Al-Azhar International Medical Journal

Volume 5 | Issue 7 Article 18

7-31-2024
Section: Ophthalmology

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How to Cite This Article

kamel, Ahmed Ismail; Hussien, Mostafa Othman; and Ali, Ezzat Ali Ezzat (2024) "Changes of Corneal higher order Aberrations in Dry Eye Patients before and after Treatment with Artificial Drops," *Al-Azhar International Medical Journal*: Vol. 5: Iss. 7, Article 18.
DOI: https://doi.org/10.58675/2682-339X.2536

ORIGINAL ARTICLE

Changes of Corneal higher order Aberrations in Dry Eye Patients before and after Treatment with Artificial Drops

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Abstract

Background: ***One of the most prevalent conditions in ophthalmology clinics is dry eye, which causes symptoms of discomfort in the eyes, such as redness, dryness, pain, and a feeling of a foreign body. It also impairs night vision because of aberrant tear film function or a lack of tears.***

Aim and objectives: ***To evaluate the differences in corneal higher-order aberrations between patients with dry eyes who received a 0.3% hydroxypropyl cellulose (methylcellulose) eye drop or a 0.2% sodium hyaluronate eye drop. to contrast the two and examine variations for every single eye drop.***

Patients and methods: ***This prospective investigation includes thirty patients (60 eyes divided into two groups) with dry eyes at the El-Hussein outpatient Clinic from January 2021 to December 2023.***

Results: ***Spherical aberration (SA), coma, and trefoil significantly decreased after treatment with the advantage of Hyfresh over Tear's guard. Thus, 0.2% sodium hyaluronate eye drops are highly recommended for dry eye patients with higher-order aberrations (HOAs).***

Conclusion: ***Compared to 0.3% Hydroxy Propyl Methyl Cellulose eye drops (Tears guard), 0.2% Sodium Hyaluronate eye drops (Hyfresh) Patients with dry eyes had much less alterations in their corneal higher order aberrations.***

Keywords: Cornea; Aberrations; Dry Eye; Artificial Drops

1. Introduction

A vital component supporting the maintenance of the ocular optical quality is the precorneal tear film.[1]

When the tear film, which is the eye's most anterior refractive surface, breaks, the optical surface becomes uneven and could potentially cause further aberrations in the optical system.[2]

Previous research backs up the theory that dry eye causes more irregularities and dynamic changes in the tear film, which results in higher optical aberrations when compared to normal eyes.[3] Deterioration of optical quality and visual function may result from these modifications.[4]

Eye drops containing artificial tears are intended to lubricate the ocular surface and alleviate discomfort in individuals with dry eyes. As a result, the cornea will become smoother, improving optical quality. After using artificial tears eye drops, the majority of patients say that their symptoms of dry eyes and vision have improved.[5]

Prior studies have demonstrated a notable enhancement in optical quality due to a considerable decrease in aberrations linked to uneven tear film following the implantation of artificial tears.[6]

Lower-order aberrations encompass Myopia (positive defocus), hyperopia (negative defocus), and ordinary astigmatism. First-order aberrations, including prisms and zero-order aberrations (pistons), are non-visually noticeable lower-order aberrations. The contribution of low-order aberrations to the total wave aberration in the eye is estimated to be around 90%. Higher-order aberrations constitute a relatively minor portion, accounting for approximately 10% of the overall aberrations of the eye.[7]

Accepted 21 July 2024.
Available online 31 July 2024

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https://doi.org/10.58675/2682-339X.2536

The prevalence of higher-order aberrations tends to rise as individuals age, while the right and left eyes exhibit mirror symmetry.[8]

The objective of this study is to examine the alterations in corneal higher-order aberrations in patients with dry eyes before and after treatment with either 0.3% Hydroxy Propyl Methyl Cellulose eye drops or 0.2% Sodium Hyaluronate eye drops. To individually assess the changes caused by each eye drop and to make a comparison of the two.

2. Patients and methods

At El-Hussein Outpatient Clinic, 30 patients with dry eyes (60 eyes total between the two groups) will participate in this prospective study between January 2021 and December 2023.

Inclusion criteria: Participants in the trial had a diagnosis of severe to moderate dry eye disease. Following the guidelines established by the Dry Eye Workshop9, every participant had to be older than 18 and have the best corrected visual acuity (BCVA) of 20/30 or higher.

