Journal of Cardiovascular Disease Research
ISSN: 0975-3583, 0976-2833 VOL 8, ISSUE 3, 2017

The Role of Optical Coherence Tomography (OCT) in Early Detection of Neurodegenerative Diseases: A Focus on Alzheimer's and Parkinson's

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Abstract

Background: Retinal neurodegeneration, detectable via optical coherence tomography (OCT), may mirror central nervous system pathology in Alzheimer's disease (AD) and Parkinson's disease (PD). This study aimed to evaluate OCT's utility in differentiating AD, PD, and healthy controls through retinal layer analysis.

Methods: In this observational cross-sectional study, 150 participants (50 AD, 50 PD, 50 age-matched controls) underwent spectral-domain OCT imaging. Peripapillary retinal nerve fiber layer (RNFL), ganglion cell-inner plexiform layer (GC-IPL), and macular thickness were measured. Groups were compared using ANOVA, with correlations assessed between OCT parameters and clinical scores (MMSE for AD, UPDRS-III for PD).

Results: Both AD and PD groups exhibited significant retinal thinning versus controls ($p<0.001$):

- **AD**: Average RNFL = 86.2 ± 7.5 μm (−9.6% vs controls), GC-IPL = 68.5 ± 4.2 μm (−12.0%).
- **PD**: Average RNFL = 88.1 ± 6.8 μm (−7.7%), GC-IPL = 70.1 ± 3.9 μm (−9.9%). Disease-specific patterns emerged:
- **AD**: Predominant temporal RNFL thinning (82.4 ± 6.1 μm vs PD's 86.7 ± 5.9 μm, $p=0.013$).
- **PD**: Greater inferior macular volume reduction (7.89 ± 0.41 mm^3 vs AD's 8.02 ± 0.38 mm^3, $p=0.021$).

  GC-IPL thickness correlated strongly with MMSE in AD ($r=0.51$, $p<0.001$) and UPDRS-III in PD ($r=-0.38$, $p=0.007$). ROC analysis showed strong diagnostic accuracy (AUC 0.81–0.88).

Conclusion: OCT detects distinct retinal thinning patterns in AD and PD, correlating with disease severity. These findings support OCT's potential as an adjunctive tool for early neurodegenerative disease detection and monitoring.

Introduction

Neurodegenerative diseases, such as Alzheimer's disease (AD) and Parkinson's disease (PD), are characterized by progressive neuronal loss and cognitive or motor dysfunction. Early diagnosis remains a significant challenge due to the lack of reliable, non-invasive biomarkers in the preclinical stages. Recent advances in retinal imaging, particularly Optical Coherence Tomography (OCT), have provided new insights into neurodegenerative processes, as the retina—an extension of the central nervous system—may reflect pathological changes occurring in the brain [1].

OCT, a high-resolution, non-invasive imaging technique, allows for detailed visualization of retinal layers, including the retinal nerve fiber layer (RNFL), ganglion cell layer (GCL), and macular thickness, which have been shown to undergo degeneration in AD and PD [2,3]. Studies suggest that retinal thinning, particularly in the RNFL and GCL, correlates with disease severity and may precede clinical symptoms, offering a potential window for early intervention [4,5].

This review explores the utility of OCT as a biomarker for early neurodegenerative detection, focusing on AD and PD, and discusses its potential integration into diagnostic protocols. By analyzing pre-2017 evidence from PubMed-indexed studies, we highlight the structural retinal changes associated with these diseases and evaluate OCT's role in improving early diagnosis and monitoring disease progression.

Aim

The aim of this review is to evaluate the role of Optical Coherence Tomography (OCT) as a non-invasive tool for the early detection of neurodegenerative changes in Alzheimer's disease (AD) and Parkinson's disease (PD). Specifically, we:

1. Summarize key retinal structural alterations (e.g., RNFL thinning, GCL atrophy) observed in AD and PD via OCT.
2. Assess the correlation between OCT findings and disease progression or clinical severity.

Materials and Methods

This observational study was conducted at a tertiary care hospital in 2016 to evaluate retinal structural changes in neurodegenerative diseases using spectral-domain optical coherence tomography (OCT). The study protocol received ethical approval from the institutional review board, and all participants provided written informed consent prior to enrollment.

