# Optical coherence tomography angiography evaluation of the effects of phacoemulsification cataract surgery on macular hemodynamics in Chinese normal eyes

**Xinyu Jia**
Tianjin Medical University
**Yinjuan Wei**
Tianjin Eye Hospital
**Hui Song** (songh221@hotmail.com)

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# Abstract

Background: To quantitatively evaluate the possible effects of phacoemulsification cataract surgery on macular hemodynamics using optical coherence tomography angiography (OCTA). Methods： Prospective observational study. Superficial and deep macular vascular densities as well as parameters of foveal avascular zone (FAZ) were measured preoperatively (baseline) and at 1 day, 1 week and 4 weeks postoperation in normal eyes (≥22 mm and≤24 mm) of patients scheduled for phacoemulsification cataract surgery with intraocular lens implantation. Correlations between the rate of change of pre- and post-operative vascular densities and surgical parameters were analyzed. Results : 123 eyes of 107 patients were recruited. Compared with baseline measurements, no statistically significant variation was found in macular vascular densities of day one after surgery ($P>0.05$). While both superficial and deep macular vascular densities were significantly increased postoperatively on week 1 and week 4 ($P<0.05$; $P<0.05$). There were no statistically significant differences in any of the FAZ parameters between the baseline measurements and the entire follow-up period ($P>0.05$ for all). There were no statistically significant correlations between main surgical parameters and the macular vascular densities. Conclusions : In normal eyes, macular blood perfusion gradually increased after phacoemulsification cataract surgery and was stabilized in one week. Foveal avascular zone was basically stable before and after surgery. Main parameters and intraoperative perfusion of phacoemulsification surgery may not be the key factors affecting macular hemodynamics.


# 1. Background

Since the first phacoemulsifier was invented by Kelman in 1967, with the technological innovation during half a century, phacoemulsification cataract surgery with intraocular lens implantation has become the most commonly used procedure for the treatment of cataract as a result of its small incision, short operation time, and rapid postoperative recovery. Specific perfusion is necessary to maintain the stability of the anterior chamber during cataract extraction. And this may cause transient intraocular pressure (IOP) fluctuations during surgery which consequently result in corneal edema, poor visual acuity, and longer time to recovery after surgery[1–2]. Whether the intraoperative perfusion and other surgical factors may cause fundus hemodynamic changes, especially macular microcirculation changes is worth exploring. However, there has been little research of this issue due to technical limitations[3–4]. Therefore, this study was designed to prospectively evaluate hemodynamic changes of the macular microcirculation in patients before and after phacoemulsification cataract surgery using OCTA.

# 2. Methods

## 2.1 Participants

All subjects were from a Han Chinese population and were recruited from May 5, 2019 to June 22, 2019 in Tianjin Eye Hospital (Tianjin, China). All participants were informed of the purpose of the research and provided written informed consent prior to entering the study. This prospective study was approved by the

Ethical Review Committee of the Tianjin Eye Hospital and adhered to the provisions of the Declaration of Helsinki for research involving human subjects.

All subjects underwent a comprehensive preoperative ophthalmologic examination. Cataract severity was assessed using the Lens Opacities Classification system III (LOCS scale)[5]. Demographic information and medical history were recorded for all subjects, and their heart rates (HR) and blood pressures (BP) were measured before the time of the OCTA imaging. Subjects were included if they met the following criteria: patients diagnosed with age-related cataracts; age 60–70 years old; normal eyes (≥ 22 mm and ≤ 24 mm) and normal IOP; LOCS-N: 2–3+. Exclusion criteria were patients with diabetes, hypertension and other systemic vascular disease; history of intraocular surgery or history of ocular trauma; history of laser treatment of the eye; history of high intraocular pressure or glaucoma; history of any fundus disease. In addition, patients with obvious postoperative anterior chamber inflammation or corneal edema under slit lamp examination will be excluded.

A single experienced surgeon operated in all patients included in the study. Tropicamide eye drops (Santen Pharmaceutical Co., Ltd., Osaka, Japan) were used for mydriasis 30 min before surgery, and cimetidine hydrochloride eye drops (Alcon, Fort Worth, TX, USA) were used for surface anesthesia. A 3.0-mm clear corneal tunnel incision was made above the temporal or the nasal of eyes with a scalpel. Continuous circular capsulorhexis were made, and nuclear hydrodissection were carried out. The lens was removed by phacoemulsification (Stellaris, Bausch & lomb Incorporated Rochester, NY, USA) with the bottle height of 90 cm. After polishing, IOLs were placed to the capsular bag and the incision was sealed. The effective phacoemulsification time (EPT) and cumulative dissipated energy (CDE) were noted at the end of each case from the metrics of the phacoemulsification machine.

