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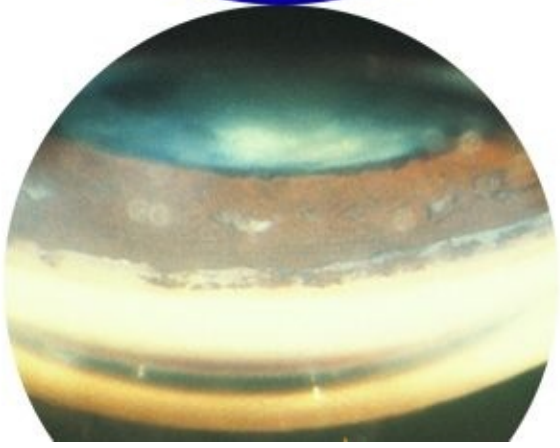
13

Refractive Surgery

2016–2017
BCSC
Basic and Clinical
Science Course™



Protecting Sight. Empowering Lives.™

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OF OPHTHALMOLOGY

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Refractive Surgery

Last major revision 2014–2015

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BCSC

Basic and Clinical Science Course™

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Published after collaborative review with the European Board of Ophthalmology subcommittee

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Cover image: From BCSC Section 10, *Glaucoma*. Typical gonioscopic appearance of angle recession. *Courtesy of Steven T. Simmons, MD*.

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General Introduction

The Basic and Clinical Science Course (BCSC) is designed to meet the needs of residents and practitioners for a comprehensive yet concise curriculum of the field of ophthalmology. The BCSC has developed from its original brief outline format, which relied heavily on outside readings, to a more convenient and educationally useful self-contained text. The Academy updates and revises the course annually, with the goals of integrating the basic science and clinical practice of ophthalmology and of keeping ophthalmologists current with new developments in the various subspecialties.

The BCSC incorporates the effort and expertise of more than 80 ophthalmologists, organized into 13 Section faculties, working with Academy editorial staff. In addition, the course continues to benefit from many lasting contributions made by the faculties of previous editions. Members of the Academy's Practicing Ophthalmologists Advisory Committee for Education, Committee on Aging, and Vision Rehabilitation Committee review every volume before major revisions. Members of the European Board of Ophthalmology, organized into Section faculties, also review each volume before major revisions, focusing primarily on differences between American and European ophthalmology practice.

Organization of the Course

The Basic and Clinical Science Course comprises 13 volumes, incorporating fundamental ophthalmic knowledge, subspecialty areas, and special topics:

1 Update on General Medicine
2 Fundamentals and Principles of Ophthalmology
3 Clinical Optics
4 Ophthalmic Pathology and Intraocular Tumors
5 Neuro-Ophthalmology
6 Pediatric Ophthalmology and Strabismus
7 Orbit, Eyelids, and Lacrimal System
8 External Disease and Cornea
9 Intraocular Inflammation and Uveitis
10 Glaucoma

11 Lens and Cataract
12 Retina and Vitreous
13 Refractive Surgery

References

Readers who wish to explore specific topics in greater detail may consult the references cited within each chapter and listed in the Basic Texts section at the back of the book. These references are intended to be selective rather than exhaustive, chosen by the BCSC faculty as being important, current, and readily available to residents and practitioners.

Study Questions and CME Credit

Each volume of the BCSC is designed as an independent study activity for ophthalmology residents and practitioners. The learning objectives for this volume are given following the Visual Acuity Chart. The text, illustrations, and references provide the information necessary to achieve the objectives; the study questions allow readers to test their understanding of the material and their mastery of the objectives. Physicians who wish to claim CME credit for this educational activity may do so by following the instructions given at the end of the book.

Conclusion

The Basic and Clinical Science Course has expanded greatly over the years, with the addition of much new text and numerous illustrations. Recent editions have sought to place a greater emphasis on clinical applicability while maintaining a solid foundation in basic science. As with any educational program, it reflects the experience of its authors. As its faculties change and as medicine progresses, new viewpoints are always emerging on controversial subjects and techniques. Not all alternate approaches can be included in this series; as with any educational endeavor, the learner should seek additional sources, including such carefully balanced opinions as the Academy's Preferred Practice Patterns.

The BCSC faculty and staff are continually striving to improve the educational usefulness of the course; you, the reader, can contribute to this ongoing process. If you have any suggestions or questions about the series, please do not hesitate to contact the faculty or the editors.

The authors, editors, and reviewers hope that your study of the BCSC will be of lasting value and that each Section will serve as a practical resource for quality patient care.

Visual Acuity Conversion Chart

Snellen Fraction					
Feet	Meters	4-Meter Standard	Decimal Notation (Visus)	Visual Angle Minute of Arc	LogMAR (Minimum Angle of Resolution)
20/10	6/3	4/2	2.00	0.50	–0.30
20/15	6/4.5	4/3	1.33	0.75	–0.12
20/20	**6/6**	**4/4**	**1.00**	**1.00**	**0.00**
20/25	6/7.5	4/5	0.80	1.25	0.10
20/30	6/9	4/6	0.67	1.50	0.18
20/40	6/12	4/8	0.50	2.00	0.30
20/50	6/15	4/10	0.40	2.50	0.40
20/60	6/18	4/12	0.33	3.00	0.48
20/80	6/24	4/16	0.25	4.00	0.60
20/100	6/30	4/20	0.20	5.00	0.70
20/120	6/36	4/24	0.17	6.00	0.78
20/150	6/45	4/30	0.13	7.50	0.88
20/200	6/60	4/40	0.10	10.00	1.00
20/400	6/120	4/80	0.05	20.00	1.30

For discussion of this chart, see BCSC Section 3, *Clinical Optics*.

Objectives

Upon completion of BCSC Section 13, *Refractive Surgery,* the reader should be able to

- state the contributions of the cornea's shape and tissue layers to the optics of the eye and how these components are affected biomechanically by different types of keratorefractive procedures
- describe the basic concepts of wavefront analysis and its relationship to different types of optical aberrations
- identify the general types of lasers used in refractive surgeries
- explain the steps--including medical and social history, ocular examination, and ancillary testing--in evaluating whether a patient is an appropriate candidate for refractive surgery
- for incisional keratorefractive surgery (radial keratotomy, transverse keratotomy, arcuate keratotomy, and limbal relaxing incisions), describe the history, patient selection, surgical techniques, outcomes, and complications
- list the various types of corneal onlays and inlays that have been used for refractive correction
- for surface ablation procedures, describe patient selection, epithelial removal and laser calibration techniques, refractive outcomes, and complications
- describe patient selection, surgical techniques, outcomes, and complications for laser in situ keratomileusis (LASIK)
- describe the different methods for creating a LASIK flap using a microkeratome or a femtosecond laser as well as the instrumentation and possible complications associated with each
- explain recent developments in the application of wavefront technology to surface ablation and LASIK
- for conductive keratoplasty, provide a brief overview of history, patient

selection, and safety issues

- describe how intraocular surgical procedures, including refractive lens exchange with intraocular lens (IOL) implantation or phakic IOL implantation, can be used in refractive correction, with or without corneal intervention
- describe the different types of IOLs used for refractive correction
- explain the leading theories of accommodation and how they relate to potential treatment of presbyopia
- describe nonaccommodative and accommodative approaches to the treatment of presbyopia
- state considerations for, and possible contraindications to, refractive surgery in patients with preexisting ocular and/or systemic disease
- list some of the effects of prior refractive procedures on later IOL calculations, contact lens wear, and ocular surgery
- describe the role of the US Food and Drug Administration (FDA) in the development and approval of ophthalmic devices used in refractive surgery

Introduction

Of all the subspecialties within ophthalmology, refractive surgery may be the most rapidly evolving. The language associated with visual acuity assessments is likewise changing in an effort to clarify intended meanings. With this edition, the BCSC Section 13 Committee introduces a switch in the manner in which the Section refers to the assessment of corrected and uncorrected visual acuity to reflect trends in the ophthalmic literature. Where the Section used the term *best-corrected visual acuity (BCVA)* in previous editions, it will now use *corrected distance visual acuity (CDVA)*. Similarly, *uncorrected visual acuity (UCVA)* will be replaced by *uncorrected distance visual acuity (UDVA)*. A visual acuity conversion chart is available on the inside front cover.

Refractive surgeons, as in all medical specialties, also use numerous abbreviations and acronyms in discussing and describing their field, especially for the continually emerging and changing refractive procedures. Thus, this edition also debuts another addition: the following list of frequently used terms as an aid to readers while reading this text as well as the refractive surgery literature in general.

Abbreviations and Acronyms Common to Refractive Surgery

ACS anterior ciliary sclerotomy

AHWP Asian Harmonization Working Party (for device regulation)

AK arcuate keratotomy

ArF argon-fluoride (laser)

ASA advanced surface ablation

BCVA best-corrected visual acuity (replaced by *corrected distance visual acuity,* ***CDVA,*** in this edition)

CCD charge-coupled device

CCL collagen crosslinking (also CXL)

CDVA corrected distance visual acuity (also called *best-corrected visual acuity, **BCVA***)

CE mark Conformite Europeene mark (product approval used in European countries, similar to US FDA approval)

CK conductive keratoplasty

CXL collagen crosslinking (also CCL)

D diopter

DLK diffuse lamellar keratitis

Epi-LASIK epipolis laser in situ keratomileusis

Femto-LASIK femtosecond laser in situ keratomileusis

FLEx femtosecond lenticule extraction

GAT Goldmann applanation tonometry

GHTF Global Harmonization Task Force (international medical device regulation)

HDE Humanitarian Device Exemption

Hex K hexagonal keratotomy

Ho:YAG holmium-yttrium-aluminum-garnet (laser)

ICL implantable collamer lens

ICRS intrastromal corneal ring segments

IOL intraocular lens

IOP intraocular pressure

I-S inferior-superior (value)

KC keratoconus

LASEK laser subepithelial keratomileusis

LASIK laser in situ keratomileusis

logMAR base-10 logarithm of the minimum angle of resolution

LRI limbal relaxing incision

LTK laser thermokeratoplasty

Nd:YAG neodymium-doped yttrium aluminum garnet (laser)

OCT optical coherence tomography

PCO posterior capsule opacification

PERK Prospective Evaluation of Radial Keratotomy (study)

PIOL phakic intraocular lens

PISK pressure-induced stromal keratopathy

PKP penetrating keratoplasty

PMD pellucid marginal degeneration

PMMA polymethylmethacrylate

PRK photorefractive keratectomy

PTK phototherapeutic keratectomy

ReLEx refractive lenticule extraction

RGP rigid gas-permeable (contact lenses)

RK radial keratotomy

RLE refractive lens exchange

RMS root mean square

RSB residual stromal bed

SIM K corneal power (K) simulation measurements

SMILE small-incision lenticule extraction

UCVA uncorrected visual acuity (replaced by *uncorrected distance visual acuity,* ***UDVA,*** in this edition)

UDVA uncorrected distance visual acuity (also called *uncorrected visual acuity,* ***UCVA***)

CHAPTER 1

The Science of Refractive Surgery

The goal of refractive surgery is to reduce dependence on contact lenses or spectacles for use in routine daily activities. A wide variety of surgical techniques and technologies are available, and all require an appropriate presurgical evaluation to determine the best technique and ensure the optimal outcome for each patient individually.

Refractive surgical procedures can be categorized broadly as *corneal* or *intraocular* (Table 1-1). Keratorefractive (corneal) procedures include incisional, laser ablation, lamellar implantation, corneal collagen shrinkage, and collagen crosslinking techniques. Intraocular refractive procedures include phakic intraocular lens (PIOL) implantation and cataract surgery or refractive lens exchange (RLE) with implantation of a monofocal, toric, multifocal, or accommodative intraocular lens. Each technique has advantages and disadvantages and should be specifically matched to the individual patient.

Table 1-1

Table 1-1 Overview of Refractive Procedures

Location	Type of Procedure	Specific Procedures	Common Abbreviations	Refractive Error Treated
Corneal	Incisional	Radial keratotomy	RK	Myopia (historical)
		Astigmatic keratotomy		
		Arcuate keratotomy	AK	Astigmatism
		Limbal relaxing incisions	LRI	Astigmatism
		Ruiz procedure		Astigmatism (historical)
		Hexagonal keratotomy	Hex K	Hyperopia (historical)
	Excimer laser	Surface ablation		Myopia, hyperopia, astigmatism
		Photorefractive keratectomy	PRK	+6.00 to –14.00 D
		Laser subepithelial keratomileusis	LASEK	+6.00 to –14.00 D
		Epipolis laser in situ keratomileusis	Epi-LASIK	+6.00 to –14.00 D
		Lamellar		
		Laser in situ keratomileusis	LASIK	+6.00 to –14.00 D
		Femtosecond laser in situ keratomileusis	Femto-LASIK	+6.00 to –14.00 D
		Refractive lenticule	ReLEx FLEx, SMILE	Investigational
	Nonlaser lamellar	Epikeratophakia, epikeratoplasty		Myopia, hyperopia, astigmatism (historical)
		Myopic keratomileusis		Myopia (historical)
		Intrastromal corneal ring segments	ICRS	Myopia, keratoconus
	Collagen shrinkage	Laser thermokeratoplasty	LTK	Hyperopia, astigmatism (historical)
		Conductive keratoplasty	CK	Hyperopia, astigmatism +0.75 to +3.25 D
	Collagen crosslinking		CCL, CXL	Keratoconus (investigational)
Intraocular	Phakic	Anterior chamber phakic intraocular lens (IOL) implantation		Myopia (in development)
		Iris-fixated phakic IOL implantation		Myopia (–5.00 to –20.00 D)
		Posterior chamber phakic IOL implantation		Myopia (–3.00 to –20.00 D)
	Pseudophakic	Refractive lens exchange (multifocal/ accommodating IOL)	RLE	Myopia, hyperopia, presbyopia
		Refractive lens exchange (toric IOL)		Myopia, hyperopia, astigmatism

This chapter reviews the fundamental corneal properties relevant to refractive surgery (focusing on keratorefractive procedures), corneal imaging for refractive surgery, and the effects of keratorefractive surgery on the cornea. It includes review of the optical principles discussed in BCSC Section 3, *Clinical Optics;* refractive errors (both lower- and higher-order aberrations); corneal biomechanics; corneal topography and tomography; wavefront analysis; laser biophysics and laser-tissue interactions; corneal biomechanical changes after surgery; and corneal wound healing.

Corneal Optics

The air-tear-film interface provides the majority of the optical power of the eye. Although a normal tear film has minimal deleterious effect, an abnormal tear film can have a dramatic impact on vision. For example, either excess tear film (eg, epiphora) or altered tear film (eg, dry eye or blepharitis) can decrease visual quality.

The optical power of the eye derives primarily from the anterior corneal curvature, which produces about two-thirds of the eye's refractive power, approximately +48.00 diopters (D). The overall corneal power is less (approximately +42.00 D) as a result

of the negative power (approximately -6.00 D) of the posterior corneal surface. Standard keratometers and Placido-based corneal topography instruments measure the anterior corneal radius of curvature and *estimate* total corneal power from these front-surface measurements. These instruments extrapolate the central corneal power *(K)* by measuring the rate of change in curvature from the paracentral 4-mm zone; this factor takes on crucial importance in the determination of IOL power after keratorefractive surgery (see Chapter 11). The normal cornea flattens from the center to the periphery by up to 4.00 D (this progressive flattening toward the peripheral cornea is referred to as a *prolate* shape) and is flatter nasally than temporally.

Almost all keratorefractive surgical procedures change the refractive state of the eye by altering corneal curvature. The tolerances involved in altering corneal dimensions are relatively small. For instance, changing the refractive status of the eye by 2.00 D may require altering the cornea's thickness by less than 30 mm. Thus, achieving predictable results is sometimes problematic because minuscule changes in the shape of the cornea may produce large changes in refraction.

Refractive Error: Optical Principles and Wavefront Analysis

One of the major applications of the wave theory of light is in wavefront analysis (see also BCSC Section 3, *Clinical Optics*, Chapter 6). Currently, wavefront analysis can be performed clinically by 4 methods: Hartmann-Shack, Tscherning, thin-beam single-ray tracing, and optical path difference. Each method generates a detailed report of lower-order aberrations (sphere and cylinder) and higher-order aberrations (spherical aberration, coma, and trefoil, among others). This information is useful both in calculating custom ablations to enhance vision or correct optical problems and in explaining patients' visual symptoms.

Measurement of Wavefront Aberrations and Graphical Representations

Although several techniques are available for measuring wavefront aberrations, the most popular in clinical practice is based on the Hartmann-Shack wavefront sensor. With this device, a low-power laser beam is focused on the retina. A point on the retina acts as a point source, and the reflected light is then propagated back (anteriorly) through the optical elements of the eye to a detector. In an aberration-free eye, all the rays would emerge in parallel, and the reflected wavefront would be a flat plane. In reality, the wavefront is not flat. To determine the shape of the reflected wavefront, an array of lenses samples parts of the wavefront and focuses light on a detector (Fig 1-1A). The extent of the divergence of the lenslet images from their expected focal points determines the wavefront error (Fig 1-1B). Optical aberrations measured by the aberrometer can be resolved into a variety of basic *shapes*, the combination of which represents the total aberration of the patient's ocular system, just as conventional

refractive error is a combination of sphere and cylinder.

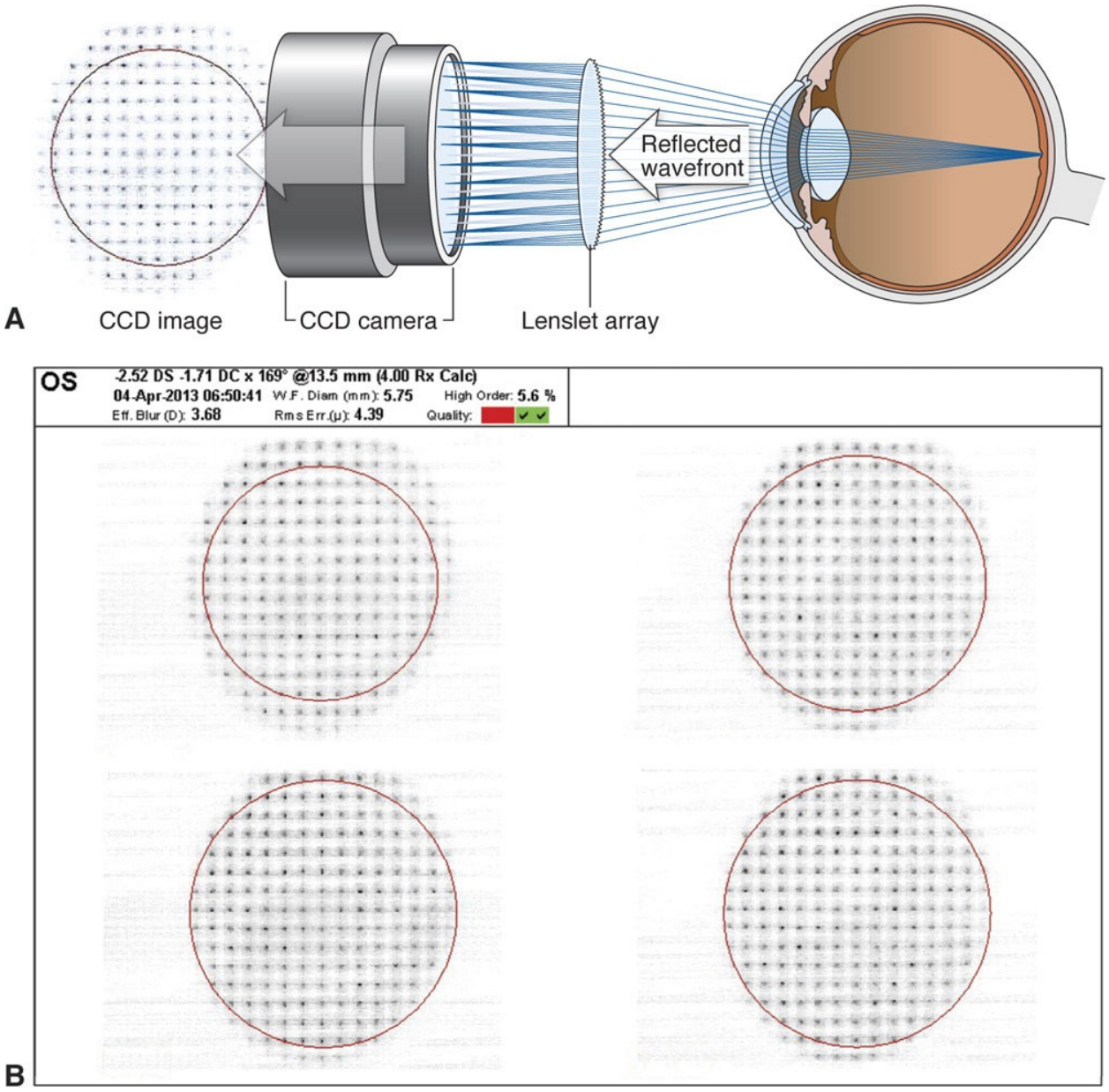


Figure 1-1 A, Schematic of a Hartmann-Shack wavefront sensor. As can be seen, the reflected wavefront passes through a grid of small lenses (the *lenslet array*), and the images formed are focused onto a charge-coupled device (CCD) chip. The degree of deviation of the focused images from the expected focal points determines the aberration and thus the wavefront error. **B,** An example of the images formed after the wavefront passes through the lenslet array. *(Part A redrawn by Mark Miller from a schematic image courtesy of Abbott Medical Optics Inc.; part B courtesy of M. Bowes Hamill, MD.)*

Currently, wavefront aberrations are most commonly specified by *Zernike polynomials*, which are the mathematical formulas used to describe the surfaces shown in Figures 1-2 through 1-6. Each aberration may be positive or negative in value and induces predictable alterations in the image quality. The magnitude of these aberrations

is expressed as a root mean square (RMS) error, which is the deviation of the wavefront averaged over the entire wavefront. The higher the RMS value is, the greater is the overall aberration for a given eye. The majority of patients have total RMS values less than 0.3 mm. Most higher-order Zernike coefficients have mean values close to zero. The most important Zernike coefficients affecting visual quality are coma, spherical aberration, and trefoil.