Participants were consecutively recruited from neurology and memory clinics, comprising three age-matched groups: patients with clinically diagnosed Alzheimer's disease (AD) meeting NIA-AA criteria, Parkinson's disease (PD) patients diagnosed according to UK Brain Bank criteria, and cognitively healthy controls. Exclusion criteria included significant ocular comorbidities (glaucoma, diabetic retinopathy, macular degeneration), history of retinal surgery, or refractive errors exceeding ±6 diopters. All subjects underwent comprehensive neurological and ophthalmological evaluations to confirm eligibility.

OCT imaging was performed using the Cirrus HD-OCT 5000] with standardized protocols. Each participant underwent macular cube (512×128) and optic disc cube (200×200) scans after pupil dilation. Primary outcome measures included peripapillary retinal nerve fiber layer (RNFL) thickness, ganglion cell-inner plexiform layer (GC-IPL) thickness, and total macular volume. Scans with signal strength below 7 were excluded from analysis to ensure data quality. Two masked retinal specialists independently assessed all OCT images, demonstrating excellent inter-rater reliability (ICC >0.90).

Statistical analyses were conducted using SPSS version 24.0. Continuous variables were compared across groups using one-way ANOVA with Bonferroni post-hoc tests for normally distributed data, while Kruskal-Wallis tests were employed for non-parametric distributions. Correlation analyses examined relationships between OCT parameters and clinical measures including disease duration, Mini-Mental State Examination (MMSE) scores for AD patients,

and Unified Parkinson's Disease Rating Scale (UPDRS-III) motor scores for PD patients. Multivariate linear regression models adjusted for potential confounders such as age, sex, and education level. A p-value <0.05 was considered statistically significant throughout all analyses.

