MEDWIN PUBLISHERS
Committed to Create Value for Researchers

Open Access Journal of Ophthalmology
ISSN: 2578-465X

Comparing Corneal OCT Findings in High Irradiance Corneal Crosslinking Combined with Femtosecond Laser In Situ Keratomileusis versus Femtosecond Laser In Situ Keratomileusis

Hosny M[1]*, Hassaballah M[1], Azzam SA[2] and Hany M[3]

[1]Professor of Ophthalmology, Cairo University, Egypt

[2]Lecturer of Ophthalmology, Cairo University, Egypt

[3]Resident of Ophthalmology, Memorial Ophthalmology Institute, Egypt

***Corresponding author:** Mohamed Hosny, Professor of Ophthalmology, Cairo University, 84 Shehab Street, Mohandeseen, Giza 1241, Egypt, Tel: +201000007675; Email: mohamedhosny@kasralainy.edu.eg

Research Article

Volume 6 Issue 1

Received Date: January 08, 2021

Published Date: January 21, 2021

DOI: 10.23880/oajo-16000209

Abstract

Objective: To study Corneal OCT findings in the interface and the demarcation line under or over the interface in patients that undergo Femtosecond laser in situ Keratomeulisis compared to patients that undergo Femtosecond laser in situ Keratomeulisis combined with high irradiance corneal cross linking (Femto-Lasik Xtra).

Study Design: Prospective Randomized Comparative Study.

Methods: Our study included 40 eyes of 20 patients divided into 2 groups, a group of 10 patients with 20 eyes underwent Femto-Lasik & the other group of 10 patients of 20 eyes underwent Femto-Lasik Xtra. The Femto Lasik procedure was done using Alcon Wave Light FS200 laser machine. The Femto-Lasik XTRA procedure entails the administration of half fluence high irradiance cross-linking subsequent to refractive correction. A higher concentration 0.25% riboflavin is applied on the stromal bed and the flap subsequent to laser ablation with a soak time of 90 seconds, UV-A irradiance is delivered as a homogenous beam of 30 mW/cm2 for 90 s to deliver a total fluence of 2.7J/cm2. Patients were randomly observed and HEIDELBERG AS-OCT was performed after 1 week, 1 month & 3 months post-operative.

Results: A demarcation line was noted in femto Lasik Xtra patients, appeared more evident in the peripheral cornea and faded as it approached the central cornea. It became less evident after 1 month and 3 months period respectively. Also the flap hinge was more hyper reflective and evident in femto Lasik Xtra patients when compared to femto Lasik patients. Anterior crosslinked stroma appeared more hyper reflective than posterior stroma in femto Lasik Xtra patients. Flap edge was also more hyper reflective and better demarked in femto Lasik Xtra treated corneas when compared to femto Lasik treated corneas.

Conclusion: AS-OCT showed significant differences between femto Lasik and Femto Lasik Xtra treated corneas. Significant changes were noted in the demarcation line in Femto Lasik Xtra patients along different time periods post-operative.

Keywords: Femto-LASIK; Femto-LASIK Xtra; Demarcation Line; AS-OCT

Abbreviations: OCT: Optical Coherence Tomography; AS-OCT: Anterior Segment OCT; PI: Patient Interface; MRSE: Manifest Refraction Spherical Equivalent; CXL: Corneal Cross-Linking.

Introduction

Optical coherence tomography (OCT) is a noncontact technology that produces high-resolution cross-sectional images of ocular tissues. Anterior segment OCT (AS-OCT) enables the precise visualization of anterior segment structures. AS-OCT is a useful tool to demonstrate thickness of flap and depth of demarcation line after Femto-Lasik Xtra patients [1].

Over the last few years, numerous studies have shown promising results with Femto-Lasik Xtra. Majority of the studies demonstrated greater stability of refraction. The incidence of post-Lasik regression is high in hyperopic eyes is related to ciliary muscle relaxation and also a serial of topographic changes which happens post-operatively. Contralateral study comparing the results of LASIK with or without concomitant cross-linking in hyperopic eyes demonstrated a significantly lower regression in the LASIK Xtra group [2]. Encouraging results have been shown in the treatment of high myopia as well. A study compared the results of LASIK Xtra for high myopic correction (upto -8.00 D) with a spherical equivalent matched historical cohort. A greater refractive accuracy of the Xtra group was noted at 3 months with 98% of the eyes attaining a UDVA of 20/25 or better against 61% eyes in the LASIK group. A longitudinal observational study of 140 eyes with a 2-year follow-up showed lower refractive shift and greater keratometric stability in the Xtra group [2].

The application of CXL along with refractive correction also had an influence on epithelial remodeling post-LASIK, especially while treating higher degrees of myopia. A study showed a significantly lower increase in mid-peripheral thickness when LASIK was combined with CXL (3.79μ) as compared to LASIK alone (9.32μ). A greater refractive stability was noted with no progressive flattening. The procedure demonstrated a good safety profile with stable endothelial cell count and no visually significant haze development. In a large study of 601 eyes, a stable uncorrected visual acuity with no significant changes in spherical equivalent or keratometry was noted at 1year follow-up [3,4].

The LASIK XTRA procedure entails the administration of half fluence high irradiance cross-linking subsequent to refractive correction. A higher concentration 0.25% riboflavin is applied on the stromal bed subsequent to laser ablation with a soak time of 90's [5]. The interface is washed thoroughly and the flap is repositioned. UV-A irradiance is delivered as a homogenous beam of 30 mW/cm^2 for 90 s to deliver a total fluence of 2.7J/cm^2. This is precisely half the energy delivered during conventional cross-linking in the Dresden protocol [5].