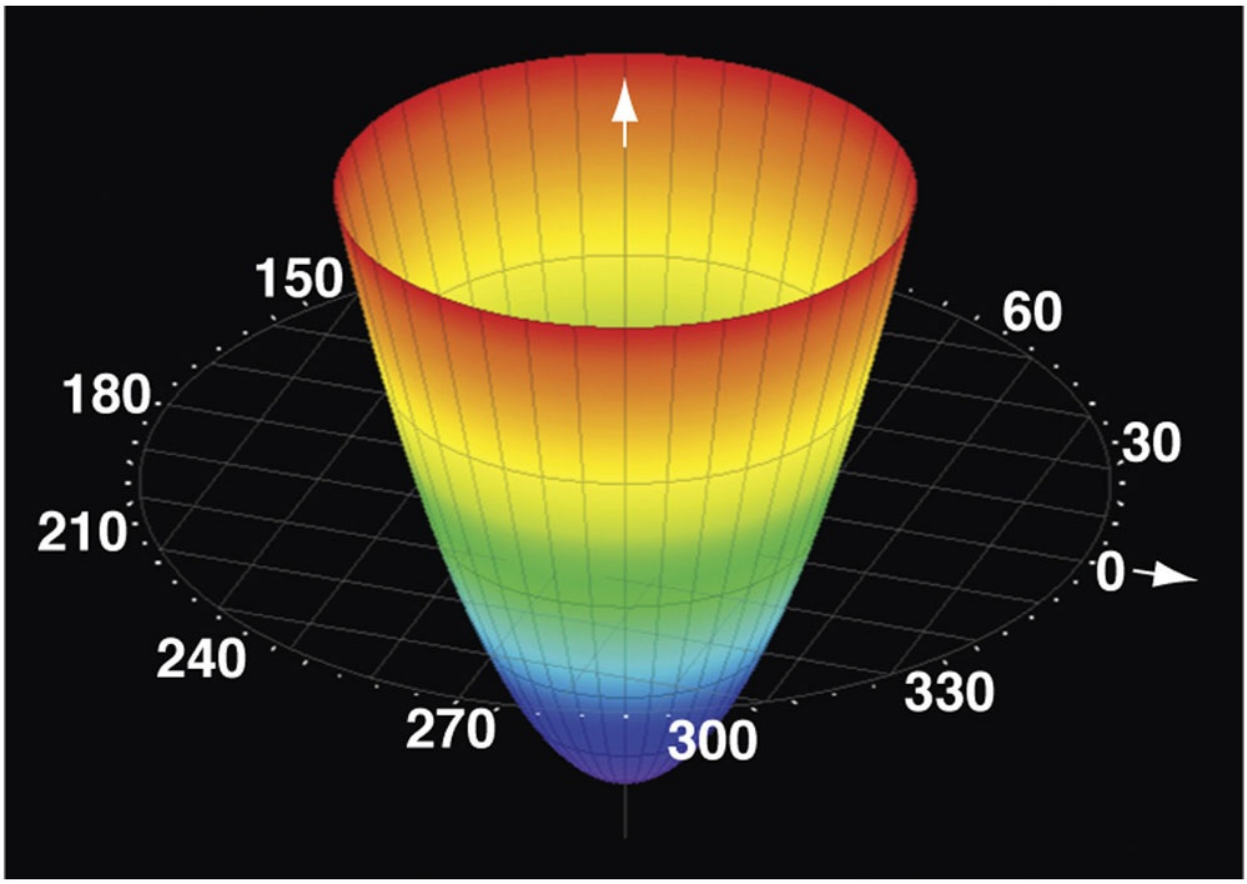


Figure 1-2 Zernike polynomial representation of defocus. *Arrows* indicate *z* axis (*arrow* emerging from cone) and zero axis. *(Courtesy of Tracey Technologies.)*

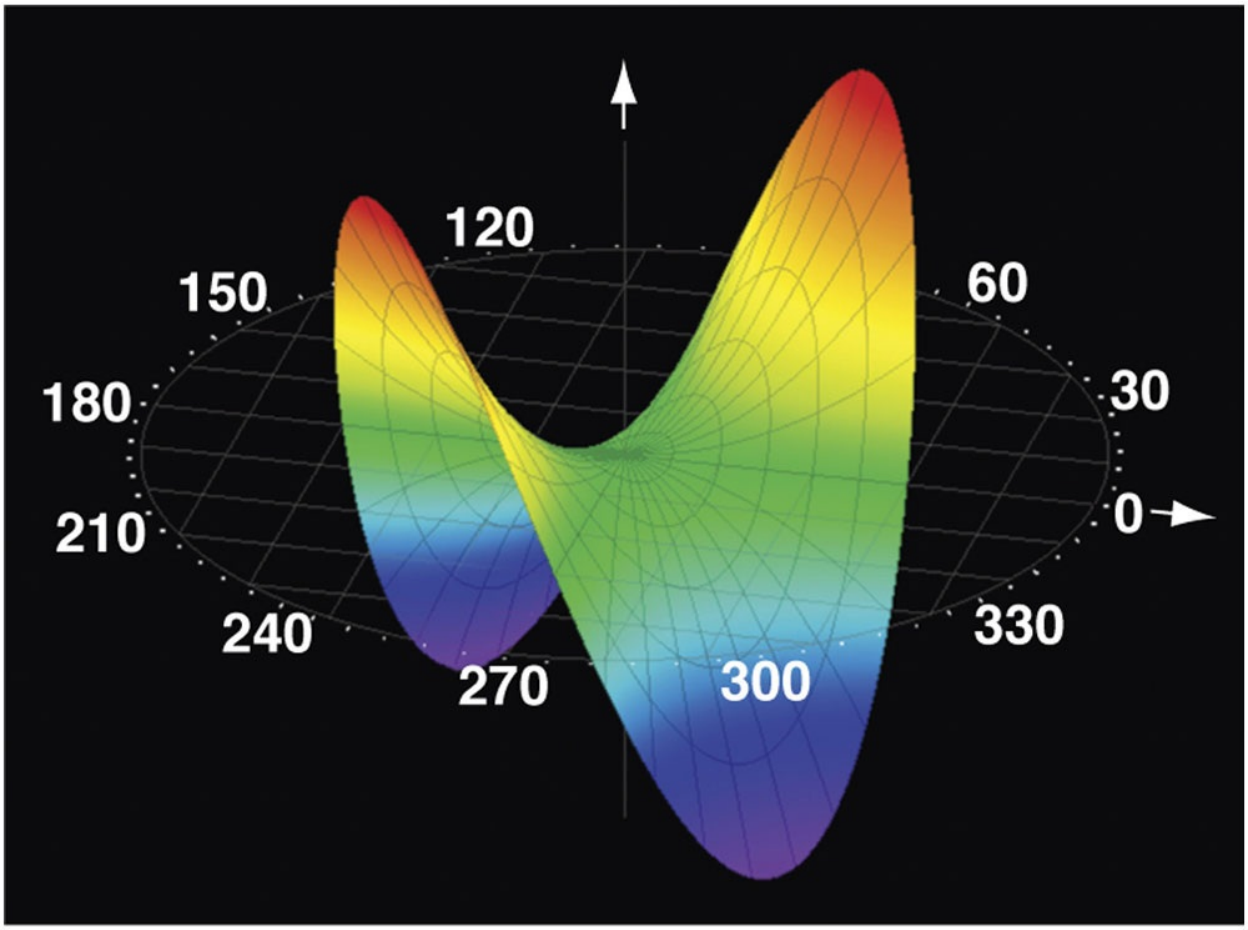


Figure 1-3 Zernike polynomial representation of astigmatism. *(Courtesy of Tracey Technologies.)*

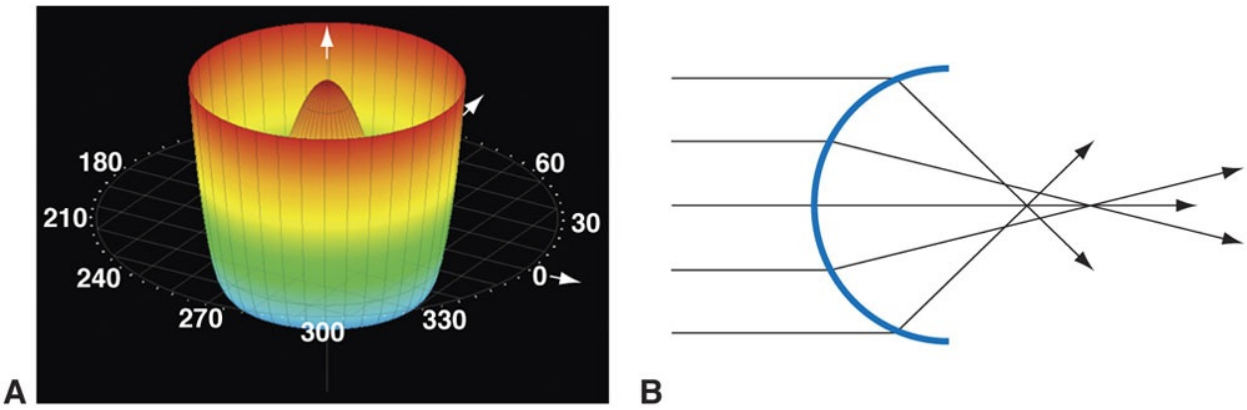


Figure 1-4 A, Zernike polynomial representation of spherical aberration. **B,** A schematic diagram of spherical aberration. Parallel rays impacting a spherical lens are refracted more acutely in the periphery than in the center of the lens. *(Part A courtesy of Tracey Technologies; part B developed by M. Bowes Hamill, MD.)*

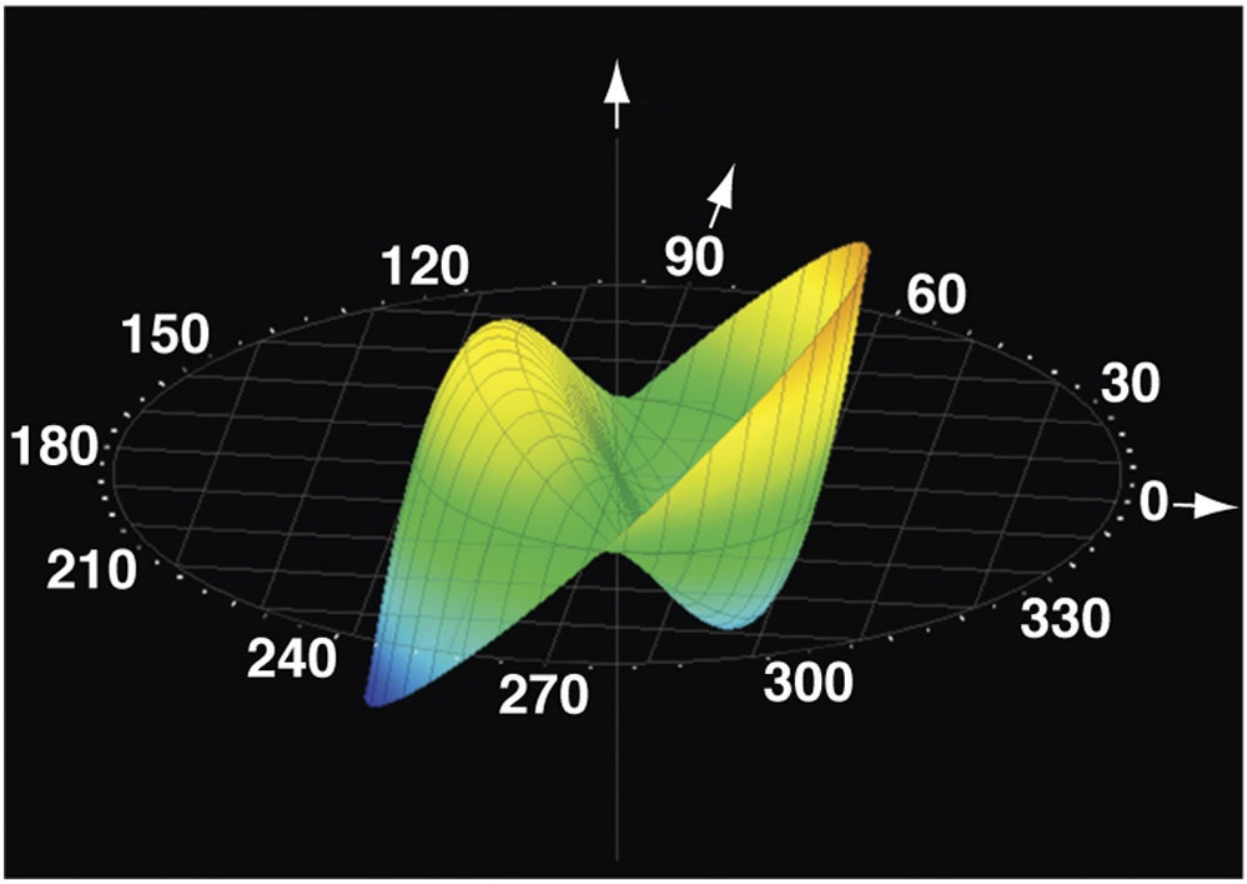


Figure 1-5 Zernike polynomial representation of coma. *(Courtesy of Tracey Technologies.)*

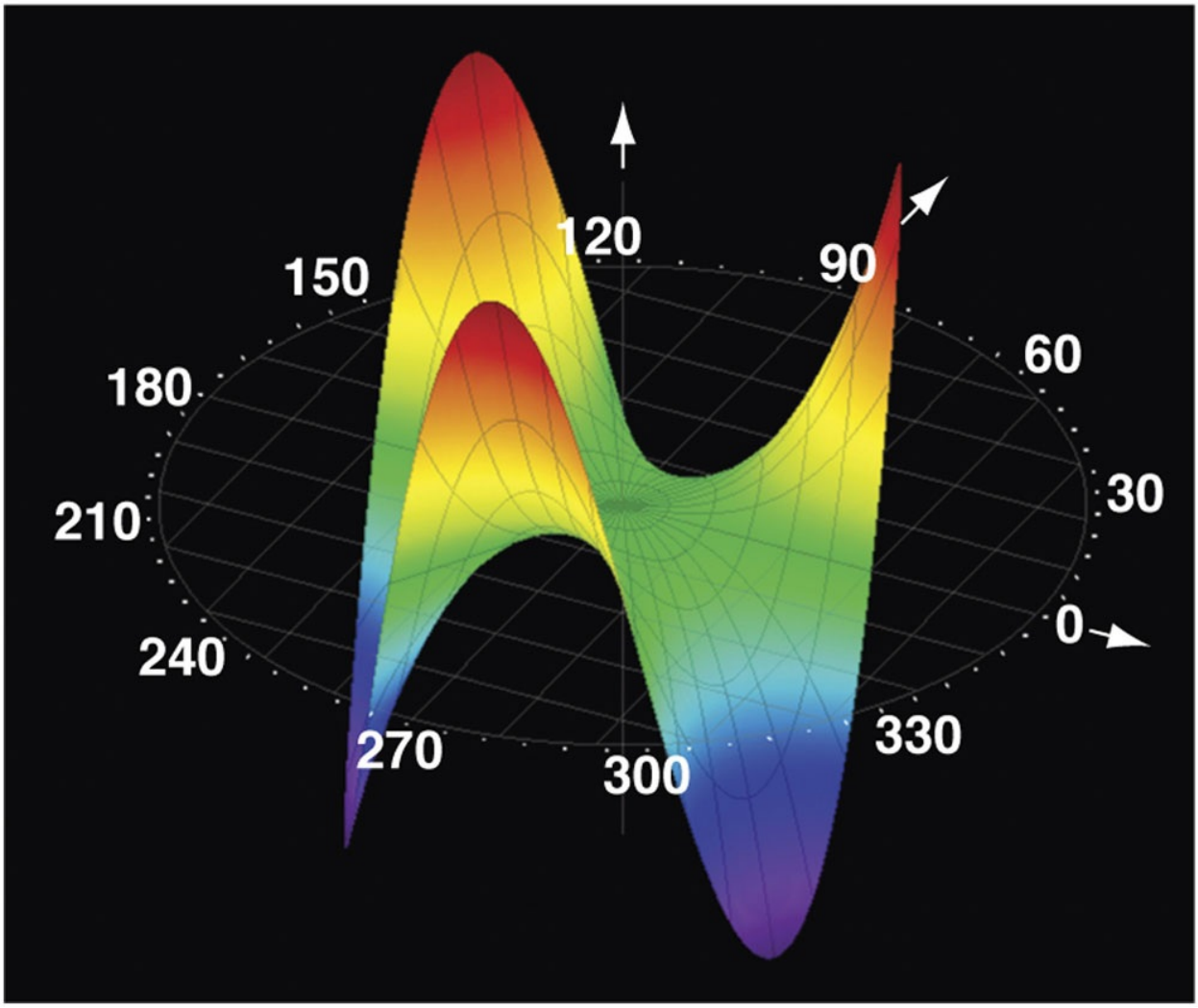


Figure 1-6 Zernike polynomial representation of trefoil. *(Courtesy of Tracey Technologies.)*

Fourier analysis is an alternative method of evaluating the output from an aberrometer. Fourier analysis involves a sine wave-derived transformation of a complex shape. Compared with shapes derived from Zernike polynomial analysis, the shapes derived from Fourier analysis are more detailed, theoretically allowing for the measurement and treatment of more highly aberrant corneas.

Lower-Order Aberrations

Myopia, hyperopia, and regular astigmatism are all lower-order (second-order) aberrations that can be expressed as wavefront aberrations. Myopia produces *positive defocus* (see Fig 1-2), whereas hyperopia produces *negative defocus*. Regular (cylindrical) astigmatism produces a wavefront aberration that has orthogonal (ie, facing at right angles) and oblique components (see Fig 1-3). Other lower-order

aberrations are non-visually significant aberrations known as *first-order aberrations*, such as vertical and horizontal prisms and zero-order aberrations (piston).

Higher-Order Aberrations

Wavefront aberration is highly dependent on pupil size, with increased higher-order aberrations apparent as the pupil dilates. Higher-order aberrations also increase with age, although the clinical effect is thought to be balanced by the increasing miosis of the pupil with age. Although lower-order aberrations decrease after laser vision correction, higher-order aberrations, particularly spherical aberration and coma, may increase after conventional surface ablation or laser in situ keratomileusis (LASIK) for myopia. This increase is correlated with the degree of preoperative myopia. After standard hyperopic laser vision correction, higher-order aberrations increase even more than they do in myopic eyes but in the opposite (toward negative values) direction. Compared with conventional treatments, customized excimer laser treatments may decrease the number of induced higher-order aberrations and provide a higher quality of vision, particularly in mesopic conditions.

Spherical aberrations

When peripheral light rays impacting a lens or the cornea focus in front of more central rays, the effect is called spherical aberration (see Fig 1-4A, B). Clinically, this radially symmetric fourth-order aberration is the cause of night myopia and is commonly increased after myopic LASIK and surface ablation. It results in halos around point images. Spherical aberration is the most significant higher-order aberration. It may increase depth of field but decreases contrast sensitivity.

Coma and trefoil

With coma, a third-order aberration, rays at one edge of the pupil come into focus before rays at the opposite edge do. The effective image resembles a comet, having vertical and horizontal components (see Fig 1-5). As can be seen by examining the illustrations, light rays entering the system do not focus on a plane; rather, one edge of the incoming beam focuses either in front of or behind the opposite edge of the beam. If one were to examine the image generated by an incoming light beam passing through an optical system with a coma aberration, the image would appear "smeared," looking somewhat like a comet with a zone of sharp focus at one edge of the image tailing off to a fuzzy focus at the opposite edge of the beam. Coma is common in patients with decentered corneal grafts, keratoconus, and decentered laser ablations.

Trefoil, also a third-order aberration, can occur after refractive surgery and produces less degradation in image quality than does coma of similar RMS magnitude (see Fig 1-6).

Other higher-order aberrations

There are numerous other higher-order aberrations, of which only a small number are of clinical interest. As knowledge of surgically induced aberration increases, more of the basic types of aberrations may become clinically relevant.

Effect of excimer laser ablation on higher-order aberrations

Whereas use of conventional (non-wavefront-guided) excimer laser ablations typically increases higher-order aberrations, both wavefront-optimized and wavefront-guided ablations tend to induce fewer higher-order aberrations and may, in principle, be able to reduce preexisting higher-order optical aberrations.

Klyce SD, Karon MD, Smolek MK. Advantages and disadvantages of the Zernike expansion for representing wave aberration of the normal and aberrated eye. *J Refract Surg.* 2004; 20(5):S537-S541.

Salmon TO, van de Pol C. Normal-eye Zernike coefficients and root-mean-square wavefront errors. *J Cataract Refract Surg.* 2006;32(12):2064-2074.

Stonecipher KG, Kezirian GM. Wavefront-optimized versus wavefront-guided LASIK for myopic astigmatism with the ALLEGRETTO WAVE: three-month results of a prospective FDA trial. *J Refract Surg.* 2008;24(4):S424-S430.

Corneal Biomechanics

The cornea consists of collagen fibrils arranged in approximately 200 parallel lamellae that extend from limbus to limbus. The fibrils are oriented at angles to the fibrils in adjacent lamellae. This network of collagen is responsible for the mechanical strength of the cornea. The fibrils are more closely packed in the anterior two-thirds of the cornea and in the axial, or prepupillary, cornea than they are in the peripheral cornea. (See BCSC Section 8, *External Disease and Cornea.*)

Structural differences between the anterior and posterior stroma affect the biomechanical behavior of the cornea. These include differences in glycosaminoglycans as well as more lamellar interweaving in the anterior corneal stroma; thus, the anterior cornea swells far less than the posterior cornea does. Stress within the tissue is partly related to intraocular pressure (IOP) but not in a linear manner under physiologic conditions (normal IOP range). When the cornea is in a dehydrated state, stress is distributed principally to the posterior layers or uniformly over the entire cornea. When the cornea is edematous, the anterior lamellae take up most of the strain. Most keratorefractive procedures alter corneal biomechanical properties either directly (eg, radial keratotomy weakening the cornea to induce refractive change) or indirectly (eg, excimer laser surgery weakening the cornea by means of tissue removal). The lack of uniformity of biomechanical load throughout the cornea explains the variation in corneal biomechanical response to different keratorefractive procedures. For instance, LASIK has a greater overall effect than does photorefractive keratectomy (PRK) on corneal biomechanics, not only because a lamellar flap is created but also because the laser ablation occurs in the deeper, weaker corneal stroma (a more detailed discussion can be found later in this chapter and in Chapter 5).

Corneal Imaging for Keratorefractive Surgery

Corneal shape, curvature, and thickness profiles can be generated from a variety of technologies such as Placido disk-based systems and elevation-based systems (including scanning-slit systems and Scheimpflug imaging). Each technology conveys different information about corneal curvature, anatomy, and biomechanical function. In addition, computerized topographic and tomographic systems may display other data: pupil size and location, indices estimating regular and irregular astigmatism, estimates of the probability of having keratoconus, simulated keratometry, and corneal asphericity. Other topography systems may integrate wavefront aberrometry data with topographic data. Although this additional information can be useful in preoperative surgical evaluations, no automated screening system can supplant clinical experience in evaluating corneal imaging.

The degree of asphericity of the cornea can be quantified by determining the *Q* value, with $Q = 0$ for spherical corneas, $Q < 0$ for prolate corneas (relatively flatter periphery), and $Q > 0$ for oblate corneas (relatively steeper periphery). A normal cornea is prolate, with an asphericity *Q* value of -0.26. Prolate corneas minimize spherical aberrations by virtue of their relatively flat peripheral curve. Conversely, oblate corneal contours, in which the peripheral cornea is steeper than the center, increase the probability of having induced spherical aberrations. After conventional refractive surgery for myopia, with the resulting flattening of the corneal center, corneal asphericity increases in the oblate direction, which may cause degradation of the optics of the eye.

