The preoperative intraocular pressure level predicts the amount of underestimated intraocular pressure after LASIK for myopia

E Chihara, H Takahashi, K Okazaki, M Park, M Tanito

Aims: To evaluate the statistical significance of the parameters that affect underestimation of intraocular pressure (IOP) after laser in situ keratomileusis (LASIK) for myopia.

Methods: In this prospective case series study, patient age, axial length, preoperative corneal curvature, preoperative central corneal thickness (CCT), preoperative IOP, and ablation depth were studied to determine whether they affect the underestimation of IOP in the right eyes of 100 consecutive patients who underwent LASIK.

Results: The preoperative IOP was the most important parameter for an amount of underestimated Goldmann applanation tonometric IOP (GAT) and non-contact tonometric IOP (ncIOP) at 1 month (r=0.654, p<0.0001, R²=0.427, and r=0.694, p<0.0001, R²=0.481, respectively) and 3 months (r=0.637, p<0.0001, R²=0.406, and r=0.726, p<0.0001, R²=0.527, respectively). Patient age was statistically significant for underestimating the GAT at 1 month, and both the ablation depth and CCT were statistically significant parameters for underestimating the ncIOP at 1 month and at 3 months by stepwise multiple regression analysis (F>4.000). However, these parameters had small bivariate correlation coefficients, and were considered as minor parameters.

Conclusion: Preoperative IOP is the most important parameter that affects an underestimation of IOP after LASIK for myopia. Eyes with a higher true IOP have a larger underestimation of the IOP after LASIK for myopia. From these results, the importance of the modulus of elasticity on IOP measurements was discussed.

The assessment of precise intraocular pressure (IOP) is of clinical importance for detecting early glaucoma and evaluating the efficacy of hypotensive treatment in patients with glaucoma and ocular hypertension. If the IOP is underestimated after refractive surgeries, especially those for myopia, clinical problems may ensue. Continuing efforts to estimate the precise IOP is of clinical importance, because myopia is a risk factor for primary open angle glaucoma.1 Patients with myopia and glaucoma may have rapid deterioration of the visual fields,2 and patients affected are at risk for selective impairment of macular function.3,4

Recently, several reports have been published on the underestimation of IOP after various refractive procedures such as radial keratotomy,5 photorefractive keratectomy,6 and laser in situ keratomileusis (LASIK).7 The effect of latanoprost may also be underestimated.8 Thus, efforts are being made to obtain precise IOP measurements.9–10

To obtain precise IOP data subsequent to refractive surgery, studies of various parameters that may impact the underestimation of the IOP are of considerable importance. Parameters that have been evaluated include ablation depth,11 age,12 preoperative IOP,11 interstitial tissue fluid,12 decreased corneal resistance toplanation,13 and corneal curvature.14

In normal eyes there is a positive correlation between corneal thickness and IOP.15 Thus, it may be reasonable to expect a positive correlation between the ablation depth and the amount of underestimated IOP. However, the reported findings on this putative correlation after LASIK are controversial. While several authors have reported a significantly positive correlation,11 others have not.5,13,17

Furthermore, in some reports, underestimation of the IOP occurs after radial keratotomy, in which there is no tissue loss,9 or after LASIK for hyperopia, in which central corneal ablation is minimal.17

It may well turn out that the cause of underestimation of the IOP after LASIK is multifactorial, and thus a multivariate analysis would be more appropriate to assess the importance of contributing parameters.

PATIENTS AND METHODS

Patients

Clinical data were obtained prospectively from the right eyes of 100 consecutive patients who underwent LASIK for myopia between April 2001 and April 2002 at Sensho-kai Eye Institute. The patients included in the study were healthy myopic subjects who were scheduled for LASIK treatment and had no systemic or ocular diseases other than myopia. All patients were treated according to the institutional treatment protocol. Patients with a cornea of less than 480 μm thickness, active anterior segment diseases, a history of ocular surgery, glaucomatous optic neuropathy, IOP greater than 21 mm Hg as determined by a Goldmann applanation tonometer, dry eye, a known history of trauma, undergoing treatment with topical or systemic steroid therapy, those who do not adhere to the follow up protocol, and those who underwent re-treatment during follow up, were excluded. Based on these exclusion criteria, data from seven patients were excluded, and the ultimate statistical analysis was based on the data from 93 eyes in 93 patients. Informed consent was obtained from all patients before LASIK, and all procedures followed the tenets of the 1989 Declaration of Helsinki.

