



Published in final edited form as:

*J Cataract Refract Surg*. 2010 June ; 36(6): 947–953. doi:10.1016/j.jcrs.2009.12.032.

## Differences in the early biomechanical effects of hyperopic and myopic laser in situ keratomileusis

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### Abstract

**PURPOSE**—To compare changes in corneal hysteresis (CH) and the corneal resistance factor (CRF) in myopic and hyperopic laser in situ keratomileusis (LASIK) and evaluate their relationship with the number of photoablative pulses delivered, a surrogate for ablation volume.

**SETTING**—Cleveland Clinic Cole Eye Institute, Cleveland, Ohio, USA.

**METHODS**—Preoperative and 1-week postoperative Ocular Response Analyzer measurements in eyes that had femtosecond-assisted LASIK were studied retrospectively. Changes in CH and CRF were compared and tested for correlation with the number of excimer laser pulses.

**RESULTS**—Thirteen myopic eyes and 11 hyperopic eyes were evaluated. Preoperative corneal thickness, CH, CRF, programmed correction magnitude, flap thickness, and total number of fixed spot-size photoablative pulses were similar in the 2 groups ( $P > .1$ ). Decreases in CH and CRF were greater after myopic LASIK than after hyperopic LASIK ( $P < .005$ ), and changes in CRF were correlated with the number of excimer laser pulses in the myopic group only ( $r = -0.63$ ,  $P = .02$ ). Regardless of ablation profile, changes in CH were more strongly correlated with preoperative CH values than with attempted ablation volume.

**CONCLUSIONS**—With comparable flap thickness and attempted ablation volumes, myopic photoablation profiles were associated with greater decreases in CRF and CH than hyperopic profiles. Results indicate that preoperative corneal biomechanical status, ablation volume, and the spatial distribution of ablation are important factors that affect corneal resistance and viscous dissipative properties differently. Preferential tissue removal in the natively thicker paracentral cornea in hyperopia may partially account for the rarity of ectasia after hyperopic LASIK.

During laser in situ keratomileusis (LASIK), photorefractive keratectomy (PRK), phototherapeutic keratectomy, and other photoablative corneal procedures, immediate

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Dr. Dupps received a travel grant from Reichert, Inc., in 2008.

**Financial Disclosure:** No author has a financial or proprietary interest in any material or method mentioned. Additional disclosures are found in the footnotes.

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circumferential severing of anterior corneal lamellae occurs in the ablation zone. The resulting structural alteration of the cornea has been proposed to decrease resistance to stromal swelling pressure peripheral to the ablation, shift tension to the intact lamellae deep to the interrupted lamellae, and generate centripetal stresses that favor central corneal flattening and a shift toward farsightedness.<sup>1,2</sup> Because intraocular pressure (IOP) also manifests as a force against the posterior corneal surface, deeper ablations concentrated in the cornea's thinnest regions can lead to offsetting corneal steepening effects.<sup>3,4</sup> These unintended biomechanically mediated effects may be an important source of variability in refractive surgery outcomes and in some cases may contribute to refractive instability, ectasia, and loss of visual acuity.

The phenomenon of post-LASIK or post-PRK ectasia is much less commonly reported after hyperopic surgery than after myopic surgery.<sup>5-7</sup> The ablation patterns used to correct myopia and hyperopia are fundamentally different. In myopia, the central cornea is preferentially ablated, while in farsighted patients, a paracentral annulus of tissue is ablated to steepen the central cornea. Hyperopic ablations involve tissue removal predominantly in the thicker tissue of the cornea, where additional interlamellar weaving of collagen imparts mechanical characteristics that approximate those of the densely interwoven limbus and sclera.<sup>8</sup> These observations suggest that both the volume and the pattern of tissue removal are important factors in corneal biomechanical stability and may influence measurements that reflect the viscoelastic status of the cornea and surrounding structures. As a step toward addressing this hypothesis, the current study compared surgically induced changes in 2 variables in biomechanical analysis—corneal hysteresis (CH) and the corneal resistance factor (CRF)—in eyes having myopic or hyperopic LASIK with similar overall amounts of attempted tissue removal and similar flap construction. We propose that intrinsic differences in the spatial distribution of ablation in these groups may result in measurably less effect on corneal biomechanical measures in hyperopic LASIK than in myopic LASIK. We also evaluated the relationship between surgically induced changes in biomechanical waveform variables and the number of excimer laser pulses delivered to the cornea during surgery.

