Ocular Aberrations and Corneal Thickness-Intraocular Pressure Relationship One Year after Laser in situ Keratomileusis (LASIK) Enhancement with An Aspheric Ablation Profile

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Abstract

Objective: To evaluate the effect of an aspheric LASIK refractive enhancement performed by relifting the original flap on the higher order aberrations (HOA) of the eye and the relationship between central corneal thickness (CCT) and intra-ocular pressure (IOP).

Methods: Consecutive case series of 30 eyes requiring refractive enhancement from 1804 uncomplicated primary LASIK procedures performed in 2012. Flap relift and wavefront optimized ablation (WaveLight Allegro Eye Q 400 Hz excimer laser) were performed in all cases. Pre- and post-operative examination included Shack-Hartmann aberrometry for 3 mm and 6 mm pupil sizes, CCT and IOP. Postoperative results at 1 year were compared to baseline values.

Results: Changes in average values of coma, spherical aberration (SA), trefoil, CCT and IOP were not significant. Linear regression revealed significant associations between change (y) in trefoil and pre-enhancement value of trefoil for 3 mm pupil (0.828x-0.045, r=0.722, p<0.001), coma and pre-enhancement value of coma for 5 mm pupil (y=0.281x-0.030, r=0.501, n=30, p=0.048), SA for 3 mm pupil compared with change in CT (y=0.080x-0.0009x, r=0.378, p=0.0392), and SA for 5 mm pupil compared with change in CCT (y=0.053x-0.0541, r=0.524, p=0.0029). Also there was a significant association between IOP and CCT both pre-(IOP=0.0313CT-3.3, r=0.740, p<0.0001) and post-enhancement (IOP=0.0243CT-0.018, r=0.675, p=0.0001).

Conclusion: LASIK enhancement with an aspheric ablation profile did not significantly impact on the average values for HOAs, IOP or CCT. For individual cases, the likely shift in magnitude of coma, trefoil and SA can be estimated and, the change in SA is correlated with changes in CCT. The change in the abscissa value linking IOP with CCT may be an indication of changes in biomechanical properties of the cornea in the central region.

Keywords: Corneal thickness; High order aberrations (Hoas); Intraocular pressure (IOP); LASIK enhancement; Excimer laser; Wavefront; Wavelet allegretto

Introduction

Laser in situ keratomileusis (LASIK) is the most frequently applied corneal refractive surgical procedure today [1]. Patients’ satisfaction has risen as the technology has advanced. The reported rate of refractive enhancement or retreatment has been reducing over the last two decades. Miscorrections ≥ 1.00 D were prevalent in up to 59% of cases in reports over the period 1994-97 [2-8]. More recently, a retrospective study on 37,932 procedures treated between 1998-2007 revealed post-op refractive error target greater than ± 1D in just 7% of cases [9]. Since 2000, the reported rate for retreatment averages at about 4% [10-12], increasing to 20% in myopic patients after 10 years according to one source [13]. The original nomograms for excimer laser photoablation were based on relatively simple spherical optics. This led to an increase in the magnitude of other higher order aberrations of the eye, and this was associated with reduced visual performances. Opinions have changed and an accepted view is that, besides the correction of sphero-cylindrical refractive error, there is a need to either maintain or reduce the magnitude of higher order aberrations of the eye such as coma and spherical aberration [14-27]. This culminated in the development of more complex algorithms, such as aspheric and wavefront corrected ablation profiles, as mechanisms to control the ocular higher order aberrations [28-30]. There is evidence suggesting that complex algorithms may not, in themselves, lead to more acceptable clinical outcomes [31]. Do these complex algorithms retain, reduce or increase the HOA of the eye after enhancement procedures? The evidence in the literature is inconclusive regarding enhancement procedures.