Abbreviations: CCT, central corneal thickness; GAT, Goldmann applanation tonometric IOP; IOP, intraocular pressure; IOPT, true IOP; LASIK, laser in situ keratomileusis; ncIOP, non-contact tonometric IOP

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Methods

In this prospective case series investigation, the preoperative and postoperative IOP levels were the primary outcome. Before LASIK, uncorrected and best corrected visual acuity, spherical equivalent refractive error, the axial length as determined by A-mode ultrasonography (AL-010, Tomey, Aichi, Japan), endothelial cell count (Noncon ROBO-CA, Konan-Keeler, Kobe, Japan), pupil diameter, the keratomic corneal curvature (RT, Tomey), the central corneal thickness (CCT), and topography as determined by an Orbscan system (Version 3D, Canon-Bausch & Lomb, Tokyo, Japan), the Goldmann applanation tonometric IOP (GAT), the non-contact (air puff) tonometric IOP (ncIOP) as determined by a Topcon CT90A, Tokyo, tear film break up time, and the size of the palpebral fissure, and the ablation depth, which was defined as a CCT loss displayed on the control panel of the excimer laser (EC5000, Nidek, Aichi, Japan), were all collected in the right eyes of 93 patients. The acoustic factor of the Orbscan system was set at 0.92. Post-surgical data were obtained at 1 week, 1 month, and 3 months after LASIK. Corneal topography and CCT (Orbscan), refractive error, and ncIOP were studied at 1 week, 1 month, and 3 months after LASIK. Before the LASIK surgery, CCT was examined by both the Orbscan and an ultrasonic pachymeter (AL3000, Tomey). However, the follow up examinations were made by means of a non-invasive Orbscan system out of safety considerations. For Goldmann applanation tonometric examinations, one tonometer, calibrated to within 0.1 degree of error, was employed, and the GAT was measured at 1 and 3 months after LASIK in a special room set aside for LASIK between 5 and 7 o’clock in the evening. Non-contact tonometric IOP was examined by two skilful technicians, both of whom were masked to the type of treatment.

Interventions

One surgeon (KO) performed all LASIK procedures on both eyes simultaneously. The room temperature was maintained at 20°C (SD 4°C), and the humidity at 40% (SD 15%). After topical anaesthesia was induced using 4% lidocaine (Xylocaine, Astra Zeneca Japan, Osaka, Japan), an 8 mm corneal flap (160 μm thickness) was created with a microkeratome (M2, Moria, Tokyo, Japan). The corneal stroma was ablated with an excimer laser. The optical and transition zones were 5.0–5.5 mm and 6.0–7.0 mm, respectively.

Topical ofloxacin (5 mg/ml, Santen, Osaka, Japan), and 0.1% fluorometholone and 0.1% hyaluronic acid (Santen) were administered postoperatively four times daily for 1 week and 1 month, respectively.

Statistical analysis

Stepwise multiple regression analysis with a forward selection procedure was used to study the parameters that may affect IOP readings. Parameters with an F value greater than or equal to 4.000 were considered statistically significant.