Exclusion criteria: Contact lens wearer, blepharitis, pterygium, and other ocular surface disease and laser in-situ keratomileusis surgery (LASIK).

Ethical consideration: Obtaining informed consent from every study participant.

All study subjects were subjected to a standard protocol consisting of the following:

History taking: Ophthalmologic and general history.

Examination of dry eye patients: Visual acuity testing (uncorrected and best corrected). Slit lamp examination, Tear break-up time (TBUT), and fluorescein staining were done for each eye. When the patient looks up, a FL strip will be used to contact the inferior fornix. The patient will be instructed to blink multiple times to ensure that the dye is mixed sufficiently before holding their eye open. All exams are conducted between 9 and 11 a.m. in order to avoid variations in the light. Corneal topography is utilized to identify corneal high-order aberrations (HOAs) ranging from third to fifth order in the middle 3 and 5 mm zones.

Treatment of dry eye patients: Instillation of 0.3% hydroxypropyl methylcellulose eye drops for the first group (30 eyes) and 0.2% sodium hyaluronate eye drops for 30 eyes in the second group, both four times a day for one month.

After treatment of dry eye patients: After one month, all the patients come back to the hospital. Previous examinations and tests have been done. Inquiries regarding each sensory dry eye symptom were also made of the patients. MediWorks Dry Eye Products (Shanghai MediWorks Precision Instruments Co., Ltd.) enable a complete, comprehensive, and precise evaluation that fully covers reports on Dry Eye Diagnosis. Meibomian Glands checking is 1 of them.

Figure 1. MediWorks Dry Eye Diagnostic System.

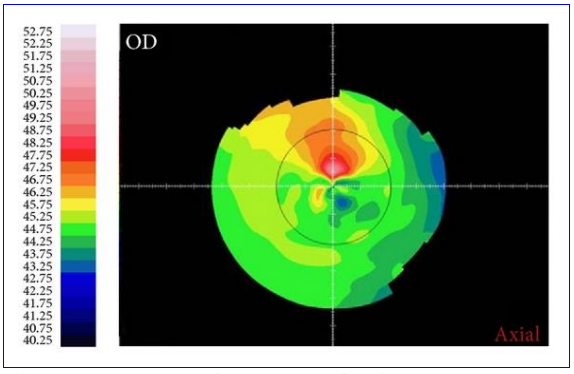

Figure 2. Corneal topography image.

Statistical analysis:

Data was uploaded to the computer, and analysis was done using IBM SPSS software version 20.0 (Armonk, New York: IBM Corp.). The qualitative data was described using percentages and numbers. We used the Shapiro-Wilk test to ensure the distribution was normal. The phrase range (minimum and maximum), mean, standard deviation, median, and interquartile range (IQR) were employed to describe the quantitative data. The significance of the findings was evaluated at the 5% level.

The test that was employed was the chi-square test, which compares different groups based on categorical variables. Fisher's Exact correction is a chi-square correction applied when the predicted count is less than five in more than 20% of the cells. Student t-test: To compare two groups under study for quantitative variables that are regularly distributed. Paired t-test: To compare two periods of customarily distributed quantitative data. Mann-Whitney test: To compare quantitative parameters that are generally not distributed between two research groups. Test of ranks signed

by Wilcoxon: For quantitative variables that are not normally distributed, comparing two periods.

3. Results

Table 1. Comparison between the two studied groups according to demographic data.

	Eye drop				Test of Sig.	p
	Hyfresh (n=30)		Tears guard (n=30)			
	No.	%	No.	%		
Sex						
Male	8	26.7	8	26.7	χ^2=0.0	1.000
Female	22	73.3	22	73.3		
Age (years)						
Min.-Max.	19.0-55.0		20.0-55.0		t=0.000	1.000
Mean±SD.	35.0±10.80		35.0±10.75			
Median (IQR)	33.0 (24.0-43.0)		36.0 (26.0-45.0)			

IQR: Inter quartile range SD: Standard deviation t: Student t-test

χ2: Chi square test p: p value for comparing between the studied groups

Sex and age were insignificantly different between the studied groups.

Table 2. Comparison between the two studied groups according to NIBUT and MGD.

