

Comparison of Two Different Accelerated Corneal Cross-linking Procedures Outcomes in Patients with Keratoconus

Özülken et al. Effect of Accelerated Crosslinking on Aberrations

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Received: 16 August 2019

Accepted: 06 January 2020

DOI: 10.4274/balkanmedj.galenos.2019.8.45

Cite this article as: Özülken K, Aksoy Aydemir G, Aydemir E, Kızıltoprak H, Yüksel E. Comparison of Two Different Accelerated Corneal Cross-linking Procedures Outcomes in Patients with Keratoconus. *Balkan Med J*

Background: Corneal Cross-linking (CXL) treatment is the unique treatment method that can cease the progression of keratoconus disease. Due to the long duration of conventional treatment, accelerated crosslinking treatment methods are being developed.

Aims: To compare two different accelerated CXL protocols in terms of postoperative visual acuity and topographic findings (Higher-order aberrations and keratometry values).

Study Design: Retrospective comparative study

Methods: Sixty-five eyes of 43 patients (30 males, 13 females) who underwent 2 different accelerated CXL protocols (10 minutes, 9 mW / cm² or 5 minutes, 18 mW / cm²) for progressive keratoconus were retrospectively analyzed. Patients were divided into two groups as group 1 (10 min, 9 mW / cm², 32 eyes of 21 patients) and group 2 (5 min, 18 mW / cm², 33 eyes of 22 patients) according to the accelerated CXL treatment protocol. Uncorrected visual acuity (UCVA) and best corrected visual acuity (BCVA) values and topographic findings (central corneal thickness, flat and steep keratometry values) were recorded preoperatively and 6 months after CXL treatment. Higher-order aberration values measured with pentacam preoperatively and 6 months after CXL were also recorded.

Results: In both groups, a significant improvement was detected in UCVA and BCVA levels between the preoperative and postoperative sixth month (Group 1; p=0.001, p=0.001 and Group 2; p=0.001, p=0.001 respectively). In addition, central corneal thickness (CCT) values decreased significantly in both groups (p=0.006, p=0.001). Trefoil values showed no significant difference between preoperative and postoperative 6th month in group 1 (p = 0.160 and p = 0.620, respectively). In group 1 and group 2, coma values were found to decrease significantly in the sixth postoperative month compared to preoperative values (p = 0.001, p = 0.020 respectively). There was no significant difference between preoperative and postoperative 6th month horizontal and vertical trefoil values in both groups. (p = 0.850 and p = 0.140, respectively). There was no significant difference between the two groups in terms of preoperative and postoperative 6th month Higher-order aberrations (HOAs), refractive errors, keratometry values, UCVA and BCVA levels.

Conclusion: Both accelerated CXL procedures were found to be able to stop the progression of keratoconus, provide a significant improvement in topography findings and coma values, and lead to an increase in visual acuity.

Key words: Accelerated Cross-linking; Corneal Cross-linking, CXL, Coma, Keratoconus, Higher order aberrations

Keratoconus is a progressive degenerative disease which is usually seen bilaterally, and is characterized by the progressive thinning of the central cornea and protrusion of the corneal stroma.¹ This thinning of the stroma layer in keratoconus patients results from biochemical, genetic and environmental factors. Treatment options for keratoconus disease may include glasses, contact lenses, intracorneal segment implantation, or a combination of all these.² However, these treatment options cannot stop the progression of keratoconus disease, and corneal

transplantation may be the only option for future rehabilitation. In 1997, Spöerl et al. showed that corneal cross-linking (CXL) with riboflavin and ultraviolet A (UV-A) could prevent the progression of keratoconus disease and reduce the need for keratoplasty.³ Corneal CXL treatment for progressive keratoconus patients; increases the number of cross linkages between the collagen fibers in the corneal stroma, making the cornea more rigid and regular.⁴

The most commonly used method for CXL treatment is the conventional CXL method described by Wollensak.⁵ In this method, corneal iso-osmolar riboflavin solution is applied for 30 minutes, then after saturation of cornea with riboflavin, a 3mW/cm² UV-A beam is applied. Thus, the duration of treatment is about 1 hour and the cumulative UV-A dose is 5.4 J / cm². Because surgical procedure takes a long time, it may cause the corneal stroma to become more dry and thinner and increase the risk of infection.⁶ Furthermore, the long duration of the procedure makes it more difficult for the patient to endure. Also in the centers providing intensive polyclinic service, the number of operations that can be performed on the same day can be limited.

