

Retinal Vascularity Index in Parkinson’s Disease

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Background

- **Parkinson’s Disease (PD)** is the fastest growing neurodegenerative disease worldwide¹
- Diagnosis relies primarily on clinical evaluation²
- Many diagnostic tools for PD are invasive and expensive
- Retinal imaging reveals structural and vascular changes mirroring neurodegenerative processes in the brain^{3,4}
- There is still no universally accepted biomarker
- Visible changes in vessel caliber are under-studied
- We employ a novel calculation of the retinal arteriovenous ratio (AVR) known as retinal vascularity index (RVI)
- **We calculated RVI on ultra-widefield (UWF) retinal images and compared RVI between patients with PD and controls**

Results

- 168 eyes of 108 PD participants and 115 eyes of 71 control participants were included
- **RVI was significantly higher in PD compared to controls**
- This difference was significant overall and in each of four quadrants within our ROI
- ROC analysis revealed moderate discriminative ability

Table 1. Demographics

Variable	Statistic	PD (N=108)	Control (N=71)	P-value*
Age	Mean (SD)	69.2 (7.9)	66.4 (8.1)	0.018
Sex	N (%)			<0.001
Female		39 (36.1)	47 (66.2)	
Male		69 (63.9)	24 (33.8)	
Years of Education	Mean (SD)	16.7 (2.9)	17.5 (2.5)	0.079
MMSE	Mean (SD)	28.5 (2.1)	29.3 (1.1)	0.006
Race	N (%)			0.027
White		105 (97.2)	63 (88.7)	
Other		3 (2.8)	8 (11.3)	
Hypertension	N (%)	30 (27.8)	17 (23.9)	0.606
Cataract Surgery	N (%)	23 (21.3)	11 (15.5)	0.436
HY Stage	N (%)			
1		19 (17.6)		
1.5		5 (4.6)		
2		46 (42.6)		
2.5		19 (17.6)		
3		11 (10.2)		
4		8 (7.4)		

*P-value for continuous variables based on Wilcoxon rank sum test. P-value for categorical variables based on Fisher’s exact test.

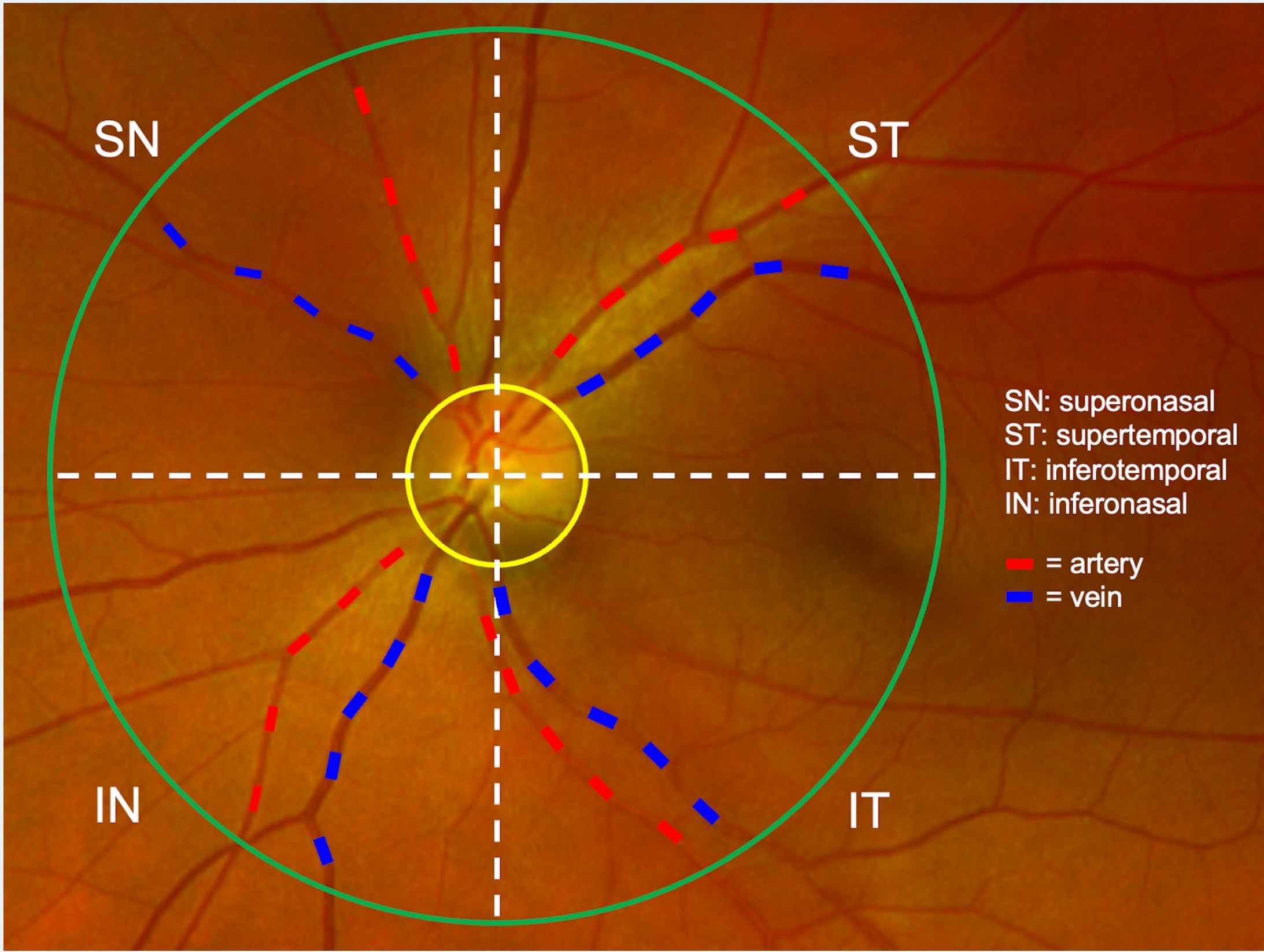
Abbreviations: SD, standard deviation; MMSE, Mini-Mental State Examination; PD, Parkinson’s Disease; HY, Hoehn & Yahr.