## 2.2 OCTA Image acquisition and data collection

Optical coherence tomography (OCTA) has emerged as a novel, rapid, non-invasive imaging modality that allows generating volumetric vascular images in seconds without the need to intravenously administer fluorescent dyes. It has broad applicability to retinal choroidal vascular disease and provides quantitative measurements of retinal vascular density[6–8]. This study used the OCTA system (RTVue-XR; Optovue, Inc., Fremont, CA, USA) to detect blood flow. During the study, OCTA measurements were performed four times in each subject eye. The first measurement was performed one day before the cataract surgery (baseline), the second measurement was performed one day after the cataract surgery, and the last two measurements was performed one week and four weeks after the cataract surgery. To evaluate macular vessels, a 6 mm × 6 mm scanning area centered on the macula was acquired and automatically divided into two segments, including the superficial (ILM to IPL-10 μm) and deep capillary plexuses (IPL-10 μm to OPL + 10 μm). Superficial and deep vascular density (%) were automatically quantified by the OCT machine’ s inner software (version 2014.2.0.93). Image acquisition and evaluation were performed by two experienced researchers independently, and images with low quality (scan quality < 6) and excessive artifacts were excluded. Subsequently, parameters including superficial and deep macular vascular densities of the whole image, foveal avascular zone (FAZ) area, FAZ perimeter (PERIM) and acircularity index (AI) were derived and recorded. The rate of change in vascular density was calculated by the difference in vascular density before and one day after surgery, divided by preoperative blood vascular density. See Fig. 1 for details.

## 2.3 Statistical analysis

SPSS (IBM, SPSS statistics, Version 20.0; SPSS Inc, Chicago, IL) was used for statistical analysis. The distribution of numeric variables was assessed by inspecting histograms and using Shapiro-Wilk tests of normality. Qualitative data are expressed in terms of frequency and numeric data are presented as the mean ± standard deviation (SD). $\chi^2$ test were used for categorical variables. Repeated measures of variance analysis were used to compare the four-time repeated measurements. The relationships between the rate of change of pre- and post-operative vascular densities and surgical parameters (EPT and CDE) were analyzed using Pearson correlation analysis. $P < 0.05$ was assumed to be statistically significant.

## 3. Results

Of all subjects enrolled in the study,6 eyes were excluded due to unclear refractive interstitial or poor fixation which conducted low quality scans. In the end, a total of 123 eyes of 107 patients were included in the study. The mean age of these patients was 63.2 ± 2.7 years. The demographic and clinical characteristics of the subjects were summarized and compared in Table 1.

Table 1
Demographic and clinical characteristics of the included patients.

| Parameters | Subclass | Numerical value |
| --- | --- | --- |
| Gender, n (%) | Male | 45 (42%) |
| | Female | 62 (58%) |
| Age, n (%) | 60 < Age ≦ 65 | 52 (49%) |
| | 65 < Age ≦ 70 | 55 (51%) |
| Eye, n (%) | Right | 73 (60%) |
| | Left | 50 (40%) |
| LOCS-N, n (%) | 2 ≦ nuclear < 3 | 67 (54%) |
| | 3 ≦ nuclear < 4 | 56 (46%) |
| Intraocular pressure, IOP (mmHg)* | Baseline | 15.27 ± 4.21 |
| | 1 day post-operation | 14.49 ± 3.92 |
| | 1 week post-operation | 12.04 ± 3.07 |
| | 4 weeks post-operation | 12.55 ± 3.29 |
| Pre-operative BCVA | | .480 ± .152 |

LOCS = Lens Opacities Classification system; N = nuclear; BCVA = best-corrected visual acuity;

*Repeated measures of variance analysis (IOP): Baseline/1 Day > 1Wk/4Wk.

Numeric data are presented as means ± standard deviations where applicable.

Vascular density is defined as the percentage of the area occupied by blood vessels in the en face image. The preoperative superficial and deep macular vascular densities were (45.29 ± 4.06)% and (44.15 ± 5.67)%. The postoperative superficial macular vascular densities were (44.59 ± 3.85)%, (47.92 ± 3.45)%, and (48.10 ± 3.67)%, respectively. Meanwhile, the postoperative deep macular vascular densities were (43.12 ± 6.13)%, (46.46 ± 4.47)%, and (47.35 ± 5.42)%, respectively. The results indicated that macular vascular densities changed significantly over time in the two layers (both $P < 0.05$). The minimum macular vascular densities were both at 1 day after surgery, but no significant difference compared with parameters before surgery (both $P > 0.05$). Then, marked increases were subsequently exhibited on week one and week four (all $P < 0.05$). The trend of vascular density is shown in Fig. 2.

