Retinal Vascular changes in Femtosecond Laser-Assisted Cataract Surgery by Optical Coherence Tomography Angiography

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Abstract

Purpose To assess the changes in retinal vasculature and thickness after femtosecond laser-assisted cataract surgery (FLACS) using optical coherence tomography angiography (OCTA).

Methods Fifty-six eyes of 56 patients with age-related cataract were enrolled in this study. Patients were divided into FLACS or conventional phacoemulsification surgery (CPS) due to the choice of operation. Vessel density (VD) and thickness at the macular area and optic nerve head (ONH) were checked by OCTA at baseline and at 1 day, 1 month and 3 months after cataract surgery.

Results In the FLACS group: The radial peripapillary capillary (RPC) density displayed a significant reduction during the follow-up ($P < 0.05$), even when the retinal nerve fiber layer (RNFL) thickness was not significantly changed. There was a significant negative correlation between the changes in RPC density and femtosecond laser-assisted pre-treatment time (FLAPT) at 1 day and 1 month after cataract surgery respectively (both $P < 0.05$). At 3 months postoperatively, the macular thickness had a significant increase in all regions (all $P < 0.05$). In the CPS group, the retinal VD and thickness did not show statistically significant changes in all regions during the follow-up (all $P > 0.05$). However, the best corrected visual acuity (BCVA) was significantly improved in both groups postoperatively (both $P < 0.001$).

Conclusions OCTA provided a promising analysis of retinal vascular alterations, demonstrating the reduction of RPC density and the increase of macular thickness after FLACS. However, these changes had no effect on the improvement of visual acuity after cataract surgery.

Introduction

Femtosecond laser-assisted cataract surgery (FLACS) has gained popularity in recent years. It has been used in several different stages of cataract surgery, including capsulotomy, lens fragmentation and liquefaction, and corneal incision []. The safety, efficacy, and predictability of FLACS have been confirmed by previous study [1]. However, some studies have reported that the cystoid macular edema was found after FLACS [,]. Moreover, Emeriewen et al. [] studied that patients experienced a decrease in visual acuity at different time-points caused by ischemic optic neuropathy after conventional cataract surgery. Li et al. [] indicated that there was a significantly reduction in superficial retinal vessel density in patients with myopia after conventional cataract surgery. Therefore, it remains unknown whether the vision decrease or retinal ischemic occurs after FLACS.

OCTA is a rapidly developing technology that allows the direct and non-invasive visualisation of retinal flow density. It works by tracking the motion of erythrocytes and comparing continuous B-scan signals from the same location. In addition, the technique also provides additional information on the retinal and choroidal capillary networks [,]. Therefore, OCTA has been used for the quantitative and qualitative investigation of the ocular vasculature [,]. The purpose of this study was to assess the retinal vasculature and thickness after cataract surgery using OCTA.

Subjects And Methods

Study Design

Fifty-six eyes of 56 consecutive patients with age-related cataract who underwent intraocular lens (IOL) implantation via either FLACS or CPS from August 2018 to July 2020 were included in this retrospective, interventional comparative case series. These procedures were performed uniformly at a single University Hospital (Tianjin Medical University Eye Hospital, Tianjin, China). Written informed consents were obtained from each subject based on their decision to proceed with either FLACS or CPS. The ethics committee of Tianjin Medical University approved the study, which is in accordance with the Declaration of Helsinki.

Exclusion criteria included the following: myopia or hyperopia to avoid the influence of magnification of the OCTA images, inflammatory cells in the anterior chamber > 5 postoperation, presence of amblyopia, media opacities which prevented high-quality imaging, dense cataracts, and ocular hypertension; and a history of systemic diseases such as hypertension, diabetes mellitus and cardiovascular disease, which might interference the ocular circulation; a history of previous ocular surgery; evidence of retinal pathologies, such as retinal vascular diseases; a history of trauma; and complications such as large fluctuation of blood pressure and posterior capsular rupture during operation.

