Chapter 5

Customized Corneal Treatments for Refractive Errors

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Core Messages

- The ultimate goal of custom corneal treatments is to satisfy patient's visual needs and can be achieved through anatomical, optical, and functional optimization.
- After establishing the safety of custom corneal treatment, the focus is now to reduce the incidence of postoperative "outliers," which results in decreased visual performance.
- Visual and refractive outcome following custom corneal treatment is influenced by many variables, which include wavefront measurement, and laser, surgical, biomechanical, and environmental factors.
- Significant improvement in the predictability of postoperative visual and refractive outcome can be achieved using nomogram adjustments and understanding the role of the epithelium in the corneal healing process.

5.1 Introduction

Laser refractive surgery has advanced rapidly, since the inception of excimer laser ablation in 1985 and LASIK (laser-assisted in situ keratomileusis) in 1990, and millions of patients worldwide have benefited from its use. Advancements such as scanning spot lasers to create smoother and subtler ablations, and eye movement tracking to precisely deliver treatment, have considerably refined laser refractive surgery. These refinements have improved the delivery system of excimer ablation, but the basic diagnostic and treatment input driving the ablation process has remained relatively unchanged. The treatment patterns have been driven by the manifest and cycloplegic subjective refractions that relied on the patient's subjective assessment.

The incorporation of wavefront technology into refractive surgery has signaled an important transition to the use of objective methods of measuring and treating refractive error vision correction. This chapter provides a brief practical overview of wavefront-guided refractive surgical ablation.

5.2 Some Basics of Customized Laser Refractive Surgery

A comprehensive review of laser refractive surgery is beyond the scope of this chapter. The reader is directed to numerous excellent overviews of this field [24, 32]. The chapter will focus on the basic requirements and some of the challenges encountered with the refinement of customized refractive surgery techniques.

Simple myopia treatment is performed by removal of cornea tissue, more central than peripheral, to effect central corneal flattening. There is one transition point per semi meridian, which is at the juncture of the ablation and the untreated cornea as shown in Fig. 5.1A. Astigmatic treatment is possible by removing a cylindrical mass of tissue, which flattens one meridian more than the meridian 90° away (Fig. 5.1B). There is one transition point per semi meridian in the steep meridian and two transition points per semi meridian in the flat meridian, one at the outer edge

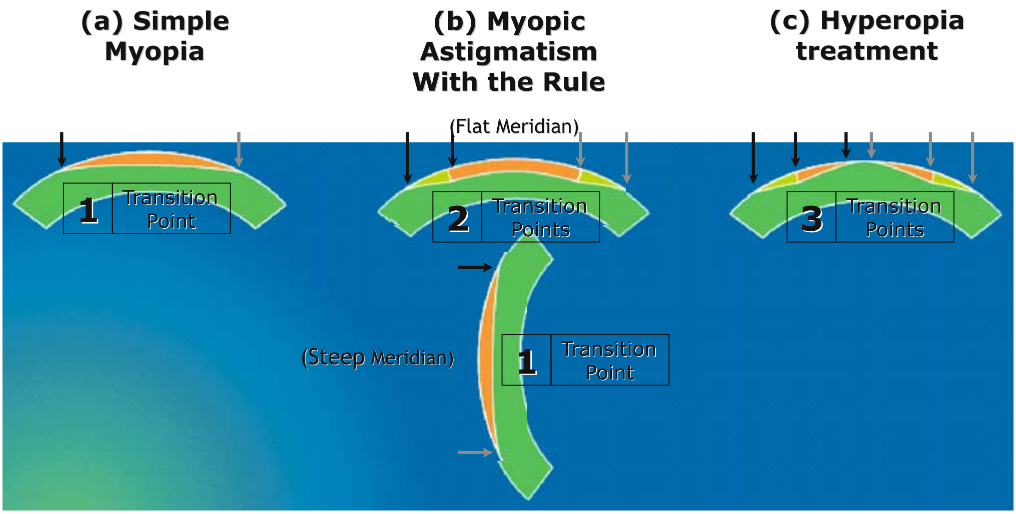

Fig. 5.1 Excimer ablation optical zone and transition zone profiles are shown in *green* for **a** myopic, **b** myopic-astigmatic, and **c** hyperopic or hyperopic-astigmatic treatments. **a** A simple myopic treatment involves more tissue removal from the central cornea than the peripheral cornea. **b** Myopic astigmatic treatment involves tissue removal of uniform thickness in the flatter meridian. This causes no change in power in the flat meridian. The steep meridian, shown below, has a convex shape, which is removed to flatten the steep meridian. **c** In hyperopic treatments, a donut-shaped ablation is performed to remove more tissue in the peripheral portion of the ablation optical zone than in the central cornea. This treatment steepens the central cornea. Hyperopic astigmatism simply applies this same pattern to steepen the flat meridian, while the steep meridian is untreated

of the ablation optical zone and one at the outer edge of the transition zone. Hyperopic treatment removes more corneal tissue in the mid-periphery of the cornea leaving the central cornea with less treatment (Fig. 5.1C). A doughnut-like mass of tissue is removed, which steepens the central cornea. There are three transition points per semi meridian with hyperopic correction, one at the central cornea, one at the deepest part of the trough, and one at the outer edge of the transition zone.

