Development of an Advanced Nomogram for Myopic Astigmatic Wavefront-Guided Laser In Situ Keratomileusis (LASIK)

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■ **BACKGROUND AND OBJECTIVE:** To identify the relationship between preoperative parameters and postoperative overcorrection or undercorrection in eyes with myopic astigmatism treated with wavefront-guided laser in situ keratomileusis (LASIK), and to develop an advanced surgical nomogram.

■ **PATIENTS AND METHODS:** A retrospective chart review of 468 eyes that underwent wavefront-guided LASIK for myopia with astigmatism with the Alcon LADARVision 4000 (Alcon Laboratories, Fort Worth, TX), of which 235 had flaps created by microkeratome (OneUse; Moria Surgical, Doylestown, PA) and 233 by femtosecond laser (Intralase; AMO, Santa Ana, CA). Manifest sphere, cylinder, and spherical equivalent were recorded preoperatively and 3 months postoperatively. Various parameters from patient records were analyzed to identify which had greatest influence on outcomes.

■ **RESULTS:** Manifest spherical equivalent was the most important predictor of surgical overcorrection, with the second being spherical aberration. In both groups, there was a statistically significant ($P < .0001$) correlation of spherical aberration with the amount of overcorrection. Using these two parameters, compensatory nomograms were derived.

■ **CONCLUSION:** Surgical overcorrection in wavefront-guided LASIK for myopic astigmatism correlates positively with the amount of spherical equivalent treated and preoperative spherical aberration. Nomograms incorporating spherical aberration may improve accuracy of outcomes.

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INTRODUCTION

Wavefront-guided laser in situ keratomileusis (LASIK) has been established as a reliable and accurate procedure for the treatment of refractive errors, often with greater than 83% of patients achieving an uncorrected visual acuity (UCVA) of 20/20 or better.[1-4] Nonetheless, a small but significant subset of patients are left with a residual refractive error.

Unadjusted laser ablation profiles can result in spherical overcorrection or undercorrection, with the former typically being less desirable due to residual hyperopia. Surgical nomograms have been devised to compensate for predictable factors leading to overcorrection, primarily the amount of attempted change in manifest refraction spherical equivalent (MRSE). Nomograms have also accounted for differences in patient age.[5] Individual surgeons use their own results to derive their own personalized nomograms, which take into account factors such as surgical technique, laser type, treatment algorithm, and the temperature and humidity of the laser suite.

Wavefront-guided technology has the ability to measure and treat a wide variety of higher order aberrations, allowing for a more complete neutralization of refractive error and decreasing the risk of night vision disturbances.[6] The treatment of higher order aberrations has been demonstrated to have an effect on spherical equivalent outcomes.[7] The Rochester Nomogram, which takes into account preoperative higher order aberrations, was developed and incorporated into the Technolas Zyoptix laser.[8] This is a proprietary algorithm and details have not been openly published. However, in a study population with myopia, the authors have reported a decreased tendency toward hyperopic overcorrection and a tighter distribution of outcomes around the intended target compared with the standard Zyoptix nomogram.[8] A recent independent study of 100 eyes with myopia treated with LASIK or laser-assisted subepithelial keratectomy using the Rochester Nomogram revealed a low level of hyperopic overcorrections (4.1% of subjects ⩾ +1.00 diopters [D]), and a mean spherical equivalent close to plano.[9]

In the current study, we sought to identify the preoperative parameters, including higher order aberrations, that are most closely linked with refractive spherical equivalent outcomes, and to develop a nomogram applicable for the treatment of myopic astigmatism.

PATIENTS AND METHODS

Patient Selection

The charts of all patients undergoing wavefront-guided myopic/astigmatic LASIK at the UCLA Laser Refractive Center with the Alcon LADARVision 4000 System (Alcon Laboratories, Fort Worth, TX) from April 2004 to March 2008 were retrospectively identified. Retrospective review of medical records was approved by the Institutional Review Board of the University of California, Los Angeles.

Treatment and Measurement

All subjects underwent a comprehensive preoperative evaluation, consisting of measurement of UCVA, best spectacle-corrected visual acuity (BSCVA), manifest and cycloplegic refraction, corneal topography, pachymetry, intraocular pressure, LADARWave aberrometry, slit-lamp examination, and dilated funduscopic examination.

On the day of surgery, the patients' eyes were dilated with 2.5% phenylephrine and 1% tropicamide. After waiting a minimum of 20 minutes, a series of five measurements from the LADARWave aberrometer was obtained, with the best three images averaged to determine a composite wavefront treatment profile using a 6.5-mm aperture.