Data Collection

Each participant underwent a comprehensive preoperative ophthalmic examination. Assessed metrics included the best-corrected visual acuity (BCVA); the intraocular pressure (IOP), as measured by Goldmann applanation tonometry; a refractive status assessment, as determined by an automatic refractometer; slit-lamp examination; and fundoscopy. Axial length (AL) was measured using the IOL Master system (Carl Zeiss, Meditec, Germany). Corneal topography was measured with a Scheimpflug device (Pentacam, Oculus Optikger ate GmbH). Endothelial cell count was determined with a specular microscope (SP-1P, Topcon Europe Medical B.V., Netherlands). B-scan ultrasound recording was also documented (AVISO, Quantel Medical, Clermont-Ferrand, France). Any performed procedures or analyses were conducted by an optometrist or technician.

OCTA image acquisition and processing

OCTA image was obtained using RTVue XR OCT (Optovue, Inc., Fremont, CA, USA; Software V.2017.1.0.155). The split-spectrum amplitude decorrelation algorithm (SSADA) was used to extract OCTA images, which operates A-scan of 70, 000 HZ scans per second. During image processing, the Motion Correction Technology function was used to correct the horizontal and vertical scans for eye movement []. Automatic segmentation was performed by the Optovue software to generate en face projection images. All scans with layer segmentation error, signal strength index < 50, or significant motion artefacts in images were excluded to ensure the accuracy of the measurement.

The ONH area was measured using a 4.5 × 4.5-mm OCTA scan. The RPC density was automatically captured from the optic disc segment that extended in a 0.75-mm-wide elliptical annulus from the ONH boundary []. The RNFL thickness measurements were obtained using a 3.45 mm radius ring centred on the optic disc (Fig. 1). The macular area was covered using a 3.0 × 3.0-mm OCTA scan. The superficial capillary plexus (SCP) was automatically selected from 3 μm below the inner limiting membrane (ILM) to 15 μm below the inner plexiform layer (IPL) (Fig. 2); the deep capillary plexus (DCP) was automatically selected from 15 μm to 70 μm below the IPL []. The macular thickness was measured from the ILM to the middle of the retinal pigment epithelium (RPE)-Bruch membrane complex. The measurement area of fovea was 1 mm diameter in the centre of macula. The measurement area of parafovea was 2 mm ring zone surrounding the fovea. Blood flow was calculated automatically in a selected area of 3144 mm^2, which was centered on the fovea in the choriocapillary bed from 31 μm below RPE to 59 μm below the RPE [12].

Femtosecond laser-assisted pre-treatment and cataract surgical procedures

The femtosecond laser-assisted pre-treatment was performed by a surgeon, using a femtosecond laser (Lensx, Alcon Laboratories, Inc.). The LenSx system consists of a 50 kHz femtosecond infrared laser with a pulse width of 600–800 femtoseconds, a central laser wavelength of 1,030 nm, and a maximum pulse energy of 15 μJ. The laser pulse energy setting was 6 μJ for performing the anterior capsulotomy (diameter: 5.2 mm). This laser is combined with a 3D spectral-domain OCT system providing visualization of the entire anterior segment during the surgical procedure and a liquid-free curved patient interface (SoftFit). The femtosecond laser system was used for capsulotomy, lens fragmentation, and corneal incision. All cataract surgical procedures were performed under local anaesthesia.

After the femtosecond laser treatment, each participant was transferred to another operating room for the remainder of the procedure. Phacoemulsification was completed using torsional phacoemulsification on an active-fluidics-based platform (Centurion® Alcon Laboratories, Inc., USA). Patients undergoing CPS were prepared for surgery in the same way as those in the femtosecond laser arm. Instead of receiving laser pre-treatment, they directly underwent the operation. The default intraocular len (IOL) used in the capsular bag was a hydrophobic acrylic IOL (Alcon Laboratories, Inc., USA). Patients received levofloxacin (Cravit) and prednisolone acetate 1% (Pred Forte) eyedrops four times a day for 1-week after the surgery, followed by tapering for 3 weeks for both groups.

Statistical Analysis

The normality of data distribution was tested using the Kolmogorov-Smirnov test. After confirmation of the normality assumption, data are generally presented as mean ± standard deviation (SD) values. The comparisons of baseline were performed using t-test. The preoperative and postoperative measurements were compared using repeated measures analysis of variance tests with Bonferroni corrections. Pearson correlation analyses were performed to determine the relationships between the changes in peripapillary vessel density at each timepoint postoperatively and related clinical factors. Statistical analyses were performed using SPSS version 22.0 (SPSS, Inc., Chicago, IL, USA). Probability values of $P < 0.05$ were considered statistically significant.

