Relationship between Induced Spherical Aberration and Depth of Focus after Hyperopic LASIK in Presbyopic Patients

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Objective: To evaluate to what extent the modification of corneal asphericity to induce spherical aberration (SA) can improve the depth of focus and to determine whether preoperative adaptive optics assessment (Voptica SL) can predict an optimal SA value for each patient.

Design: Comparative, prospective clinical trial with paired eye control.

Participants: Patients ≥45 years old who are hyperopic from +1.00 to +2.50 diopters (D), with eyes suitable for LASIK surgery.

Intervention: Bilateral hyperopic LASIK surgery using a 200-Hz Allegretto excimer laser. The dominant eye was operated using a conventional profile. The nondominant eye was programmed with an aspheric ablation profile and −0.75 D monovision.

Main Outcome Measures: Primary outcome was the correlation between postoperative SA and depth of focus, defined as the pseudo-accommodation value (PAV = [1/reading distance {m}] − minimum addition [D]). Main secondary outcome was the comparison of depth of focus between patients with an induced SA close to the optimal one (group 1), patients with an induced SA far from the optimal one (group 2), and patients for whom SA induction did not increase the depth of focus (control group).

Results: We included 76 patients. Between preoperative and postoperative assessment, the mean increase of distance-corrected PAV for near vision was +0.25±0.64 D ($P < 0.001$) for dominant eyes and +0.63±0.55 D ($P < 0.001$) for nondominant eyes. As the level of negative or positive postoperative SA increased, PAV for intermediate and near vision increased. Among the 37 eyes that followed the preoperative adaptive optics assessment, the mean PAV increase at near was significantly higher ($P < 0.05$) in group 1 (0.93±0.50 D) than in group 2 (0.46±0.42 D) and than in the control group (0.35±0.32 D). The mean optimal SA value determined by the dynamic simulation procedure to optimize the depth of focus was −0.18±0.13 μm at 4.5 mm.

Conclusions: Aspheric hyperopic LASIK can increase the depth of focus without impairing far vision, but this benefit would be maximal and reproducible if we could define and achieve an optimal SA value determined by preoperative assessment using an adaptive optics instrument. *Ophthalmology 2014;■:1−11 © 2014 by the American Academy of Ophthalmology.*

Refractive correction for presbyopia with the Excimer laser system has recently been among the most discussed topics in refractive surgery. Several principles have been defined. Monovision LASIK is an extended technique published for the first time in 1999.[1] This procedure has been found to produce high levels of patient satisfaction in many studies.[2] However, the success of this technique has been limited by the ability of individuals to adapt to monovision itself and works best for people who are only mildly presbyopic. Nonetheless, to date, that kind of procedure does not prevent visual acuity (VA) at reading distance from diminishing with advancing age.

McDonnell et al[3] described improved VA from a multifocal effect after radial keratotomy. This opened new concepts for correction of presbyopia based on the induction of pseudoaccommodative cornea. Moreira et al[4] were the first

to report the use of laser refractive surgery to reduce symptoms of presbyopia. Attempts based on inferior off-center ablation[5,6] have been abandoned owing to the decrease of the best spectacle-corrected VA. Ablation profiles in the form of a peripheral near zone[7−10] (concentric ring for near vision) or in the form of a central near zone[11−13] (central disk for near vision) are other used options. Even if presbyopia LASIK surgery is common, the coexistence of so many different and opposing techniques for approaching the same presbyopic problem shows that a satisfying corneal laser correction is yet to be found.

Many recent LASIK techniques for correcting hyperopia and presbyopia are based on corneal asphericity and the related induction of spherical aberration (SA) to increase the depth of focus.[14] Reinstein et al[15] combined extended depth of focus with monovision in a micro-monovision protocol,

whereas Epstein and Gurgos[16] combined monocular peripheral presbyLASIK on the nondominant eye with monofocal distance correction on the dominant eye. Jackson et al[17] performed bilateral aspheric treatment and observed that negative SA was highly correlated with postoperative improvement of distance-corrected near VA. Despite their generally satisfactory results, these techniques present an unsatisfactory predictability concerning the induced depth of focus and consequent patient satisfaction.

In this context, we studied the relationship between corneal asphericity, SA, and depth of focus before and after the operative procedure to determine an optimal SA value. The primary objective of our study was to evaluate to what extent the modification of corneal asphericity and SA value could increase the depth of focus. The secondary objective was to determine whether preoperative assessment by using an adaptive optics instrument was able to predict the most useful SA value for each patient.

Methods

Study Design and Patients

This comparative, prospective study was conducted in the Department of Ophthalmology, Purpan Hospital, Toulouse, France. We included 76 consecutive hyperopic patients from December 1, 2012, to September 1, 2013. Study inclusion criteria were as follows: ≥ 45 years old, spherical hyperopia between +1.00 and +2.50 diopters (D) with an astigmatism lower than 1.25 D, a best-corrected VA of 10/10 Parinaud 2 (40 cm) or better for each eye, cornea suitable for LASIK with central corneal pachymetry of ≥ 520 μm, and a normal corneal topographic pattern.

We excluded patients with clinically significant ocular disease such as cataract or glaucoma, corneal diseases such as keratoconus or previous herpes keratitis, and previous corneal or intraocular surgery. The study was approved by the Ethical Committee of Purpan Hospital (HyperVOPTICA study no. 2012-AO1278-35) and conducted in accordance with the Declaration of Helsinki.

Patient Examinations

The evaluators (C.T. and B.L.) did not participate in the surgical process and the surgeon (F.M.) was not involved in postoperative data collection and analyses. The investigators (B.L. and M.C.) were asked to complete standardized data forms on all patients.

Patients were examined preoperatively and postoperatively at day 1, week 1, and month 3. All of the following analyses were performed preoperatively and 3 months after surgery for all patients: ocular dominance determination, manifest refraction, cycloplegic refraction, slit-lamp microscopy of the anterior segment, dilated fundoscopy, applanation tonometry, corneal topography with determination of Q factor at 6 mm and keratometry (Pentacam, Oculus Inc, Arlington, WA), pupillometry (Tonoref 2, Nidek), aberrometry at 4.5 and 6 mm (AOVIS-1, Voptica SL, Murcia, Spain), handheld ultrasound pachymetry (Corneo-Gage Plus; Sonogage, Cleveland, OH), and contrast sensitivity (CVS-1000; Vector Vision, Greenville, OH).

The visual assessment was performed using an adaptive optics–based instrument[18] preoperatively for the last 37 patients because of the unavailability of the instrument at the beginning of the study.

At the 1-day and 1-week time points after surgery, we performed a biomicroscopic examination, including a complete record of potential complications, such as interface fibrosis, epithelial ingrowth, folds, and opacities. Moreover, at each visit patients completed a subjective satisfaction questionnaire, reporting adverse events such as glare and halos and their vision quality in daily life on a scale of 3 to 0 (3, no change; 2, slight impact; 1, moderate impact; 0, intense impact).

Ocular Dominance Testing

Ocular dominance was assessed using 3 methods: the "hole test" and determining which eye was used for aiming through a camera and a rifle. The hole test involved the patient binocularly aligning a distant object through a hole in a sheet of white A4 paper, held at arm's length in landscape format, with each hand holding either end. The eyes were alternately covered while looking through the hole. The eye with which the object seemed to be centered through the hole was considered the dominant eye. Dominance was confirmed if the result was the same for all tests. If the 3 tests were inconclusive, the monovision assessment was repeated with each eye in turn as the dominant eye and the dominance was determined according to which setup felt more natural for the patient.

VA and Depth of Focus Examination

Concerning far vision testings, distance VA was assessed using a standardized scotopic Monoyer projection chart at a viewing distance of 5 m converted into minimum angle of resolution notation. A line of acuity was considered read if ≥ 3 of the 5 letters of that line were recognized correctly.