### Table 1  Time course of the CCT, refractive error, and IOP (mean (SD))

<table>
<thead>
<tr>
<th></th>
<th>1 week postoperative</th>
<th>1 month postoperative</th>
<th>3 month postoperative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reduction in CCT (μm by Orbscan)</td>
<td>78.9 (37.0)</td>
<td>61.5 (33.0)</td>
<td>50.3 (27.9)</td>
</tr>
<tr>
<td>Improved refractive error (D)</td>
<td>4.95 (2.1)</td>
<td>4.72 (1.98)</td>
<td>4.55 (1.97)</td>
</tr>
<tr>
<td>Reduction in ncIOP (mm Hg)</td>
<td>5.1 (2.6)</td>
<td>5.1 (2.6)</td>
<td>4.8 (2.6)</td>
</tr>
<tr>
<td>Reduction in GAT (mm Hg)</td>
<td>NA</td>
<td>2.9 (3.1)</td>
<td>3.2 (2.8)</td>
</tr>
<tr>
<td>Post-LASIK ncIOP (mm Hg)</td>
<td>10.3 (2.3)</td>
<td>10.2 (2.3)</td>
<td>10.4 (2.1)</td>
</tr>
<tr>
<td>Post-LASIK GAT (mm Hg)</td>
<td>NA</td>
<td>13.0 (2.5)</td>
<td>12.7 (2.5)</td>
</tr>
</tbody>
</table>

IOP, intraocular pressure; op, LASIK surgery; CCT, central corneal thickness; GAT, Goldmann applanation tonometric intraocular pressure; ncIOP, non-contact tonometric intraocular pressure; NA, not applicable.

RESULTS

The mean (SD) of the preoperative values were as follows: age of the patients (51 men, 42 women) 33.2 (8.6) years,
refractive error –5.70 (2.22) dioptres (D), axial length 26.1 (1.02) mm, keratometric reading 7.74 (0.25) mm, refractive power within a 3 mm circle 43.2 (1.4) D, CCT by means of Orbscan 529 (32) μm, GAT 15.9 (3.0) mm Hg, and ncIOP 15.3 (3.1) mm Hg. The corneal ablation depth was 66.1 (22.9) μm.

The amount of reduced CCT and the improved refractive error in dioptres (D) tend to decline during the follow up period of 3 months (table 1). During the postoperative period, reduction of the IOPs (GAT and ncIOP) and the IOP period of 3 months (table 1). During the postoperative error in dioptres (D) tend to decline during the follow up period of 3 months (table 1).

Bivariate correlation (R2 = 0.406) and that between the preoperative GAT (with D indicating a difference between the preoperative and postoperative data) at 1 month and the preoperative IOP was significant in both the GAT (r = 0.654, p<0.0001, R2 = 0.427) and ncIOP (r = 0.694, p<0.0001, R2 = 0.481) (table 2, figs 1 and 2). Parameters other than the preoperative IOP—that is, patient age, axial length, preoperative corneal curvature, preoperative CCT, and ablation depth, did not exhibit significant bivariate correlation with ΔGAT (1 month) or ΔncIOP (1 month) (table 2).

Bivariate correlation coefficients between ΔGAT (3 months) or ΔncIOP (3 months) and six parameters are listed in table 3. Here again, the preoperative IOP exhibited a significant correlation with ΔGAT and ΔncIOP (r = 0.637, p<0.0001, R2 = 0.406 and r = 0.726, p<0.0001, R2 = 0.527, respectively). Other than this, only ablation depth (r = 0.242, p = 0.0282 R2 = 0.059) exhibited a significant correlation with ΔncIOP (3 months). Parameters other than the preoperative IOP and ablation depth, did not exhibit significant bivariate correlation with ΔGAT (3 months) or ΔncIOP (3 months) (table 3).

The multivariate effects of six independent parameters on the underestimation of IOP at 1 and 3 months were analysed by stepwise multiple regression with a forward selection procedure. When the ΔGAT values at 1 month were set as a dependent variable, two of the six parameters were statistically significant based on the stepwise multiple regression analysis (F>4.000); the preoperative GAT (R2 = 0.427) was the most important, followed by patient age (R2 = 0.027). Thus, 42.7% and 2.7% of the underestimation were explainable by the preoperative GAT and patient age, respectively. The regression equation obtained was ΔGAT (1M) = −6.079 – 0.059 × age + 0.678 × preoperative GAT (R2 = 0.453 for this equation). When the ΔncIOP (1 month) was set as a dependent variable for stepwise multiple regression, three of the six parameters significantly affected the ΔncIOP (1 month) (F>4.000). The preoperative ncIOP was the most significant parameter (R2 = 0.481), followed by ablation depth (R2 = 0.037) and preoperative CCT (R2 = 0.003). The regression equation obtained was ΔncIOP (1M) = 3.063 + 0.628 × preoperative ncIOP − 0.017 × preoperative CCT + 0.021 × ablation depth (R2 = 0.535 for this equation). Neither axial length nor preoperative corneal curvature was a significant parameter in either analysis.