		EYE DROP		TEST OF SIG.	P
		Hyfresh (n=30)	Tears guard (n=30)		
NIBUT (SEC)	Before				
	Min.-Max.	6.50-12.0	3.45-13.0	t=0.238	0.813
	Mean±SD.	9.41±1.77	9.29±2.33		
	Median (IQR)	9.68 (7.9-11.2)	8.97 (8.2-11.3)		
	After				
	Min.-Max.	10.0-14.50	8.15-15.70	t=0.688	0.495
	Mean±SD.	13.18±1.12	12.90±1.94		
	Median (IQR)	13.55 (12.6-14.0)	13.10 (12.5-14.2)		
	Increase	3.77±1.28	3.61±2.0	U=423.0	0.690
	$^{t0}p_0$	<0.001*	<0.001*		
MGD (%)	Before				
	Min.-Max.	15.0-46.0	20.0-67.0	U=254.50*	0.004*
	Mean±SD.	32.40±7.93	39.67±11.78		
	Median (IQR)	34.50 (25.0-37.0)	40.0 (35.0-45.0)		
	After				
	Min.-Max.	0.0-27.0	0.0-35.0	U=227.0*	0.001*
	Mean±SD.	16.60±6.27	22.20±9.84		
	Median (IQR)	16.50 (14.0-20.0)	25.0 (20.0-28.0)		
	Decrease	15.80±5.36	17.47±6.67	U=386.0	0.342
	$^{Z}p_0$	<0.001*	<0.001*		

IQR:Inter quartile range SD:Standard deviation t:Student t-test U:Mann Whitney test

t0:Paired t-test Z:Wilcoxon signed ranks test p:p value for comparing between the two studied groups

p0:p value for comparing between Before and After in each group *:Statistically significant at p≤0.05

NIBUT before and after treatment was insignificantly different between the studied groups while it was significantly increased after treatment than before in hyfresh and tears guard groups (P value<0.001). Meibomian gland dysfunction (MGD) before and after treatment was significantly decreased in hyfresh group than tears guard group (P value=0.004 and 0.001 respectively) and it was significantly decreased after treatment than before in hyfresh and tears guard groups (P value<0.001).

Table 3. Comparison between the two studied groups according to Tear height and corneal thickness.

		EYE DROP		TEST OF SIG.	P
		Hyfresh (n=30)	Tears guard (n=30)		
TEAR HEIGHT (ML)	Before				
	Min.-Max.	0.14-0.53	0.08-0.80	U=317.00*	0.049*
	Mean±SD.	0.27±0.09	0.23±0.12		
	Median (IQR)	0.26 (0.20-0.33)	0.20 (0.17-0.25)		
	After				
	Min.-Max.	0.20-0.70	0.20-0.47	U=369.50	0.233
	Mean±SD.	0.36±0.12	0.31±0.07		
	Median (IQR)	0.35 (0.27-0.40)	0.30 (0.25-0.36)		
	Increase	0.09 ± 0.07	0.08±0.13	U=371.50	0.244
	$^{Z}p_0$	<0.001*	<0.001*		
CORNEAL THICKNESS	Before				
	Min.-Max.	458.0-607.0	450.0-566.0	t=1.933	0.059
	Mean±SD.	535.1±45.13	515.5±32.68		
	Median (IQR)	542.5 (492.0-492.0)	512.0 (495.0-544.0)		
	After				
	Min.-Max.	475.0-621.0	458.0-581.0	t=2.176*	0.034*
	Mean±SD.	545.7±42.94	524.3±32.81		
	Median (IQR)	546.0 (506.0-574.0)	519.5 (509.0-551.0)		
	Increase	10.60±9.93	8.80±4.50	U=421.50	0.672
	$^{t}p_0$	<0.001*	<0.001*		

IQR:Inter quartile range SD:Standard deviation. t:Student t-test. U:Mann Whitney test.

t0:Paired t-test. Z:Wilcoxon signed ranks test, p:p value for comparing between the two studied groups.

p0:p value for comparing between Before and After in each group. *:Statistically significant at p≤0.05.

Tear height before treatment was significantly increased in hyfresh group than tears guard group (P value=0.049) while after treatment it was insignificantly different between the studied groups. Tear height was significantly increased after treatment than before in hyfresh and tears guard groups (P value<0.001). Corneal thickness before treatment was insignificantly different between the studied groups while after treatment it was significantly increased in hyfresh group than tears guard group (P value=0.034). Corneal thickness was significantly increased after treatment than before in hyfresh and tears guard groups (P value<0.001).