Concerning reading tests, we used standard procedures. The reading chart was the Parinaud scale. The results were also converted into minimum angle of resolution notation. Measurements were recorded for each eye separately and binocularly at a viewing distance of 40 cm (near vision) and 67 cm (intermediate vision). The reading distance between the trial frame and the reading chart was precisely determined using a graduated ruler.

All tests were performed under the same conditions of luminance. The luminance of the chart and the background was measured with a luminance meter (LS100; Minolta, Osaka, Japan). The luminance of the chart and the walls were 64.71 and 0.884 cd/m^2, respectively. Uncorrected and best-corrected VA were determined for distance vision and for near vision.

For the evaluation of the depth of focus, we decided not to use dynamic clinical methods (push up, push down, and minus lens procedure) owing to the great variability in the measurements. We used the minimum addition for reading. The minimum addition was determined by adding positive lenses by step of 0.25 D over the best distance correction until the patient reported he could read Parinaud 2 for near vision and Parinaud 3 for intermediate vision. The pseudo-accommodation value (PAV) was defined as (1/reading distance [m]) − minimum addition (D).

Adaptive Optics Visual Assessment Procedure

The instrument used in the study was the monocular Adaptive Optics Visual Analyzer (Voptica SL). It is a clinical instrument to perform visual testing with full control of the optical aberrations noninvasively induced in the patient's eye. It includes a Hartmann-Shack wave-front sensor to measure refraction and aberrations,[19] a liquid crystal on a silicon spatial light modulator to induce any desired aberration profile on the patient's eye, and a microdisplay to present the visual stimuli to the patient.[20] The instrument allows the operator to perform visual testing after induction of any optical aberration, particularly different amounts of SA.

All measurements were performed after instillation of cyclopentolate (repeated 3 times) 45 minutes before the procedure. The procedure was conducted in 2 phases. During the first phase, the aberrations were measured in both eyes at 4.5- and 6-mm pupil sizes.

Three series of measurements of optical aberrations, particularly SA and vertical and horizontal coma aberrations, were recorded. Concerning the reapeatability of the SA measurements, data obtained on these triplicate consecutive repeated series with the Voptica aberrometer on all patients produced a mean standard deviation of 0.0118 μm for the spherical aberration at 4.5 mm (4.5 C12).

During the second phase, the visual testing was performed with a 4.5-mm pupil size only for the nondominant eye. This pupil size was chosen for dynamic procedure as a compromise between photopic and mesopic vision in common life because testing 2 different pupil sizes would take too long (about 20 minutes per tested pupil size) and induce a too important variability in relation with patient cooperation, considering that in our study the pupil size was 4.35±0.63 mm in the photopic condition and 5.72±0.59 mm in the mesopic condition. It first consisted of distance vision assessment divided in 3 steps: reading with the best objective correction for far vision (determined by 3 measurements during the first phase), reading after adding +0.50 D to manifest refraction (to induce a myopisation), and reading after inducing additional negative SA in 0.1-μm steps from 0 to −0.50 μm of induced SA. The same procedure was repeated for near vision. The induction of SA was combined with a small myopic refractive error to increase the depth of focus. Different myopic shifts could be selected, but to simplify the procedure we set it at 0.50 D for 2 reasons: (1) This value induces a modest deterioration of far vision when combined with the selected SA amounts (with the Swaine rule, 0.50 D of myopia corresponds to a far VA of 5/10). (2) The mean postoperative spherical equivalent of nondominant eyes previously operated with postoperative refraction target of −0.75 D was −0.45±0.51 D, which is close to the selected value of 0.50 D.

The visual simulation for far and near (40 cm) distances was carried out in the nondominant eyes of 37 patients. The ideal SA to induce for a particular patient was the value that increased near vision without significantly degrading far vision. Patients with no improvement of near vision by SA induction were not considered valid to increase the depth of focus using this procedure and were included in the control group. To optimize the visual performance for near vision with an acceptable distance vision, the optimal values of SA were those that gave the highest near VA and fulfilled 2 conditions: (1) far VA higher than 0.50 and (2) near VA higher than 0.60.

These optimal values of SA were not taken into account in the ablation profile set with an identical Q factor target for all nondominant eyes. However, there was an high intersubject variability in postoperative values of SA. So, visual parameters, PAV and uncorrected near vision, were compared between eyes with large and small differences between final and optimal SA.

Surgical Procedure

The same surgeon (F.M.) performed LASIK under low illumination for both eyes in the same session using an Allegretto Excimer laser (200 Hz; Alcon, Fort Worth, TX). The effective ablation spot size was 0.7 mm at a pulse-rate frequency of 250 Hz. Optical treatment zone diameter used was 6 mm for all patients. The suction ring of the microkeratome was centered on the limbus. Flaps were created by using a One Use + large-cut microkeratome (Moria SA, Antony, France). Even if laser centration in hyperopic eyes is still a matter of debate,[21] we decided to center the laser beam on the pupil according to our previous results,[22] using the active Eye Tracker System.

For all subjects we planned monovision: The dominant eye was set for a full correction of refractive error (WaveFront Optimized), and correction of the nondominant eye was intended to reach a 0.75-D myopic refraction. Furthermore, the nondominant eye was operated with an aspherical ablation profile (Custom Q) aimed at a target Q factor of −0.80. Ablation profiles were based on the preoperative subjective and cycloplegic refraction.

Outcome Measures

The primary outcome was postoperative PAV and the correlation between SA and depth of focus. Two methods were used to assess this relationship: comparing preoperative with postoperative PAV for intermediate and near vision for the dominant eyes and for the nondominant eyes (operated with an aspherical ablation profile) and comparing preoperative and postoperative PAV for intermediate and near vision between both eyes of the same patient.

The secondary outcome was the comparison of depth of focus concerning a group of patients with an induced SA value close to the optimal one (according to the preoperative adaptive optics visual assessment), a group of patients with an induced SA value far from the optimal one, and a control group of patients for whom SA induction did not increase the depth of focus.

Other outcomes were safety index (defined as the ratio of the mean postoperative best distance-corrected VA [BDCVA] to the mean preoperative BDCVA), efficacy index for the dominant eyes (defined as the ratio between the mean postoperative uncorrected distance vision and the mean preoperative BDCVA), accuracy index (percentage of eyes within ±0.50 D of the intended refraction), contrast sensitivity, and subjective quality of vision.

Statistical Analysis

We compared before and after LASIK treatment, and between both eyes, criteria such as PAV and SA using paired tests: Z-test and Student *t* test (when there were <30 samples). We compared with the same tests the differences between groups of eyes classified according to their postoperative SA value. For correlation studies, we measured the *r* correlation coefficient. Statistical significance was set at $P < 0.05$.

Results

Population Characteristics

The study population included 76 subjects (35 males and 41 females) aged 56±4.5 years (range, 47−65 years). All patients included completed the study. Principal ocular features are summarized in Table 1. There were no differences in the baseline ophthalmic characteristics between the dominant and the nondominant eyes.

Efficacy

Uncorrected distance vision 3 months after surgery is presented for dominant eyes, nondominant eyes, and binocularly in Figure 1. For dominant eyes, the efficacy index was 0.980. The same postoperative visual outcomes are presented for uncorrected near vision in Figure 2.

Accuracy

Figure 3 shows scatterplots of attempted versus achieved spherical equivalent refraction 3 months after treatment. Concerning the accuracy index, 89.5% of dominant eyes and 64.5% of nondominant eyes were within ±0.50 D of the intended refraction. Nondominant eyes were undercorrected from +0.50 to +1.50 D from attempted refraction (−0.75 D) in 43.4% of cases.

