# Changes In Corneal Surface Aberrations And Nerve Density After Cataract Surgery Of Patients With Dry Eye Disease

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Research Article

**Keywords:** dry eye disease, corneal nerve, corneal vortex, corneal aberrations, cataract surgery,

**Posted Date:** February 17th, 2022

**DOI:** https://doi.org/10.21203/rs.3.rs-1352536/v1

## Abstract

**Purpose:** To evaluate the change patterns in corneal aberrations and nerve density after cataract surgery in dry eye disease (DED).

**Methods:** One hundred and six eyes of 69 patients with dry eye were included in this study. The preoperative, 1-month and 3-month postoperative dry eye-related indices were obtained by the Oculus keratograph and the ocular surface disease index (OSDI) questionnaire. The corneal aberrations and corneal surface regularity indices were measured using a Pentacam HR system. In vivo confocal microscopy (ICVM) was performed to observe sub-basal corneal nerves of vortex and superior periphery, and corneal endothelial number. An artificial intelligence (AI) technique run by the deep learning model generated the sub-basal nerve fibre parameters.

Results: One hundred and six eyes of 69 patients with DED (mean age, 69.32±8.91 years) were recruited. Corneal aberrations on the anterior and total corneal surfaces increased significantly at 1 month after surgery compared with the baseline values but gradually returned to the baseline by 3 months after surgery. Significant changes in posterior corneal HOAs occurred at 1-month and 3-month. Corneal endothelial cells decreased continuously until 3 months after operation. There were significantly lessen in corneal vortical nerve maximum length and average density after operation, these damages were present after 3 months. But for corneal peripheral nerve, these damages lasted only 1 month after operation. The corneal vortical nerve maximum length and average density were negatively correlated with anterior corneal surface aberrations before and one month after surgery.

**Conclusions:** After cataract surgery, changes in corneal aberrations occurred mainly both on the anterior and posterior surface. However, the change of posterior lasts longer. The corneal vortical nerve maximum length and average density are reduced after cataract surgery in patients with DED. Although the anterior corneal aberration will recover one month after cataract surgery, the dry eye state continues to worsen. IVCM is a useful tool to evaluate corneal sub-basal nerve changes in dry eye patients before and after cataract operation.


## Introduction

Modern cataract surgery has meet higher standards of safety and visual performance. While many patients have complained of postoperative dry eye symptoms and studies have documented an increase in the prevalence and severity of dry eye diseases (DED).[1,2] There are numerous causes of exacerbation of dry eye, such as damage of corneal nerve and epithelial caused by surgical incisions,[3] light exposure from the operating microscope,[4] topical anaesthesia and eye drops containing preservatives using [5]and so on. One study reported a reduction in corneal nerves length and density after cataract surgery.[6] Previous studies reported that corneal sub-basal nerve density and length tended to decrease in DED, indicating damaged nerve fibers.[7] They indicated cataract surgery aggravated the dry eye by damaging corneal nerves. Their study location focused on the center of the cornea, while due to less observed range and on positioning function, these result in each measurement was conducted in different position, increased variability, poor reproducibility, as well as decreased comparability. An effective and standard examination location is needed for the preoperative and postoperative comparison. Corneal vortex is a recently recognized peculiar structure which is universally present in population.[8] Additionally, it is easy to recognize and has relatively fixed site compared with corneal center.[9]

Guirao et al.[10]found increased corneal aberrations after conventional cataract surgery. Especially the development of higher-order aberrations (HOA) can affect visual quality.[11] Patients with DED have greater optical aberrations, mainly cornea. This can be attributed to the instability and irregularity of the tear film. These symptoms naturally lead to visual function impairment, thus affecting the quality of life.[12,13] While these literatures did not pay attention on corneal intrinsic aberrations. There are many similarities in ocular surface changes between the two. Prior studies focused on one certain aspect-the changes of corneal nerve or aberration.