Table 4. Comparison between the two studied groups according to UCVA and BCVA.

		EYE DROP		U	P
		Hyfresh (n=30)	Tears guard (n=30)		
UCVA	Before				
	Min.-Max.	0.30-0.70	0.05-0.60	155.00*	<0.001*
	Mean±SD.	0.57±0.10	0.42±0.14		
	Median (IQR)	0.60 (0.50-	0.50 (0.40-		

	0.60)	0.50)		
After				
Min.-Max.	0.50-0.90	0.10-0.70	199.00*	<0.001*
Mean±SD.	0.71±0.10	0.56±0.17		
Median (IQR)	0.70 (0.60-0.80)	0.60 (0.50-0.70)		
Increase	0.14±0.06	0.14±0.05	421.50	0.623
$^{Z}p_0$	<0.001*	<0.001*		
Before				
Min.-Max.	0.60-0.90	0.40-0.90	186.00*	<0.001*
Mean±SD.	0.75±0.08	0.65±0.09		
Median (IQR)	0.70 (0.70-0.80)	0.70 (0.60-0.70)		
After				
Min.-Max.	0.70-1.0	0.60-1.0	302.00*	0.021*
Mean±SD.	0.89±0.09	0.82±0.10		
Median (IQR)	0.90 (0.80-1.0)	0.80 (0.80-0.90)		
Increase	0.13±0.06	0.17±0.06	309.00*	0.019*
$^{Z}p_0$	<0.001*	<0.001*		

BCVA

IQR:Inter quartile range. SD:Standard deviation. U:Mann Whitney test.

Z:Wilcoxon signed ranks test. p:p value for comparing between the two studied groups.

p0:p value for comparing between Before and After in each group. *:Statistically significant at p≤0.05.

Uncorrected visual acuity (UCVA) before and after treatment was significantly increased in hyfresh group than tears guard group (P value<0.001) and it was significantly increased after treatment than before in hyfresh and tears guard groups (P value<0.001). Best corrected visual acuity (BCVA) before and after treatment was significantly increased in hyfresh group than tears guard group (P value<0.001 and 0.021 respectively) and it was significantly increased after treatment than before in hyfresh and tears guard groups (P value<0.001).

Table 5. Comparison between the two studied groups according to Coma.

COMA		EYE DROP		U	P
		Hyfresh (n=30)	Tears guard (n=30)		
$(Z3)^1$	Before				
	Min.-Max.	-0.46-0.38	-0.47-0.23	343.00	0.114
	Mean±SD.	-0.04±0.24	-0.14±0.26		
	Median (IQR)	0.04 (-0.27-0.14)	-0.06 (-0.41-0.13)		
	After				
	Min.-Max.	-1.33-1.43	-1.33-0.74	410.50	0.559
	Mean±SD.	-0.16±0.73	-0.31±0.48		
	Median (IQR)	-0.26 (-0.60-0.21)	-0.36 (-0.54-0.11)		
	Decrease	0.12±0.56	0.17±0.35	420.00	0.657
	$^{Z}p_0$	0.036*	0.026*		
$(Z3)^{-1}$	Before				
	Min.-Max.	-0.80-1.38	-1.48-3.52	439.50	0.877
	Mean±SD.	0.10±0.75	0.24±1.24		
	Median (IQR)	-0.04 (-0.62-0.61)	-0.07 (-0.49-0.36)		
	After				
	Min.-Max.	-2.65-2.76	-2.66-1.49	430.00	0.767
	Mean±SD.	-0.25±1.24	-0.30±1.10		
	Median (IQR)	-0.29 (-1.08-0.57)	-0.37 (-1.06-0.66)		
	Decrease	0.35±0.81	0.54±0.93	438.00	0.859
	$^{Z}p_0$	0.014*	0.001*		

IQR:Inter quartile range. SD:Standard deviation. U:Mann Whitney test.

Z:Wilcoxon signed ranks test. p:p value for comparing between the two studied groups.

p0:p value for comparing between Before and After in each group. *:Statistically significant at p≤0.05.

Coma (Z3)1 and (Z3)-1 before and after treatment were insignificantly different between the studied groups while they were significantly decreased after treatment than before in hyfresh and tears guard groups (P value<0.05).

