



# Transorbital sonography for evaluation of optic nerve and its vascularization in multiple sclerosis: a correlation study with clinical variables and visual evoked potentials.



Sartori A<sup>a</sup>, Rossi L<sup>a</sup>, Marangoni D<sup>b</sup>, Inferrera L<sup>b</sup>, Carraro N<sup>a</sup>, Favero A<sup>a</sup>, Cerutti R<sup>a</sup>, Leonelli R<sup>b</sup>, Drigo A<sup>b</sup>, Bratina A<sup>a</sup>, Bosco A<sup>a</sup>, Tognetto D<sup>b</sup>, Manganotti P<sup>a</sup>

<sup>a</sup>Neurology Unit, Department of Medical, Surgical and Health Sciences, University of Trieste, Trieste, Italy

<sup>b</sup>Ophthalmology Unit, Department of Medical, Surgical and Health Sciences, University of Trieste, Trieste, Italy

## INTRODUCTION

Multiple sclerosis (MS) frequently involves the optic nerve, both in terms of acute inflammation, e.g. optic neuritis (ON) and degenerative processes. Traditionally, visual evoked potentials (VEPs) allow a detailed functional assessment of optic pathways involvement in MS. Morphological involvement can be detected with magnetic resonance imaging (MRI), Transorbital sonography (TOS) has emerged as a non-invasive, cost-effective imaging technique to evaluate the optic nerve and its vascularization in MS patients, with low cost and bedside assessment capabilities. According to previous studies, MS patients exhibit reduced optic nerve diameter (OND) and altered optic nerve sheath diameter (ONSD) compared to healthy controls, correlating with disease duration and disability scores. Furthermore, TOS has shown potential in detecting subclinical optic nerve changes in MS patients without a history of ON. The integration of TOS with Doppler ultrasound allows for a comprehensive evaluation of both morphological and hemodynamic alterations in the optic nerve.

## OBJECTIVES/AIMS

The aim of the study was to investigate the correlations between transorbital sonography (TOS) and visual evoked potentials (VEPs) to analyze optic pathways and their correlations with clinical variables, in PwMS (People with Multiple Sclerosis).

## PATIENTS AND METHODS

PwMS from our MS centre were enrolled. Inclusion criteria were: both relapsing or progressive forms, age  $\geq 18$  years; exclusion criteria were: CNS comorbidities, relapse within the prior 3 months, ophthalmic comorbidities (amblyopia, glaucoma, known macular degeneration, diabetic retinopathy history of retinal detachment, macular pucker or macular hole, previous retinal surgery, cataract).

The following clinical data were collected: sex, age, disease duration, EDSS, annualized delta EDSS, annual relapse rate (ARR). PwMS underwent ophthalmic evaluation (including visual acuity, Goldmann tonometry, slit lamp examination, fundoscopy, Ishihara test). Patients also underwent VEPs evaluation.