Corneal Topography

Corneal topography provides highly detailed information about corneal curvature. Topography is evaluated using keratoscopic images, which are captured from Placido disk patterns that are reflected from the tear film overlying the corneal surface and then converted to computerized color scales (Fig 1-7). Because the image is generated from the anterior surface of the tear film, irregularities in tear composition or volume can have a major impact on the quality and results of a Placido disk-based system. Because of this effect, reviewing the Placido image (image of the mires) prior to interpreting the maps and subsequent numerical data is a wise approach. Additionally, Placido disk-based systems are referenced from the line that the instrument makes to the corneal surface (termed the *vertex normal*). This line may not necessarily be the patient's line of sight or the visual axis, which may lead to confusion in interpreting topographic maps. For a more extensive discussion of other uses of computerized corneal topography, refer to BCSC Section 3, *Clinical Optics*, and Section 8, *External Disease and Cornea*. Generally, data from the reflection of the mires from the topographic instruments are presented not only numerically but--more important for clinical

evaluation--also as an image, with corneal curvature typically represented utilizing axial and tangential methods.

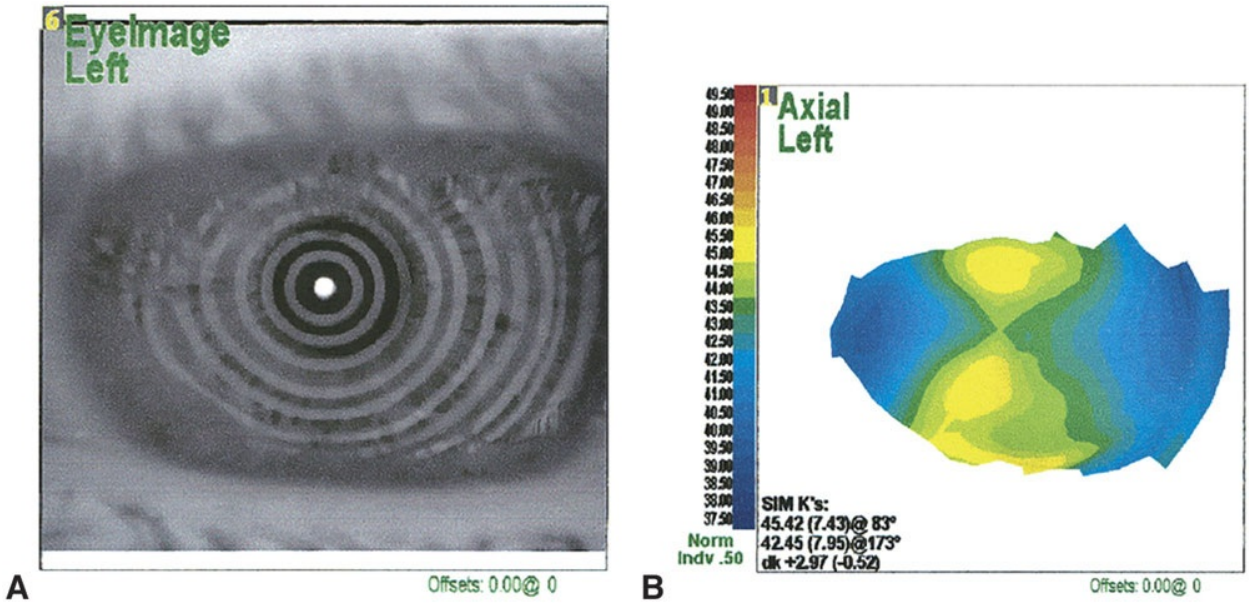


Figure 1-7 Placido imaging of the cornea. **A,** The raw Placido disk image; **B,** computer-generated color map derived from data in **A.** *(Courtesy of J. Bradley Randleman, MD.)*

Axial power and curvature

Axial power representation comes from the supposition that the cornea is a sphere and that the angle of incidence of the instrument is normal to the cornea. Axial power is based on the concept of "axial distance" (Fig 1-8). As can be seen from the illustration, axial power underestimates steeper curvatures and overestimates flatter curvatures. This representation also is extremely dependent on the reference axis employed--optical or visual.

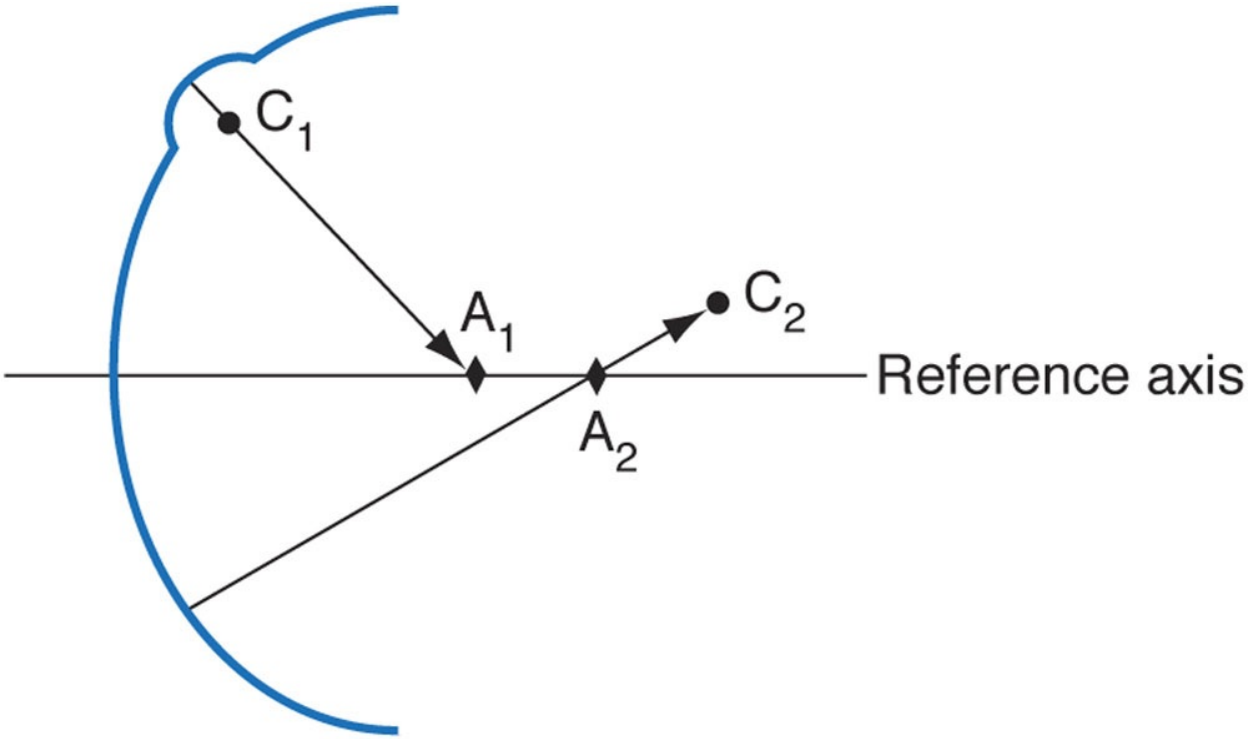


Figure 1-8 Schematic representation of the difference between axial distance (axial curvature) and radius of curvature for 2 points on a curved surface. Points C_1 and C_2 represent the centers of curvature of their respective surface points. Points A_1 and A_2 represent the endpoints of the axial distances for the given axis. As can be seen, local, steeper areas of curvature are underestimated, whereas flatter areas are overestimated. *(Adapted from Roberts C. Corneal topography: a review of terms and concepts.* J Cataract Refract Surg. *1996;22(5):624-629, Fig 3.)*

Maps generated from the same cornea but using different reference axes look very different from one another. Axial power representations actually average the corneal powers and thereby provide a "smoother" representation of corneal curvature than does the tangential, or "instantaneous," method. Recall that the curvature and power of the central 1-2 mm of the cornea are generally not well imaged by Placido disk techniques but can be closely approximated by the axial power and curvature indices (formerly called *sagittal curvature*); however, the central measurements are extrapolated and thus are potentially inaccurate. These indices also fail to describe the true shape and power of the peripheral cornea. Topographic maps displaying axial power and curvature provide an intuitive sense of the physiologic flattening of the cornea but do not represent the true refractive power or the true curvature of peripheral regions of the cornea (Fig 1-9).

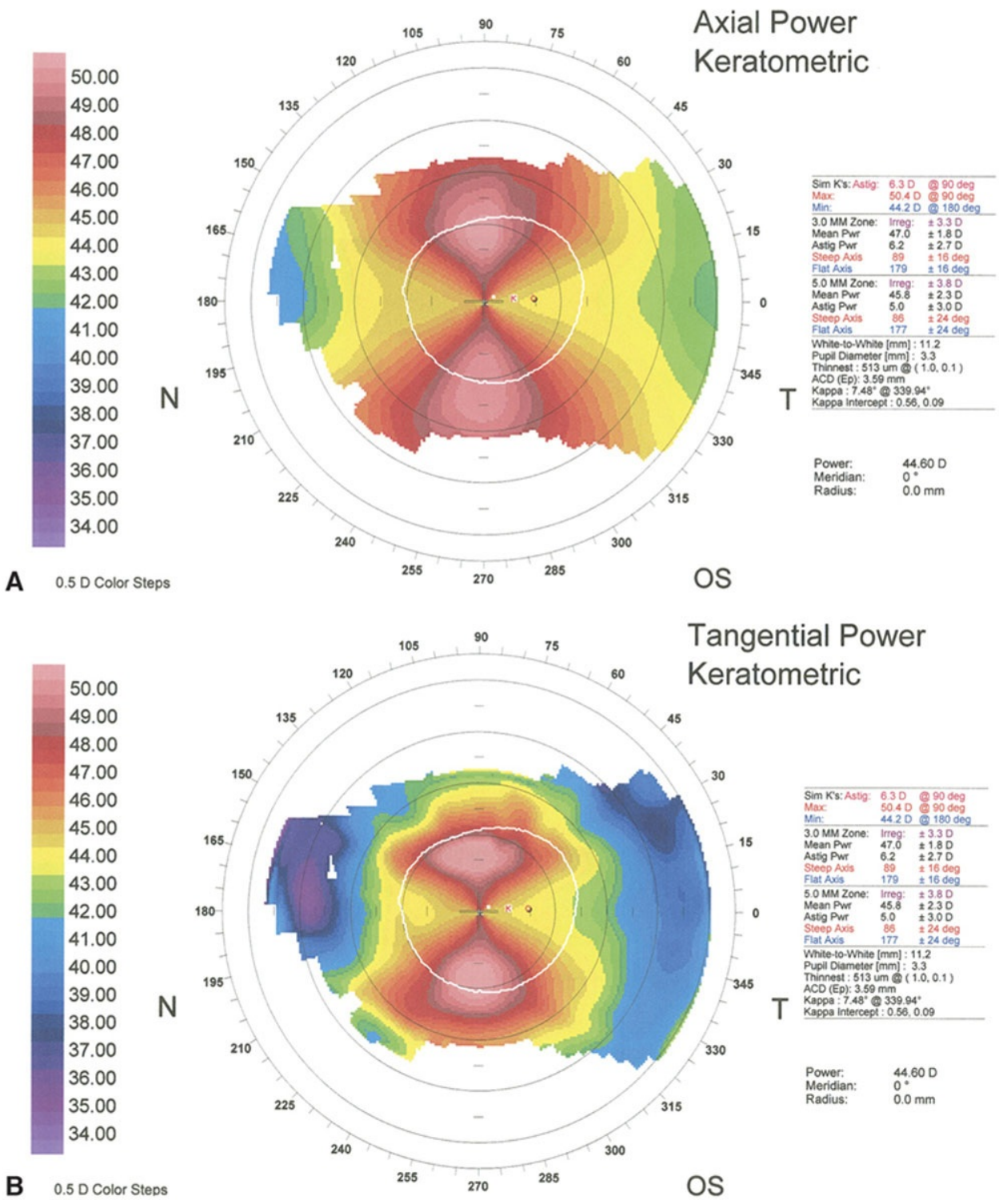


Figure 1-9 Examples of curvature maps. **A,** Axial (sagittal); **B,** instantaneous (tangential). *(Courtesy of J. Bradley Randleman, MD.)*

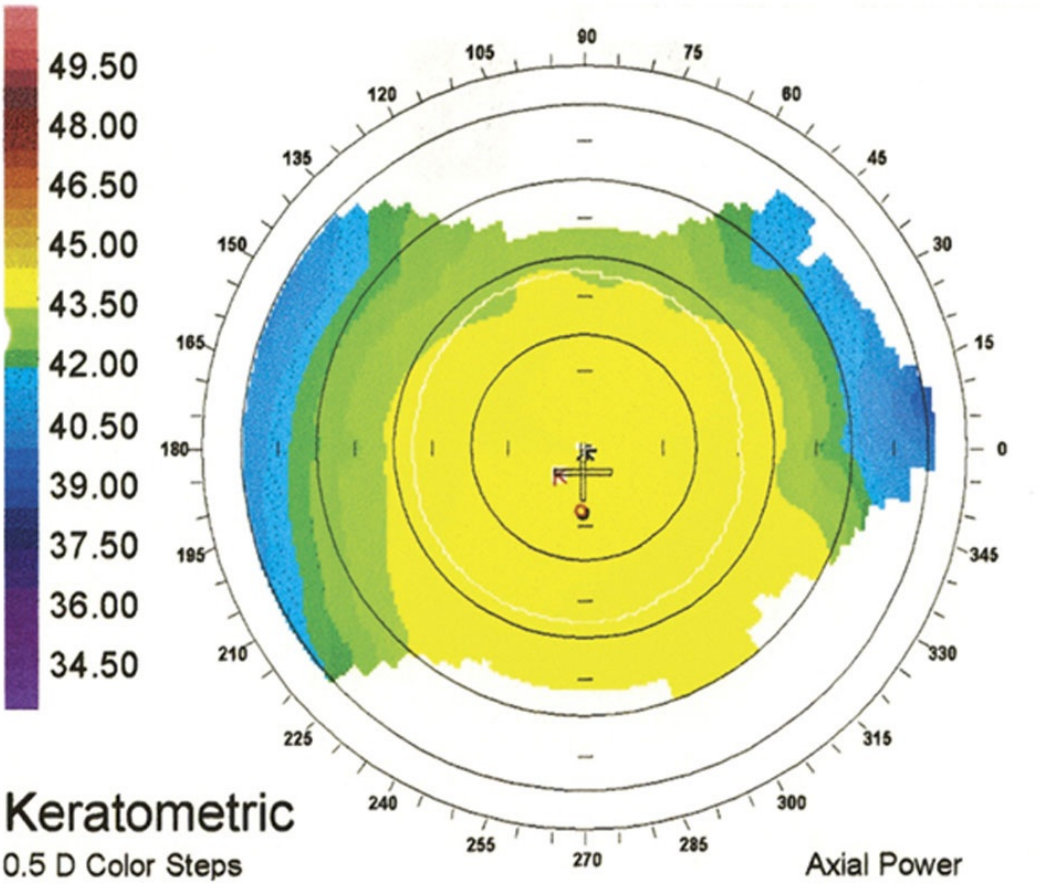
Instantaneous power and curvature

A second method of describing the corneal curvature on Placido disk-based topography is the *instantaneous radius of curvature* (also called *meridional* or *tangential power*). The instantaneous radius of curvature is determined by taking a perpendicular path through the point in question from a plane that intersects the point and the visual axis, while allowing the radius to be the length necessary to correspond to a sphere with the same curvature at that point. The curvature, which is expressed in diopters, is estimated by the difference between the corneal index of refraction and 1.000, divided by this tangentially determined radius. A tangential map typically shows better sensitivity to peripheral changes with less "smoothing" of the curvature than an axial map shows (see Fig 1-9). In these maps, diopters are relative units of curvature and are not the equivalent of diopters of corneal power. The potential benefit of this method's increased sensitivity is balanced by its tendency to document excessive detail ("noise"), which may not be clinically relevant.

For routine refractive screening, most surgeons have the topographic output in the axial (sagittal) curvature mode rather than the instantaneous (tangential) mode.

Corneal topography and astigmatism

A normal topographic image of a cornea without astigmatism demonstrates a relatively uniform color pattern centrally with a natural flattening in the periphery (Fig 1-10). *Regular astigmatism* is uniform steepening along a single corneal meridian that can be fully corrected with a cylindrical lens. Topographic imaging of regular astigmatism demonstrates a symmetric "bow-tie" pattern along a single meridian with a straight axis on both sides of center (Fig 1-10B). The bow-tie pattern on topographic maps is an artifact of Placido-based imaging; that is, because the Placido image cannot detect curvature at the central measurement point, the corneal meridional steepening seems to disappear centrally and become enhanced as the imaging moves farther from center.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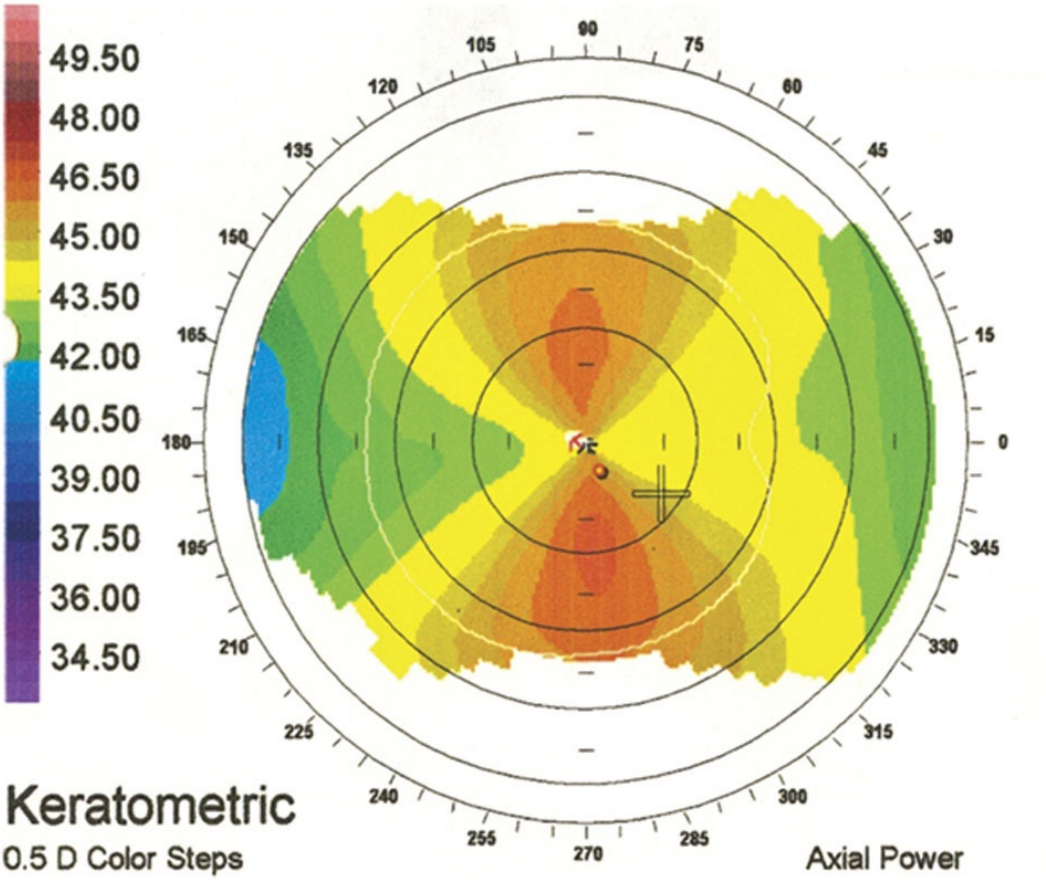
A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225
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195
180
165
150
135
120
105
Keratometric
0.5 D Color Steps
Axial Power

B

Figure 1-10 Normal corneal topographic patterns. **A,** Round; **B,** symmetric bow tie. *(Courtesy of J. Bradley Randleman, MD.)*

Irregular astigmatism is nonuniform corneal steepening from a variety of causes that cannot be corrected by cylindrical lenses. Irregular astigmatism decreases corrected distance visual acuity (CDVA; also called *best-corrected visual acuity, BCVA*) and may reduce contrast sensitivity and increase visual aberrations, depending on the magnitude of irregularity. Rigid gas-permeable and hard contact lenses can correct visual acuity reductions resulting from corneal irregular astigmatism by bridging the irregular corneal surface and the contact lens with the tear film. For more information on irregular astigmatism, see BCSC Section 3, *Clinical Optics*.

Corneal topography is very helpful in evaluating eyes with irregular astigmatism. Topographic changes include nonorthogonality of the steep and flat axes (Fig 1-11). Asymmetry between the superior and inferior or nasal and temporal halves of the cornea may also be revealed by corneal topography, although these patterns are not necessarily indicative of corneal pathology. In contrast, wavefront analysis can demonstrate higher-order aberrations (such as coma, trefoil, quadrafoil, or secondary astigmatism). The ability to differentiate regular from irregular astigmatism has clinical significance in keratorefractive surgery. Traditional excimer laser ablation can treat spherocylindrical errors but does not effectively treat irregular astigmatism. Topography-guided ablation may be useful in treating irregular astigmatism not caused by early corneal ectatic disorders.