## PATIENTS AND METHODS

Charts of patients who had LASIK by 1 of 2 surgeons (W.J.D., S.E.W.) at Cole Eye Institute between November 2006 and November 2007 were reviewed in this retrospective study after protocol approval by the Institutional Review Board, Cleveland Clinic Foundation (study #07-305). Only patients with preoperative and 1-week postoperative biomechanical waveform measurements were included in the analysis. Hyperopic and myopic patients with the requisite measurements were selected from the same time period on the basis of comparable preoperative central corneal thickness (CCT) values.

All patients had screening evaluations comprising manifest and cycloplegic refractions, topographic analysis (Atlas, Carl Zeiss Meditec), wavefront aberrometry (LADARWave, Alcon, Inc.), dilated fundus examination, IOP (pneumotonometer, Mentor Corp.), CCT measurements by ultrasound (US) pachymetry of (CorneaGage Plus, Sonogage), slitlamp examination, and 3 to 4 replicate biomechanical waveform measurements (Ocular Response Analyzer, Reichert, Inc.) in each eye.

The Ocular Response Analyzer used in the study delivers a several millisecond-duration air impulse and rapidly samples the intensity of infrared light reflected off the central corneal surface during the resulting corneal deformation.<sup>9</sup> Reflected infrared intensity at the detector reaches a maximum when the cornea is predominantly flat. It then falls during the corneal excursion into concavity and rises again to a peak when the cornea recovers to a second predominantly applanated state. The resulting applanation/pressure curves are superimposed in time, and the difference in the plenum pressures recorded at the 2 applanation events is reflected

in the CH variable. Pressure at the first applanation event is higher than that at the second due to complex interactions of elastic and viscous properties that allow for time-dependent dissipation of the air-puff energy. Luce<sup>9</sup> first described a reduction in CH, which explains the dissipative capacity in keratoconus, Fuchs endothelial corneal dystrophy, and myopic LASIK patients. The CRF is derived from the same 2 applanation event measurements but is expressed in linear combination with an empirically determined constant designed to maximize the dependence of CRF on CCT. The CRF is weighted toward the first applanation event and is thought to reflect the overall viscoelastic resistance to the air jet.

The biomechanical waveform measurements were repeated 1 week after surgery and included CH, CRF, corneal-compensated IOP, and Goldmann-correlated IOP (ie, mean of first applanation event and second applanation event).

All patients had LASIK with an excimer laser (LadarVision 4000, Alcon, Inc.) and flap creation with a 60 KHz femtosecond laser (IntraLase FS, IntraLase Corp.). This femtosecond system delivers hyperopic and hyperopic astigmatism corrections in a plus-cylinder format that combines paracentral and peripheral tissue removal with preferential treatment of the flattest axis. The treatment pattern does not incorporate ablation of the most central cornea. Although a wavefront-guided hyperopic treatment could result in delivery of some central pulses in an attempt to correct certain higher-order aberrations, the custom hyperopia software was not used in this study. The reported SD of the central thickness of the flap created with the femtosecond laser is 10  $\mu\text{m}$ .<sup>10,11</sup> The femtosecond laser energy settings and all flap dimensions except depth were identical in the myopic group and hyperopic group. The mean attempted flap thickness was 104.1  $\mu\text{m}$  in both groups; the measured flap thicknesses were obtained by the subtraction method (total corneal thickness – residual stroma after flap lift) using US pachymetry. The optical zone diameter and transition zone were 6.5 mm and 1.25 mm, respectively, in myopic treatments, and 6.0 mm and 1.5 mm, respectively, in hyperopic treatments. The total number of excimer laser pulses was recorded from the computer-generated surgical report for each treatment and was used as a surrogate for the approximate corneal volume removed because the excimer laser in the study uses a fixed spot size regardless of treatment algorithm. Eyes were treated with a wavefront-guided or conventional spherocylindrical algorithm.

