

Assessment of Microvascular Changes using Optical Coherence Tomography Angiography after Phacoemulsification Surgery in an Indian Population

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ABSTRACT

Purpose: To identify changes in superficial retinal capillary microvasculature before and after cataract surgery using optical coherence tomography angiography (OCTA).

Setting: Rajan eye care, Tertiary care center in Chennai, India.

Design: Prospective observational study.

Methods: Patients above 40 years who underwent uncomplicated cataract surgery had 6 × 6 mm OCTA fovea-centered scans using Zeiss Angioplex 5000 OCTA before and 4 weeks postoperatively. Signal strength and automated values obtained for perfusion density (PD) and vascular density (VD) were recorded.

Results: Fifty-eight eyes of 33 patients aged 67 ± 5 years were enrolled. Signal strength (3.9 ± 2.3 vs. 5.7 ± 2.1, p<0.001), PD (16.4 ± 10.4 vs. 26.6 ± 10.3, p<0.001) and VD (7.4 ± 4.5 vs. 11.4 ± 4.0, p<0.001) increased significantly after surgery. Strong positive correlation was seen between signal strength and PD (r=0.86, p<0.001) and VD (r=0.79, p<0.001). Linear mixed model analysis with eye as grouping factor, time (i.e. pre and post-surgery) and signal strength as covariates showed, surgery independently caused an increase in PD (β=3.63 increment in PD after surgery, p<0.001) and VD (β=1.61 increment in VD after surgery, p=0.003). After adjusting for signal strength, a 20% increment in macular PD and VD was observed in central 1 mm area around fovea. Foveal avascular zone (FAZ) area, perimeter and circularity, did not change after surgery.

Conclusion: Macular perfusion and vascularity indices increase immediately after cataract surgery independent of improvement in signal strength, though FAZ is not influenced.

Keywords: OCT angiography; Microvascular changes; Phacoemulsification; Superficial retinal capillary layer; Vascular density; Perfusion density

INTRODUCTION

Cataract surgery is the most commonly performed intraocular procedure worldwide. There have been paradigm shifts to improve the safety of surgery and ensure excellent refractive outcomes. However, cataract surgery has been known to induce transient inflammation leading to increased retinal circulation

and clinically significant cystoid macular edema in a minority of cases [1,2]. Evaluation of retinal morphology has shifted from the routine use of fluorescein angiography to optical coherence tomography (OCT) over the past decade. Studies have shown a slight increment in the macular thickness after uncomplicated cataract surgery using automated OCT measurements, thereby providing surrogate evidence of an increase in retinal perfusion

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after cataract surgery [3,4]. However, quantitative measurements of the retinal vascular density and perfusion status after cataract surgery have not been studied extensively.

Optical coherence tomography angiography (OCTA) is an exciting and new imaging modality that has revolutionized our understanding of the retinal and choroidal vasculature in a non-invasive manner in normal as well as diseased states [5]. This technology has been recently used to study changes in retinal circulation following cataract surgery with most authors confirming an increment in circulation at the level of the superficial and deep capillary plexus [6-8]. However, there is controversy regarding whether OCTA measurements denote a true increment in blood flow or whether a mere improvement in signal strength post cataract removal gives a pseudo impression of enhanced blood flow [9]. This potential source of error is compounded by the fact that OCTA scans are prone to motion artifacts and segmentation errors, are influenced by signal strength [10] and every OCTA machine uses different software algorithms to automatically denote vascularity indices.

In view of this, it is important to statistically adjust for variability in signal strength and re-evaluate the OCTA parameters to understand whether cataract surgery has a truly pro-inflammatory influence on retinal circulation. We performed a study to understand changes in the superficial retinal capillary microvasculature before and after cataract surgery using the OCTA in an Indian population.

MATERIALS AND METHODS

This was a prospective observational study on consecutive consenting patients undergoing uncomplicated cataract surgery for routine age-related cataracts. The study was approved by the institutional ethics committee and was carried out as per the tenets of the declaration of Helsinki and good clinical practice guidelines. Informed consent was obtained from all patients before undertaking the cataract surgery.

