Higher Order Aberrations (HOA) Changes after Femto-LASIK in Topography and Wavefront-guided Treatments

Georgi Taskov, Todor Taskov

Eye Hospital Luxor, Plovdiv, Bulgaria

Corresponding author: Georgi Taskov, Luxor Eye Hospital, 47A Bulgaria Blvd., 4003 Plovdiv, Bulgaria; E-mail: taskovmd@gmail.com; Tel.: 032 968 881

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Abstract

Background: Publications have focused on comparing the effect of various methods of refractive surgery or ablation profiles on higher order aberrations (HOA), yet the effect of WG compared to TG ablation in femtosecond laser-assisted in-situ keratomileusis femto-LASIK on HOAs has not been studied adequately.

Materials and methods: We reviewed the changes of HOAs before and after femto-LASIK for simple myopia or compound myopic astigmatism after topography-guided (TG) and wavefront-guided (WG) ablation profiles. In this retrospective study, 42 eyes underwent TG and 31 WG femto-LASIK.

Results: The total HOAs increased from 0.41±0.16 μm pre-operatively to 0.66±0.30 μm post-operatively in the TG group and from 0.42±0.13 μm pre-operatively to 0.59±0.27 μm post-operatively in the WG group without statistically significant difference between the two groups. However, the postoperative change of secondary astigmatism showed a statistically significant difference between the two groups [0.20 (0.0-0.53) vs. 0.0 (0.0-0.20) for TG and WG groups, respectively; \(p=0.009\)].

Conclusions: The total HOAs increased compared to pre-operative data, in both the TG and WG ablation profile groups. The extent of increase of secondary astigmatism was significantly lower in the WG group, which might favour the postoperative quality of vision.

Keywords

astigmatism, femto-LASIK, higher order aberrations, myopia, topography, wavefront

INTRODUCTION

Visual complaints even after successful refractive surgery have been reported by 3% to 40% of patients, mainly due to an increase in the eye's existing natural higher-order aberrations (HOAs) (spherical aberrations, coma, trefoil, etc.). Induction of HOAs has been associated with poor quality of vision, leading to a higher incidence of glare,
halos, starbursts, and deterioration of contrast function.\textsuperscript{2} The increase in HOAs following refractive surgery can be attributed to flap-induced irregularities, decentration, a variation in hydration of cornea during ablation, and biomechanical changes resulting from the laser surgery.\textsuperscript{3} Compared to the initial flap, which is traditionally created by a microkeratome in laser-assisted in-situ keratomileusis (LASIK), femtolaser-assisted in-situ keratomileusis (femto-LASIK) creates planar flaps of uniform thickness (or with at least small deviation in thickness) which is correlated with significantly decreased flap-associated complications.\textsuperscript{4} Femto-LASIK has gained widespread popularity as a safe, effective and predictable treatment for correcting myopia and myopic astigmatism.\textsuperscript{2,5} Nevertheless, HOAs have been shown to increase post-operatively despite the use of femtosecond lasers.\textsuperscript{6,7}

Since HOAs cannot be corrected by conventional refraction parameters, customized excision treatment profiles, such as wavefront-guided (WG) or topography-guided (TG), have been developed to balance and compensate for pre-existing HOAs.\textsuperscript{8,9} WG ablation addresses the overall ocular wavefront aberrations in addition to the refractive errors, whereas TG ablation aims to treat the corneal irregularities in addition to the defocus and astigmatism. Both customized ablation profiles have advantages and disadvantages. The TG ablation algorithm, in addition to treating spherocylindrical refractive errors, addresses the irregularities of the corneal elevation in an effort to reshape the cornea into an ideal curve and achieve a planar wavefront postoperatively. Unlike the WG profiles, the TG ablation profiles do not attempt to correct the aberrations arising from the crystalline lens or other ocular structures.\textsuperscript{10,11} Various publications have focused on comparing the effect of various methods of refractive surgery or various ablation profiles on HOAs.

In this report, the effect on the general image quality, as assessed by total HOAs, of WG and TG femto-LASIK for simple myopia and/or compound myopic astigmatism was investigated pre-operatively and at 1 month postoperatively.