In the early years of refractive surgery, patients were treated with broad beam excimer lasers, 6 mm in diameter, and the optical zones were often even smaller, sometimes as small as 4.0–5.0 mm, which tended to cause night glare and halos when the pupil dilated beyond 6 mm, making driving at night problematic. Although these patients had symptoms because of their small optical zone, the photorefractive keratectomy (PRK) refractive correction has remained relatively stable based on 12 years of follow-up as noted by Rajan and coworkers [52].

Current excimer laser systems are more sophisticated and use small spot treating systems with fast eye tracking systems, which minimize decentrations. The use of larger optical zones and limiting the treatment to less than 12 D has reduced the likelihood of patients having problems postoperatively. Now, many patients receiving customized excimer laser eye treatment experience fewer night driving symptoms than they noted before the surgery. Patients with larger amounts of myopic refractive error often undergo correction with phakic intraocular lenses [22, 47].

Wavefront sensors were initially utilized for research in ophthalmology and visual sciences. Liang, Grimm, Goelz, and Bille [26] introduced the Shack–Hartmann wavefront sensor in 1994 into ophthalmology and subsequently in 1997, Liang, Williams, and Miller [27] used a Shack–Hartmann system and coupled it with an adaptive optics deformable mirror to improve in vivo retinal imaging and demonstrate marked improvement in visual performance with higher

Table 5.1 Summary of customized laser-assisted in situ keratomileusis (LASIK) results from industry-sponsored FDA studies. *BCVA* best corrected visual acuity testing

Customized platform	Vision without glasses ≥20/20 at 6 months postoperatively (%)	Prescription within ±0.50 D of intended correction (%)	Loss of ≥2 lines BCVA postoperatively (%)
Alcon LadarVision[a]	85.8	80.2	0
Bausch and Lomb Technolas 217z[b]	91.5	90.9	0.6
Visx Star S4 and WaveScan[c]	93.9	90.3	0
Visx Star S4 and WaveScan for hyperopia	61.8	64.9	0

Source documents available at: www.fda.gov/cdrh/LASIK/lasers.htm

[a] Autonomous LadarVision data on myopic eyes collected with 4,000-Hz eye tracker.

[b] B+L Technolas data collected on myopic eyes with 217z model with a 120-Hz eye tracker

[c] Does not include 12 myopic eyes that were retreated within the first 6 months of surgery

Table 5.2 Summary of myopic conventional LASIK results from industry-sponsored FDA studies

Customized platform	Vision without glasses ≥20/20 at 6 months postoperatively (%)	Prescription within ±0.50 D of intended correction (%)	Loss of ≥2 lines BCVA postoperatively (%)
Alcon LadarVision	65.2	82	1.9
Bausch and Lomb Technolas 217a	87.3	87.6	0.4
Visx Star S3 and WaveScan	54.1	72.5	0
Wavelight Allegreto[a]	87.7	85.3	0.7
Nidek	47.4	60.3	1.2

Source documents available at: www.fda.gov/cdrh/LASIK/lasers.htm

[a] Wavefront optimized procedure; does not include 10 eyes that were retreated before 6 months after surgery

order aberration correction. In 2000, Seiler [59] coupled the Tscherning diagnostic wavefront sensor with a flying spot excimer laser to treat patients with customized ablation. Pallikaris et al. [43] were also able to couple a Shack–Hartmann wavefront sensor with another flying spot laser later that year and perform wavefront-driven customized ablation as well. By 2003, three wavefront driven excimer laser systems were approved by the US FDA (Federal Drug Administration) and even more were being utilized worldwide. The results of the clinical trials (Table 5.1) indicate improved visual and refractive outcome compared with the equivalent conventional treatment platforms for myopia (Table 5.2) and hyperopia (Table 5.3). The exciting field of wavefront technology and ocular higher order aberration correction had been established, but

Table 5.3 Summary of hyperopic conventional LASIK results from industry-sponsored FDA studies

Customized platform	Vision without glasses ≥20/20 at 6 months postoperatively (%)	Prescription within ±0.50 D of intended correction (%)	Loss of ≥2 lines BCVA postoperatively (%)
Alcon LadarVision	48.8	65	1.4
Bausch and Lomb Technolas 217a	61.4	66.5	2.8
Visx Star S3 and WaveScan	48.1	76.4	3.8
Wavelight Allegreto	67.5	72.3	0.8

Source documents available at: www.fda.gov/cdrh/LASIK/lasers.htm

there were and remain many important challenges.

5.3 Forms of Customization

The ultimate goal of customized ablation is to optimize the treatment to help satisfy a patient's visual needs. This goal is best achieved by performing three forms of customization [33]:

1. Optical,
2. Anatomical,
3. Functional.

5.3.1 Optical Customization

Optical customization involves treating refractive error by measuring and treating the second (lower) order aberrations of sphere, either myopia or hyperopia, and astigmatism and higher order (third and above) aberrations. This includes third order aberrations like coma and trefoil as well as positive spherical aberrations (fourth order), which are also found in the normal population. The wavefront sensor measures the ocular aberrations and a treatment file developed to treat the aberrations using 193 nm argon fluoride excimer laser.