LASIK flaps were created with either the Moria OneUse automated disposable microkeratome (Moria Surgical, Doylestown, PA) with a 130-micron head or the Intralase 60-kHz femtosecond laser (AMO, Santa Ana, CA). In the microkeratome group, a fresh, sterile blade was used for each eye. Intraoperative pachymetry was performed to determine the actual flap thickness and to estimate the residual stromal bed.

Treatment was performed using the CustomCornea Myopic Astigmatism algorithm on the LADARVision 4000 excimer laser (Alcon Laboratories), with a 6.5-mm optical zone and a 1.25-mm blend zone. All surgeries were performed by a single surgeon (DRH). Postoperative treatment included moxifloxacin and prednisolone eye drops four times a day for 1 week.

Postoperative assessment at the 3-month visit included determination of UCVA, BSCVA, manifest and cycloplegic refraction, topography, and dilated wavefront aberrometry.

TABLE

Preoperative Patient Characteristics[a]

Characteristic	Microkeratome	Femtosecond Laser
No. of eyes	235	233
No. of patients	135	129
% male	37.0%	39.0%
Preoperative manifest refraction	-4.15 ± 1.83	-4.11 ± 1.95
Postoperative manifest refraction (3 mo)	-0.12 ± 0.41	-0.05 ± 0.56
Δ manifest refraction	4.03 ± 1.83	4.06 ± 1.96
Programmed laser spherical equivalent	-3.87 ± 1.72	-3.58 ± 1.76
Age (y)	37.5 ± 9.20	35.90 ± 10.10
Manifest refraction		
Preoperative sphere	-3.81 ± 1.83	-3.76 ± 1.95
Preoperative cylinder	-0.68 ± 0.68	-0.70 ± 0.70
Preoperative spherical equivalent	-4.15 ± 1.80	-4.11 ± 1.95
Wavefront refraction		
Preoperative sphere	-3.78 ± 1.88	-3.65 ± 1.96
Preoperative cylinder	-0.90 ± 0.74	-0.91 ± 0.77
Preoperative spherical equivalent	-4.23 ± 1.91	-4.11 ± 1.98
Wavefront measurements[b]		
Defocus RMS	6.60 ± 2.63	6.46 ± 2.75
Cylinder RMS	0.87 ± 0.74	0.89 ± 0.76
Coma RMS	0.24 ± 0.13	0.23 ± 0.13
Spherical aberration RMS	0.20 ± 0.17	0.23 ± 0.18
Total higher order aberrations RMS	0.45 ± 0.14	0.45 ± 0.15

RMS = root mean square.
[a]Values given as mean ± standard deviation.
[b]Across a 6.5-mm pupil.

Data and Statistical Analysis

Manifest sphere, cylinder, and spherical equivalent were recorded for each eye from the preoperative and 3-month postoperative visit. In addition, age, gender, preoperative wavefront spherical equivalent, root mean square (RMS) values for defocus, cylinder, coma, spherical aberration (SA), and total higher order aberrations, as well as the actual laser setting spherical equivalent at the time of treatment (LaserSE), were recorded.

Multiple stepwise linear regression was performed separately on the microkeratome and femtosecond laser groups, using SAS software (version 9.1; SAS Institute, Inc., Cary NC), to identify those parameters with the greatest influence on postoperative outcome. A P value of less than .05 was considered to be statistically significant. A linear regression model was then created and used to derive a nomogram for each group incorporating the most significant factors. The "r" value, or correlation coefficient, was calculated for each linear regression model to indicate the linear relationship between the parameter and outcome, with values closer to 1 indicating a strong correlation between the two.

RESULTS

A total of 468 eyes met inclusion criteria, of which 235 had flaps created by microkeratome and 233 by femtosecond laser. Baseline parameters were similar between the two groups (Table). The microkeratome treatments were performed between April 2004 and

August 2006. The femtosecond laser treatments were performed from April 2006 to March 2008.

In the microkeratome group, stepwise regression revealed that spherical equivalent was the most important predictor of overcorrection ($P < .0001$). This was followed by spherical aberration RMS ($P < .0001$) and cylinder RMS ($P < .046$). In the femtosecond laser group, spherical equivalent was again the most influential factor ($P < .0001$), followed by spherical aberration ($P < .0001$).