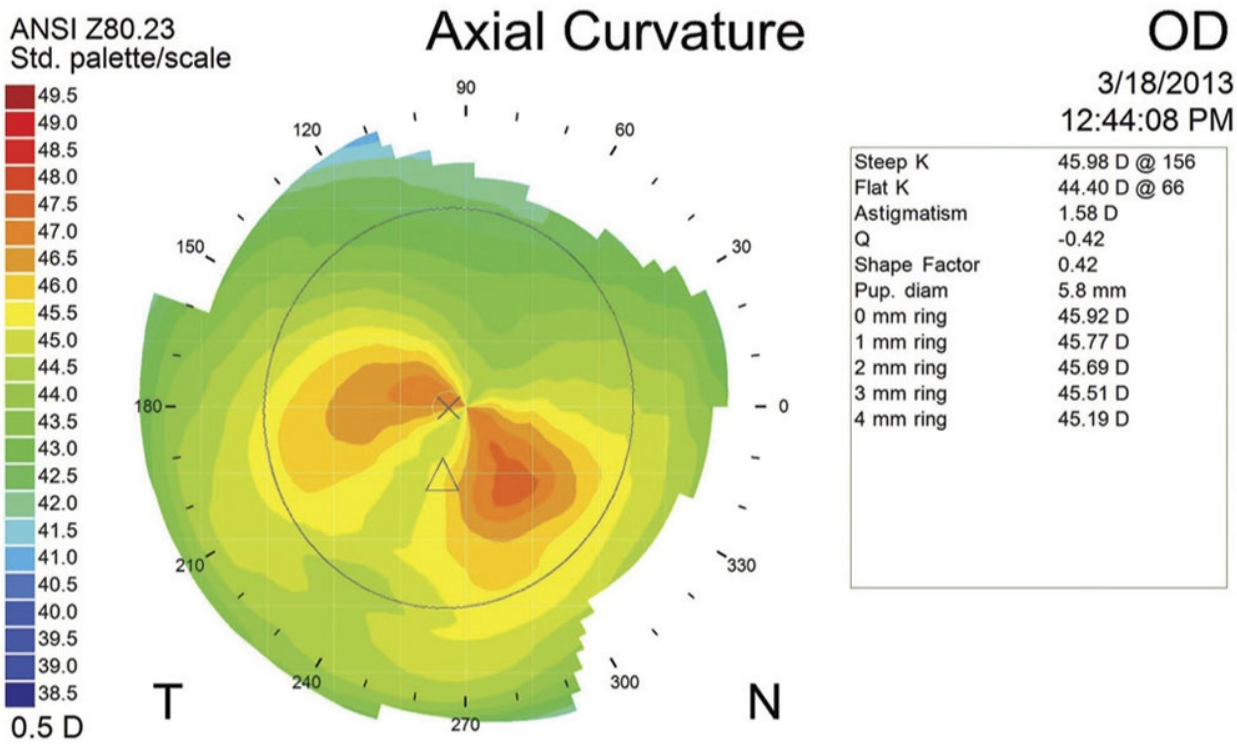


Figure 1-11 A curvature map showing nonorthogonal axes, which may indicate pathology that would contraindicate refractive surgery. *(Courtesy of Gregg J. Berdy, MD.)*

Limitations of corneal topography

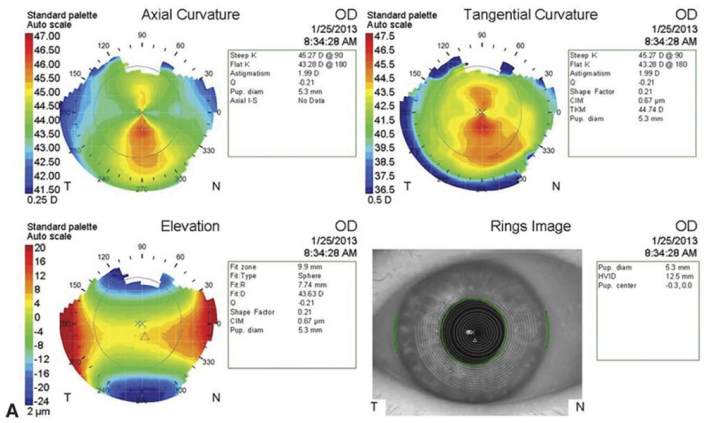
In addition to the limitations of the specific algorithms and the variations in terminology among manufacturers, the accuracy of corneal topography may be affected by other potential problems:

- tear-film effects
- misalignment (misaligned corneal topography may give a false impression of corneal apex decentration suggestive of keratoconus)
- instability (test-to-test variation)
- insensitivity to focus errors
- limited area of coverage (central and limbal)
- decreased accuracy of corneal power simulation measurements (SIM K) after refractive surgical procedures
- decreased accuracy of posterior surface elevation values in the presence of corneal opacities or, often, after refractive surgery (with scanning-slit technology)

Roberts C. Corneal topography: a review of terms and concepts. *J Cataract Refract Surg.* 1996; 22(5):624-629.

Corneal Tomography

Whereas surface corneal curvature (power) is best expressed by Placido imaging, overall corneal shape, including spatial thickness profiles, is best expressed by computed tomography. A variety of imaging systems are available that take multiple slit images and reconstruct them into a corneal-shape profile, including anterior and posterior corneal elevation data. These include scanning-slit technology and Scheimpflug-based imaging systems (Fig 1-12). To represent shape directly, color maps may be used to display a *z-height* from an arbitrary plane such as the iris plane; however, in order to be clinically useful, corneal surface maps are plotted to show differences from best-fit spheres or other objects that closely mimic the normal corneal shape (Fig 1-13). In general, each device calculates the best-fit sphere for each map individually. For this reason, comparing elevation maps is not exact because they frequently have different referenced best-fit sphere characteristics.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Axial Curvature
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Steep K 45.27 D @ 90
Flat K 43.28 D @ 180
Astigmatism 1.99 D
Q -0.21
Pup. diam 5.3 mm
Axial I-S No Data
Tangential Curvature
Shape Factor 0.21
CIM 0.67 µm
TKM 44.74 D
Elevation
Fit zone 9.9 mm
Fit Type Sphere
Fit R 7.74 mm
Fit D 43.63 D
Rings Image
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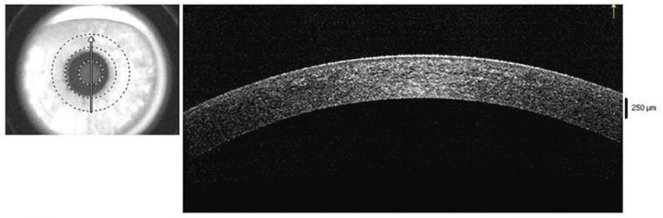
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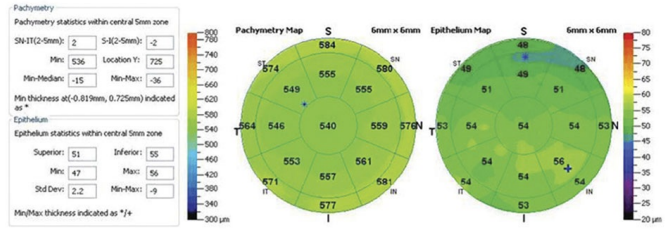
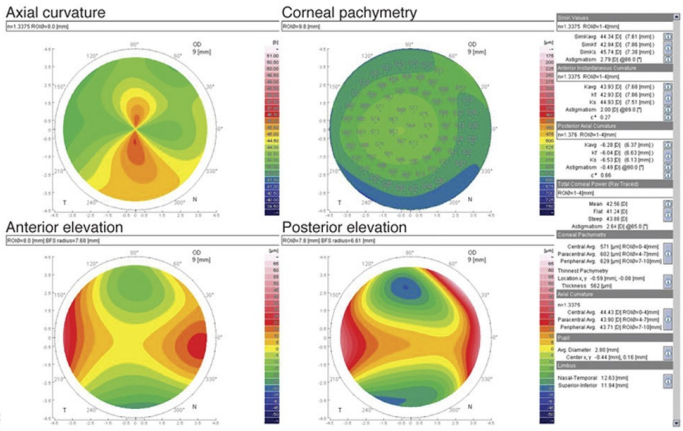
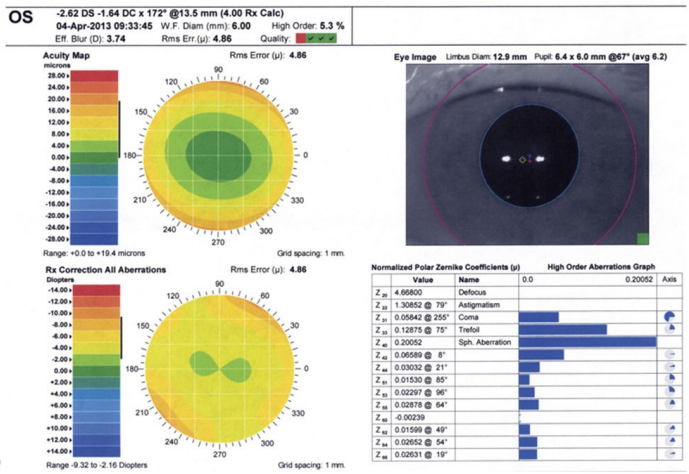

Pachymetry
Pachymetry statistics within central 5mm zone
SN-IT(2-5mm): 2
S-I(2-5mm): -2
Minc 536
Location Y: 725
Min-Median: -15
Min-Max: -36
Min thickness at(-0.819mm, 0.725mm) indicated as *
Epithelium
Epithelium statistics within central 5mm zone
Superior: 51
Inferior: 55
Minc 47
Max: 56
Std Dev: 2.2
Min-Max: -9
Min/Max thickness indicated as */+
Pachymetry Map
6mm x 6mm
Epithelium Map
B


Axial curvature
Corneal pachymetry
Anterior elevation
Posterior elevation
C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Eff. Blur (D): 3.74 Rms Err.(µ): 4.86 Quality:
Acuity Map
Rms Error (µ): 4.86
Range: +0.0 to +19.4 microns
Grid spacing: 1 mm.
Eye Image
Limbus Diam: 12.9 mm Pupil: 6.4 x 6.0 mm @67° (avg 6.2)
Rx Correction All Aberrations
Rms Error (µ): 4.86
Range -9.32 to -2.16 Diopters
Grid spacing: 1 mm.
Normalized Polar Zernike Coefficients (µ)
High Order Aberrations Graph
Value
Name
Axis
4.66800 Defocus
1.30852 @ 79° Astigmatism
0.05842 @ 255° Coma
0.12875 @ 75° Trefoil
0.20052 Sph. Aberration
0.06589 @ 8°
0.03032 @ 21°
0.01530 @ 85°
0.02297 @ 96°
0.02878 @ 64°
-0.00239
0.01599 @ 49°
0.02652 @ 54°
0.02631 @ 19°
D

Figure 1-12 Different options for corneal imaging. All images are of the same patient taken at the same visit. **A,** Placido disk-based corneal curvature map showing axial and tangential curvature maps as well as the elevation map and the Placido rings image. Recall that this mapping technology analyzes *only* the surface characteristics of the cornea. **B,** Optical coherence tomography (OCT) image of the same cornea shown in **A.** Note that the corneal thickness profile (of the stroma as well as the epithelium) is well demonstrated, but the overall surface curvature is not. Had this patient previously undergone either LASIK or Descemet membrane-stripping keratoplasty (DSEK), which he has not, the demarcation line would have been well imaged with this technology. **C,** Corneal tomography image using dual Scheimpflug/Placido-based technology of the same patient and eye shown in **A** and **B.** The surface curvature, pachymetry, and anterior and posterior elevation mappings are demonstrated. Numerical values are shown along the right side. **D,** Wavescan image from a device like that illustrated in Fig 1-1A, taken of the fellow eye to that represented in **A, B,** and **C.** Note that this map does not show any corneal surface contours or features but rather provides information about the optics of the entire ocular system. As such, it can provide information on the refractive error and aberrations of the entire eye. *(Images courtesy of M. Bowes Hamill, MD.)*

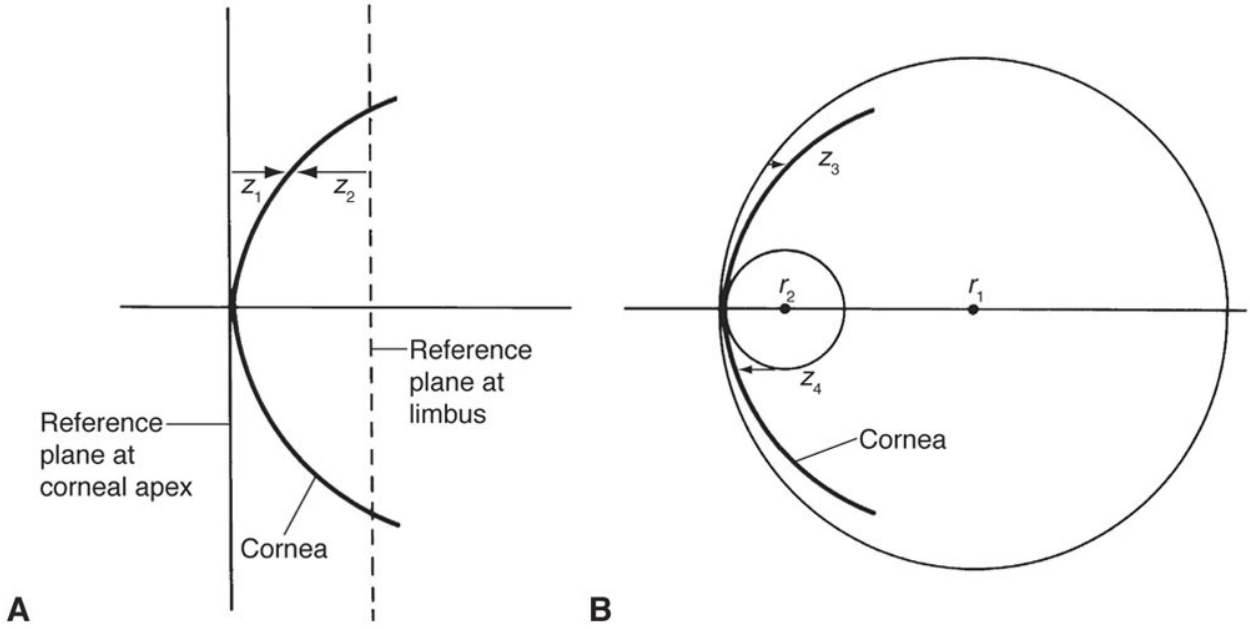


Figure 1-13 Height maps (typically in mm). **A,** Height relative to plane surface; z_1 is below the surface parallel to the corneal apex, and z_2 is above the surface parallel to the corneal limbus. **B,** Height relative to reference sphere; z_3 is below a flat sphere of radius r_1, and z_4 is above a steep sphere of radius r_2. *(Illustration by Christine Gralapp.)*

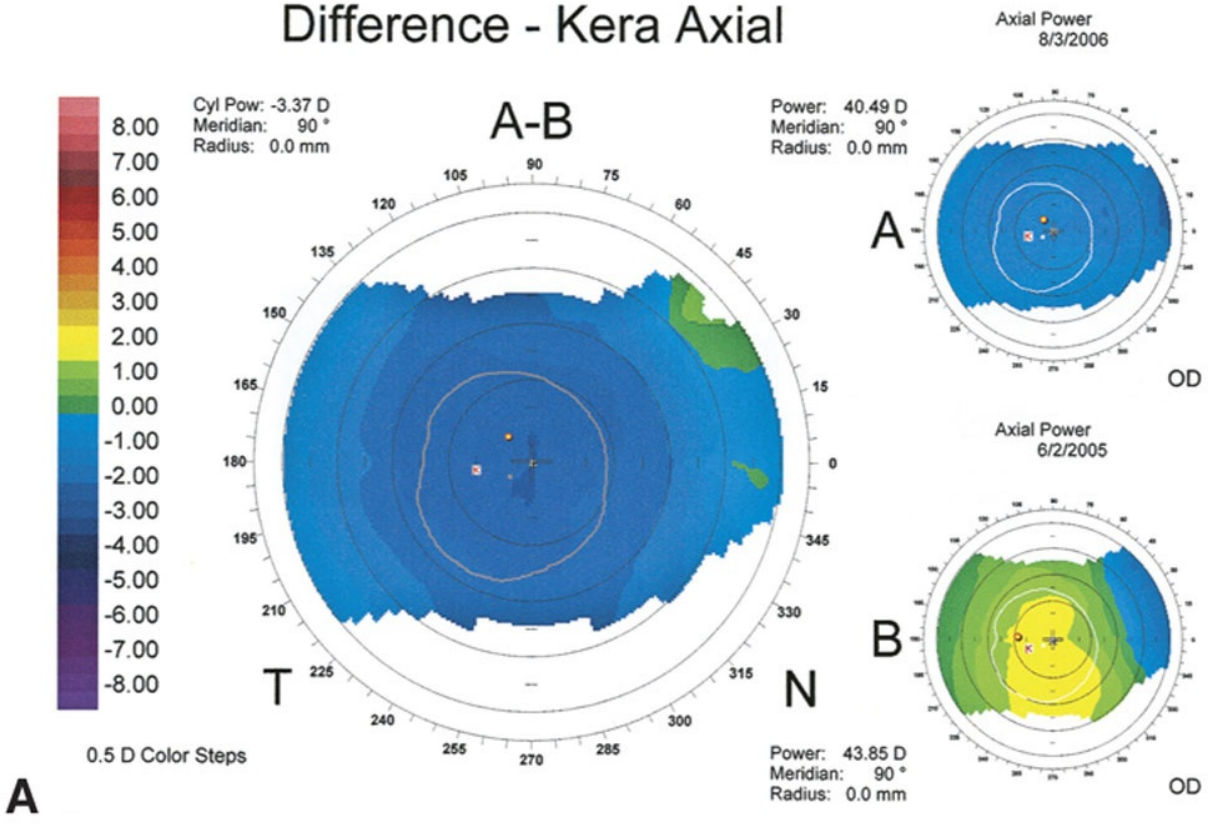
Elevation-based tomography is especially helpful in refractive surgery for depicting the anterior and posterior surface shapes of the cornea and lens. With such information, alterations to the shape of the ocular structures can be determined with greater accuracy, especially postoperative changes.

Indications for Corneal Imaging in Refractive Surgery

Corneal topography is an essential part of the preoperative evaluation of refractive surgery candidates. About two-thirds of patients with normal corneas have a symmetric astigmatism pattern that is round, oval, or bow-tie shaped (see Fig 1-10). Asymmetric patterns include asymmetric bow-tie patterns, inferior steepening, superior steepening, skewed radial axes, or other nonspecific irregularities.

Corneal topography detects irregular astigmatism, which may result from abnormal tear film, contact lens warpage, keratoconus and other corneal ectatic disorders, corneal surgery, trauma, scarring, and postinflammatory or degenerative conditions. Repeat topographic examinations may be helpful when the underlying etiology is in question, especially in cases of suspicious steepening patterns in patients who wear contact lenses or who have an abnormal tear film. Contact lens wearers often benefit from extended periods without contact lens wear prior to preoperative planning for refractive surgery; this period allows the corneal map and refraction to stabilize. Patients with keratoconus or other ectatic disorders are not routinely considered for ablative keratorefractive surgery because the abnormal cornea has an unpredictable response and/or progressive ectasia. Forme fruste, or subclinical, keratoconus typically is considered a contraindication to ablative refractive surgery. Studies are under way to determine the suitability of some keratorefractive procedures in combination with corneal collagen crosslinking as alternative therapeutic modalities for these patients (see also Chapter 7).

Corneal topography and tomography can also be used to demonstrate the effects of keratorefractive procedures. Preoperative and postoperative maps may be compared to determine the refractive effect achieved (*difference map;* Fig 1-14). Corneal mapping can also help explain unexpected results, including undercorrection and overcorrection, induced astigmatism, and induced aberrations from small optical zones, decentered ablations, or central islands (Fig 1-15).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Axial Power
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Radius: 0.0 mm
A-B
Power: 40.49 D
Meridian: 90 °
Radius: 0.0 mm
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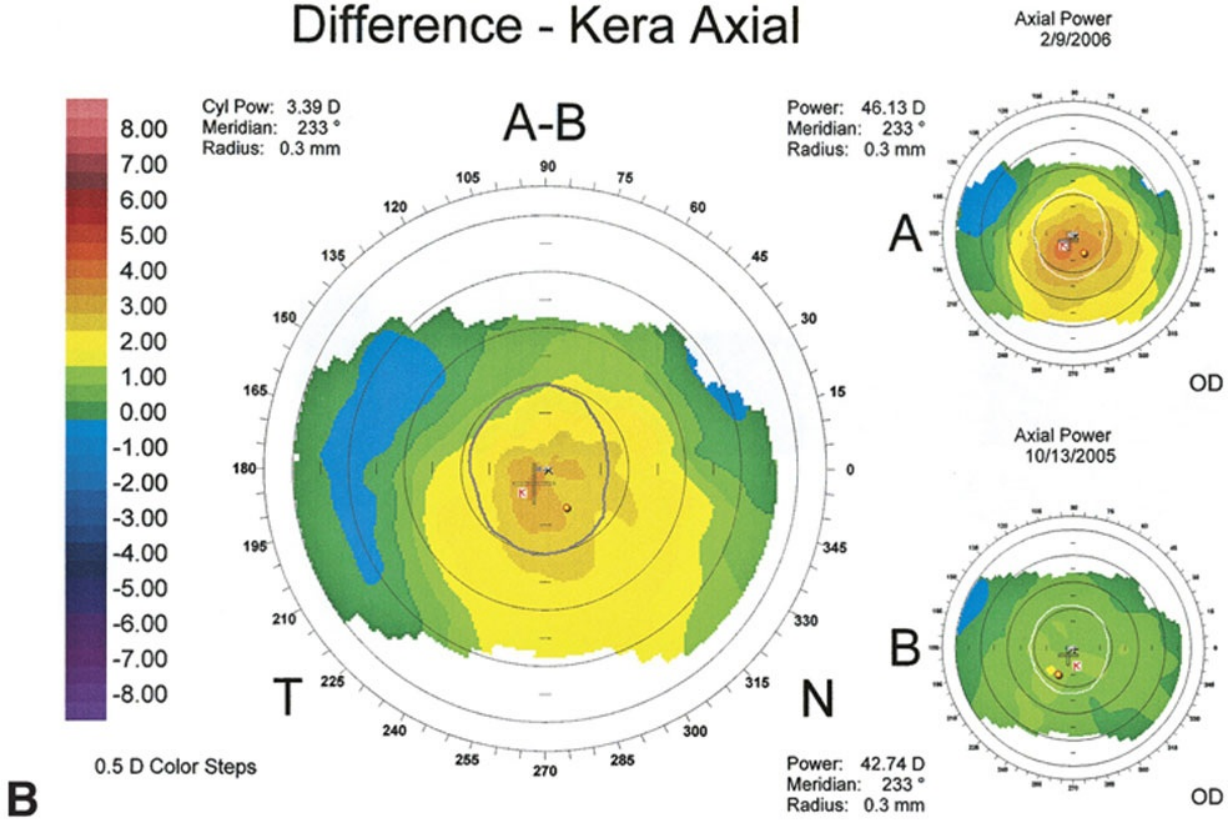
Radius: 0.0 mm
A


Difference - Kera Axial
Axial Power
2/9/2006
Cyl Pow: 3.39 D
Meridian: 233 °
Radius: 0.3 mm
A-B
Power: 46.13 D
Meridian: 233 °
Radius: 0.3 mm
A
OD
Axial Power
10/13/2005
B
OD
8.00
7.00
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-5.00
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-7.00
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T
N
Power: 42.74 D
Meridian: 233 °
Radius: 0.3 mm
B

Figure 1-14 Difference maps demonstrating corneal power change before and after myopic **(A)** and hyperopic **(B)** LASIK. *(Courtesy of J. Bradley Randleman, MD.)*

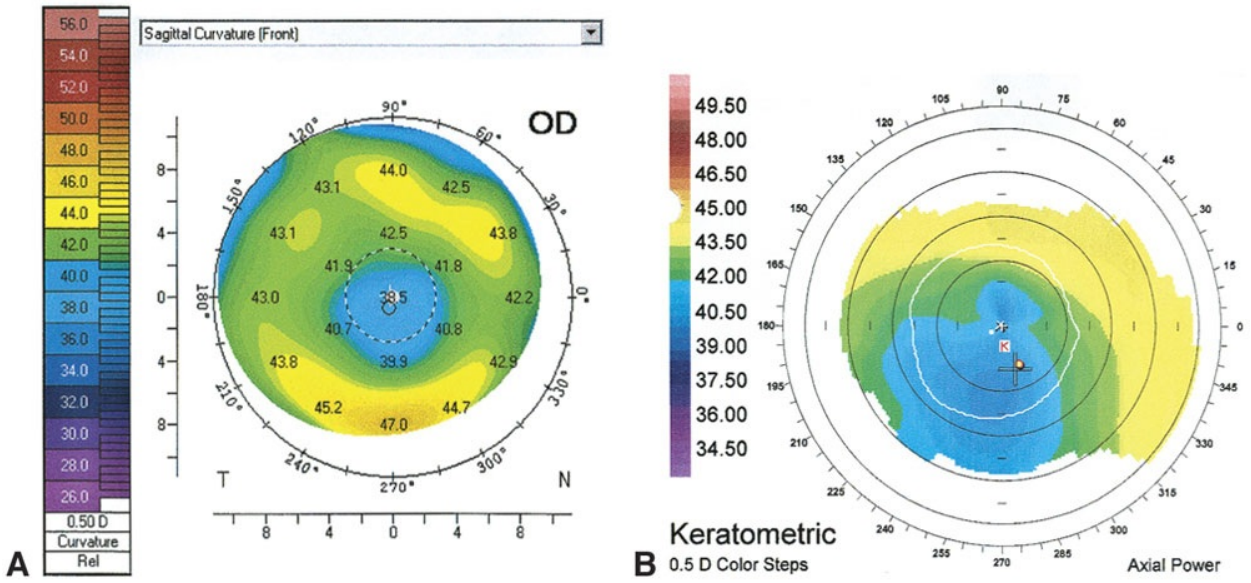

Figure 1-15 Topographic maps showing small optical zone after excimer laser ablation **(A)** and decentered ablation **(B).** *(Courtesy of J. Bradley Randleman, MD.)*

De Paiva CS, Harris LD, Pflugfelder SC. Keratoconus-like topographic changes in keratoconjunctivitis sicca. *Cornea.* 2003;22(1):22-24.