Various commercial wavefront sensors allow optical customization by measuring the ocular aberrations based on techniques that include Shack–Hartmann [26], Tscherning [40], and the Scanning Slit, a subjective system [57] using spatially resolved refractometry. The most popular of the systems is the Shack–Hartmann technique, which is used by at least four of the laser refractive surgical eye companies offering customized ablation. Each system has relative strengths and weaknesses and there are trade-offs. Some wavefront sensors have greater dynamic range, but may sacrifice accuracy or vice versa. A more detailed discussion is included elsewhere and is beyond the scope of this chapter [24].

5.3.2 Anatomical Customization

This form of customization involves careful measurement of the corneal curvature using corneal topography, the corneal thickness [29] using ultrasonic pachymetry [35, 62], and the pupil size [35, 38] under low light (mesopic) conditions. These measurements are critical in helping to design an optimal ablation pattern, which gives an adequate ablation optical zone diameter [14, 30], while avoiding treating with too deep an ablation. The larger the optical zone the deeper the tissue removal [30].

The normal cornea is about 500–540 μ. LASIK creates a flap that is usually between 90–180 μm, and laser ablation is performed to remove tissue either over the central cornea for myopia correction, or in the corneal mid-periphery for hyperopia treatment. The laser ablation can be anywhere between 10 and 160 μm depending on the amount of myopia or hyperopia and the diameter of the optical zone. Most surgeons prefer not to ablate deeper than the posterior or remaining 250 μm of the cornea (to avoid corneal ectasia). The thickness of the flap has an indirect influence on the surgeon's options in optical zone sizes since a thick flap may limit the amount of ablation the surgeon can apply before ablating deeper than the posterior 250 μm. If there is not enough room to treat with an adequate optical zone, the surgeon may opt for "surface ablation," which has the advantage of conserving tissue with surgery.

There are three common surface ablations, PRK or LASEK (laser-assisted epithelial keratoplasty). In PRK the superficial layer of the cornea, the corneal epithelium, is removed and the laser treatment applied. LASEK is a variant of PRK where the superficial layer, the corneal epithelium, is peeled back (like an apron), the laser treatment is applied, then the epithelial layer is floated back over the treated cornea, and a bandage soft contact lens is applied over the cornea for comfort. PRK and LASEK have longer recovery periods than LASIK, usually 2–4 days, and there may be more discomfort because the surface layer of the cornea is disrupted [33]. Epi LASIK is a variant of LASEK where a mechanical microkeratome with a dulled blade is used to remove the epithelium in a single sheet without the use of dilute alcohol and may have the advantage of less tissue damage to the epithelium than LASEK, but this remains to be demonstrated [45].

Interestingly, the outcomes for LASIK, PRK, and LASEK are similar in the few studies that have compared the treatments in the same patients in paired eye studies [12, 31]. LASIK is used for the typical patient while PRK or LASEK are used more commonly in patients who have thin corneas that are not deep enough for LASIK [2]. Surface ablation is also used preferentially in patients who have a tendency toward dry eyes since it tends not to increase dryness symptoms in patients who have dry eyes [4]. The popularization of Intralase, which uses a femtosecond laser to create the flap with LASIK, has further encouraged surgeons to use thinner flaps and strive for lower standard deviation when making LASIK flaps. One study has shown that thinner flaps (<100 μm), are associated with better efficacy, predictability, and contrast sensitivity suggesting that better control of flap thickness may improve outcomes [8]. The optimal anatomical approach is still being clarified, although we have become much more sophisticated in our approach to anatomical customization in recent years.

5.3.3 Functional Customization

Functional customization requires an understanding of the visual needs of the patient and factors such as age, occupation, hobbies, and the patient's expectations. Myopic (nearsighted) individuals see poorly at distance, but often can take off their glasses and see well close up. These patients need to be alerted that their ability to read may be reduced, but they will probably get a dramatic improvement in their distance vision. A number of studies have shown that elderly myopes, over 45 years of age, are more susceptible to hyperopic overcorrection [13, 17]. Furthermore, treating younger myopes more aggressively and hyperopes less aggressively result in greater patient satisfaction. Young myopes have large accommodative amplitudes and hence tolerate a slight hyperopic overcorrection postoperatively. Conversely, older patients prefer emmetropic or slight myopia postoperatively to compensate for reduced accommodative amplitudes. An overcorrection or hyperopic outcome would blur both distance and near vision and is highly undesirable. Presbyopic patients may be treated with monovision where one eye is fully corrected for distance and one eye is intentionally left with a moderate amount of nearsightedness, or monovision (an intentional correction to make one eye −1.25 to 1.50 D myopic) or mini monovision (one eye made −0.25 to −0.75 D myopic). This gives the patient a greater dynamic working range when using both eyes together and allows the presbyopic patient more independence from reading glasses. Most patients who need to see well with both eyes at distance prefer being treated by aiming for optimal distance vision in both eyes. The use of a soft contact lens trial to allow the patient to simulate mono or mini monovision is also helpful in making a decision whether or not this is a viable option for the patient [9]. The use of multifocal or aspheric ablations is being advocated to correct presbyopic patients, but the long-term viability remains to be established [6, 63].