MATERIALS AND METHODS

Patient population

In this retrospective report, data was collected from 73 eyes of patients (42 in the TG group and 31 in the WG group) that were admitted for the correction of myopia and compound myopic astigmatism with Femto-LASIK. The refractive surgery was performed in Luxor Eye Hospital, Plovdiv in Bulgaria from October 2015 to July 2018. Study enrolment took place after the approval of the Ethics Committee of the hospital and signed informed consent from each participant. All patients included in the study were adults, with no other eye conditions or systemic diseases and with a postoperative uncorrected visual acuity (UCVA) 1.0 (20/20) or more. Optimal postoperative visual acuity would allow the appropriate comparison of the aberrations involved, whereas patients with a lower UCVA would require further enhancement procedures that would eventually lead to new end-state of aberrations. During the collection period, only 1 case of suboptimal postoperative UCVA (20/25) was present, not allowing for the development of a study subgroup.

Regarding patient allocation to WG or TG treatment, certain safety requirements were taken into consideration. Using the calculation: percentage tissue altered minus (ablation plus flap) divided by minimum central corneal thickness, the per cent value was obtained. If this value exceeded 40% in the WG treatment plan, TG treatment was selected instead. This is due to the fact that, while being the preferred treatment in our clinic, the WG ablation would expose the eye to more damage. Additional safety evaluations that were taken into consideration were residual stromal bed, type of topography, value of the ablated diopters, and age of the patients.

Pre-operative examination

All patients had a pre-operative ophthalmic examination including the subjective best corrected visual acuity (BCVA), autorefractometry (ARF), slit lamp exam, pachymetry (corneal thickness value), topography exam (using ATLAS 995\textsuperscript{TM} by Carl Zeiss), wavefront analysis (WASCA G210\textsuperscript{TM} by Carl Zeiss), and subjective BCVA after cycloplegia. In these samples, the WASCA Analyser of Carl Zeiss was used to assess the root mean square high order aberrations (RMS HOAs) and the scotopic pupil size. The cycloplegic subjective refraction, refined using the nomogram, was used for operative planning. Save for two patients in which topography exam was used in one eye and wavefront analysis in the contralateral eye, the remaining patients had the same evaluation in both eyes.

Femto-LASIK Surgery

All flaps were created by Alcon LenSx\textsuperscript{TM} at 120 microns depth and the ablation was performed using Carl Zeiss MEL 80. All surgeries were performed by the same surgeon, who had high confidence and equal experience with both methods (TG and WG). Two drops of proxymetacaine hydrochloride 0.5% 5 minutes apart, 1 drop proxymetacaine 0.5%, 1 drop of dexamethasone, 1% plus tobramycin 0.3% were used throughout the steps of the procedure.

Post-operative follow-up

Complete ophthalmic evaluations were performed at 1 month postoperatively and the following parameters were obtained: BCVA, ARF, slit lamp exam, pachymetry (corneal thickness value), topography exam, and wavefront analysis. The % RMS HOA normal values (calculated as the %
HOA Changes after Femto-LASIK Treatments

**Statistical analysis**

All calculations were made using SPSS 21. Continuous data were presented as mean ± SD or median and interquartile range (IQR). Comparisons between the two treatment groups at baseline were performed with Welch’s test for unequal variances for testing between-group differences in continuous variables. The Welch’s test for unequal variances, which is a modified Student’s t-test was selected in order to compensate for bias in the comparison of the two unequal-in-size patients’ groups (the non-parametric Mann-Whitney test was used when data deviated from normality). Additionally, pre- and post-operative HOAs in each treatment group were compared by paired t-test or by the non-parametric Wilcoxon signed-rank test in case of non-normally distributed data. Linear regression analysis was performed in order to identify which factors can be independent prognostic factors of the postoperative HOA. P-values < 0.05 were considered statistically significant.

**RESULTS**

In this retrospective study, 73 eyes were included. TG and WG femto-LASIK were performed in 42 (26 males and 16 females) and 31 eyes (19 males and 12 females), respectively. The mean age of the patients in the TG group was 32±6 years, while those of the WG group had a result of 27±6 years (p=0.001). The majority of the patients in both groups were male (61.9% and 61.3% of the patients in the TG and WG groups, respectively).

The mean ± SD Spherical Equivalent (SE) refractive error in the TG and WG groups preoperatively was -4.72±2.27 and -2.93±1.19 diopters (D), respectively (p<0.001). Similarly, the mean ± SD refractive spherical and cylindrical error was -4.09±2.31 and -1.25±0.92 D for the TG group and -2.67±1.22 and -0.51±0.44 D for the WG group (p<0.05).