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Table 1. Ocular Characteristics of the 76 Subjects

Characteristics	Dominant Eyes		Nondominant Eyes	
	Mean ± SD	Range	Mean ± SD	Range
Spherical equivalent (D)	+1.80±0.47	+0.63 to +3	+1.81±0.38	+1 to +2.75
Treated refraction (D)	+1.80±0.47	+0.63 to +3	+2.56±0.38	+1.75 to +3.50
Intermediate vision PAV (D)	+0.70±0.44	−0.50 to +1.50	+0.68±0.43	−0.50 to +1.50
Near vision PAV (D)	0.98±0.48	+0 to +2.50	0.96±0.44	+0 to +2.25
Q value	−0.08±0.21	−0.61 to +0.34	−0.09±0.21	−0.81 to 0.32
4.5 C12 (μm)	0.106±0.042	−0.030 to +0.205	0.108±0.057	−0.097 to + 0.226
6 C12 (μm)	0.325±0.145	0.035−0.786	0.314±0.185	−0.084 to 0.938

4.5 C12 = Spherical aberration at 4.5 mm; 6 C12 = spherical aberration at 6 mm; D = diopters; PAV = pseudo-accommodation value.

Safety

Three months after surgery, only 1 nondominant eye (0.66%) lost 2 lines (0.8 postoperatively instead of 1 preoperatively). All other eyes achieved a (1/minimum angle of resolution) BDCVA of ≥1 postoperatively. The safety index was 0.999.

Results concerning contrast sensitivity are presented in Table 2. For nondominant eyes, the only noticeable postoperative differences were a lower contrast sensitivity for 12 and 18 cycles per degree in no-glare situations after surgery ($P = 0.02$ and $P = 0.04$, respectively). These differences were not found under the glare condition. For dominant eyes, we found a significant increase ($P = 0.03$) in contrast sensitivity for 3 cycles per degree under the glare condition but not in no-glare situations. These findings were not consistent with findings for other frequencies. After surgery, the subjective satisfaction score was 2.45±0.54/3.

Asphericity and SA Induction

After surgery, the mean Q value (6 mm) was −0.62±0.25 for the dominant eyes and −0.76±0.30 for the nondominant eyes ($P < 0.001$). The mean postoperative 4.5 C12 was 0.039±0.045 μm for the dominant eyes and −0.054±0.057 μm for the nondominant

eyes ($P < 0.001$). The mean postoperative SA at 6 mm was −0.032±0.214 for the dominant eyes and −0.135±0.247 μm for the nondominant eyes ($P < 0.001$).

As shown in Figure 4, for all eyes the SA value varied with the corneal asphericity value. Indeed, ΔQ (postoperative Q−preoperative Q) was correlated with ΔC12 (postoperative C12−preoperative C12) at 6 mm ($r = 0.275$; $P < 0.05$).

Correlation between SA and Depth of Focus

After full correction for far vision, the mean increase in PAV between preoperative and postoperative assessment (Fig 5) was significantly greater for the nondominant eyes. The difference between nondominant eyes and dominant eyes was +0.38±0.49 D for near vision and +0.29±0.35 D for intermediate vision.

We studied the correlation between the postoperative 4.5 C12 and the ΔPAV (postoperative PAV−preoperative PAV) for intermediate and near vision (Figs 6 and 7). For all eyes, negative and positive postoperative SA were statistically correlated with the change of PAV for intermediate ($r = -0.320$ [$P < 0.01$] for negative SA; $r = 0.270$ [$P < 0.05$] for positive SA) and near vision ($r = -0.348$ [$P < 0.01$] and $r = 0.268$ [$P < 0.05$], respectively).

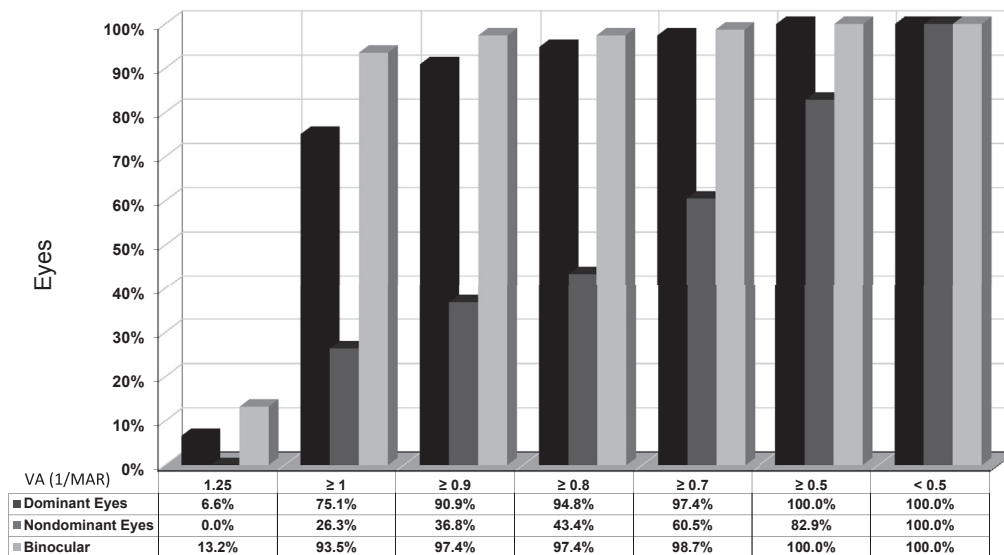| VA (1/MAR)	1.25	≥ 1	≥ 0.9	≥ 0.8	≥ 0.7	≥ 0.5	< 0.5
■ Dominant Eyes	6.6%	75.1%	90.9%	94.8%	97.4%	100.0%	100.0%
■ Nondominant Eyes	0.0%	26.3%	36.8%	43.4%	60.5%	82.9%	100.0%
■ Binocular	13.2%	93.5%	97.4%	97.4%	98.7%	100.0%	100.0%

Figure 1. Cumulative histogram of uncorrected distance visual acuity 3 months after bilateral hyperopic LASIK. The graph presents visual outcomes for dominant eyes (black) set for distance vision, nondominant eyes (dark grey) operated with an aspherical ablation profile and intended to reach a 0.75-diopter myopic refraction, and for binocular vision (light grey). MAR = minimum angle resolution; VA = visual acuity.
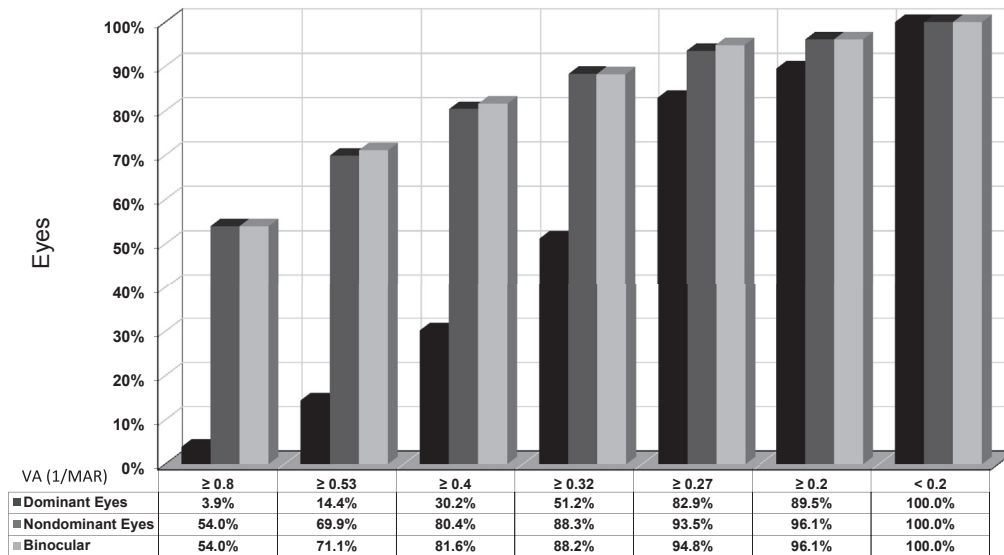
Figure 2. Cumulative histogram of uncorrected near visual acuity 3 months after bilateral hyperopic LASIK. The graph presents visual outcomes for dominant eyes (black) set for distance vision, nondominant eyes (dark grey) operated with an aspherical ablation profile and intended to reach a 0.75-diopter myopic refraction, and for binocular vision (light grey). MAR = minimum angle resolution; VA = visual acuity.

