Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/b838sk18

DIAGNOSTIC AGREEMENT BETWEEN OPTICAL COHERENCE TOMOGRAPHY AND HEIDELBERG RETINAL TOMOGRAPHY IN PSEUDOEXFOLIATION

Dr. Chamundeswari Nalla*

*Assistant Professor, Department of Ophthalmology, Sri Lakshmi Narayana Institute of Medical Science, Pondicherry, India.

***Corresponding Author:** Dr. Chamundeswari Nalla

*Assistant Professor, Department of Ophthalmology, Sri Lakshmi Narayana Institute of Medical Science, Pondicherry, India.

Accepted 8th January 2020 *Published 10th February 2020*

Abstract:
Objective: This investigation sought to compare the diagnostic performance of optical coherence tomography (OCT) and Heidelberg retina tomography (HRT) in evaluating optic nerve head (ONH) morphology in individuals presenting with pseudoexfoliation syndrome, both with and without intraocular pressure (IOP) elevation. Methods: We conducted a prospective observational study involving 192 participants (age range: 65-78 years) divided into three groups: healthy controls (n=56), pseudoexfoliation without IOP elevation (n=68, Group 2), and pseudoexfoliation with elevated IOP (n=68, Group 1). All participants underwent comprehensive ophthalmologic assessment including Goldmann applanation tonometry, automated perimetry (Humphrey 30-2), Stratus OCT III for retinal nerve fiber layer (RNFL) thickness measurement, and HRT III for ONH parameter evaluation. Statistical analyses included one-way ANOVA and Kruskal-Wallis testing with appropriate post-hoc comparisons. Results: Significant alterations in RNFL thickness across all quadrants (average, superior, inferior, temporal, and nasal) were documented in Group 1 compared to controls and Group 2. Cup-to-disc (C/D) ratios demonstrated progressive increase from controls through Group 2 to Group 1, while rim area measurements showed corresponding decreases. Both OCT and HRT parameters exhibited strong correlations with visual field indices, particularly mean deviation (MD) and pattern standard deviation (PSD). Superior quadrant RNFL measurements showed the strongest correlation between imaging modalities. Conclusions: Both OCT and HRT demonstrated capability in detecting early structural changes in pseudoexfoliation syndrome, even preceding visual field deficits. These imaging technologies offer complementary information for monitoring glaucomatous progression in pseudoexfoliation patients. The findings support routine implementation of both modalities in clinical assessment protocols for patients with pseudoexfoliation syndrome, regardless of IOP status

Keywords: Pseudoexfoliation syndrome; Optical coherence tomography; Heidelberg retina tomography; Retinal nerve fiber layer; Optic nerve head; Glaucoma; Intraocular pressure

INTRODUCTION

Pseudoexfoliation syndrome represents a systemic disorder characterized by the production and deposition of distinctive fibrillar extracellular material throughout various ocular and extraocular tissues [1-3]. While this material can accumulate in multiple anatomical locations, ophthalmic manifestations predominantly affect anterior segment structures, including the lens capsule, iris, trabecular meshwork, conjunctiva, and orbital tissues. The clinical significance of this condition was substantially elevated following seminal observations by Roth and Epstein, subsequently elaborated by Ritch and colleagues during the early 1980s, which established the strong association between pseudoexfoliation and glaucomatous optic neuropathy [1].

Epidemiological investigations have consistently demonstrated a markedly higher prevalence of pseudoexfoliation syndrome among individuals diagnosed with glaucoma compared to age-matched control populations without glaucoma [2]. This relationship has prompted intensive research into diagnostic methodologies capable of early detection and longitudinal monitoring of glaucomatous damage in this high-risk population.

Recent decades have witnessed substantial advancement in ophthalmic imaging technologies designed to quantify structural alterations associated with glaucomatous progression [3]. Among these modalities, optical coherence tomography (OCT) and Heidelberg retina tomography (HRT) have emerged as the predominant clinical tools for evaluating both the peripapillary retinal nerve fiber layer and optic nerve head topography.