Inpatient correlation of CH and CRF between right eyes and left eyes was tested using Statistical Package for the Social Sciences software (SPSS, Inc.) at a significance level of 0.05 to determine whether both eyes could be included in the study and treated as independent for the purposes of analysis. Based on significant intraclass correlation, only the right eye of each patient was included in the analysis. After data were assessed for normality using histograms and residual plots, paired Student *t* tests were applied to assess changes in biomechanical waveform variables in the myopic group and hyperopic group. Regression analysis was performed to assess the relationship between the total number of excimer laser photoablative pulses and biomechanical waveform variables within groups, and analyses of Cook's distance were performed to identify outliers or influential points. Software used for analysis included SigmaStat (version 3.5, Systat Software, Inc.), Excel (version 7, Microsoft Corp.), and Minitab (version 14.20, Minitab, Inc.). The significance level was set at 0.05.

## RESULTS

The hyperopic group comprised 11 eyes of 11 patients (4 women, 7 men) and the myopic group, 13 eyes of 13 patients (7 women, 6 men). The chart review found no cases of previous surgical procedures, ocular comorbidities (glaucoma, retinal detachment, corneal scars), or preoperative clinical suspicion for keratoconus on the basis of CCT or topography. Table 1

compares the preoperative data between the myopic group and hyperopic group. The only significant difference between the groups was in age ( $P < .001$ ).

All but 1 eye in the myopic group was treated with a wavefront-guided algorithm; all eyes in the hyperopic group had LASIK with a conventional spherocylindrical algorithm. Table 2 compares the intraoperative variables. The attempted astigmatic correction ranged from 0.00 to  $-1.36$  diopters (D) in the myopic group and from 0.00 to  $-4.41$  D in the hyperopic group. The flap thickness by intraoperative subtraction pachymetry was  $107 \mu\text{m} \pm 13$  (SD) in all eyes, which compared favorably with the mean programmed femtosecond flap thickness. There was no statistically significant difference between the 2 groups in any intraoperative variable.

Table 3 compares the preoperative and postoperative CH and CRF in the myopic group and hyperopic group. There were no statistically significant differences between groups in preoperative CH or CRF ( $P = .6$  and  $P = .2$ , respectively; 2-sample Student  $t$  test). The CH and CRF decreased significantly after myopic LASIK, with a mean reduction in CH of 21% and a mean reduction in CRF of 29%. The CRF was not significantly different after hyperopic LASIK; a statistically significant decrease in CH after hyperopic LASIK was minimal in magnitude (6%). Decreases in CH and CRF with myopic LASIK were significantly greater than the decreases associated with hyperopic LASIK ( $P < .001$  and  $P = .005$ , respectively).

Figures 1 and 2 show the results of regression analyses of the changes in CH and CRF, respectively, as a function of the number of excimer laser pulses delivered. Analyses of Cook's distance showed no outliers or influential data points. The CRF decreased as a function of the number of ablative pulses in myopic LASIK ( $r = -0.63$ ,  $P = .02$ ), while the relationship between CH change and myopic ablation pulses was not significant ( $r = -0.52$ ,  $P = .07$ ). Neither CH ( $r = 0.51$ ,  $P = .1$ ) nor CRF ( $r = -0.04$ ,  $P = .9$ ) changed in proportion to the number of ablative pulses delivered during hyperopic LASIK. In myopic LASIK, the change in CH was related to preoperative CH ( $r^2 = 0.47$ ,  $P = .01$ , Figure 3), whereas the change in CRF was not significantly correlated with preoperative CRF ( $r^2 = 0.07$ ,  $P = .4$ ). In hyperopic LASIK, most of the variance in the changes in CRF and CH was explained by the preoperative CRF ( $r^2 = 0.53$ ,  $P = .01$ ) and preoperative CH ( $r^2 = 0.67$ ,  $P = .002$ ), respectively.