Patients and Methods

This study was conducted under the applicable institutional research regulations. All patients received a thorough explanation of the study design and aims. All have signed an informed written consent. The study was performed on a total of 40 eyes of 20 patients, 20 eyes of 10 patients underwent Femtosecond Lasik and 20 eyes of 10 patients underwent Femtosecond Lasik Xtra. The patients were recruited from the outpatient ophthalmology clinics of Dar El-Oyoun Hospital in Sheik Zayed city from the period from April 2018 till October 2018. This is a Prospective randomized comparative study for comparing AS-OCT findings in patients underwent FemtoLASIK vs. Patients underwent FemtoLASIK Xtra. The patients were randomized by block randomization. The protocol was revised and approved by the Ophthalmology ethical committee in faculty of medicine, Cairo University.

Inclusion Criteria

a) Patients age 18-35.

b) Myopes up to -8 D.

c) Hypermetrope up to +4. D.

d) Astigmatism less than 4. D.

e) Stable refraction for 1 year.

f) Central corneal thickness was 500 microns or more.

g) Normal Corneal tomography with a Belin Ambrosio big D value of less than 1.85.

h) Expected post-LASIK residual stromal bed was 300 microns or more.

Exclusion Criteria

a) Age less than 18years, more 35 than years.

b) Myopes more than 8. D.

c) Hypermetrope more than 4. D.

d) Astigmatism more than 4. D.

e) Unstable refraction for 1 year.

f) Corneal thickness less than 500 microns.

g) Abnormal corneal tomography with a Belin Ambrosio big D value more than 1.85.

h) Expected post LASIK residual stromal bed less than 300 microns.

i) Any patient has anterior or posterior segment abnormality.

j) Dry eye syndrome from autoimmune diseases e.g. rheumatoid arthritis and other autoimmune diseases.

Evaluation of Patients

All patients meeting inclusion criteria were subjected to full ophthalmic examination of both eyes in the form of:

1) Measurement of UCVA and BCVA at baseline (Snellen chart) and conversion to decimal units for statistical analysis.
2) Full slit lamp examination, IOP measurement with Goldmann applanation tonometry.
3) Dilated fundus examination using slit lamp bio microscopy with +90D Volk lens and/or +78D Volk lens in some cases.
4) Oculus Pentacam® topography was performed for both eyes before surgery.

Femto LASIK Procedure

The process started by moving a swivel motion-based bed to place the patients head under the Alcon WaveLight FS200 laser machine. Topical anesthetic was used Benoxinate hydrochloride 0.4% (Eipico® pharmaceuticals) then standard draping is applied, and a lid speculum is used to maintain the lids retracted throughout the FS laser treatment. Fixation suction ring is well centered on the cornea and suction no.1 is activated manually to fix the globe. The patient interface (PI) was then lowered slowly to dock onto the suction ring, when perfectly aligned; suction no.2 started automatically to applanate the cornea beginning the corneal flap creation step. (Immediately after the start of suction no.2, the surgeon can re-adjust the position of the flap before pressing the FS firing button). The FS process started by creating a tunnel passing beneath the hinge to facilitate the escape of gas formed during femto-dissection, followed by creating the flap bed in a raster manner and finally creating the side cut. Then the suction turned off automatically. A superior hinge was created with 100 µm flap thickness and an inverted side cut was at 115º.

Femto LASIK XTRA Procedure

a) Administration of half fluence high irradiance cross-linking subsequent to refractive correction. A higher concentration 0.25% riboflavin was applied on the stromal bed and soaks the flap subsequent to laser ablation with a soak time of 90 sec.

b) The interface was washed thoroughly and the flap is repositioned. UV-A irradiance was delivered as a homogenous beam of 30 mW/cm^2 for 90 s to deliver a total fluence of 2.7J/cm^2.

Post-Operative Medications: Patients were on topical antibiotic eye drops (gatifloxacin) 5 times a day , topical steroids (flurometholol) 5 times a day & topical artificial tears 5 times a day for 1 week. Medications were reduced to 3 times a day for the next 3 weeks. After 1 month, patients maintained a twice a day dose of steroid (flurometholol) and topical artificial tears for the period of the next 3 months.

Post-operative follow-up: patients were followed up 1 day, 1 week, 1 month, 3 months & 6 months after the initial surgery. All patients performed Measurement of UCVA and BCVA at follow up using Snellen chart and conversion to decimal units for statistical analysis. Full slit lamp examination, IOP measurement with Goldmann applanation tonometry.

Post-operative assessment: Patients performed AS-OCT using HEIDELBERG® Spectralis® Anterior segment add-on module after 1 week, 1 month & 3 months post-operative.

Results

Statistical Analysis

A total of 40 eyes of 20 patients who fulfilled the inclusion criteria were included in our study, the mean age was 24± (6) years in the femto Lasik group and 21±(3) years in the femto Lasik Xtra group.

BCVA was recorded in Snellen units and converted to decimal notation for statistical analysis. Mean spherical equivalent for the Femto Lasik group pre-operative was -5.33D±3.00D for the myopia patients and +3.25D±1.00D for the hyperopia patients. Mean spherical equivalent for the Femto Lasik Xtra group pre-operative was -5.00D±2.00D for the myopia group and +3.50D±1.00D for the hyperopia group.

The femto Lasik group included 20 eyes of 6 female patients and 4 male patients, while the femto Lasik Xtra group included 20 eyes of 3 male patients and 7 female patients. No intraoperative nor post-operative complications occurred to any of the patients included in our study (Figure 1,Table 1).

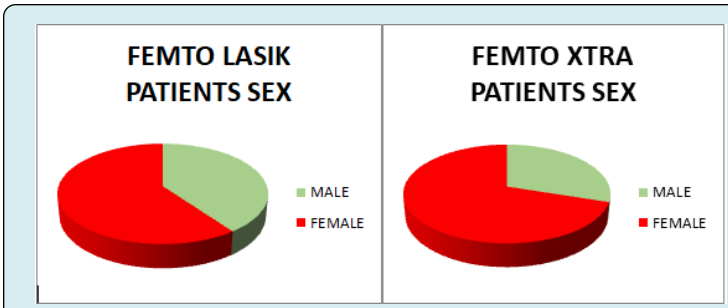

Figure 1: Sex distribution in patients in our study.