The preoperative FAZ area, PERIM and AI were (0.35 ± 0.13) $mm^2$, (2.25 ± 0.46) mm and 1.14 ± 0.02, respectively. The postoperative FAZ area were (0.38 ± 0.15) $mm^2$, (0.35 ± 0.16) $mm^2$ and (0.33 ± 0.17) $mm^2$ in the next 3 visits. The postoperative PERIM values were (2.34 ± 0.59) mm, (2.17 ± 0.59) mm and

(2.12 ± 0.58) mm. And postoperative AI values were 1.12 ± 0.61, 1.10 ± 0.26 and 1.12 ± 0.04, respectively. There were no statistically significant differences in any of the FAZ measurements for the entire study period ($P > 0.05$). The trend of FAZ parameters is shown in Fig. 3.

Correlation analyses of the measurement parameters are presented in Table 2 and Fig. 4. The rate of change in vascular density was calculated by the difference in vascular density before and one day after surgery, divided by preoperative blood vascular density. No statistically significant correlations were observed between EPT and rate of change in both superficial and deep macular vascular densities. And there were no statistically significant correlations between CDE and the changes of macular vascular densities.

Table 2
Relationships between the surgical parameters and changes of macular vascular densities

| Surgical parameters | Rate of change in superficial macular vascular density | | Rate of change in deep macular vascular density | |
|---|---|---|---|---|
| | r | P | r | P |
| EPT | .008 | .960 | − .029 | .856 |
| CDE | − .112 | .478 | − .066 | .667 |
| P < 0.05 was assumed to be statistically significant. | | | | |

# 4. Discussion

In this study, we performed a quantitative assessment of macular vascular density using OCTA and compared the macular blood perfusion before and after phacoemulsification cataract surgery in Chinese normal eyes. We limited the patient's axial length and age to a small range, because these factors may affect the fundus blood flow [9]. Of note, we found that blood flow parameters in the macula area increased gradually and stabilized in about one week after surgery. FAZ related parameters are stable before and after surgery. Main parameters of phacoemulsification surgery have no statistically significant correlations with changes of macular hemodynamics.

The development of phacoemulsification technology has made it one of the most popular techniques in treating cataracts. Surgeons use maximum vacuum to reduce direct damage by the power of phacoemulsification, but it brings the effect of high perfusion pressure at the same time. Previous reports have reported that the instability of the fluidics system during cataract surgery results in a longer operation time and an increase in CDE, which in turn will lead to longer recovery time and even poor visual function in postoperative patients [1–2]. So we wonder whether the fluctuation of intraocular perfusion pressure during phacoemulsification affect fundus microcirculation and then affect the patient's postoperative vision. A few studies have reported the effects of cataract surgery on ocular hemodynamics[10–12]. However, there is a shortage of research on this issue and there is a lack of quantitative study and large number of cases. The emergence of OCTA provides us with new ideas to explore.

The main methods of studying ocular blood flow reported in the literature can be divided into non-invasive and invasive techniques. Invasive techniques primarily involve scanning laser ophthalmoscopic angiography with fluorescein and/or indocyanine green (ICG) dye. These two methods often result in an allergic reaction due to the intravenous administration of dye before examination, and are relatively expensive and time consuming.[13]. Many non-invasive methods based on Doppler technology for detecting ocular blood flow, such as color Doppler imaging (CDI), laser Doppler velocimetry (LDV), laser Doppler flowmetry (LDF)[14]. However, their ability to visualize retinal blood vessels, especially retinal microvessels, is limited. Moreover, methods like laser speckle technique and blue field entoptic technique have a large degree of dependence on the subject's cooperation and the study of the fundus structure are limited [3–4]. With the development of OCTA and the gradual application in ophthalmology, non-invasive and quantitative research of fundus blood vessels has become possible[6–8]. It use the split-spectrum amplitude-decorrelation angiography (SSADA) algorithm through the intrinsic motion contrast provided by the flowing erythrocytes, making it possible to noninvasively obtain three-dimensional mapping of the retina and choroidal microvasculature[15, 16]. Good reproducibility and repeatability of OCTA on vascular and FAZ measurements have already been demonstrated[17–18]. So our study used this quantitative method to figure out whether transient hyperperfusion in cataract surgery affects fundus blood flow.

Many literatures have reported the effects of phacoemulsification cataract surgery with intraocular lens implantation on ocular hemodynamics by using various techniques[19–22]. EJR Hilton et al. found that small incision cataract surgery led to an 8.3% postoperative increase in pulsatile ocular blood flow (POBF) after one month following surgery, which was comparable with our present results [19]. However, Spraul CW et al. described a post-operative decrease in POBF and pulse amplitude at 3 days that was not apparent 12 months later [20], Rainer G. et al reported no change in fundus pulse amplitude, or blood-flow velocities and resistance of the retrobulbar vessels up to 1 month following cataract surgery [21]. And Adam Turk et al. indicated that there were no significant differences in IOP, POBF, and ocular pulse amplitude (OPA) between one week and three weeks after cataract surgery in a study of 52 eyes of 26 subjects[22]. Nevertheless, due to the different equipment used as well as the diversity of the group properties, the conclusions of those previous studies were not highly comparable with our present results.