Models produced by 2-predictor linear regression analyses to further evaluate the relative predictive value of the number of ablation pulses and the preoperative biomechanical wavefront variables on surgically induced biomechanical changes showed results that were qualitatively similar to those above. In myopic LASIK, the preoperative CH value was a significant predictor of the change in CH ( $P = .02$ ) and the number of ablation pulses was not a significant predictor ( $P = .1$ ) in a model that accounted for 60% of the variance in CH change. Conversely, a model of the change in CRF ( $r^2 = 50\%$ ) was significant in the ablation pulses term ( $P = .02$ ) but not in the preoperative CRF term ( $P = .2$ ). In hyperopic LASIK, changes in CH and CRF were related to their respective preoperative values ( $P = .005$  and  $P = .02$ , respectively) but not to the number of ablation pulses ( $P = .2$  and  $P = .8$ , respectively). The 2-predictor hyperopic regression models accounted for a high percentage of variance in CH change ( $r^2 = 74\%$ ) and CRF change ( $r^2 = 53\%$ ). Analysis of Cook's distance showed no outliers. In every analysis with a statistically significant correlation, higher preoperative CH and CRF values favored larger decreases in the same variable after LASIK. Patient age, the only preoperative characteristic that was significantly different between the myopic group and hyperopic LASIK group, was not a significant predictor of LASIK-associated change in CH or CRF in either group ( $r^2 < 0.04$ ,  $P > .5$ ).

The decrease in Goldmann-correlated IOP from preoperatively to 1 week postoperatively (mean  $14.5 \pm 3.8$  mm Hg versus  $10.6 \pm 4.2$  mm Hg) was statistically significant in the myopic group ( $P = .001$ , paired Student  $t$  test) but not in the hyperopic group (mean  $17.3 \pm 4.4$  mm Hg

versus  $17.2 \pm 4.1$  mm Hg) ( $P = .9$ ). The corneal-compensated IOP was not significantly affected by myopic LASIK (mean  $14.0 \pm 3.4$  mm Hg versus  $13.3 \pm 3.1$  mm Hg) ( $P = .5$ ) or by hyperopic LASIK (mean  $16.0 \pm 3.3$  mm Hg versus  $16.7 \pm 2.1$  mm Hg) ( $P = .4$ ).

## DISCUSSION

In this study, the biomechanical analysis was used to assess the relative effects of patient-specific and surgery-specific variables on the biomechanical changes 1 week after LASIK. Corneal hysteresis and CRF values have been shown to be significantly lower after myopic LASIK and in eyes with keratoconus.<sup>9,12-14</sup> In this study, we compared the effect of 2 fundamentally different ablation profiles—myopic and hyperopic—in otherwise similar LASIK procedures and found that myopic LASIK caused much greater reductions in CH and CRF than hyperopic LASIK. In myopic LASIK, the decrease in CRF was related to the number of ablative pulses (a surgical variable) and was unrelated to preoperative CRF (1 of 2 patient-specific biomechanical variables studied). Conversely, the decrease in CH in myopic LASIK was more affected by preoperative CH than by the attempted ablation volume. In hyperopic LASIK, changes in CH and CRF were more strongly related to their respective preoperative values than to the attempted volume of tissue removal.

The major predictors of changes in CH and CRF were notably different. Reductions in CRF were predicted primarily by attempted ablation volume, while the change in CH was more dependent on preoperative CH values. Recalling the weighting of CRF toward the first appplanation event, CRF is determined largely by the initial resistance to deformation by the air jet. The greater the resistance, the slower the initial corneal deformation and the higher the air pressure achieved before the air jet is turned off, an event that is triggered on detection of the first appplanation. Only in a centrally biased myopic photoablation did corneal resistance decrease in proportion to the attempted ablation volume.

In a paracentrally biased hyperopic procedure, the decrease in overall viscoelastic resistance (CRF) was unrelated to the volume of ablation. Instead, the decrease was related to the preoperative CRF value; the higher the preoperative CRF value, the larger the decrease in viscoelastic resistance in hyperopic LASIK. Changes in the viscoelastic dissipative capacity (CH) of the cornea—whether after myopic or hyperopic ablation—were primarily related to preoperative CH values and decreased more when the preoperative CH value was high. An overarching conclusion is that the early postoperative biomechanical effects of LASIK depend not only on surgical factors, such as volume and pattern of ablation, but also on preoperative patient-specific measures of viscoelastic resistance and stress dissipation capacity. Also, ablation volume appears to be a less critical factor than preoperative biomechanical status when assessing the effect of LASIK on viscoelastic dissipative properties such as CH.