Summary for the Clinician

- Customized correction involves consideration of anatomical, functional, and optical factors that would provide optimal visual performance based on the patient's requirements.
- Correction of preoperative higher order aberrations could provide greater visual benefit through improvement in uncorrected visual acuity and contrast sensitivity.

5.4 Technological Requirements for Customized Refractive Surgery

Laser refractive surgery has evolved rapidly from the first treatments, which were carried out in blind eyes by Seiler in 1985 [58] and then on sighted eyes in 1987 using PRK [25]. In 1990, Pallikaris combined the lamellar splitting of the corneal stroma with treatment using an excimer laser, which formed the basis of modern-day LASIK surgery [42]. Since the advent of LASIK, several technological advancements have revolutionized the treatment procedure. These include physical properties of the laser, eye movement tracking, wavefront measurement, and laser–wavefront interface.

5.4.1 Physical Properties of the Laser

In order to correct the complex nature of the higher order aberrations, the laser system must be precise to make the eye near diffraction limited. When the ablation depth is small, the ablation depth per pulse limits the precision of the laser system. Current excimer lasers have an ablation depth per pulse of about 0.30 μm, which is sufficient for such a level of precision treatment [18].

A smaller spot size such as a <1 mm spot can treat finer aberrations, but larger spot sizes (>2 mm) can treat a sphere or cylinder. The trend over recent years has been to use smaller spot sizes and faster laser repetition rates from 50 to 500 Hz. These faster Hertz rates for lasers are preferable since they reduce treatment time, which reduces variability due to the dehydration of the cornea that occurs with longer treatment times. Thus, shorter treatment times allow for more uniform and predictable ablations. The excimer laser spot sizes for customized correction have decreased, sometimes to less than 1.0 mm and rapidity of the treatment has increased from 10 Hz to sometimes as fast as 500 Hz. Guirao and coworkers [16], as well as Huang and Arif [19], have noted that a spot size of 0.5–1.0 mm is capable of reducing lower and higher order aberrations. A study by Bueeler and Mrochen (cited in [23, 24]) comparing ablation depths of 0.25 and 1.0 μ with laser spot diameters of 0.25 and 1.0 mm and tracker latencies of 0, 4, 32, and 96 ms as well as no eye tracking, and looking at the simulated efficacy of a scanning spot correction of a higher order aberration of 0.6 mm vertical coma with a 5.7 mm pupil diameter. They found that the shallower ablation depth of 0.25 μm combined with a larger spot size of 1.0 mm is more stable and less dependent on tracker latency, but less capable of treating very finely detailed aberrations. A shorter latency is advantageous since it reduces the time the target has to move before the laser mirrors react to the movement [23, 24].

5.4.2 Eye Movement Tracking

The eye makes frequent saccades during fixation that could reduce the effectiveness of customized vision correction. A laser ablation driven by a robust eye tracking system, which can follow such rapid eye movements, can allow effective customized vision correction. Eye tracking has been incorporated into treatments using video-based and laser radar tracking, with tracking rates varying between 60 and 4,000 Hz. Porter, Yoon, and coworkers indicate that over 90–95% of eye movement during laser refractive surgery could be captured by a 1- to 2-Hz closed loop tracking system [50]. In addition, these studies indicated that the most critical component of eye tracking was the accuracy of the centering of the tracker over the pupil center at the time the tracker was activated. Small decentrations of 200–400 µm were not uncommon in the above study, even with meticulous centering by the surgeon, suggesting that greater magnification and a more automated system may be advantageous.

Small eye movements do occur during ablation as noted above as well as static decentration errors, which occur when attempting to center the tracker over the pupil. Guirao and coworkers found that a translation of 0.3–0.4 mm or a rotation of 8–10° could still correct up to 50% of the higher order aberrations in a normal eye [15]. The corollary of this is that 50% of the benefit of the correction of a higher order aberration would be lost with such translation or rotation, stressing the importance of proper centration and an adequate tracking system.

5.4.3 Wavefront Measurement and Wavefront–Laser Interface

More recently, clinicians have begun using wavefront sensing to measure and treat the subtle aberrations of the eye in addition to sphere and cylinder. Different types of wavefront sensors exist, including Tscherning and subjective wavefront sensors, but the most popular used by the laser companies is the Shack–Hartman system. The latter system is an objective technique that measures the slope of the wavefront exiting the pupil using a Shack–Hartman lenslet array. The wavefront image provides an image of the lower and higher order aberrations that patients have.

In order to obtain optimal results, a very reproducible and accurate map needs to be created. This is achieved through multiple captures, comparisons, and often combining (or averaging) information to generate a composite wavefront map based on 3–5 wavefront scans. The wavefront error can be documented and then transferred to the excimer laser via a floppy disc. The corneal ablation pattern is then formulated, which is the reverse of the wavefront error to correct the wavefront aberrations. When implementing this step, the diameter of the measured wavefront needs to be at least the scotopic or low mesopic pupil diameter if possible [24]. To achieve a large pupil diameter, pharmacological dilating agents such as 2.5% neosynephrine or tropicamide may be used. Recently, we have demonstrated that the use of a nonpharmacologically dilated pupil in 90 eyes achieves equivalent results to 155 eyes dilated with a mild noncycloplegic dilating agent such as 2.5% neosynephrine. In those studies, 93.4% and 94.6% of eyes obtained an uncorrected visual acuity of 20/20 or better in the above respective groups. The final step in this process is the design of a laser shot pattern, which is determined by the laser characteristics described above and the treatment of the optic zone diameter.