VA (1/MAR)	≥ 0.8	≥ 0.53	≥ 0.4	≥ 0.32	≥ 0.27	≥ 0.2	< 0.2
▪ Dominant Eyes	3.9%	14.4%	30.2%	51.2%	82.9%	89.5%	100.0%
▪ Nondominant Eyes	54.0%	69.9%	80.4%	88.3%	93.5%	96.1%	100.0%
▪ Binocular	54.0%	71.1%	81.6%	88.2%	94.8%	96.1%	100.0%

Optimal SA Value

The visual simulation for far and near (40 cm) distances was carried out in nondominant eyes of 37 patients using the Voptica adaptive optics instrument following the protocol described. In 10 patients, visual simulation showed no increase of depth of focus after SA induction. In 6 patients (16.2%), there was no improvement of near vision by SA induction, and in 4 cases (10.8%) far and/or near VA were too low (<0.50 and <0.60 for distance and near vision, respectively). These patients were used as a control group to compare with the rest of the patients grouped, depending on the difference between the values of postoperative and optimal SA.

Thus, the optimal SA value to induce was found for 27 patients (73.0%). For these patients, the mean VA values for the 6 values of induced SA are shown in Figure 8. As negative SA increased, far VA decreased and near VA increased. The mean optimal additional predicted 4.5 C12 value to induce (i.e., the value to add to the

preoperative 4.5 C12 value) was -0.28 ± 0.12 μm. The mean preoperative 4.5 C12 value was $+0.11\pm0.04$. The optimal postoperative calculated 4.5 C12 for each patient was estimated as the sum of the optimal additional predicted value plus the preoperative value, being the mean value -0.18 ± 0.13 μm.

Optimal postoperative calculated 4.5 C12 values for each tested eye and the postoperative 4.5 C12 values are shown in Figure 9. In some eyes, a range of SA values fulfilled all conditions of optimization, which are displayed in the figure as errors bars.

The influence of the deviations between optimal postoperative calculated 4.5 C12 values and the postoperative amounts of 4.5 C12 values on visual performance are shown in Figures 10 and 11 in comparison with the control group. In addition to correlation analysis, the average values and the standard deviations were calculated in 3 groups: 15 eyes with SA deviation <0.075 microns (group 1), 12 eyes with SA deviation >0.075 microns (group 2),
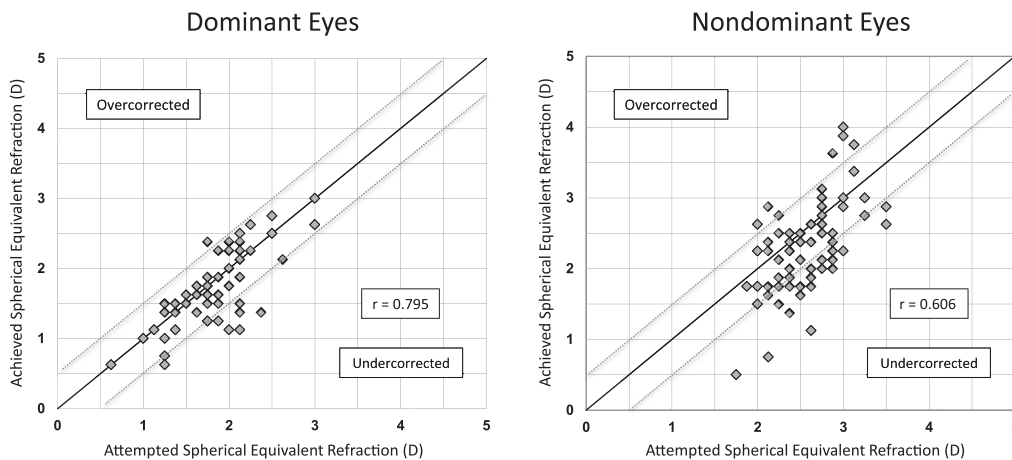

Figure 3. Scatterplots of the attempted versus achieved spherical equivalent refraction 3 months after bilateral hyperopic LASIK for dominant eyes (left) and nondominant eyes (right). The coefficients of determination are displayed. D = diopters.

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Table 2. Contrast Sensitivity Average Data

| cpd	Dominant Eyes			Nondominant Eyes		
	Preoperative	Postoperative	P value	Preoperative	Postoperative	P value
Without glare						
3	4.98±1.90	5.19±1.33	0.26	4.75±1.75	4.87±1.59	0.63
6	4.98±1.64	5.41±1.63	0.15	4.98±2.00	4.57±1.81	0.19
12	4.75±1.98	4.89±1.79	0.65	4.58±1.78	3.83±1.86	0.02*
18	4.25±1.97	4.63±1.64	0.20	4.42±2.08	3.80±1.95	0.04*
With glare						
3	4.84±1.51	5.28±1.45	0.03*	4.82±1.38	4.91±1.38	0.52
6	4.75±1.58	5.06±1.82	0.18	4.60±1.60	4.39±1.83	0.60
12	4.32±1.81	4.52±2.03	0.43	4.35±2.18	3.78±2.15	0.17
18	4.25±1.93	4.22±2.14	0.85	4.30±1.89	3.80±1.99	0.10

cpd = cycles per degree.
*$P < 0.05$.

Figure 4. Scatterplot of the change of spherical aberration (C12) and corneal asphericity (Q) at 6 mm between preoperative and postoperative assessment. Coefficient of determination and *P* values are displayed. Postop = mean postoperative value; preop = mean preoperative value.

and 10 eyes in which SA induction did not increase the depth of focus (control group). In Figure 10, PAV increased relatively ($r = 0.41$) as SA deviations decreased. The mean increment of PAV at near was significantly greater ($P < 0.05$) in group 1 (0.93±0.50 D) with respect to the group of eyes with larger SA deviations (0.46±0.42 D) and with respect to the control group (0.35±0.32 D).

Figure 11 compares uncorrected VA at far and near distances as a function of SA deviations. In group 1, there was less intersubject variability. Indeed, 11 of 15 eyes (73.3%) had far VA > 0.6 and near VA equal to 0.8. In most eyes, far and near values of VA were similar, with differences ≤0.2 in 13 of 15 eyes. However, in 5 of 12 eyes in group 2, there were larger differences between far and near VA (>0.4). The far VA was >0.6 in 9 of 12 eyes (75%) and the near VA was ≥0.8 in only 6 of 12 eyes (50%). Similar results were found in the control group; in 5 of 10 eyes, the differences between far and near VA were ≥0.4, the far VA was >0.6 in 60% of the eyes, and the near VA was ≥0.8 in 50% of the eyes. In group 1, the average values of VA were 0.69±0.22 for far vision and 0.78±0.07 at near distance, whereas in group 2, the average VA was 0.76±0.28 for far vision and 0.62±0.22 at near distance. In both groups, the far VA was not different ($P = 0.28$), but the difference in near VA was significant ($P = 0.014$). The mean values of the control group, 0.76±0.30 and 0.63±0.20 at far and near distances, respectively, were similar to those of group 2 ($P > 0.70$).

Postoperative refraction data were not different ($P > 0.20$) among the 3 groups. The values of spherical equivalent were −0.48±0.48, −0.29±0.54, and −0.55±0.55 D, and cylinders −0.30±0.29, −0.42±0.40, and −0.35±0.29 D, for groups 1 and 2 and the control group, respectively. Therefore, VA differences between groups at near distance cannot be attributed to differences in postoperative refraction data between groups.