Based on the Bunsen-Roscoe law of reciprocity, it has been proposed that it could be possible to shorten the duration of treatment using higher irradiation.⁷ Accordingly, it has been argued that by modifying the intensity and time of irradiation, the photochemical effect will be similar. The results of experimental and clinical studies have shown that similar biological effects can be achieved with accelerated CXL treatment, which reduces the irradiation time and increases the radiation intensity.⁷

Progressive distortion in keratoconus causes irregular astigmatism, progressive myopia and increased high-order aberrations (HOAs). Therefore, attempts have been made to benefit from high-order aberrations in the diagnosis and classification of keratoconus. Recently, CXL treatment applied to stop keratoconus disease has also been shown to regularize the optic surface and improve HOAs and have positive effects on visual functions.^{8,9} In the literature, it was seen that most of the studies investigating the effects of CXL treatment on high-order aberrations were performed by conventional CXL treatment or conventional CXL treatment was compared with the accelerated CXL treatment.

The aim of this study was to compare the effects of two different accelerated CXL treatment protocols (9mw / cm²-10min vs. 18Mw / cm²-5min) on HOAs and best corrected visual acuity (BCVA).

MATERIALS AND METHODS

Patients who were diagnosed as progressive keratoconus in our clinic and underwent accelerated CXL were retrospectively analyzed. The patients were divided into two groups as group 1 (10 min, 9 mW/cm²) and group 2 (5 min, 18 mW/cm²) according to the accelerated CXL treatment protocol. The following changes within 1 year were accepted as progression criteria: Greater than 1 Diopter (D) increase in maximum keratometry value, worsening of visual acuity due to keratoconus and increase in manifest astigmatism value more than 1 D, manifest spherical value or spherical equivalent increase more than 0.5 D, and ≥ 2 % decrease in central cornea thickness (CCT) from baseline.¹² Patients who underwent anterior segment surgery, had an existing corneal scar and history of corneal trauma, herpetic keratitis, dry eye, autoimmune disease, who had undergone CXL treatment and those with a thinnest point of corneal thickness less than 400 microns on topography were excluded.

The study was approved by the Local Ethics Committee and was conducted in accordance with the Declaration of Helsinki. All participants were given detailed information before the operation and after their written informed consent was obtained.

Demographic characteristics of the patients, preoperative and postoperative 6th month manifest refraction values, uncorrected visual acuity (UCVA), best corrected visual acuity (BCVA), biomicroscopy, funduscopy examination, keratometry values (CCT, flat ve steep keratometry values), and corneal aberrations were evaluated. The BCVA and UCVA of patients were recorded using Snellen's chart and then converted to logMAR for statistical analysis.

Keratoconus was diagnosed with a Scheimpflug camera and Placido disk based topography

WaveLight®Oculyzer II (Pentacam, Germany) and the same topographic device was used in the follow-up of the patients. Topographic measurements were taken by the same technician at the same time of the day to avoid any corneal hydration differences during the day. Furthermore, the measurements were repeated until an optimum measurement was obtained.

Aberration measurements and corneal topography were analyzed using the WaveLight®Oculyzer II (Pentacam, Germany). Total corneal HOAs including coma, horizontal and vertical trefoil, spherical aberration, total HOA and Q value (corneal asphericity) in the Zernike analysis were recorded. Total corneal aberrations, calculated from the elevation values by the Pentacam software, were evaluated in a 6.0-mm-diameter central area with respect to the pupil center in a dark environment, and the pupil was not dilated.

