AI- Mapping the Genetic Basis of Retinal Thickness Using AI-Derived imaging Phenotypes

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The retina is the light-sensitive area of neural tissue at the back of the eye that enables vision. Comprised of several layers of highly specialised cells, the retina receives, and transmits light signals to the brain via the optic nerve. Optical coherence tomography (OCT), is a non-invasive imaging technique, from which morphological measures such as retinal thickness, may be derived. Changes in retinal thickness are a key feature of several eye diseases, and more recently have been suggested as a biomarker for neurodegenerative disease. The regions in which retinal thinning, or thickening occurs can be highly disease specific. Understanding the genetic drivers of retinal thickness, across specific retinal regions, may give insight into the biological processes underlying a range of diseases and eye health more generally.

Over 67,000 individuals from the UK Biobank underwent OCT imaging, as part of an ophthalmic assessment. Using these OCT data and AI-enabled image segmentation methods, we generated high resolution maps of retinal thickness, giving measurements at 29,041 locations (pixels) across the retina. We combined these retinal thickness measures, with genome-wide genotype data, to uncover the genetic drivers of retinal thickness using two approaches: 1) functional principal component (fPC) analysis was used to identify gross spatial patterns representing the major contributors to the variation of retinal thickness. We then undertook genome-wide association analyses (GWAS) using the top fPC scores as phenotypes. 2) by undertaking GWAS for all 29,041 pixels, allowing the examination of spatial patterns of associated genetic variants, at ultra-high resolution.