Fundus Refraction Offset (FRO) as an individualized myopia biomarker (2158-A0338)

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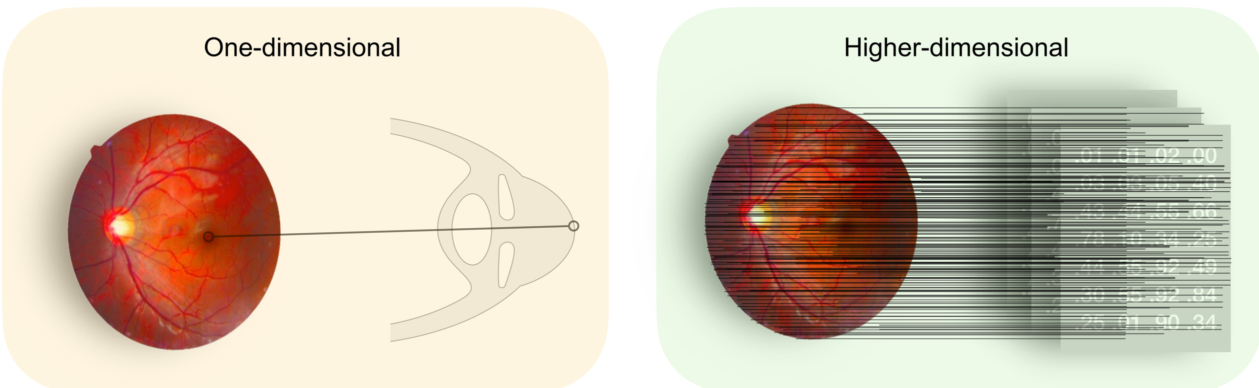
Introduction

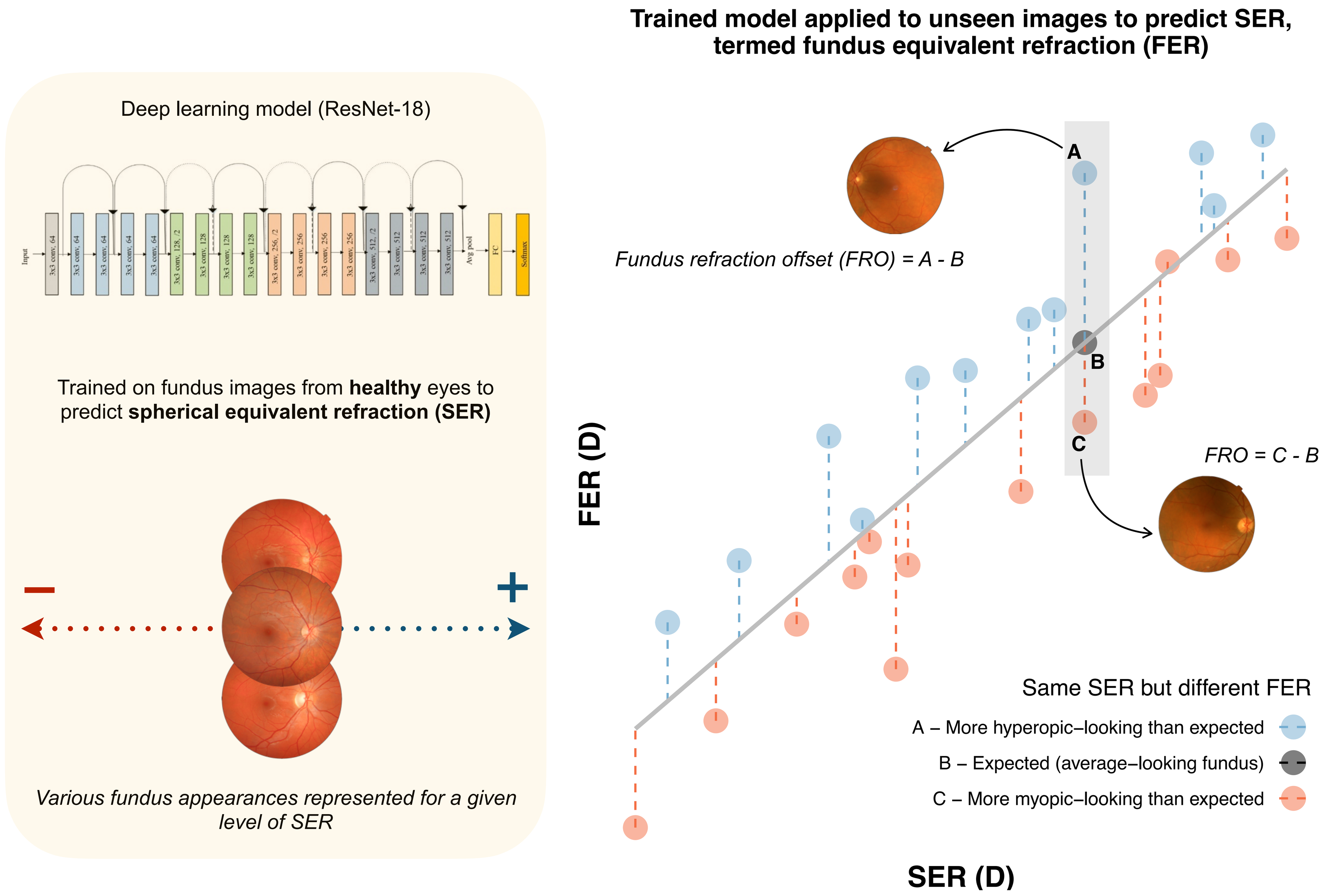
- As *on-axis* metrics, spherical equivalent refraction (SER) and axial length (AL) are limited in capturing individual-level differences in posterior segment anatomy.
- This may explain why fundi of eyes with similar myopia severity do not always 'look' equally myopic.
- To address this problem, we proposed a fundus-level metric—fundus refraction offset (FRO)—and investigated its association with OCT-derived parameters.