Surgical Technique

A single experienced surgeon (k.o) performed all surgeries. Under sterile conditions at the operating room, following draping, 0.5% proparacaine HCL ophthalmic solution (Alcaine, Alcon Inc., Hünenberg, Switzerland) were instilled into the eyes. 9.0 mm diameter corneal epithelium was peeled after stripping with the help of

spatul 0.1% riboflavin solution (0.1% solution VibeX; Avedro Inc., Waltham, MA) was applied to cornea every 3 minutes for half an hour. In group 1, after the control of the riboflavin solution penetrates the entire cornea with a surgical microscope, the cornea was irradiated with UV-A light at a wavelength of 370 nm and 9 mW / cm² for 10 minutes, and in group 2, the cornea was irradiated with a 18mW / cm² UVA light at 370 nm for 5 minutes. In both groups, a drop of riboflavin solution was applied every 3 minutes also during the irradiation period. After the procedure, all patients were fitted with soft contact lenses (Lotrafilcon B, Air Optix Hydraglyde, Alcon Laboratories Inc.) with a diameter of 14.0 mm and a base curve of 8.6 and a maximum of 140 barrers. Postoperative treatment was prescribed as 0.5% moxifloxacin hydrochloride, 0.1% fluorometholone, topical eye drops 4 times a day. Patients were monitored daily until the corneal epithelium recovered and the contact lenses were removed after epithelial healing. Follow-up examinations of the patients were made in the second week, first month, third month and sixth month.

Statistical Analysis

Descriptive data were presented as the mean \pm standard deviations, frequency distributions, and percentages. The Shapiro-Wilk test was used to assess conformity of the data to normal distribution. The Wilcoxon test was used for the analysis of data that were not normally distributed in dependent groups and the Mann-Whitney U test was used for non-normal distributed data in nondependent groups. Data were analyzed using SPSS Windows 20.0 software (IBM, Armonk, New York, USA). A value of $p < 0.05$ was considered statistically significant. The results of a priori power analysis via PASS 11 (Power and Sample Size Calculation Software, Version 11) showed the need to enroll at least 30 eyes in each group. Therefore, 32 eyes were included in group 1 and 33 eyes were included in group 2, the power of the study was found to be 82.3%. The primary outcomes of our study are visual acuity, corneal keratometry, refractive error and higher order aberration values and their changes between preoperatively and 6 months after CXL treatment. From the references, articles using variables similar to our study were selected and effect size and minimum sample size were calculated. The effect size was accepted as 0.60, type 1 error rate was accepted as 0.05 and type 2 error rate was accepted as 0.20. The primary outcomes are UCVA, BCVA, corneal keratometry and aberrations values and their changes between preoperatively and 6 months after CXL treatment.

RESULTS

The study included 65 eyes of 43 patients (30 male, 13 female). Group 1 comprised 32 eyes of 21 patients (17 male, 4 female) with a mean age of 23.23 ± 4.21 years (16-33 years). Group 2 comprised 33 eyes of 22 patients (13 male, 9 female) with a mean age of 23.90 ± 4.44 years (17-34 years). There was no significant difference between two groups in terms of preoperative keratometry, HOAs, visual acuity, and spherical cylindrical values ($p > 0.05$ for each)

Visual Acuity And Refraction Results

Preoperative values were compared between groups. No significant differences were detected ($p = 0.008$). The visual acuity and refraction values of the patients before and at 6 months after CXL treatment are shown in Table 1. In Group 1, a significant difference was found between UCVA and BCVA before and at 6 months after the CXL treatment ($p = 0.001$ for each). Refractive examination revealed a significant decrease in spherical and cylindrical values at 6 months after treatment ($p = 0.001$, for each). In group 2, there was a significant difference in UCVA and BCVA before and at 6 months after the treatment ($p = 0.001$ for each). Refractive examination at 6 months showed a significant improvement in spherical and cylindrical values ($p = 0.001$ for each). When visual acuity levels of two groups were compared preoperatively and 6 months postoperatively, no significant difference was found between the two groups ($p = 0.123$). Changes from the pre-post treatment in UCVA and BCVA in each group showed no statistically significant difference between groups ($p > 0.05$ for each) which is shown as Table 2.