Therefore, in our study, we investigated the changes of corneal aberrations, corneal regularity, corneal nerve density, corneal endothelial number and symptoms and signs of dry eye in DED patients before and after cataract operation. Moreover, these parameters were further evaluated to identify their relationship.

## Material And Methods

This prospective study adhered to the tenets of the Declaration of Helsinki and was approved by the Ethics Committee of the Peking University Third Hospital. (#M2019236). All patients were fully informed of the details and possible risks of the procedure, and written informed consents were obtained from all the participated patients. 106 eyes of 69 patients with dry eye meeting the inclusion and exclusion criteria were evaluated before and after cataract surgery. Participants were eligible if the patients were diagnosed with age-related cataract and DED which based on the 2017 Report of the Tear Film & Ocular Surface Society International Dry Eye Workshop (TFOS DEWS). [14] Criteria for diagnosis of dry eye included symptoms of dryness, foreign body sensation, burning, fatigue or blurred vision, and tear break-up time (TBUT) < 10 s. The exclusion criteria were: age younger than 50 years or older than 80 years; any ocular surface and corneal abnormalities; history of contact lens wear within 1-month; recent eye surgery; nasolacrimal duct obstruction; glaucoma; ocular fundus diseases; diabetes and immunologic systemic disease.

Preoperative clinical assessment included the following: collection of demographic information, OSDI questionnaire,[15] Catquest questionnaire,[16] best corrected Snellen visual acuity (BCVA) [converted to logarithm of the minimum angle of resolution or (logMAR) for the purpose of statistical analysis], slit-lamp biomicroscopy. The keratograph 5M (Oculus Optikgeräte GmbH, Wetzlar, Germany) was used to measure the non-invasive tear break-up time (TBUT), tear meniscus height (TMH) and Meibography scores.[17,18] The Pentacam HR system (Oculus Inc., Wetzlar, Germany) was used to measure corneal intrinsic

aberrations and corneal surface regularity indices. In vivo confocal microscopy (IVCM) was performed to assess sub-basal plexus morphology and endothelial cell count.

The Pentacam HR system is a non-invasive system for measuring and featuring the anterior segment. The raw data from the Scheimpflug camera were obtained in the 50-picture corneal-fine scan mode over a measurement zone diameter of 4.0 mm on the anterior corneal surface and posterior corneal surface. The elevation data of the rotating Scheimpflug camera images were reconstructed to a 3-dimensional corneal structure, which can eliminate the tear film's effect, thus measuring the corneal intrinsic aberrations. It allows the quantification of corneal surface regularity as computed indices, namely index of surface variance (ISV), index of vertical asymmetry (IVA), index of height asymmetry (IHA), and index of height decentration (IHD). The Zernike polynomials of the corneal wavefront were automatically generated using the integrated software. The Zernike coefficients up to 8th order over the central 4.0mm diameter zones of total, anterior, and posterior corneal surfaces were extracted, including the total root mean square (RMS) aberrations, RMS of the higher-order aberrations (RMS HOA), and RMS of the lower-order aberrations (RMS LOA).

Corneal images were obtained by the IVCM had a definition of 384 × 384 pixels over an area of 400 μm ×400 μm, with lateral spatial resolution of 0.5 μm and a depth resolution of 1–2 μm. ICVM was performed on each eye in two different areas: corneal vortex and superior peripheral cornea. Periphery was determined as an outside one-sixth part of the cornea (apart from the temporal surgical incision). Approximately 30 pictures were captured, from the corneal epithelium to the endothelium, and images with good quality were selected for analysis.

We selected each of 5 the high-quality images in corneal vortex and periphery with no overlapping for analysis of the corneal nerve parameters by the CNS-Net. The method demonstrated high accuracy, fast speed, and quantified in the sub-basal corneal nerve segmentation with IVCM.[19] The AI technique produced the maximum length of the corneal vortical nerve, and average density of the corneal vortical nerve, the maximum length of the corneal peripheral nerve, and average density of the corneal peripheral nerve. With regarding to corneal endothelium count, we select a clear image for cell counting, and the counting is completed by automatic camera.