Rabinowitz YS, Yang H, Brickman Y, et al. Videokeratography database of normal human corneas. *Br J Ophthalmol.* 1996;80(7):610-616.

The Role of Corneal Topography in Refractive Surgery

Corneal topography is one of the key evaluative technologies in refractive surgery, crucial not only in preoperative screening but also in postoperative evaluation of patients with unexpected results. Topographic analysis should be undertaken in all patients being considered for refractive surgery in order to identify patients who should not undergo the procedure. Although refractive surgery has numerous contraindications (see Chapter 2), some of the most important to recognize are the corneal ectatic disorders: keratoconus and pellucid marginal degeneration (see BCSC Section 8, *External Disease and Cornea*, for further discussion).

Keratoconus (KC) and pellucid marginal degeneration (PMD) are generally progressive conditions in which thinning occurs in the central, paracentral, or peripheral cornea, resulting in asymmetric corneal steepening and reduced spectacle-corrected visual acuity. These 2 conditions may be separate entities or different clinical expressions of the same ectatic process; in either case, they are currently contraindications for excimer laser surgery. The topographic pattern in keratoconic

eyes usually demonstrates substantial inferonasal or inferotemporal steepening, although severe central and even superior steepening patterns may occur (Fig 1-16). The classic topographic pattern in PMD is inferior steepening, which is most dramatic between the 4 and 8 o'clock positions, with superior flattening. This inferior steepening often extends centrally, coming together in what has been described as a "crab-claw" shape (see Chapter 10, Fig 10-2). There may be substantial overlap in the topographic patterns of KC and PMD.

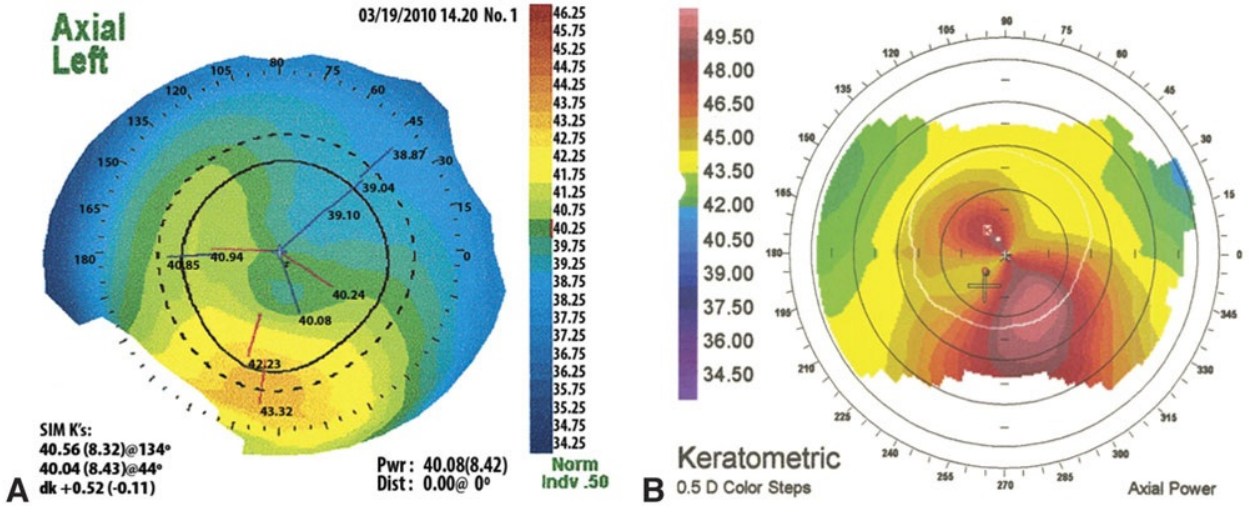

Figure 1-16 Corneal topography in keratoconus. Topography of suspected case **(A)** and confirmed case **(B).** *(Courtesy of J. Bradley Randleman, MD.)*

The patient who poses the greatest difficulty in preoperative evaluation for refractive surgery is the one in whom KC ultimately develops but who shows no obvious clinical signs at the time of examination. Corneal topography may reveal subtle abnormalities that should alert the surgeon to this problem. Although newer screening indices take into account a variety of topographic factors that may indicate a higher likelihood of subclinical KC, none of these indices is definitive. Inferior-superior (I-S) values are useful in screening for KC. The I-S value is derived by calculating the difference between inferior and superior corneal curvature measurements at a defined set of 5 points above and below the horizontal meridian. I-S values greater than 1.4, central corneal powers greater than 47.2 D, and skewed radial axes are all suggestive of corneal ectatic disorders, but there is some overlap between normal and abnormal eyes.

In addition to these topographic metrics, substantial displacement of the thinnest area of the cornea from the center as revealed by corneal tomography is also suggestive of KC. Normal corneas are substantially thicker peripherally than centrally (by approximately 50-60 mm), and corneas that are not thicker peripherally suggest an ectatic disorder. Newer technologies such as high-resolution anterior segment optical

coherence tomography (OCT), ultra-high-frequency ultrasound, and hysteresis analysis may be helpful as screening tests for keratoconus by aiding in evaluating the relative position of the posterior and anterior apex, epithelial thickness, and corneal biomechanical properties; however, these technologies have yet to be validated.

Ambrosio R Jr, Alonso RS, Luz A, Coca Velarde LG. Corneal-thickness spatial profile and corneal-volume distribution: tomographic indices to detect keratoconus. *J Cataract Refract Surg.* 2006;32(11):1851-1859.

Lee BW, Jurkunas UV, Harissi-Dagher M, Poothullil AM, Tobaigy FM, Azar DT. Ectatic disorders associated with a claw-shaped pattern on corneal topography. *Am J Ophthalmol.* 2007;144(1):154-156.

Rabinowitz YS. Videokeratographic indices to aid in screening for keratoconus. *J Refract Surg.* 1995;11(5):371-379.

Rabinowitz YS, McDonnell PJ. Computer-assisted corneal topography in keratoconus. *Refract Corneal Surg.* 1989;5(6):400-408.

Post-penetrating keratoplasty

Corneal topography is helpful in identifying the irregularity, magnitude, and meridian of postoperative astigmatism after penetrating keratoplasty (PKP). Complex peripheral patterns may result in a refractive meridian of astigmatism that is not aligned with the topographic meridian. Conventional, wavefront-optimized, wavefront-guided, or topography-guided ablations may be considered in post-PKP eyes after all sutures have been removed and the refraction has stabilized, depending on the resulting refractive error and corneal shape.

Corneal Effects of Keratorefractive Surgery

All keratorefractive procedures induce refractive changes by altering corneal curvature; however, the method by which the alteration is accomplished varies by procedure and by the refractive error being treated. Treatment of myopia requires a *flattening*, or decrease, in central corneal curvature, whereas treatment of hyperopia requires a *steepening*, or increase, in central corneal curvature. Corneal refractive procedures can be performed using a variety of techniques, including incisional, tissue addition or subtraction, alloplastic material addition, collagen shrinkage, and laser ablation (see the section Laser Biophysics for discussion of laser ablation).

Overall patient satisfaction after refractive surgery depends largely on the successful correction of refractive error and creation of a corneal shape that maximizes visual quality. The natural shape of the cornea is *prolate*, or steeper centrally than peripherally. In contrast, an *oblate* cornea is steeper peripherally than centrally. The natural prolate corneal shape results in an aspheric optical system, which reduces spherical aberration and therefore minimizes fluctuations in refractive error as the pupil changes size. Oblate corneas increase spherical aberrations. Common complaints in patients with substantial spherical aberration include glare, halos, and decreased night vision.

Incisional Techniques

Incisions perpendicular to the corneal surface predictably alter its shape, depending on the direction, depth, location, and number of incisions (see Chapter 4). All incisions cause a local flattening of the cornea. Radial incisions lead to flattening in both the meridian of the incision and the one 90deg away. Tangential (arcuate or linear) incisions lead to flattening in the meridian of the incision and steepening in the meridian 90deg away that may be equal to or less than the magnitude of the decrease in the primary meridian (Fig 1-17); this phenomenon is known as *coupling* (see Chapter 3, Fig 3-5).

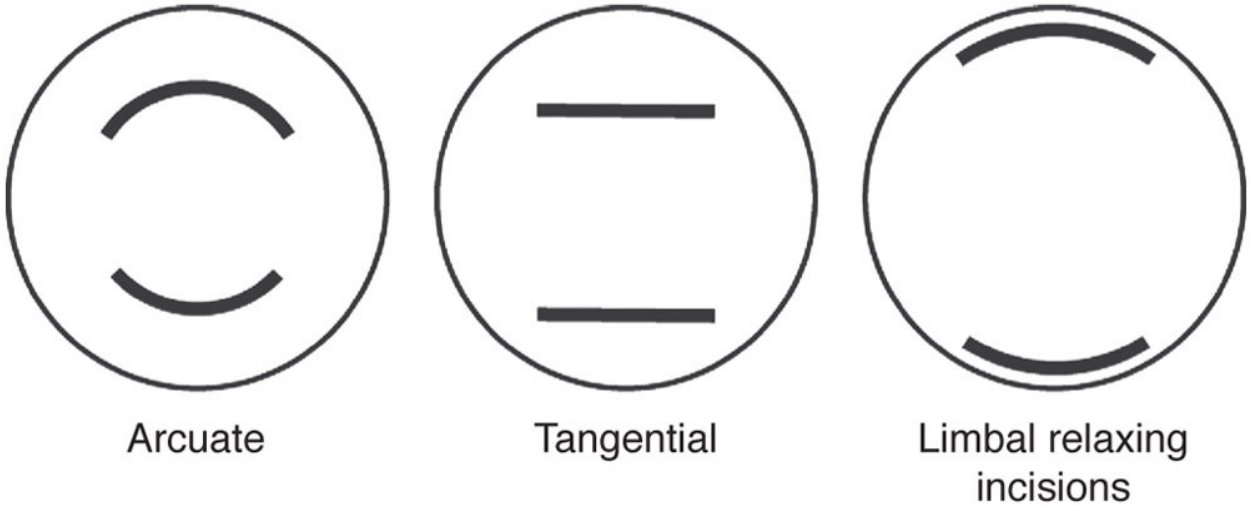

Figure 1-17 Schematic diagrams of incisions used in astigmatic keratotomy. Flattening is induced in the axis of the incisions (at 90deg in this case), and steepening is induced 90deg away from the incisions (at 180deg in this case). *(Illustrations by Cyndie C. H. Wooley.)*

The closer the radial incisions approach the visual axis (ie, the smaller the optical zone), the greater their effect; similarly, the closer tangential incisions are placed to the visual axis, the greater is the effect. The longer the tangential incision, up to 3 clock-hours, the greater the effect.

For optimum effect, an incision should be 85%-90% deep to retain an intact posterior lamella and maximum anterior bowing of the other lamellae. Nomograms for numbers of incisions and optical zone size can be calculated using finite element analysis, but surgical nomograms are typically generated empirically (eg, see Table 3-1). The important variables for radial and astigmatic surgery include patient age and the number, depth, and length of incisions. The same incision has greater effect in older patients than it does in younger patients. IOP and preoperative corneal curvature are not significant predictors of effect.

Tissue Addition or Subtraction Techniques

With the exception of laser ablation techniques (discussed in the section Laser

Biophysics), lamellar procedures that alter corneal shape through tissue addition or subtraction are primarily of historical interest only. *Keratomileusis* for myopia was originated by Barraquer as "carving" of the anterior surface of the cornea. It is defined as a method to modify the spherical or meridional surface of a healthy cornea by tissue subtraction. *Epikeratoplasty* (sometimes called *epikeratophakia*) adds carved donor tissue to the surface to induce hyperopic or myopic changes. *Keratophakia* requires the addition of a tissue lenticule or synthetic inlay intrastromally (see Chapter 4). There is, however, recurring interest in femtosecond laser techniques to excise intrastromal lenticules to alter corneal curvature without the need for excimer laser ablation. These procedures are termed *refractive lenticule extraction (ReLEx)*, *femtosecond lenticule extraction (FLEx)*, and *small-incision lenticule extraction (SMILE)*. Although early results are promising, these procedures are currently under clinical investigation.

Alloplastic Material Addition Techniques

The shape of the cornea can be altered by adding alloplastic material such as hydrogel on the surface or into the corneal stroma to modify the anterior shape or refractive index of the cornea. For example, the 2 arc segments of an intrastromal corneal ring can be placed in 2 pockets of the stroma to directly reshape the surface contour according to the profile of the individual rings (Fig 1-18). For further discussion, see Chapter 4.

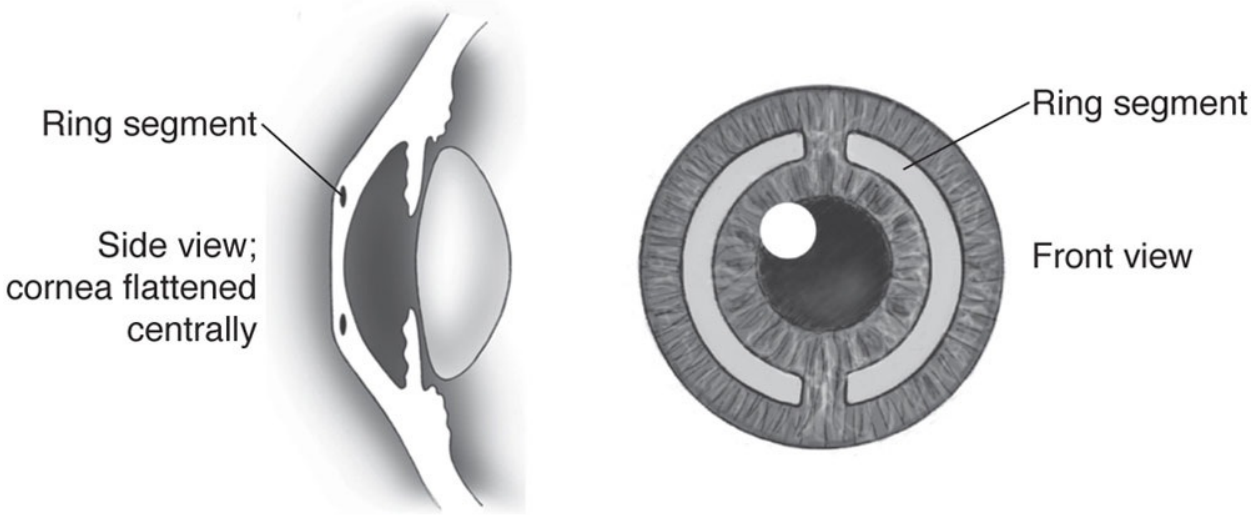

Figure 1-18 Schematic illustrations showing placement of intrastromal corneal ring segments. *(Illustrations by Jeanne Koelling.)*

Collagen Shrinkage Techniques

Alteration in corneal biomechanics can also be achieved by collagen shrinkage.

Heating collagen to a critical temperature of 58deg-76degC causes it to shrink, inducing changes in the corneal curvature. *Thermokeratoplasty* and *conductive keratoplasty (CK)* are avoided in the central cornea because of scarring but can be used in the midperiphery to cause local collagen contraction with concurrent central corneal steepening (Fig 1-19; also see Chapter 7).

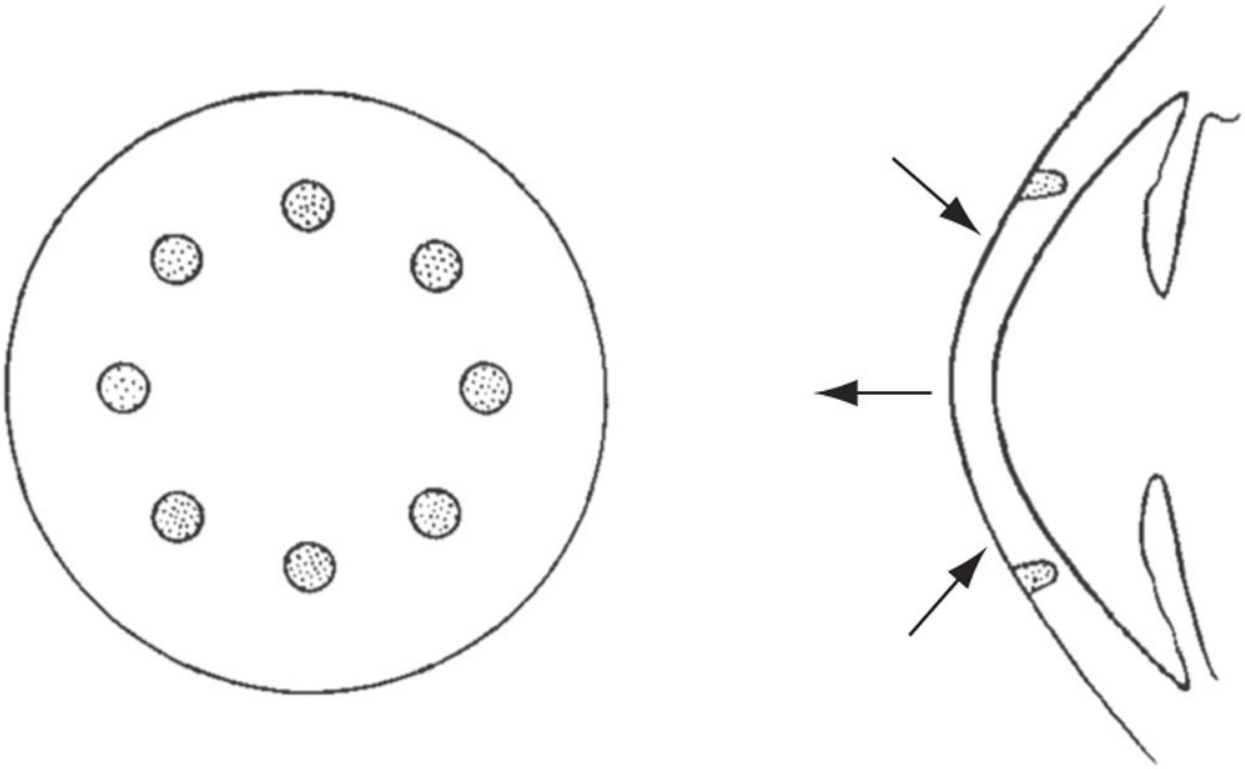

Figure 1-19 Schematic diagrams of thermokeratoplasty and conductive keratoplasty. Heat shrinks the peripheral cornea, causing central steepening *(arrows).*

Laser Biophysics

Laser-Tissue Interactions

Three different types of laser-tissue interactions are used in keratorefractive surgery: photoablation, photodisruption, and photothermal. *Photoablation*, the most important laser-tissue interaction in refractive surgery, breaks chemical bonds using excimer (from "*exci*ted di*mer*") lasers or other lasers of the appropriate wavelength. Laser energy of 4 eV per photon or greater is sufficient to break carbon-nitrogen or carbon-carbon tissue bonds. Argon-fluoride (ArF) lasers are excimer lasers that use electrical energy to stimulate argon to form dimers with the caustic fluorine gas. They generate a wavelength of 193 nm with 6.4 eV per photon. The 193-nm light is in the ultraviolet C

(high ultraviolet) range, approaching the wavelength of x-rays. In addition to having high energy per photon, light at this end of the electromagnetic spectrum has very low tissue penetrance and thus is suitable for operating on the surface of tissue. This laser energy is capable of great precision, with little thermal spread in tissue; moreover, its lack of penetrance or lethality to cells makes the 193-nm laser nonmutagenic, enhancing its safety. (DNA mutagenicity occurs in the range of 250 nm.) Solid-state lasers have been designed to generate wavelengths of light near 193 nm without the need to use toxic gas, but the technical difficulties in manufacturing these lasers have limited their clinical use.

The femtosecond laser is approved by the US Food and Drug Administration (FDA) for creating corneal flaps for LASIK and may also be used to create channels for intrastromal ring segments and for lamellar keratoplasty and PKP. It uses a 1053-nm infrared beam that causes *photodisruption*, a process by which tissue is transformed into plasma, and the subsequent high pressure and temperature generated lead to rapid tissue expansion and formation of microscopic cavities within the corneal stroma. Contiguous photodisruption allows for creation of the corneal flap, channel, or keratoplasty incision.

Photothermal effects are achieved by focusing a holmium:YAG laser with a wavelength of 2.13 mm into the anterior stroma. The beam's energy is absorbed by water in the cornea, and the resulting heat causes local collagen shrinkage and subsequent surface flattening. This technique is approved by the FDA for treating low hyperopia but is not commonly used at present.