This strategy did not take into account the biomechanics of the cornea, which resulted in patients developing positive spherical aberration after myopic treatment and negative spherical aberration with the treatment of hyperopia. The laser companies have incorporated correction factors in an attempt to minimize the induced positive or negative spherical aberration created by the ablation with refractive surgery.

Summary for the Clinician

- Wavefront sensors deduce ocular aberrations based on the measured slope of the wavefront error at a discrete set of points. Pupil size and wavefront aperture diameter have a profound effect on the magnitude of the higher order aberrations measured.
- A 2-mm laser spot diameter is adequate for correcting defocus and astigmatism and a 1-mm spot size for correction up to fourth order Zernike modes.
- Greater laser frequencies reduce treatment time and thereby minimize corneal dehydration time.

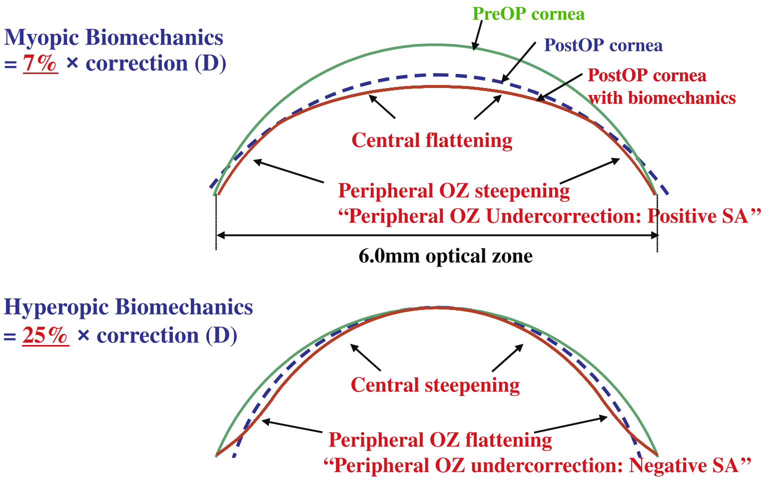

Fig. 5.2 A hypothesis by Yoon et al. [43] of the biomechanical response of the cornea to excimer laser refractive surgery after a **a** myopic and **b** hyperopic procedure. Preoperative corneal shape, postoperative corneal shape, and postoperative corneal shape including biomechanical effects are denoted using *solid gray*, *dashed black* and *solid black* lines, respectively. **a** In myopic laser correction, the central cornea is flattened while the peripheral portion of the optical zoned steepens (causing peripheral optical zone undercorrection) and flattens, causing positive spherical aberration. **b** In hyperopia, the central cornea and ablation optical zone steepens, but the peripheral part of the ablation optical zone flattens (resulting in peripheral optical zone undercorrection), causing negative spherical aberration. (Figure is courtesy of Dr. Geunyoung Yoon)

5.5 Biomechanics of Refractive Surgery

The biomechanical effects on the cornea have direct relevance to optimizing customized ablation because the biomechanical changes caused by creating a flap or carrying out an ablation may induce higher order aberrations. The biomechanics of refractive surgery is a complicated subject, but there are several empiric observations that help clarify the cornea's response to refractive laser eye treatment. The most prominent change that occurs with myopic excimer laser surgery is an increase in positive spherical aberration, while hyperopic treatment tends to cause an increase in negative spherical aberration [5, 37]. Normally, most individuals in the population have a slight positive spherical aberration, which means that the central light rays would fall directly on the macula in an emmetropic individual, but the peripheral light rays coming in closer to the edge of the pupil would be focused in front of the retina. Roberts has shown that the cornea actually steepens and thickens slightly in the mid-periphery after myopic excimer laser treatment, which accounts for the positive spherical aberration noted after myopic ablation with either LASIK PRK [10, 21, 54].

Huang et al. [20] developed a mathematical model of corneal smoothing to explain regression and induction of postoperative higher order aberrations observed clinically. Mrochen and Seiler postulated that the ablation in the central cornea is more effective than the more peripheral cornea [39], while Dupps and Roberts [10] and Roberts [54, 55, 56] proposed that the corneal shape or curvature change is caused by the biomechanical response of the cornea. Yoon et al. [66] have modeled the cornea calculating the variable ablation rate as one moves to the periphery of the optical zone and the effect of biomechanics and wound healing. In this model, the variable ablation rate in which the efficacy of the laser pulses decreases as one moves to the peripheral part of the optical zone accounts for up to a maximum 8% decrease in efficacy when one reaches the peripheral part of a 6.0-mm diameter optical zone. In the same model noted above, the biomechanical/biologic healing would increase positive spherical aberration by 7% of the spherical value of myopia being treated and negative spherical aberration by 25% of the spherical value in hyperopia treatment (see Fig. 5.2).