Nomogram equations were derived from these parameters to adjust the LaserSE based on these identified preoperative parameters. Cylinder RMS was barely statistically significant in the microkeratome model; therefore, it was excluded from the microkeratome nomogram equation to unify and simplify the two equations. Thus, both models depend on magnitude of attempted MRSE and amount of preoperative SA.

For the microkeratome group:

$$\text{LaserSE} = -0.08 - 0.98 \times \text{MRSE} + 0.77 \times \text{SA} \ (r = 0.964).$$

For the femtosecond laser group:

$$\text{LaserSE} = 0.05 - 0.95 \times \text{MRSE} + 0.98 \times \text{SA} \ (r = 0.952).$$

(LaserSE = spherical equivalent of the laser setting in diopters; MRSE = postoperative target spherical equivalent – preoperative spherical equivalent in diopters; SA = preoperative spherical aberration over a 6.5-mm aperture in microns).

DISCUSSION

Wavefront-guided LASIK provides for exceptional refractive accuracy and high levels of patient satisfaction. Despite this, there remains a group of patients who end up with postoperative refractive errors requiring enhancement.[4] In this article, we consider the factors that contribute to overcorrection of spherical equivalent refraction in myopic patients.

Recent studies have established a connection between preoperative higher order aberrations and postoperative spherical equivalent outcome.[8] However, the specific higher order aberrations involved and their relative significance with regard to primary LASIK procedures have not been published. A study by Steinert and Fynn-Thompson[10] evaluated the role of higher order aberration in postoperative refractive error in a population of previously treated LASIK eyes undergoing enhancement procedures, and found that preoperative spherical aberration was the higher order abberation most closely correlated with consecutive hyperopia following enhancement. The relationship was described with a linear equation in which the amount of overcorrection was directly proportional to the amount of preoperative spherical aberration.

We describe a multi-variable regression analysis based on a large sample size of patients undergoing LASIK for myopia for the first time to determine which preoperative factors have the highest correlation with postoperative ametropia. As expected, the most important preoperative risk factor is the magnitude of spherical equivalent treated. After preoperative spherical equivalent, spherical aberration was found to correlate significantly with overcorrection. In the microkeratome model, preoperative cylinder RMS was barely statistically significant, and improved the overall correlation of the model slightly (from $R = 0.9204$ to $R = 0.9305$). In the femtosecond laser model, preoperative cylinder RMS was not statistically significant. Consequently, cylinder was excluded from the final model to simplify the nomogram and maintain the uniformity between the microkeratome and femtosecond laser groups.

Patients in the microkeratome and femtosecond laser groups were analyzed separately due to anticipated differences in treatment response attributable to the biomechanical properties of the cornea. Previous studies have demonstrated differences in the biomechanical response of the cornea depending on whether the flap is created using a microkeratome or femtosecond laser.[11] A microkeratome flap has a meniscus shape, extending deeper in the cornea periphery and shallower toward the center. A femtosecond laser flap has a planar profile with an equal depth across its entire length. The planar flap invades the peripheral cornea less, leading to preservation of tensile strength of the cornea, which seems to be depth-dependent and is most significant in the cornea periphery. In general, femtosecond laser flaps also heal stronger in the periphery than microkeratome flaps.[12] Because there are known differences in the biomechanical effects the two methods of flap creation have on the cornea, they were analyzed separately to avoid confounding factors in the nomogram development.

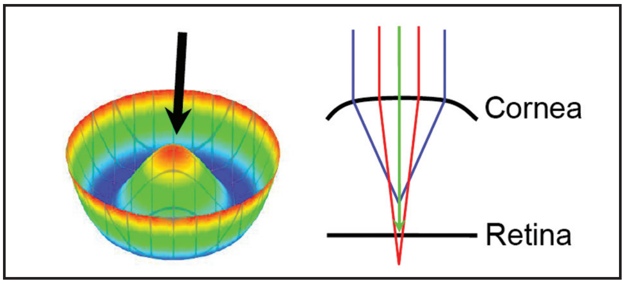

Figure 1. Positive spherical aberration. The wavefront profile features hyperopia around the central visual axis (arrow), due to flattening of the central cornea relative to the periphery.