Fundamentals of Excimer Laser Photoablation

All photoablation procedures result in the removal of corneal tissue. The amount of tissue removed centrally for myopic treatments is estimated by the *Munnerlyn formula:*

$$\text{Ablation Depth } (\mu\text{m}) \approx \frac{\text{Degree of Myopia (D)} \times (\text{Optical Zone Diameter})^2 \text{ (mm)}}{3}$$

Clinical experience has confirmed that the effective change is independent of the initial curvature of the cornea. The Munnerlyn formula highlights some of the problems and limitations of laser vision correction. The amount of ablation increases by the square of the optical zone, but the complications of glare, halos, and regression increase when the optical zone decreases. To reduce these adverse effects, the optical zone should be 6 mm or larger.

With surface ablation, the laser treatment is applied to the Bowman layer and the anterior stroma, whereas LASIK combines an initial lamellar incision with ablation of the cornea, typically in the stromal bed (see Chapter 5 for further details of surgical technique). Theoretical limits for residual posterior cornea apply the same as they do

for PRK. Flaps range in thickness from ultrathin (80-100 mm) to standard (130-180 mm). The thickness and diameter of the LASIK flap depend on instrumentation, corneal diameter, corneal curvature, and corneal thickness.

Treatments for myopia flatten the cornea by removing central corneal tissue, whereas those for hyperopia steepen the cornea by removing a doughnut-shaped portion of mid-peripheral tissue. Some lasers use a multizone treatment algorithm to conserve tissue by employing several concentric optical zones to achieve the total correction required. This method can provide the full correction centrally, while the tapering peripheral zones reduce symptoms and allow higher degrees of myopia to be treated. For an extreme example, 12.00 D of myopia can be treated as follows: 6.00 D are corrected with a 4.5-mm optical zone, 3.00 D with a 5.5-mm optical zone, and 3.00 D with a 6.5-mm optical zone (Fig 1-20). Thus, the total 12.00 D correction is achieved in the center using a shallower ablation depth than would be necessary for a single pass (103 mm instead of 169 mm). For hyperopia, surface ablation and LASIK use a similar formula to determine the maximum ablation depth, but the ablation zone is much larger than the optical zone. The zone of maximal ablation coincides with the outer edge of the optical zone. A transition zone of ablated cornea is necessary to blend the edge of the optical zone with the peripheral cornea.

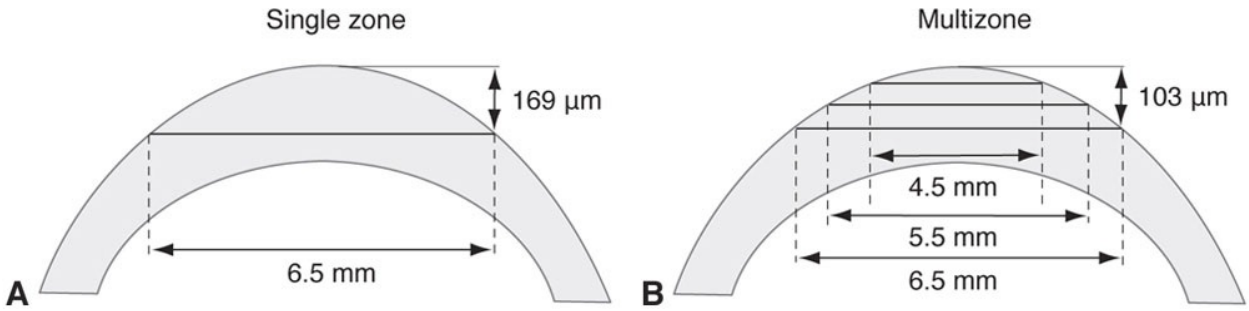

Figure 1-20 Diagrammatic comparison of single and multizone keratectomies. **A,** Depth of ablation required to correct 12.00 D of myopia in a single pass. **B,** Depiction of how the use of multiple zones reduces the ablation depth required. *(Illustrations by Cyndie C. H. Wooley.)*

Care must be taken to ensure that enough stromal tissue remains after creation of the LASIK flap and ablation to maintain adequate corneal structure. The historical standard has been to leave a minimum of 250 mm of tissue in the stromal bed, although the exact amount of remaining tissue required to ensure biomechanical stability is not known and likely varies among individuals. See Chapters 2 and 5 for further discussion of these issues.

Types of Photoablating Lasers

Photoablating lasers can be subdivided into broad-beam lasers, scanning-slit lasers, and flying spot lasers. *Broad-beam lasers* have larger-diameter beams and slower repetition rates and rely on optics or mirrors to create a smooth and homogeneous multimode laser beam of up to approximately 7 mm in diameter. These lasers have very high energy per pulse and require a small number of pulses to ablate the cornea. *Scanning-slit lasers* generate a narrow-slit laser beam that is scanned over the surface of the tissue to alter the photoablation profile, thus improving the smoothness of the ablated cornea and allowing for larger-diameter ablation zones. *Flying spot lasers* use smaller-diameter beams (approximately 0.5-2.0 mm) that are scanned at a higher repetition rate; they require use of a tracking mechanism for precise placement of the desired pattern of ablation. Broad-beam lasers and some scanning-slit lasers require a mechanical iris diaphragm or ablatable mask to create the desired shape in the cornea, whereas the rest of the scanning-slit lasers and the flying spot lasers use a pattern projected onto the surface to guide the ablation profile without masking. The majority of excimer lasers in current clinical use utilize some form of variable or flying spot ablation profile.

Wavefront-optimized and wavefront-guided laser ablations

Because conventional laser treatment profiles have small blend zones and create a more oblate corneal shape postoperatively, they are likely to induce some degree of higher-order aberration, especially spherical aberration and coma. These aberrations occur because the corneal curvature is relatively more angled peripherally in relation to laser pulses emanating from the central location; thus, the pulses hitting the peripheral cornea are relatively less effective than are the central pulses.

Wavefront-optimized laser ablation improves the postoperative corneal shape by taking the curvature of the cornea into account and increasing the number of peripheral pulses; this approach minimizes the induction of higher-order aberrations and often results in better-quality vision and fewer night-vision complaints. As in conventional procedures, the patient's refraction alone is used to program the wavefront-optimized laser ablation. This technology does not directly address preexisting higher-order aberrations; however, recent studies have found that the vast majority of patients do not have substantial preoperative higher-order aberrations. It also has the advantage of being quicker than wavefront-guided technology and avoids the additional expense of the aberrometer.

In *wavefront-guided laser ablation,* information obtained from a wavefront-sensing aberrometer (which quantifies the aberrations) is transferred electronically to the treatment laser to program the ablation. This process is distinct from those in conventional excimer laser and wavefront-optimized laser treatments, in which the subjective refraction alone is used to program the laser ablation. The wavefront-guided

laser attempts to treat both lower-order (ie, myopia or hyperopia and/or astigmatism) and higher-order aberrations by applying complex ablation patterns to the cornea to correct the wavefront deviations. The correction of higher-order aberrations requires non-radially symmetric patterns of ablation (which are often much smaller in magnitude than ablations needed to correct defocus and astigmatism). The difference between the desired and the actual wavefront is used to generate a 3-dimensional map of the planned ablation. Accurate registration is required to ensure that the ablation treatment actually delivered to the cornea matches the intended pattern. Such registration is achieved by using marks at the limbus before obtaining the wavefront patterns or by iris registration, which matches reference points in the natural iris pattern to compensate for cyclotorsion and pupil centroid shift. The wavefront-guided laser then uses a pupil-tracking system, which helps maintain centration during treatment and allows accurate delivery of the customized ablation profile.

The results for both wavefront-optimized and wavefront-guided ablations for myopia, hyperopia, and astigmatism are excellent, with well over 90% of eyes achieving 20/40 or better uncorrected distance visual acuity (UDVA; also called *uncorrected visual acuity, UCVA*). Although most visual acuity parameters are similar between conventional and customized treatments (including both wavefront-optimized and wavefront-guided treatments), the majority of recent reports demonstrate improved vision quality when customized treatment profiles are used. Outcomes with wavefront-optimized treatments are similar to those of wavefront-guided treatments for most patients, with the exception of patients with substantial preoperative higher-order aberrations.

Topography-guided laser ablations

Topography-guided lasers are currently investigational in the United States. Although similar in concept to wavefront-guided lasers, topography-guided devices link the treatment to the corneal topography rather than to the wavefront data. Although experience is still early, these instruments may offer significant benefit in the treatment of highly aberrated eyes, such as eyes with previous RK or PKP.

Myrowitz EH, Chuck RS. A comparison of wavefront-optimized and wavefront-guided ablations. *Curr Opin Ophthalmol.* 2009;20(4):247-250.

Netto MV, Dupps W Jr, Wilson SE. Wavefront-guided ablation: evidence for efficacy compared to traditional ablation. *Am J Ophthalmol.* 2006;141(2):360-368.

Padmanabhan P, Mrochen M, Basuthkar S, Viswanathan D, Joseph R. Wavefront-guided versus wavefront-optimized laser in situ keratomileusis: contralateral comparative study. *J Cataract Refract Surg.* 2008;34(3):389-397.

Pasquali T, Krueger R. Topography-guided laser refractive surgery. *Curr Opin Ophthalmol.* 2012;23(4):264-268.

Perez-Straziota CE, Randleman JB, Stulting RD. Visual acuity and higher-order aberrations with wavefront-guided and wavefront-optimized laser in situ keratomileusis. *J Cataract Refract Surg.* 2010;36(3):437-441.

Rowsey JJ. Ten caveats in refractive surgery. *Ophthalmology.* 1983;90(2):148-155.

Schallhorn SC, Farjo AA, Huang D, et al; American Academy of Ophthalmology. Wavefront-guided LASIK for the correction of primary myopia and astigmatism: a report by the American Academy of Ophthalmology. *Ophthalmology.* 2008;115(7):1249-1261.

Schallhorn SC, Tanzer DJ, Kaupp SE, Brown M, Malady SE. Comparison of night driving performance after wavefront-guided and conventional LASIK for moderate myopia. *Ophthalmology.* 2009;116(4):702-709.

Stonecipher KG, Kezirian GM. Wavefront-optimized versus wavefront-guided LASIK for myopic astigmatism with the

Corneal Wound Healing

All forms of keratorefractive surgery are exquisitely dependent on corneal wound healing to achieve the desired results. Satisfactory results require either modifying or reducing wound healing or exploiting normal wound healing for the benefit of the patient. For example, astigmatic keratotomy requires initial weakening of the cornea followed by permanent corneal healing, with replacement of the epithelial plugs with collagen and remodeling of the collagen to ensure stability and avoid long-term hyperopic drift. PRK requires the epithelium to heal quickly, and with minimal stimulation of the underlying keratocytes, to avoid corneal scarring and haze. Lamellar keratoplasty requires intact epithelium and healthy endothelium early in the postoperative period to seal the flap. Later, the cornea must heal in the periphery to secure the flap in place and avoid late-term displacement while minimizing irregular astigmatism; also, the cornea must remain devoid of significant healing centrally to maintain a clear visual axis. In addition to stromal healing, regeneration of the corneal nerves is crucial to a normal ocular surface and good visual function. Delay or difficulty in re-innervation can lead to problems with corneal sensation and tear-film stability and to dry eye symptoms.

The understanding of corneal wound healing has advanced tremendously with recognition of the multiple factors involved in the cascade of events initiated by corneal wounding. The cascade is somewhat dependent on the nature of the injury. Injury to the epithelium can lead to loss of underlying keratocytes from apoptosis. The remaining keratocytes respond by generating new glycosaminoglycans and collagen, to a degree dependent on the duration of the epithelial defect and the depth of the stromal injury. Corneal haze is localized in the subepithelial anterior stroma and may persist for several years after surface ablation. Clinically significant haze, however, is present in only a small percentage of eyes. The tendency toward haze formation is greater with deeper ablations, increased surface irregularity, and prolonged absence of the epithelium. Despite loss of the Bowman layer, normal or even enhanced numbers of hemidesmosomes and anchoring fibrils form to secure the epithelium to the stroma.

Controversy persists over the value of different drugs for modulating wound healing in surface ablation. Typically, clinicians in the United States use corticosteroids in a tapering manner following surgery to reduce inflammation. Mitomycin C has been applied to the stromal bed after excimer surface ablation to attempt to decrease haze formation (see Chapters 5 and 6). Vitamin C has been postulated to play a role in protecting the cornea from ultraviolet light damage by the excimer laser, but no randomized, prospective clinical trial has yet been performed. Various growth factors that have been found to promote wound healing after PRK, including transforming growth factor b, may be useful in the future.

Haze formation does not seem to occur in the central flap interface after LASIK, which may be related either to lack of significant epithelial injury and consequent subcellular signaling or to maintenance of some intact surface neurons. LASIK shows very little long-term evidence of healing between the disrupted lamellae and only typical stromal healing at the peripheral wound. The lamellae are initially held in position by negative stromal pressure generated by the endothelial cells aided by an intact epithelial surface. Even years after treatment, the lamellar interface can be broken and the flap lifted, indicating that only a minimal amount of healing occurs. LASIK flaps can also be dislodged secondary to trauma many years postoperatively.

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CHAPTER 2

Patient Evaluation

A thorough preoperative patient evaluation is crucial for achieving a successful outcome after refractive surgery. It is during this encounter that the physician begins to develop an impression as to whether the patient is a good candidate for refractive surgery. Perhaps the most important goal of this evaluation is to identify who should *not* have refractive surgery.

Patient History

The evaluation actually begins before the physician sees the patient. Receptionists or refractive surgical coordinators who speak with a patient before the visit may get a sense of the patient's goals and expectations for refractive surgery. If the patient is particularly quarrelsome about the time or date of the appointment or argues about cost, the surgeon should be informed. Such a patient may be too demanding to be a good candidate for surgery.

Important parts of the preoperative evaluation include an assessment of the patient's expectations; his or her social, medical, and ocular history; manifest and cycloplegic refractions; a complete ophthalmic evaluation, including slit-lamp and fundus examinations; and ancillary testing (Table 2-1). If the patient is a good candidate for surgery, the appropriate refractive surgery procedures, benefits, and risks need to be discussed, and informed consent must be obtained.

Table 2-1

Table 2-1 Important Parts of the Preoperative Refractive Surgery Evaluation

Patient expectations and motivations
Assessment of specific patient expectations
Discussion of uncorrected distance versus reading vision
History
Social history, including vision requirements of profession and hobbies, tobacco and alcohol use
Medical history, including systemic medications and diseases such as diabetes mellitus and rheumatologic diseases
Ocular history, including history of contact lens wear
Ocular examination
Uncorrected near and distance vision, ocular dominance
Manifest refraction (pushing plus)
Monovision demonstration, if indicated
External evaluation
Pupillary evaluation
Motility
Slit-lamp examination, including intraocular pressure measurement
Corneal topography
Wavefront analysis, if indicated
Pachymetry
Cycloplegic refraction (refining sphere, not cylinder)
Dilated fundus examination
Informed consent
Discussion of findings
Discussion of medical and surgical alternatives and risks
Answering of patient questions
Having patient read informed consent document when undilated and unsedated, ideally before the day of procedure, and sign prior to surgery

Because accurate testing results are crucial to the success of refractive surgery, the refractive surgeon must closely supervise office staff members who are performing the various tests (eg, corneal topography or pachymetry) in the preoperative evaluation. Likewise, the surgeon should make sure the instruments used in the evaluation are properly calibrated, as miscalibrated instruments can result in faulty data and poor surgical results.

Patient Expectations

One of the most important aspects of the entire evaluation is assessing the patient's expectations. Inappropriate patient expectations are probably the leading cause of patient dissatisfaction after refractive surgery. The results may be exactly what the surgeon expected, but if those expectations were not conveyed adequately to the patient before surgery, the patient may be quite disappointed.

The surgeon should explore expectations relating to both the refractive result (eg, uncorrected distance visual acuity [UDVA; also called *uncorrected visual acuity, UCVA*]) and the emotional result (eg, improved self-esteem). Patients need to understand that they should not expect refractive surgery to improve their corrected distance visual acuity (CDVA; also called *best-corrected visual acuity, BCVA*). In addition, they need to realize refractive surgery will not prevent possible future ocular problems such as cataract, glaucoma, or retinal detachment. If the patient has obviously unrealistic hopes, such as a guarantee of 20/20 uncorrected visual acuity or perfect uncorrected reading *and* distance vision, even though he or she has presbyopia, the patient may need to be told that refractive surgery cannot currently fulfill his or her needs. The refractive surgeon should exclude patients with unrealistic expectations.

Social History

The social history and medical history can identify the vision requirements of the patient's profession. Certain occupations require that best vision be at a specific distance. For example, a minister may desire that best uncorrected vision be at arm's length, so that reading can be done at the pulpit without glasses. Military personnel, firefighters, or police may have restrictions on minimum UDVA and CDVA and on the type of refractive surgery allowed. Knowledge of a patient's recreational activities may help guide the surgeon to the most appropriate refractive procedure or determine whether that patient is even a good candidate for refractive surgery. For example, a surface laser procedure may be preferable to a lamellar procedure for a patient who is active and at high risk of ocular trauma. Someone with highly myopic and presbyopic vision who is used to examining objects a few inches from the eyes without the use of glasses (eg, jeweler or stamp collector) may not be happy with postoperative emmetropia. Tobacco and alcohol use should be documented.

Medical History

The medical history should include systemic conditions, prior surgeries, and current and prior medications. Certain systemic conditions, such as connective tissue disorders and diabetes mellitus, can lead to poor healing after refractive surgery. In addition, potentially recurrent conditions such as herpes simplex virus infection should be recognized so that preventive measures can be instituted. An immunocompromised state--for example from cancer or HIV infection/AIDS--may increase the risk of infection after refractive surgery (see Chapter 10). Medications that affect healing or the ability to fight infection, such as systemic corticosteroids or chemotherapeutic drugs, should be specifically noted. The use of corticosteroids increases the risk of cataract development, which could compromise the long-term postoperative visual outcome. Use of certain medications--for example, isotretinoin and amiodarone--traditionally has been thought to increase the risk of poor results with photorefractive keratectomy (PRK) and laser in situ keratomileusis (LASIK) due to a potentially increased risk of poor corneal healing; however, there is no evidence for this association in the peer-reviewed literature. Previous use of isotretinoin can damage the meibomian glands and predispose a patient to dry eye symptoms postoperatively. In addition, caution needs to be taken with patients using sumatriptan who are undergoing PRK or LASIK and with patients using hormone replacement therapy or antihistamines who are undergoing PRK because of a possible increased risk of delayed epithelial healing.

Although laser manufacturers do not recommend excimer laser surgery for patients with cardiac pacemakers and implanted defibrillators, many such patients have undergone the surgery without problems. It may be best to check with the pacemaker and defibrillator manufacturer before laser surgery. Refractive surgery is also generally contraindicated in pregnant and breastfeeding women because of possible changes in

refraction and corneal hydration status. Many surgeons recommend waiting at least 3 months after delivery and cessation of breastfeeding before performing the refractive surgery evaluation and procedure.

de Rojas Silva V, Rodriguez-Conde R, Cobo-Soriano R, Beltran J, Llovet F, Baviera J. Laser in situ keratomileusis in patients with a history of ocular herpes. *J Cataract Refract Surg*. 2007;33(11):1855-1859.

Pertinent Ocular History

The ocular history should focus on previous and current eye problems such as dry eye symptoms, blepharitis, recurrent erosions, glaucoma, and retinal tears or detachments as well as on systemic conditions such as diabetes mellitus and connective tissue disorders. Ocular medications should be noted. A history of previous methods of optical correction, such as spectacles and contact lenses, should be taken. The stability of the current refraction is very important. Has the prescription for glasses or contact lenses changed substantially in the past few years? A significant change is generally thought to be greater than 0.50 D in either sphere or cylinder over the past year. A contact lens history should be taken. Important information includes the type of lenses used (eg, soft, rigid gas-permeable [RGP], polymethylmethacrylate [PMMA]); the wearing schedule (eg, daily-wear disposable, daily-wear frequent replacement, overnight wear indicating number of nights worn in a row); the type of cleaning, disinfecting, and enzyming agents used; and how old the lenses are. Occasionally, a patient may have been happy with contact lens wear and needs only a change in lens material or wearing schedule to eliminate a recent onset of uncomfortable symptoms.

Because contact lens wear can change the shape of the cornea (corneal warpage), it is recommended that patients discontinue contact lens wear before the refractive surgery evaluation as well as before the surgery. The exact length of time the patient should be without contact lens wear has not been established. Current clinical practice typically involves discontinuing use of soft contact lenses for at least 3 days to 2 weeks (toric lenses may require longer) and of rigid contact lenses for at least 2-3 weeks. Some surgeons keep patients out of rigid contact lenses for 1 month for every decade of contact lens wear. Patients with irregular or unstable corneas should discontinue wearing their contact lenses for a longer period and then be re-refracted every few weeks until the refraction and corneal topography stabilize before being considered for refractive surgery. For patients who wear RGP contact lenses and find glasses a hardship, some surgeons suggest changing to soft contact lenses for a period to aid stabilization and regularization of the corneal curvature.

Patient Age, Presbyopia, and Monovision

The age of a patient is important in predicting postoperative patient satisfaction. The loss of near vision with aging should be discussed with all patients. Before age 40

years, individuals with emmetropic vision generally do not require reading adds to see a near target. After this age, patients need to understand that if their eyes are made emmetropic through refractive surgery, they will require reading glasses for near vision. They must also understand that "near vision" tasks include all tasks performed up close, such as applying makeup, shaving, or seeing the computer or cell phone screen--not just reading. These points cannot be overemphasized for patients with myopia who are approaching age 40 years. Before refractive surgery, these patients can read well with and without their glasses. Some may even read well with their contact lenses. If their eyes are emmetropic after surgery, many will not read well without reading glasses. The patient needs to understand this phenomenon and must be willing to accept this result before undergoing any refractive surgery that aims for emmetropia. In patients who wear glasses, a trial with contact lenses will approximate the patient's reading ability after surgery.

A discussion of monovision (ie, 1 eye corrected for distance and the other eye for near/intermediate vision) often fits well into the evaluation at this point. The alternative of monovision correction should be discussed with all patients in the age groups approaching or affected by presbyopia. Many patients have successfully used monovision in contact lenses and want it after refractive surgery. Others have never tried it but would like to, and still others have no interest. If a patient has not used monovision before but is interested, the attempted surgical result should first be demonstrated with glasses or temporary contact lenses at near and distance. Generally, the dominant eye is corrected for distance and the nondominant eye to approximately -1.50 to -1.75 D. For most patients, such refraction allows good uncorrected distance and near vision without intolerable anisometropia. Some surgeons prefer a "mini-monovision" procedure, whereby the near-vision eye is corrected to approximately -0.75 D, which allows some near vision with better distance vision and less anisometropia. The exact amount of monovision depends on the desires of the patient. Higher amounts of monovision (up to -2.50 D) can be used successfully in selected patients who want excellent postoperative near vision. However, in some patients with a higher degree of postoperative myopia, improving near vision may lead to unwanted adverse effects of loss of depth perception and anisometropia. It is often advisable to have a patient try monovision with contact lenses before surgery to ensure that distance and near vision as well as stereovision are acceptable and that no muscle imbalance is present, especially with higher degrees of monovision.