The vast majority of both group patients had combined myopia with astigmatism (83% of the TG and 81% of the WG group). The mean ± SD pupil diameter pre-operatively was 6.89±0.68 and 6.94±0.43 mm for the TG and the WG, respectively (p>0.05). Mean corneal thickness, ablation depth, and optical zone did not differ significantly between the two groups. Paired t-test was used to assess the change in all normally distributed HOAs postoperatively (RMS HOA, % of the normal HOA values, coma), while Wilcoxon signed-rank test was used for the HOAs who deviated from normality (trefoil, secondary astigmatism and tetrafoil). Median and IQR are also given for the latter parameters. The presentation of all HOAs (RMS) and their % normal values in both groups increased postoperatively (Table 1), although the between-group differences did not reach statistical significance (Table 2).

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Topography (N=42)</th>
<th>Wavefront (N=31)</th>
</tr>
</thead>
<tbody>
<tr>
<td>RMS HOA (µm)</td>
<td>Pre-op (N=42)</td>
<td>Post-op (N=42)</td>
</tr>
<tr>
<td></td>
<td>0.41±0.16</td>
<td>0.66±0.30</td>
</tr>
<tr>
<td>% of the normal HOA values</td>
<td>62.3±23.8</td>
<td>101.3±42.6</td>
</tr>
<tr>
<td>Coma (µm)</td>
<td>0.66±0.46</td>
<td>1.05±0.73</td>
</tr>
<tr>
<td>Trefoil (µm)</td>
<td>0.40 (0.20-0.63)</td>
<td>0.50 (0.28-0.80)</td>
</tr>
<tr>
<td>Secondary astigmatism (µm)</td>
<td>0.20 (0.10-0.30)</td>
<td>0.35 (0.20-0.60)</td>
</tr>
<tr>
<td>Tetrafoil (µm)</td>
<td>0.30 (0.10-0.40)</td>
<td>0.20 (0.10-0.40)</td>
</tr>
</tbody>
</table>

HOA: higher-order aberrations; RMS: root mean square; *: paired t-test; ** Wilcoxon signed-rank test; ¶: median and IQR will be given also for all HOAs which deviate from normality.
There were no statistically significant differences between the 2 groups in the total HOAs and in the % of the normal HOA values pre-operatively. At 1-month postoperatively, secondary astigmatism showed a statistically significant increase in the TG group compared to the WG group (Table 2).

Fig. 1 shows the difference between the two groups of the mean % of normal HOA values pre- and post-operatively.

Linear regression analysis was performed in order to identify which factors could be independent prognostic factors of the postoperative measurement of the RMS of HOA, with explanatory variables being patient demographics (such as sex, age, type of operation), as well as all the pre-operative parameters (sphere, cylinder, SE, optical zone, pachymetry, ablation depth, and pupil diameter). More specifically, several univariate regression models were implemented in order to test the statistical significance of each factor separately. The parameters used for the univariate regression models were sex, age, operation, spherical and cylindrical error, spherical equivalent, optical zone, pachymetry, ablation depth, and pupil diameter. The statistically significant factors (p<0.05) were then inserted into a multivariate linear regression model. Based only on the statistically significant factors derived from the univariate regression models, the final implemented model is a multivariate regression model with cylindrical error and pupil diameter pre-operatively as explanatory variables. The Pearson correlation coefficients between each explanatory variable and the dependent one were alternatively calculated to identify the significant factors to be used in a multivariate model. Therefore, the only variables

Table 2. Comparison of between-group difference from preoperative HOAs

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Topography (N=42)</th>
<th>Wavefront (N=31)</th>
<th>Change from pre-op</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>RMS HOA (μm)</td>
<td>0.25±0.26</td>
<td>0.18±0.25</td>
<td></td>
<td>0.230*</td>
</tr>
<tr>
<td>% of the normal HOA values</td>
<td>39.0±39.7</td>
<td>25.9±32.6</td>
<td></td>
<td>0.137*</td>
</tr>
<tr>
<td>Coma (μm)</td>
<td>0.40 (-0.20-0.65)</td>
<td>0.10 (-0.10-0.40)</td>
<td></td>
<td>0.149**</td>
</tr>
<tr>
<td>Trefoil (μm)</td>
<td>0.10 (-0.20-0.40)</td>
<td>-0.10 (-0.20-0.10)</td>
<td></td>
<td>0.238**</td>
</tr>
<tr>
<td>Secondary astigmatism (μm)</td>
<td>0.20 (0.0-0.53)</td>
<td>0.0 (0.0-0.20)</td>
<td></td>
<td>0.009**</td>
</tr>
<tr>
<td>Tetrafoil (μm)</td>
<td>0.05 (-0.10-0.10)</td>
<td>0.10 (-0.10-0.20)</td>
<td></td>
<td>0.309**</td>
</tr>
</tbody>
</table>