Table 6. Comparison between the two studied groups according to SA (Z4)0.

$SA\ (Z4)^0$	EYE DROP		U	P
	Hyfresh (n=30)	Tears guard (n=30)		
BEFORE				
MIN.-MAX.	1.06-1.83	0.62-1.55	175.00*	<0.001*
MEAN±SD.	1.32±0.21	1.04±0.25		
MEDIAN (IQR)	1.27 (1.2±1.4)	1.06 (0.88-1.2)		
AFTER				
MIN.-MAX.	-2.25-2.16	-2.26-1.45	398.50	0.446
MEAN±SD.	0.02±1.15	-0.28±1.09		
MEDIAN (IQR)	-0.16 (-0.81-0.61)	-0.28 (-0.84-0.81)		
DECREASE	1.30±1.10	1.33±1.13	422.00	0.679
$^{Z}p_0$	<0.001*	<0.001*		

IQR:Inter quartile range. SD: Standard deviation. U:Mann Whitney test. Z:Wilcoxon signed ranks test.

p:p value for comparing between the two studied groups. p0:p value for comparing between Before and After in each group. *:Statistically significant at p≤0.05.

SA (Z4)0 before treatment was significantly increased in hyfresh group than tears guard group (P value <0.001) while after treatment it was insignificantly different between the studied groups. SA (Z4)0 was significantly decreased after treatment than before in hyfresh and tears guard groups (P value <0.001).

4. Discussion

Similar to our finding, the Gao et al.[10] study assessed alterations in optical clarity in individuals with dry eye syndrome prior to and following therapy. It observed a noteworthy enhancement in visual acuity after treatment, as shown by a substantial improvement in best-corrected visual acuity (p=0.02).

Liu et al.[11] The effect of dry eye on (BCVA) was confirmed by the investigation. The comparative results showed that when compared to the standard group, the dry eye group's BCVA was much worse. These results validate our pre-treatment results from before.

Consistent with our findings, Lu et al.[12] conducted an assessment of corneal aberration alterations in individuals with dry eye following treatment with artificial eye drops. They reported that the best-corrected visual acuity (BCVA)

LogMar (0.10±0.05) showed a substantial improvement compared to the initial measurement (0.14±0.09) after two weeks (p<0.001).

Coma (Z3)1 and (Z3)-1 before and after treatment were insignificantly different between the studied groups. At the same time, they were significantly decreased after treatment than before in the Hyfresh and Tears guard groups (P value<0.05).

Coma (Z3)1 decreased from -0.04±0.24 to -0.16±0.73 after treatment with Hyfresh and from -0.14±0.26 to -0.31±0.48 after treatment with Tears Guard, with a significant difference within the group.

Coma (Z3)-1 decreased from 0.10±0.75 to -0.25±1.24 after treatment with Hyfresh and from 0.24±1.24 to -0.30±1.10 after treatment with Tears Guard, with a significant difference within the group.

Trefoil (Z3)3 and (Z3)-3 before and after treatment were insignificantly different between the studied groups, while they significantly decreased after treatment than before in the Hyfresh and Tears guard groups (P value<0.05).

When compared to the initial values of 0.0192±0.0458 μm and 0.0145±0.0289 μm, respectively, the vertical and horizontal coma terms for the investigation of a 3 mm zone were dramatically reduced (−0.0181±0.0454 μm & 0.0032±0.0215 μm, respectively). The reduction in these terms was statistically significant (p<0.001 and p=0.008) Liu et al.,[11]

Spherical aberration (SA) (Z4)0 before treatment was significantly increased in the Hyfresh group than in the Tears guard group (P value<0.001). In contrast, after treatment, it was insignificantly different between the studied groups. SA (Z4)0 was significantly decreased after treatment than before in the Hyfresh and Tears guard groups (P value<0.001).

Liu et al.[11] Our outcomes were not up to par. As noted in the 3 mm zone investigation, the SA term did not show any statistically significant changes (t=0.1470, t=0.884).

