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Cluster stability and its relationship to blood pressure, intraocular pressure and hemodynamic variables in the human retina

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Footnotes

Commercial Relationships **Daphne Zou** None; **James Keller** None; **Alon Harris** AdOM, Qlaris, Luseed, Cipla, Code C (Consultant/Contractor), AdOM, Luseed, Oxymap, Qlaris, Phileas Pharma, SlitLed, QuLent, Code I (Personal Financial Interest), AdOM, Qlaris, Phileas Pharma, Code S (non-remunerative); **Giovanna Guidoboni** Foresite Healthcare LLC, Qlaris, Code C (Consultant/Contractor), Gspace LLC, Code I (Personal Financial Interest)

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Abstract

Purpose : Clustering helps identify eyes with similar hemodynamic conditions, which is useful for individualizing treatments. However, which hemodynamic variables are most relevant for clustering is not known. Here, we study the influence of flow rate (Q), vascular pressures (P), and vascular resistances (R) on cluster stability.

Methods : A validated mathematical model for the retinal circulation is used to create a synthetic dataset. Intraocular pressure (IOP), and systolic and diastolic blood pressures (SBP, DBP) are sampled randomly in the intervals (5,40) mmHg, (100,220) mmHg and (50,130) mmHg, respectively, assuming that pulse pressure falls within (20,120) mmHg. For each combination of SBP, DBP and IOP, the synthetic dataset includes the model-predicted values of Q, P, and R. The Fuzzy C-Means (FCM) algorithm is run under 8 scenarios, differing by the variables considered for clustering (Tab.1). For each scenario, FCM is run 1000 times with random initialization of the cluster centers, and the resulting fuzzy partitions are examined as an indication of stability. Based on cluster validity measures, C=3 has been selected as the number of clusters to be identified.

Results : Fig.1 reports the final locations of the cluster centers projected on the MAP-IOP plane, with $MAP = \frac{1}{3} SBP + \frac{2}{3} DBP$. Cluster centers are quite stable with respect to the random initialization for S4-S8 (Figs.1d-h). In contrast, when S1 is considered, the cluster centers

cover a pseudo-circle over the plane (Fig.1a), thereby indicating a marked lack of robustness. For S2 and S3, the cluster centers alternate among few selected locations (Figs.1b,c). These results suggest that not including R would cause instability in the FCM results (Figs.1a-c). If R is not included, robustness is achieved by accounting for both Q and P (Fig.1g).

Conclusions : Clusters identify hemodynamically-similar eyes for different MAP-IOP combinations. This study suggests that vascular resistance is essential in establishing hemodynamic similarities, either through its value R or its consequences on both flow rate Q and pressure distribution P. Considering only SBP, DBP, IOP, and blood flow Q (Fig.1b) does not yield robust clusters. This study helps define the concept of hemodynamically-similar eyes and, ultimately, enable personalized treatment approaches.

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SCENARIO	VARIABLES					
	SBP	DBP	IOP	Q	P	R
S1	√	√	√			
S2	√	√	√	√		
S3	√	√	√		√	
S4	√	√	√			√
S5	√	√	√		√	√
S6	√	√	√	√		√
S7	√	√	√	√	√	
S8	√	√	√	√	√	√

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Summary of Clustering Scenarios

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Final FCM cluster centers on the MAP-IOP plane

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