

## Optical Coherence Tomography in Parkinson's Disease: A Potential in-vivo Retinal $\alpha$ -Synuclein Biomarker in Parkinson's Disease

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**Abstract :** Background: Parkinson's Disease (PD) is a neuro degenerative disorder associated with the loss of dopaminergic cells and the presence  $\alpha$ -synuclein (AS) aggregation in of Lewy bodies. Both dopaminergic cells and AS are found in the retina. Optical coherence tomography (OCT) allows high-resolution in-vivo examination of retinal structure injury in neuro degenerative disorders including PD. Methods: We performed a cross-section OCT study in patients with definite PD and healthy controls (HC) using Spectral Domain SD-OCT platform to measure the peripapillary retinal nerve fiber layer (pRNFL) thickness and total macular volume (TMV). We performed intra-retinal segmentation with fully automated segmentation software to measure the volume of the RNFL, ganglion cell layer (GCL), inner plexiform layer (IPL), inner nuclear layer (INL), outer plexiform layer (OPL), and the outer nuclear layer (ONL). Segmentation was performed blinded to the clinical status of the study participants. Results: 101 eyes from 52 PD patients (mean age 65.8 years) and 46 eyes from 24 HC subjects (mean age 64.1 years) were included in the study. The mean pRNFL thickness was not significantly different (96.95  $\mu$ m vs 94.42  $\mu$ m,  $p=0.07$ ) but the TMV was significantly lower in PD compared to HC (8.33 mm<sup>3</sup> vs 8.58 mm<sup>3</sup>  $p=0.0002$ ). Intra-retinal segmentation showed no significant difference in the RNFL volume between the PD and HC groups (0.95 mm<sup>3</sup> vs 0.92 mm<sup>3</sup>  $p=0.454$ ). However, GCL, IPL, INL, and ONL volumes were significantly reduced in PD compared to HC. In contrast, the volume of OPL was significantly increased in PD compared to HC. Conclusions: Our finding of the enlarged OPL corresponds with mRNA expression studies showing localization of AS in the OPL across vertebrate species and autopsy studies demonstrating AS aggregation in the deeper layers of retina in PD. We propose that the enlargement of the OPL may represent a potential biomarker of AS aggregation in PD. Longitudinal studies in larger cohorts are warranted to confirm our observations that may have significant implications in disease monitoring and therapeutic development.

**Keywords :** Optical Coherence Tomography, biomarker, Parkinson's disease, alpha-synuclein, retina

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