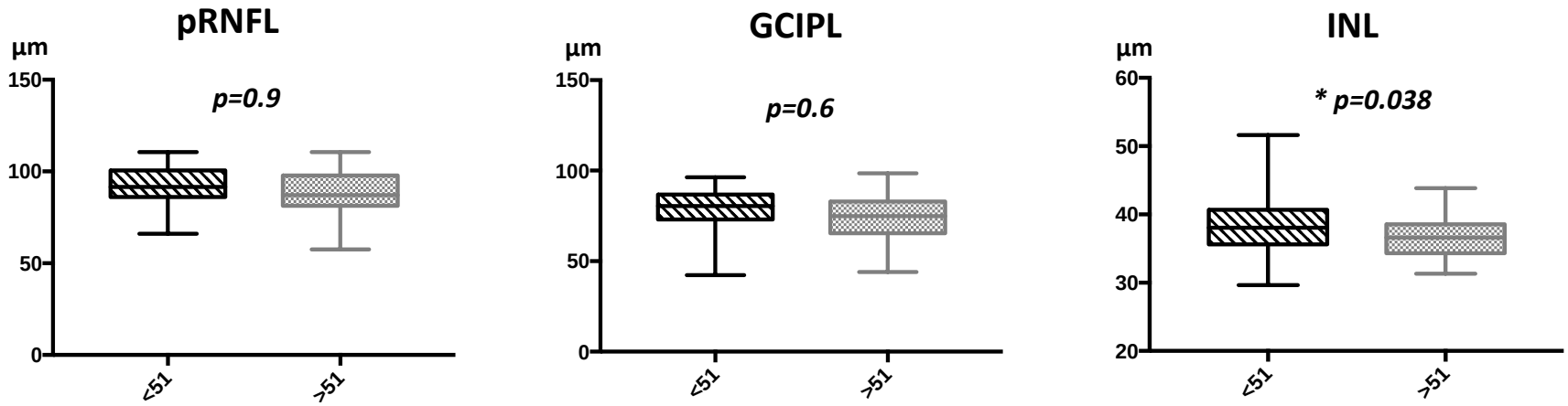
Population characteristics according to age

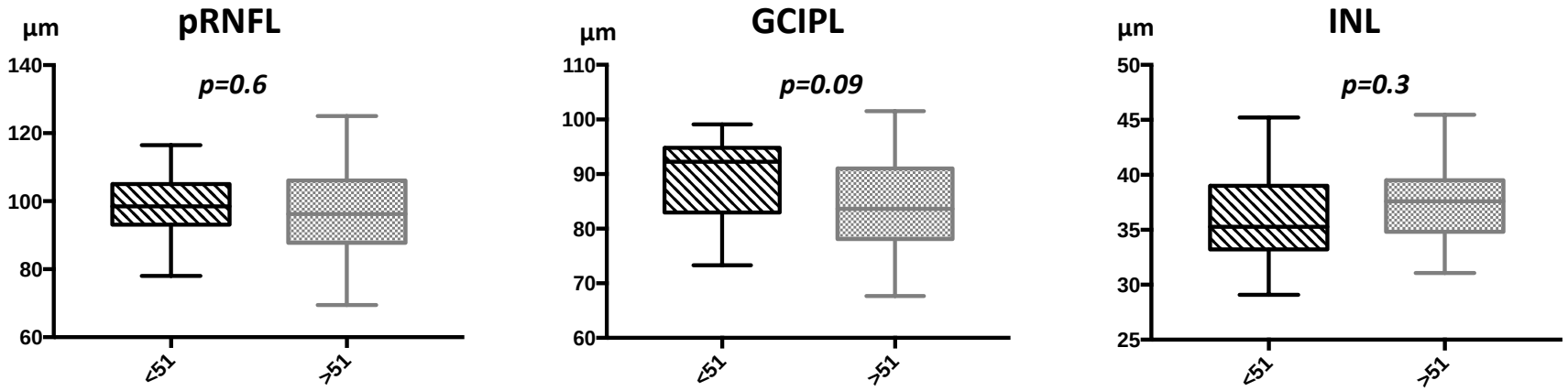
	Patients < 51y (n=43)	Patients > 51y (n=41)	p-values
Mean (SD) age, y	41.8 (7.3)	59.2 (5.8)	<0.0001
Female, no (%)	19 (44%)	23 (56%)	0.2
Mean (SD) disease duration, y	9.9 (6.5)	14.9 (10.04)	**0.049**
PPMS, no (%)	32 (74%)	30 (73%)	0.5
Treated patients, no (%)	36 (83%)	15 (36%)	**<0.0001**
Median (range) baseline EDSS score	6 (2-7)	5.5 (2.5-7.5)	0.7
Mean (SD) T2LV	15.86 (20.3)	15.17 (16.6)	0.2
Mean (SD) T1LV	6.76 (9.4)	8.44 (11.0)	0.4
	Controls < 51y (n=14)	Controls > 51y (n=22)	p-values
Mean (SD) age, y	35.3 (8.1)	61.2 (7.0)	<0.0001
Female, no (%)	6 (43%)	12 (54%)	0.5