	Femto Lasik (n=10)		Femto Lasik Xtra (n=10)		Test of Significance	p
	No.	%	No.	%		
Sex						
Male	4	40	3	30	χ^2= 0.22	^{FE}p= 1
Female	6	60	7	70		
Age (years)						
Min. –Max.	19.0-32.0		18.0–28.0		t= 2.057	0.054
Mean ± SD.	24.50 ± 4.35		21.0 ± 3.16			
Median	24		20			

χ^2: Chi square test; FE: Fisher Exact; t: Student t-test
p: p value for comparing between the two studied groups
Table 1: Comparison between the two studied groups according to demographic data.

Base line UCVA in the femto Lasik group was 0.2 pre-op. Baseline BCVA in the femto Lasik group was 0.9 preoperatively. SD UCVA PRE-OP 0.13165, SD BCVA PRE-OP 0.07378 (Figure 2).

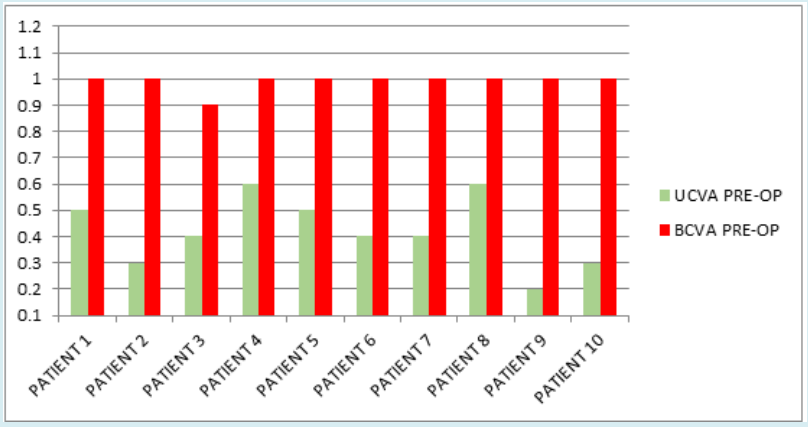

Figure 2: Baseline UCVA & BCVA pre-operative in Femto Lasik group.

Baseline UCVA in femto Xtra group was 0.2 and baseline BCVA was 0.9 preoperatively. SD UCVA PRE-OP 0.126491106, SD BCVA PRE-OP 0.042163702 (Figure 3).

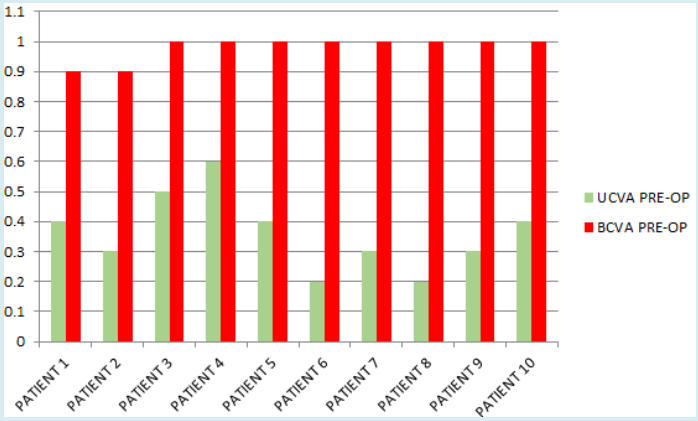

Figure 3: Baseline UCVA & BCVA pre-operative in Femto Lasik Xtra group.

Baseline UDVA postoperatively in the Femto Lasik group was 0.9 and baseline BCVA was 0.9. Mean spherical equivalent was -0.25D±0.75D post-operative (Figure 4).
SD UCVA POST-OP 0.042163, SD BCVA POST-OP 0.0316227.

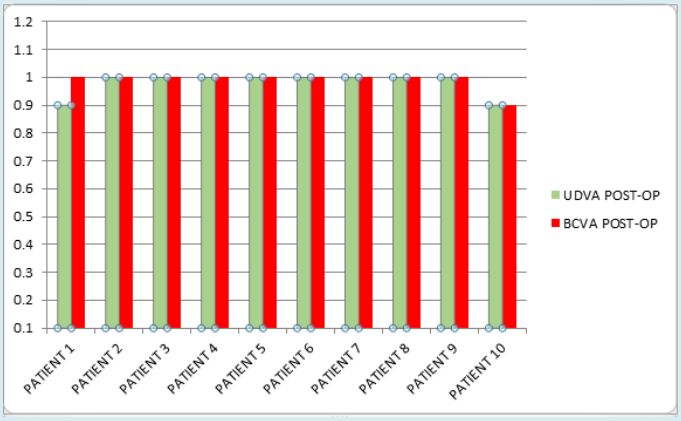

Figure 4: Baseline UDVA & BCVA Post-operative in Femto Lasik group.

Baseline UDVA postoperatively in the femto Lasik Xtra group was 0.9 and baseline BCVA in the femto Lasik Xtra group was 0.9. Mean spherical equivalent was -0.25D±0.75D post-operative (Figure 5).
SD UCVA POST-OP 0.048304, SD BCVA POST-OP 0.0421637

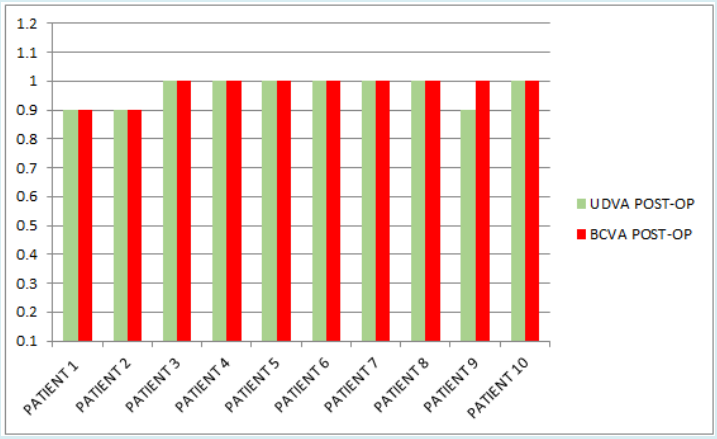

Figure 5: Baseline UDVA & BCVA post-operative in Femto Lasik Xtra group.