Topography Results

Preoperative corneal topography results were compared between groups. No significant differences were detected ($p = 0.128$). The corneal topography results of the patients before and at 6 months after treatment are shown in Table 3. In group 1, a statistically significant decrease of was determined in steep and flat keratometry values at 6 months after CXL treatment compared to the pre-treatment values ($p = 0.001$ for each). The thinnest corneal thickness decreased by approximately 6 μm ($p = 0.006$). In group 2, flat and steep keratometry values at 6 months after the CXL treatment decreased by 0.2 D, and 0.5 D respectively and the differences were statistically significant ($p = 0.030$ and $p = 0.001$ respectively). A decrease of 8.5 μm was found to be statistically significant in the thinnest corneal thickness ($p = 0.001$). When topography results of two groups were compared preoperatively and 6 months postoperatively, no significant difference was found between the two groups ($p = 0.092$). Changes from the pre-post treatment in topography results in each group showed no statistically significant difference between groups ($p > 0.05$ for each) which is shown as Table 4.

High Order Aberation Results

Preoperative HOAs results were compared between groups. No significant differences were detected ($p = 0.487$). The HOAs results of the patients before and at 6 months after treatment are shown in Table 5. There was no significant difference in the horizontal and vertical trefoil values of the patients in group 1 before and at 6

months after treatment ($p=0.160$ and $p=0.620$ respectively). Significant difference was observed in coma before and after CXL treatment in group 1 ($p=0.001$). A significant difference was observed in the total HOA ($p=0.001$) whereas no significant difference was observed in spherical aberration in group 1 before and at 6 months after treatment ($p=0.420$).

In group 2, no significant difference was observed in the horizontal and vertical trefoil values before and at 6 months after CXL treatment ($p=0.850$ and $p=0.140$ respectively). There was a significant difference in coma ($p=0.020$). Although there was no significant difference in spherical aberration ($p=0.060$), a significant difference was observed in total HOA ($p=0.001$). When HOA values of two groups were compared preoperatively and 6 months postoperatively, no significant difference was found between the two groups ($p=0.140$). Changes from the pre-post treatment in HOA values in each group showed no statistically significant difference between groups ($p>0.05$ for each) which is shown as Table 6.

DISCUSSION

The present study investigated the effects of two different accelerated CXL treatments on visual acuity and topographic parameters. It is known that structural changes of the cornea can decrease visual quality by increasing HOAs.

Ocular aberrations are divided into two groups as monochromatic and chromatic aberrations. Monochromatic aberrations are divided into two subgroups as low-order aberrations (spherical and cylindrical refractive defects) and HOAs (spherical aberration, secondary astigmatism, coma, trefoil, quadrofoil, tetrafoil, and pentafoil).¹⁰ Since ocular aberrations are a major cause of visual impairment in keratoconus,⁸⁻¹⁰ difference of HOAs between the two different accelerated CXL protocols was evaluated in this study.