5.5.1 LASIK Flap

Potgieter et al. [51] followed corneal topography and ocular wavefront changes after a lamellar flap creation. They observed that statistically significant changes in wavefront data that showed significant change in four Zernike modes—90/180° astigmatism, vertical coma, horizontal coma, and spherical aberration. The topography data indicated that the corneal biomechanical response was significantly predicted by stromal bed thickness in the early follow-up period and by total corneal pachymetry and flap diameter in a two-parameter statistical model in the late follow-up period. They concluded that uncomplicated lamellar flap creation was responsible for changes in corneal topography and induction of higher-order optical aberrations. Predictors of this response include stromal bed thickness, flap diameter, and total corneal pachymetry.

Further studies by Porter, MacRae, and coworkers [49] noted that the increase in positive spherical aberrations with LASIK is primarily related to the excimer laser ablation and not the cutting of peripheral collagen fibers caused by the microkeratome incision. The microkeratome or laser incision to create the corneal flap generally cuts a flap approximately 100–180 µm deep. This study involved making a superior hinged microkeratome flap with a Hansatome (Bausch and Lomb) and observing the flap-induced aberrations for 2 months. In one group the flap was lifted and a sham ablation was performed using a microkeratome, which created a flap with a superior hinge. In another group the flap was not lifted and the eye was simply observed for 2 months. In the group where the flap was lifted, there was a 0.19 µm (50%) increase in higher order root mean square (RMS) wavefront error, while a negligible increase was measured in the group with no flap lift. Horizontal trefoil was the only higher aberration that consistently increased. After 2 months, the flap was lifted and the cornea ablated with the excimer laser to treat myopia. With the ablation, we found an increase in positive spherical aberration. The increase in positive spherical aberration was proportional to the amount of myopia treated with greater amounts of myopic treatment causing larger amounts of positive spherical aberration. Overall, we noted that most of the increase in higher order aberration was induced by the ablation with conventional LASIK [61]. We were impressed that flap manipulation also contributed significantly to an increase in higher order aberrations and recommend that clinicians minimize flap hydration and meticulously reposition the flap after ablation.

Pallikaris and coworkers noted an increase in horizontal coma and spherical aberration when they made a microkeratome flap using a nasal hinged microkeratome and observed the effects of the flap cut alone for several months [44]. Waheed and coworkers have also created a flap using a Moria 2 and an SKBM microkeratome and noted a mild hyperopic shift of 0.5 D, but they did not observe this shift in the SKBM group [65].

Interestingly, they noted that post-flap aberrations accounted for less than one-quarter of the increase in post-laser aberrations suggesting that the ablation contributes significantly to the post-LASIK higher order aberration increase with conventional LASIK treatments. This finding is also similar to those noted by our group as reported above by Porter et al. [49].

In a contralateral study comparing the Bausch and Lomb Hansatome with the Intralase, Tran et al. found in eight paired eyes a significant increase in higher order aberration 10 weeks post-flap creation in the microkeratome group, which was driven mainly by trefoil and quadrafoil [64]. The difference in higher order aberration between the microkeratome eye and Intralase was subtle and even though they found a statistically significant difference, the change in higher order aberrations (microkeratome with a 0.055-µm RMS (32%) increase vs. Intralase, with a 0.03-µm RMS (20%) increase, 6.0-mm pupil) is of equivocal clinical significance. Further paired-eye studies are warranted to clarify the differences in mechanical vs. Laser-created flaps and the clinical meaning of any differences noted. Control of hydration and flap thickness may also be helpful in such studies. As noted previously, Cobo Soriano et al. reported that thinner flaps of less than 100 µm tend to achieve better uncorrected visual acuity and contrast sensitivity results than eyes that have thicker flaps [8]. Thus, further studies comparing varying flap creation techniques need to attempt to use flaps of similar thickness and diameters to make comparisons more meaningful.

We have also noted that we can improve on results in eyes that averaged a spherical equivalent of almost –5.00 D and had more higher order aberration than the normal myopic population using the Rochester Nomogram, a nomogram that modifies the spherical correction based on the amount of preoperative higher order aberration, as we will discuss later.

Thus, in myopic laser treatment, there is a tendency for the central cornea to flatten more, but the cornea in the periphery optical zone steepens and thickens causing an unanticipated positive spherical aberration. This causes the peripheral light rays to be focused more anteriorly than the central light rays. In hyperopic corneal laser surgery, the tendency is for the central cornea to steepen, but the peripheral optical zone cornea tends to flatten slightly causing unanticipated negative spherical aberration. In this case the central light rays are focused on the retina with emmetropia, but the mid-peripheral lights rays passing through the pupil are focused behind the retina.

One strategy to minimize spherical aberration is to use an aspheric curvature to compensate for the spherical aberration, which is induced by conventional refractive surgery. This strategy uses an aspheric constant for a given amount of correction, which is based on the average amount of aspheric change induced in a previously treated group of eyes. Most eyes have a small amount of positive spherical aberration in the normal population of people who have never had refractive surgery [36].