An important finding in the study is the similarity of the myopic and hyperopic LASIK groups with respect to femtosecond flap thickness, magnitude of refractive error, attempted volume of photoablative tissue removal, preoperative CH, preoperative CRF, and simulated keratometry values from Placido-based corneal topography. An excimer laser system with a fixed spot size was used in this study. Thus, the number of ablation pulses could be used to estimate the attempted volumetric tissue removal. The similarity of this variable in the myopic group and hyperopic group helped mitigate the effects of inequalities in (1) the magnitudes of attempted corrections and (2) the use of wavefront-guided and conventional treatment algorithms. The use of the femtosecond laser to create thin flaps with similar dimensions in both groups minimized the biomechanical impact and variability<sup>10,11</sup> associated with this step. In addition, using a femtosecond laser rather than a mechanical microkeratome has advantages in biomechanical studies. One-week postoperative data were analyzed to capture the early differential effects of myopic and hyperopic photoablation without significant confounding by

acute postoperative edema or later collagen remodeling effects. A significant difference in the mean age between the myopic group and the hyperopic group is a potential confounding variable because age may be a proxy for corneal stiffness. The preoperative CH and CRF values were similar in the 2 groups; however, in an Asian population,<sup>15</sup> CH and CRF were found to have very weak correlations with age ( $r = -0.17$  and  $r = -0.18$ , respectively) across a much wider range of ages (19 to 89 years) than we encountered in this study.

Other factors may influence the observed differences in the effect of myopic and hyperopic photoablation on CH and CRF. We used the number of ablation pulses as a surrogate for ablation volume to address the hypothesis that similar volumes of tissue removal can produce disparate biomechanical changes due to the spatial location of the pulses. Although the number of pulses did not differ significantly between groups, the ablative efficiency of paracentral and peripheral pulses may be lower than in central ablation due to the more oblique angle of incidence of the excimer beam and beam defocus.<sup>16</sup> These effects could lead to lower effective volumes of tissue removal in hyperopia than the number of delivered pulses implies; however, it is unlikely that they explain the marked differences observed in this study. The maximum depth of stromal ablation has been proposed as a key variable in determining the biomechanical response to refractive surgery due to its theoretical relationship to the number of disrupted lamellae.<sup>17</sup> The theoretical relationship between maximum ablation depth and ablation volume in spherical myopia and hyperopia is complex and has been described by Gatinel et al.<sup>18</sup> In the current study, there were no significant differences in the maximum ablation depths in the myopic and hyperopic groups. This further implicates the structural importance of the spatial distribution of pulses (central versus paracentral) in myopic and hyperopic surgery.

The mechanism of measurement by the Ocular Response Analyzer may also have had an impact on the differences in CH and CRF between myopic and hyperopic patients. The infrared beam used to monitor the inward and outward applanation events is reflected off the central 3.0 mm of the cornea and may provide more effective sampling of central corneal change than paracentral and peripheral changes. This sampling bias might favor greater reductions in CH and CRF in centrally biased myopic procedures. Although Kamiya et al.<sup>19</sup> found no correlation between corneal curvature and CH in a nonsurgical population, this does not rule out the possibility that curvature changes in a LASIK population also contribute to some of the changes in CH and CRF.

The differential response to myopic and hyperopic surgery may provide insight into the decrease in applanation pressures after myopic PRK and LASIK. This change was initially attributed to decreases in CCT.<sup>20</sup> Munger et al.<sup>21</sup> observed a decrease in central applanation pressure without a decrease in CCT after hyperopic LASIK, which suggests that paracentral corneal ablation reduces corneal bending resistance and affects IOP measurement independently of CCT. However, the magnitude of the reduction in applanation pressure is generally lower after hyperopic LASIK than after myopic LASIK.<sup>22</sup> In the current study, Goldmann-correlated IOP decreased significantly only in the myopic group and corneal-compensated IOP did not change significantly in either group. This may be due to both explanations we propose in this report as follows: (1) some degree of central sampling bias with applanation tonometry and with the Ocular Response Analyzer, and (2) a broader distribution of tissue removal in the thicker paracentral and peripheral regions of the cornea that results in a measurably lower biomechanical impact on the cornea as a whole. A contoured tonometer effectively bypasses the issue of bending resistance and provides another effective approach for measuring IOP after LASIK.<sup>23</sup>

A recent study comparing changes in CH and CRF after laser-assisted subepithelial keratectomy for myopia, LASIK for myopia, and LASIK for hyperopia<sup>24</sup> found similar changes in CH and CRF 3 months myopic LASIK and hyperopic LASIK. In that study, the

authors saw no relationship between CCT change and the change in CH or CRF. The lack of such a relationship may be attributable to the fact that CCT change is not representative of the total area or volume treated, especially in cases of wavefront-guided treatment and hyperopic ablation. The study also differs in that a mechanical microkeratome was used and flap depth, attempted refractive correction, and the number of ablation pulses were not reported or compared for equivalence in the myopic and hyperopic groups.