Although typically the nondominant eye is corrected for near, some patients prefer that the dominant eye be corrected for near. Of several methods for testing ocular dominance, one of the simplest is to have the patient point to a distant object, such as a small letter on an eye chart, and then close each eye to determine which eye he or she was using when pointing; this is the dominant eye. Another is to have a patient make an "okay sign" with one hand and look at the examiner through the opening.

Examination

Uncorrected Visual Acuity and Manifest and Cycloplegic Refraction

The refractive elements of the preoperative examination are extremely important because they directly determine the amount of surgery to be performed. Visual acuity at distance and near should be measured. The current glasses prescription and visual acuity with those glasses should also be determined, and a manifest refraction should be performed. The sharpest visual acuity with the least amount of minus ("pushing plus") should be the final endpoint (see BCSC Section 3, *Clinical Optics*). The duochrome test should not be used as the final endpoint because it tends to overminus patients. Document the best visual acuity obtainable, even if it is better than 20/20. An automated refraction with an autorefractor or wavefront aberrometer may be helpful in providing a starting point for the manifest refraction. A cycloplegic refraction is also necessary; sufficient waiting time must be allowed between the time the patient's eyes are dilated with appropriate cycloplegic eye drops--tropicamide, 1%, or cyclopentolate, 1%, is generally used--and the refraction. For full cycloplegia, waiting at least 30 minutes (with tropicamide, 1%) or 60 minutes (with cyclopentolate, 1%) is recommended. The cycloplegic refraction should refine the sphere and not the cylinder from the manifest refraction, as it is done to neutralize accommodation. For eyes with greater than 5.00 D of refractive error, a vertex distance measurement should be performed to obtain the most accurate refraction. When the difference between the manifest and cycloplegic refractions is large (eg, >0.50 D), a postcycloplegic manifest refraction may be helpful to recheck the original. In patients with myopia, such a large difference is often caused by an overminused manifest refraction. In patients with hyperopia, substantial latent hyperopia may be present, in which case the surgeon and patient need to decide exactly how much hyperopia to treat. If there is significant latent hyperopia, a pushed-plus spectacle or contact lens correction can be worn for several weeks or months preoperatively to reduce the postoperative adjustment from treating the true refraction.

Refractive surgeons have their own preferences for whether to program the laser using the manifest or cycloplegic refraction, based on their individual nomogram and technique and on the patient's age. Many surgeons plan their laser input according to the manifest refraction, especially for younger patients, if that refraction has been performed with a careful pushed-plus technique.

Pupillary Examination

After the manifest refraction (but before dilating eye drops are administered), the external and anterior segment examinations are performed. Specific attention should be given to the pupillary examination; the pupil size should be evaluated in bright room

light and under dim illumination, and the surgeon should look for any afferent pupillary defect. A variety of techniques are available for measuring pupil size in dim illumination, including use of a near card with pupil sizes on the edge (with the patient fixating at distance), or a pupillometer. The dim-light measurement should be taken using an amount of light entering the eye that closely approximates the amount entering during normal nighttime activities such as night driving; it should not necessarily be done under completely dark conditions.

Pupil size measurements should be standardized as much as possible. Large pupil size may be a risk factor for postoperative glare and halo symptoms after refractive surgery. Measuring the low-light pupil diameter preoperatively and using that measurement to direct surgery remains a controversial approach. Conventional wisdom suggests that the optical zone should be larger than the pupil diameter to minimize vision disturbances such as glare and halos. Recent evidence, however, does not support an association between preoperative pupil size and an increased incidence of either glare or halo complaints 1 year postoperatively. It is not clear, therefore, that pupil size can be used to predict which patients are more likely to have such symptoms. The size of the effective optical zone--which is related to the ablation profile and the level of refractive error--may be more important in minimizing visual adverse effects than is the low-light pupil diameter.

When asked, patients often note that they had glare under dim-light conditions even before undergoing refractive surgery. Thus, it is important that patients become aware of their glare and halo symptoms preoperatively, as this knowledge may minimize postoperative complaints or misunderstanding.

Chan A, Manche EE. Effect of preoperative pupil size on quality of vision after wavefront-guided LASIK. *Ophthalmology.* 2011;118(4):736-741. Epub 2010 Nov 20.

Edwards JD, Burka JM, Bower KS, Stutzman RD, Sediq DA, Rabin JC. Effect of brimonidine tartrate 0.15% on night-vision difficulty and contrast testing after refractive surgery. *J Cataract Refract Surg.* 2008;34(9):1538-1541.

Pop M, Payette Y. Risk factors for night vision complaints after LASIK for myopia. *Ophthalmology.* 2004;111(1):3-10.

Schallhorn SC, Kaupp SE, Tanzer DJ, Tidwell J, Laurent J, Bourque LB. Pupil size and quality of vision after LASIK. *Ophthalmology.* 2003;110(8):1606-1614.

Schmidt GW, Yoon M, McGwin G, Lee PP, McLeod SD. Evaluation of the relationship between ablation diameter, pupil size, and visual function with vision-specific quality-of-life measures after laser in situ keratomileusis. *Arch Ophthalmol.* 2007;125(8):1037-1042.

Ocular Motility, Confrontation Fields, and Ocular Anatomy

Ocular motility should also be evaluated. In patients with asymptomatic tropia or phoria, symptoms may develop after refractive surgery if the change in refraction causes the motility status to break down. If there is a history of strabismus (see Chapter 10) or a concern about ocular alignment postoperatively, a trial with contact lenses before surgery should be considered. A sensory motor evaluation can be obtained preoperatively if strabismus is an issue. Confrontation fields should be considered as well, if clinically indicated.

The general anatomy of the orbits should also be assessed. Patients with small

palpebral fissures and/or large brows may not be ideal candidates for LASIK or epipolis LASIK (epi-LASIK) because there may be inadequate exposure and difficulty in achieving suction with the microkeratome or laser suction ring.

Intraocular Pressure

The intraocular pressure (IOP) should be checked after the manifest refraction is completed and corneal topography measurements are taken. Patients with glaucoma (see Chapter 10) should be advised that during certain refractive surgery procedures the IOP is dramatically elevated, potentially aggravating optic nerve damage. Also, topical corticosteroids are used after most refractive surgery procedures and, after a surface ablation procedure, may be used for months. Long-term use of topical corticosteroids may cause marked elevation of IOP in corticosteroid responders.

Samuelson TW. Refractive surgery in glaucoma. *Curr Opin Ophthalmol.* 2004;15(2):112-118.

Slit-Lamp Examination

A complete slit-lamp examination of the eyelids and anterior segment should be performed. The conjunctiva should be examined specifically for conjunctival scarring, which may cause problems with microkeratome suction. The cornea should be evaluated for surface abnormalities such as decreased tear breakup time (Fig 2-1) and punctate epithelial erosions (Fig 2-2). Significant blepharitis (Fig 2-3), meibomitis, and dry eye syndrome should be addressed before refractive surgery, as they are associated with increased postoperative discomfort and decreased vision, and dry eye symptoms frequently increase postoperatively. A careful examination for epithelial basement membrane dystrophy (Fig 2-4) is required, because its presence increases the risk of flap complications during LASIK. Patients with epithelial basement membrane dystrophy are not ideal candidates for LASIK and may be better candidates for a surface ablation procedure. Signs of keratoconus, such as corneal thinning and steepening, may also be found. Keratoconus is typically a contraindication to incisional or ablative refractive surgery (see Chapter 10). The endothelium should be examined carefully for signs of cornea guttata and Fuchs and other dystrophies. Poor visual results have been reported in patients with cornea guttata and a family history of Fuchs dystrophy. Corneal edema is generally considered a contra-indication to refractive surgery. The deposits of granular and Avellino corneal dystrophies may increase substantially in size and number in the flap interface after LASIK, resulting in poor vision.

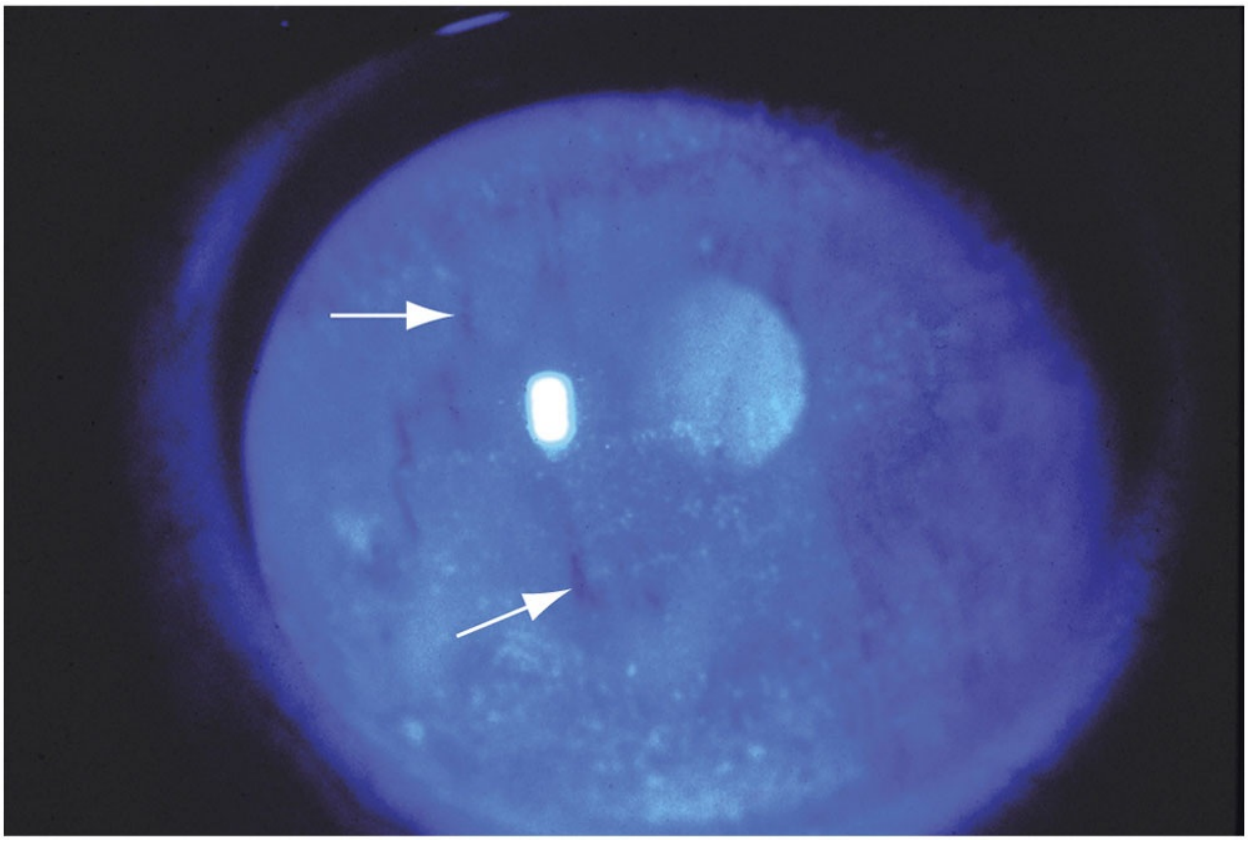

Figure 2-1 Slit-lamp photograph showing decreased tear breakup time. After instillation of fluorescein dye, the patient keeps the eye open for 10 seconds, and the tear film is examined with cobalt blue light. Breaks, or dry spots, in the tear film *(arrows)* are visible in this image. Punctate epithelial erosions are also present. *(Courtesy of Christopher J. Rapuano, MD.)*

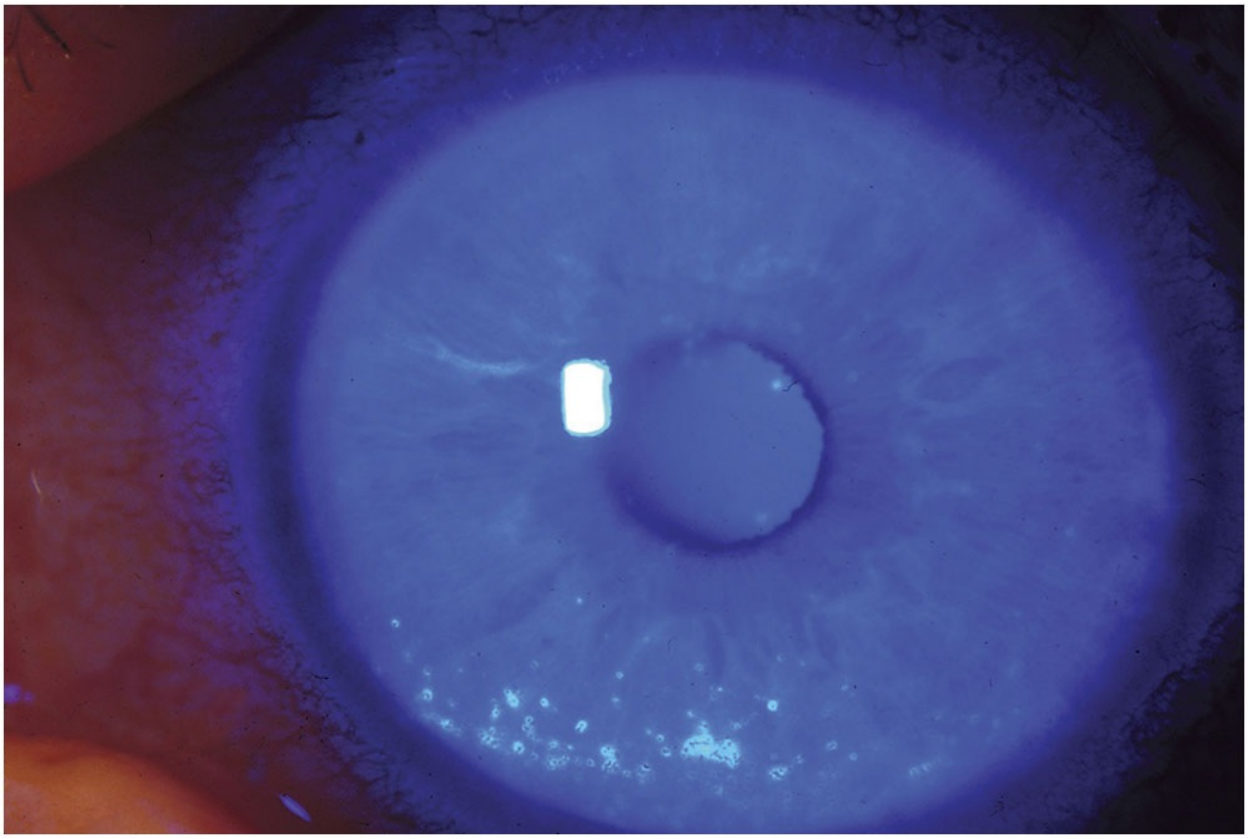

Figure 2-2 Slit-lamp photograph, showing punctate epithelial erosions. Inferior punctate fluorescein staining is noted in this image from a patient with moderately dry eyes. *(Courtesy of Christopher J. Rapuano, MD.)*

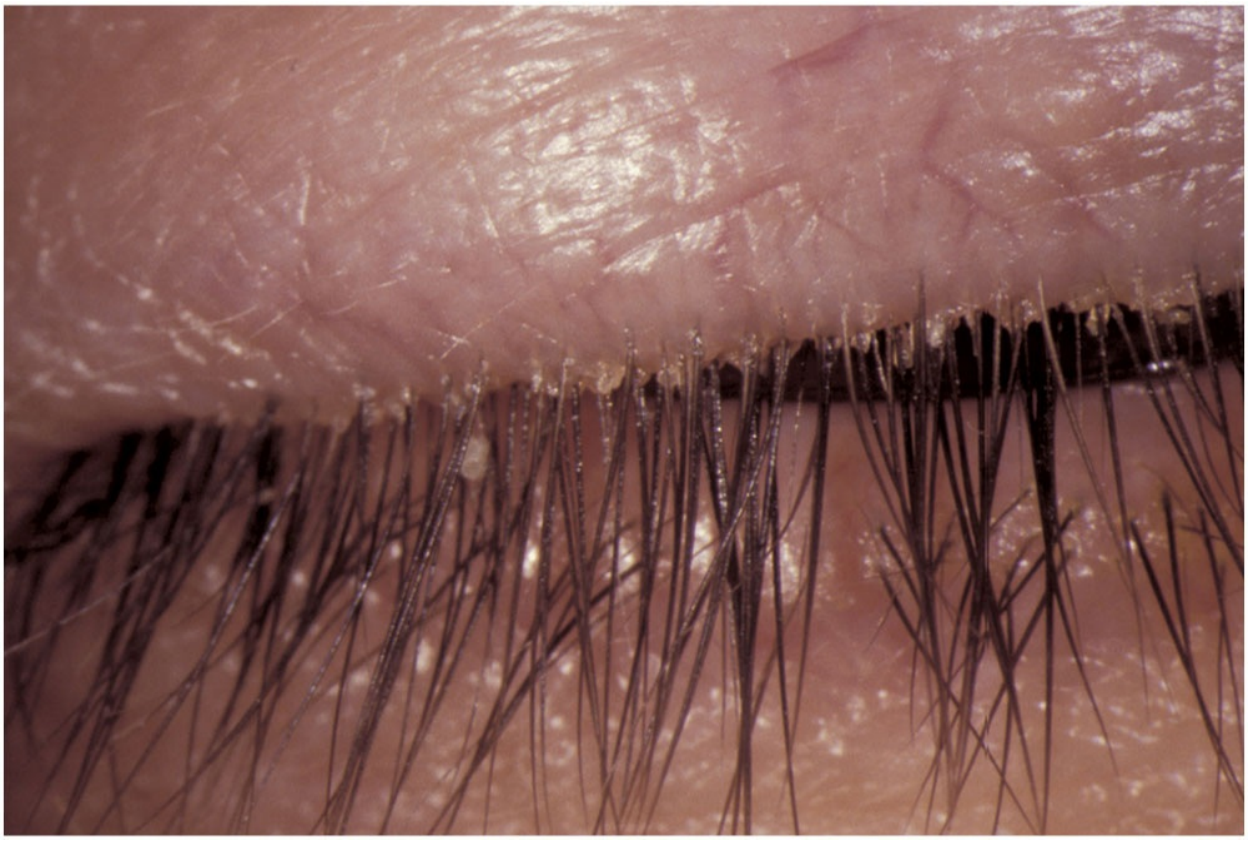

Figure 2-3 Example of blepharitis. Moderate crusting at the base of the lashes is shown in this image of a patient with seborrheic blepharitis. *(Courtesy of Christopher J. Rapuano, MD.)*

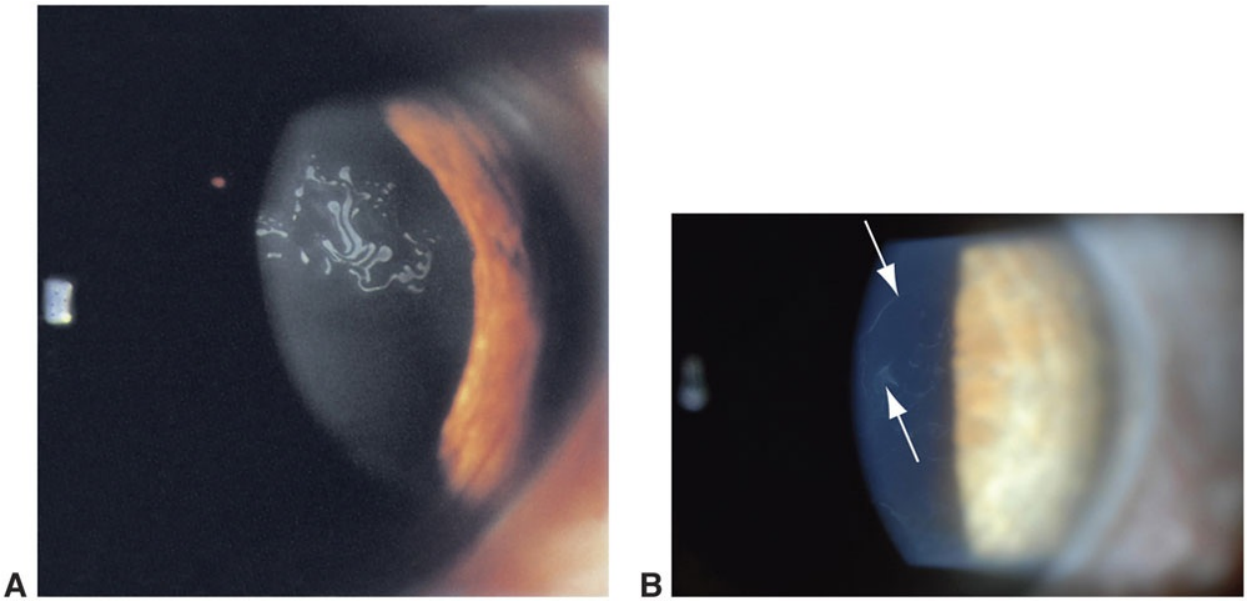

Figure 2-4 Images of epithelial basement membrane dystrophy. Epithelial map changes can be obvious **(A)** or more subtle **(B).** *Arrows* show geographic map lines. *(Part A courtesy of Vincent P. deLuise, MD; part B courtesy of Christopher J. Rapuano, MD.)*

The anterior chamber, iris, and crystalline lens should also be examined. A shallow anterior chamber depth may be a contraindication for insertion of certain phakic intraocular lenses (PIOLs) (see Chapter 8). Careful evaluation, both undilated and dilated, of the crystalline lens for clarity is essential, especially in patients older than 50 years. Surgeons should be wary of progressive myopia due to nuclear sclerosis. Patients with mild lens changes that are visually insignificant should be informed of these findings and advised that the changes may become more significant in the future, independent of refractive surgery. They should also be told that IOL power calculations are not as accurate when performed after keratorefractive surgery. In patients with moderate lens opacities, cataract extraction may be the best form of refractive surgery. Some surgeons give patients a record of their preoperative refractions and keratometry measurements along with the amount of laser ablation performed and the postoperative refraction.

Kim TI, Kim T, Kim SW, Kim EK. Comparison of corneal deposits after LASIK and PRK in eyes with granular corneal dystrophy type II. *J Refract Surg.* 2008;24(4):392-395.

Moshirfar M, Feiz V, Feilmeier MR, Kang PC. Laser in situ keratomileusis in patients with corneal guttata and family history of Fuchs' endothelial dystrophy. *J Cataract Refract Surg.* 2005;31(12):2281-2286.