Furthermore, research methods mentioned above focused more on large vessels than the microvasculature in eye, which is a limitation to show pathophysiologic changes in macular vessels [23]. And the pulsatile component we used to measured is thought to be primarily choroidal in origin which could hardly describe the retinal, especially the macular vessels in a precise way. However, OCTA provides segmented image of the macular vessels and quantitatively measure blood flow at a given location. Siqing Yu et al. used OCTA to study 13 cataract eyes and observed that there was a increase of either perfusion or vessel density on superficial capillary plexus (SCP) and deep capillary plexus (DCP) in a 3 mm × 3 mm en face image one week after surgery[24], which is consistent with our results. Siqing Yu et al. attributed this increase as the result of the different refractive interstitial conditions before and after surgery. But they did not measure patients' ocular blood flow status immediately after the surgical intervention was performed, which ignoring the impact of cataract surgery on the macular hemodynamics. Zhennan Zhao et al. studied 32 cases of uncomplicated phacoemulsification surgeries by using OCTA[25]. Significant increases in macular vessel density and macular thickness were found in one month and three months postoperatively. This is basically consistent with the conclusions of our larger sample study. Previous studies have pointed out that fundus perfusion will eventually improve due to the IOP-lowering effect of cataract surgery, which is believed to result from the widening of the anterior chamber[26–29] and vasodilator effect of inflammatory factors[30, 31]. The interpretation of these studies is in support of our findings. Moreover, most of the subjects had earlier cataracts (LOCS scale,median: N3, C4, P3) in current study in order to ensure the imaging quality of larger en face images (6mm × 6 mm), so the effect of lens opacities were diminished.

Previous clinical studies of FAZ have used techniques such as fluorescein fundus angiography (FFA), fundus photography (FP) and adaptive optics scanning laser ophthalmoscopy (AOSLO), all of which have limitations on clinical application due to their invasiveness, complex equipment and long scanning time[32–35]. Some clinical studies using OCTA to analyze FAZ[36–40] are mainly focused on diabetic retinopathy(DR) have shown a decrease in total retinal blood flow associated with an increase in FAZ area with increasing age[41, 42]. Our inclusion criteria have avoided the interference of age factors on the results. Meanwhile, studies[37, 43] of DR patients have showed that the size of FAZ was negatively correlated with both the macular vascular density and BCVA. Therefore, FAZ parameters may detect the impairments of macular micro-vessels and visual function to some extent. In our study, the FAZ area of subjects after cataract surgery increased first and then decreased, while the differences were not significant ($P > 0.05$). This difference may be due to participants in our study have no systemic vascular disease. The postoperative microcirculation change was only transient and mild, with no qualitative vascular changes. Our result is consistent with the findings of Siqing Yu et al.[24] that there were no significant differences in FAZ area and perimeter between preoperative measurements and one week after cataract surgery. However, unlike our findings, Zhennan Zhao et al[25] found a decrease in the foveal avascular zone after cataract surgery. We analyzed this difference may be contributed to the inconsistency in the axial length of enrolled patients included in the two studies.

The effects of various surgical parameters on ocular structures have been of concern and efforts have been made to evaluate the same[44, 45]. However,there is a shortage of literature on the effect of different flow parameters on the posterior segment. Previous studies[46] demonstrated that phacoemulsification ultrasound energy can induce the production of some cytokines, which in turn affects ocular hemodynamics. This prompts us to explore the correlations between surgical parameters and changes in ocular blood flow. A 6mm × 6 mm OCTA image were used in this study to quantitatively calculate the rate of change of macular vascular density before and after surgery. In our study, no statistically significant correlations were observed between the two parameters (EPT and CDE) and rate of change in both superficial and deep macular vascular densities. It suggests that the main parameters of phacoemulsification surgery may not be the key factors affecting macular hemodynamics. However, the

LOCS nuclear opalescence score of our subjects between 2 + and 3+, which may result in a very small fluctuation of surgical parameter and reduce its influence.

The main limitation of this study is the lack of research on patients with more severe cataracts. However, this study is the basis for exploring the effects of phacoemulsification on macular hemodynamics in different populations in the future. Furthermore, studies in the future are needed to focus on abnormal eyes, especially patients who with high myopia, glaucoma and systemic vascular disease. This will give clinicians more reference for practice. For example, a highly myopic patients who have long eyes, weak eyeball wall and liquefying vitreum, will have greater intraoperative IOP fluctuations. Comparison of ocular vasculature changes between long eyes and normal eyes before and after surgery can guide clinicians to further optimize surgical parameters and clinical medication. This study can also be a basis for further studies of fundus hemodynamic changes after vacuum application in femtosecond laser-assisted cataract surgery.