All examinations were performed preoperatively, 1 month and 3 months postoperatively. Povidone–iodine (PI) 5% solution was instilled before and after placement of the lid speculum. Patients underwent standard phacoemulsification through a 3.0 mm clear corneal incision and intraocular lens implantation (Tecnis ZCB00, Abbott, United States) by the same surgeon (LXM). The Centurion microsurgical system (Alcon Laboratories, Inc., Ft. Worth, TX) was employed for phacoemulsification and cataract removal. Prednisolone acetate 1% eye drops (Allergan, Ireland) and levofloxacin 0.5% eye drops (Santen, Japan), both 4 times a day, were prescribed for 1 month postoperatively.

All analyses were performed using SPSS version 23.0 software. We verified the normality of data distribution by the Kolmogorov-Smirnov test. Descriptive parameters were expressed as the number of patients (%) or mean ± standard deviation (SD)/median with interquartile range, depending on the distribution pattern. The paired t test and Wilcoxon signed rank test were used for the preoperative data and postoperative data comparisons. The Pearson and Spearman correlation coefficients were calculated. A *P* value less than 0.05 was considered statistically significant.

## Results

One hundred and six eyes of 69 patients (mean age, 69.32 ± 8.91 years) were recruited. Twenty-five participants (36.2%) were men. Fifty-three right eyes and 53 left eyes underwent cataract surgery. No eye had surgical complications throughout the 3-month follow-up.

Table 1 summarises the comparison results of visual function, ocular symptoms and signs before and after cataract. The BCVA and Catquest-9SF score in all cases were significantly better 1 month and 3 months postoperatively than preoperatively, while there were no significant differences in these between the 1 month and 3 months. OSDI score was significantly different preoperatively and 3 months postoperatively. Ocular pain was aggravated in 1 month after cataract surgery. Poor vision improved compared with preoperation. However, other symptoms did not change significantly. At 1 month postoperatively, TMH was significantly better than before cataract surgery. TBUT and Meibography scores were worsen in 1 month after operation.

Table 1
Preoperative and postoperative visual function, ocular symptoms and signs

| Parameters | Baseline | 1 month | 3 months | P value | | |
|---|---|---|---|---|---|---|
| | | | | Baseline vs 1 month | Baseline vs 3 months | 3 months vs 1 month |
| BCVA[#] | 0.59 ± 0.47 | 0.23 ± 0.38 | 0.21 ± 0.21 | 0.00 | 0.00 | 0.66 |
| Catquest-9SF rasch score[$] | 1.00(-0.90,2.71) | -0.54(-1.82,0.01) | -0.69(-1.86, -0.02) | 0.00 | 0.03 | 0.57 |
| OSDI score[$] | 37.50(20.45,53.73) | 20.00(9.38,41.15) | 14.29(6.25,25.00) | 0.20 | 0.03 | 0.13 |
| Sensitivity to light[$] | 1.00(1.00,3.00) | 1.00(0.00,3.00) | 1.00(0.25,3.00) | 0.97 | 0.13 | 0.45 |
| Foreign body sensation[$] | 1.00(0.00,1.00) | 1.00(0.00,2.00) | 1.00(0.00,1.50) | 0.64 | 0.16 | 0.72 |
| Painful eyes[$] | 0.00(0.00,1.00) | 1.00(0.00,3.00) | 0.50(0.00,2.50) | 0.01 | 0.23 | 0.45 |
| Blurred vision[$] | 1.00(0.00,3.00) | 1.00(0.00,2.00) | 1.00(0.75,2.25) | 0.32 | 0.26 | 0.15 |
| Poor vision[$] | 1.00(1.00,3.00) | 0.00(0.00,1.00) | 0.00(0.00,1.00) | 0.00 | 0.02 | 0.06 |
| TBUT(s) [$] | 4.01(2.87,5.166) | 3.50(2.52,4.91) | 4.33(3.01,6.73) | 0.54 | 0.43 | 0.72 |
| TMH (mm) [$] | 0.16(0.15,0.20) | 0.19(0.15,0.22) | 0.19(0.15,0.23) | 0.01 | 0.29 | 0.59 |
| Meibography score[$] | 2.00(2.00,3.00) | 3.00(2.00,3.00) | 3.00(2.00,3.50) | 0.00 | 0.08 | 0.32 |
| BCVA: best corrected Snellen visual acuity; TBUT: tear break-up time; TMH: tear meniscus height; OSDI: ocular surface disease index; | | | | | | |
| [#], Paired t test; mean ± standard deviation was reported | | | | | | |
| [$], Wilcoxon signed rank test, median (25% quantile, 75% quantile) was reported | | | | | | |