Average UDVA in the femto Lasik group was 0.4 and 0.36 in the femto Lasik Xtra group pre-operatively. Post-operative UDVA in the femto Lasik group was 0.98 and 0.97 in the femto Lasik Xtra group (no statistical significance) (Figure 6, Tables 2-4).

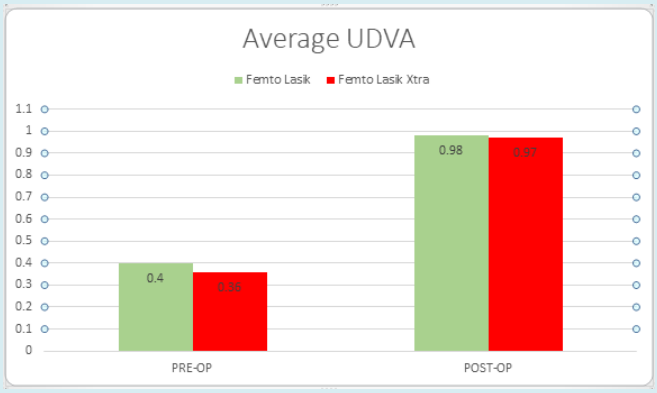

Figure 6: Average UDVA pre-op and post-op in femto Lasik and femto Lasik Xtra groups.

Studied Groups	Preoperative		Z	p
	UCVA	BCVA		
Femto Lasik (n=20)			3.943*	<0.001*
Min. –Max.	0.20 – 0.60	0.90 – 1.20		
Mean ± SD.	0.42 ± 0.13	1.01 ± 0.07		
Median	0.4	1		
Femto Lasik Xtra (n=20)				
Min. –Max.	0.20 – 0.60	0.90 – 1.0	3.943*	<0.001*
Mean ± SD.	0.36 ± 0.12	0.98 ± 0.04		
Median	0.35	1		

Z: Wilcoxon signed ranks test
p: p value for comparing between UCVA and BCVA in each group
*: Statistically significant at p ≤ 0.05
Table 2: Comparison between UCVA and BCVA preoperative in each group.

Studied Groups	Postoperative		Z	p
	UCVA	BCVA		
Femto Lasik (n=20)				
Min. –Max.	0.90 – 1.0	0.90 – 1.0	1.414	0.157
Mean ±SD.	0.98 ± 0.04	0.99 ± 0.03		
Median	1	1		
Femto Lasik Xtra (n=20)				
Min. –Max.	0.90 – 1.0	0.90 – 1.0	1.414	0.157
Mean ± SD.	0.97 ± 0.05	0.98 ± 0.04		
Median	1	1		

Z: Wilcoxon signed ranks test
p: p value for comparing between UCVA and BCVA in each group
Table 3: Comparison between UCVA and BCVA postoperative in each group.

UCVA	Femto Lasik (n=20)	Femto Lasik Xtra (n=20)	U	p
Preoperative				
Min. –Max.	0.20 –0.60	0.20 –0.60	146	0.149
Mean ±SD.	0.42 ± 0.13	0.36 ± 0.12		
Median	0.4	0.35		
Postoperative				
Min. –Max.	0.90 –1.0	0.90–1.0	180	0.602
Mean ± SD.	0.98 ± 0.04	0.97 ± 0.05		
Median	1	1		
p_1	<0.001*	<0.001*		

U: Mann Whitney test
p: p value for comparing between the two studied groups
p_1: p value for comparing between preoperative and postoperative in each group
*: Statistically significant at p ≤ 0.05
Table 4: Comparison between the two studied groups according to UCVA.

AS-OCT Findings

First week Post-Operative

Non-crosslinked corneas: corneas show a uniform flap thickness of about (123µm±30µm), flap edge is hyper reflective with no demarcation line in corneal stroma (Figure 7).

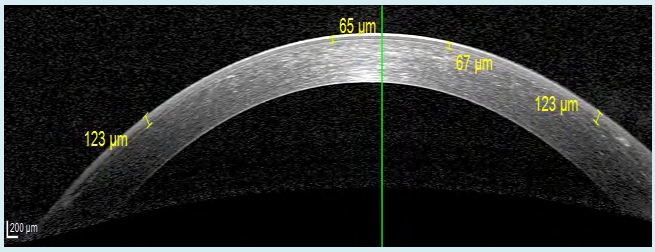

Figure 7: Non-crosslinked corneas 1 week post-operative: no demarcation line and uniform flap thickness.

Crosslinked corneas: treated corneas show a hyper reflective line, starts at the hinge of the flap, it deepens in the anterior stroma approximately between the depths of 130µ-174µm in the anterior stroma. This demarcation line is consistent with the stromal bed at the central and Para central cornea and hard to distinguish from the flap edge as it fades while approaching the Para central & central cornea. This line appears to be in different depth levels along the stroma and disappears at the central cornea. The edge of the flap appears to be hyper reflective, more hyper reflective than the Femto Lasik treated corneas, especially at the hinge of the flap. Hyper reflectivity is noted in the anterior cross linked stroma and flap, but there is an area of hypo reflectivity anterior to the demarcation line and the hyper reflective cross linked stroma at the hinge of the flap. A hyper reflective subepithelial line is also noted in the central and Para central corneas (Figures 8 & 9).