The relative importance of patient and surgical factors in the risk for ectasia continues to be a subject of debate. Our study shows that both play a role in measurable biomechanical alterations after LASIK. Even in routine cases with no ectasia, the biomechanical response affects optical outcomes and may contribute to differences in induced aberrations between myopic eyes and hyperopic eyes.<sup>25,26</sup> By characterizing biomechanical changes in 2 markedly different patterns of photoablation with comparable attempted ablation volumes, we provide evidence of the importance of the spatial distribution of ablation. More detailed analyses of the signal waveform<sup>27</sup> of the Ocular Response Analyzer may provide additional insight into corneal behavior after LASIK, and efforts are underway to assess the sensitivity of certain waveform derivative variables to ablation volume and pattern.

## Acknowledgments

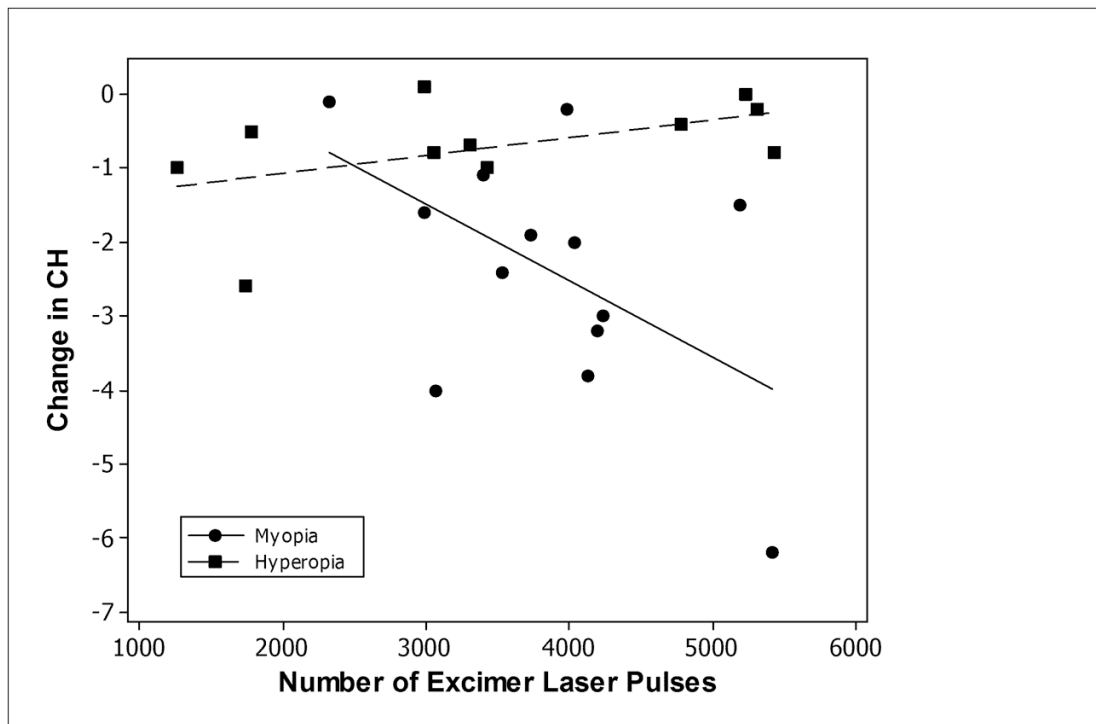
Supported in part by National Institutes of Health 8K12 RR023264/1KL2RR024990, EY10056, EY15638, Bethesda, Maryland, and a Research to Prevent Blindness Challenge Grant to the Department of Ophthalmology, Cleveland Clinic Lerner College of Medicine of Case Western Reserve University, Ohio.

