First name: Chiara

Last name: Zanetta

City: Milano

Country: Italy

Date of birth: 11/08/1988

Institution/organization: Neurological Department, INSPE-Institute of Experimental Neurology, University Hospital San Raffaele, Milan

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Abstract Title: A longitudinal evaluation of RNFL thickness in Clinically Isolated Syndrome

Abstract short title (max 45 characters): RNFL thickness changes and Multiple Sclerosis risk

Authors: Chiara Zanetta (presenting author), Simone Guerrieri, Marco Pisa, Gloria Dalla Costa, Gabriela Girafa, Letizia Leocani, Vittorio Martinelli, Giancarlo Comi

Neurological Department, INSPE-Institute of Experimental Neurology, University Hospital San Raffaele, Milan

Background: Optical coherence tomography (OCT) allows evaluation of afferent visual pathway involvement in both visual and nonvisual Clinically Isolated Syndrome (CIS). Our aim was to explore longitudinal retinal nerve fiber layer-RNFL thickness changes in patients with CIS and evaluate its prognostic value for conversion to clinically definite multiple sclerosis (CDMS).

Methods: Forty-nine consecutive CIS patients (27 females, mean age 33.8 ± 10, 17 acute optic neuritis-AON) underwent OCT at baseline and after a mean follow up of 30.8 (12.27-62.70) months. Disability, presence of oligoclonal bands (BOIgG) and number of T2 hyperintense and gadolinium-enhancing lesion (GD+) at baseline were collected. Multilevel mixed effects models were used to explore longitudinal changes in RNFL, Ganglion Cell Layer-GCL, Inner Plexiform Layer-IPL, Inner Nuclear Layer-INL and ganglion cell-inner plexiform layer-GCIPL of each eye. Data were analyzed both including and excluding eyes with AON and corrected considering basal T2 lesion load, age, sex and BOIgG.

Results: Patients who developed CDMS (20.4%, 5 AON at baseline) were younger, showed higher T2 (60.0 vs 43.5% with > 9 T2 lesions) and GD+ (40.0 vs 30.8%) lesion load and presence of BOIgG (80.0 vs 61.5%). Mean baseline RNFL thickness was 95.13± 12.62 μm, significantly lower in CIS with > 9 T2 and GD+ lesions ($p<0.05$ in all instances). Longitudinal changes in RNFL thickness significantly differed between patients who developed CDMS and who did not: a mean RNFL decrease of 0.15 and 0.12 μm per month was observed in converters with respect to non-converters when considering and excluding eyes with AON, respectively ($p=0.004$ and $p=0.012$), regardless of basal T2 lesion load, age, sex and BOIgG**.**

Conclusions: RNFL thickness may be a useful biomarker for monitoring CIS patients and predicting conversion to CDMS. Larger longitudinal studies on CIS patients are needed to confirm our preliminary findings and the utility of OCT in clinical practice.