Non-invasive dual-conjugate adaptive optics imaging of human foveal capillary network

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Background

Imaging of retinal capillaries is a difficult task because of their small size (down to approximately 5 µm), low contrast, and arrangement in multiple planes of varying retinal depth. Even good-quality color retinal imaging fails to capture any of the finest capillary details.

In fluorescein angiography (FA), the current clinical gold standard for capillary imaging, a contrast agent is injected in the patient's bloodstream to enhance the contrast of the retinal vasculature. This is not performed on healthy eyes because of a small risk for adverse reactions.[1,2] However, many capillaries are not visualized in FA. An apparent discrepancy has been shown between capillary densities determined using histology and FA in both macaque and human retinas.[3,4] Smaller capillaries in the foveal slope and in deeper planes are often missed.

The technique of adaptive optics (AO) allows high-contrast imaging of retinal features on the order of microns, thus allowing for non-invasive imaging of the smallest capillaries.

Purpose

To demonstrate non-invasive imaging of foveal capillary networks with a high-resolution wide-field dual-conjugate adaptive optics (DCAO) imaging instrument,[5,6] and compare morphological findings with published data from the literature.

Method

The foveal capillary network of five normal subjects with no prior history of ocular or neurologic disease or surgery was imaged with a high-resolution wide-field DCAO instrument.

Images, scaled using individual retinal scaling factors (RSF), were postprocessed to correct for uneven illumination and to enhance contrast, and the foveal avascular zone (FAZ) in each image was defined using a manual procedure (Fig. 1). An automated algorithm, based on publicly available[7] and custom written software (MatLab; MathWorks, Natick, MA), was used to identify vessels and extract morphological FAZ and vessel parameters.

Capillary densities were calculated in two annular regions of interest (ROI) outside the FAZ (500 µm and 750 µm outer radius from the foveal center) and the superior, inferior, temporal, and nasal quadrants within the two ROI (Fig. 2).

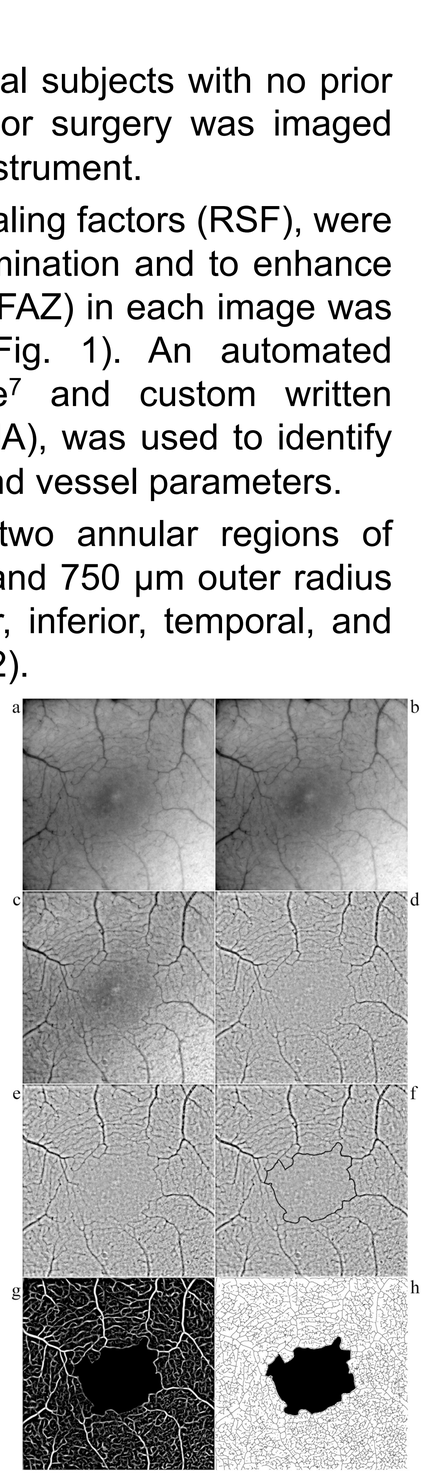

Fig. 1. Image postprocessing procedure: (**a**) Raw image, (**b**) spatial filtering, (**c**) CLAHE-filtering, (**d**) flat-fielding, (**e**) smoothing (Gaussian [σ = 1]), (**f**) spline curve fit to FAZ border, (**g**) vesselness filtering, (**h**) skeletonized tracing of identified vessels.

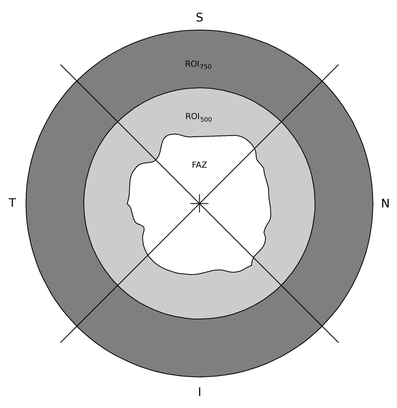

Fig. 2. Schematic drawing of ROIs and quadrants (N, nasal; I, inferior; T, temporal; S, superior) used in capillary density analysis in a right eye. Quadrants were horizontally mirrored to maintain nasotemporal classification for left eyes.