Results

A total of 56 eyes of 56 individuals were included in this study. 26 cases were enrolled in the FLACS group. The remaining 26 cases were enrolled in the CPS group. No cases were excluded because of poor scan quality or complications after the surgery. Results of statistical analysis of the patient characteristics are presented on Table 1.

Table 1
Patient demographic and clinical characteristics.

Parameters	FLACS group(n = 30)	CPS group(n = 26)	*P*
Sex, male/female (n)	12/18	14/12	0.324
Age (y)	63.13 ± 5.28	65.50 ± 6.85	0.151
BCVA	0.63 ± 0.14	0.62 ± 0.12	0.760
IOP(mmhg)	15.35 ± 3.53	14.24 ± 3.10	0.217
SE (D)	-0.05 ± 0.57	-0.22 ± 0.68	0.321
CCT(μm)	540.07 ± 19.85	537.38 ± 20.63	0.581
ACD (mm)	3.74 ± 0.17	3.70 ± 0.14	0.318
AL (mm)	23.45 ± 0.73	23.43 ± 0.66	0.921
SBP(mmHg)	117.47 ± 5.77	118.23 ± 8.32	0.688
DBP (mmHg)	75.20 ± 7.43	74.19 ± 7.96	0.626
MAP (mmHg)	89.31 ± 5.40	88.87 ± 6.58	0.785
MOPP (mmHg)	49.31 ± 4.02	49.75 ± 4.31	0.688
Pulse (bpm)	75.13 ± 7.07	76.65 ± 8.61	0.471
Glucose (mmol/L)	5.31 ± 0.44	5.35 ± 0.48	0.706
HbA1c (%)	5.09 ± 0.51	5.09 ± 0.59	0.953
Cholesterol (mmol/L)	4.32 ± 1.04	4.48 ± 0.89	0.543
Triglycerides(mmol/L)	1.31 ± 0.22	1.47 ± 0.59	0.172

Means ± SD;

BCVA: best corrected visual acuity, IOP: intraocular pressure, SE: spherical equivalent, CCT: central corneal thickness, ACD: anterior chamber depth, AL: axial length, SBP: systolic blood pressure, DBP: diastolic blood pressure, MAP: mean arterial pressure, MOPP: mean ocular perfusion pressure, bpm: beat per minute, MAP = DBP + 1/3(SBP - DBP), MOPP = 2/3MAP - IOP;

The FLACS group showed a longer surgical time compared to the CPS group (FLACS: 371.47 ± 62.95 s vs. CPS: 337.35 ± 40.10 s; $P = 0.021$). In addition, the irrigation/aspiration time (I/A T) was significantly shorter when patients were treated via CPS than via FLACS (FLACS: 100.90 ± 15.31 s vs. CPS: 90.92 ± 8.28 s, $P = 0.004$). There was no difference in either effective phacoemulsification time (EPT) or balanced salt solution (BSS) in both groups (EPT: $P = 0.220$; BSS: $P = 0.083$). Table 2 summarises the intraoperative outcomes of participants.

Table 2
Intraoperative outcomes for all eyes in the FLACS or CPS group.

Parameters	FLACS group	CPS group	*P*
FLAPT (s)	135.37 ± 19.99	-	—
EPT (s)	69.93 ± 15.75	64.92 ± 14.28	0.220
I/A T (s)	100.90 ± 15.31	90.92 ± 8.28	0.004
BSS (ml)	78.00 ± 14.24	71.92 ± 10.96	0.083
CDE (%)	2.08 ± 1.26	2.35 ± 0.67	0.333
TOT (s)	371.47 ± 62.95	337.35 ± 40.10	0.021

Means ± SD;

FLAPT: femtosecond laser-assisted pretreatment time, EPT: effective phacoemulsification time, I/A T: irrigation/aspiration time, BSS: balanced salt solution, CDE: cumulative dissipated energy, TOT: total operating time;

The BCVA was significantly better in each group at all time-points after surgery (FLACS: $P < 0.001$; CPS: $P < 0.001$). The IOP were similar in each group during the follow-up (FLACS: $P = 0.580$; CPS: $P = 0.526$). There were no differences in BCVA and IOP at each time point between the FLACS and CPS groups (all $P > 0.05$).