The advantage of this technique is that it helps minimize the amount of spherical aberration induced for the average eye [48]. One disadvantage of this approach is that a moderate number of eyes in the normal preoperative population are not close to the population average; some eyes actually have negative spherical aberration and may actually experience an increase in spherical aberration, while some eyes have much larger amounts of positive spherical aberration and would benefit more from a larger amount of aspheric adjustment to reduce their preoperative spherical aberration. The second disadvantage is that it is not a customized ablation and would not be suitable for eyes that had even modest amounts of higher order aberration. These eyes with mild and greater amounts of higher order aberrations do benefit from treatment with customized ablation, which improves contrast sensitivity under photopic and mesopic conditions [61]. These strategies are being employed to treat eyes with minimal amounts of higher order aberration and are currently being used by Nidek, Bausch, and Lomb as well as Wavelight (Wavelight's results are noted in Table 5.2).

Summary for the Clinician

- Postoperative higher order aberrations are induced by flap creation, magnitude of treatment, loss of ablation depth per pulse, and the corneal healing response.
- Among myopes, postoperative regression and increased positive spherical aberration results from unanticipated steepening of the midperipheral cornea.
- Among hyperopes, the midperipheral cornea flattens postoperatively, resulting in unanticipated negative spherical aberration.

5.6 Clinical Results of Customized Excimer Laser Ablation

Laser companies have performed a number of large, well-controlled clinical trials to provide evidence of the relative success, and to establish the safety and efficacy of customized excimer laser treatment. Several reports have been published to establish the safety and efficacy of the customized LASIK treatment for myopia using the Bausch and Lomb Zyopitx system [1, 34], the Alcon CustomCornea platform [3, 46], the VISX Wavescan system [28], the Carl Zeiss Meditec platform [53], the Allegretto Wavelight [41], and the Nidek NAVEX platform [7].

Tables 5.1 and 5.2 provide information on the visual outcome of the customized LASIK procedure compared with that following conventional

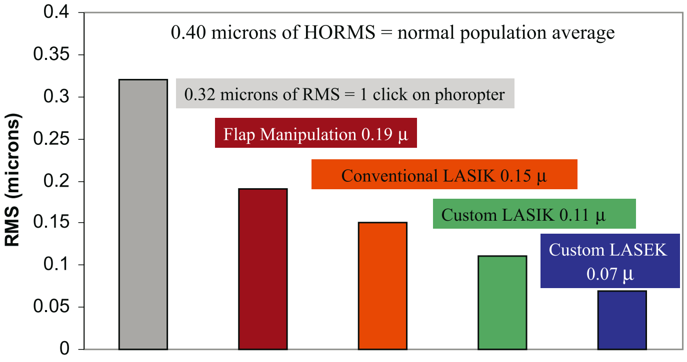

Fig. 5.3 Summary of higher order aberration induction with several different refractive surgery interventions. Flap manipulation associated with lifting the flap caused the greatest amount of higher order aberration increase due to flap swelling and less meticulous attention to symmetric lying down of the flap

LASIK treatment for myopia. In the conventionally treated myopic eye groups the data suggest that 20/20 or better uncorrected vision (vision without spectacles or contacts) ranges between 40 and 90% depending on the preoperative myopia and the laser used. The eyes treated with customized or wavefront-guided ablation range between a 60 and 95% likelihood of obtaining 20/20 or better uncorrected visual acuity under high contrast conditions (Table 5.1). The conventional hyperopic eyes have about a 40–88% chance of achieving 20/20 or better uncorrected vision as noted in Table 5.3.

Most treatments with customized LASIK or customized surface treatments do introduce slight increases in higher order aberration. We have carried out other studies [31] comparing the use of the Customized LASEK with the Bausch and Lomb Zyoptix System and compared that with conventional (noncustomized) LASIK using the same Bausch and Lomb Planoscan system. In a paired study of 24 patients where one eye was treated with customized LASEK and the contralateral eye treated with conventional LASIK, we found a 0.07-µm increase (6.0-mm aperture) in higher order aberration in the customized LASIK eyes compared with a 0.15-µm increase with conventional LASIK. We compared these results with those of an equivalent group of 340 eyes in the US FDA Bausch and Lomb Zyoptix clinical trial where there was a 0.11-µ increase in higher order aberration (6.0-mm aperture). The amount of increase in higher order aberration is relatively trivial when one compares this with the amount of wavefront error (0.32 µm RMS—6.0-mm aperture) introduced with 0.25 D of spherical refractive error (one click on the phoropter). Thus, the amount of higher order aberrations introduced with customized ablation is equivalent to about one half of a click of a sphere on a phoropter. These results are summarized in Fig. 5.3.