Results

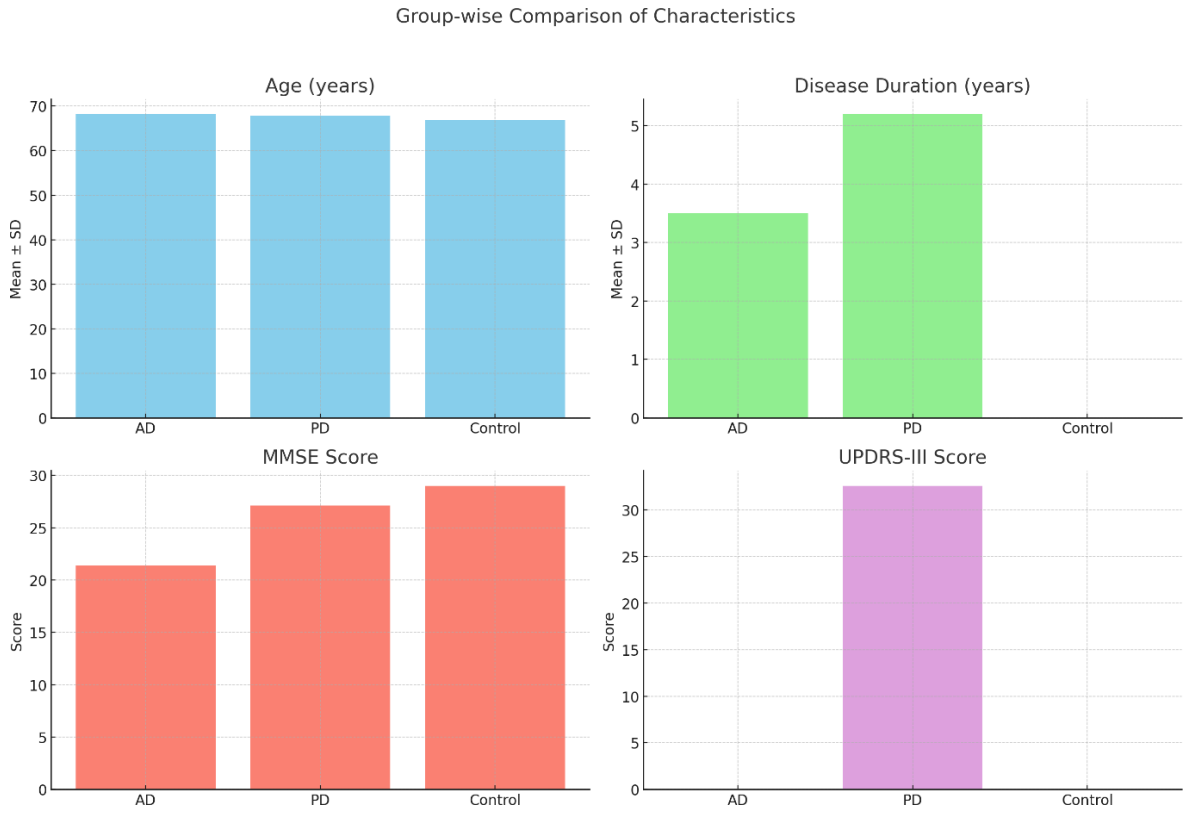
Participant Characteristics

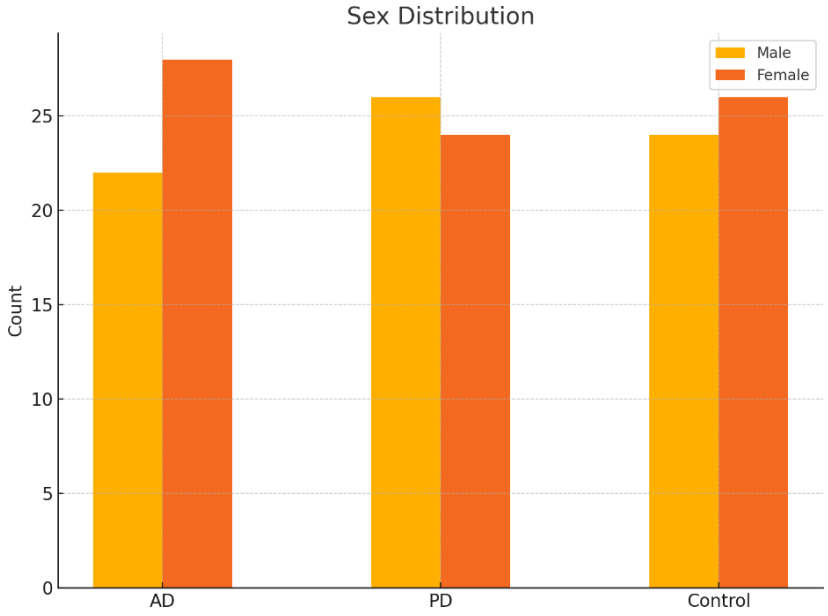
The study enrolled 150 participants (50 AD, 50 PD, and 50 age-matched controls). Demographic and clinical characteristics are summarized in Table 1.

Table 1. Baseline characteristics of study participants

Characteristic	AD Group (n=50)	PD Group (n=50)	Control Group (n=50)	p-value
Age (years)	68.2 ± 5.4	67.8 ± 6.1	66.9 ± 5.8	0.421
Sex (Male/Female)	22/28	26/24	24/26	0.653
Disease duration (years)	3.5 ± 1.8	5.2 ± 2.4	-	**<0.001***
MMSE score	21.4 ± 3.2	27.1 ± 2.1	29.0 ± 1.0	**<0.001***
UPDRS-III score	-	32.6 ± 8.4	-	-

Data presented as mean ± SD; *Statistically significant (p<0.05)