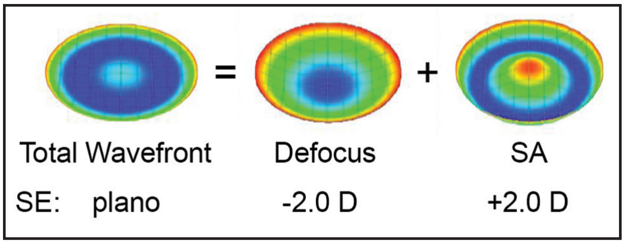

Figure 2. Wavefont profile of a patient with myopia after LASIK with plano spherical equivalent. When broken down into Zernike components, it is apparent that this patient has a hyperopic contribution from spherical aberration and a myopic contribution from defocus. SA = spherical aberration; SE = spherical equivalent; D = diopters.

The derived nomogram equations demonstrate the linear relationship between preoperative MRSE, preoperative SA, and refractive outcome, and can be used to calculate the surgeon offset for a particular case. Caution must be exercised, however, because these data represent the experience of a single surgeon under fixed conditions with the Alcon LADARVision 4000 excimer laser. Although similar relationships may exist under alternative surgical conditions, generalizability of this specific nomogram may be limited. In particular, this nomogram should not be generalized to excimer lasers produced by other manufacturers, or other types of treatment (hyperopic astigmatism, mixed astigmatism, conventional ablations, wavefront-optimized ablations, etc.). The findings of this study should serve merely to alert the refractive surgeon to be aware of the level of spherical aberration in the patient undergoing wavefront-guided treatment and that significant levels of positive or negative spherical aberration may impact outcomes.

The wide range of spherical aberration found in the population can have a considerable effect on the output of this nomogram. In our study population, preoperative spherical aberration ranged from -0.48 to +1.00 microns. Consider a patient with a myopia of -4.00 D undergoing LASIK with the femtosecond laser desiring emmetropic target refraction. With an extreme negative spherical aberration measuring -0.48 microns, the adjusted laser spherical equivalent would be -4.22 D, resulting in a negative surgeon-entered offset of -0.22 D to account for an anticipated undercorrection. The same patient with a myopia of -4.00 D with extremely high spherical aberration (+1.00 microns) would call for a dramatically reduced laser spherical equivalent of -2.77 D, or a surgeon-entered offset of +1.23 D. Failure to reduce the laser setting by this amount would likely lead to significant overcorrection in the second case. Simply put, without the compensatory nomogram, treatment of the patient with extreme negative spherical aberration would result in undercorrection, whereas overcorrection would result in the patient with extreme positive spherical aberration.

The results of this study beg the question: why does a large amount of positive spherical aberration correlate with an overcorrected outcome in the patient with myopia undergoing wavefront guided LASIK? The authors would like to propose the following hypothesis.

Consider the wavefront shape for positive spherical aberration (Fig. 1). Note that near the visual axis the wavefront has a hyperopic contour, indicating a hyperopic contribution to the overall wavefront. Consider the following extreme example to illustrate the hypothesis. Figure 2 shows the overall wavefront map of a particular eye with a plano sphere manifest refraction. This example might represent a patient after LASIK who had undergone a relatively high conventional myopic treatment, was left with a large amount of positive spherical aberration, and is seeking enhancement to correct quality of vision issues, despite a plano refraction. If we break up this wavefront into its defocus and spherical aberration components, we see that the defocus waveform contributes -2.0 D to the refractive error, whereas the spherical aberration waveform contributes +2.0 D to the refractive error. If the surgeon programs the laser with no defocus offset in this example, the laser is effective at correcting the myopic defocus portion of the wavefront because the laser beam is perpendicular to the central cornea, resulting in maximal laser fluence, and fully corrects the -2.0 D (Fig. 3). Because of the cosine effect,[13] the relatively peripheral laser pulses that are aimed to correct spherical aberration hit the peripheral cornea at an oblique angle, increasing the surface area over which the energy is delivered, decreasing the laser fluence (Fig. 4). As a result, the laser is less effective at correcting

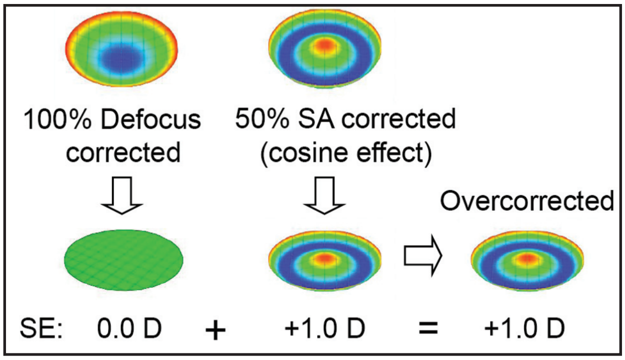

Figure 3. Hypothetical wavefront-guided treatment of the patient in Figure 2. The laser fully corrects the defocus component, eliminating its myopic contribution entirely. Due to the cosine effect, the laser only partially corrects the spherical aberration component, resulting in a net overcorrection and a hyperopic result. SA = spherical aberration; SE = spherical equivalent; D = diopters.

