The association between serum neurofilament light chain and OCT measures in multiple sclerosis

Jesper Hagemeier[1], Eleonora Tavazzi[1], Murali Ramanathan[2], Dejan Jakimovski[1], Niels Bergsland[1], Davorka Tomic[3], Harald Kropshofer[3], David Leppert[3], Zuzanna Michalak[4], Michael Dwyer[1], Ralph Benedict[5], Bianca Weinstock-Guttman[5], Jens Kuhle[4], Robert Zivadinov[1,6]

[1]Buffalo Neuroimaging Analysis Center, Department of Neurology, Jacobs School of Medicine and Biomedical Sciences, University at Buffalo, State University of New York, [2]Department of Pharmaceutical Sciences, Jacobs School of Medicine and Biomedical Sciences, University at Buffalo, State University of New York, [3]Novartis Pharma AG, [4]Neurologic Clinic and Policlinic, Departments of Medicine, Biomedicine and Clinical Research, University Hospital Basel, University of Basel, [5]Jacobs MS Center, Department of Neurology, Jacobs School of Medicine and Biomedical Sciences, University at Buffalo, State University of New York, [6]Center for Biomedical Imaging at Clinical Translational Science Institute, University at Buffalo, State University of New York

Objective: To investigate the association between serum levels of neurofilament light chain (sNfL), retinal nerve fiber layer thickness (RNFLT), fovea volume (FV) and total macular volume (TMV) in multiple sclerosis (MS).

Background: Optical coherence tomography (OCT) detects retinal changes in MS. Brain atrophy and clinical disability were reported to be associated with high sNfL in MS, but association with OCT measures was not explored.

Design/Methods: MS patients and healthy controls (HC) were prospectively enrolled. At baseline and after an average of 5.5 years, sNfL levels were measured using Simoa assay and OCT was performed, obtaining RNFLT, FV and TMV for both eyes. Linear regression analysis, controlling for age and sex, was used to investigate associations between sNfL levels and OCT measures.

Results:
127 MS (85 relapsing remitting-RRMS, 42 progressive MS-PMS), 20 clinically isolated syndrome (CIS) and 52 HC were enrolled. SNfL levels were significantly higher in MS than HC at both time points ($p<0.0001$). In the MS cohort, baseline SNfL was associated in both eyes with RNFLT ($p \leq 0.002$), TMV ($p \leq 0.034$) and FV ($p \leq 0.034$). Baseline sNfL was associated with RNFLT of both eyes ($p \leq 0.006$) and FV of right eye ($p=0.027$) in RRMS, and with TMV of left eye ($p=0.025$) in CIS. There was no significant association in HC nor in PMS. Furthermore, no significant association was found between sNfL change over time and changes of any OCT variable in the entire MS cohort. Finally, MS patients with sNfL ≥30 pg/ml at baseline had significantly lower RNFLT ($p \leq 0.036$) and TMV ($p \leq 0.014$) in both eyes at baseline than patients with <30 pg/ml.

Conclusions:
SNfL is associated with OCT measures reflective of neuroaxonal damage, and higher sNfL levels are associated with reduced RFNLT and TMV in MS. These findings support the role of sNfL as a marker of neurodegeneration in MS.