Bivariate correlations between the ΔGAT (1 month) and age (r = −0.163, p = 0.12, fig 3), that between the ΔncIOP (1 month) and the ablation depth (r = 0.191, p = 0.063; fig 4), and that between the ΔncIOP (1 month) and the preoperative CCT (r = 0.053, p = 0.61, fig 5) were not significant despite the positive correlations by multivariate analysis (table 2).

When the ΔGAT and ΔncIOP at 3 months were set as the dependent variables for stepwise multiple regression, only the preoperative IOP was a significant parameter for the ΔGAT (3 months). ΔGAT (3M) = −6.455 + 0.596 × preoperative GAT (R2 = 0.406). At the same time, three parameters, which were the same as the three important parameters for ΔncIOP (1 month), were found to be significant parameters for the ΔncIOP (3 months). ΔncIOP (3M) = 3.501 + 0.638 × preoperative ncIOP + 0.028 × ablation depth − 0.019 × preoperative CCT (R2 = 0.615 for this equation).

### Table 2: Correlation coefficients between underestimated IOP (ΔGAT and ΔncIOP) at 1 month for six parameters

| Parameter   | Correlation coefficient (95% CI) | p Value | | Parameter   | Correlation coefficient (95% CI) | p Value |
|-------------|----------------------------------|---------|-------------|----------------------------------|---------|
| Preop GAT   | 0.654 (0.519 to 0.757)           | <0.0001*| Preop GAT   | 0.694 (0.572 to 0.785)           | <0.0001*|
| Preop ncIOP | 0.163 (-0.355 to 0.042)          | 0.12    | Preop ncIOP | 0.026 (-0.226 to 0.177)          | 0.81    |
| Age         | -0.024 (-0.218 to 0.189)         | 0.89    | Age         | 0.153 (-0.344 to 0.144)          | 0.14    |
| Ablation depth | -0.036 (-0.169 to 0.238)       | 0.73    | Ablation depth | 0.018 (-0.219 to 0.184)         | 0.86    |
| Preop CCT   | 0.075 (-0.131 to 0.274)          | 0.48    | Preop CCT   | 0.053 (-0.151 to 0.252)          | 0.61    |
| Preop corneal curvature | 0.015 (-0.272 to 0.134) | 0.49    | Preop corneal curvature | 0.191 (-0.011 to 0.378) | 0.063    |

### Table 3: Correlation coefficients between underestimated IOP (ΔGAT and ΔncIOP) at 3 months for six parameters

| Parameter   | Correlation coefficient (95% CI) | p Value | | Parameter   | Correlation coefficient (95% CI) | p Value |
|-------------|----------------------------------|---------|-------------|----------------------------------|---------|
| Preop GAT   | 0.637 (0.478 to 0.756)           | <0.0001*| Preop GAT   | 0.726 (0.604 to 0.814)           | <0.0001*|
| Preop ncIOP | 0.095 (-0.317 to 0.137)          | 0.423   | Preop ncIOP | 0.012 (-0.206 to 0.228)          | 0.918   |
| Age         | -0.024 (-0.251 to 0.205)         | 0.838   | Age         | 0.219 0.002 to 0.414             | 0.014   |
| Ablation depth | 0.130 (-0.102 to 0.348)       | 0.272   | Ablation depth | 0.219 (-0.21 to 0.209)         | 0.946   |
| Preop corneal curvature | 0.008 (-0.229 to 0.228) | 0.996   | Preop corneal curvature | 0.024 (-0.225 to 0.209) | 0.04    |
| Preop CCT   | -0.001 (-0.325 to 0.127)         | 0.377   | Preop CCT   | 0.026 (-0.026 to 0.436)         | 0.0282* |

Δ, difference between preoperative and 1 month postoperative data; CI, confidence interval; GAT, Goldmann applanation tonometric intraocular pressure; ncIOP, non-contact tonometric intraocular pressure; preop, preoperative; CCT, central corneal thickness.