All patients above the age of 40 who presented to our institution with senile cataracts without any coexisting ocular or systemic comorbidity were offered participation and consenting patients were enrolled. Eyes with posterior polar, brown, black or mature cataracts, those with poor mydriasis, pseudoexfoliation, zonular weakness and eyes that experienced a surgical complication such as posterior capsular rupture were excluded from the analysis. All patients underwent a routine preoperative work up including evaluation of the best corrected visual acuity (BCVA), intraocular pressure (IOP), dilated slit lamp evaluation of the anterior segment and thorough evaluation of the posterior segment followed by optical biometry for intraocular lens power estimation.

Patients also underwent preoperative OCTA assessment in the eye to be operated using the Zeiss Angioplex-5000 OCTA system (Carl Zeiss Meditec, USA). The scans were acquired by a technician well trained in obtaining OCTA. A 6 × 6 mm scan centered on the fovea was acquired and en face retinal angiograms were created using the proprietary Optical Micro Angiography (OMAGc) Algorithms from the manufacturer that utilizes amplitude and phase OCT signal data to deliver the

angiography images. Preoperative signal strength of minimum of 3/10 was required to register the scan for analysis without any motion artifacts. The technician checked for segmentation errors as well before admitting the scan for automated analysis. A postoperative signal strength of minimum 5/10 was required for the scan to be admissible.

After acquisition, automated measurements from the superficial capillary plexus were used for study purposes. Parameters used were perfusion density, vascular density and the size of the foveal avascular zone (FAZ). These parameters from the central (circle with a diameter of 1 mm), parafoveal (circle with a diameter of 3 mm) and perifoveal (circle with a diameter of 6 mm) regions, as described previously by Zhao et al. [6], were used for analysis.

All patients underwent routine clear corneal phacoemulsification with intraocular lens implantation and received topical prednisolone acetate eye drops in a tapering fashion for four weeks.

At the end of 4 weeks, the OCTA measurements were again performed by the same technician using the same protocols described above. The primary outcome measures were changes in perfusion density, vascular density and size of the FAZ at 4 weeks post cataract surgery compared to preoperative values.

Statistical analysis

All continuous variables were described as means with standard deviation and categorical variables were described as proportions (n,%). Differences between pre and postoperative measurements were done using the paired t test.

To study changes of perfusion and vascularity density as well as FAZ in time we performed a linear mixed model analysis with these dependent variables and with time (i.e. pre and post-surgery) and signal strength as covariates. Data were recorded using Microsoft Excel and statistical analyses were done with SPSS statistical software (version 25, IBM Corp, Armonk, USA). A p-value of <0.05 was considered significant.

RESULTS

In this study we included 58 eyes of 33 subjects (21 female, 12 male), aged 67 ± 5 years. Table 1 shows pre and post-surgery values for the perfusion density vascular density, and FAZ in the central, perifoveal and parafoveal zones.

The signal strength improved significantly after surgery. Similarly, the perfusion density and vascular density also increased significantly after surgery ($p < 0.001$). Figure 1A and 1B shows OCTA images of an eye before and after surgery showing increased perfusion and vascular density.