Discussion

A current surgical approach for treating hyperopic presbyopic patients is the LASIK procedure. We used in our study an Alcon laser (Wavelight Allegretto 200 Hz) with the WaveFront Optimized software for the dominant eyes and obtained refractive results in the same range (efficacy index, 0.980; accuracy index, 89.5%; safety index, 0.999) as reported in other recent studies.[23–25]
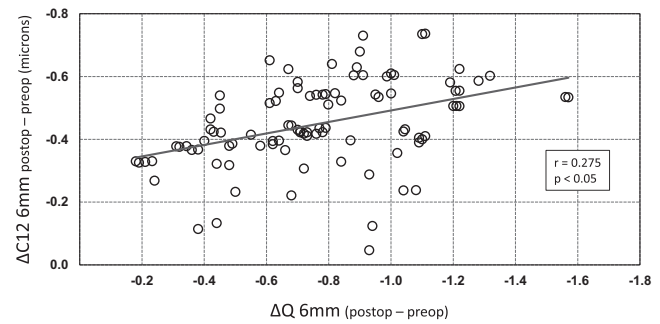
To improve near vision performance for hyperopic presbyopic patients undergoing a LASIK procedure, many combinations can be proposed. Because the presence of high-order aberrations, in particular SA, has also been shown to improve depth of focus,[26–29] we aimed to induce for nondominant eyes some defocus and a negative SA value for each patient. Theoretically, this approach is the most simple and promising because the standard ablation for hyperopic eyes leads to a more prolate cornea and we just have to exaggerate the aspheric shape to induce more negative SA. The advantage of this combination is that the generated asphericity reinforces monovision[30,31] and makes it possible to reduce the degree of myopia, thus making monovision tolerable.

The main objective of our study was to evaluate to what extent corneal shape modification and negative SA induction could increase the depth of focus.

We first confirmed that, in hyperopic LASIK surgery, the ablation induces a more prolate cornea and, consequently, SA tends toward negative values, as our and other groups previously reported.[22,29,32,33] Because we performed an aspherical procedure, we observed a bigger decrease of the Q value, and this change of corneal asphericity was correlated with the change of SA value at 6 mm ($r = 0.275$; $P < 0.05$). In this study, we could not investigate this correlation at 4.5 mm because the Pentacam does not measure the Q value below 6 mm. Thus, the SA value always becomes more negative as we program an aspherical ablation profile; however, we were surprised to find many eyes with a postoperative positive value at or sometimes near zero. These eyes had a high preoperative positive SA value and the laser treatment was unable to induce a negative value; it only reduced the degree of positive SA, which theoretically decreases the depth of focus.

Second, to evaluate the effect of these different groups of induced SA on the depth of focus, we compared the distance-corrected PAV for near and intermediate vision preoperatively and postoperatively and between both eyes. The bilateral study design, comparing hyperopia corrected in both eyes of the same patient, largely reduces the variability induced by interindividual differences (no bias related to age or accommodative reserve) and allows us to compare the postoperative near vision performances
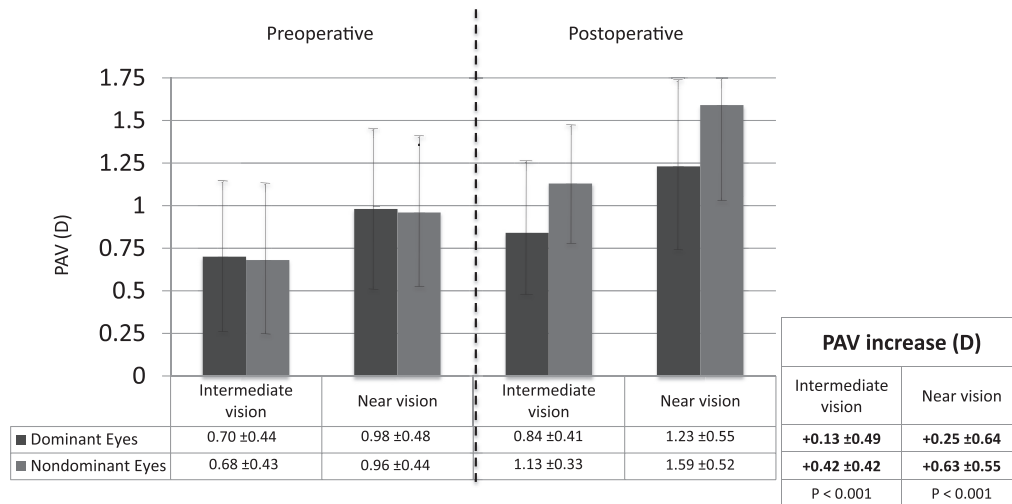
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	Preoperative		Postoperative		PAV increase (D)	
	Intermediate vision	Near vision	Intermediate vision	Near vision	Intermediate vision	Near vision
Dominant Eyes	0.70 ±0.44	0.98 ±0.48	0.84 ±0.41	1.23 ±0.55	**+0.13 ±0.49**	**+0.25 ±0.64**
Nondominant Eyes	0.68 ±0.43	0.96 ±0.44	1.13 ±0.33	1.59 ±0.52	**+0.42 ±0.42**	**+0.63 ±0.55**
					P < 0.001	P < 0.001

Figure 5. Preoperative and postoperative pseudo-accommodation values (PAVs) of dominant eyes (black) and nondominant eyes (grey) for intermediate and near vision after full correction for far vision. Increases in PAV between preoperative and postoperative assessment are reported. The postoperative differences between both eyes are significant (P < 0.001). D = diopters.

obtained after 2 different procedures. We demonstrated a mean improvement of +0.63±0.55 D of PAV in near vision for the nondominant eyes versus +0.25±0.64 D for the dominant eyes (P < 0.001). In addition, the postoperative SA value correlated statistically with the PAV change. As the magnitude of negative or positive SA increased, intermediate and near PAV improved. This point was also reported recently by Jackson et al[17] after hyperopic LASIK for negative SA but on a multivariable analysis with a small population of 33 patients.

Then, a question regularly discussed is which kind of optics aberrations are the more efficient to improve the depth of focus. Zheleznyak et al[31] recently observed that myopia associated with positive SA was better for intermediate vision, whereas myopia associated with negative SA was better for near vision, for a 4-mm pupil. Rocha

et al[34] concluded that depth of focus increased independently of the sign of the added SA with a 6-mm pupil. Yi et al[35] and Benard et al[36] reported similar results and found that depth of focus increased especially with a combination of primary and secondary SA in opposite signs, with a 6 mm pupil size for Yi et al and with 3-, 4.5-, and 6-mm pupil sizes for Benard et al. However, these outcomes were obtained with an adaptive optics vision simulator, which simulated the effect of SA in a few young subjects (3−10 subjects maximum) and, except for the study by Benard et al, the depth of focus was tested with only 1 pupil size (4 or 6 mm), which does not correspond to a real-life diameter. In addition, for the studies by Yi et al and Benard et al, the subject was asked to indicate the "unacceptable blur" to evaluate adverse effects, a subjective judgment that does not take into account potential neuronal adaptation over time. In
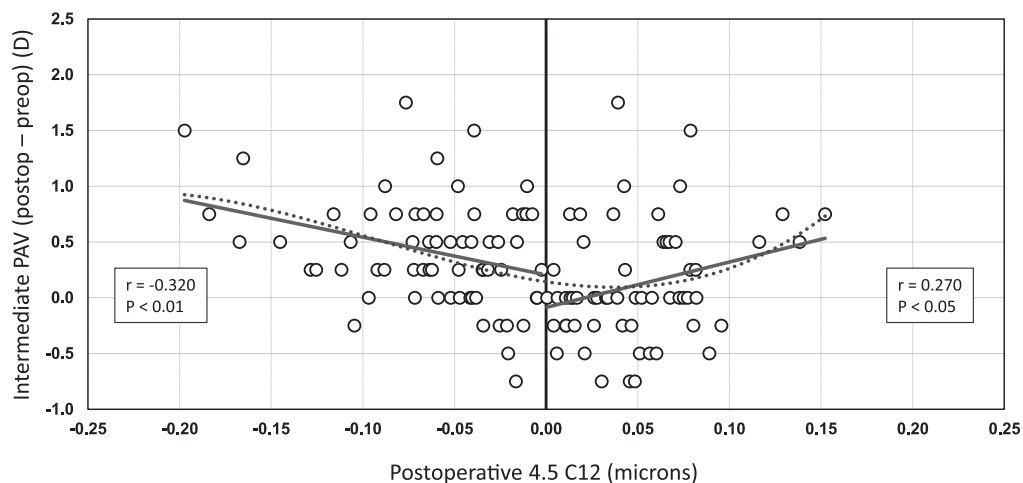