We also found that with customized ablation, eyes with greater amounts of preoperative higher aberration obtained greater benefit with customized ablation. This is similar to what we have noted in eyes with astigmatism. If patients have more astigmatism, it is more worthwhile to treat these eyes with an astigmatism treatment. In our FDA study evaluating the Bausch and Lomb Zyoptix customized ablation in 340 eyes, we found that eyes with greater amounts of preoperative higher order aberration (>0.35 µm of RMS; 6.0-mm pupil) wavefront error were more likely to experience an improvement in contrast sensitivity of one to two patches than eyes with lower amounts of preoperative higher order aberrations and eyes were five times as likely to gain one patch of contrast sensitivity than lose one patch of contrast in the study. Two percent of eyes had a two-patch contrast sensitivity loss compared with 24% of eyes that had a two-patch gain in mesopic contrast sensitivity and that gain in contrast was related to a reduced increase in higher order aberration compared with the eyes that lost mesopic contrast. In the study, mesopic contrast sensitivity gains were ten times more likely than losses and the gains in contrast were related to a decrease or minimal increase in higher order aberration, while those eyes that lost contrast had a higher increase in higher order aberration than the eyes that gained contrast [61]. The greatest gain in vision with customized ablation is under low light conditions when the pupil is more dilated and not in visual acuity. Thus, measurements of contrast sensitivity changes are more helpful at articulating the visual gains using customized ablation than high-contrast visual acuity changes. In the future, we will carry out more studies that evaluate the visual benefit of customized ablation by evaluating the changes in contrast sensitivity under normal and low lighting conditions.

Treatment using a customized correction method may need an adjustment of sphere when treating higher order aberrations. Durrie and coworkers noted a tendency of hyperopic overcorrection in LASIK retreatment eyes, particularly in eyes with larger amounts of spherical aberration and cautioned users to reduce myopic sphere in customized retreatments. They also cautioned the user to sometimes plan for a second retreatment to treat the residual hyperopia when retreating myopic eyes with larger amounts of spherical aberration using the Alcon Ladarwave System [11]. Recent studies by our group have also demonstrated that the treatment of preoperative higher order aberration using the Bausch and Lomb Zyoptix may secondarily affect sphere and cylinder [61]. We noted in the 340-eye US FDA trial that eyes with larger amounts of preoperative coma, trefoil, or spherical aberration were more likely to result in hyperopic overcorrection. We noted that 21.8% of eyes were likely to have a mild overcorrection of 0.5 D or more, while only 2% of eyes were likely to be undercorrected. The overcorrections were strongly associated with preoperative coma, trefoil, and spherical aberrations. We also noted that the postoperative cylinder is also more likely with eyes that had preoperative coma. Since this study, we have improved our results using a nomogram (the Rochester Nomogram), which modifies the treatment sphere based on the amount of preoperative higher order aberration and the preoperatively manifest sphere and cylinder.

Using the Rochester Nomogram, we subsequently treated 175 eyes that were more myopic and had more higher order aberration than in the FDA study and yet we achieved better results than in the FDA study. Using this nomogram, 160 out of 175 eyes (91.5%) were within ±0.5 D, or less, and all eyes (100%) were within ±1 D of the target refraction. Five out of 175 eyes (2.8%) had an overcorrection or residual hyperopia (>0.5 D), while 10 other eyes (5.7%) had undercorrection or residual myopia (>-0.5 D) demonstrating that the tendency toward hyperopic overcorrection with higher order aberration treatment was minimized.

In comparison, if we used a simple theoretical linear regression that only uses the preoperative wavefront sphere to optimize the postoperative sphere, our results would not have been as good. The simple theoretic linear regression recommended we use 93% of the Zywave wavefront sensor's preoperative Predicted Phoropter Refraction. If we had used the theoretic 93% nomogram, which does not take into account the effect of preoperative higher order aberration and manifest refraction, only 121 of the 175 eyes (69.1%) would have been within ±0.5 D or less of the target spherical equivalent (compared with 91.5% with the Rochester Nomogram). Thirty-nine of the 175 eyes (22.3%; compared with 2.8% with the Rochester Nomogram) would have been overcorrected and would have obtained residual hyperopia >0.5 D. In addition, 15 out of 175 eyes (8.6%) would have been undercorrected and would have had myopia (>–0.5 D) postoperatively (compared with 5.7% with the Rochester Nomogram). Note that the tendency toward greater accuracy and the reduced rate of postoperative hyperopic overcorrection with the Rochester Nomogram, which takes into account the amount of preoperative higher order aberration and manifest refraction compared with the theoretical 93% of the preoperative Zywave sphere, which only considers the relationship between the preoperative wavefront sphere and the postoperatively manifest sphere. We believe this approach of considering the effect of the preoperative manifest sphere and cylinder as well as the preoperative higher order aberrations on postoperative sphere and cylinder may have some merit and may warrant further studies by other groups using different laser platforms. We are currently working on clarifying the effect of third-order terms, coma, and trefoil on astigmatism.

5.7 Summary

The field of refractive surgery has been revolutionized by the use of wavefront sensing, which has helped us understand how effective our attempts were in reducing or minimizing an increase in ocular aberrations. With this understanding, we have been able to correct our patients' refractive errors, minimizing the increase in higher order aberration. Customized refractive surgery provides very good outcomes among normal eyes, but a better understanding of the role of biomechanics and tissue healing as well as how correction of preoperative higher order aberrations effects the correction of the sphere and cylinder is warranted [11, 60, 61]. The knowledge gained from such understanding will allow significant enhancements to outcomes and provide insights into customized treatment of eyes with increased higher order aberrations such as transplant eyes, post-refractive surgery, irregular astigmatism, etc. This exciting field has been led by the synergy between basic scientists and clinicians who have worked together to allow us to apply space age technology to improve patients' quality of vision.

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