HOA: higher-order aberrations; RMS: root mean square; *: Independent samples t-test; **: Mann-Whitney test; ¶: Median and IQR will be given also for all HOAs who deviate from normality.

Table 3. Summary of the multivariate model

<table>
<thead>
<tr>
<th>Factor</th>
<th>Estimate</th>
<th>Standard Error</th>
<th>p-value</th>
<th>R²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Constant</td>
<td>-1.014</td>
<td>0.351</td>
<td>0.005*</td>
<td>0.267</td>
</tr>
<tr>
<td>Cylinder (D)</td>
<td>-0.086</td>
<td>0.035</td>
<td>0.018*</td>
<td></td>
</tr>
<tr>
<td>Pupil diameter (mm)</td>
<td>0.226</td>
<td>0.050</td>
<td>&lt;0.0001*</td>
<td></td>
</tr>
</tbody>
</table>

*Statistically significant parameters.
HOA Changes after Femto-LASIK Treatments

statistically significantly correlated with the post-operative HOA were cylindrical error ($r=-0.23, p=0.025$) and pupil diameter ($r=0.45, p<0.001$) pre-operatively, leading to the same fitted model as resulted by the univariate regression models.

The summary statistics for the final fitted multivariate model are presented in Table 3 below. Pre-operative astigmatism and pupil diameter were found to be the only independent prognostic factors of post-operative HOA (RMS).

Figs 2 and 3 illustrate the partial scatterplots of the exploratory variables vs. the response from the above multivariate regression analysis.

DISCUSSION

In this retrospective study, the induction of both total HOAs RMS and individual HOAs (third and fourth order) before and after femto-LASIK surgery for the correction of myopia and/or myopic compound astigmatism was examined. Both TG and WG cause minimal corneal tissue ablation compared to other non-customized ablation profiles and thus have important clinical implications.

The present study showed that HOAs were induced postoperatively in both groups (TG and WG) to a statistically significant degree, a finding that is in accordance with previous studies.12-15

Although the increase in HOAs RMS was statistically significant compared to pre-operative values in either group, there was no statistically significant difference in the pre-operative and postoperative HOAs RMS between the 2 groups, which is in agreement with the results of Jain et al.10 More specifically, in the TG group coma, trefoil, and secondary astigmatism increased statistically significantly post-operatively, while in the WG group only secondary astigmatism and trefoil increased to a statistically significant degree. In the study of Jain et al. TG induced significantly lower coma aberrations after LASIK for myopia in virgin eyes. However, in the aforementioned study less stromal tissue was ablated in the TG group compared to the WG optimized group ($p<0.001$)10, whereas in the present study, the ablation depth in the TG group was slightly lower, without reaching statistical significance. The inconsistency between the two studies can be at least partly attributed to the fact that in the study of Jain et al. all patients (in both groups) suffered only from myopia, whereas in the present study the cylindrical error in the TG group was statistically significantly higher compared to the WG group. In addition, the spherical error in the WG group was significantly lower than in the TG group. Furthermore, the LASIK surgical method that was implemented was different between the two studies. Other studies that compared WG aberration with other methods showed also that WG was at least non-inferior in inducing postoperative HOAs. More specifically, in the study of Anderle et al. that compared the standard with the WG myopic femto-LASIK, both methods had equivalent postoperative aberration score at one-year postoperatively.13 Similarly, Perez-Straziota et al. found that WG LASIK and wavefront-optimized LASIK produced equivalent visual outcomes and no differences in HOAs.16 In the study of Yu et al. that compared LASIK outcomes between small-spot and variable-spot WG laser, the small-spot scanning laser group had significantly fewer spherical aberrations and significantly less mean total HOA RMS, while patients reported that the clarity of their night and day vision was significantly better in the eye treated with the small-spot scanning laser.17 In the present study, the change from pre-operative secondary astigmatism value showed a statistically significant difference between the two groups, which is not reported in the literature to the best of our knowledge. This could be attributed to the fact that the aforementioned studies that compared the impact of different methods of LASIK on high HOAs do not include results regarding secondary astigmatism. However, a source of bias is that the two groups of the present study were not perfectly matched regarding both the spherical and the cylindrical error. In fact, the TG group that showed the greater increase in secondary astigmatism had a significantly higher cylindrical and spherical error. Nevertheless, although the pre-operative low order aberrations (LOAs) differed statistically significantly between the two groups, pre-operative HOAs did not show any statistically significant difference, which is in alignment with the literature so far. Namely, the type and severity of LOAs pre-operatively have not been proven to be clearly associated with the type and incidence of both pre- and post-operative HOAs. Furthermore, the interaction among individual HOAs needs to be further elucidated.18