Figure 6. Scatterplot of the change of intermediate pseudo-accommodation value (PAV) between preoperative and postoperative assessment versus postoperative spherical aberration at 4.5 mm (4.5 C12). Coefficient of determination and P values are calculated for negative and positive postoperative spherical aberration. Tendency is represented as a dotted curve. D = diopters; postop = mean postoperative value; preop = mean preoperative value.
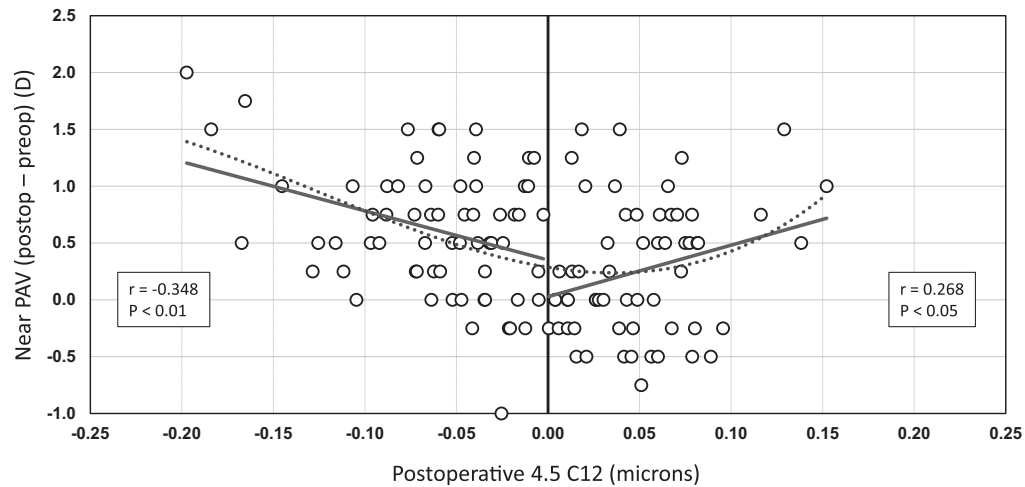
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Figure 7. Scatterplot of the change of near pseudo-accommodation value (PAV) between preoperative and postoperative assessment versus postoperative spherical aberration at 4.5 mm (4.5 C12). Coefficient of determination and *P* values are calculated for negative and positive postoperative spherical aberration. Tendency is represented as a dotted curve. D = diopters; postop = mean postoperative value; preop = mean preoperative value.

clinical practice, after surgery, we observed that negative and positive SA were correlated with PAV improvement at all reading distances in our hyperopic population. Negative SA seemed to be more linked to PAV increase than positive SA for intermediate vision ($r = -0.320$ vs $r = 0.270$) and for near vision ($r = -0.348$ vs $r = 0.268$). Nevertheless, the small number of eyes with low or high positive SA in our postoperative results (because of the ablation profile settings) could explain this difference.

A striking observation of our results is that there is a high individual variability. In our population, an SA value can be associated with different degrees of PAV change (from -0.75 to $+2$ D) as shown by the large standard deviation of mean PAV improvement for near and intermediate vision. In a word, a standardized aspherical ablation

procedure seems to be useless for some patients and beneficial for others. One possible explanation is the well-reported nature of the neural adaptation to optical aberrations.[37] Another explanation is the unreliable values of SA induced by the intrinsic variability. In a few patients, we observed an unexpected decrease in PAV with increased SA. Although modest, this may be due to a particular combination with a residual hyperopia, limiting the benefit of SA for near vision. Some measurement variability and/or particular neural responses could be also responsible for this.

Considering this low predictability, we need to find a way to identify the most appropriate SA value to set for each eye. The approach we used is the visual assessment with an adaptive optics clinical instrument to determine preoperatively the optimal postoperative SA to obtain the best patient
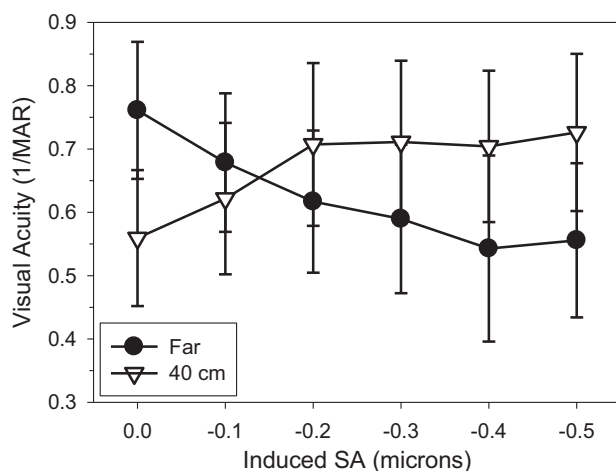

Figure 8. Mean visual acuity values for the 6 induced spherical aberrations (SAs) simulated in 27 nondominant eyes for far (circles) and near (triangles) vision using the Voptica instrument. As the magnitude of negative SA increases, far visual acuity decreases and near visual acuity increases. MAR = minimum angle of resolution.
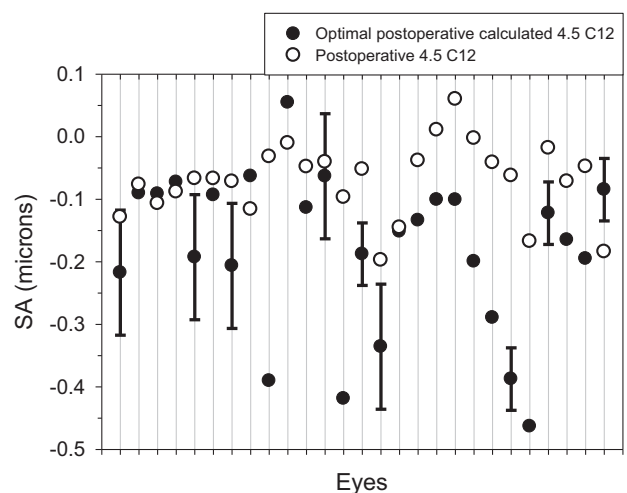

Figure 9. Optimal values of spherical aberration (SA; black circles) and real postoperative SA values (white circles) for each tested nondominant eye. In some eyes, a range of SA values fulfilled all conditions of optimization, which are displayed as errors bars.
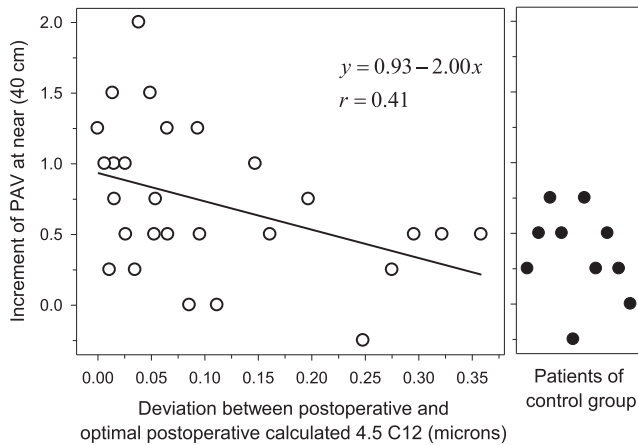
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Figure 10. Scattergram of the increment of the near pseudo-accommodation value (PAV) between preoperative and postoperative assessment versus deviation between postoperative and optimal spherical aberration. As a reference, the image on the right presents the control group of randomly ordered patients. The PAV increases significantly ($r = 0.41$) as SA deviation decreases, indicating that the visual benefit would be maximal if an optimal SA could be achieved.

satisfaction in near vision without impairing distance vision. The adaptive optics technology has made possible not only the measurement but also the modification and correction of wavefront errors. It could predict for any patient the most appropriate SA value to induce a "personalized" treatment. Ideally, this technology should require coupling to the laser photoablation software to induce a more accurate optimal postoperative SA value.