The number of corneal endothelia decreased significantly 1 month and 3 months after operation. There were significantly lessen in corneal vortical nerve maximum length and average density after operation, these damages were present after 3 months. But for corneal peripheral nerve, these damages lasted only 1 month after operation. Other comparisons among ICVM parameters are shown in the Table 2.

Table 2
Preoperative and postoperative ICVM parameters

| Parameters | Baseline | 1 month | 3 months | P value | | |
|---|---|---|---|---|---|---|
| | | | | Baseline vs 1 month | Baseline vs 3 months | 3 months vs 1 month |
| Corneal endothelial number | 2832.55 ± 344.91 | 2311.97 ± 559.27 | 2382.08 ± 585.54 | 0.00 | 0.00 | 0.08 |
| Corneal vortical nerve maximum length(mm) | 2.58 ± 0.70 | 2.23 ± 0.69 | 2.13 ± 0.85 | 0.00 | 0.00 | 0.03 |
| Corneal vortical nerve average density(mm/mm$^2$) | 14.99 ± 4.11 | 12.98 ± 4.17 | 12.41 ± 5.16 | 0.00 | 0.00 | 0.01 |
| Corneal peripheral nerve maximum length(mm) | 3.02 ± 0.63 | 2.68 ± 0.64 | 2.70 ± 0.49 | 0.00 | 0.00 | 0.25 |
| Corneal peripheral nerve average density(mm/mm$^2$) | 16.08 ± 3.68 | 13.71 ± 3.61 | 13.48 ± 2.95 | 0.00 | 0.04 | 0.31 |

Patients had an increased in anterior and total corneal HOAs at 1-month. Significant changes in posterior corneal HOAs occurred at 1-month and 3-month. Total corneal aberration analysis found that there had significant changes at both timepoints, the rule is that aberration increases and then decreases. ISV and IVA increased at 1-month, but the IVA returned to the baseline values at 3-month. Further details are provided in Table 3.

Table 3 Preoperative and postoperative total, higher-order and lower-order aberrations of the total, anterior, and posterior surface of cornea

| Parameters | Baseline | 1 month | 3 months | P value | | |
|---|---|---|---|---|---|---|
| | | | | Baseline vs 1 month | Baseline vs 3 months | 3 months vs 1 month |
| RMS (CF) | 0.69(0.55,0.91) | 0.75(0.57,0.99) | 0.65(0.45,0.95) | 0.09 | 0.92 | 0.07 |
| RMS HOA (CF) | 0.20(0.14,0.26) | 0.23(0.15,0.28) | 0.20(0.13,0.29) | 0.00 | 0.44 | 0.43 |
| RMS LOA (CF) | 0.67(0.52,0.87) | 0.72(0.53,0.95) | 0.62(0.43,0.90) | 0.13 | 0.91 | 0.07 |
| RMS (CB) | 0.25(0.21,0.32) | 0.28(0.23,0.35) | 0.27(0.24,0.33) | 0.00 | 0.06 | 0.59 |
| RMS HOA (CB) | 0.07(0.06,0.09) | 0.09(0.07,0.12) | 0.08(0.07,0.11) | 0.00 | 0.03 | 0.43 |
| RMS LOA (CB) | 0.24(0.20,0.31) | 0.26(0.22,0.32) | 0.26(0.22,0.31) | 0.00 | 0.17 | 0.55 |
| RMS (Cornea) | 0.75(0.53,0.99) | 0.83(0.59,1.07) | 0.64(0.45,1.03) | 0.04 | 0.96 | 0.02 |
| RMS HOA (Cornea) | 0.21(0.15,0.29) | 0.25(0.17,0.33) | 0.23(0.14,0.34) | 0.00 | 0.22 | 0.34 |
| RMS LOA (Cornea) | 0.72(0.50,0.95) | 0.78(0.54,1.01) | 0.62(0.43,0.98) | 0.09 | 0.95 | 0.02 |
| ISV | 19.00(14.00,25.00) | 21.50(16.75,29.00) | 21.00(15.00,29.75) | 0.00 | 0.01 | 0.75 |
| IVA | 0.15(0.12,0.22) | 0.19(0.13,0.24) | 0.17(0.11,0.27) | 0.01 | 0.17 | 0.39 |
| IHA | 4.15(1.68,8.05) | 4.80(2.28,9.88) | 5.20(1.70,9.48) | 0.06 | 0.75 | 0.66 |
| IHD | 0.01(0.01,0.02) | 0.01(0.01,0.02) | 0.01(0.01,0.02) | 0.18 | 0.89 | 0.01 |