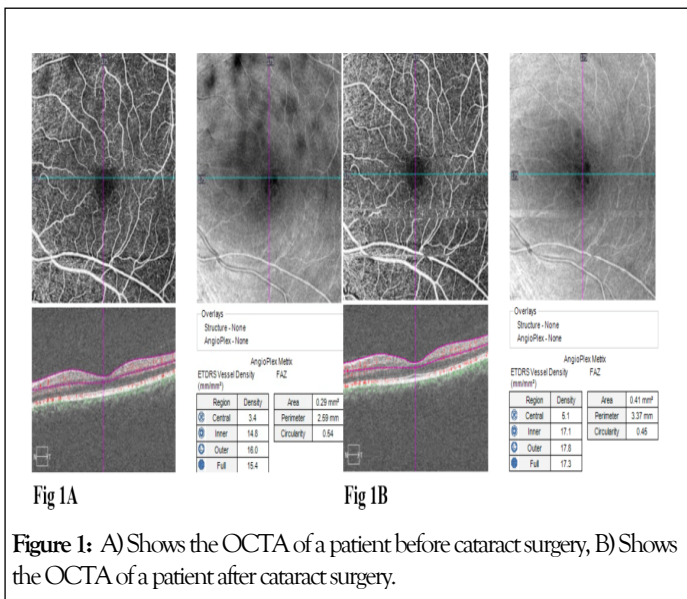


Figure 1: A) Shows the OCTA of a patient before cataract surgery, B) Shows the OCTA of a patient after cataract surgery.

	VA pre	VA post	p1
Signal strength	3.9 ± 2.3	5.7 ± 2.1	<0.001
PD central	3.4 ± 3.3	6.9 ± 5.3	<0.001
PD inner	14.1 ± 10.6	25.2 ± 11.7	<0.001
PD outer	17.5 ± 10.8	27.8 ± 10.3	<0.001
PD full	16.4 ± 10.4	26.6 ± 10.3	<0.001
VD central	1.8 ± 1.5	3.3 ± 2.5	<0.001
VD inner	6.6 ± 4.7	10.9 ± 4.7	<0.001
VD outer	8.2 ± 4.5	11.8 ± 4.0	<0.001
VD full	7.4 ± 4.5	11.4 ± 4.0	<0.001
FAZ area	0.23 ± 0.18	0.20 ± 0.21	0.32
FAZ perimeter	2.04 ± 1.00	1.57 ± 0.61	0.62
FAZ circularity	0.65 ± 0.14	0.62 ± 0.09	0.59

Abbreviations: PD: Perfusion Density; VD: Vascular Density; FAZ: Foveal Avascular Zone; 1 paired T-test

Table 1: OCTA parameters acuity pre and post-surgery.

A strong positive correlation was found between signal strength and the perfusion and vascular density (Table 2). The scatter plots in Figure 2A and 2B, show the association between signal strength and perfusion and vascular density.

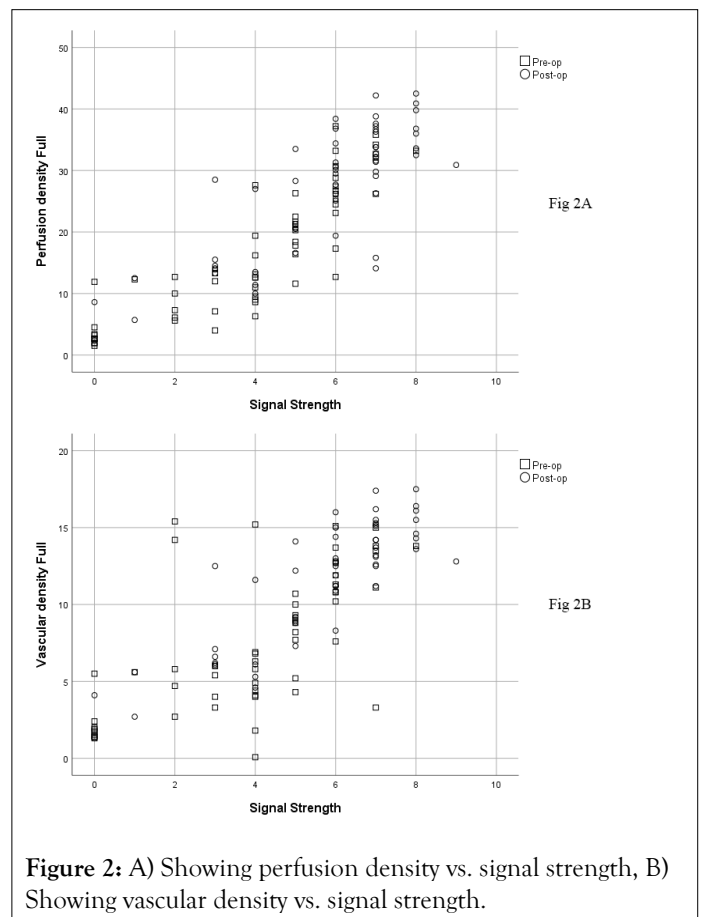


Figure 2: A) Showing perfusion density vs. signal strength, B) Showing vascular density vs. signal strength.

