Phenotypic Expression of the Optic Disc in Primary Open Angle Glaucoma

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Purpose

We performed a retrospective study to identify demographic and ocular characteristics associated with six identifiable optic disc phenotypes in Primary Open Angle Glaucoma (POAG) patients.

Methods

Inclusion Criteria

Diagnosis of POAG, one disc photo within two years of a visual field (VF), ≥ 2, VFs with Mean Deviation (MD) > -10dB, Pattern Standard Deviation (PSD) probability <0.05, and a Cirrus Optical Coherence Tomography (OCT) with optic disc area between 1.14 and 3mm².

Phenotypic Classification

The photos were classified independently by three masked glaucoma specialists into disc phenotypic subgroups, according to standard reference photographs:

Figure 1. Phenotypic subgroups.

Agreement:
The three graders agreed on 89% of the total images (1083). All remaining discrepancies (11%) were resolved by a consensus between the graders to decide the final phenotype.

Results

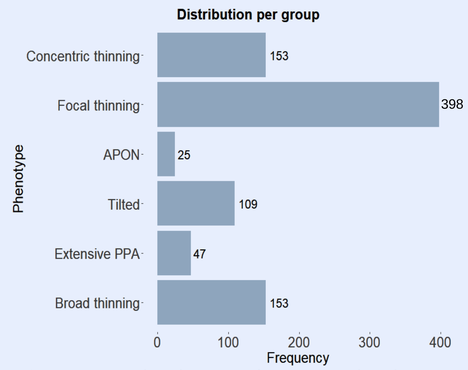

Figure 2. Bar plot showing phenotypes distribution

Table 1. Summary Statistics showing statistically significant variables based on ANOVA (continuous) and Chi-Squared test (categorical)

	All	Gender (%)		Race (%)					Age	IOP	LogMAR	CCT	Refraction	MD	PSD	Disc Area	RNFL
	n =	Male	Female	Caucasian	Asian	African Descent	Hispanic	Other	Mean (±SD)	Mean (±SD)	Mean (±SD)	Mean (±SD)	Mean (±SD)	Mean (±SD)	Mean (±SD)	Mean (±SD)	Mean (±SD)
All	885	41.8	58.2	57.4	16.5	9.5	4.3	12.3	70.5 (11.5)	13.4 (3.6)	0.1 (0.2)	546.1 (42.9)	-1.8 (2.8)	-4.6 (2.2)	5.8 (2.2)	1.8 (0.4)	65.8 (25.9)
Concentric Th.	153	54.2	45.8	56.9	9.2	11.8	6.5	15.7	70.9 (12.9)	13.9 (3.8)	0.2 (0.3)	549.2 (37.2)	-0.7 (1.9)	-4.3 (2.2)	5.1 (1.7)	1.9 (0.4)	70.2 (16.8)
Focal Thinning	398	37.9	62.1	59.8	14.1	9.5	4.0	12.6	71.0 (11.1)	13.5 (3.7)	0.1 (0.2)	545.9 (42.5)	-1.4 (2.7)	-4.4 (2.2)	6.0 (2.4)	1.8 (0.3)	66.3 (29.3)
APON	25	40.0	60.0	68.0	12.0	12.0	0.0	8.0	68.8 (9.5)	12.3 (3.4)	0.1 (0.1)	558.4 (49.3)	-1.5 (1.8)	-4.5 (2.1)	7.1 (2.8)	1.9 (0.3)	67.6 (10.8)
Tilted	109	43.1	56.9	39.4	42.2	6.4	2.8	9.2	65.1 (11.1)	13.3 (2.9)	0.1 (0.2)	551.5 (45.2)	-3.9 (3.4)	-4.5 (2.1)	6.0 (2.4)	1.7 (0.4)	66.4 (22.0)
Extensive PPA	47	46.8	53.2	70.2	8.5	4.3	4.3	12.7	74.0 (11.0)	13.3 (4.5)	0.1 (0.2)	551.4 (46.9)	-2.3 (3.4)	-5.6 (2.5)	5.5 (1.6)	1.7 (0.5)	62.1 (24.3)
Broad Thinning	153	37.3	62.7	58.8	15	10.5	4.6	11.2	71.8 (10.8)	12.6 (3.5)	0.2 (0.2)	535.0 (44.2)	-1.9 (2.6)	-5.0 (2.2)	5.7 (2.1)	1.9 (0.4)	60.7 (27.9)
P-values:		0.015				0.000			0.000	0.044	0.024	0.030	0.000	0.001	0.000	0.000	0.000

Table 2. Gender Pairwise comparison using Chi-Squared Test

Pheno 1	Pheno 2	p-value	p adjusted
CT	FT	0.001	0.011

Only statistically significant P Value adjusted are shown.