In the FLACS group, the RPC density was significantly decreased after surgery ($P < 0.001$). However, there was no statistically significant change in the macular VD during the follow-up (all $P > 0.05$). In the CPS group, there was no significant change in the VD in the ONH and macular area at any time-point after surgery (all $P > 0.05$) (Table 3 and Table 4).

Table 3
OCTA parameters in the FLACS group.

	Baseline	**1 day**	**1 m**	**3 m**	***P***
SCP (%)					
Whole Image	42.73 ± 4.37	42.34 ± 4.24	41.47 ± 4.09	40.82 ± 3.88	0.280
Parafovea	46.93 ± 5.3	46.56 ± 5.20	45.65 ± 4.27	45.51 ± 4.45	0.608
Fovea	17.25 ± 2.64	17.41 ± 2.48	16.78 ± 2.65	16.40 ± 2.39	0.410
DCP (%)					
Whole Image	47.44 ± 4.31	45.21 ± 3.80	46.75 ± 4.20	46.92 ± 4.02	0.182
Parafovea	49.37 ± 5.72	47.11 ± 5.68	48.17 ± 5.63	49.05 ± 5.49	0.409
Fovea	26.75 ± 5.88	25.06 ± 5.66	25.60 ± 5.83	26.55 ± 5.76	0.636
RPC (%)					
Whole Image	49.39 ± 2.89	47.26 ± 2.18	47.71 ± 2.79	48.04 ± 2.53	0.014
Peripapillary	54.23 ± 3.66	51.17 ± 2.54	51.35 ± 2.76	52.10 ± 3.59	< 0.001

Means ± SD;

SCP: superficial capillary plexus, DCP: deep capillary plexus, RPC: radial peripapillary capillary;

Table 4
OCTA parameters in the CPS group.

	Baseline	**1 day**	**1 m**	**3 m**	***P***
SCP (%)					
Whole Image	44.54 ± 2.39	44.84 ± 2.35	44.13 ± 2.34	44.99 ± 2.26	0.546
Parafovea	46.66 ± 2.74	47.02 ± 3.06	46..33 ± 2.80	46.66 ± 2.85	0.861
Fovea	18.39 ± 4.36	19.05 ± 4.06	18.35 ± 3.96	19.02 ± 4.22	0.880
DCP (%)					
Whole Image	47.71 ± 4.46	47.24 ± 4.51	48.30 ± 4.34	47.50 ± 4.45	0.844
Parafovea	50.47 ± 4.91	49.25 ± 5.10	50.88 ± 5.09	51.06 ± 4.91	0.562
Fovea	30.99 ± 7.01	29.65 ± 6.60	31.25 ± 6.82	32.05 ± 5.96	0.622
RPC (%)					
Whole Image	48.40 ± 2.26	48.99 ± 2.66	49.53 ± 1.99	49.56 ± 3.37	0.339
Peripapillary	52.89 ± 2.89	53.25 ± 2.76	53.32 ± 2.19	53.40 ± 3.50	0.925
Means ± SD;					
SCP: superficial capillary plexus, DCP: deep capillary plexus, RPC: radial peripapillary capillary;					

In the FLACS group, there was a statistically significant change in the macular thickness after surgery. At 3 months postoperatively, the macular thickness had a significant increase in all regions (all $P < 0.05$). However, there was no significant change in the macular thickness in the CPS group at any time-point after surgery (all $P > 0.05$). Moreover, no significant change was found in the RNFL thickness in both groups during the follow-up (all $P > 0.05$) (Table 5).

Table 5
Measured macular thickness and RNFL thickness in both groups.

		Baseline	1 d	1 m	3 m	*P*
FLACS group	Macular thickness (μm)					
	Whole image	306.07 ± 7.54	301.87 ± 7.37	307.66 ± 7.21	308.73 ± 7.13	0.002
	Parafovea	315.63 ± 9.68	312.20 ± 8.35	319.50 ± 7.56	319.17 ± 8.20	0.003
	Fovea	248.63 ± 11.95	243.50 ± 9.69	252.10 ± 8.64	250.53 ± 18.32	0.006
	RNFL (μm)					
	Average	110.37 ± 12.82	115.17 ± 14.05	114.27 ± 14.07	112.90 ± 15.15	0.575
CPS group	Macular thickness (μm)					
	Whole image	305.12 ± 8.71	303.65 ± 6.99	306.12 ± 7.92	306.39 ± 6.91	0.173
	Parafovea	315.04 ± 11.82	312.46 ± 11.67	317.19 ± 14.25.	318.38 ± 11.37	0.329
	Fovea	248.96 ± 13.73	245.45 ± 11.11	252.19 ± 14.25	253.39 ± 11.38	0.113
	RNFL (μm)					
	Average	110.81 ± 10.77	117.42 ± 12.08	114.46 ± 12.23	115.19 ± 11.82	0.240
Means ± SD;						
RNFL: retinal nerve fiber layer;						