Another substantial finding of the present study was that pre-operative pupil diameter ($p<0.001$) and astigmatism ($p=0.018$) were both independent prognostic factors of postoperative HOAs in the total study population. Previous studies have also found that a large pupil induces more postoperative aberrations19,20, a finding that could be attributed to the small transition zone of the laser ablation.21 AL-Zeraid et al. who studied the induced HOAs six months after WG intraLase Femtosecond Laser in moderate-to-high astigmatism (which was not the case in the WG group of the present study) found that the change only in the 4th-order spherical aberration postoperatively correlated positively with pre-operative myopia.22 However, the present study indicates the prognostic role of the pre-operative LOA astigmatism in predicting the HOAs one-month post-operatively and more specifically the 4th-order aberration secondary astigmatism, as the pre-operative cylindrical error was statistically significantly correlated with the post-operative secondary astigmatism in the total study population ($r=-0.44, p<0.001$).
CONCLUSIONS

The results of this study suggest a promising role for the use of WG femto LASIK in patients with myopia or compound myopic astigmatism, since it results in fewer post-operative aberrations compared to TG. Furthermore, this study indicates that apart from the pupil size, the cylindrical error is an independent prognostic factor of post-operative HOAs. Further randomized prospective studies, with longer follow-up periods comparing the two methods ideally between the contralateral eyes of the same patients, might be useful to elucidate the impact of the two methods on the induction of HOAs.

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Author Contributions

All authors were equally involved in the execution of the study and preparation of the manuscript.

Conflict of Interest

The authors declare no conflict of interest.

REFERENCES

Изменения в отклонениях в порядке возрастания (ОПВ) после Femto-LASIK в топографии и лечении с применением волнового фронта

Георги Тасков, Тодор Тасков
Офтальмологическая клиника „Луксор”, Пловдив, Болгария

Автор для корреспонденции: Георги Тасков, Офтальмологическая клиника „Луксор”, бул. „Болгария” № 47А, 4003 Пловдив, Болгария
E-mail: taskovmd@gmail.com; Тел.: 032 968 881

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Резюме

Введение: Публикации фокусируются на сравнении эффекта различных методов рефракционной хирургии или различных профилей абляции на отклонения в порядке возрастания (ОПВ) и, тем не менее, влияния волнового фронта (ВФ) по сравнению с топографической абляцией при фемтосекундном лазерном кератомилёзе in situ AS femto на ОПВ не был адекватно изучен.

Материалы и методы: Мы рассмотрели изменения ОПВ до и после Femto-LASIK для общей миопии или сочетанного миопического астигматизма после топографических (TG) и WG профилей абляции. В этом ретроспективном исследовании 42 глаза подвергались TG, а 31 – WG Femto-LASIK.

Результаты: Общие ОПВ увеличиваются с 0,41 ± 0,16 μm до операции до 0,66 ± 0,30 μm после операции в группе TG и с 0,42 ± 0,13 μm до операции до 0,59 ± 0,27 μm в группе WG без статистически значимой разницы между двумя группами. Однако послеоперационные изменения вторичного астигматизма не выявили статистически значимой разницы между двумя группами [0,20 (0,0-0,53) против 0,0 (0,0-0,20) для групп TG и WG соответственно; p = 0,009].

Выводы: Общее ОПВ увеличилось по сравнению с предоперационными данными в профильных группах абляции TG и WG. Степень увеличения вторичного астигматизма была значительно ниже в группе WG, что может улучшить послеоперационное качество зрения.

Ключевые слова

астигматизм, femto-LASIK, отклонения в порядке возрастания, миопия, топография, волновой фронт