# 5. Conclusions

In our study, macular blood perfusion in normal eyes gradually rose one day to one week after phacoemulsification cataract surgery in Chinese normal eyes. Finally, it stabilized in a short period of time (a week or so). FAZ measurements seems to be stable before and after surgery. Main parameters and intraoperative perfusion of phacoemulsification surgery may not be the key factors affecting macular hemodynamics.

# Declarations

### 6.1 Ethics approval and consent to participate

This prospective observational study was approved by the ethics committee of Tianjin Eye Hospital, and written informed consent was obtained from all patients.

### 6.2 Consent for publication

Not applicable.

### 6.3 Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

### 6.4 Competing interests

The authors declare that they have no competing interests.

### 6.5 Funding

No funding received.

### 6.6 Authors' contributions

Design of the study (XJ, YW); data collection (XJ, YW); statistical analysis (XJ, YW); drafting of the manuscript (XJ); critical revision (YW,HS). All authors read and approved the manuscript to be published.

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### 7 Footnotes

Xinyu Jia and Yingjuan Wei contributed equally to this work.

Xinyu Jia and Yingjuan Wei are co-first authors.

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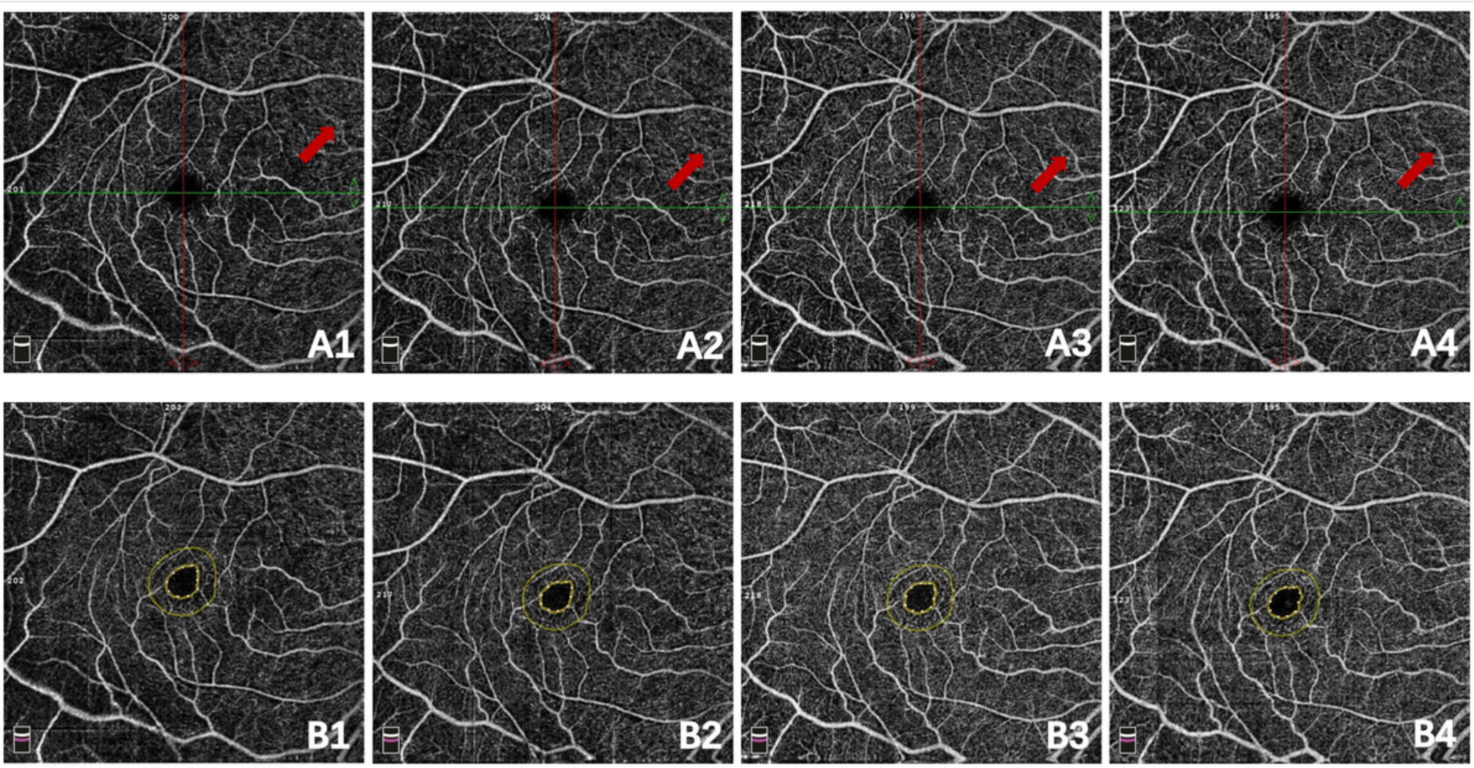
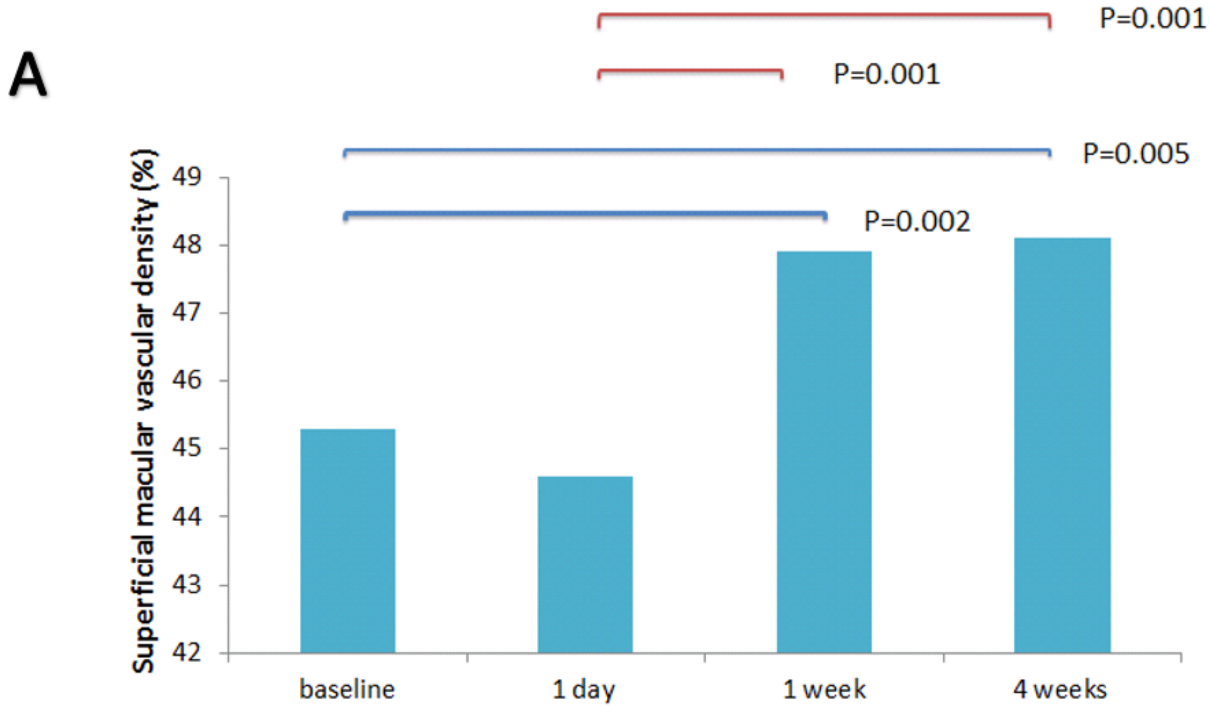
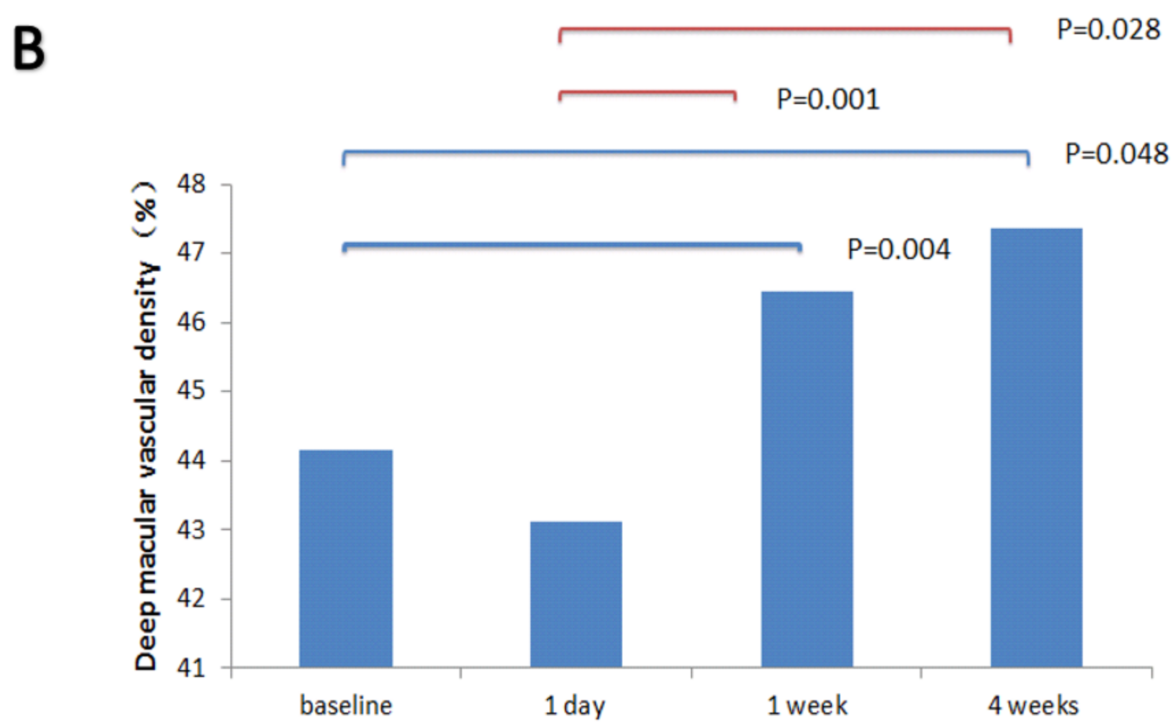
# Figures



