Clinical Ophthalmology

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RESPONSE TO LETTER

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

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Dear editor

We would like to sincerely thank Dr. Elsaddig for taking the time to read our article "AI-Based Ocular Age Estimation from Combined OCT and OCTA Metrics: Decade-Stratified Normative Modelling in Healthy Eyes – a Pilot Study" and for providing such thoughtful and detailed comments, especially in the context of the rapidly growing literature in this field.

We fully agree with the key points raised regarding sample size, decade-wise balance, systemic covariates, and the need for external validation and model interpretability. These are indeed genuine limitations of our current work and were deliberately and explicitly acknowledged in the manuscript, as well as reflected in the designation of this study as a pilot study.

Our primary aim was to provide a proof-of-concept normative framework that integrates structural and vascular OCT/OCTA metrics for ocular age estimation, and to do so in a transparent manner that clearly exposes its current limitations. We share entirely Dr Elsaddig's view that:

- Larger, better-balanced, and ethnically more diverse cohorts,
- Systematic collection of systemic cardiovascular and metabolic variables,
- Independent external validation, ideally across different OCT/OCTA platforms, and
- More explicit model interpretability tools (eg SHAP or permutation-based feature importance)

These are all crucial next steps before any strong clinical claims can be made.

In fact, these elements form the core of our ongoing work. We are currently planning to extend the dataset in a multicentre setting, incorporating standardised systemic assessments and planning external validation on additional devices. We are also implementing feature-attribution approaches to better understand which structural and vascular components drive age predictions and to make the models more clinically interpretable.

We are grateful that Dr Elsaddig has highlighted these aspects so clearly. We see his letter as a constructive contribution that helps to frame our study in the appropriate context: not as a definitive statement, but as an early step towards robust, multimodal AI-based biomarkers of ocular ageing and, potentially, glaucoma susceptibility. It is precisely through such collegial critique and open discussion that the field can progress responsibly.

We thank Dr Elsaddig once again for his careful reading and valuable insights.

Received: 6 November 2025
Accepted: 10 November 2025
Published: 13 November 2025

Disclosure

The authors report no conflicts of interest in this communication.

https://doi.org/10.2147/OPTH.S579539