INL thickness increased in patients aged<51 years

a) patients



b) controls

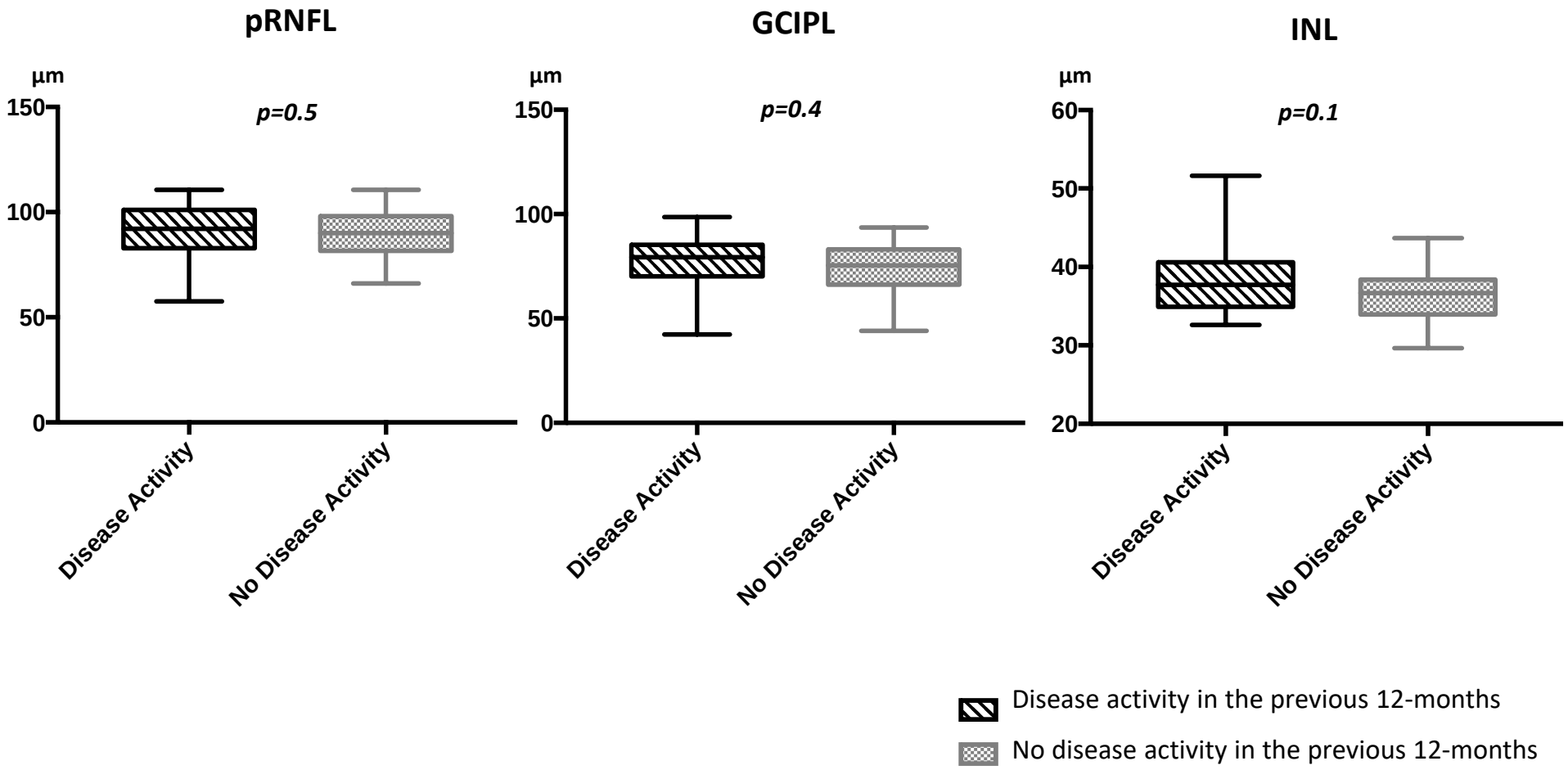


ANCOVA adjusted for gender, disease duration, treatment use and MRI scanner

Population characteristics according to disease activity

	Disease activity (n=42)	No disease activity (n=35)	p-values°
Mean (SD) age, y	46.3 (10.3)	54.3 (9.6)	**0.001**
Female, no (%)	21 (50%)	19 (54%);	0.7
Mean (SD) disease duration, y	12.2 (9.6)	13.02 (8.2)	0.3
PPMS, no (%)	27 (64%)	29 (83%)	0.1
Treated patients, no (%)	31 (74%)	19 (54%)	**0.007**
Median (range) baseline EDSS score	5.5 (2.5-7)	5.5 (2.5-7.5)	0.1
Mean (SD) T2LV	19.2 (20.1)	12.2 (16.2)	0.3
Mean (SD) T1LV	8.18 (9.8)	7.2 (10.5)	0.9