The Pearson correlation analyses between the changes in RPC density and other clinical factors revealed that the FLAPT was significantly correlated with the changes in the RPC density at 1 day and 1 month respectively after surgery (r = 0.506, $P = 0.004$; r = 0.367, $P = 0.046$) (Fig. 3). However, no significant correlation was found for age, mean ocular perfusion pressure (MOPP), EPT, I/A T, BSS, cumulative dissipated energy (CDE), total operating time (TOT) and RNFL (all $P > 0.05$, Table 6).

Table 6
Correlation between the changes in RPC density postoperatively and variation in FLACS group.

Factors	1 d		1 m		3 m	
	r	p	r	p	r	p
Age(yrs)	0.031	0.873	0.069	0.718	0.144	0.448
MOPP (mmHg)	0.150	0.428	0.002	0.993	0.341	0.065
FLAPT (S)	0.506	0.004	0.367	0.046	0.223	0.236
EPT (S)	0.093	0.624	0.034	0.860	0.002	0.990
I/A T (S)	0.288	0.123	0.159	0.400	0.185	0.329
BSS (ml)	0.068	0.721	0.047	0.806	0.141	0.458
CDE	0.044	0.819	0.160	0.398	0.023	0.903
TOT (S)	0.017	0.928	0.070	0.714	0.127	0.504
RNFL (μm)	0.074	0.697	0.106	0.579	0.101	0.596
Means ± SD;						
BSS: balanced salt solution, CDE: cumulative dissipated energy, EPT: effective phacoemulsification time, FLAPT: femtosecond laser-assisted pretreatment time, MOPP: mean ocular perfusion pressure, I/A T: Irrigation/aspiration time, IOP: intraocular pressure, RNFL: retinal nerve fiber layer, TOT: total operating time;						

Discussion

In this study, the RPC density was significantly decreased postoperatively in the FLACS group, even when the RNFL thickness was not significantly changed. However, OCTA detected no statistically significant changes in the RPC density and RNFL thickness in the CPS group during the follow-up.

The reason for the changes in RPC density was not fully clear. Radial peripapillary capillaries constitute a superficial layer of capillaries with a relatively constant calibre, and these run parallel to the retinal nerve fibre layer in the peripapillary region []. Considering the unique pattern and distribution of the vessels, the RPC was considered to be particularly vulnerable to elevated IOP when compared with other retinal capillarie []. Previous studies on laser in the femtosecond pre-treatment in cataract surgery reveal that the application of docking may cause a transient and irregular elevation of IOP [,]. Ecsedy et al. [] determined that the application of the suction ring increased patient's IOP by up to 40 mmHg. While the IOP decreased after removing the suction ring, it remained above baseline [15]. A broad IOP fluctuation can restrict ocular blood flow and lead to retinal ischaemic and neuropathic injury [-]. Therefore, we speculate that the intense intraoperative IOP fluctuations may produce an acute injury to the retina, leading to RPC density reduction after FLACS surgery.

Another reason for the changes in RPC density might be postoperative inflammation. It has been shown that prostaglandin levels increase more noticeably after FLACS than after CPS [,]. The release of prostaglandins can lead to postoperative inflammation and consequently, the breakdown of the blood-retinal barrier []. Furthermore, thermal damage from prolonged laser treatment and mechanical microtrauma from femtosecond laser pulses may also contribute to the elevated inflammation [,]. Residual particulate lens material can stimulate inflammation and lens fragmentation following FLACS additionally cause prostaglandin-associated inflammation []. The changes in inflammatory factors and prostaglandin levels may result in the reduction of RPC density in FLACS.