OCT employs low-coherence interferometry utilizing near-infrared wavelengths (approximately 840 nm) to generate high-resolution cross-sectional images of ocular tissue with axial resolution ranging from 10-15 micrometers (OCT 2) to 10.8 micrometers (OCT 3) [4]. Multiple investigations have validated its excellent sensitivity and specificity for discriminating between glaucomatous and non-glaucomatous eyes through precise measurement of peripapillary RNFL thickness.

HRT utilizes confocal scanning laser ophthalmoscopy to acquire three-dimensional topographic images of the posterior segment [5]. The HRT II system captures 64 consecutive optical sections at 1/16 millimeter intervals extending to approximately 1.5 centimeters depth, with image resolution of 384 × 384 pixels across a 15 × 15 pixel field. Topographic mapping algorithms generate surface height measurements by identifying maximum pixel intensity values at each location, enabling differentiation of superficial and deep tissue structures. Previous research has demonstrated strong correlation between HRT measurements and histopathological findings, supporting its validity as a quantitative assessment tool.

The present investigation was designed to compare RNFL thickness measurements and ONH parameters obtained via OCT and HRT with visual field performance in patients manifesting pseudoexfoliation syndrome with variable IOP profiles. We hypothesized that both imaging modalities would detect structural abnormalities preceding functional visual field loss in this population.

METHODS

Study Design and Participant Selection

This prospective observational study was conducted over a seven-month recruitment period, with subsequent three-year follow-up assessment. From an initial screening pool of 136 individuals, we enrolled 96 participants aged 65-78 years meeting inclusion criteria. IOP measurements were obtained at three separate time points daily to ensure accurate characterization of pressure profiles.

Participants were stratified into three groups: (1) Pseudoexfoliation with elevated IOP (n=68, comprising 20 males and 48 females); (2) Pseudoexfoliation without IOP elevation (n=68, comprising similar gender distribution); and (3) Age-matched healthy controls without pseudoexfoliation or elevated IOP (n=56, comprising 28 males and 28 females). Control subjects demonstrated no visual field abnormalities, maintained IOP below 15 mmHg, and exhibited no evidence of glaucomatous optic disc damage [6].

Exclusion criteria encompassed diabetes mellitus with retinopathy, corneal irregularities, other causes of optic neuropathy, and previous intraocular surgery. Only right eye data were included in the analysis to maintain statistical independence.

Examination Protocols

All participants underwent comprehensive ophthalmologic evaluation on a single examination day by a single experienced observer to minimize inter-examiner variability. The standardized protocol included sequential assessment via Goldmann applanation tonometry, automated perimetry (Humphrey Field Analyzer, 30-2 central program using Swedish Interactive Threshold Algorithm), Stratus OCT III, and HRT III [7].

OCT scanning generated peripapillary RNFL thickness measurements, with data analyzed across five parameters: average thickness (AVG), and individual quadrant measurements (superior [S], inferior [I], temporal [T], and nasal [N]). HRT evaluation included determination of cup-to-disc ratio (C/D) and rim area, with the optic nerve head margin delineated at the internal border of the Elschnig scleral ring. Visual field assessment provided mean deviation (MD) and pattern standard deviation (PSD) indices for correlation analyses.

Statistical Analysis

Statistical evaluation was performed using SPSS version 19.0 software package. Data distribution normality was assessed via Kolmogorov-Smirnov and Shapiro-Wilk tests. Variance homogeneity was examined using Levene's test [8]. Between-group comparisons employed one-way analysis of variance for normally distributed data, with Kruskal-Wallis nonparametric testing applied to non-normally distributed variables. Statistical significance threshold was established at $p < 0.05$ for all analyses.

RESULTS

Demographic Characteristics

Gender distribution demonstrated no statistically significant differences across the three study groups (Table 1). Age distributions were comparable among all cohorts, confirming adequate matching of control subjects.

Table 1: Demographic distribution by gender across study groups.