Hu et al. [32] claimed that intra-ocular pressure influenced the HOA induced by LASIK. The average intra-ocular pressure (IOP) measured by Goldmann tonometry tends to reduce after either PRK or LASIK [33-36] and, the influence of central corneal thickness (CCT) on the measured IOP by applanation tonometry has long been recognized [37-43]. When this is taken into consideration, the change in measured IOP after LASIK is strongly associated with the change in central corneal thickness. Therefore, it is possible that changes in the HOA after LASIK are mediated not just by the measured IOP but also the measured CCT. Enhancement procedures involving further

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diminution of central corneal thickness are expected to affect the measured IOP and possibly the numerical indices associated with the CCT-IOP relationship. In an extensive review of corneal biomechanics, Garcia-Porta et al. [44] provided a definition of corneal biomechanics as "a branch of science that studies deformation and equilibrium of corneal tissue under application of any force". Young's modulus is the constant for a material linking the force per unit area and the corresponding deformation per unit length. This modulus is a marker for the elastic response of the cornea. If Young's modulus of the treated corneal tissue under application of any force is larger, then the cornea stiffens and easier to deform during applanation tonometry. Changes in Young's modulus may affect the numerical indices of the CCT-IOP relationship.

The aim of this study was to evaluate the results of refractive enhancement after primary uncomplicated LASIK procedure by lifting the original flap and applying an aspheric excimer laser ablation profile by assessing the ocular wavefront aberrations and the relationship between central corneal thickness and intra-ocular pressure (IOP).

Patients and Methods

Study design

This was a consecutive case-by-case series of patients referred for refractive enhancement due to non-tolerated residual refractive error and uncorrected distance visual acuity (UDVA) after primary LASIK performed during 2012. All patients had a mechanical microkeratome cut flap with 90 µm head and superior hinge position (Moria M2 Single Use, Moria, Anthony, France) at the time of the first surgical intervention. Criteria for LASIK refractive enhancement were, unchanged refraction between two consecutive visits 2 months apart, residual spherical equivalent ≥±0.75D, UDVA worse than 0.9 decimal lines (Snellen equivalent 20/22), and residual corneal stromal bed thickness ≥ 300 µm.

All patients were previously treated in our clinic using Wavelight Allegretto Eye-Q 400 Hz (Alcon, Forth Worth, Texas, USA) excimer laser for correction of myopia and, all refractive enhancement procedures were performed on the same excimer laser.

The study was approved by the Ethical Committee of Specialty Eye Hospital "Svjetlost". The tenets of the Helsinki agreement were followed throughout. All refractive enhancements were performed by the same surgeon.

Preoperative assessment

All patients underwent a complete preoperative ophthalmologic examination prior to deciding if the patient met the criteria for enhancement. Measurements included UDVA (Snellen chart at 6 m), manifest and cycloplegic refraction, corneal topography (Pentacam HR, Oculus Optikgeräte GmbH, Wetzlar, Germany), whole eye aberrometry (L 80 wave+, Luneau SAS, Prunay-le-Gillon, France) for pupil sizes of 3 mm and 5 mm, anterior optical coherence tomography (Visante OCT anterior segment imaging, Carl Zeiss Meditec, Jena, Germany) for evaluation of flap thickness and thickness of residual corneal bed, tonometry (Auto Non-Contact Tonometer, Reichert Inc., Buffalo, NY, USA). Slit lamp and dilated fundus examination were also performed. The higher order aberrations (HOAs) evaluated were coma, spherical aberration and trefoil. The L 80 wave+ is a combined autorefractometer, corneal topographer and whole eye aberrometer. The design is based on the Shack-Hartmann aberrometer. Its' modus operandi has been extensively described elsewhere [45]. The HOAs were measured after 10 minutes adaptation in a dark room without mydriasis. The value for coma was taken as the RMS of the sum of the squared Z-13 and Z13 coefficients. Similarly, the value for trefoil was the RMS of the sum of the squared Z-33 and Z33 coefficients. The value for spherical aberration was the value for the Z04 coefficient. Each of these Zernike polynomials describing the wavefront were computed using the manufacturer's software built into the L80 wave+. Central corneal thickness values were read off the captured OCT images. All instruments were checked and calibrated according suppliers' recommendations before use on subjects.

Surgical procedure

The position, diameter and integrity of the flap, site and size of the hinge were inspected just before patients were transferred to the preparation room. Two drops of topical anesthetic were instilled at two minute intervals over 5 minutes before surgery. The eye was cleaned with 2.5% povidone iodine just before lifting the flap. The edge of the flap was located and locally de-epithelized with Merocel sponge (Alcon, Fort Worth, Texas, USA) at the nasal or temporal edge 90° away from hinge. Flat blunt LASIK spatula (Moria, Antony, France) was slid under the flap gently separating flap from underlying corneal bed. After lifting the flap and folding it by placing it on superior conjunctiva, stromal bed thickness was measured using ultrasound pachymeter (PachPen, Acutome, Malvern, PA, USA).