## Figure 1

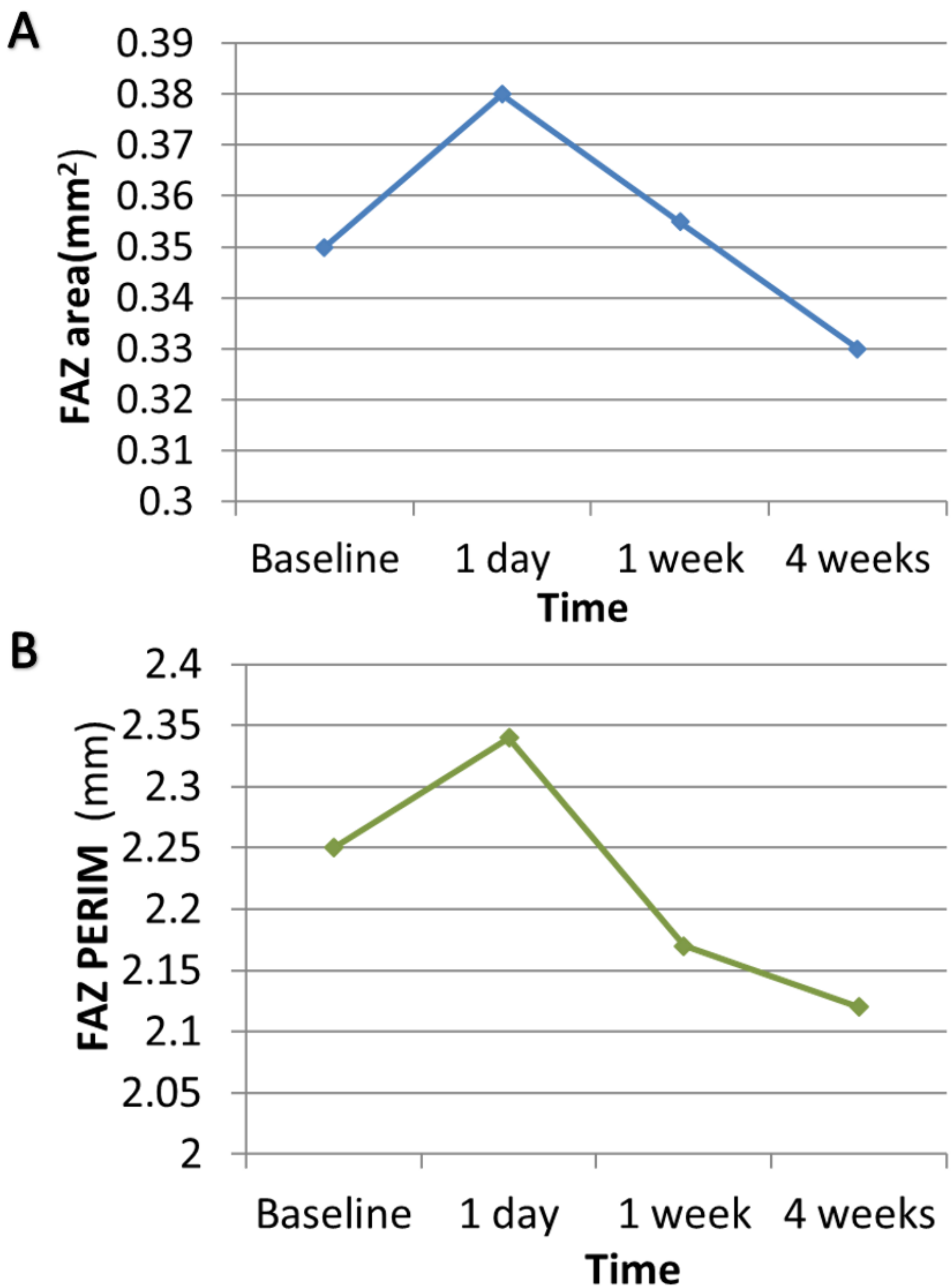
Vascular image(A) and FAZ circular band analysis image(B) in the OCTA enface image Figure 1 shows the follow-up results of the right eye of a patient aged 60-65 (LOCSIII: C3N2P3). A1-A4 corresponds to the macular vessel image before surgery, one day after surgery, one week after surgery, and one month after surgery, respectively. We can see that the vascular signals in Figures A3 and A4 are significantly stronger than those in Figures A1 and A2. The areas indicated by the red arrows can be used as examples. Meanwhile, yellow rings on Figure B1-B4 corresponds to FAZ images at four visits.