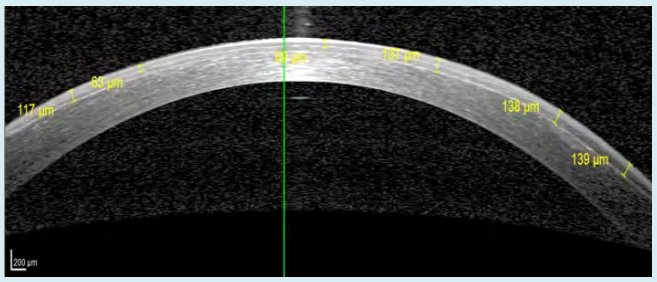

Figure 8: Cross-linked cornea 1 week post-operative: demarcation line at variable depths in the corneal stroma, fading in the Para central and central cornea.

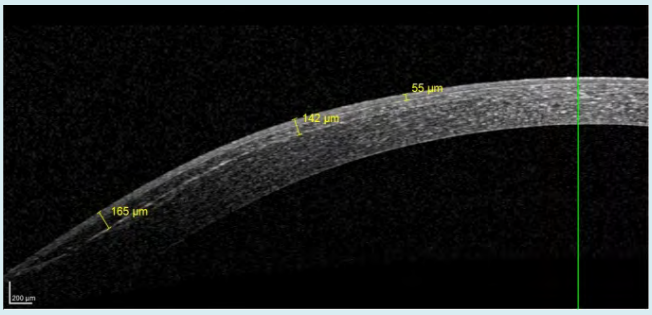

Figure 9: Cross-linked cornea 1 week post-operative: hyper reflectivity of flap hinge, demarcation line fading in para central cornea, a hypo reflective zone between the demarcation line and the anterior crosslinked stroma and flap.

One Month Post-Operative

Non-Crosslinked Corneas: AS-OCT shows uniform cornea with no haze in the interface and uniform flap thickness (Figure10).

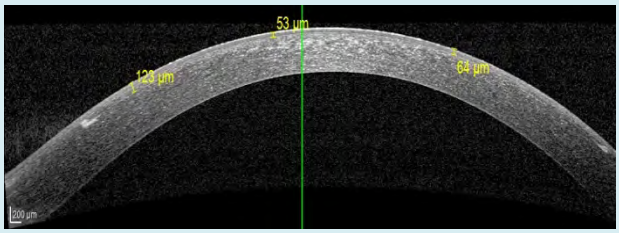

Figure 10: Non-crosslinked cornea 1 month post-operative: uniform flap thickness.

Crosslinked Corneas: The demarcation line starts fading and becomes less evident in the peripheral cornea; traces of the demarcation line remain in the peripheral sector of the flap. The demarcation line appears as if shifted anteriorly (shallower than 1-week post-operative) between 100-150µm, this might be related to shrinkage and decrease corneal thickness after CXL. Hyper reflectivity of the anterior corneal stroma is noted, more in the peripheral cornea than central. The hyper reflectivity of the flap hinge almost fades (less hyper reflective than 1-week post-operative) (Figures 11 & 12).

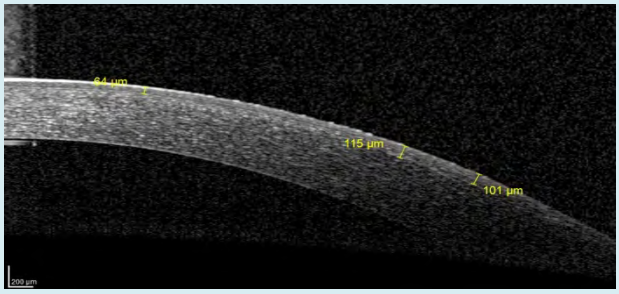

Figure 11: Cross-linked cornea 1 month post-operative: hyper reflectivity of the anterior stroma with traces of the demarcation line.

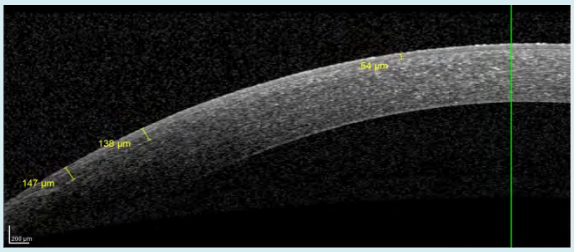

Figure 12: crosslinked cornea 1 month post-operative: traces of the demarcation line with disappearance of flap hinge hyper reflectivity.

Three Months Post-Operative

Non-crosslinked corneas: stable uniform flap, hard to distinguish from the corneal stroma in the central and para central cornea, no demarcation line is noted. Flap hinge is barely visible (Figures 13-15).

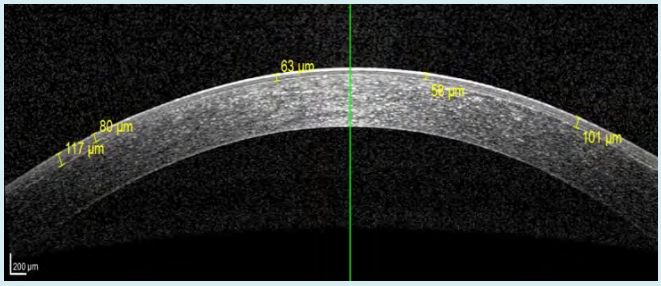

Figure 13: Non crosslinked cornea 3 months post-operative: uniform femto Lasik flap, hard to distinguish in Para central and central cornea.

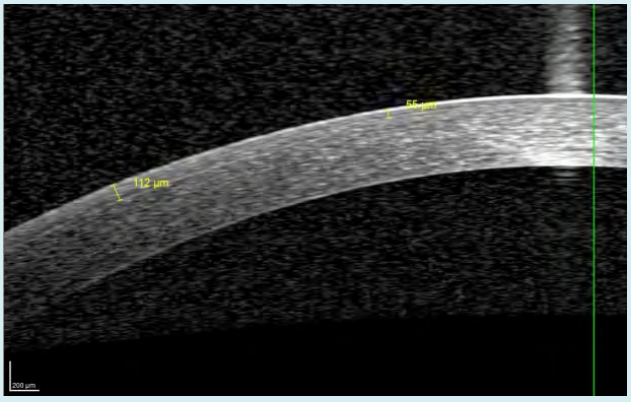

Figure 14: Non crosslinked cornea 3 months post-operative: flap edge barely visible In femto Lasik corneas.