No differences in terms of INL according to disease activity

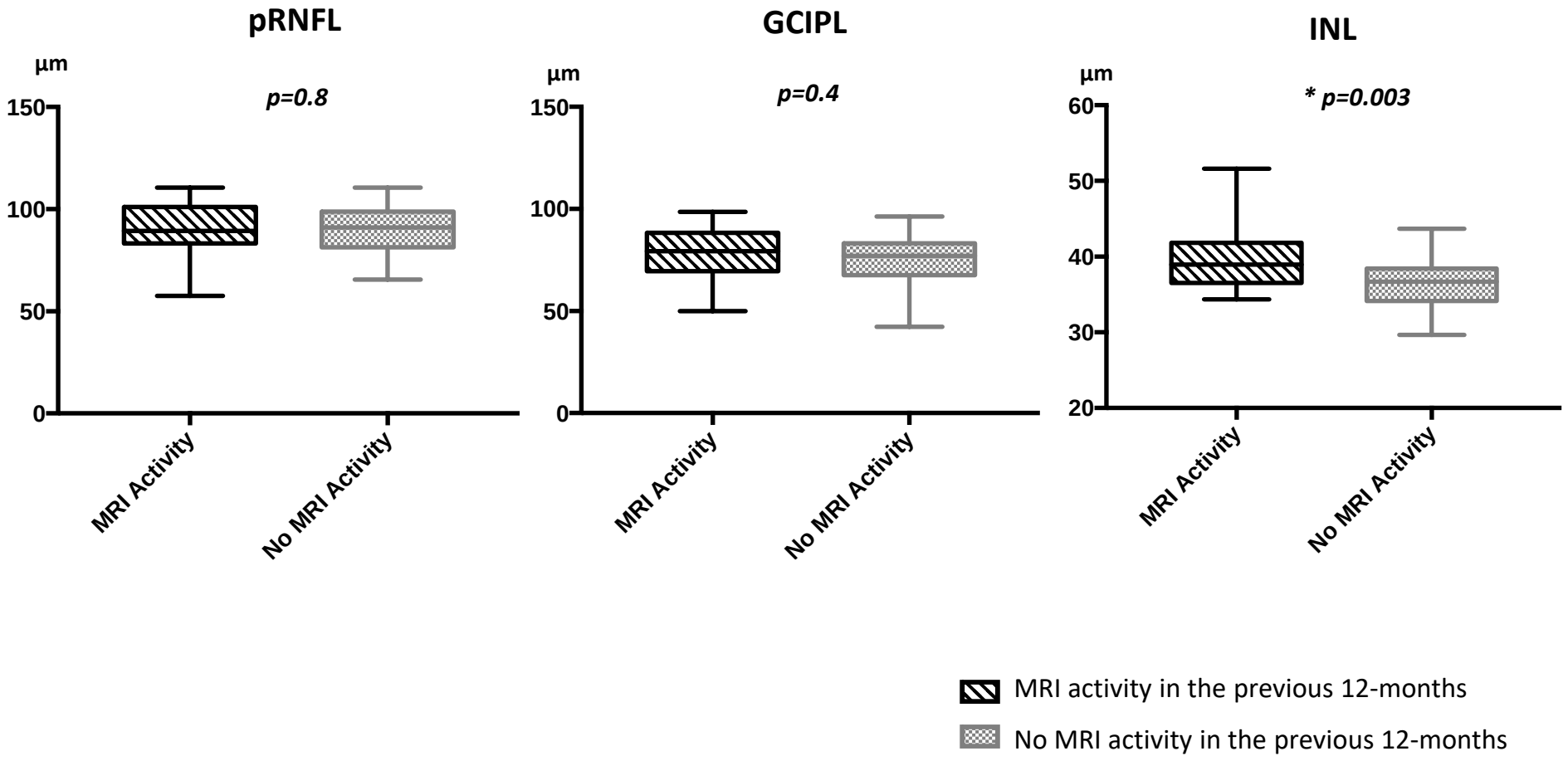


ANCOVA adjusted for gender, age, disease duration, treatment use and MRI scanner

Population characteristics according to clinical/MRI activity

	Clinical activity (n=33)	No clinica activity (n=44)	p-values§
Mean (SD) age, y	45.2 (10.3)	53.1 (9.8)	**0.001**
Female, no (%)	16 (48%)	24 (54%);	0.6
Mean (SD) disease duration, y	11.6 (10.1)	13.1 (8.1)	0.4
PPMS, no (%)	21 (63.6%)	35 (79.5%)	0.1
Treated patients, no (%)	25 (76%)	25 (57%)	**0.001**
Mean (SD) T2LV	20.3 (21.1)	12.7 (15.9)	0.1
Mean (SD) T1LV	9.2 (10.5)	6.5 (10.7)	0.2
	MRI activity (n=20)	No MRI activity (n=57)	p-values*
Mean (SD) age, y	43.9 (10.5)	52.1 (10.04)	**0.003**
Female, no (%)	9 (45%)	31 (54%);	0.4
Mean (SD) disease duration, y	10.8 (7.1)	13.2 (9.5)	0.3
PPMS, no (%)	14 (70%)	42 (73.7%)	0.7
Treated patients, no (%)	17 (85%)	33 (58%)	**0.03**
Mean (SD) T2LV	14.9 (15.1)	16.4 (19.8)	0.6
Mean (SD) T1LV	4.99 (5.1)	8.72 (11.2)	0.2

INL thickness increased in patients with evidence of MRI activity in the previous 12-months



ANCOVA adjusted for gender, age, disease duration, treatment use and MRI scanner

CONCLUSIONS

- We observed **reduced pRNFL and GCIPL thickness in PMS compared to controls**; no differences in terms of INL between PMS patients and controls

- A significant **correlation** emerged **between INL thickness and T2LV and between CGIPL thickness and T1LV in progressive patients**

- In our study **INL thickness resulted significantly higher in younger (<51 years) PMS patients and in those with recent T2- and/or gadolinium-enhancing lesions in the previous 12-months**

If our finding is confirmed in longitudinal studies, **INL** may be considered as a useful **biomarker of neuroinflammation and a potential predictor of response to treatment in PMS**