Methods

- Cross-sectional study design (NCT03233646)
- Individuals with PD were diagnosed by neurologists specializing in movement disorders
- Control individuals had normal cognition and no PD symptoms
- **Exclusion criteria:** <50 years age, diabetes, glaucoma, vitreoretinal pathology, any non-PD dementia, corrected Snellen visual acuity worse than 20/40
- **UWF images were acquired** using scanning laser ophthalmoscopy (California, Optos, Marlborough, MA) in undilated eyes
- **UWF images were analyzed** using a semi-automated software embedded in the Comprehensive Ocular Imaging Network (COIN, ocularimaging.net)
- A trained grader manually identified the size and location of the optic disc and fovea to define the **region of interest (ROI) of five disc diameters (DD)—47° field—centered on the optic disc**
- The largest arteriole and venule in each quadrant (superonasal [SN], superotemporal [ST], inferotemporal [IT], inferonasal [IN]) were segmented at consistent distances from the optic disc center to measure vessel diameter (*d*)
- Cross-sectional area of each vessel was automatically calculated and averaged (*A*) for arterioles and venules separately

$$A = \frac{\sum_{i=1}^n \left(\frac{\pi}{4} \times d_i^2 \right)}{n}$$

RVI = the ratio between arteriolar *A* and venular *A*, calculated overall within our ROI and within each quadrant.



- **Statistical analysis:** main outcome analysis using generalized estimating equations with exchangeable correlation structure and discriminatory analysis using receiver operating curves (ROC)

Results

Table 2. Retinal Vascularity Index (RVI)

Variable	Statistic	PD	Control	P-value*
Superonasal RVI	N	168	115	
	Mean (SD)	0.875 (0.241)	0.769 (0.239)	<0.001
	Min, Median, Max	0.382, 0.841, 1.760	0.264, 0.724, 1.788	
Superotemporal RVI	N	168	115	
	Mean (SD)	0.755 (0.203)	0.680 (0.191)	0.005
	Min, Median, Max	0.316, 0.722, 1.431	0.328, 0.626, 1.337	
Inferotemporal RVI	N	168	115	
	Mean (SD)	0.688 (0.193)	0.599 (0.156)	<0.001
	Min, Median, Max	0.263, 0.663, 1.280	0.308, 0.604, 1.120	
Inferonasal RVI	N	168	115	
	Mean (SD)	0.813 (0.221)	0.690 (0.176)	<0.001
	Min, Median, Max	0.303, 0.783, 1.427	0.250, 0.674, 1.244	
Total RVI	N	168	115	
	Mean (SD)	0.790 (0.134)	0.696 (0.117)	<0.001
	Min, Median, Max	0.387, 0.785, 1.074	0.478, 0.685, 1.003	

Outcomes were compared at the eye level between groups using the Z-test of difference in means between groups with generalized estimating equations (GEE) with an exchangeable correlation structure.

*P-values after GEE analyses were adjusted for age, sex, and race.

Abbreviations: SD, standard deviation; PD, Parkinson’s Disease

Conclusions

- **We observed an increased RVI in PD compared to controls**
- Increased RVI may reflect changes in retinal vascular structure related to α -synuclein deposition⁵, dopamine dysregulation⁶, and/or neuroinflammation⁷
- Discriminative analysis suggests that RVI may not stand alone as a diagnostic tool
- Further study is warranted to determine if **RVI derived from a 47° ROI on UWF images may serve as a potential retinal biomarker of PD**

References + Supplemental Material

