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Physiology-enhanced transfer learning discovers combinations of intraocular pressure and blood pressure associated with structural biomarkers of glaucoma eyes in a population-based study

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Footnotes

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Abstract

Purpose : The role of blood pressure in relationship to intraocular pressure (IOP) as a risk factor for open angle glaucoma (OAG) remains elusive. In this study, a novel physiology-enhanced transfer learning method is developed to identify clusters of eyes for which IOP and mean arterial pressure (MAP) levels have similar hemodynamic implications. Statistical correlations between clusters and structural markers are explored a posteriori in healthy and OAG eyes in a population-based study.

Methods : Clusters identified via Fuzzy-C-means (FCM) on a synthetic dataset are transferred onto a population-based dataset (Thessaloniki Eye study; 2438

healthy, 170 OAG eyes). Clustering is based on IOP, MAP and hemodynamic variables (flow rate, vascular pressure, vascular resistance) obtained via a validated physiology-based mathematical model for the retina circulation using eye-specific IOP and MAP as inputs. The Fuzzy Nearest Prototype Classifier is used for transferring the FCM clusters from the synthetic to the real dataset. A linear mixed model analysis with a subject-specific random effect to account for subject-induced dependence between left and right eyes is used to compare subcluster means of vertical and horizontal cup-to-disc ratios (vC/D, hC/D), where the effect of age and gender were considered.

Results : Healthy eyes do not exhibit statistically significant differences in vC/D and hC/D across clusters. In OAG eyes, both vC/D and hC/D are found to be higher in cluster c than in cluster b ($p<0.05$) (Tab. 1). Eyes in clusters b and c have comparable IOP but different MAP, with MAP being lower in cluster c. Due to the number of eyes in each cluster, clusters a-e and b-e were considered in the analysis for healthy and OAG eyes, respectively.

Conclusions : The proposed physiology-enhanced transfer learning method identifies specific MAP-IOP combinations that correlate with higher C/D in OAG. Such correlations are not found in healthy eyes, suggesting that compromised regulatory mechanisms in OAG eyes leave them more susceptible to glaucomatous damage.

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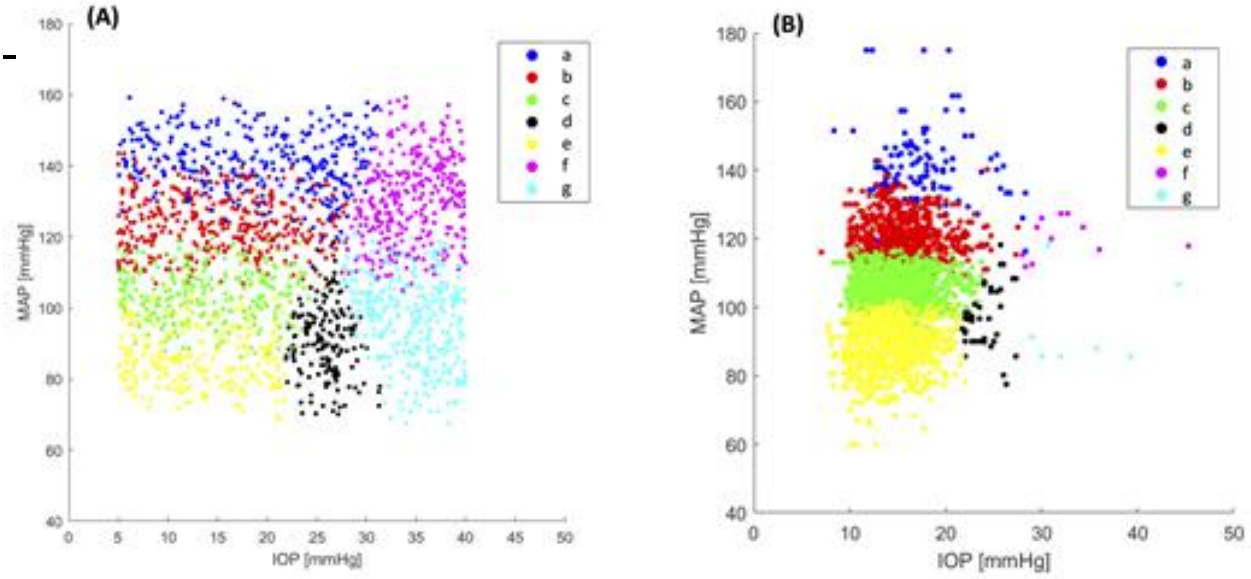

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Fig. 1. FCM clusters based on IOP, MAP and model-predicted hemodynamic variables are projected onto the MAP-IOP plane for synthetic dataset (A) and transferred onto population-based dataset (B)

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	Clusters						
	a	b	c	d	e	f	g
Healthy Eyes							
Number of Eyes	89	542	1009	12	785	0	1
vC/D (mean±std)	0.29±0.18	0.25±0.18	0.23±0.17	0.29±0.23	0.24±0.18	-	0.2±0
hC/D (mean±std)	0.26±0.17	0.23±0.17	0.21±0.16	0.24±0.18	0.21±0.16	-	0.2±0
OAG Eyes							
Number of Eyes	4	36	67	12	43	6	2
vC/D (mean±std)	0.45±0.19	0.54±0.21	0.67±0.21	0.62±0.23	0.59±0.23	0.65±0.18	0.3±0.28
hC/D (mean±std)	0.33±0.13	0.45±0.21	0.58±0.2	0.5±0.19	0.49±0.21	0.53±0.22	0.3±0.28

	p values	
	Healthy Eyes (*)	OAG Eyes (**)
vC/D	0.13	0.036 (#)
hC/D	0.09	0.049 (#)

(*) clusters a, b, c, d, e are compared
(**) clusters b, c, d, e are compared
(#) significant difference between clusters b and c

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Tab. 1. Summary of statistical analysis across clusters for healthy and OAG eyes