Stromal bed, especially its edges, was thoroughly cleaned with Merocel sponge in radial fashion to remove any residue of epithelial cells. Irrigation was avoided to make sure stromal hydration remained unchanged. After the cleaning of stromal bed, excimer laser ablation was performed on Allegretto Eye Q 400 Hz excimer laser. Wavefront optimized ablation profile was used with the same nomogram adjustment as that used for primary LASIK. The ablation profile was adapted to correct the patients' cycloplegic refraction. After the ablation one drop of oxybuprocaine 0.4% (Novesin, OmniVision GmbH, Puchheim, Germany) was instilled on top the corneal bed while stromal side of the flap was thoroughly cleaned with Merocel sponge to remove any epithelial cells and to prevent flap striae. The flap was repositioned back to its' original position and the interface was irrigated copiously with balanced salt solution. The flap was smoothed out with a wet Merocel sponge. A silicon bandage contact lens was placed on the eye and left in situ for one week.

Postoperative treatment and assessment

All patients were examined one day, one week, one month, three months and one year after the surgery. Evaluation included measurement of UDVA and CDVA, manifest refraction, whole eye aberrometry for pupil sizes of 3 mm and 5 mm, anterior optical coherence tomography for evaluation of corneal thickness, slit lamp and dilated fundus examination, tonometry and corneal topography.

Postoperatively patients were given a combination of topical antibiotic and steroid drops (Tobradex, Alcon, Forth Worth, Texas, USA) 4 times daily for two weeks, and artificial tears (Blink, Abbott Medical Optics, Santa Ana, CA, USA) 6-8 times daily for at least one month.
Data were analyzed to determine the significance of change in the mean high order aberrations (HOAs), central corneal thickness (CCT), and measured intraocular pressure (IOP) in comparison to baseline values (Student t-test, 2-sample assuming unequal variances for data with normal distribution and, where appropriate, Mann Whitney U test for nonparametric analysis). Differences were considered significant when p<0.05.

Data were further analyzed by linear regression to determine the significance of any correlation between the induced change in each high order aberration (HOA) with pre-enhancement HOA value, between CCT and IOP both pre- and post-enhancement, and the change in each HOA with the change in CCT. Correlations were considered significant when p<0.05. If a significant correlation was found between CCT and IOP both before and after enhancement then, the difference between the two correlation coefficients were tested for significance of any apparent difference by first, converting each correlation coefficient to a z score using Fischer’s ‘r to z’ transformation (http://quantpsy.org).

**Results**

Twenty two patients (31 eyes) required a refractive enhancement procedure out of 1804 primary LASIK procedures performed in 2012 leading to a refractive enhancement rate of 1.72%. These patients consisted of 8 females and 14 males. Mean patient age was 43.71 ± 8.67 years (range 25 to 60 years). One eye (one patient) was lost to follow up at one year. Of the patients that completed the study, 23 eyes required sphero-cylindrical correction, 4 eyes required spherical correction and 3 eyes required a cylindrical correction only. Twenty six eyes were predominately myopic and 4 were hyperopic prior to enhancement. Residual refractive errors on case-by-case basis are presented in table 1.