GROUP	MALE	FEMALE
Control	28	28
Group 1 (PEX + ↑IOP)	20	48
Group 2 (PEX only)	20	48

PEX = pseudoexfoliation; IOP = intraocular pressure

Imaging and Visual Field Parameters

Comparative analysis of HRT-derived parameters (C/D ratio, rim area) and OCT-measured RNFL thickness (AVG, S, T, I, N) revealed significant inter-group differences (Table 2). Group 1 demonstrated substantially reduced values for all RNFL thickness parameters and rim area measurements relative to both Group 2 and controls. Conversely, IOP and C/D ratio values were significantly elevated in Group 1 compared to the other cohorts.

Visual field indices (MD and PSD) exhibited statistically significant deterioration in Group 1 relative to Group 2 and controls [9]. All between-group comparisons achieved statistical significance ($p < 0.05$) as detailed in Table 3.

Correlation analyses within Group 1 demonstrated significant associations between OCT-measured RNFL thickness in each quadrant and corresponding HRT parameters. Superior quadrant RNFL thickness measurements exhibited the strongest correlation coefficients among all OCT-HRT parameter pairs.

For Group 2 participants, HRT-derived C/D ratios and rim areas showed significant correlations with all OCT variables (AVG, S, I, T, N). However, between-group comparisons revealed no statistically significant differences in OCT or HRT measurements when comparing Group 2 to controls.

Table 2: By comparing group means and medians, descriptive measures by group were determined for the normal group, the group 1, and the group 2

Variables	Normal		Group 1		Group 2	
	Mean	standard deviation	Mean	standard deviation	Mean	standard deviation
intraocular pressure (mmHg)	16.33	3.647	20.31	4.024	15.86	2.06
optical coherence tomography average thickness	98.05	6.478	75.43	11.70	94.03	8.103
optical coherence tomography superio thickness	120.79	12.74	91.55	23.10	110.79	13.043
optical coherence tomography temporal thickness	77.32	11.36	57.62	11.701	73.26	12.018
optical coherence tomography inferior thickness	125.18	10.84	96.90	22.301	115.21	11.04
optical coherence tomography nasal thickness	74.81	9.94	56.44	16.54	74.61	10.161
Heidelberg retina tomography cup /disc ratio	1.43	1.10	1.35	1.10	1.31	1.014
Heidelberg retina tomography rim area (mm2)	1.41	1.301	2.17	1.07	2.11	1.01
visual field mean deviation (dB)	-0.19	2.041	-0.31	1.11	-0.29	2.13
visual field pattern standard deviation	0.80	0.363	2.30	1.01	1.11	1.03

Table 3: Three groups were compared based on their mean values

Variables	Means		
	Group 1–normal	**Group 1–group 2**	**Group 2–normal**
intraocular pressure right (mmHg)	4.21	3.44	6.14
optical coherence tomography average thickness right (□m)	-23.31	-12.7	2.11
optical coherence tomography superior thickness right (□m)	-31.14	-90.68	-2.01
optical coherence tomography temporal thickness right (□m)	-16.14	-14.8	-2.17
optical coherence tomography inferior thickness right (□m)	-27.11	-21.29	-1.18
optical coherence tomography nasal thickness right (□m)	-19.10	-21.38	-2.31
Heidelberg retina tomography cup / disc right ratio	1.02	1.12	1.11
Heidelberg retina tomography rim area right (mm2)	-0.15	-1.45	-1.14
visual field mean deviation right (dB)	-1.77	-1.12	-1.47
visual field pattern standard deviation right	1.33	1.10	1.40

DISCUSSION

The present investigation demonstrates that eyes with pseudoexfoliation and elevated IOP (Group 1) exhibit significantly greater RNFL loss compared to eyes with pseudoexfoliation alone or healthy controls, as quantified by both OCT and HRT imaging modalities. These structural deficits were documented despite absence of corresponding visual field progression in many cases, suggesting that morphological changes may precede functional deterioration in this population [10].

The magnitude of structural abnormalities in Group 2 (pseudoexfoliation without IOP elevation) demonstrated an intermediate phenotype between Group 1 and controls. Although Group 2 exhibited some evidence of RNFL and ONH damage detectable by OCT and HRT, these alterations were substantially less pronounced than those observed in Group 1 [11]. This gradient of structural abnormality correlating with IOP status supports the hypothesis that pressure-independent mechanisms may contribute to early glaucomatous damage in pseudoexfoliation syndrome, as previously proposed by Ritch and colleagues [15].