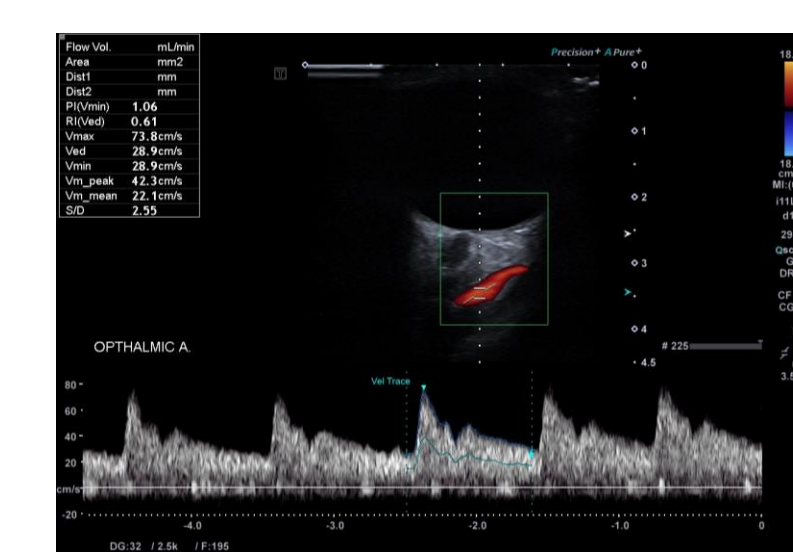
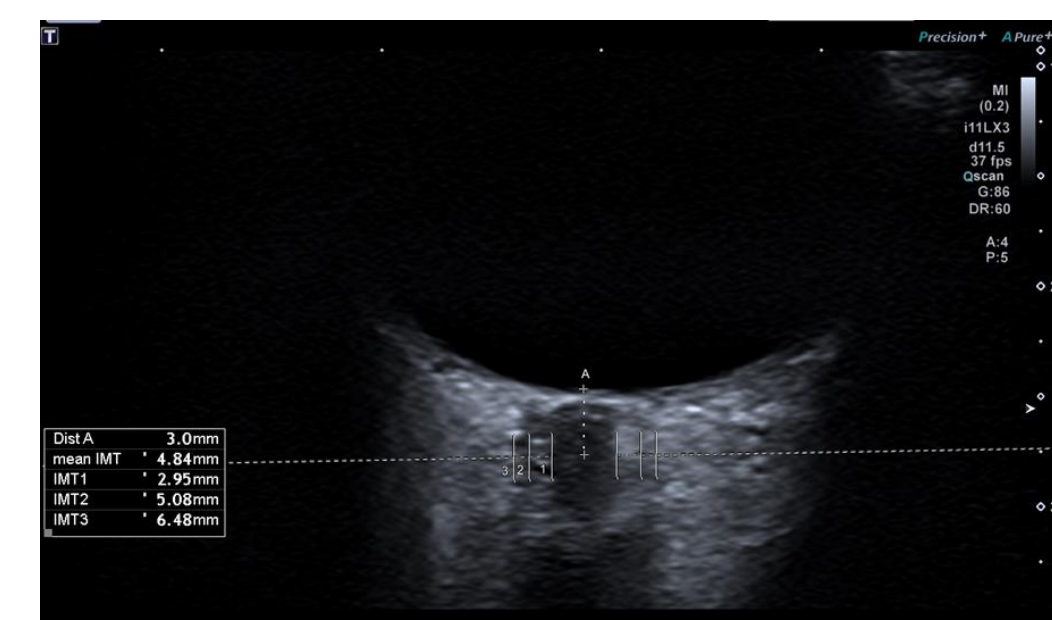
Ocular ultrasound was performed following the ONSD POCUS Quality Criteria Checklist. Patients were insonated in a supine position with a neutral gaze, and images were obtained through the closed upper eyelid, a linear probe with a frequency of 7.5 MHz was used. Axial images were captured, with the retina serving as the reference structure for depth, measurement depth was set at 3 mm. The following structures were measured: optic nerve diameter (OND), internal optic nerve sheath diameter (ONSDi) and external optic nerve sheath diameter (ONSDe).

We assessed the ophthalmic artery (Oph A) and central retinal artery (Centr Ret A) flow velocities expressed as cm/s (peak systolic velocity [PSV], end diastolic velocity [EDV], mean velocity [mV]), and the central retinal Vein (Centr Ret V) flow velocities (highest velocity [HV], lowest velocity [LV], mV) and calculated, for each blood vessel, the pulsatility index (PI) and the Resistive Index (RI).

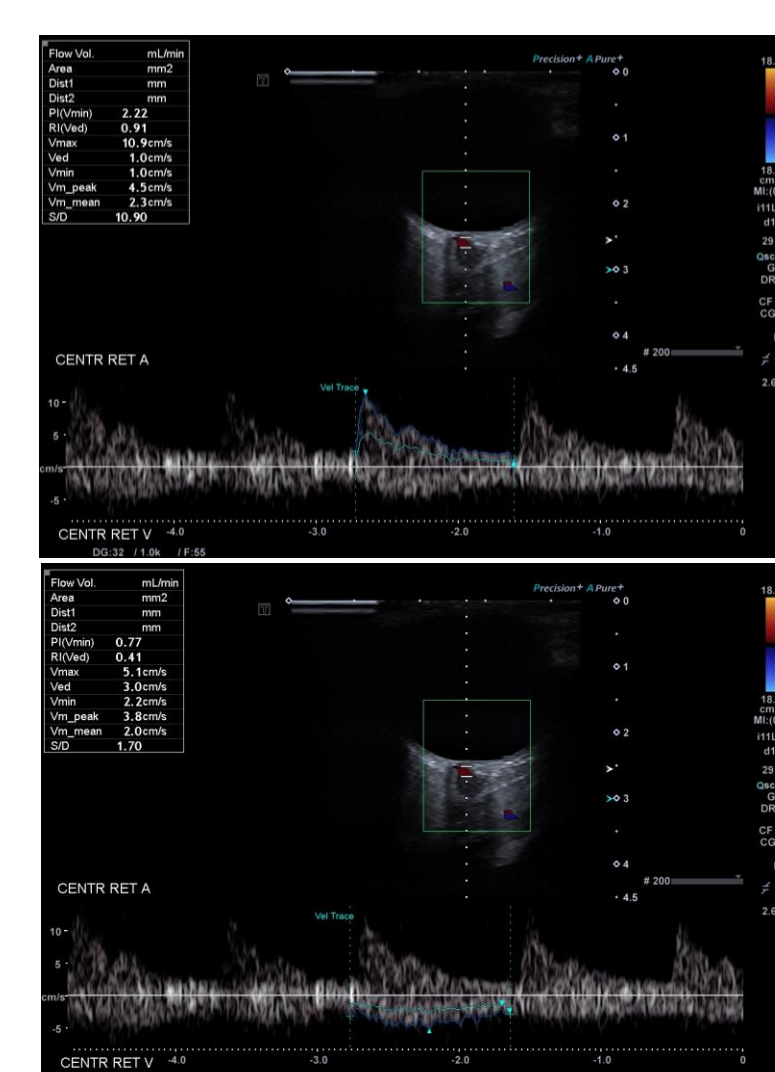
Normality of variables was assessed using the Shapiro-Wilk test, and parametric correlations were calculated using Pearson's correlation coefficient ( $r$ ), while non-parametric correlations were assessed with Spearman's Rho ( $\rho$ ).