$3\text{mW}/\text{cm}^2$ 30 minute conventional CXL treatment has been shown to stop keratoconus disease, improve vision, topographic parameters, and HOAs.¹¹ However, in conventional CXL treatment, 30 minutes of riboflavin and 30 minutes of UVA administration for a total of 1 hour can be very demanding for both the patient and the surgeon. Moreover, occupying the operating room for about 1 hour reduces the total number of operations that can be performed, thereby reducing efficiency.¹² In addition, it may be risky for infection to expose the cornea for 1 hour after corneal epithelial peeling.¹³ Therefore, based on the Bunsen-Roscoe reciprocity law, the same biological effect can be achieved with higher irradiation for a much shorter time, and this has been described as accelerated CXL treatments.¹⁴ The shortening of the total treatment time by providing a much higher irradiance by shortening the exposure time was described as accelerated CXL.¹⁵ Accelerated CXL was started to be used in ophthalmology practice as it provided both patient and doctor a high degree of convenience by shortening the treatment period.¹⁶ However, the biggest concern in accelerating CXL was whether it was as effective as standard treatment. In ex vivo studies on corneal biomechanical properties, Wernli J. et al. demonstrated that Bunsen-Roscoe reciprocity law was valid for irradiance values up to $40\text{--}45\text{ mW}/\text{cm}^2$ (treatment time of less than 2 minutes), and that porcine corneas up to these values acceptable corneal stiffness has been shown to be obtained.¹⁷ In addition, Hammer A et al. observed that $9\text{mW}/\text{cm}^2$ treatment showed similar corneal stiffness with the standard treatment, but values above this ($18\text{mw}/\text{cm}^2$) were not different from the control group. They consider this to be due to the fact that oxygen consumption in accelerated procedures is very fast, that the oxygen in the environment is exhausted very quickly and that oxygen cannot diffuse sufficiently into the cornea.⁷ As is known, oxygen and oxygen radicals are responsible for the formation of a type 2 reaction, which plays an important role in the initiation and continuation of the CXL process.¹⁸ However, Viciguerra P. stated that the smoothing effect of CXL on the cornea was not directly related to the increase in best spectacle-corrected visual acuity and the increase in corneal biomechanics.¹⁹ These results have encouraged many surgeons to accelerated CXL, and many studies have been conducted.²⁰⁻²²

In their study comparing accelerated (5 minutes, 18mW , 5.4 J) and standard (30 minutes, 30mW , $5.4\text{ J}/\text{cm}$) CXL treatment, Kato N et al. reported a significant decrease in keratometric values in both methods at the end of 1 year and no difference was found between the two methods.²³ Likewise, Yildirim Y et al. observed that topographic and refractive changes improved significantly and similarly at the end of 12 months after both accelerated CXL and standard CXL treatment.²⁴ In our study, accelerated CXL treatment in two different protocols showed a significant increase in visual acuity and a significant decrease in spherical and cylindrical values and in K1 and K2 values. We did not observe a significant difference between these two protocols.

Despite studies indicating that there was no difference between the two methods in terms of topographic improvement, in their study of Kirgiz A et al. comparing accelerated CXL of 10 minutes (9mW) and 5 minutes (18mW), it was found that 10 minutes CXL was better in terms of topographic recovery.²⁰ Choi et al. found that the topographic improvement was better at 3 mW irradiance, even if it increased 30 mW irradiance and total energy to 6.6 (j/cm) .²¹ When Hashemi et al. compared the long-term results of standard (3mW) and accelerated (18mW) CXL, they found that standard treatment significantly improved topographic flattening and refractive correction.²² The possible explanation of obtaining different results in studies comparing accelerated and standard CXL can be the age of patients, different devices used, and different preoperative keratometric and visual values. However, the reason for less topographic flattening with accelerated CXL was interpreted as the appearance of a more superficial demarcation line with accelerated CXL.^{21,22} This is thought to be due to the fact

that the oxygen in the environment is exhausted at high energy and the oxygen cannot diffuse sufficiently into the cornea.¹⁸ In our study, we did not evaluate the demarcation line with OCT. This can be considered as the weakness of our study.

In keratoconus disease, visual impairment is caused by high irregular astigmatism as well as increased HOAs.²⁵ Coma-like aberrations in keratoconus patients are known to be much higher than in normal eyes.²⁶ In addition to stopping keratoconus disease, CXL treatment leads to topographic changes, leading to an increase in visual acuity, and an improvement in visual quality by lowering HOAs.⁸

In this study, the HOA values of two groups were examined. When the values of patients in group 1 (10 min, 9mW/cm²) and group 2 (5 min, 18 mW/cm²), before and after CXL were compared, a significant decrease was observed only in coma and total HOA. Although visual acuity and topography findings improved, similar findings were not obtained in aberrations. Further studies are needed to elucidate the effects of the changes in HOAs after CXL treatment on visual function and contrast sensitivity, as well as possible relationships with low-contrast visual acuity.

