

AI-Based Ocular Age Estimation from Combined OCT and OCTA Metrics: Decade-Stratified Normative Modelling in Healthy Eyes – A Pilot Study [Letter]

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Dear editor

I read with great interest the article by Pourjavan et al¹ evaluating artificial intelligence (AI)-based ocular age estimation from combined optical coherence tomography (OCT) and OCT angiography (OCTA) metrics. The authors present a novel pilot study providing decade-stratified normative data and demonstrating that multimodal integration markedly enhances biological age prediction accuracy. This research offers valuable insights into vascular ageing and its potential role in glaucoma risk stratification. However, several methodological and interpretive aspects merit further discussion.

First, while the inclusion of both OCT and OCTA data is innovative, the modest cohort size (120 subjects, 221 eyes) limits the applicability of the normative values reported. The distribution of participants across decades, particularly in older age groups, was uneven, which may affect the precision of decade-stratified estimates and contribute to the non-linear or U-shaped vascular density trends observed. Larger normative studies such as that by Tan et al² have consistently demonstrated a near-linear decline in vessel density with age when adequately powered, suggesting that the present findings should be interpreted cautiously until validated in larger, demographically diverse cohorts.

Second, the reliance on self-reported systemic health without formal cardiovascular screening introduces a potential confounding factor. Undetected hypertension, diabetes, or smoking exposure can significantly influence microvascular parameters. Given the sensitivity of peripapillary and macular vessel density to systemic vascular risk factors,³ incorporating standardised systemic assessments (blood pressure, HbA1c, smoking history, lipid profile) in future work would strengthen the dataset's validity and enhance translational value.

Third, while the use of support vector regression (SVR) is appropriate for small datasets, the lack of external validation limits claims of model generalisability. The reported R^2 of 0.895, while impressive, may still reflect some degree of residual overfitting despite subject-level cross-validation. Replication on an independent dataset, ideally using a different OCTA platform, would help to establish reproducibility. Furthermore, while principal component analysis (PCA) efficiently simplifies complex data, it could obscure which anatomical or vascular features most strongly influence age prediction. Hence, using analytical approaches such as SHAP or permutation importance could clarify which features most influence the model's predictions and improve clinical understanding.⁴

Fourth, the decision to analyse both eyes from most subjects, albeit within grouped cross-validation, may still inflate apparent performance due to intra-subject correlation. Future normative studies should consider restricting analyses to one eye per participant to ensure statistical independence.

Finally, the proposal that AI-derived “ocular age” might serve as a biomarker for glaucoma susceptibility is intriguing but remains preliminary. While accelerated ocular ageing could conceivably reflect neurovascular vulnerability, prospective studies evaluating whether deviations between predicted and chronological age (Δ Age) precede structural or functional

glaucomatous progression are needed to substantiate clinical utility. This approach has shown promise in systemic ageing biomarkers but requires longitudinal validation before risk stratification applications can be justified.⁵

In conclusion, Pourjavan et al provide a valuable contribution by integrating vascular and structural imaging for AI-based modelling of ocular ageing. The study highlights the potential of multimodal analytics in advancing our understanding of neurovascular ageing in ophthalmology. However, the limited sample size, lack of systemic covariate adjustment, and absence of external validation indicate that these findings should be regarded as preliminary. Future multicentre studies with larger, ethnically diverse cohorts and transparent model interpretability frameworks will be important to confirm the robustness and clinical relevance of AI-based ocular age estimation.

Disclosure

The author reports no conflicts of interest in this communication.

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