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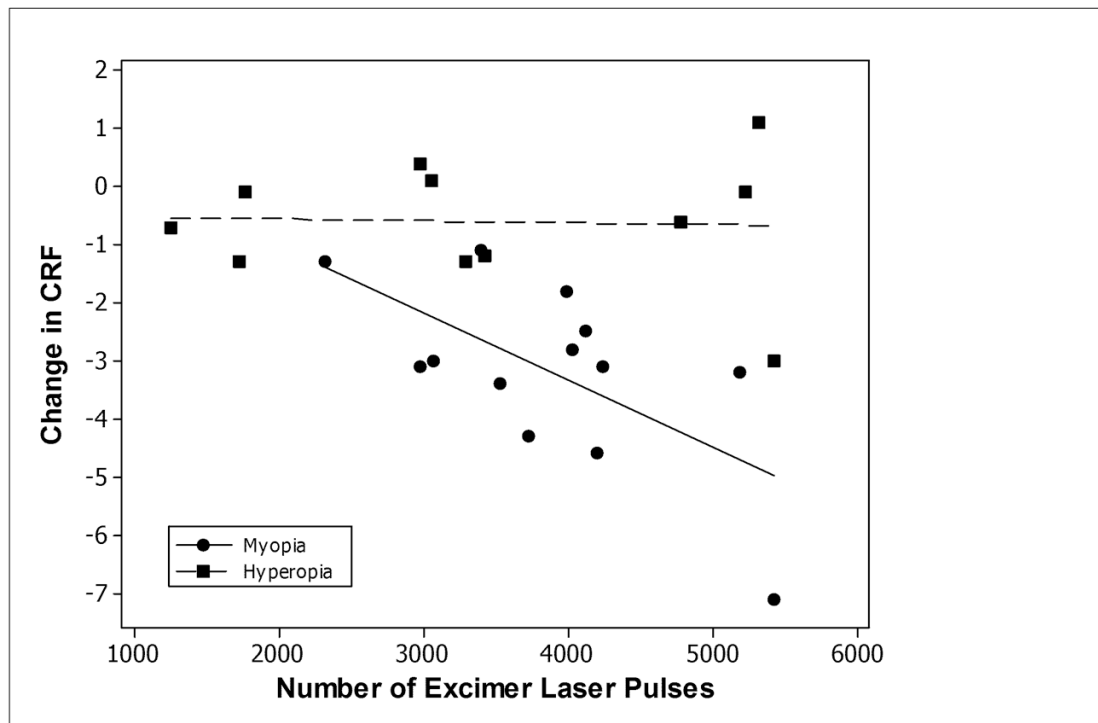
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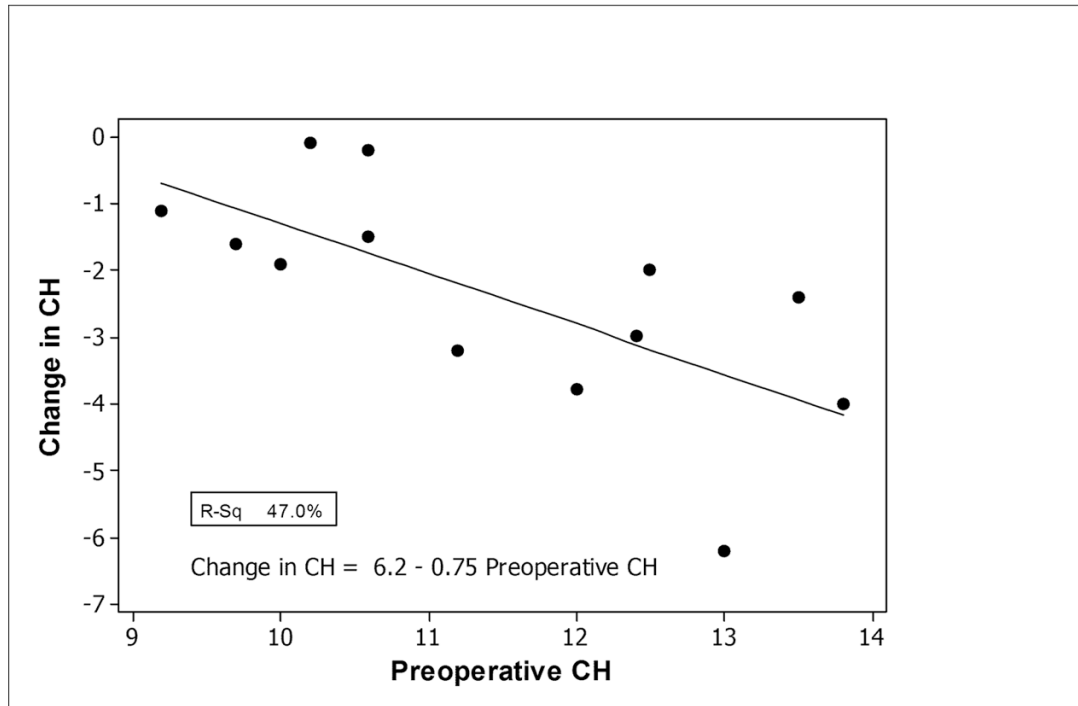