In contrast to the improvement in visual acuity and K1-K2 values, one of the reasons for not having similar results in high-order aberrations may be the difference in the preoperative topographic cone location in patients. Unlike the current study, Greenstein et al.²⁷ found a significant reduction in HOAs in the 1st year follow-up of the standard protocol CXL (3 mw / 30 min) for the keratoconus and post-LASIK ectasia. Unlike our study, this study had a long follow-up period and standard protocol CXL was applied. Kocamiş et al.²⁸ applied the standard protocol CXL to 37 keratoconus patients and evaluated the HOAs in the 1st, 3rd, 6th, 12th and 18th months. In the early follow-up period, especially in vertical coma and they found a significant decrease in HOAs and total corneal aberrations in the 18th month examination. Caporossi et al.²⁹ found a statistically significant decrease in HOAs after 48 months of follow-up. Baumeister et al.³⁰ examined the short-term effects of CXL therapy, and in the 6th month, a decrease in coma aberration was observed and no statistically significant decrease was found in total HOAs. Kirgiz A et al also reported that coma-like HOAs were significantly lower in the 9mW group than in the 18mW group.²⁰ In the current study, the short follow-up period and the application of 2 different accelerated cxl protocols instead of standard cxl protocol may have been the reason that significant difference only observed in coma and total HOA in group 1 and group 2.

The lack of aberrometer for the measurement of HOAs, the low number of patients and the lack of a control group with the standard protocol CXL treatment were among the factors limiting this study. In addition, the comparison of patients with data only in the 6th month after CXL is the another missing side of our study. Another limitation of the study is the lack of endothelial cell density measurement, so there were no data on the effects on the corneal endothelium of accelerated CXL treatment applied with higher energy. However, a retrospective examination of the patients revealed no postoperative complications such as corneal decompensation, cataract or chronic epithelial defect due to endothelial loss.

Future studies are needed to elucidate the impact of changing HOAs on visual function after CXL treatment, this studies can also investigate the possible relationships of HOAs with contrast sensitivity and low-contrast visual acuity

In conclusion, despite the difference of CXL treatment protocols, similar findings were obtained in both groups. Although the effect on HOAs cannot be demonstrated, there is a need for further studies with larger patient groups and longer follow-up period to be able to re-evaluate and draw more definitive conclusions.

Declaration of Conflicting Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

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TABLE 1. Preoperative/postoperative visual acuity and refraction values

	Group 1 (10 mw/cm ² , 9 minute)			Group 2 (18 mw/cm ² , 5 minute)		
	Preoperative	Postoperative	P	Preoperative	Postoperative	p
UCVA (LogMAR)	0.86±0.17	0.54±0.13	0.001	0.92±0.25	0.62±0.13	0.001
BCVA (LogMAR)	0.35±0.16	0.12±0.08	0.001	0.45±0.33	0.30±0.27	0.001
Spheric, D (min-max)	-2.57±0.31 (-6.00, +1.00)	-1.75±0.27 (-5.00, +1.50)	0.001	-1.69±0.30 (-6.00, +1.25)	-1.05±0.26 (-5.00, +1.75)	0.001
Cylindrical, D (min-max)	-3.22±0.27 (-6.75, -0.50)	-2.25±0.23 (-5.75, -0.25)	0.001	-3.79±0.22 (-6.00, -1.50)	-3.32±0.24 (-5.75, -1.25)	0.001

BCVA: Best corrected visual acuity, D: Diopter, logMAR: Logarithm of the minimal angle of resolution, mw: miliwatt, UCVA: Uncorrected visual acuity

TABLE 2. Changes between preoperative and postoperative visual acuity and refraction values between groups

	Group 1 (10 mw/cm ² , 9 minute)	Group 2 (18 mw/cm ² , 5 minute)	P
UCVA (LogMAR)	-0.32±0.15	-0.30±0.17	0.546
BCVA (LogMAR)	-0.23±0.10	-0.15±0.30	0.402
Spheric, D	-0.82±0.30	-0.70±0.28	0.383
Cylindrical, D	-0.97±0.25	-0.52±0.21	0.058