	r	p
PD central	0.56	<0.001
PD inner	0.83	<0.001
PD outer	0.86	<0.001
PD full	0.86	<0.001
VD central	0.49	<0.001
VD inner	0.75	<0.001
VD outer	0.8	<0.001
VD full	0.79	<0.001
FAZ area	-0.029	0.84
FAZ perimeter	-0.069	0.63
FAZ circularity	-0.082	0.57

Abbreviations: PD: Perfusion Density; VD: Vascular Density; FAZ: Foveal Avascular Zone

Table 2: Pearson correlation, r, between signal strength and the different OCTA parameters.

A linear mixed model analysis with eye as grouping factor, the different OCTA parameters as dependent variable and time (i.e. pre and post-surgery) and signal strength as covariates showed that both signal strength and surgery independently caused an increase in perfusion density and vascular density (Table 3). Assuming a constant signal strength of 8, associated with an excellent signal, this would imply an increment in perfusion density of 20% in the central zone, of 12% in the inner zone and of 10% in the outer zone. For the vascular density this would be 11%, 12% and 8% respectively. The FAZ parameters i.e. area, perimeter and circularity, did not change after surgery and showed no correlation with the signal strength. None of the patients showed any changes of cystoid macular edema at the study end point of 4-6 weeks.

	Constant		Signal Strength		Post vs. Pre -Surgery	
	β	β	p	β	p	
PD central	1.42	0.97	<0.001	1.85	0.012	
PD inner	2.98	3.94	<0.001	4.2	0.001	
PD outer	6.18	3.93	<0.001	3.64	<0.001	
PD full	5.28	3.79	<0.001	3.63	<0.001	
VD central	1.17	0.83	<0.001	0.85	0.023	
VD inner	2.61	1.5	<0.001	1.78	0.009	
VD outer	3.77	1.45	<0.001	1.27	0.02	
VD full	3.41	1.44	<0.001	1.61	0.003	

Abbreviations: PD: Perfusion Density; VD: Vascular Density

Table 3: Linear mixed model analysis for the different OCTA parameters with time and signal strength as covariates.

DISCUSSION

In this prospective study, measuring OCTA parameters before and after cataract surgery, in a cohort of patients who underwent routine uncomplicated cataract surgery, we found that there was a significant increment retinal capillary perfusion and vascular density in the superficial capillary plexus. This relation persisted even after adjusting for the proportionally increased signal strength due to cataract removal. The maximum increment in vascular parameters was seen in the central zone and least in the perifoveal zone between 3-6 mm from center of fovea. The FAZ dimensions did not show any change on OCTA

parameters after the cataract surgery and was not affected by the signal strength.

In a recent study with a similar methodology, Zhao et al. evaluated the macular vasculature of 32 consecutive eyes undergoing uncomplicated cataract surgery using a split-spectrum amplitude-decorrelation angiography algorithm (RTVue-XR Avanti (Optovue, Inc.) [11]. They reported that the mean vessel density increased by 6% and 3% in the parafoveal and perifoveal area at 3 months after surgery. The authors also reported a 27% reduction the size of the FAZ. Contrary to these results, we did not find any change in the FAZ and also found greatest increment in vascularity on the central 1 mm zone of about 20% from baseline. These differences could be explained on the basis of the different algorithms used to analyze the OCTA data with different machines, and importantly, adjustment for signal strength done in our study as opposed to unadjusted measures reported by Zhao et al. [11]. Tan et al. [9] have pointed out this ambiguity of unadjusted values presented by Zhao et al. and have cast doubts on the results published.