ISV: index of surface variance; IVA: index of vertical asymmetry; IHA: index of height asymmetry; IHD: index of height decentration; RMS(CF) total root mean square (corneal front); RMS HOA(CF): root mean square of higher-order aberrations (corneal front); RMS LOA(CF): root mean square of lower-order aberrations (corneal front); RMS(CB): total root mean square (corneal back); RMS HOA(CB): root mean square of higher-order aberrations (corneal back); RMS LOA(CB): root mean square of lower-order aberrations (corneal back); RMS(Cornea): total root mean square (cornea); RMS HOA(Cornea): root mean square of higher-order aberrations (cornea); RMS LOA(Cornea): root mean square of lower-order aberrations (cornea);

The results of correlation between ICVM parameters and corneal aberrations before and after cataract operation are shown in Table 4. As we can see, the corneal vortical nerve maximum length and average density were negatively correlated with anterior corneal surface aberrations before surgery. While at 1-month, only the corneal vortical nerve maximum length was negatively correlated with anterior corneal surface aberrations. At 3-months, the corneal vortical nerve maximum length and average density were positively correlated with posterior corneal surface aberrations. Moreover, the corneal endothelial number was negatively associated with posterior corneal surface aberrations.

Table 4
Correlation Analysis of Sub-basal Nerve Parameters and Corneal Parameters Using Pentacam

| | | RMS (CF) | RMS HOA (CF) | RMS LOA (CF) | RMS (CB) | RMS HOA (CB) | RMS LOA (CB) | RMS (Cornea) | RMS HOA (Cornea) | RMS LOA (Cornea) | ISV | IVA | IHA | IHD |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Corneal endothelial number | Baseline | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS |
| | 1 month | NS | -0.27* | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS |
| | 3 months | NS | NS | NS | 0.59** | NS | 0.59** | NS | NS | NS | NS | NS | NS | NS |
| Corneal vortical nerve maximum length(mm) | Baseline | -0.26* | -0.25* | -0.26* | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS |
| | 1 month | -0.28* | NS | -0.30* | NS | NS | NS | -0.28* | NS | -0.29* | NS | NS | NS | NS |
| | 3 months | NS | NS | NS | 0.61** | NS | NS | 0.75** | NS | NS | NS | NS | NS | NS |
| Corneal vortical nerve average density(mm/mm$^2$) | Baseline | -0.25* | -0.26* | -0.24* | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS |
| | 1 month | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS |
| | 3 months | NS | NS | NS | 0.57** | NS | 0.66** | NS | NS | NS | NS | NS | NS | NS |
| Corneal peripheral nerve maximum length(mm) | Baseline | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS |
| | 1 month | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS |
| | 3 months | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS |
| Corneal peripheral nerve average density(mm/mm$^2$) | Baseline | NS | NS | NS | NS | NS | NS | NS | NS | -0.21* | NS | NS | NS | -0.22* |
| | 1 month | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS |
| | 3 months | NS | -0.43* | NS | NS | NS | NS | NS | -0.53* | NS | NS | NS | NS | NS |