Our findings showed a significant negative correlation between the changes in RPC density and FLAPT at 1 day and 1 month after surgery. However, there were no statistically significant correlations between the changes in RPC density and other clinical factors, such as: I/A time and total operating time. In this study, the FLACS required a longer surgical time and I/A time than did the CPS. Perhaps the vertical application of the femtosecond laser to the cortex below the anterior capsule can cause a structural change, which can in turn make cortical cleaving hydrodissection more difficult. The remaining cortical layer also has the potential to render I/A more difficult to perform []. Moreover, in order to reduce the intraoperative damage of blood-retinal barrier, we specifically excluded patients with moderate to severe cataract to lower the CDE. This may be why we did not observe correlations between the changes in RPC density and I/A time and total operating time.

Although there was no statistically significant change of the VD in the macular area in both groups, we observed increases in macular thickness at 1 month postoperatively and this increase remained 3 months after surgery. These changes had no effect on the improvement of visual acuity after cataract surgery, even though the differences reached the threshold of statistical significance in FLACS group instead of CPS group. Several researches reported the increase of retinal thickness after cataract removal, which was suggested to result from the breakdown of the blood-retinal barrier [,]. In the present study, the TOT was 371.47 ± 62.95 s in the group and 337.35 ± 40.10 s in the CPS group. There was a significant difference in the operating time between the two groups, which was in accordance with the comparison of I/A time [27]. Furthermore, the intraoperative CDE was 2.08 ± 1.26% in the FLACS and 2.35 ± 0.67% in the CPS group as the patients enrolled with mild cataract. In addition, phacoemulsification was completed using torsional phacoemulsification on an active-fluidics-based platform, which could maintain the relatively minor changes in IOP []. Therefore, the shorter operation time, less intraoperative injury and the relatively minor changes in IOP could contribute to the result.

One limitation of this study is that the number of included participants represents a relatively small sample size, and therefore, our results may have been influenced by the short follow-up time. Further longitudinal studies involving larger numbers of patients are thus needed.

In conclusion, OCTA provided a promising analysis of retinal vascular alterations, demonstrating the reduction of RPC density and the increase of macular thickness after FLACS. However, these changes had no effect on the improvement of visual acuity after cataract surgery.

Declarations

Declaration of conflicting interests

The authors declare that there is no conflict of interest regarding the publication of this article.

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Data Availability

The data used to support the findings of this study are available from the corresponding author on request.