*Pearson’s correlation coefficient.

*Statistically significant correlation.
Underestimation of IOP after LASIK

The reduced IOP reading. However, corneal ablation explain the positive correlation between ablation depth and nevertheless it is a parameter of minor importance. This finding suggests that the ablation depth is not ignorable, analysis (Fsignificant parameter by stepwise multiple regression analysis (\(F>4.000\)); however, it is not significant by single regression analysis (\(r=−0.163, p=0.12\)). This finding suggests that the age is a parameter of minor importance.

DISCUSSION

For a follow up study of the CCT, an Orbscan system, in which we set an acoustic factor of 0.92, was used in this study because of its non-invasive character, to protect against damage to the corneal flap. The Orbscan system has highly reproducible data\(^6\); however, the corneal thickness or standard deviation obtained with this system may be greater than that obtained with an ultrasonic pachymeter.\(^{16,20}\) To avoid problems with the Orbscan, we used the ablation depth data displayed on the control panel of the EC5000 for statistical analysis.

From a theoretical point of view, the positive correlation between corneal thickness and the IOP readings\(^8\) may explain the positive correlation between ablation depth and the reduced IOP reading.\(^{11,16,20}\) However, corneal ablation by the refractive surgery is lenticularly shaped and not uniform. This may be one of the reasons for the poor correlation between the ablation depth and reduced IOP reading in our study and in the studies of others.\(^5,7,11,17,20,27\) Wound healing processes may cause time dependent loss of initially positive correlation between the ablation depth and the reduced IOP reading.\(^{24}\)

There is clinical evidence that casts doubt on the positive correlation between the post-LASIK ablation depth and the underestimation of IOP. Firstly, the amount of underestimated IOP after LASIK for hyperopia was similar to that after LASIK for myopia.\(^{17,24}\) Thus, differences in ablation depth at the central or the peripheral cornea were not reflected in differences in the amount of the underestimated IOP. Secondly, the IOP measured at the peripheral cornea, where the corneal parenchyma was not ablated after LASIK for myopia, was not free of underestimation, even though the underestimation at the peripheral cornea was milder than at the centre.\(^{24}\) Finally, underestimation of the IOP was found after radial keratotomy, in which procedure the corneal parenchyma is not ablated.\(^1\) A poor correlation between the ablated depth and reduced IOP measurement in this study and the clinical evidence mentioned above suggest that the ablation depth per se may not be the principal cause of IOP underestimation after refractive surgery.

According to a report by Goldmann and Schmidt, the IOP reading can be affected by corneal thickness, ocular rigidity, tear film, and corneal curvature.\(^{29}\) Because the changes in corneal curvature after LASIK are correlated closely with the ablation depth, the first three factors may be the main parameters that affect the IOP measurement after LASIK.

In our study, the ablation depth was able to account for only 3.7% or 5.9% of the total underestimation of the ncIOP at 1 month or 3 months, and this is of far less importance than the preoperative ncIOP, which was able to account for 48.1% and 52.7% of the total underestimation at 1 month and 3 months, respectively. The effect of the preoperative IOP on the underestimation of IOP was reported previously,\(^11\) and our results confirmed the earlier findings. According to Orsengo and Pye,\(^8\) the modulus of elasticity (E) is a function of the true IOP (IoPT), and those authors formulated the equation E = 0.0229IoPT in the normal eye; thus, eyes with a higher IoPT have a higher E. Purslow and Karwatowski reported an equation of\(^4\)

\[
\frac{dP}{dV} = \frac{t}{\pi} \frac{E}{R^2}
\]

Thus, E can affect dP. As the collagen fibrils are cut after refractive surgery and cut collagen fibres do not have tensile force, refractive surgery can lead to reduced corneal rigidity.\(^{32}\) While the E is greater in eyes with higher IoPT, the absolute reduction of E may be greater in eyes with a higher IoPT when the percentage of cut collagen fibres in the cornea is nearly constant.