The high order aberration results are shown in table 2. There was no significant change in the average RMS values for coma, spherical aberration or trefoil for both pupil sizes of 3 mm and 5 mm. Further analysis of the data revealed a significant correlation between the change (Δ) in each HOA and the pre-enhancement HOA value for trefoil (3 mm pupil, r=0.722, p=0.00007) and coma (5 mm pupil r=0.501, p=0.048). These data are shown in figures 1 and 2.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Eye</th>
<th>Sphere (D)</th>
<th>Cylinder (D)</th>
</tr>
</thead>
<tbody>
<tr>
<td>N 1</td>
<td>R</td>
<td>0</td>
<td>-1.00</td>
</tr>
<tr>
<td></td>
<td>L</td>
<td>0.25</td>
<td>0</td>
</tr>
<tr>
<td>N 2</td>
<td>R</td>
<td>0</td>
<td>-0.25</td>
</tr>
<tr>
<td></td>
<td>L</td>
<td>0.25</td>
<td>-0.50</td>
</tr>
<tr>
<td>N 3</td>
<td>R</td>
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<td>-0.50</td>
</tr>
<tr>
<td>N 4</td>
<td>R</td>
<td>0.75</td>
<td>-1.00</td>
</tr>
<tr>
<td>N 5</td>
<td>R</td>
<td>0</td>
<td>-0.25</td>
</tr>
<tr>
<td></td>
<td>L</td>
<td>0.37</td>
<td>-1.00</td>
</tr>
<tr>
<td>N 6</td>
<td>L</td>
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<td>0</td>
</tr>
<tr>
<td>N 7</td>
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<td>0</td>
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<tr>
<td>N 8</td>
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</tr>
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<td>0</td>
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<tr>
<td>N 9</td>
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<tr>
<td>N10</td>
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<tr>
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<tr>
<td>N18</td>
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<td>0</td>
<td>-0.25</td>
</tr>
</tbody>
</table>

Table 1: Case-by-case residual refractive error after LASIK enhancement.

**High order aberrations before and after enhancement**

<table>
<thead>
<tr>
<th>Variable</th>
<th>3 mm pupil</th>
<th>5 mm pupil</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>preoperative</td>
<td>postoperative</td>
</tr>
<tr>
<td>RMS (µm)</td>
<td>0.553 ± 0.20</td>
<td>0.307 ± 0.19</td>
</tr>
<tr>
<td>Coma (µm)</td>
<td>0.055 ± 0.05</td>
<td>0.064 ± 0.06</td>
</tr>
<tr>
<td>Trefoil (µm)</td>
<td>0.053 ± 0.04</td>
<td>0.054 ± 0.04</td>
</tr>
<tr>
<td>SA (µm)</td>
<td>-0.005 ± 0.02</td>
<td>0.003 ± 0.03</td>
</tr>
</tbody>
</table>
Higher Order Aberrations (HOA) before and after enhancement.

Table 2: Higher Order Aberrations (HOA) before and after enhancement.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Preop.</th>
<th>Postop.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Central corneal thickness (µm)</td>
<td>518.67 ± 43.68 (448 to 591)</td>
<td>499.8 ± 50.81 (423 to 586)</td>
</tr>
<tr>
<td>Intraocular pressure (mmHg)</td>
<td>12.87 ± 1.85 (10 to 17)</td>
<td>12.17 ± 1.86 (9 to 16)</td>
</tr>
<tr>
<td>Flap thickness (µm)</td>
<td>102.74 ± 4.85 (95 to 112)</td>
<td>102.74 ± 4.85 (95 to 112)</td>
</tr>
<tr>
<td>Intraoperative pachymetry (µm)</td>
<td>416.63 ± 42.79 (344 to 489)</td>
<td>416.63 ± 42.79 (344 to 489)</td>
</tr>
</tbody>
</table>

Mean central corneal thickness (CCT) values are shown in Table 3. There was no significant change in average IOP and CCT. Linear regression revealed a significant correlation between individual pairs of IOP and CCT measures (r=0.7396, p<0.0001, n=30 pre-enhancement and r=0.6749, p<0.0001, n=30 post-enhancement). The difference between the two correlation coefficients was not significant (z=0.477, p=0.6331). The IOP and CCT values are shown in Figure 3. Reporting the significant findings encountered on further analysis of these data, a significant correlation was found between the change in CCT (ΔCCT) and change in spherical aberration (ΔSA) at 3 mm pupil (r=-0.378, p=0.0392) and 5 mm pupil (r=0.524, p=0.0029). There were no significant correlations between ΔCCT and changes in either coma or trefoil for both pupil sizes.