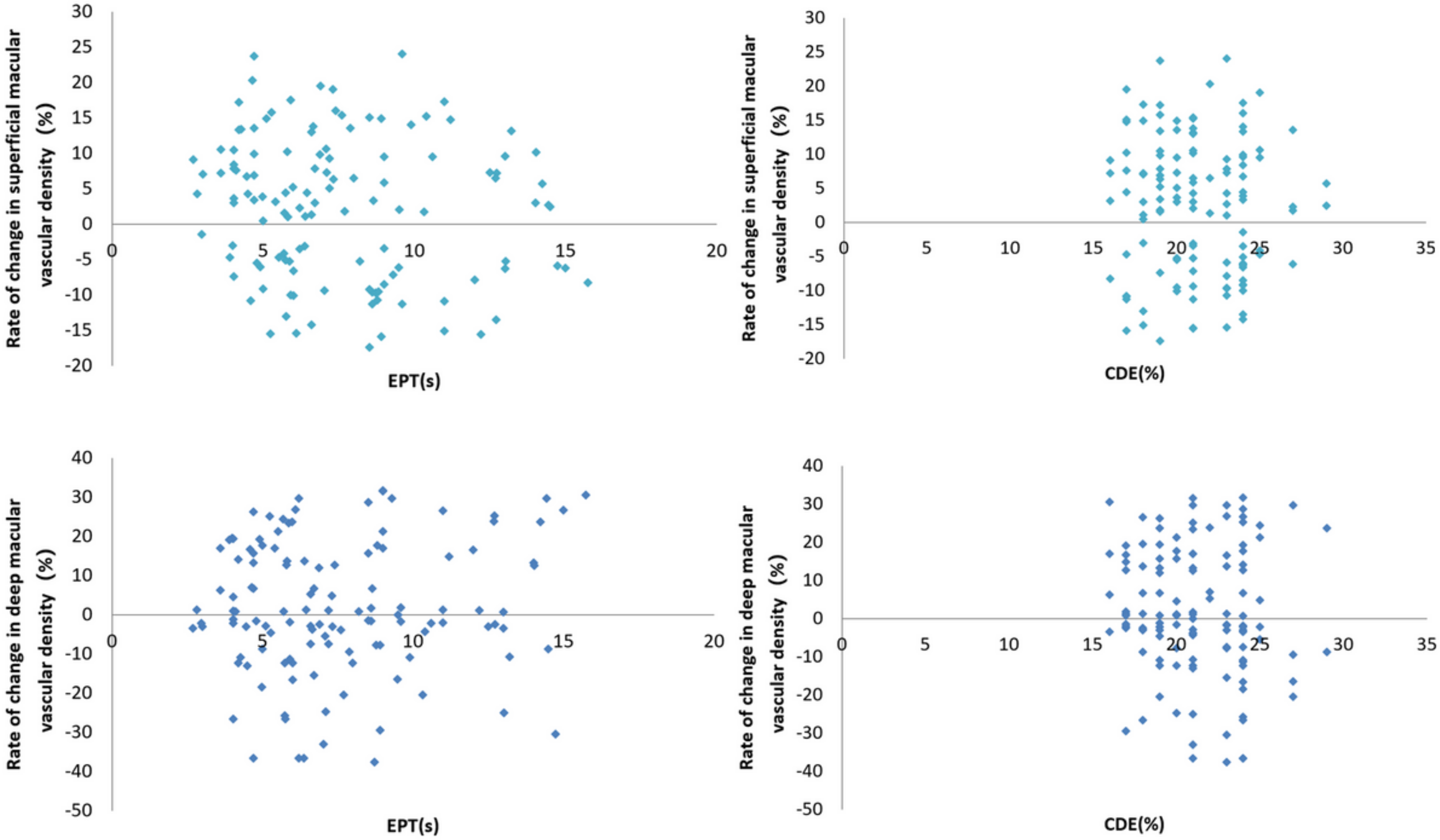
## Figure 2

Macular vascular densities obtained at various times in eyes undergoing phacoemulsification surgery Figure 2 shows the changes in macular vascular density at different follow-up times. P values less than 0.05 compared between groups were also indicated in the figure. The remaining unlabeled P values were all greater than 0.05.




## Figure 3

FAZ parameters obtained at various times in eyes undergoing phacoemulsification surgery Repeated measures of variance analysis showed no significant difference in FAZ-related parameters measured at four follow-up visits (P > 0.05).




## Figure 4

Relationships between the surgical parameters and changes of macular vascular densities No statistically significant correlations were observed (P >0.05).