Multiple investigations support our discovery by demonstrating the fluctuation of corneal surface smoothness shortly after blinking. This research has observed a notable rise in smoothness approximately 10 seconds after blinking, indicating that the dry tear film layer can impact the clarity of the cornea Xu et al.,[13] Ferrer et al.,1, and Koh et al.,[14]

2ry astigmatism (Z4)2 before treatment was insignificantly different between the studied groups, while after treatment, it was significantly decreased in the Hyfresh group than the Tears guard group (P value=0.048).

2ry astigmatism (Z4)2 was significantly less severe after treatment compared to before in the Hyfresh and Tears guard groups (P values = 0.037 and 0.028, respectively).

2ry astigmatism (Z4)-2 before and after treatment was insignificantly different between the studied groups, while it was significantly decreased after treatment than before in the Hyfresh and Tears Guard groups (P values = 0.047 and 0.033, respectively).

Tetra foil (Z4)4 and (Z4)-4 before and after treatment were insignificantly different between the studied groups, while they significantly decreased after treatment than before in the Hyfresh and Tears guard groups (P value<0.05).

2ry Coma (Z5)1 before treatment was insignificantly different between the studied groups, while after treatment, it was significantly decreased in the Hyfresh group than in the Tears Guard group (P value=0.004).

2ry Coma (Z5)1 was significantly decreased after treatment than before in the Hyfresh and Tears guard groups (P value < 0.001 and 0.004, respectively).

2ry Coma (Z5)-1 before and after treatment was insignificantly different between the studied groups, while it was significantly decreased after treatment than before in the Hyfresh and Tears guard groups (P values=0.026 and 0.031, respectively).

2ry Trefoil (Z5)3 and (Z5)-3 before and after treatment were insignificantly different between the studied groups, while they were significantly decreased after treatment than before in the Hyfresh and Tears guard groups (P value < 0.05).

Penta foil (Z5)5 and (Z5)-5 before and after treatment were insignificantly different between the studied groups, and they were insignificantly different between before and after treatment in both groups.

Our results before treatment were supported by Denoyer et al.[15] Following the act of blinking, patients with dry eye experienced a notable rise in the overall levels of (HOAs), coma, and trefoil aberrations. The control eyes did not exhibit this rise in aberrations. The presence of dry eyes resulted in considerably elevated levels of total higher-order aberrations, coma, and trefoil aberrations compared to the control eyes.

In alignment, the 5 mm zone, vertical coma, horizontal coma, and SA at two weeks all showed a statistically and mathematically significant decrease compared to those at baseline (−0.0018±0.1121 μm, 0.0181±0.0907 μm, and 0.1111±0.0575 μm; μ=0.004, μ=0.001, and μ=0.026, respectively) Liu et al.[11]

All the previous parameters before treatment were in line with the dry eye group finding of Liu et al.[11] In contrast, the wavefront aberrations in the DE group were substantially higher than in the standard group (P<0.001), including total corneal aberrations, HOA, coma, trefoil, and SA.

This demonstrates how dry eyes aggravate corneal aberrations.

Mico and Alio,[16] concluded that, compared to normal control eyes, the eyes of dry eye sufferers had more optical aberrations. Increased tear film irregularity in dry eyes led to an increase in higher-order aberrations. Nevertheless, Mico and Alio did not ascertain the impact of therapy; hence, our investigation resolves this gap.

In contrast to us, both groups' postoperative data showed a considerable increase in the combined HOA, coma, trefoil, and SA. When tested 10 seconds after blinking, the dry eye group's total HOA, coma, and trefoil rose dramatically, with the exception of SA. These values were recorded immediately after blinking.[17]

However, the difference between our findings and the Jung et al.[17] studies may contribute to his treatment by laser subepithelial keratomileusis (LASEK).

To explain the earlier findings, corneal aberrations are caused mainly by the anterior corneal surface. In contrast, the posterior corneal surface produces relatively steady aberration that is not very significant in relation to corneal aberrations. The most anterior covering layer that interacts with the air on the anterior corneal surface is called tear film Lu et al.,[12]

4. Conclusion

Compared to 0.3% hydroxypropyl methylcellulose eye drops (Tears Guard) and 0.2% sodium hyaluronate eye drops (Hyfresh), Patients with dry eyes had much fewer alterations in their corneal higher-order aberrations.

Disclosure

The authors have no financial interest to declare in relation to the content of this article.

Authorship

All authors have a substantial contribution to the article

Funding

No Funds : Yes

Conflicts of interest

There are no conflicts of interest.

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