Statistical analysis was performed with SPSS, Version 24.0. Statistical significance was set at  $p < 0.05$ .

Sagittal B-mode ultrasound scan of left eye: measure of the optic nerve diameter, with and without the meningeal sheath, at 3 mm from the retinal plane (A: distance from retina; 1-3: diameters OND, ONSDint e ONSDe ext



Color Doppler and velocity waveform of right ophthalmic artery. Measurement of the PSV (indicated as Vmax), EDV (indicated as Ved), mV (indicated as Vm\_p: mean of peak velocities) and Vm\_m (mean of mean velocities), PI and RI.



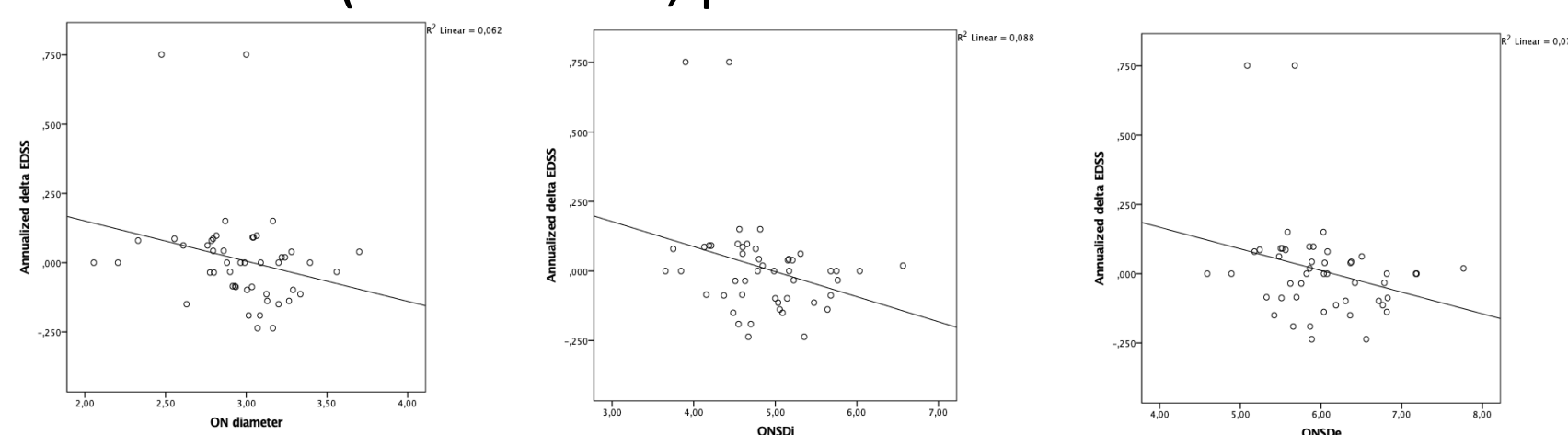
## RESULTS

Patients' characteristics are shown in Table 1.