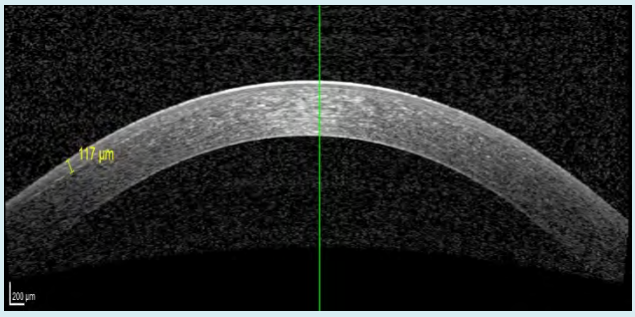

Figure 15: Non crosslinked cornea 3 months post-operative: uniform flap with hard to distinguish border at the central and Para central cornea.

Crosslinked Corneas

A demarcation line remains, more evident in the peripheral cornea. Hyper reflectivity of the anterior crosslinked stroma (Anterior to the demarcation line). Decreased flap thickness is noted with average thickness of 60±10µm. Flap hinge is more evident than Femto Lasik treated corneas (Figures 16-19).

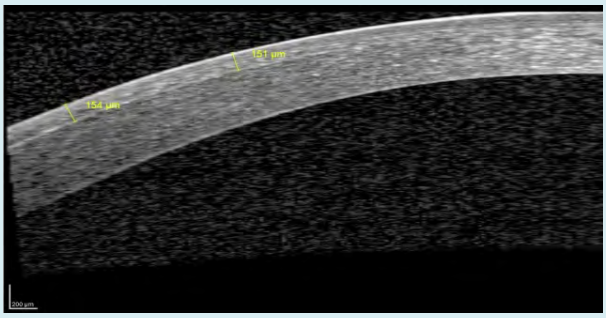

Figure 16: Crosslinked cornea 3 months post-operative: demarcation line noted at 150±10µm in the anterior stroma.

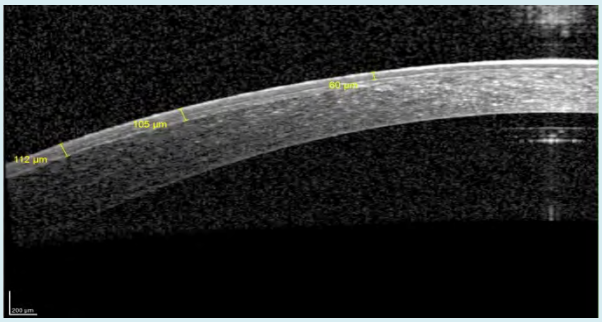

Figure 17: Crosslinked cornea 3 months post-operative: demarcation line at the peripheral cornea, fading at the Para central cornea, with flap decreased thickness.

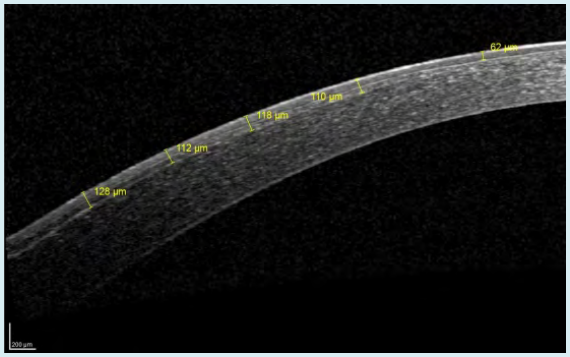

Figure 18: Crosslinked cornea 3 months post-operative: demarcation line at the level of 128µm, with flap shrinkage and decreased thickness (60µm).

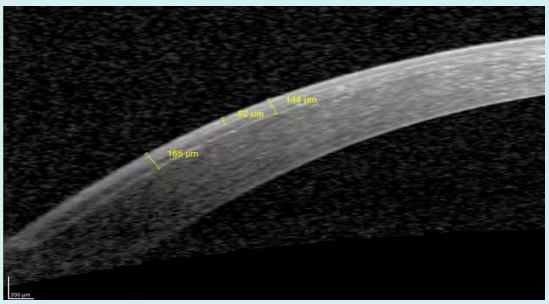

Figure 19: Crosslinked cornea 3 months post-operative: flap hinge is more visible in crosslinked corneas.

Discussion

Controversy exists regarding the effect and the benefit of Lasik Xtra in many patients including hypermetric patients, high myopic patients and young aged patients. Some surgeons employ cross-linking in all hyperopic LASIK and in all young myopic patients over 6D and under 30 years of age and in all patients with myopic astigmatism when the difference in astigmatism between the two eyes is more than 0.75D. When used in conjunction with LASIK (Lasik Xtra), the goal of CXL is to restore corneal strength without creating an additional change in refraction beyond that provided by the LASIK correction. Traditional CXL, when applied to the ecstatic cornea, is known to cause a flattening of the cornea of several diopters; therefore, it is important to consider the differences between Lasik Xtra and conventional CXL. CXL treatment for KC and corneal ectasia has been found to have a low rate of side effects. It is not surprising that, as Lasik Xtra produces similar tissue effects to these treatments, and uses lower doses for treatment effect, the safety profile is favorable. In addition to the studies described in the literature, in which there were no side effects beyond those typically associated with LASIK treatment, several papers mentioned in our review have looked at the safety of this prophylactic treatment. Adding a new data point in the ongoing controversy surrounding the impact of combined prophylactic corneal cross-linking (CXL) and LASIK flap creation, USC Roski Eye Institute published the first study to demonstrate the lack of corneal biomechanical impact using the revolutionary Brillouin microscopy, they concluded that Lasik Xtra has no benefit in increasing corneal strength [6]. Lasik Xtra treatment has been shown to significantly improve post-LASIK refractive stability, when compared to LASIK alone. This has been shown for both myopic and hyperopic refractive treatments, particularly in those with high diopter corrections who are at greater risk of refractive drift. And while the number of treatments and follow-up is not sufficient to draw definitive conclusions regarding the ability of Lasik Xtra to reduce the risk of corneal ectasia, the treatment profile may support prophylactic use [7].