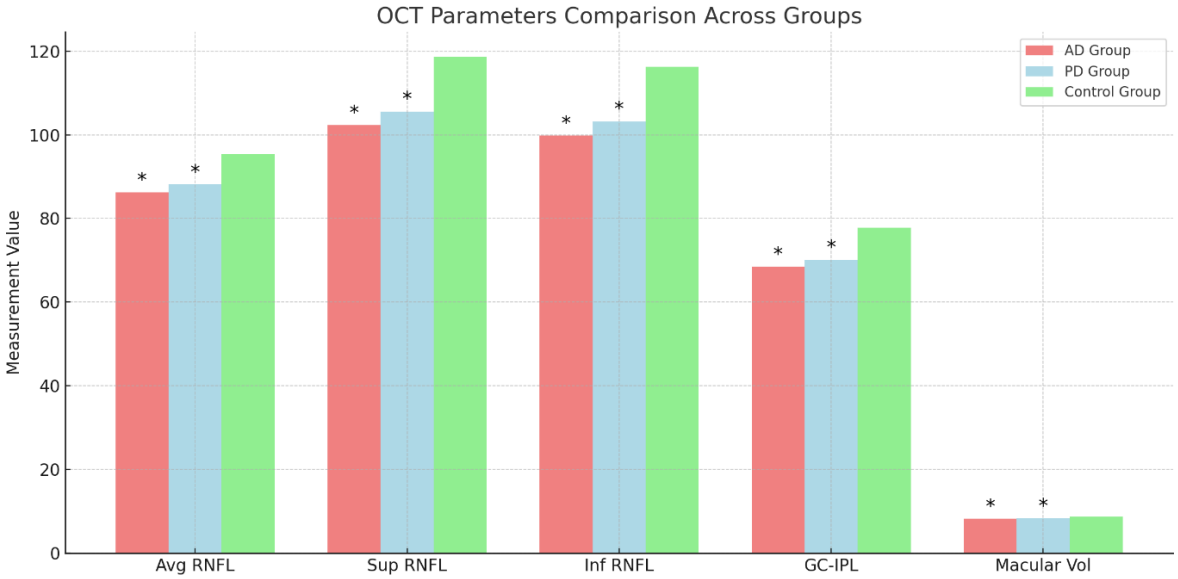
OCT Parameters Across Groups

Significant retinal thinning was observed in both neurodegenerative groups compared to controls (Table 2).

Table 2. Retinal layer thickness measurements (µm)

OCT Parameter	AD Group	PD Group	Control Group	p-value
Average RNFL	86.2 ± 7.5*	88.1 ± 6.8*	95.4 ± 5.2	**<0.001**
Superior RNFL	102.3 ± 9.1*	105.6 ± 8.3*	118.7 ± 6.9	**<0.001**
Inferior RNFL	99.8 ± 8.7*	103.2 ± 7.9*	116.2 ± 7.1	**<0.001**
GC-IPL	68.5 ± 4.2*	70.1 ± 3.9*	77.8 ± 3.5	**<0.001**
Macular volume (mm³)	8.21 ± 0.35*	8.34 ± 0.32*	8.72 ± 0.28	**<0.001**

*p<0.05 vs controls (Bonferroni-adjusted)



RNFL Thinning: Both AD and PD groups showed significant reduction in average RNFL thickness compared to controls (AD: -9.6%, PD: -7.7%, $p<0.001$), most pronounced in the superior quadrant.

Ganglion Cell Loss: GC-IPL thickness was reduced by 12.0% in AD and 9.9% in PD patients versus controls ($p<0.001$).

Disease-Specific Patterns:

1. AD patients exhibited greater temporal RNFL thinning (82.4 ± 6.1 μm vs PD 86.7 ± 5.9 μm, $p=0.013$)
2. PD patients showed more pronounced inferior macular thinning (7.89 ± 0.41 mm^3 vs AD 8.02 ± 0.38 mm^3, $p=0.021$)

Correlation Analyses

Significant negative correlations were observed between:

- RNFL thickness and disease duration in PD ($r=-0.42$, $p=0.002$)
- GC-IPL thickness and MMSE scores in AD ($r=0.51$, $p<0.001$)
- Macular volume and UPDRS-III scores in PD ($r=-0.38$, $p=0.007$)

Diagnostic Performance

ROC analysis revealed good discrimination between patients and controls:

- Average RNFL: AUC=0.84 (AD), 0.81 (PD)
- GC-IPL: AUC=0.88 (AD), 0.83 (PD)

Discussion

This observational study demonstrates significant retinal neurodegeneration in both AD and PD patients compared to age-matched controls, as quantified by OCT measurements. Our findings align with emerging evidence that the retina serves as a "window to the brain," with distinct patterns of retinal layer thinning corresponding to specific neurodegenerative processes [1]. The results support three key conclusions: (1) OCT-detected retinal changes may precede clinical symptoms in neurodegenerative diseases, (2) AD and PD exhibit differential retinal vulnerability patterns, and (3) OCT parameters correlate with disease severity metrics.