BCVA: best corrected visual acuity, D: diopter, logMAR: logarithm of the minimal angle of resolution, mw: miliwatt, UCVA: uncorrected visual acuity

TABLE 3. Preoperative And Postoperative Topographic Values

	Group 1 (10 mw/cm ² , 9 minute)			Group 2 (18 mw/cm ² , 5 minute)		
	Preoperative	Postoperative	p	Preoperative	Postoperative	p
K1, D (min-max)	45.5±0.2 (43.4-49.2)	44.3±0.2 (42.1-49)	0.001	45.3±0.3 (42.4-52.6)	45.1±0.4 (41.9-56.5)	0.038
K2, D (min-max)	48.4±0.3 (45.7-53.1)	47.2±0.3 (45.2-52.6)	0.001	49.3±0.4 (46.5-60.1)	48.8±0.5 (45.8-60)	0.001
Thinnest, µm (min-max)	472.5±5.4 (403-537)	466.8±5.4 (412-531)	0.006	461.1±6 (400-519)	452.6±6.1 (400-531)	0.001

D: diopter, K1: Flat K, K2: Steep K, mW: iliwatt, µm: mikron

TABLE 4. Changes Between Preoperative and Postoperative Topographic Values between groups

	Group 1 (10 mw/cm ² , 9 minute)	Group 2 (18 mw/cm ² , 5 minute)	P
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TABLE 5. Preoperative and postoperative high order aberration values						
K1	D	Group 1 (10 mw/cm ² , 9 minute)		Group 2 (18 mw/cm ² , 5 minute)		p
		Preoperative	Postoperative	Preoperative	Postoperative	
K2	Horizontal trefoil, μm	-0.168±0.06 (-0.94/0.57)	-0.251±0.07 (-0.96/0.87)	-0.5±0.5 (-3.87/0.86)	0.06274±0.10 (-0.7196/1.11)	0.850
	Vertical trefoil, μm	0.086±0.07 (-0.85/1.24)	0.100±0.06 (-0.49/0.80)	0.069±0.09 (-0.63/1.35)	0.207±0.06 (-0.50/1.72)	0.140
	Coma, μm (min/max)	-2.194±0.22 (-4.98/0.48)	-1.668±1.83 (-3.75/-0.20)	0.268±0.25 (-5.80/3.68)	0.343±0.22 (-4.91/2.22)	0.020*
	Spherical aberration, μm (min/max)	0.704±0.10 (-0.94/1.77)	0.731±0.12 (-0.85/3.49)	0.580±0.13 (-2.13/1.56)	0.368±0.17 (-2.49/1.74)	0.060
	Total HOA (min/max)	2.150±0.07 (1.40/3.20)	1.643±0.08 (0/2.50)	2.466±0.14 (1.30/5.60)	2.275±0.13 (1.20/5.10)	0.001*

HOA: higher order aberration, mW: miliwatt, μm :mikron, *: statistically significant change

TABLE 6. Changes between preoperative and postoperative high order aberration values between groups			
	Group 1 (10 mw/cm ² , 9 minute)	Group 2 (18 mw/cm ² , 5 minute)	p
Horizontal trefoil, μm	0.083±0.07	0.081±0.12	0.851
Vertical trefoil, μm	0.014±0.06	0.102±0.08	0.156
Coma, μm	0.526±0.72	0.168±0.24	0.188
Spherical aberration, μm	0.016±0.11	-0.198±0.18	0.061
Total HOA	-0.512±0.07	-0.284±0.12	0.065