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Figures

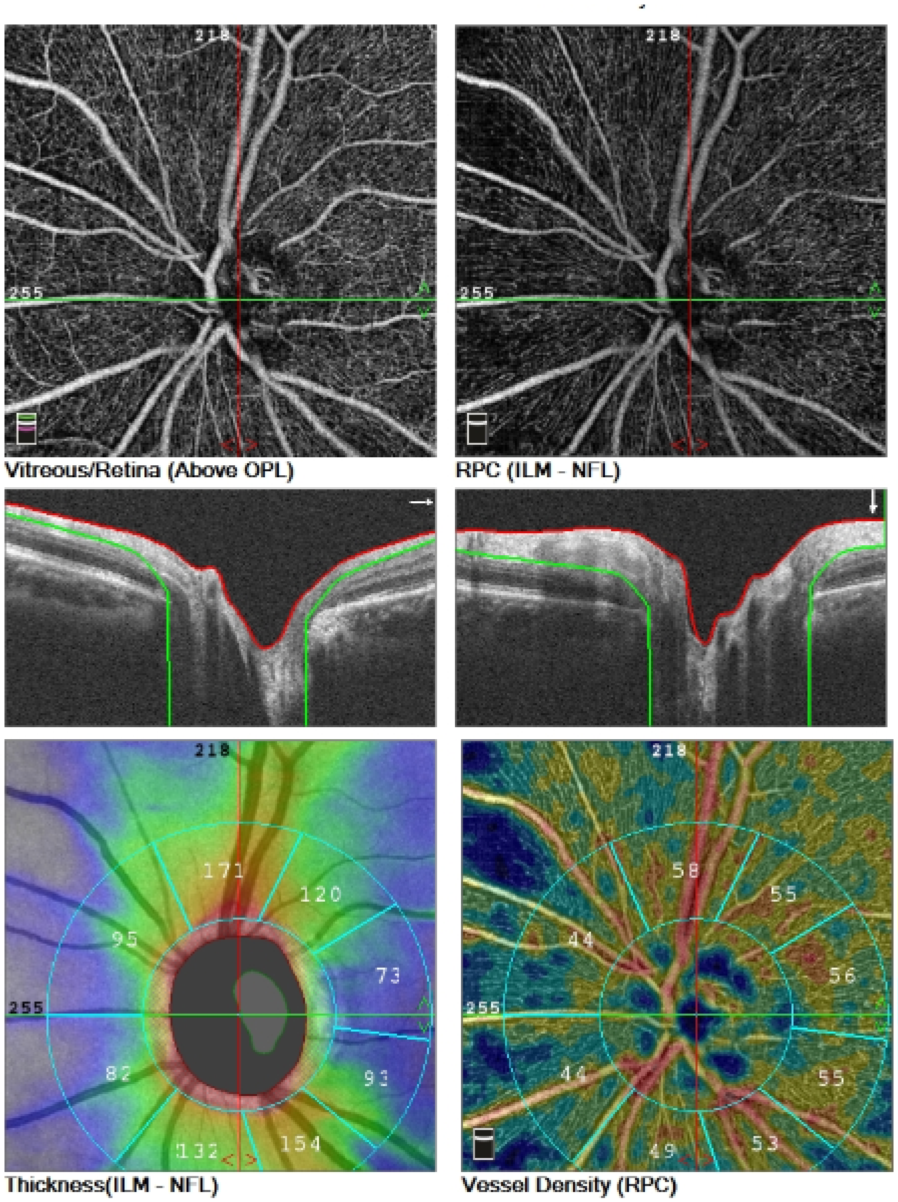

Figure 1

A 4.5 × 4.5-mm image of optic disc angiogram.