Because the Excimer laser we used (as all current lasers) is not able to accurately induce a chosen value of SA, all eyes preoperatively tested with the adaptive optics instrument were divided in 3 groups: 10 eyes where SA
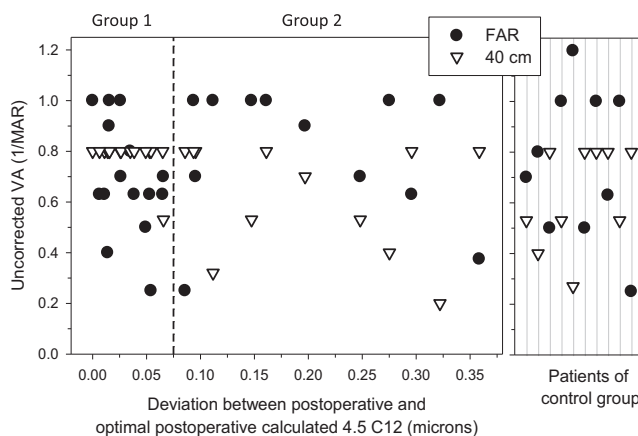

Figure 11. Scattergram of uncorrected visual acuity (VA) at far and near distances versus deviation between postoperative and optimal spherical aberration (SA). Group 1 includes 15 eyes with SA deviation of <0.075 microns. Group 2 includes 12 eyes with SA deviation of >0.075 microns. The image on the right shows randomly ordered patients from the control group. Intersubject variability is lower in group 1 and the difference in near VA is significant ($P = 0.026$) compared with group 2. MAR = minimum angle of resolution.

induction did not increase the depth of focus (control group), 15 eyes with SA deviation (from the predicted optimal value) of <0.075 microns (group 1), and 12 eyes with SA deviation of >0.075 microns (group 2). The mean increment of PAV at near was significantly higher ($P < 0.05$) in group 1 (0.93 ± 0.50 D) than in group 2 (0.46 ± 0.42 D) and in the control group (0.35 ± 0.32 D). In addition, there was less intersubject variability concerning uncorrected VA at far and near distances in group 1 (the average values of VA were 0.69 ± 0.22 for far vision and 0.78 ± 0.07 at near distance), whereas in group 2, the average VA was 0.76 ± 0.28 for far vision and 0.62 ± 0.22 at near distance (significant difference for near vision between both groups; $P = 0.014$). The mean values of VA at far and near distances were very similar in group 2 and the control group ($P > 0.70$). We need to confirm these results with a larger population, but it seems that we can create a customized optic plan with an optimal SA value to target for each eye to allow a maximal and reproducible depth of focus without impairing distance vision.

Indeed, correcting presbyopia is always a compromise. The most frequent adverse events of SA induction are reduction in contrast sensitivity, starburst, and glare symptoms after surgery.[13,38] Nonetheless, in our study, nondominant eye contrast sensitivity significantly decreased only for 12 and 18 cycles per degree in a no-glare situation, but not in the glare condition. For dominant eyes, an unexpected, significant increase in contrast sensitivity was observed for 3 cycles per degree in the glare condition but not in a no-glare situation. All differences for other frequencies, concerning dominant or nondominant eyes, between preoperative and postoperative assessment, were not significant. These findings suggest that contrast sensitivity is minimally and similarly affected after hyperopic LASIK surgery, programming either a conventional or an aspherical ablation procedure. In addition, the clinical relevance of contrast sensitivity decrease is questionable because the satisfaction score reporting this kind of adverse events was satisfactory ($2.45\pm0.54/3$) and only 1 nondominant eye lost best-corrected VA between preoperative and postoperative examinations (0.8 instead of 1), with a safety index of 0.999 for our entire population.

The preoperative adaptive optics assessment performed on the nondominant eye predicted that the mean optimal postoperative calculated 4.5 C12 was -0.18 ± 0.13 μm; the mean 4.5 C12 value measured after aspheric LASIK surgery was -0.054 ± 0.057 μm. This outcome means that, first, the SA value induced by our hyperopic LASIK procedure is generally far from the optimal predicted one. Even for eyes that had the highest postoperative negative SA values in our population (-0.197 μm), the procedure was safe. Consequently, future presbyLASIK softwares should allow targeting of a more important negative postoperative SA, because depth of focus is directly correlated with it and the optimal value is usually more negative. Rocha et al,[34,39] in simulations obtained with adaptive optics in a few unoperated young subjects with a 5- or 6-mm pupil, seem to confirm that we can add greater levels of negative SA to extend the depth of focus, and this benefit begins to plateau and decline with values (around -0.9 μm) far from the

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range of the mean predicted optimal additional ones we observed (-0.28 ± 0.12 μm). This difference can be explained by the bigger pupil size used to measure SA value (i.e., 5 or 6 mm in these studies and 4.5 mm in our study). But, even with this consideration, we can suppose that an SA value of -0.28 μm found with a 4.5-mm pupil is far from corresponding with a value of -0.9 μm with a 6-mm pupil. By way of comparison, we observed for all the 152 eyes studied a mean postoperative SA value of -0.008 ± 0.069 μm for a 4.5-mm pupil and -0.084 ± 0.236 μm for a 6-mm pupil. Second, the large standard deviation of the optimal additional predicted SA shows that we have to customize this value to obtain a maximal postoperative depth of focus. Nevertheless, in the current state of technological developments, the laser predictability about adding SA is insufficient to induce an accurate corneal shape to achieve a specific and predefined depth of focus.

Induction of SA must ideally be associated with a monovision or a micro-monovision to enable useful intermediate and near vision in daily life. However, in our study, we observed that it can be difficult to have effective monovision in nondominant eyes set for an aspherical corneal profile. Programming asphericity leads to an high refractive variability in postoperative results (accuracy index of 64.5% for nondominant eyes versus 89.5% for dominant eyes), and undercorrection is more frequent than overcorrection. Consequently, to have a real clinical benefit for patients, the predictability of future aspheric hyperopic LASIK softwares must be optimized.

In conclusion, treating hyperopia and presbyopia with aspherical presbyLASIK can significantly increase the depth of focus without impairing best-corrected distance vision, but this benefit could be maximal and reproducible if we can define and achieve an optimal SA value for each eye. We have shown in our study that preoperative visual assessment with an adaptive optics instrument helps to determine optimal SA values. Because of the versatility of the Voptica instrument, in the future, the assessment procedure could be further optimized. We could incorporate low-contrast letters or a night driving simulator and perform a similar procedure to anticipate contrast reduction and visual disturbances. We could also induce coma aberrations considering the kappa angle and pupil shift of hyperopic patients. Refinement of this procedure and laser software to accurately induce a customized SA value for each patient, associated with some degree of monovision, should allow a satisfying postoperative depth of focus without vision quality damage.