There are many published researches regarding safety and efficacy of Lasik Xtra. A study by Celik HU, et al. [2] on 8 eyes in which 4 have underwent Lasik and the other 4 eyes underwent Lasik Xtra with an age group from 29-39 years with a mean sphere of -5.56±1.5D showed a refractive outcome of sphere equivalent of -0.18±0.31D in the Lasik group vs. 0.62±0.25D sphere equivalent in the Lasik Xtra group. Early stromal haze which resolved within 1 month in the Lasik Xtra group. UDVA was similar in the Lasik Xtra vs. LASIK in all cases. No decrease in CDVA or ECC in either group. No differences in keratometric readings from 1-12 months in either group [2].

Another study by Aslianides IM, et al. [8] on a total of 10 eyes with a group of 5 eyes underwent Lasik and the other group of 5 eyes performing Lasik Xtra showed predictable refractive outcome with 4 (80%) of eyes in the Lasik Xtra achieving Plano MRSE and 1 eye having myopia of 0.25 D at 1 month follow-up. Non-significant trend toward greater refractive stability in the Lasik Xtra group. Early stromal haze resolving in 1 month noted in the Lasik Xtra group [8].

Several studies were published by Kanellopoulos AJ, et al. [9] regarding Lasik Xtra. A study on 65 eyes underwent Lasik and 75 eyes underwent Lasik Xtra showed greater percent of cases achieved UDVA of 20/20 or better (p=0.045) or 20/25 or better (p = 0.039) in the Lasik Xtra vs. the LASIK. Less refractive (p=0.065) and K (p=0.032) regression in the Lasik Xtra vs. the LASIK over 24 months (p=0.065). No significant decrease of ECC in either group. No haze was noted in both groups [9]. Another study comparing and evaluating epithelial changes between Lasik and Lasik Xtra showed no significant differences between groups, except in the -8.00 to -9.00 subgroup, where significantly less changes in epithelial thickness were observed in the Lasik Xtra group [10]. another study comparing Lasik and Lasik Xtra in topography guided hyperopic correction on 34 patients showed Less regression of keratometric readings and refraction in the Lasik Xtra group (0.22±0.31 Lasik Xtra vs. +0.72 ± 0.19, p=0.0001) [11]. A 1 year results study comparing myopic Lasik to myopic Lasik Xtra in 155 eyes, 73 eyes underwent Lasik Xtra. Group which underwent Lasik Xtra had an average postoperative MRSE of -0.23, -0.19, and -0.19 D for the 3-, 6-, and 12-month period, respectively, compared to -6.58±1.98 D preoperatively. Flat keratometry was 37.69, 37.66, and 37.67 D, compared to 43.94 D preoperatively, and steep keratometry was 38.35, 38.36 and 38.37 D, compared to 45.17 D preoperatively.

The predictability of Manifest Refraction Spherical Equivalent (MRSE) correction showed a correlation coefficient of 0.979. The other group which underwent LASIK had an average postoperative MRSE of -0.23, -0.20, and -0.27 D for the 3, 6 and 12 month period, respectively, compared with −5.14±2.34 D preoperatively. Flat keratometry was 37.65, 37.89 and 38.02 D, compared with 43.15 D preoperatively, and steep keratometry was 38.32, 38.57, and 38.66 D, compared with 44.07 D preoperatively. The predictability of MRSE correction showed a correlation coefficient of 0.970. The keratometric stability plots were stable for the LASIK Xtra group and slightly regressing in the standard Lasik group. He concluded that improved refractive and keratometric stability were noted in Lasik Xtra patients compared to standard Lasik [12].

A study by Tomita M, et al. [13] on in vivo confocal laser microscopy of morphologic changes after Lasik Xtra for myopia showed a demarcation line with mean depth of 200.04±27.01μm (178-278um) in 95.8% of eyes. No differences in visual or K outcomes, no differences in ECC [13].

A study by Xu W, et al. [14] studying biomechanical changes in myopia patients with unsatisfactory corneas after femto Lasik Xtra on a total of 22 eyes of 11 myopic astigmatism patients concluded that Lasik Xtra could correct visual acuity effectively and strengthen corneal structure satisfactorily. They also concluded that Lasik Xtra is a safe and effective strategy for myopia with high-risk corneas as none of the patients showed iatrogenic ectasia after 2 years follow-up [14].

The combination of low-risk profile and significant improvement in refractive stability supports Lasik Xtra as a promising adjunct to LASIK in reducing the likelihood of enhancement procedures, particularly in those patients with high diopter corrections, and those with hyperopic corrections. Four studies that included a total of 41,468 eyes have found that LASIK has an average retreatment rate of 12%. Most of these occur during the first 2 years after the LASIK procedure [15-18]. If the refractive results with Lasik Xtra are truly more stable, this should logically result in lower retreatment rates over time.

Regarding demarcation line after Lasik Xtra, a study was published by Ng ALK, et al. [19] comparing demarcation line on AS-OCT after simultaneous Lasik and different protocols of accelerated crosslinking. 23 patients were included in this study. The average age was 29.0±8.2 years. There was no statistical difference in preoperative spherical equivalent refraction (P>0.05). At postoperative 1 month, a well-defined demarcation line was visible in 74% and 70% in the 2- and 3-minute groups, respectively. The demarcation line depth was 282±51 μm and 284±43 μm, respectively (P=1) and the ratio of the demarcation line depth to the postoperative central corneal thickness was 0.69±0.13 and 0.72±0.10 (P=0.61). There was no difference in the percentage of eyes with grade 1 or 2 corneal haze (P=0.76) [19]. No enough

data and literature were found to date assessing the AS-OCT findings and demarcation line and behavior in femto Lasik Xtra patients.