HOA: higher order aberration, mW: miliwatt, μm :mikron

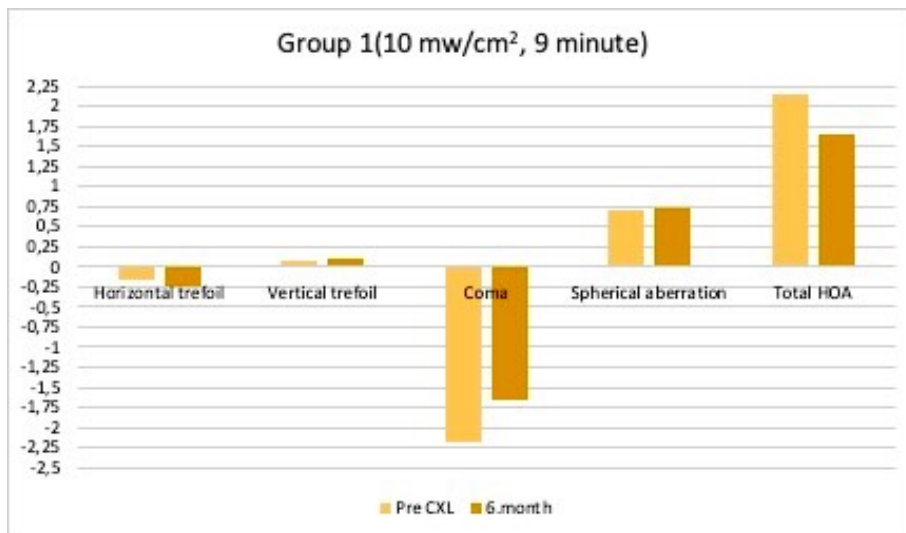


FIG. 1. Pre CXL and post CXL 6th month higher order aberration values in Group 1 (10 mw/cm², 9 minute)

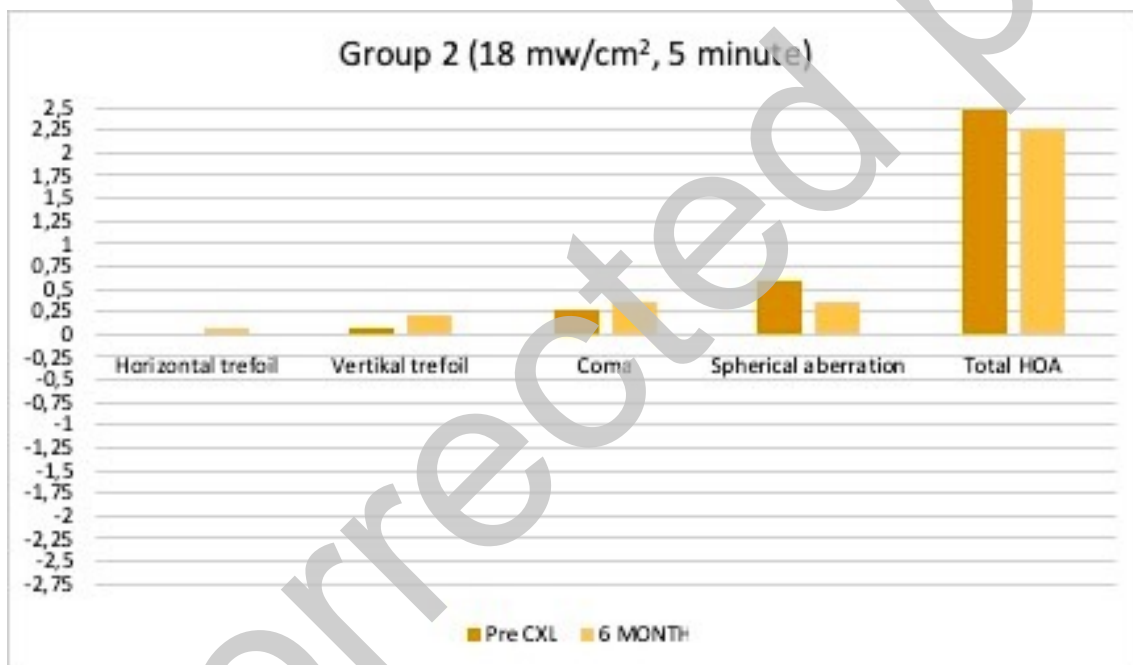


FIG. 2. Pre CXL and post CXL 6th month higher order aberration values in Group 2 (18 mw/cm², 5 minute)