Patients' clinical characteristics	PwMS (n=24)
<b>Sex:</b>	
Males	11 (45.8%)
Females	13 (54.2%)
<b>Treatment:</b>	
First line	10 (41.7%)
Second line	12 (50%)
No treatment	2 (8.3%)
Age at diagnosis (y)	35.71 $\pm$ 10.68
Age at evaluation (y)	46.25 $\pm$ 9.78
Disease duration from diagnosis (y)	10.94 $\pm$ 5.99
EDSS at diagnosis	1.5 (0-3)
EDSS at evaluation	1.5 (0-6)
EDSS variation	0 (-1.5-5)
ARR	0.338 (0.1-1)
History of optic neuritis	8 (33.3%)

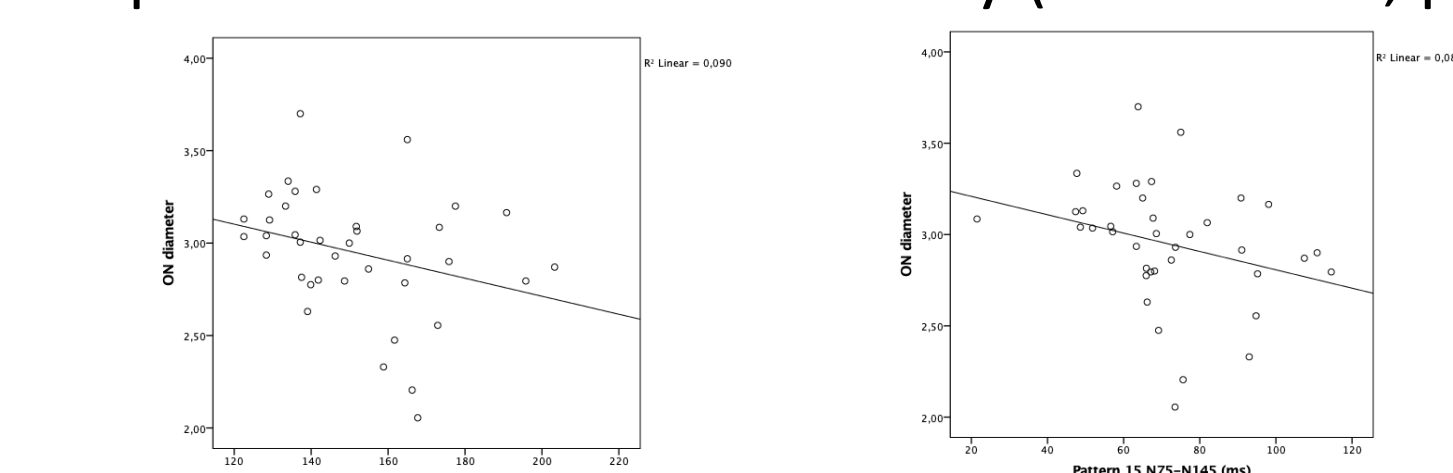
Negative correlations between annualized delta EDSS and:

- OND ( $\rho = -0.325$ ,  $p = 0.024$ )
- ONSDi ( $\rho = -0.298$ ,  $p = 0.04$ )
- ONSDe ( $\rho = -0.293$ ,  $p = 0.044$ )