In our study, patients in the femto Lasik group achieved an average of 0.99 UDVA post-operatives; Lasik Xtra group had a post-operative UDVA of 0.99 too. No statistical difference was detected between both groups in terms of UDVA post operatively. No haze or any complications occurred in both groups neither intra-operatively nor post-operatively.

Regarding AS-OCT findings in our study, a demarcation line was noted in all of our patients whom performed Femto Lasik Xtra (100% of the cases). What we found surprisingly is that the demarcation line had different patterns along the follow up period which was up to 3 months as was discussed earlier in the results. No published literatures that we know of till date studied the demarcation line behavior and pattern in Lasik Xtra patients. Further studies may be needed for studying and assessing the different patterns of the demarcation line found in Lasik Xtra patients.

Our study however had a few drawbacks; we did not have enough patients to compare to the control group, a larger number of patients would have added more strength to our study. Also, we followed our patients up with AS-OCT for a short period of time (3 months) so we could not estimate if these changes would remain stable or if further changes occur in the period beyond 3 months.

Our study has positive points too; including the prospective data collection in the real-world and hence clinically applicable setting. A standardized SD AS-OCT imaging protocol was followed allowing each follow-up AS-OCT scan to be registered and locked to the baseline scan, thus enabling accurate measures. The changes in the pattern of the demarcation line along the follow up period in the Lasik Xtra patients is also a major positive point for our study.

References

1. Lim SH (2015) Clinical Applications of Anterior Segment Optical Coherence Tomography. J Ophthalmol 1-12.

2. Celik HU, Alagoz N, Yildirim Y, Agca A, Marshall J, et al. (2012) Accelerated corneal crosslinking concurrent with laser in situ keratomileusis. J Cataract Refract Surg 38(8): 1424-1431.

3. Seven I, Dupps WJ (2013) Patient-Specific Finite Element Simulations of Standard Incisional Astigmatism Surgery and a Novel Patterned Collagen Crosslinking Approach to Astigmatism Treatment. J Med Device 7(4): 409131-409132.

4. Mazzotta C, Balestrazzi A, Traversi C, Caragiuli S, Caporossi A (2014) In vivo Confocal Microscopy Report after Lasik with Sequential Accelerated Corneal Collagen Cross-Linking Treatment. Case Rep Ophthalmol 5(1): 125-131.

5. (2018) Avedro's KXLTM System for Lasik Xtra and Accelerated Cross linking.

6. Randleman JB, Su JP, Scarcelli G (2017) Biomechanical Changes After LASIK Flap Creation Combined With Rapid Cross-Linking Measured With Brillouin Microscopy. J Refract Surg 33(6): 408-414.

7. Rajpal RK, Wisecarver CB, Williams D, Rajpal SD, Kerzner R, et al. (2015) Lasik Xtra® Provides Corneal Stability and Improved Outcomes. Ophthalmol Ther 4(2): 89-102.

8. Aslanides IM, Mukherjee AN (2013) Adjuvant corneal crosslinking to prevent hyperopic LASIK regression. Clin Ophthalmol 7: 637-641.

9. Kanellopoulos AJ, Asimellis G (2015) Combined laser in situ keratomileusis and prophylactic high-fluence corneal collagen crosslinking for high myopia: two-year safety and efficacy. J Cataract Refract Surg 41(7): 1426-1433.

10. Kanellopoulos AJ, Asimellis G (2014) Epithelial Remodeling After Femtosecond Laser-assisted High Myopic LASIK. Cornea 33(5): 463-469.

11. Kanellopoulos AJ, Kahn J (2012) Topography-guided hyperopic LASIK with and without high irradiance collagen cross-linking: initial comparative clinical findings in a contralateral eye study of 34 consecutive patients. J Refract Surg 28(11 S): 837-840.

12. Kanellopoulos AJ, Asimellis G, Karabatsas C (2014) Comparison of prophylactic higher fluence corneal cross-linking to control, in myopic LASIK, one year results. Clin Ophthalmol 8: 2373-2381.

13. Tomita M, Yoshida Y, Yamamoto Y, Mita M, Waring G (2014) In vivo confocal laser microscopy of morphologic changes after simultaneous LASIK and accelerated collagen crosslinking for myopia: One-year results. J Cataract Refract Surg 40(6): 981-990.

14. Xu W, Tao Y, Wang L, Huang Y (2017) Evaluation of Biomechanical Changes in Myopia Patients with Unsatisfactory Corneas After Femto Second-Laser In Situ Keratomileusis (FS-LASIK) Concurrent with Accelerated Corneal Collagen Cross-Linking Using Corvis-ST: Two-Year Follow-Up Results. Med Sci Monit 23: 3649-3656.

15. Jaycock PD, Lobo L, Ibrahim J, Tyrer J, Marshall J (2005)

Interferometric technique to measure biomechanical changes in the cornea induced by refractive surgery. J Cataract Refract Surg 31(1): 175-184.

16. Randleman JB, White AJ, Lynn MJ, Hu MH, Stulting RD (2009) Incidence, outcomes, and risk factors for retreatment after wavefront-optimized ablations with PRK and LASIK. J Refract Surg 25(3): 273-276.

17. Hersh PS, Fry KL, Bishop DS (2003) Incidence and associations of retreatment after LASIK. Ophthalmology 110(4): 748-754.

18. Alio JL, Muftuoglu O, Ortiz D, Santonja PJJ, Artola A, et al. (2008) Ten-Year Follow-up of Laser In Situ Keratomileusis for Myopia of up to 10 Diopters. Am J Ophthalmol 145(1): 46-54.

19. Ng ALK, Kwok PSK, Wu RTK, Jhanji V, Woo VCP, et al. (2017) Comparison of the Demarcation Line on ASOCT After Simultaneous LASIK and Different Protocols of Accelerated Collagen Crosslinking. Cornea 36(1): 74-77.