ISV: index of surface variance; IVA: index of vertical asymmetry; IHA: index of height asymmetry; IHD: index of height decentration; RMS(CF) total root mean square (corneal front); RMS HOA(CF): root mean square of higher-order aberrations (corneal front); RMS LOA(CF): root mean square of lower-order aberrations (corneal front); RMS(CB): total root mean square (corneal back); RMS HOA(CB): root mean square of higher-order aberrations (corneal back); RMS LOA(CB): root mean square of lower-order aberrations (corneal back); RMS(Cornea): total root mean square (cornea); RMS HOA(Cornea): root mean square of higher-order aberrations (cornea); RMS LOA(Cornea): root mean square of lower-order aberrations (cornea);

## Discussion

Ophthalmic surgery may have the potential to temporarily induce or worsen dry eye conditions such as photorefractive keratectomy and laser-assisted in situ keratomileusis (LASIK), in especial during the short postoperative stage. [20,21] Furthermore, cataract surgery has been shown the same effects on dry eye symptoms, with dry eye being one of the most frequent complaints in the postoperative period.[5] The multifactorial aetiology of dry eye is still not fully understood.[22] Patients with DED experienced the stimulation of cataract surgery can increased the severity of the disease. In the past, academe's study of postoperative dry eye focuses on changes of ocular symptoms and signs, such as OSDI questionnaire, TBUT, TMH, corneal fluorescein staining, Schirmer test and so on. Combined, these series are commonly used for the assessment the degrees of severity. When the inconsistent symptoms and signs, these methods provide poor direct information on ocular surface status. It is widely known that whether DED or cataract surgery would damage corneal nerve by ICVM examination. Moreover, both can increase corneal aberration by Pentacam. To assess the ocular surface status more comprehensively, our study presents a continuous and comprehensive evaluation system for dry eye of perioperative cataract period by combing the locatable IVCM, Pentacam and Oculus.

Choi et al.[23] showed the TBUT were not notably altered during the perioperative periods after cataract operation. Consistent with this report, we also found these results. While some studied shown a reduced TBUT only during the early postoperative phase.[24,25] Others reported TBUT decreased at 1 month or 3 months postoperatively.[2,26] These divergences could be partly attributed to the differences of measurements. Keratograph was used, which permits an automated, hypersensitivity, and examiner independent technique for measuring TBUT. TBUT as measured using the Keratograph was consistently lesser than the subjective observer recordings since it can record the first incident of break-up anywhere in the tear film.[27] Or the different target population in each study, we only enrolled DED patients, others enrolled patients with or without DE syndromes. Meibography scores had deteriorated dramatically in one month after the operation. One study said that Meibomian gland function may be altered without accompanying structural changes after cataract surgery.[26] Our results suggested possible transient structural changes related to cataract surgery or medication which aggravated symptoms of ocular surface discomfort. We assessed the lower tear meniscus using Oculus which has shown high repeatability.[28] And yet TMH shown significantly increased at 1 month. We compared each dry eye symptom of OSDI questionnaire, because it was hard to distinguish the reasons for changes of blurred vision. Apart from the painful eyes that aggravated at 1 month compared to pre-op, the sensitivity to light, foreign body sensation and blurred vision were not significantly changed. The results mean painful eyes may the primary manifestation of postoperative dry eye aggravation. That could be explanation for why TMH increased at 1 month, owing to irritant tear secretion.