**Figure 1.** Linear regression of CH change as a function of the number of excimer laser pulses delivered during myopic LASIK ( $r^2 = 0.27$ ,  $P = .07$ ) and hyperopic LASIK ( $r^2 = 0.26$ ,  $P = .1$ ) (CH = corneal hysteresis).



**Figure 2.** Linear regression of CRF change as a function of the number of excimer laser pulses delivered during myopic LASIK ( $r^2 = 0.40$ ,  $P = .02$ ) and hyperopic LASIK ( $r^2 = 0.002$ ,  $P = .9$ ) (CRF = corneal resistance factor).



**Figure 3.** Linear regression of CH change in myopic LASIK as a function of the preoperative CH value ( $r^2 = 0.47$ ,  $P = .9$ ) (CH = corneal hysteresis).

**Table 1**

Preoperative comparison of myopic and hyperopic LASIK groups.

Parameter	Mean $\pm$ SD		P Value
	Myopic (n = 13)	Hyperopic (n = 11)	
MRSE, absolute value (D)	3.4 $\pm$ 1.5	2.3 $\pm$ 1.3	.09
Cycloplegic refraction SE, absolute value (D)	3.0 $\pm$ 1.4	2.6 $\pm$ 1.5	.7
Refractive astigmatism (D)	0.4 $\pm$ 0.5	0.8 $\pm$ 1.2	.35
Age (y)	32 $\pm$ 10	52 $\pm$ 10	<.001
CCT ( $\mu$ m)	554 $\pm$ 32	564 $\pm$ 39	.48
Topographic simulated K (D)	44.4 $\pm$ 1.1	43.5 $\pm$ 1.1	.05

CCT = central corneal thickness, K = keratometry, MRSE = manifest refractive spherical equivalent; SE = spherical equivalent

**Table 2**

Comparison of intraoperative variables.

Parameter	Mean $\pm$ SD		P Value
	Myopic Group	Hyperopic Group	
Central flap thickness ( $\mu\text{m}$ )	107.0 $\pm$ 12.8	106.9 $\pm$ 12.8	.97
Attempted SE correction, absolute value (D)	2.6 $\pm$ 1.0	2.6 $\pm$ 1.3	.97
Delivered pulses (n)	3797 $\pm$ 932	3409 $\pm$ 1447	.4
Maximum ablation depth ( $\mu\text{m}$ )	58 $\pm$ 17	50 $\pm$ 25	.4

SE = spherical equivalent

\* Student *t* test with independent samples

**Table 3**

Preoperative and postoperative CH and CRF by group.

Value	Myopic Group			Hyperopic Group			P Value*
	Preop	Postop	Change	Preop	Postop	Change	
CH	11.4 ± 1.5	9.1 ± 1.3	-2.4 ± 1.7	11.8 ± 1.6	11.1 ± 1.1	-0.7 ± 0.7	.008
CRF	11.0 ± 1.9	7.8 ± 2.1	-3.2 ± 1.6	12.2 ± 2.3	11.5 ± 1.7	-0.6 ± 1.1	.09

CH = corneal hysteresis; CRF = corneal resistance factor; LASIK = laser in situ keratomileusis

\* Paired Student *t* test