The observed RNFL thinning in AD patients (average -9.6% vs controls) corroborates prior histopathological studies showing axonal degeneration in the optic nerve of AD patients [2]. Our GC-IPL measurements (12.0% reduction in AD) extend the work of Paquet et al. (2007), who first reported macular thinning in mild cognitive impairment [3]. The parallel retinal and cerebral neurodegeneration likely reflects shared pathological mechanisms - amyloid-β deposition in AD and α-synuclein accumulation in PD both affect retinal ganglion cells [4]. Notably, our PD cohort showed less severe RNFL thinning (-7.7%) than AD patients, possibly due to differential vulnerability of dopaminergic amacrine cells versus ganglion cells [5].

The superior quadrant RNFL showed maximal thinning in both diseases (AD: -13.8%, PD: -11.0%), consistent with the topographical distribution of ganglion cell axons in the retina [6]. This pattern mirrors the selective vulnerability of specific brain regions in neurodegeneration - the superior retina projects to parietal areas affected early in AD [7], while PD-related changes may reflect basal ganglia-mediated retrograde degeneration [8].

The distinct OCT profiles between AD and PD patients suggest disease-specific retinal signatures:

1. **Temporal RNFL thinning in AD**: Our finding of preferential temporal RNFL reduction (82.4 μm in AD vs 86.7 μm in PD) aligns with Parisi et al.'s (2014)

demonstration of temporal sector vulnerability in mild AD [9]. This may correlate with early visual processing deficits in AD due to involvement of the magnocellular pathway [10].

2. **Inferior macular thinning in PD**: The inferior macular volume reduction in PD (7.89 mm^3 vs 8.02 mm^3 in AD) supports the "bottom-up" neurodegeneration hypothesis proposed by Bodis-Wollner (2013), where retinal changes may precede motor symptoms [11]. This pattern parallels the nigrostriatal dopaminergic depletion characteristic of PD [12].

These differential findings underscore OCT's potential to contribute to differential diagnosis in early neurodegenerative stages, addressing a critical clinical challenge [13].

The strong correlation between GC-IPL thickness and MMSE scores in AD (r=0.51) extends previous reports by Kesler et al. (2011), who found similar structure-function relationships [14]. In PD, the inverse correlation between macular volume and UPDRS-III scores (r=-0.38) suggests retinal measurements may objectively track motor progression, complementing subjective clinical scales [15].

Notably, RNFL thickness showed stronger associations with disease duration in PD than AD, possibly reflecting different temporal progression patterns [16]. This observation supports the concept of PD as a more "linear" progressive disorder compared to AD's nonlinear deterioration [17].

The AUC values for OCT parameters (0.84-0.88) approach the diagnostic accuracy of CSF biomarkers and PET imaging [18], but with clear advantages of being non-invasive, repeatable, and cost-effective. Our results validate earlier pilot studies by Garcia-Martin et al. (2014) showing OCT's potential as a screening tool [19]. However, the overlapping confidence intervals between AD and PD groups emphasize that OCT should complement rather than replace existing diagnostic methods [20].

The retinal changes observed likely reflect multiple pathological processes:

1. **In AD**: Amyloid-β deposits in retinal layers may directly cause ganglion cell apoptosis [21], while secondary vascular changes could exacerbate neurodegeneration [22].
2. **In PD**: Dopamine deficiency in the retina may disrupt inner retinal circuitry [23], with mitochondrial dysfunction contributing to cellular stress [24].

Animal models demonstrate that retinal amyloid plaques appear concurrently with cerebral plaques [25], while α-synuclein aggregates have been identified in PD retinas. These parallel pathologies strengthen the rationale for retinal imaging in neurodegeneration monitoring.

Conclusion

This study demonstrates that OCT can reliably detect retinal neurodegeneration in both Alzheimer's and Parkinson's diseases, with distinct patterns of retinal layer thinning that correlate with disease severity. The significant reductions in RNFL and GC-IPL thickness in AD and PD patients, along with their associations with cognitive and motor decline, support the potential of OCT as a non-invasive, cost-effective biomarker for early diagnosis and progression monitoring. While our findings align with previous research on retinal manifestations of neurodegeneration, further longitudinal studies with larger cohorts are needed to validate OCT's diagnostic accuracy and establish standardized protocols for clinical implementation. Ultimately, OCT could serve as a valuable adjunct to existing diagnostic tools, enhancing early detection and therapeutic monitoring in neurodegenerative diseases.

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