References

1. Wright KW, Guemes A, Kapadia MS, Wilson SE. Binocular function and patient satisfaction after monovision induced by myopic photorefractive keratectomy. J Cataract Refract Surg 1999;25:177–82.
2. Braun EH, Lee J, Steinert RF. Monovision in LASIK. Ophthalmology 2008;115:1196–202.
3. McDonnell PJ, Garbus J, Lopez PF. Topographic analysis and visual acuity after radial keratotomy. Am J Ophthalmol 1988;106:692–5.
4. Moreira H, Garbus JJ, Fasano A, et al. Multifocal corneal topographic changes with excimer laser photorefractive keratectomy. Arch Ophthalmol 1992;110:994–9.
5. Anschütz T. Laser correction of hyperopia and presbyopia. Int Ophthalmol Clin 1994;34:107–37.
6. Bauerberg JM. Centered vs. inferior off-center ablation to correct hyperopia and presbyopia. J Refract Surg 1999;15: 66–9.
7. Cantú R, Rosales MA, Tepichín E, et al. Advanced surface ablation for presbyopia using the Nidek EC-5000 laser. J Refract Surg 2004;20(suppl):S711–3.
8. El Danasoury AM, Gamaly TO, Hantera M. Multizone LASIK with peripheral near zone for correction of presbyopia in myopic and hyperopic eyes: 1-year results. J Refract Surg 2009;25:296–305.
9. Telandro A. Pseudo-accommodative cornea: a new concept for correction of presbyopia. J Refract Surg 2004;20(suppl): S714–7.
10. Pinelli R, Ortiz D, Simonetto A, et al. Correction of presbyopia in hyperopia with a center-distance, paracentral-near technique using the Technolas 217z platform. J Refract Surg 2008;24: 494–500.
11. Jung SW, Kim MJ, Park SH, Joo CK. Multifocal corneal ablation for hyperopic presbyopes. J Refract Surg 2008;24: 903–10.
12. Assil KK, Chang SH, Bhandarkar SG, et al. Photopic pupillometry-guided laser in situ keratomileusis for hyperopic presbyopia. J Cataract Refract Surg 2008;34:205–10.
13. Alió JL, Chaubard JJ, Caliz A, et al. Correction of presbyopia by technovision central multifocal LASIK (presbyLASIK). J Refract Surg 2006;22:453–60.
14. Yeu E, Wang L, Koch DD. The effect of corneal wavefront aberrations on corneal pseudoaccommodation. Am J Ophthalmol 2012;153:972–81.
15. Reinstein DZ, Couch DG, Archer TJ. LASIK for hyperopic astigmatism and presbyopia using micro-monovision with the Carl Zeiss Meditec MEL80 platform. J Refract Surg 2009;25: 37–58.
16. Epstein RL, Gurgos MA. Presbyopia treatment by monocular peripheral presbyLASIK. J Refract Surg 2009;25: 516–23.
17. Jackson WB, Tuan KM, Mintsioulis G. Aspheric wavefront-guided LASIK to treat hyperopic presbyopia: 12-month results with the VISX platform. J Refract Surg 2011;27:519–29.
18. Fernández EJ, Manzanera S, Piers P, Artal P. Adaptive optics visual simulator. J Refract Surg 2002;18:S634–8.
19. Prieto PM, Vargas-Martín F, Goelz S, Artal P. Analysis of the performance of the Hartmann-Shack sensor in the human eye. J Opt Soc Am A Opt Image Sci Vis 2000;17:1388–98.
20. Piers PA, Manzanera S, Prieto PM, et al. Use of adaptive optics to determine the optimal ocular spherical aberration. J Cataract Refract Surg 2007;33:1721–6.
21. Reinstein DZ, Gobbe M, Archer TJ. Coaxially sighted corneal light reflex versus entrance pupil center centration of moderate to high hyperopic corneal ablations in eyes with small and large angle kappa. J Refract Surg 2013;29:518–25.
22. Soler V, Benito A, Soler P, et al. A randomized comparison of pupil-centered versus vertex-centered ablation in LASIK correction of hyperopia. Am J Ophthalmol 2011;152:591–9.
23. Kanellopoulos AJ, Conway J, Pe LH. LASIK for hyperopia with the WaveLight excimer laser. J Refract Surg 2006;22: 43–7.
24. George MR, Shah RA, Hood C, Krueger RR. Transitioning to optimized correction with the WaveLight ALLEGRETTO

WAVE: case distribution, visual outcomes, and wavefront aberrations. J Refract Surg 2010;26:S806–13.

25. Durrie DS, Smith RT, Waring GO IV, et al. Comparing conventional and wavefront-optimized LASIK for the treatment of hyperopia. J Refract Surg 2010;26:356–63.

26. Nio YK, Jansonius NM, Fidler V, et al. Spherical and irregular aberrations are important for the optimal performance of the human eye. Ophthalmic Physiol Opt 2002;22:103–12.

27. Cheng H, Barnett JK, Vilupuru AS, et al. A population study on changes in wave aberrations with accommodation. J Vis [serial online] 2004;4:272–80. Available at: http://www.journalofvision.org/content/4/4/3.full. Accessed August 16, 2014.

28. Cantú R, Rosales MA, Tepichín E, et al. Objective quality of vision in presbyopic and non-presbyopic patients after pseudoaccommodative advanced surface ablation. J Refract Surg 2005;21(suppl):S603–5.

29. Benito A, Redondo M, Artal P. Laser in situ keratomileusis disrupts the aberration compensation mechanism of the human eye. Am J Ophthalmol 2009;147:424–31.

30. Villegas EA, Alcón E, Mirabet S, et al. Extended depth of focus with induced spherical aberration in light-adjustable intraocular lenses. Am J Ophthalmol 2014;157:142–9.

31. Zheleznyak L, Sabesan R, Oh J-S, et al. Modified monovision with spherical aberration to improve presbyopic through-focus visual performance. Invest Ophthalmol Vis Sci 2013;54:3157–65.

32. Bottos KM, Leite MT, Aventura-Isidro M, et al. Corneal asphericity and spherical aberration after refractive surgery. J Cataract Refract Surg 2011;37:1109–15.

33. Llorente L, Barbero S, Merayo J, Marcos S. Total and corneal optical aberrations induced by laser in situ keratomileusis for hyperopia. J Refract Surg 2004;20:203–16.

34. Rocha KM, Vabre L, Chateau N, Krueger RR. Expanding depth of focus by modifying higher-order aberrations induced by an adaptive optics visual simulator. J Cataract Refract Surg 2009;35:1885–92.

35. Yi F, Iskander DR, Collins M. Depth of focus and visual acuity with primary and secondary spherical aberration. Vision Res 2011;51:1648–58.

36. Benard Y, Lopez-Gil N, Legras R. Optimizing the subjective depth-of-focus with combinations of fourth- and sixth-order spherical aberration. Vision Res 2011;51:2471–7.

37. Artal P, Chen L, Fernández EJ, et al. Neural compensation for the eye's optical aberrations. J Vis [serial online] 2004;4:281–7. Available at: http://www.journalofvision.org/content/4/8/281.long. Accessed August 16, 2014.

38. Chalita MR, Chavala S, Xu M, Krueger RR. Wavefront analysis in post-LASIK eyes and its correlation with visual symptoms, refraction, and topography. Ophthalmology 2004;111:447–53.

39. Rocha KM, Vabre L, Harms F, et al. Effects of Zernike wavefront aberrations on visual acuity measured using electromagnetic adaptive optics technology. J Refract Surg 2007;23:953–9.

Footnotes and Financial Disclosures

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Abbreviations and Acronyms:
4.5 C12 = spherical aberration at 4.5 mm; **BDCVA** = best distance-corrected visual acuity; **D** = diopters; **PAV** = pseudo-accommodation value; **SA** = spherical aberration; **VA** = visual acuity.

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