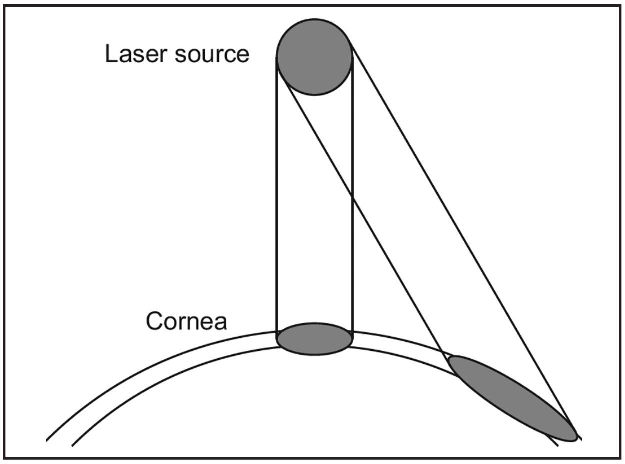

Figure 4. The "cosine effect." A circular laser beam directed at the central cornea has an angle of incidence of 90°, resulting in maximum laser fluence. The same laser beam directed at the peripheral cornea has an oblique angle of incidence, which projects the laser beam into an elliptical shape. This ellipse has much greater surface area than the circle that is achieved on the central cornea, and results in decreased laser fluence and less effective ablation.

the spherical aberration wavefront and only manages to correct 50% of the SA (ie, +1.0 D). This results in a final correction of -1.0 D instead of plano, leaving the patient with a hyperopic result (+1.0 D). Hersh et al. demonstrated, both theoretically and clinically, that myopic ablation patterns that do not take this cosine effect into account can alter corneal asphericity.[13] The theoretical model that took into account that beam fluence changes radially across the ablation zone (ie, cosine effect) accurately predicted the corneal shape change toward increasing positive SA (increasing oblate shape of the cornea postoperatively). The Hersh et al. study used the same laser, LADARVision 4000, that was used in the current study.

Newer laser platforms (eg, Alcon Wavelight Allegretto; Alcon Laboratories) take the cosine effect into account by applying additional pulses in the mid periphery to maintain a more prolate shape following excimer ablation, thus inducing less spherical aberration. This technique should be used for all wavefront-guided or topography-guided procedures when treating spherical aberration, hyperopic corrections, or any aberration that requires peripheral ablation.

Through the use of wavefront analysis, we can now appreciate the close interactions between lower-order and higher order aberrations in LASIK. Conventional treatment of lower-order aberrations has historically been associated with the induction of higher order aberrations.[14-17] It is now apparent that the treatment of higher order aberrations, specifically high levels of spherical aberration, can have a relatively significant effect on lower-order spherical equivalent outcome. Although these effects are dependent on laser platform, this study, along with the publications describing the Rochester nomogram,[7,8] suggest that at least two laser platforms (LADARVision and Technolas) benefit from the consideration of higher order aberrations when developing a nomogram. It has also been noted by Schwartz et al.[18] and Durrie et al.[19] using the LADARVision platform that a high amount of spherical aberration led to significant overcorrection of myopia in patients.

Incorporating higher order aberrations such as spherical aberration into a nomogram for myopic LASIK may allow for greater accuracy in achieving the desired target MRSE and may reduce the likelihood of hyperopic overcorrection and the need for subsequent enhancement procedures. Although the results and nomograms reported in this study are meant to illustrate this valuable clinical finding, it is important to recognize that the nomograms are not generalizable because they are based on a single surgeon's experience on a specific laser platform. Further research on a broad variety of laser platforms is necessary to derive and validate specific nomograms for use with other excimer lasers, femtosecond lasers, and microkeratome systems. As with any new laser system, the individual surgeon should start with the manufacturer's suggested nomogram and monitor his or her own results, leading to the development of a personalized nomogram unique to his or her own situation. This study suggests that, along with traditional parameters that are collected for nomograms, including amount of correction and spherical aberration may be useful to collect preoperatively for incorporation into nomogram development.

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