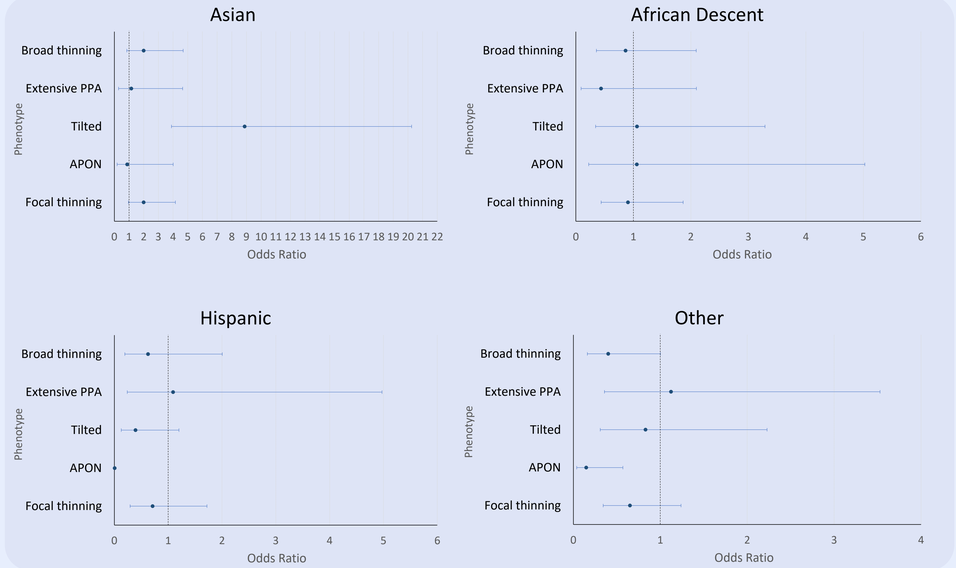

Figure 3. Forest Plot showing association between different races and Phenotypes, with Caucasian and Concentric Thinning as references.

Table 3. Pairwise Comparison using Mann-Withney-Wilcoxon Test adjusted with Bonferroni correction among all continuous variables

Pheno 1	Pheno 2	n1	n2	Mean 1	Mean 2	p	p.adj
AGE							
CT	Tilted	153	109	70.9 (±12.9)	65.1 (±11.1)	0	0.000
FT	Tilted	398	109	71.0 (±11.1)	65.1 (±11.1)	0	0.000
Tilted	EPA	109	47	65.1 (±11.1)	74.0 (±11.0)	0	0.000
Tilted	BT	109	153	65.1 (±11.1)	71.8 (±10.8)	0	0.000
DA							
CT	Tilted	153	109	1.9 (±0.4)	1.7 (±0.4)	0	0.003
Tilted	BT	109	153	1.7 (±0.4)	1.9 (±0.4)	0	0.001
LogMAR							
FT	BT	398	153	0.1 (±0.2)	0.2 (±0.2)	0	0.004
MEAN PSD							
CT	FT	153	398	5.1 (±1.7)	6.0 (±2.4)	0	0.005
RNFL							
CT	BT	153	153	70.2 (±16.8)	58.6 (±20.4)	0	0.000
FT	BT	398	153	64.3 (±20.0)	58.6 (±20.4)	0	0.001
Tilted	BT	109	153	66.4 (±22.0)	58.6 (±20.4)	0	0.000
SPHERE							
CT	Tilted	153	109	-0.7 (±1.9)	-3.9 (±3.4)	0	0.000
FT	Tilted	398	109	-1.4 (±2.7)	-3.9 (±3.4)	0	0.000
Tilted	BT	109	153	-3.9 (±3.4)	-1.9 (±2.6)	0	0.000

Summary results

- Tilted phenotype was more frequently associated with Asian race, myopia, younger age and lower Disc Area.
- Broad Thinning phenotype has a thinner Retinal Nerve Fiber Layer.
- Focal Thinning has better Visual Acuity compared to Broad Thinning.
- Focal Thinning and Broad Thinning are more associated with female gender.

Conclusion

This study reports six phenotypic classifications of POAG patients, with emergence of some ocular and systemic differences between phenotypes. Future refinement of phenotypes should allow improved individualization of patient care and enhance the ability to interpret a multitude of genetic associations with POAG.

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