At a minimum, the reduced modulus of elasticity can help explain the reduced IOP reading at the central cornea after LASIK for hyperopia or radial keratotomy and the reduced

Figure 3 Scatter graph and bivariate regression analysis between the underestimated GAT (dGAT) 1 month (1M) after LASIK and patient age. Age is a significant parameter by stepwise multiple regression analysis (F>4.000); however, it is not significant by single regression analysis (r=−0.163, p=0.12). This finding suggests that the age is a parameter of minor importance.

Figure 4 Scatter graph and bivariate regression analysis between the underestimated non-contact tonometric IOP (dncIOP) 1 month (1M) after LASIK and the ablation depth. The ablation depth is a significant parameter by stepwise multiple regression analysis (F>4.000); however, it is marginally significant by single regression analysis (r=0.191, p=0.063, dncIOP=3.649+0.022×ablation depth). This finding suggests that the ablation depth is not ignorable, nevertheless it is a parameter of minor importance.

Figure 5 Scatter graph and bivariate regression analysis between the underestimated non-contact tonometric IOP (dncIOP) and the preoperative CCT (Pre-CCT). The preoperative CCT is a significant parameter by stepwise multiple regression analysis (F>4.000); however, it is not significant by single regression analysis (r=0.053, p=0.61). Here again, it is suggested that the preoperative CCT is a parameter of minor importance.
IOP reading at the peripheral cornea where changes of the corneal curvature and corneal thickness are minimal after LASIK for myopia. If the ablation depth is greater after LASIK, the number of cut collagen fibres increases and results in a reduction in E, which in turn results in a more significant underestimation of the IOP unrelated to the ablation depth.

In previous reports, other factors that may affect underestimation of the IOP include preoperative corneal curvature,3 changes in corneal curvature,6,7 age and sex,6 and intraocular fluid.12 Corneal ablation can bring about changes in the corneal curvature, and the corneal curvature can in turn affect the IOP measurement,3 which may explain the positive correlation between the corneal curvature and ΔIOP.6,12 However, another explanation may be a proportional reduction of the corneal thickness and the consequently reduced E brought about by the cutting of the collagen fibres.

In our findings, age was determined to be a significant parameter by multivariate analysis, a finding that agrees with that of Faucher and others.9 Another study has also reported increased corneal rigidity in elderly subjects.6,12 Increased E in elderly subjects and differences in the architecture of the collagen fibres8 or weak cornea collagen fibres in females may affect the amount of underestimation of the IOP after LASIK.6 The increased thickness of the corneal epithelium3 may also affect the E of the total cornea and the IOP measurement after refractive surgery. Studies of these minor parameters of more subtle effect require necessarily larger sample sizes and will be a subject for future analysis.

Tear film, the last of the four parameters reported by Goldmann and Schmidt,27 may also affect IOP readings. Dry eye is a common finding after LASIK.2 Reduced tear film flow may increase capillary pressure, which may cause the IOP to be underestimated.

In conclusion, we studied the effect of six parameters on underestimation of the IOP after LASIK for myopia by stepwise multiple regression analysis. Among the six, the preoperative IOP level was the most important parameter, and was able to account for 42.7% to 40.6% and 48.1% to 52.7%, respectively, of the postoperative underestimation of the IOP and ΔIOP at 1 month and 3 months. Patients with a higher IOP have greater underestimation of the IOP. This finding is important for the proper diagnosis and evaluation of treatment outcome in patients with post-LASIK glaucoma.

ACKNOWLEDGEMENTS

Part of this work as been presented as a poster at the ARVO meeting in 2002 and 2003 at Fort Lauderdale, FL, USA.

The authors have no proprietary interest in any materials that appear in this paper.

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Proprietary interest: None.

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doi: 10.1136/bjo.2004.048074

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