Spherical equivalent refraction and axial length are one-dimensional summaries of ocular dimensions along the visual axis (left). In contrast, Fundus Refraction Offset is derived from pixel-level information across an individual's fundus, making it a 'higher-dimensional' metric.

Methods

- Fundus photographs from 3,1670 healthy eyes in the UK Biobank were used to train a deep learning model to predict SER, with the goal of training a model that learned to capture the non-pathological variations in fundus appearance across a broad spectrum of SER.
- The trained model was applied to the internal (UK Biobank) unseen set (9524 eyes) and an external dataset (152 eyes) to derive FRO for each eye, defined as the error (residuals) in fundus-predicted SER.
- Internal unseen set: Association of FRO with macular thickness (MT) was tested, controlling for SER, age, sex and ethnicity.
- External dataset: Associations of FRO with choroidal area, choroidal vascularity index (CVI) and MT were tested—controlling for SER (and subsequently AL), age, sex and ethnicity.



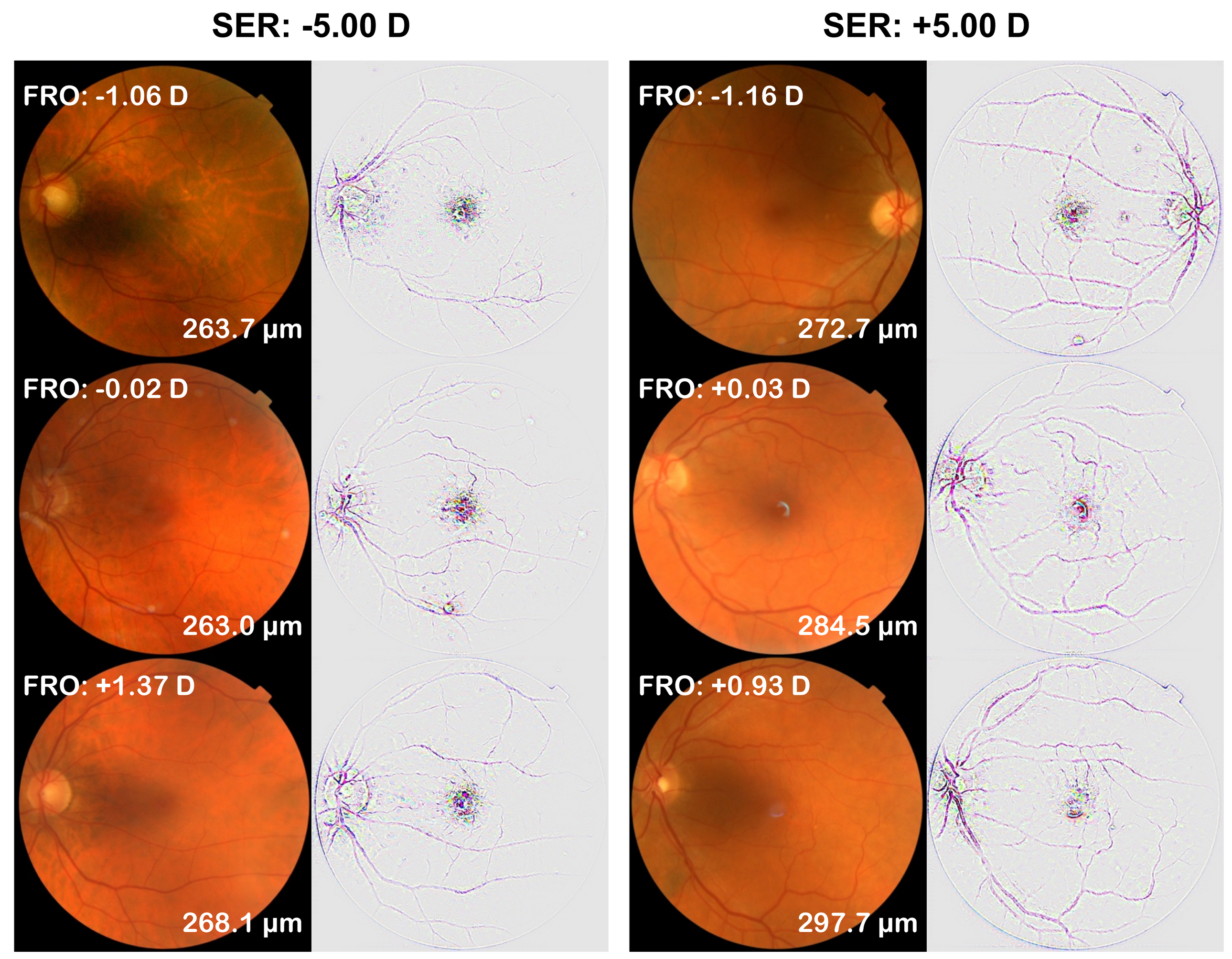
A trained deep learning model (left) was applied to unseen images to predict spherical equivalent refraction (SER) for each eye, with the predicted SER termed fundus equivalent refraction (FER) to distinguish it from SER in the strictly one-dimensional and on-axis sense. FRO was computed as the residuals from the line of best fit of FER vs SER, visually represented by the vertical dashed line in the scatterplot (right). For an eye with a given SER, a more negative FRO indicated a more myopic fundus appearance than typical for that SER.