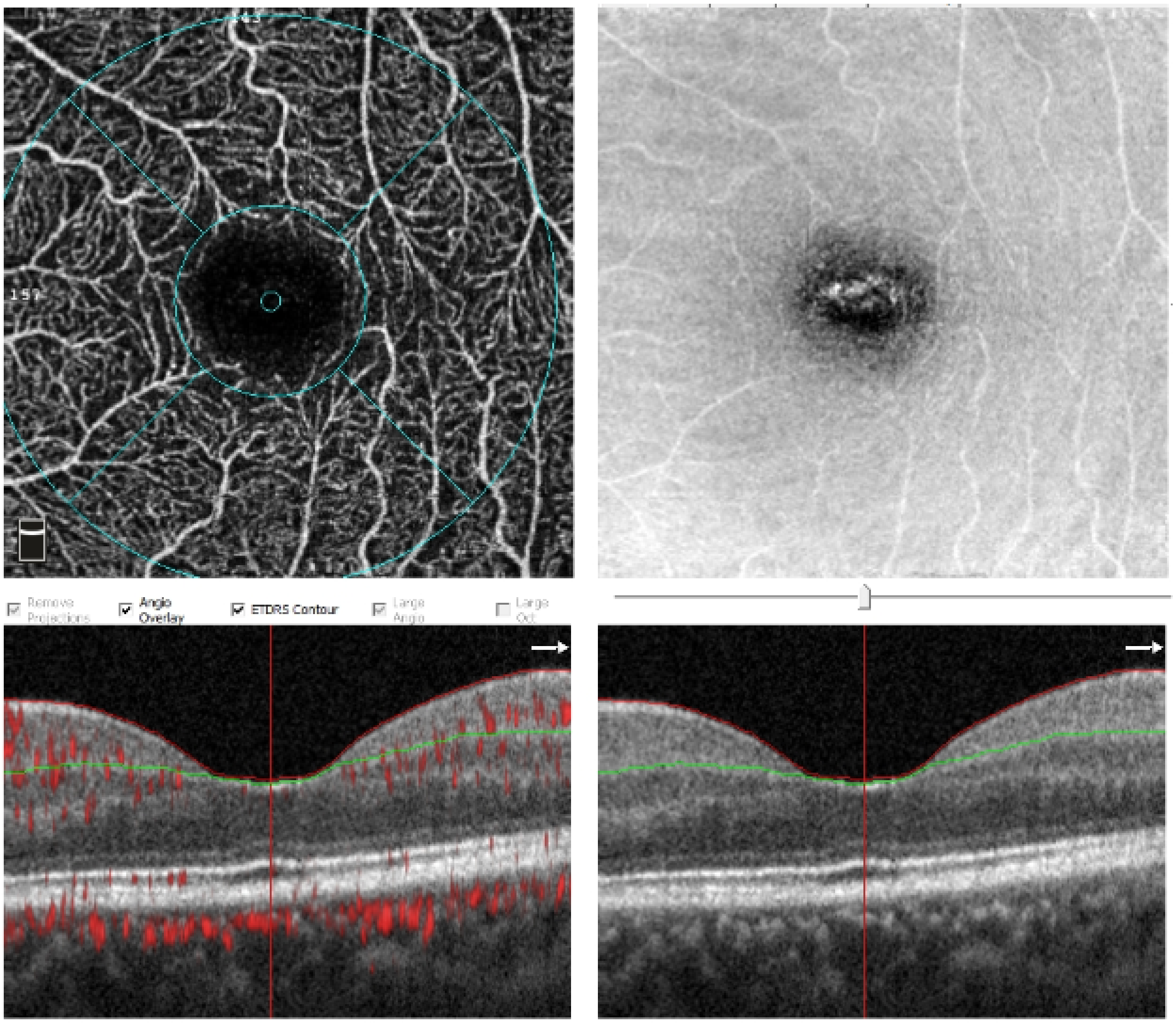

Figure 2

A 3 × 3-mm image of superficial capillary plexus angiogram.

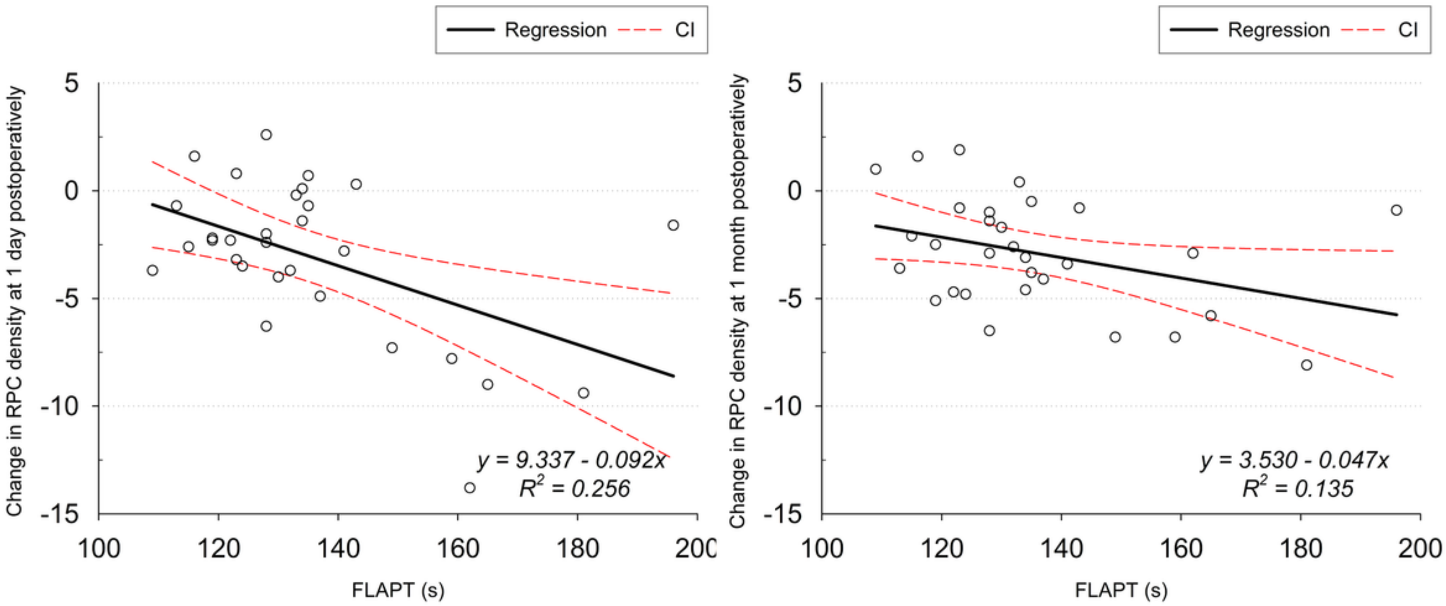

Figure 3

Scatterplots. The FLAPT is negatively correlated with the changes in RPC density at 1 d (Left) and 1 month (Right) postoperatively.