Previous studies showed that the injured nerves degenerate after cataract surgery resulting in reduced sub-basal nerve density and reflectivity and increased beading.[3,6] They usually measure the central cornea by IVCM, but due to less observed range and on positioning function. These result in each measurement was conducted in different position, increased variability, poor reproducibility, and decreased comparability. Corneal vortex is a recently recognized peculiar structure which is universally present in population.[8] Moreover, it is easy to recognize and has relatively fixed site that located in approximately 1 to 2 mm inferior or nasal to the corneal apex.[29] Dipika et al. suggested that the mean sub-basal nerve density was greatest centrally.[30] For assessment in corneal nerve at different locations, we measured separately corneal vortex and periphery before and after cataract. It turned out that corneal vortical nerve average density and maximum length significantly reduced until 3 months or longer. However, the damage around the corneal periphery only until 1 month. The corneal density and length have not yet returned to preoperative status at the last phase. Consistent with early studies, corneal central and temporal incised sub-basal nerve density is reduced one month after cataract surgery in patients.[3,6] These changes are due to temporal clear cornea incision to a small extent, as it also happened in corneal center. Our research also certainly confirmed this conjecture. However, we tested the corneal vortex which is more fixed and corneal periphery that apart from the temporal surgical incision. We ruled out the effect of corneal incision and found there had other factors affecting corneal nerve. Some people consider it is due to ultrasonic energy damage, ocular medicated toxicity or others that relating to surgery. Interestingly, the damage of peripheral corneal nerve lasted only 1 mouth, but central corneal damage until 3 months or more. It seems to have other factors that continue to harm corneal vortex. Yet there had no relevant research which concerning corneal vortical nerve after cataract surgery or of dry eye. Then, referring the studies about corneal center, we would hazard a guess that the persistent injury of corneal vortical nerve is due to lasting dry eye condition-in others word the inflammation.[31] We will explain it in combination with the changes of corneal aberration.

Patients with dry eye have greater corneal aberration that usually due to instability of tear film.[32] Based on our previous studies,[33] DED patients had increased corneal intrinsic aberrations except for the aberration caused by tear film. Pentacam was used to measure corneal intrinsic aberrations. Our research found that the anterior, posterior and total corneal surface higher-order aberrations increased one month after operation. There was no difference in corneal intrinsic aberrations after operation and before operation except from the posterior HOAs that postoperative increased between three months. They believed that corneal aberrations may be related to postoperative ocular surface condition such as dry-eye symptoms. Significant changes in the anterior, posterior and total HOAs over the 4.0 mm zone at 1-month. He et al. reported changes can only be found in the 6mm area. In part that's because we recruited DED patients who themselves with larger corneal aberration and imbalance of ocular surface homeostasis. Current strategy on dry eye treatment is also mainly based on eliminating exacerbating factors, inhibiting inflammation and restoring homeostasis.[34] It is indisputable that cataract surgery is a harsh blow to ocular surface homeostasis, especially to patients with dry eyes before operation who were already imbalance. Thus, the aberrations of dry eye patients after cataract surgery are greater and we detected significant aberration changes over the 4.0 mm zone at 1-month. One study said that persistent DE symptoms after cataract surgery were associated with a high OSDI score at baseline, low TBUT, low digital pressure score, and extended MG dropout at 1 month postoperative.[23] Undeniably, the surgical incision, intraoperative flushing, and application of eyedrops may have short-term implications for corneal HOAs.[35] Our study also found the long-term changes of the posterior surface corneal HOAs after cataract surgery and agrees with findings in previous studies and attributed to corneal inflammation ,corneal edema, keratic precipitates, the incision, endothelial damage, or localized Descemet membrane detachment can affect the posterior surface more than anterior surface.[35,36] There were no significant differences in anterior and total aberration between three months after operation and before operation. Some of these changes can be attributed to postoperative corneal remodeling. Incision remodeling continues slowly for months to years after surgery, a process that is thought to be associated with collagen deposits on the posterior endothelial surface of the incision.[37] Late posterior wound retraction can last up to 15 years, what maybe implied long-term incision remodeling. The clinical effect of posterior wound retraction may induce changes in anterior and posterior corneal curvatures and thereby alter corneal power and astigmatism.[38] Cataract surgery can damage corneal epithelium and epithelial thickness is associated with local irregularities of corneal topography that contribute to the optical power of the cornea.[39]Furthermore, significant changes in epithelial thickness have been correlated with corneal instability.[40] It was found that epithelial thickness increased 1 day postoperatively and decreased after 1 week. Then it returned to the pre-operative levels at 1-month and remained stable until at 3-months by using spectral-domain OCT measurement. These findings might clinically affect visual function.[41] When the cornea is damaged, wound healing primarily progresses toward reestablishing the continuity of the corneal epithelium, followed by remodeling of the stromal tissue via activated keratocytes.[42] Although the operation led to exacerbating of dry eye, changing of corneal regularity and then increasing of corneal intrinsic aberration, epithelial or stromal remodeling might restore corneal regularity to preoperative level. While there is no remission of dry eye. Inflammation might be the possible internal reason for epithelial changes. A previous study showed significant Langerhans cell infiltration was seen at 3 days and 5 days after cataract surgery. Langerhans cell infiltration contributed to deranged epithelial renewal and the thinning of the corneal epithelium.[43] Inevitably, the infiltration of inflammatory cells will aggravate dry eye. Thus, surgical incision leads to direct injury and indirect injury of inflammation.