Mean intraocular pressure (IOP) and central corneal thickness (CCT) values are shown in Table 3. There was no significant change in average IOP and CCT. Linear regression revealed a significant correlation between individual pairs of IOP and CCT measures (r=0.7396, p<0.0001, n=30 pre-enhancement and r=0.6749, p<0.0001, n=30 post-enhancement). The difference between the two correlation coefficients was not significant (z=0.477, p=0.6331). The IOP and CCT values are shown in Figure 3. Reporting the significant findings encountered on further analysis of these data, a significant correlation was found between the change in CCT (ΔCCT) and change in spherical aberration (ΔSA) at 3 mm pupil (r=-0.378, p=0.0392) and 5 mm pupil (r=0.524, p=0.0029). There were no significant correlations between ΔCCT and changes in either coma or trefoil for both pupil sizes.
Discussion

The flap relift and reablation technique for residual refractive error after LASIK has been reported to be both safe and effective [46]. For this reason, we accepted this as a reasonable standard procedure for enhancement cases. One of the possible restrictions of this technique is the limitation of the treatment zone with the primary flap and stromal bed diameter and position on the cornea. Our results did not reveal any significant changes in average RMS high order aberration values. Thus, across all 30 cases, the refractive enhancement appears to have corrected only the spherico-cylindrical residual refractive errors but did not affect the overall average optical profiles of the eyes. This has to be viewed with caution. The average HOA values may not change significantly, but, this is not true in each individual case. On a case by case basis, individual changes in trefoil and coma were associated with pre-enhancement values. Figure 2 shows that the algorithm of the enhancement procedure has a tendency to reduce the magnitude of coma when pre-enhancement levels of coma is higher than the average. The opposite occurring when the pre-enhancement coma is relatively low. The same can be said for trefoil as shown in Figure 1. Surprisingly, individual changes in spherical aberration were not associated with the pre-enhancement values. However, for both pupil sizes, the changes in spherical aberration were strongly correlated with changes in corneal thickness. However, there are some paradoxes in the HOA data. Firstly, Figure 4 shows that the change in spherical aberration for the 3mm pupil is inversely associated with the change in corneal thickness and in Figure 5 there is direct association between changes in spherical aberration and corneal thickness for the 5 mm pupil. Secondly, changes in the magnitude of HOAs are expected to be more significant for the larger pupil. This was true for cornea but, we found that changes in trefoil were associated with pre-enhancement values for the smaller 3 mm pupil not the 5 mm pupil. These anomalies may not be detected in larger samples of enhancement cases with different demographics. Nevertheless, the data we obtained do suggest that different lasers with different algorithms may be preferred if there is an intention to improve the overall optical performance of the eye by, for example, nullifying the HOA values.

The IOP measured by applanation tonometry is strongly associated with the corneal thickness [37-42]. Hence, surgical procedures that ultimately reduce corneal thickness are expected to cause the measured IOP values to reduce [32-36] and, the opposite occurring in procedures leading to increase in thickness [47]. Chang and Stulting [36] studied the effect of refractive correction and the lamellar flap on the measured IOP. They found 0.12 mmHg decrease in IOP per diopter of refractive change. However, extrapolation of their data to a theoretical correction of zero diopter reveals a predicted decrease in measured IOP of 1.36 mmHg. It was claimed that this predicted fall was related to the lamellar corneal flap which makes no contribution to the load bearing characteristics of the post LASIK cornea [36].

A alternative explanation to account for this extrapolated fall in measured IOP could be an induced weakness, a fall in stiffness and rigidity caused by flap creation. Corneal rigidity can be affected by the procedure used to create the flap. Compared with a femtosecond procedure, predicting the change in rigidity when the flap is created using a mechanical microkeratome is compounded by factors such as the variability in the flap thickness profile where the meniscus of the flap is much thicker in the periphery than in the center (especially with the rotatory microkeratomes as used in this investigation), variable hinge length, shallow angled side cut and decreased flap re-adherence to the underlying stromal bed. [48-50]. Our data on correlation between IOP and CCT shown in Figure 3 revealed no significant change in this correlation resulting from the refractive enhancement procedure. We found no change in mean IOP or change in the CCT-IOP gradient but, the change in the abscissa that might from subtle changes in the average biomechanical properties of the cornea. We have been unable to find any other publication showing measured IOP and CCT in cases that have been treated not once but twice with an excimer laser.

In summary, both the optical performance of the eye and expected change in measured IOP can be reasonably predicted on a case-by-case basis following an enhancement procedure using the Wavelight Allegretto Eye-Q 400 Hz excimer laser.
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Conflict of Interest Statement

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