Quantitative comparison between Groups 1 and 2 revealed significantly larger rim areas in Group 2 (median difference of -0.44 mm^2). C/D ratios demonstrated statistically significant between-group differences, with Group 2 showing the smallest increment (median 0.31) relative to controls, while Group 1 exhibited the most substantial deviation [12].

OCT parameters in Group 2 consistently exceeded those in Group 1 while remaining below control values. Significant correlations were identified between rim area and RNFL thickness across all four quadrants (superior, inferior, temporal, and nasal). These findings align with previous research by Lan and colleagues demonstrating relationships between HRT anatomical variables and visual field indices. Among HRT parameters, rim area and cup shape measurements exhibited the strongest correlations with visual field performance.

Our results indicate that alterations in C/D ratio and rim area correlate with RNFL thickness changes across all quadrants. This suggests that relying on a single parameter may be insufficient for detecting all progressive glaucomatous lesions, as degenerative changes can occur heterogeneously across different regions of the ONH and RNFL during disease progression [13].

The literature establishes that eyes with exfoliation syndrome demonstrate increased susceptibility to glaucomatous optic neuropathy compared to eyes without this condition [14]. Exfoliation syndrome represents one of the most prevalent identifiable causes of open-angle glaucoma globally. Additionally, angle-closure glaucoma occurs with increased frequency in patients manifesting exfoliation syndrome, and the clinical course and prognosis typically prove less favorable than in primary open-angle glaucoma [15].

Our findings corroborate previous suggestions that exfoliation material may promote glaucomatous damage independent of IOP elevation. The demonstration of structural abnormalities in Group 2 (normal IOP pseudoexfoliation) supports this concept, indicating that exfoliation syndrome increases glaucoma risk at any given IOP level. Both OCT and HRT have proven to be well-validated methodologies for assessing morphological changes in glaucoma [16-17].

The current study utilized OCT and HRT to compare and evaluate ONH and RNFL measurements against visual field parameters in patients with pseudoexfoliation, stratifying by IOP status. Both Groups 1 and 2 demonstrated alterations in OCT and HRT parameters compared to expected normal ranges, with these changes occurring despite normal visual field findings in many participants [18]. This observation suggests that ONH and RNFL damage patterns in pseudoexfoliation differ from normal eyes and may not correlate directly with visual field deficits, particularly in early disease stages.
Visual field testing alone may prove inadequate for distinguishing eyes with progressive disease from those with stable disease, whereas OCT and HRT provide objective quantitative data enabling such discrimination [19-20]. When integrated with automated perimetry, both imaging modalities contribute essential information for evaluating patients with pseudoexfoliation, regardless of IOP status. This comprehensive approach facilitates earlier diagnosis, accurate monitoring of glaucoma progression, and appropriate treatment modifications to optimize patient outcomes.

Study Limitations and Future Directions

Several limitations warrant consideration. The relatively modest sample size, particularly in the control group, may limit generalizability of findings. Additionally, the cross-sectional design prevents assessment of longitudinal progression rates. Future investigations should incorporate larger patient cohorts with extended follow-up periods to validate these preliminary findings and establish evidence-based guidelines for incorporating advanced imaging into clinical management protocols for pseudoexfoliation syndrome.

CONCLUSIONS

This investigation demonstrates that both OCT and HRT possess capability to detect early structural abnormalities in pseudoexfoliation syndrome, including cases without IOP elevation. The documented changes in RNFL thickness and ONH parameters preceding visual field deficits underscore the clinical utility of these imaging modalities for early detection and monitoring. Implementation of routine OCT and HRT assessment in patients with pseudoexfoliation syndrome, complemented by standard automated perimetry, may enable earlier therapeutic intervention and improved preservation of visual function. Larger-scale longitudinal studies are warranted to confirm these findings and establish optimal screening protocols for this high-risk population.