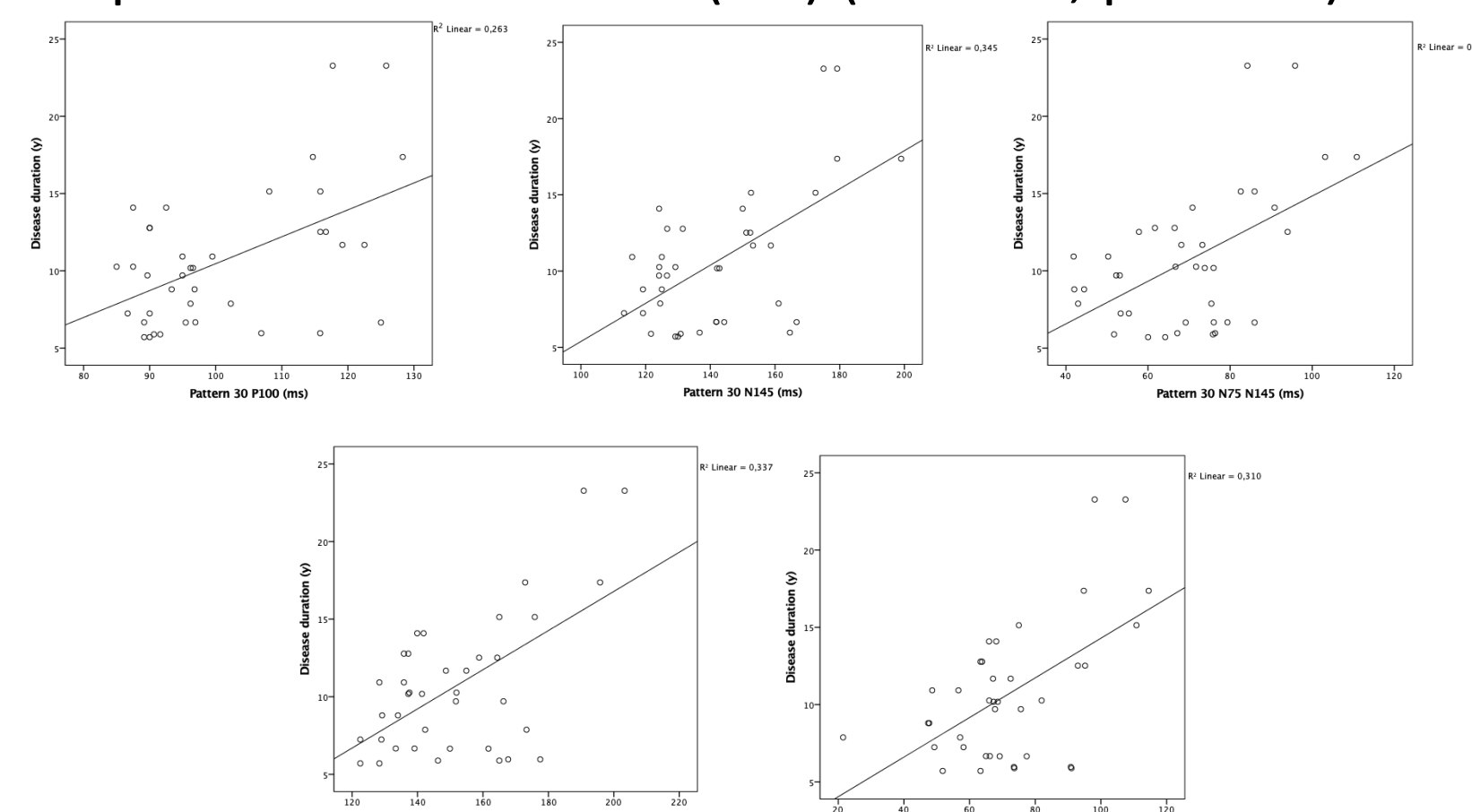
OND correlated negatively with

- pattern-15 N145 latency ( $\rho = -0.376$ ,  $p = 0.020$ )
- pattern-15 N75 N145 latency ( $\rho = -0.434$ ,  $p = 0.006$ )



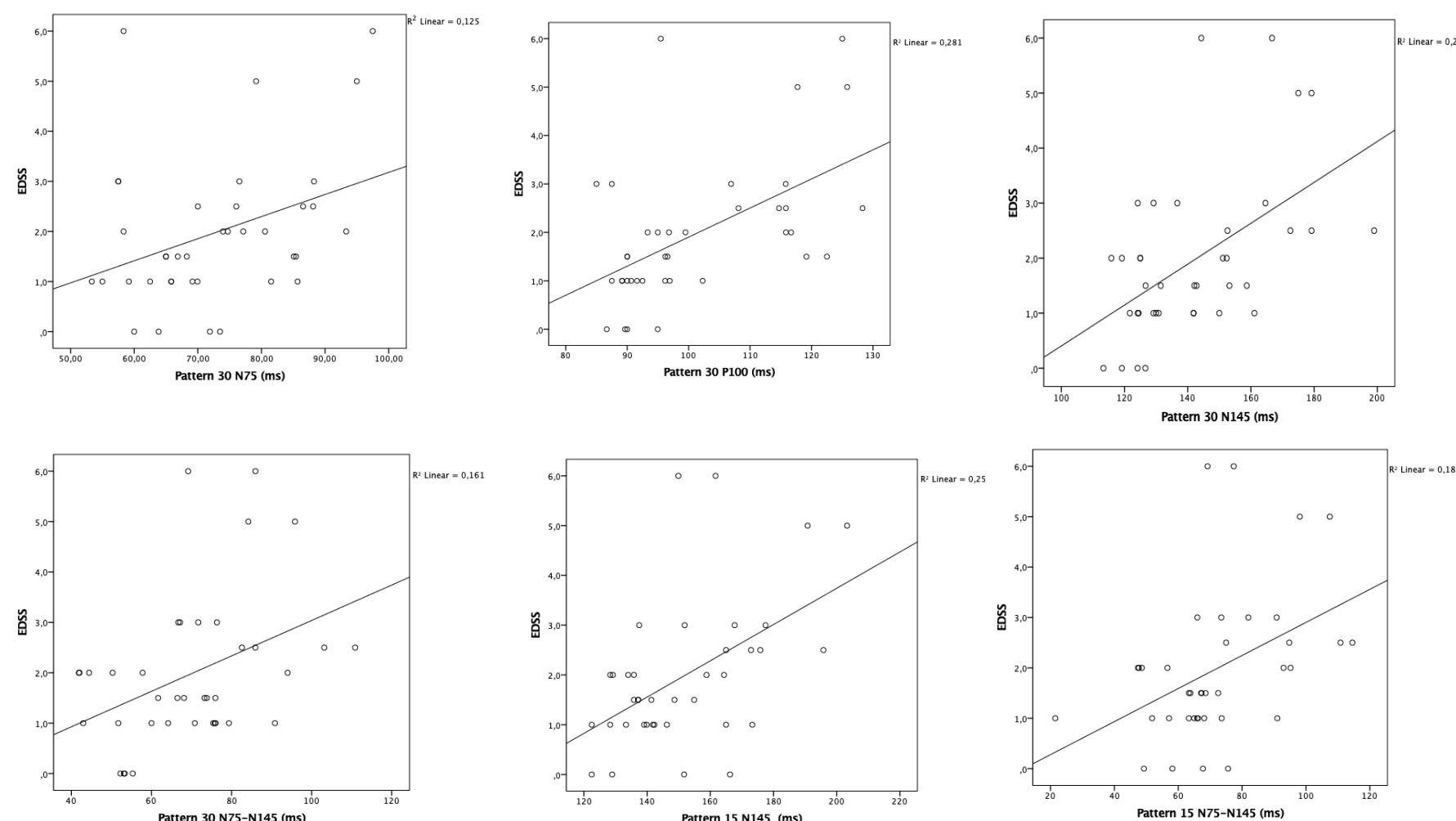
Positive correlation between disease duration and:

- pattern 30 P100 (ms) ( $\rho = 0.369$ ,  $p = 0.023$ )
- pattern 30 N145 (ms) ( $\rho = 0.405$ ,  $p = 0.012$ )
- pattern 30 N75-N145 (ms) ( $r = 0.526$ ,  $p = 0.001$ )
- pattern 15 N145 (ms) ( $\rho = 0.360$ ,  $p = 0.026$ )
- pattern 15 N75-N145 (ms) ( $r = 0.557$ ,  $p < 0.001$ )



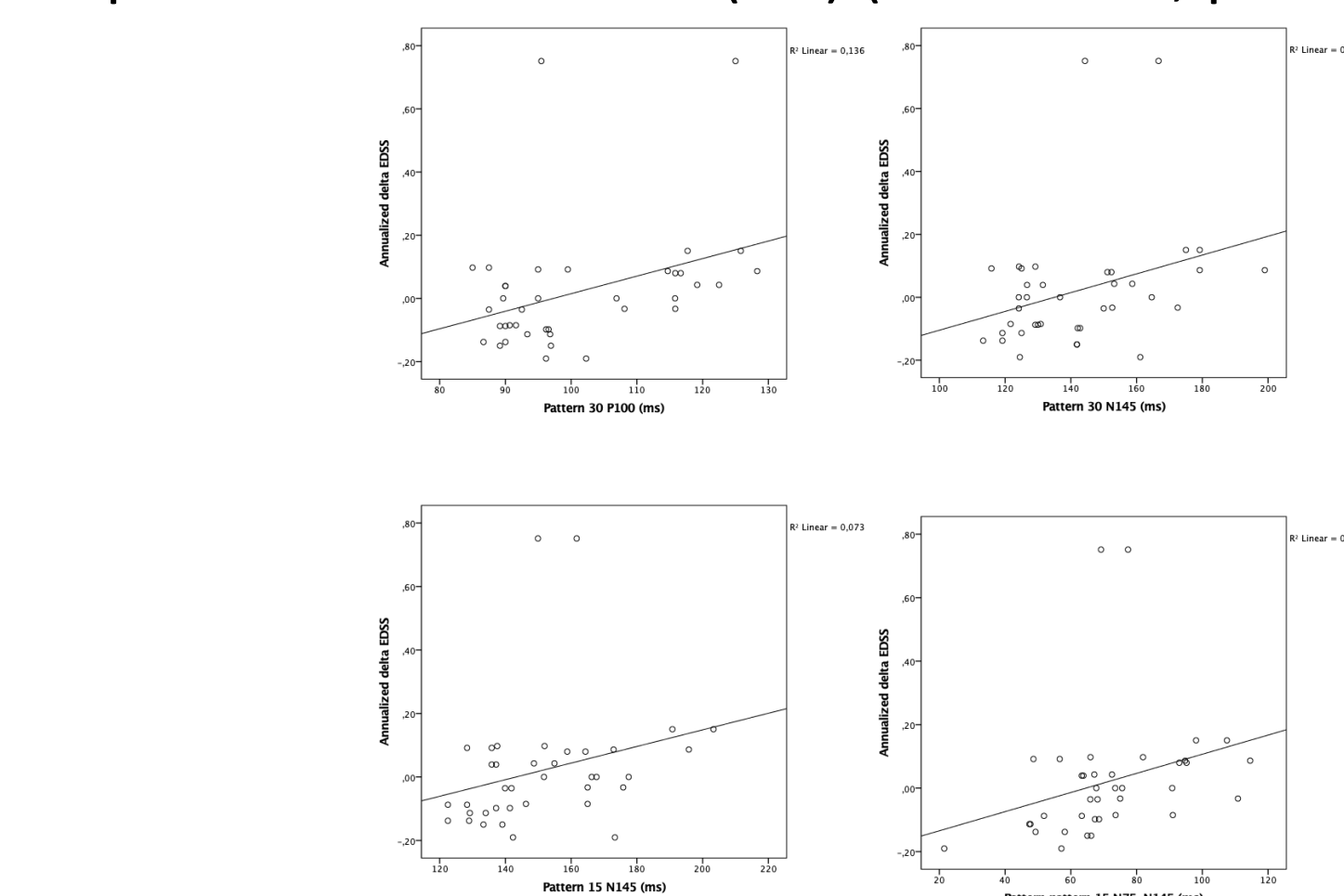
Positive correlation between EDSS and:

- pattern 30 N75 (ms) ( $\rho = 0.350$ ,  $p = 0.031$ )
- pattern 30 P100 (ms) ( $\rho = 0.530$ ,  $p = 0.001$ )
- pattern 30 N145 (ms) ( $\rho = 0.528$ ,  $p = 0.001$ )
- pattern 30 N75-N145 (ms) ( $\rho = 0.397$ ,  $p = 0.014$ )
- pattern 15 N145 (ms) ( $\rho = 0.469$ ,  $p = 0.003$ )
- pattern 15 N75-N145 (ms) ( $\rho = 0.482$ ,  $p = 0.002$ )



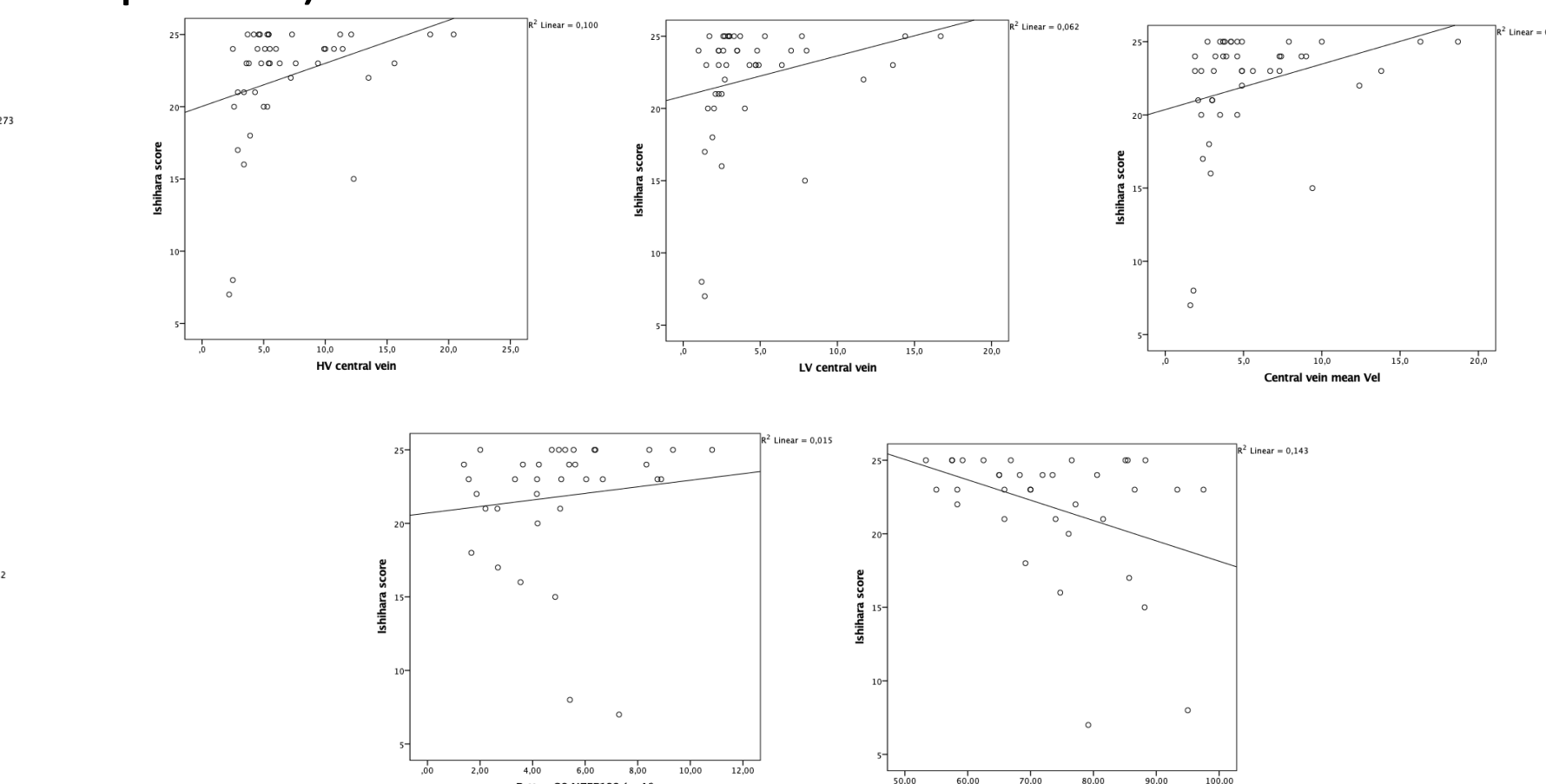
Positive correlation between annualized delta EDSS and:

- pattern 30 P100 (ms) ( $\rho = 0.362$ ,  $p = 0.025$ )
- pattern 30 N145 (ms) ( $\rho = 0.368$ ,  $p = 0.023$ )
- pattern 15 N145 (ms) ( $\rho = 0.416$ ,  $p = 0.009$ )
- pattern 15 N75-N145 (ms) ( $\rho = 0.536$ ,  $p = 0.001$ )



Ishihara score correlated:

- positively with Centr Ret V HV ( $\rho = 0.394$ ,  $p = 0.008$ )
- positively with Centr Ret V LV ( $\rho = 0.363$ ,  $p = 0.016$ )
- positively with Centr Ret V mV ( $\rho = 0.386$ ,  $p = 0.01$ )
- positively with pattern 30 N75 P100 (mcV) ( $\rho = 0.342$ ,  $p = 0.041$ )
- negatively with pattern 30 N75 (ms) ( $\rho = -0.344$ ,  $p = 0.04$ )



Ophthalmic artery (Oph A) and Centr Ret A velocities correlated negatively with VEPs latencies (data not shown).

## DISCUSSION AND CONCLUSIONS

Our data confirm a correlation between disability measures and OND (confirming previous observations of ONSD negatively correlating with the EDSS<sup>1-3</sup> and a correlation between disease duration and EDSS and VEPs increased latencies

Moreover, we report increased VEP latencies in smaller ON and a reduced velocity in Oph A and Centr Ret A and a better performance in color vision test to higher venous velocities in Centr Ret V. TOS can represent a viable method to investigate MS-related degenerative processes of the optic nerve, correlating with clinical and VEPs variables.

## DISCLOSURES

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported. A. Sartori received funding for travel and/or speaker honoraria from Biogen, Novartis, Roche; she is Principal Investigator in clinical trials of Novartis and Roche. L. Rossi: received funding for travel/accommodation/course participation from Novartis, Roche, Sandoz, Merz and AbbVie. Dario Marangoni: nothing to disclose. Leandro Inferrera: nothing to disclose. Nicola Carraro: nothing to disclose. Anna Favero: received funding for travel from Fidia. Raffaele Cerutti: nothing to disclose. Riccardo Leonelli: nothing to disclose. Alessandro Drigo: nothing to disclose. Alessio Bratina: received speaker honoraria from Argenx. Antonio Bosco: received funding for travel from Biogen, Roche, Sanofi e MBS. Daniele Tognetto: nothing to disclose. Paolo Manganotti: nothing to disclose.

## REFERENCES

- Candelieri Merlicco A, Gabaldón Torres L, Villaverde González R, Fernández Romero I, Aparicio Castro E, Lastes Arias MC. Transorbital ultrasonography for measuring optic nerve atrophy in multiple sclerosis. *Acta Neurol Scand.* 2018;138(5):388-393. doi:10.1111/ane.12976
- De Masi R, Orlando S, Conte A, et al. Transbulbar B-Mode Sonography in Multiple Sclerosis: Clinical and Biological Relevance. *Ultrasound Med Biol.* 2016;42(12):3037-3042. doi:10.1016/j.ultrasmedbio.2016.07.018
- Koraysha NA, Kishk N, Hassan A, et al. Evaluating optic nerve diameter as a possible biomarker for disability in patients with multiple sclerosis. *Neuropsychiatr Dis Treat.* 2019;15:2571-2578. Published 2019 Sep 6. doi:10.2147



55° CONGRESSO  
SOCIETÀ ITALIANA  
DI NEUROLOGIA