In our study, we found the corneal vortical nerve average density and maximum length were negatively correlated anterior corneal aberrations including total aberrations, LOAs and HOAs. As we all known the density of the corneal sub-basal nerve tends to reduce in DED.[44,45] We wonder if the changes of corneal nerve will lead to increasing corneal aberrations in DED. Our previous studies have verified this hypothesis and considered it has a certain impact. Only the corneal vortical nerve maximum length had negative correlation with correlated anterior corneal aberrations one month after the operation. However, these correlations disappeared 3 months after operation. The corneal vortical nerve average density and maximum length were positive correlatively with posterior corneal surface aberration 3 months after operation. One cause may be the loss of corneal endothelium. Other corneal anterior aberrations changes disappeared due to corneal remodeling. Moreover, preoperative and postoperative changes and correlation mostly found in corneal vortex which proved to be unique site relating to dry eye.

Our study has some limitations. The total corneal aberrations, corneal nerve length, corneal vortical and peripheral nerve density and length were analysed. However, each aberration, corneal nerve width, branch number, nerve tortuosity required further analysis. The basis of corneal remodeling is also needed, such as anterior-segment optical coherence tomography.

## Conclusions

The results of this study extend our understanding of the changes in corneal aberrations and nerve density after cataract surgery. Our data show that corneal vortical nerve maximum length and average density are decreased after cataract surgery partly because the aggravation of dry eye condition. Furthermore, corneal aberrations change mainly occurred on the anterior surface of the cornea until 1 month and posterior surface until 3 months. However, changes of anterior aberrations disappeared because of corneal remodeling instead of dry eye relief. The symptoms and signs of dry eye are inconsistent, but there are changes in objective examination, for example IVCM.

## Declarations

**Conflict of Interest**: No conflicting relationship exists for any author.

**Funding**: The publication of this paper was supported by a grant from Beijing Natural Science Foundation (Grant no. 7202229). The sponsor or funding organisation had no role in the design or conduct of this research.

**Availability of data and material:** The analysis data used in this study are available from the corresponding author upon request.

**Code availability**: Not applicable.

**Authors' contributions**: All named authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship for this article and take responsibility for the integrity of the work as a whole. **Dalan Jing:** research design, data acquisition, data analysis, and manuscript preparation. **Xiaodan Jiang:** research design, manuscript modification. **Yilin Chou:** data acquisition, data analysis. **Shanshan Wei**: data acquisition. **Ran Hao:** data analysis. **Jie Su:** data acquisition. **Xuemin Li:** research design.

**Ethics approval:** The study was approved by the Ethics Committee of Peking University Third Hospital and the research was performed in accordance with the Declaration of Helsinki.

**Consent to participate**: Written informed consent was obtained from all participants.

**Consent for publication**: All authors have given their approval for this version to be published.

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