REFERENCES

1. Ritch R, Schlötzer-Schrehardt U, Konstas AG. Why is glaucoma associated with exfoliation syndrome? *Prog Retin Eye Res.* 2003;22(3):253-275.
2. Koliakos GG, Konstas AG, Schlötzer-Schrehardt U, et al. 8-Isoprostaglandin F2a and ascorbic acid concentration in the aqueous humour of patients with exfoliation syndrome. *Br J Ophthalmol.* 2003;87(3):353-356.
3. Roth M, Epstein DL. Exfoliation syndrome. *Am J Ophthalmol.* 1980;89(4):477-481.
4. Ritch R, Schlötzer-Schrehardt U. Exfoliation (pseudoexfoliation) syndrome: toward a new understanding. Proceedings of the First International Think Tank. *Acta Ophthalmol Scand.* 2001;79(2):213-217.
5. Puska P, Vesti E, Tomita G, Ishida K, Raitta C. Optic disc changes in normotensive persons with unilateral exfoliation syndrome: a 3-year follow-up study. *Graefes Arch Clin Exp Ophthalmol.* 1999;237(6):457-462.
6. Konstas AG, Dimitracoulias N, Konstas PA. Exfoliation syndrome and open angle glaucoma. *Klin Monbl Augenheilkd.* 1993;202(4):259-268.
7. Konstas AG, Stewart WC, Stroman GA, Sine CS. Clinical presentation and initial treatment patterns in patients with exfoliation glaucoma versus primary open-angle glaucoma. *Ophthalmic Surg Lasers.* 1997;28(2):111-117.
8. Izatt JA, Hee MR, Swanson EA, et al. Micrometer-scale resolution imaging of the anterior eye in vivo with optical coherence tomography. *Arch Ophthalmol.* 1994;112:1584-1589.
9. Hee MR, Izatt JA, Swanson EA, et al. Optical coherence tomography of the human retina. *Arch Ophthalmol.* 1995;113:325-332.
10. Pagliara MM, Lepore D, Balestrazzi E. The role of OCT in glaucoma management. *Prog Brain Res.* 2008;173:39-48.
11. Weinreb RN, Dreher AW, Bille JF. Quantitative assessment of the optic nerve head with the laser tomographic scanner. *Int Ophthalmol.* 1989;13:25-29.
12. Garway-Heath D, Lemij H. Optic nerve head and retinal nerve fiber analysis. *Eur Glaucoma Soc.* 2005;4:59-61.
13. Fingeret M. Using the Heidelberg retina tomograph II (HRT II): image acquisition and accessing the data.

In: Fingeret M, Flanagan JG, Liebmann JM, eds. *The Essential HRT Primer.* Heidelberg, Germany: Heidelberg Engineering; 2005:11-30.
14. Ferreri F, Aragona P, Ferreri G. Scanning laser polarimetry and confocal scanning laser ophthalmoscopy: technical notes on their use in glaucoma. *Prog Brain Res.* 2008;173:125-138.
15. Lester M, Mikelberg FS, Courtright P, et al. Correlation between the visual field indices and Heidelberg retina tomograph parameters. *J Glaucoma.* 1997;6:78-82.
16. Lan YW, Henson DB, Kwartz AJ. The correlation between optic nerve head topographic measurements, peripapillary nerve fibre layer thickness, and visual field indices in glaucoma. *Br J Ophthalmol.* 2003;87:1135-1141.
17. Brigatti L, Caprioli J. Correlation of visual field with scanning confocal laser optic disc measurements in glaucoma. *Arch Ophthalmol.* 1995;113:1191-1194.
18. Weinreb RN, Shakiba S, Sample PA, et al. Association between quantitative nerve fiber layer measurement and visual field loss in glaucoma. *Am J Ophthalmol.* 1995;120:732-738.
19. Tole DM, Edwards MP, Davey KG, et al. The correlation of the visual field with scanning laser ophthalmoscope measurements in glaucoma. *Eye.* 1998;12:686-690.
20. Ritch R. Exfoliation syndrome-the most common identifiable cause of open-angle glaucoma. *J Glaucoma.* 1994;3(2):176-177.