Supplementary Section 1

OCT-A scanning protocol, image analysis and indices extraction

The automatically generated superficial retinal layer (SRL) and deep retinal layer (DRL) en face images from the 3 mm × 3 mm and 6 mm × 6 mm macular angiograms were exported in png format (Portable Network Graphics) from all sessions for further analysis. The SRL images with the foveal avascular zone (FAZ) boundary automatically marked by the instrument's software were also exported from the instrument for each session whereas, the FAZ boundary in the DRL images were marked manually using custom written MATLAB program (MathWorks, Natick, Massachusetts, USA). To make sure that the OCT-A indices were obtained from the same retinal region and corrected for magnification between the sessions, the SRL and DRL images were analysed using a custom image analysis software. Figure S1 below provides an overview of the image analysis and index extraction process for SRL image of 3mm scan size. Firstly, image registration was performed to align the images captured at different times of the day for each participant to ensure that the indices within subjects were derived from the same retinal region. A set of three corresponding landmarks were manually tagged by a single observer first on the reference SRL image chosen randomly from either of the sessions for each participant and then on all the 14 SRL images one after the other. These points were then used to determine the transformation required for the 14 images to align them with respect to the reference image. Using this information, these 14 SRL and 14 DRL images aligned with each other respectively, compensating for any translation, rotation, and scaling between them. Then, the delineated FAZ from these images were adjusted for magnification calculated using the previously described schematic eye method⁷ and FAZ measurements were extracted.

These images were then binarised using local Sauvola binarization method followed by skeletonization. A modified ETDRS (Early Treatment Diabetic Retinopathy Study) with foveal zone (1mm region) and parafovea (2.5mm annulus) zone and its quadrants was rotated to the average amount of rotation from 7 sessions and adjusted for magnification (averaged magnification of the 7 sessions) for each participant using the previously described 3-surface schematic eye method ¹ to ensure that the indices between subjects were derived from the same sized retinal regions and centred on the 3mm images. Similar steps were used for the SRL and DRL images of 6mm scans, except that the modified ETDRS grid constructed here consists of central (2.5mm annulus) and perifovea (5mm annulus). The perifoveal annulus from the 6mm images were used for extracting indices. The ETDRS zones for the 3mm and 6mm OCT-A images have been depicted in Figure 1 of the manuscript.

Since vessel density has a linear component in it, to appropriately rescale vessel density apart from adjusting retinal regions, an additional correction i.e., Corrected vessel density = Vessel Density / magnification correction factor was also incorporated to the extracted vessel density values.

OCT scanning protocol, image analysis and thickness extraction

Two 5-line raster enhanced depth imaging (EDI) foveal centred OCT scans were captured. Raw raster OCT data were exported in img file and analysed using a custom written software in MATLAB. The OCT-A images from the raster line centred on the fovea were analysed using previously described automated deep learning methods to segment outer boundary of retinal pigment epithelium (RPE), outer nuclear plexiform layer/ outer plexiform layer (ONL/OPL) boundary, inner nuclear layer/inner plexiform layer (INL/IPL) boundary, and internal limiting membrane (ILM) (Figure 2).² All the images with their corresponding boundaries were manually corrected for any errors by a single experienced observer masked to the sessions. The transverse scale of the OCT data was then adjusted to account for ocular magnification for each session and participant using the schematic eye model ¹ and were used to derive mean total retinal thickness (axial distance from the RPE to the ILM), SRL thickness (axial distance from the INL/IPL boundary) ³ over the central 1mm foveal zone, 1.5mm parafoveal zone and 2.5mm perifoveal zone (Figure 2 of the manuscript).



Figure S1. Overview of the image analysis and indices extraction process for the SRL en face image from 3 mm × 3 mm macular angiogram (SRL: Superficial Retinal Layer, FAZ: Foveal Avascular Zone, ETDRS: Early Treatment Diabetic Retinopathy Study)