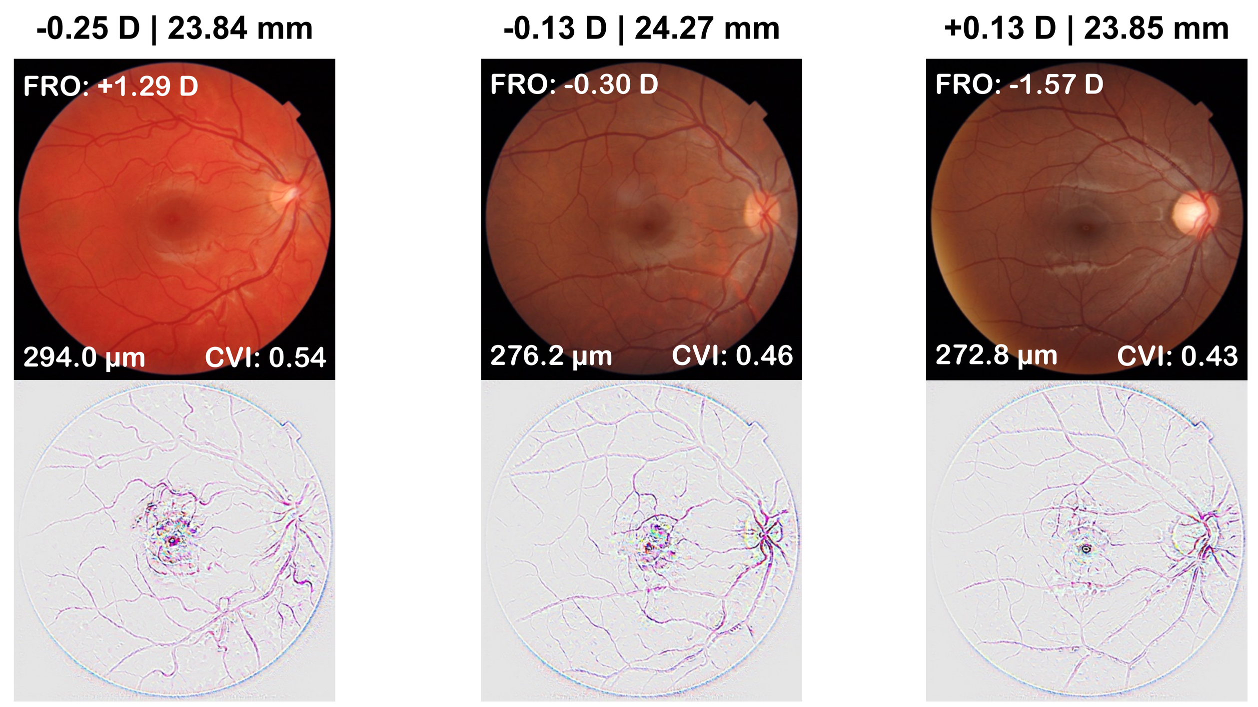
Results

- Internal unseen set: MT decreased with more negative FRO (β=0.64, 95% CI: 0.37-0.90, *P*<.001).
- External dataset: MT decreased with more negative FRO—in the SER-adjusted (β=2.45, 95% CI: 0.64-4.26, *P*=.008) and AL-adjusted (β=2.09, 95% CI: 0.28-3.91, *P*=.02) models. CVI also decreased with more negative FRO—in the SER-adjusted (β=0.01, 95% CI: 0.01-0.02, *P*<.001) and AL-adjusted (β=0.01, 95% CI: 0.004-0.02, *P*=.001) models.

Conclusions

- FRO reflects individual-level mismatch between on-axis measures of ametropia (SER or AL) and the 'anatomical' appearance of ametropia. This may have prognostic relevance for assessing the risks of myopia and its complications among eyes with similar SER or AL.





The top panel displays fundus photographs from eyes in the internal (UK Biobank) unseen set with similar spherical equivalent refraction (SER)—but varying fundus refraction offset (FRO)—along with their macular thickness. The bottom panel shows fundus photographs from eyes in the external dataset with similar SER and axial length (but varying FRO), along with their overall macular thickness and choroidal vascularity index (CVI). Attention maps highlighting fundus regions important for the prediction of fundus equivalent refraction are also displayed.

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