Table Subject data, individual retinal scaling factors (RSF*), and descriptive FAZ parameters.

Subject	Age	Eye	Axial length AL (mm)	q (mm/deg)	Retinal scaling factor RSF (µm/pixel)	FAZ perimeter (mm)	FAZ area (mm^2)	Major FAZ axis (µm)	Minor FAZ axis (µm)	Equivalent diameter# (µm)
TR	36	R	23.59	0.284	0.904	0.406	3898	830	651	719
JT	44	L	25.82	0.313	0.997	0.200	3030	580	488	505
PK	32	R	24.62	0.298	0.947	0.354	3008	692	660	671
HK	30	L	24.37	0.295	0.937	0.189	2498	602	413	491
BL	58	L	24.80	0.300	0.954	0.359	4409	816	604	676
Mean	40		24.64	0.298	0.948	0.302	3369	704	563	612
SD	10.2		0.72	0.009	0.030	0.100	769	116	108	106

* RSF = IPS† · P‡ · q

† Instrument plate scale, IPS = 0.43 deg/mm

‡ Instrument pixel size, P = 7.4 µm/pixel

The diameter of a circle with the same area as the FAZ.

Results

Mean FAZ area was 0.302 ± 0.100 mm^2 and mean equivalent diameter was 612 ± 106 µm. Mean capillary density (length/area) was 38.0 ± 4.0 mm^{-1} in the inner ROI and 36.4 ± 4.0 mm^{-1} in the outer ROI. The difference in ROI capillary density was not significant. There was no significant difference in capillary density between inner or outer ROI quadrants, nor between quadrants irrespective of ROI.

Conclusions

Mean FAZ area and mean equivalent diameter were similar to published data from the literature.[8-11] Non-invasive DCAO imaging yields lower capillary densities than histology[4] but similar results compared to published data from fluorescein angiography[4] and AO-SLO[11] studies.

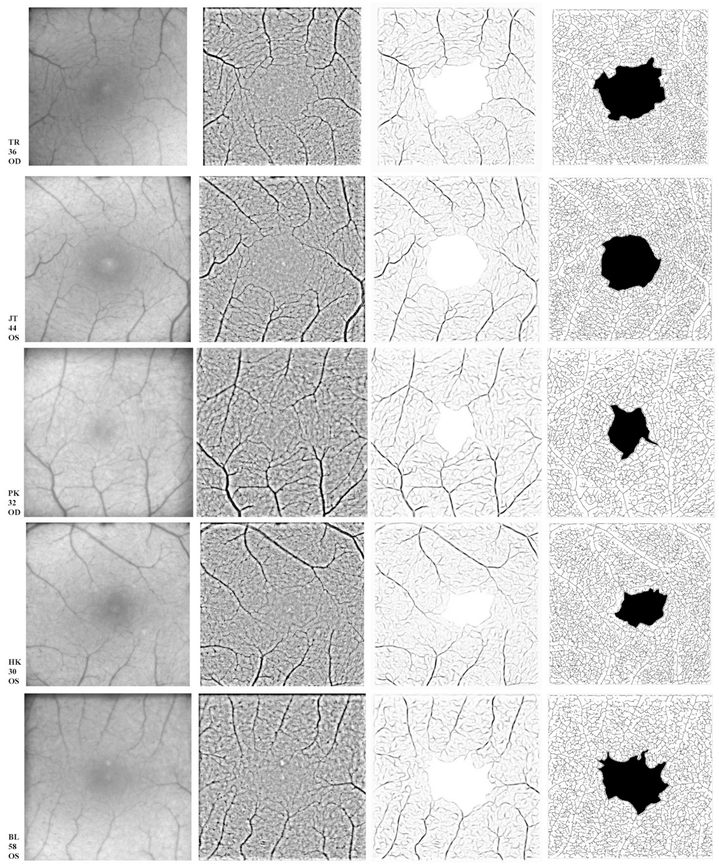

Fig. 5. Unprocessed images (left), processed images (middle left), image with identified vessels (middle right), and images of skeletonized vessels and FAZ (black central area). Images are scaled according to individual retinal scaling factor.

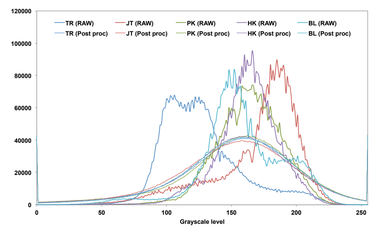

Fig. 4. Grayscale distribution of camera raw and post-processed images. The mean gray scale value of post-processed images was 152.7 ± 1.0 (mean ± SD).

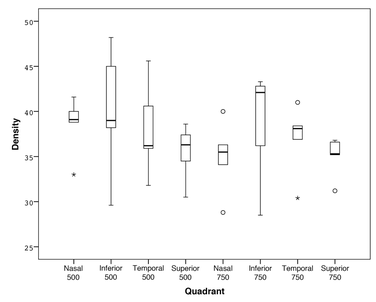

Fig. 5. Box plot of capillary densities in the N, I, T, and S quadrants of ROI500 and ROI750.

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