Similarly, Yu et al. have demonstrated the influence of cataract density and grade on the OCTA measurements using a swept source OCTA in 12 eyes [8]. Authors showed increment in the perfusion and vessel densities in both the superficial and deep capillary plexus after cataract surgery within the 3 × 3 mm images obtained. Authors also observed significantly better distinguishability of FAZ border postoperatively, however, FAZ area and perimeter measurements did not significantly change after cataract surgery, a finding similar to ours. Lim et al. have also shown that the signal strength as an important factor in the analysis of microvascular density using OCTA [10]. In view of these publications, we thought it was prudent to evaluate changes in the macular vascularity after adjustment of the increase in signal strength. Age is another factor known to influence these measurements [12]. However, given the small range of age in our study and the limited numbers, we did not include age as a covariate in our statistical modeling when adjusting for signal strength.

We observed maximum increment in vascularity in the central 1 mm zone around the FAZ. This could be because of the way the algorithm computed the thickness with maximum averaging done at the macula, or it could be because the pro inflammatory cytokines produced after cataract surgery gravitate to the center of the fovea and lead to increased vascular density and permeability. However, none of the eyes developed cystoid macular edema, making it difficult to provide a direct clinical application to these findings. Yet, it may be prudent to perform OCTA before cataract surgery, especially in eyes with diabetic retinopathy and other diseases prone to developing macular edema postoperatively. Also, these findings may be transient and studies with longer follow up are required to determine this.

The drawbacks of the study are the lack of assessment of the deep capillary plexus and lack of correlation with macular thickness values using the structural OCT. The merits are the adequate number of eyes studied and the statistical adjustment done to compensate for the influence of signal strength on macular vessel density.

CONCLUSION

In conclusion, even after adjusting for changes in signal strength, we observed a near 20% increment in the macular perfusion and vascular density in the central 1 mm area around the fovea. These increments were slightly lower but still statistically significant even in the parafoveal and perifoveal regions. FAZ was not influenced by cataract surgery. The clinical relevance of these findings needs to be studied further with larger samples and longer follow up periods.

What was known

- Signal strength while obtaining OCT images improves after cataract surgery due to media clarity.
- Studies have shown a slight increment in the macular thickness after uncomplicated cataract surgery using automated OCT measurements, thereby providing surrogate evidence of an increase in retinal perfusion after cataract surgery
- Quantitative measurements of the retinal vascular density and perfusion status after cataract surgery have shown slight increment after surgery, however, there is controversy regarding whether OCTA measurements denote a true increment in blood flow.

What this paper adds

- There is significant increment in retinal capillary perfusion and vascular density in the superficial capillary plexus after cataract surgery and this relation persisted even after adjusting for the proportionally increased signal strength due to cataract removal.
- The maximum increment in vascular parameters was seen in the central zone within 1 mm of fovea and least in the perifoveal zone between 3-6 mm from center of fovea.
- The FAZ dimensions did not show any change on OCTA parameters after the cataract surgery and was not affected by the signal strength.

COMPLIANCE WITH ETHICAL STANDARDS

Funding

Nil

Conflicts of interest

None of the authors have any conflicts of interest.

Ethics approval

This study was performed in line with the principles of the Declaration Of Helsinki. Approval was granted by the Ethics committee of Rajan Eye Care.

This article does not contain any studies with human participants or animals performed by any of the authors.

Informed consent

Informed consent was obtained from all individual participants included in the study.

Consent to publish

Patients signed informed consent regarding publishing their data and photographs.

Availability of data and material (data transparency)–Datasheet with anonymized patient data will be made available to anyone who wants access.

Code availability (software application or custom code)

SPSS code used for statistical analysis will be made available to anyone who wants access.

Author contributions

All authors contributed to the study conception and design. All authors read and approved the final manuscript.

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