Dilated Fundus Examination

A dilated fundus examination is also important before refractive surgery to ensure that the posterior segment is normal. Special attention should be given to the optic nerve (glaucoma, optic nerve drusen) and peripheral retina (retinal breaks, detachment). Patients and surgeons should realize that highly myopic eyes are naturally at increased risk of retinal detachment (see Chapter 10), unrelated to refractive surgery.

Packard R. Refractive lens exchange for myopia: a new perspective? *Curr Opin Ophthalmol.* 2005;16(1):53-56.

Ancillary Tests

Corneal Topography

The corneal curvature must be evaluated. Although manual keratometry readings can be quite informative, they have largely been replaced by computerized corneal topographic analyses. Several different methods are available to analyze the corneal curvature, including Placido disk, scanning-slit-beam, rotating Scheimpflug photography, high-frequency ultrasound, and ocular coherence tomography techniques. (See also the discussion of corneal topography in Chapter 1.) These techniques image the cornea and provide color maps showing corneal power and/or elevation. Patients

with visually significant irregular astigmatism are generally not good candidates for corneal refractive surgery. Early keratoconus, pellucid marginal degeneration (Fig 2-5), and contact lens warpage should be considered possible causes of visually significant irregular astigmatism. Irregular astigmatism secondary to contact lens warpage usually reverses over time, although the reversal may take months. Serial corneal topographic studies should be performed to document the disappearance of visually significant irregular astigmatism before any refractive surgery is undertaken.

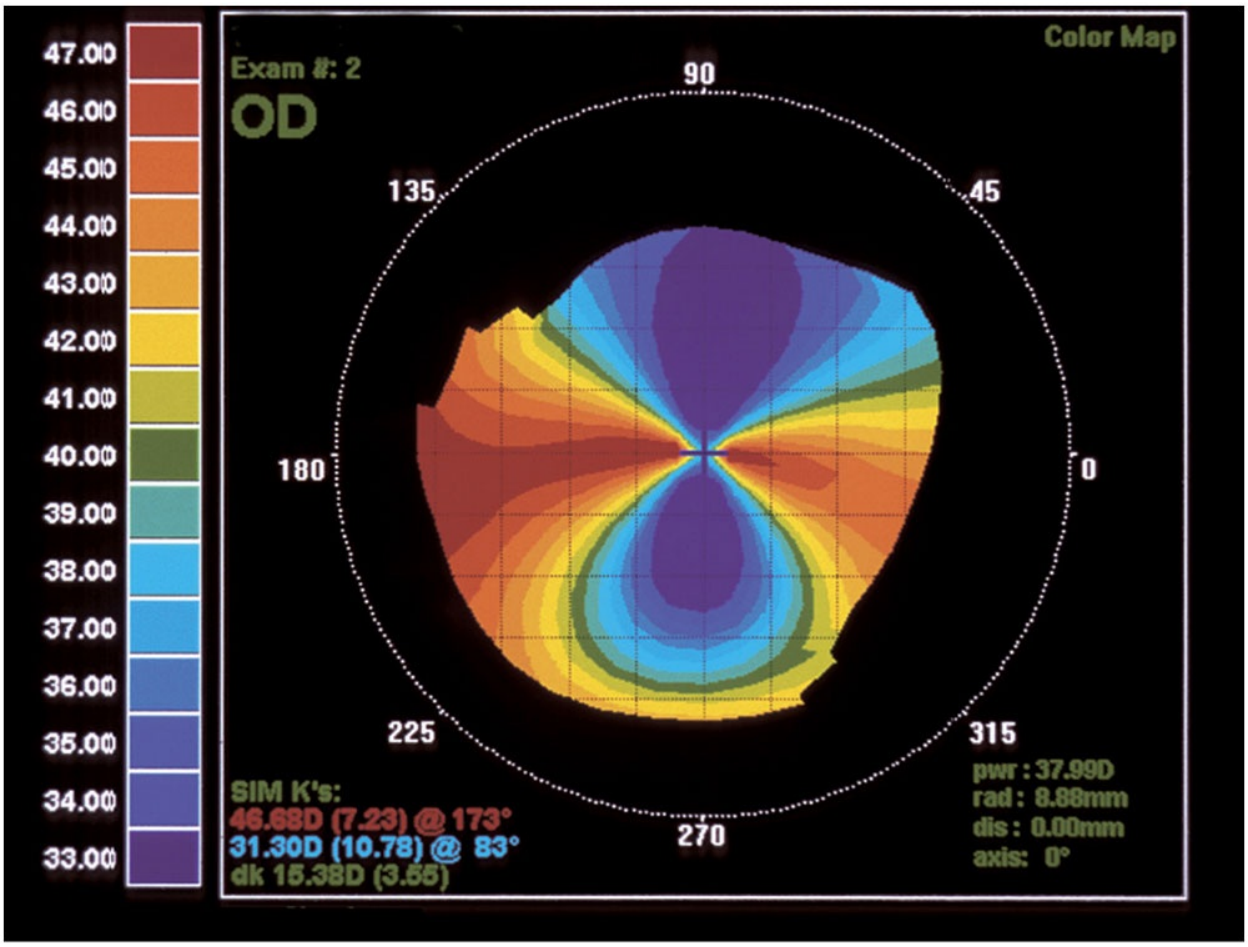

Figure 2-5 A corneal topographic map of the typical irregular against-the-rule astigmatism found in eyes with pellucid marginal degeneration. Note that the steepening nasally and temporally connects inferiorly. *(Courtesy of Christopher J. Rapuano, MD.)*

Unusually steep or unusually flat corneas can increase the risk of poor flap creation with the microkeratome. Femtosecond laser flap creation theoretically may avoid these risks. When keratometric or corneal topographic measurements reveal an amount or an axis of astigmatism that differs significantly from that determined through refraction, the refraction should be rechecked for accuracy. Lenticular astigmatism or posterior corneal curvature may account for the difference between refractive and

keratometric/topographic astigmatism. Most surgeons will treat the amount and axis of the refractive astigmatism, as long as the patient understands that after any future cataract surgery, some astigmatism may reappear (after the astigmatism contributed by the natural lens has been eliminated).

Pachymetry

Corneal thickness should be measured to determine whether it is adequate for keratorefractive surgery. This procedure is usually performed with ultrasound pachymetry; however, certain non-Placido disk corneal topography systems can also be used if properly calibrated. Most newer systems can provide a map showing the relative thickness of the cornea at various locations. The accuracy of the pachymetry measurements of scanning-slit systems decreases markedly for eyes that have undergone keratorefractive surgery. Because the thinnest part of the cornea is typically located centrally, a central measurement should always be taken. The thickness of the cornea is an important factor in determining whether the patient is a candidate for refractive surgery and which procedure may be best. In a study of 896 eyes undergoing LASIK, the mean central corneal thickness was 550 mm +- 33 mm (range, 472-651 mm). It has been suggested that an unusually thin cornea (beyond 2 standard deviations) indicates that the patient may not be ideal for any refractive surgery. Many surgeons would not consider LASIK refractive surgery if the central corneal thickness is less than 480 mm, even if the calculated residual stromal bed (RSB) is thicker than 250 mm. If LASIK is performed and results in a relatively thin RSB--for example, around 250 mm--future enhancement surgery that further thins the stromal bed may not be possible. If there is a question of whether endothelial integrity is causing an abnormally thick cornea, specular microscopy may be helpful in assessing the health of the endothelium.

Price FW Jr, Koller DL, Price MO. Central corneal pachymetry in patients undergoing laser in situ keratomileusis. *Ophthalmology.* 1999;106(11):2216-2220.

Wavefront Analysis

Wavefront analysis is a technique that can provide an objective refraction measurement (see also discussion of this topic in Chapters 1 and 5). Certain excimer lasers can use this wavefront analysis information directly to guide the ablation, a procedure called *wavefront-guided,* or *custom, ablation.* Some surgeons use wavefront analysis to document levels of preoperative higher-order aberrations. Refraction data from the wavefront analysis unit can also be used to refine the manifest refraction. If the manifest refraction and the wavefront analysis refraction are very dissimilar, the patient may not be a good candidate for wavefront treatment. Note that a custom wavefront ablation generally removes more tissue than does a standard ablation in the same eye.

Calculation of Residual Stromal Bed Thickness After LASIK

A lamellar laser refractive procedure such as LASIK involves creation of a corneal flap, ablation of the stromal bed, and replacement of the flap. The strength and integrity of the cornea postoperatively depend greatly on the thickness of the RSB. RSB thickness is calculated by subtracting the sum of the flap thickness and the calculated laser ablation depth from the preoperative corneal thickness. For example, if the central corneal thickness is 550 mm, the flap thickness is estimated to be 140 mm, and the ablation depth for the patient's refraction is 50 mm, the RSB would be 550 mm - (140 mm + 50 mm) = 360 mm thick. When the surgeon determines the RSB, the amount of tissue removed should be based on the actual intended refractive correction, not on the nomogram-adjusted number entered into the laser computer. For example, if a patient with -10.00 D myopia that is being fully corrected, the amount of tissue removed is 128 mm for a 6.5-mm ablation zone for the VISX laser. Even if the surgeon usually takes off 15% of the refraction for a conventional ablation and enters that number into the laser computer, approximately 128 mm of tissue will be removed, not 85% of 128 mm.

Most surgeons believe the RSB should be at least 250 mm thick. Others want the RSB to be greater than 50% of the original corneal thickness. If the calculation reveals an RSB that is thinner than desired, LASIK may not be the best surgical option. In these cases, a surface ablation procedure may be a better option because no stromal flap is required; this results in a thicker RSB postoperatively.

Discussion of Findings and Informed Consent

Once the evaluation is complete, the surgeon must analyze all the information and discuss the findings with the patient. If the patient is a candidate for refractive surgery, the risks and benefits of the various medical and surgical alternatives must be discussed. (Table 2-2 provides an overview of the most common refractive surgery procedures, their typical refractive ranges, and their key limitations.) Important aspects of this discussion are the expected visual acuity results for the amount of refractive error (including the need for distance and/or reading glasses, the chance of needing an enhancement, and whether maximal surgery is being performed during the initial procedure), the risk of decreased CDVA or severe vision loss, the adverse effects of glare and halos or dry eyes, the change in vision quality, and the rare need to revise a corneal flap (eg, for flap displacement, significant striae, or epithelial ingrowth). The patient should understand that the laser ablation might need to be aborted if there is an incomplete, decentered, or buttonholed flap. The pros and cons of surgery on 1 eye versus both eyes on the same day should also be discussed and patients allowed to decide which is best for them. Although the consequences of bilateral infection are higher with bilateral surgery, serial unilateral surgery may result in temporary anisometropia and is more inconvenient. Nonsurgical alternatives, such as glasses and

contact lenses, should also be discussed.

Table 2-2

Table 2-2 Limitations of the Most Common Refractive Surgery Procedures

Procedure	Typical Spherical Range	Typical Cylinder Range	Limitations
LASIK	−10.00 to +4.00 D	Up to 4.00 D	Thin corneas (thin residual stromal bed); epithelial basement membrane dystrophy; small palpebral fissures; microkeratome flap complications, especially with flat and steep corneas; preoperative severe dry-eye syndrome; certain medications; wavefront-guided ablations may have more restricted FDA-approved treatment parameters
Surface ablation	−10.00 to +4.00 D	Up to 4.00 D	Postoperative haze at high end of treatment range but range may be extended with the use of mitomycin C; preoperative severe dry eye syndrome; certain medications; prolonged vision-recovery time and more postoperative discomfort compared with LASIK
Intrastromal corneal ring segments	−1.00 to −3.00 D	None	Not FDA approved to correct cylinder; glare symptoms; white opacities at edge of ring segments; not after radial keratotomy
Intrastromal corneal ring segments	FDA approved to treat myopia in keratoconus	NA	Approved for patients 21 years or older; contact lens intolerance; corneal thickness ≥450 μm at incision site; no corneal scarring
Phakic intraocular lenses	−3.00 to −20.00 D	None	FDA approved for myopia; intraocular surgery; long-term complications such as glaucoma, iritis, cataract, pupil distortion, corneal edema
Refractive lens exchange	All ranges	Up to 3.00 D	Not FDA approved; same complications as with cataract extraction with a lens implant

FDA = US Food and Drug Administration; LASIK = laser in situ keratomileusis; NA = not applicable.

If a patient is considering refractive surgery, he or she should be given the informed consent document to take home and review. The patient should be given an opportunity to discuss any questions related to the surgery or the informed consent form with the surgeon preoperatively. The consent form should be signed before surgery and never when the patient is dilated and/or sedated. For sample informed consent forms, see Appendix 2, as well as the website of the Ophthalmic Mutual Insurance Company (OMIC; www.omic.com/risk-management/consent-forms/).

CHAPTER 3

Incisional Corneal Surgery

Incisional refractive surgery has largely been replaced by other modalities but is still used in limited circumstances for treatment of primary and residual astigmatism after both cataract and keratorefractive surgery (limbal relaxing incisions) and following penetrating keratoplasty (arcuate keratotomy).

The history of incisional keratotomy dates back to the 1890s. Lans examined astigmatic changes induced in rabbits after partial-thickness corneal incisions and thermal cautery. Sato made significant contributions to incisional refractive surgery in the 1930s and 1940s. He observed central corneal flattening and improvement in vision after the healing of spontaneous ruptures of the Descemet membrane (corneal hydrops) in patients with advanced keratoconus, which led him to develop a technique to induce artificial ruptures of the Descemet membrane. His long-term results in humans were poor, because incisions were made posteriorly through the Descemet layer, inducing late corneal edema in 75% of patients. In the 1960s and 1970s, Fyodorov, using radial incisions on the anterior cornea, established that the diameter of the central optical clear zone was inversely related to the amount of refractive correction: smaller central clear zones yield greater myopic corrections.

Incisional Correction of Myopia

Radial Keratotomy in the United States

Radial keratotomy (RK) is now largely considered an obsolete procedure, but it did play an important role in the history of refractive surgery. The excimer laser was originally intended to produce more accurate incisions for RK, not for surface ablation or laser in situ keratomileusis (LASIK), for which the excimer laser is now used. Radial keratotomy differs from surface ablation and LASIK in that it does not involve removal of tissue from the central cornea; rather, there is a redistribution of power from the center to the periphery.

To evaluate the safety and efficacy of RK, the Prospective Evaluation of Radial

Keratotomy (PERK) study was undertaken in 1982 and 1983 for patients with myopia from -2.00 D to -8.75 D (mean, -3.875 D). The sole surgical variable was the diameter of the central optical clear zone (3.00, 3.50, or 4.00 mm), based on the level of preoperative myopia. It was later found that the older the patient, the greater the effect achieved with the same surgical technique. In the PERK study, 8 radial incisions were used for all patients; repeat surgery, if necessary, involved an additional 8 incisions. Ten years after the procedure, 53% of the 435 study patients had 20/20 or better uncorrected distance visual acuity (UDVA; also called *uncorrected visual acuity, UCVA*) and 85% had 20/40 or better. Of the patients who had bilateral surgery, only 30% reported the use of spectacles or contact lenses for distance refractive correction at 10 years. Complications related to the procedure included loss of corrected distance visual acuity (CDVA; also called *best-corrected visual acuity, BCVA;* 3%), delayed bacterial keratitis, corneal scarring, irregular astigmatism, and epithelial erosions.

The most important finding in the 10-year PERK study was the continuing long-term instability of the procedure. A hyperopic shift of 1.00 D or greater was found in 43% of eyes between 6 months and 10 years postoperatively. There was an association between length of the incision and hyperopic shift, particularly if the incisions extended into the limbus.

Waring GO III, Lynn MJ, McDonnell PJ; PERK Study Group. Results of the Prospective Evaluation of Radial Keratotomy (PERK) study 10 years after surgery. *Arch Ophthalmol.* 1994;112(10):1298-1308.

Surgical technique

Radial corneal incisions severed collagen fibrils in the corneal stroma. This produced a wound gape with midperipheral bulging of the cornea, compensatory central corneal flattening, and decreased refractive power, thereby decreasing myopia (Fig 3-1).

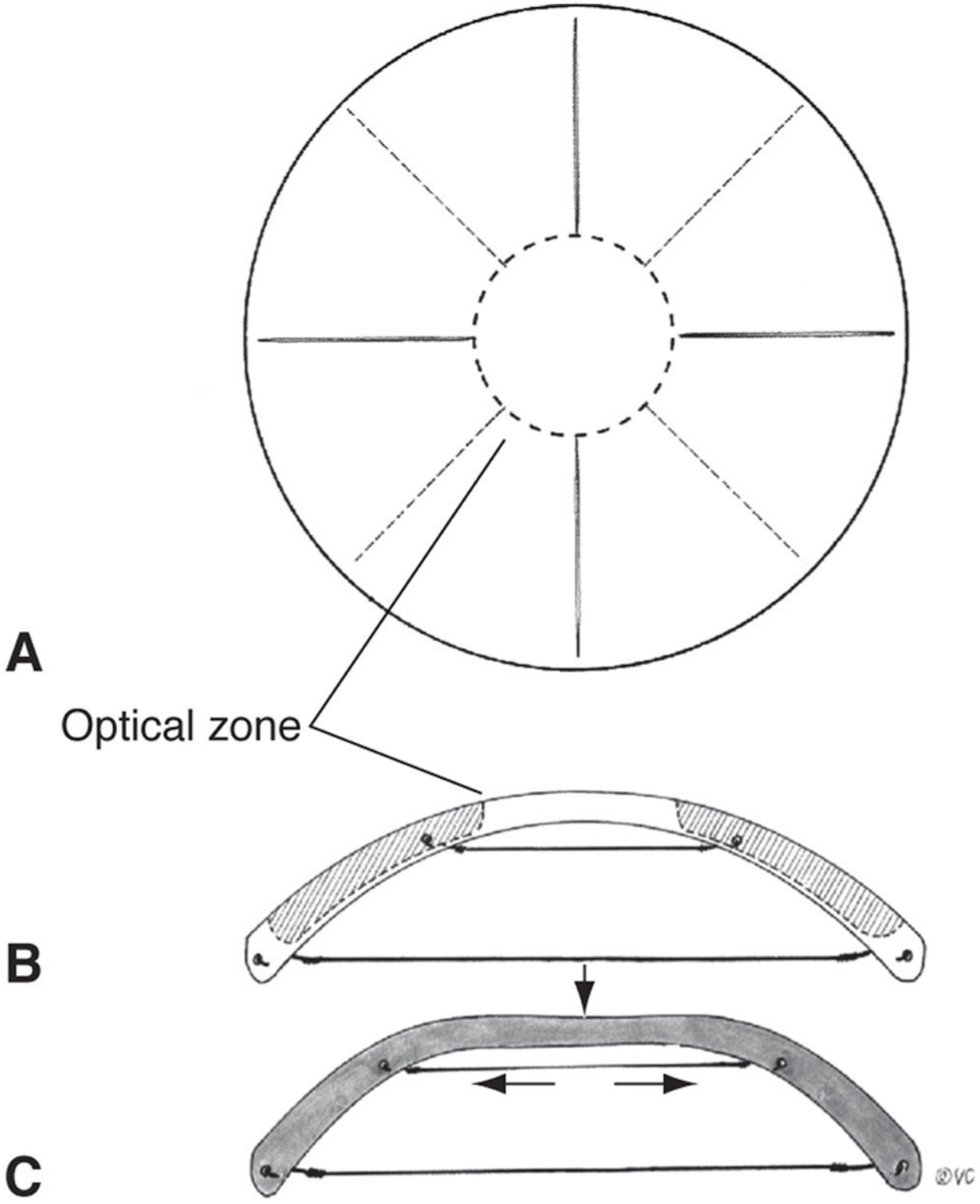

Figure 3-1 Schematic diagrams of the effect of radial incisions. **A,** 8-incision radial keratotomy (RK) with circular central optical zone *(dashed circle),* which shows the limit of the inner incision length. **B,** Cross-sectional view of the cornea, showing RK incisions *(shaded areas).* **C,** Flattening is induced in the central cornea. *(Modified from Troutman RC, Buzard KA.* Corneal Astigmatism: Etiology, Prevention, and

Management. *St Louis: Mosby-Year Book; 1992.)*

The design of the diamond-blade knife (angle and sharpness of cutting edge, width of blade, and design of footplate) influenced both the depth and the contour of incisions (Fig 3-2). The footplates reduced the risk of penetration and stabilized the blade. The guard on the front of the blade prevented inadvertent entry into the central optical zone. The length of the knife blade and the associated depth of the incisions were set according to the corneal thickness, which was usually measured with an ultrasonic pachymeter. The ideal depth of RK incisions was 85%-90% of the corneal thickness.

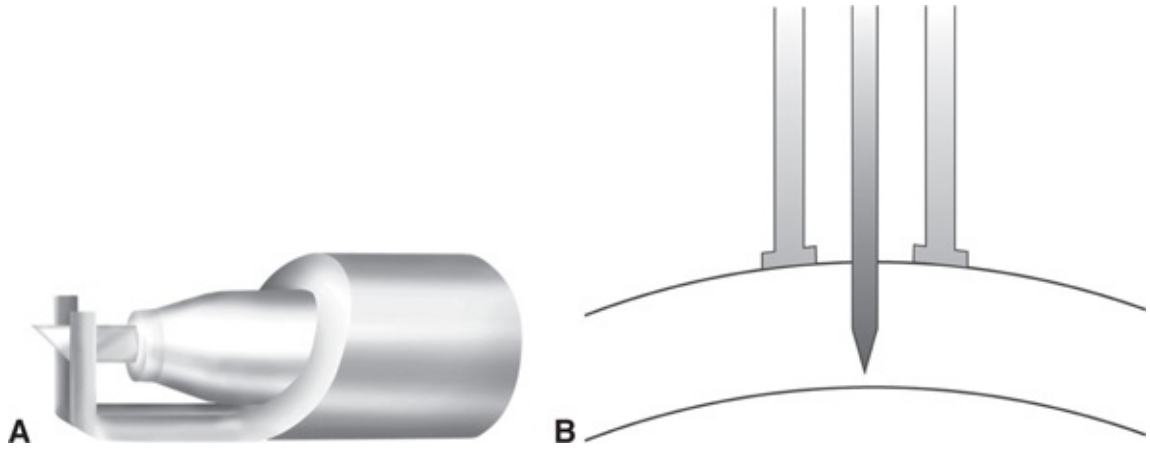

Figure 3-2 A, Illustration of the guarded diamond knife used in RK surgery. Note the footplates and blade between them. The distance from the tip of the blade to the footplates is adjustable. **B,** Diagram of RK diamond blade with footplates that rest on the cornea, reducing the risk of penetration into the anterior chamber. *(Part A courtesy of KMI Surgical; redrawn by Cyndie C. H. Wooley.)*

Postoperative refraction, visual acuity, and corneal topography

Radial keratotomy changed not only the curvature of the central cornea but also its overall topography, creating an oblate cornea--flatter in the center and steeper in the periphery. The procedure reduced myopia but increased spherical aberration. The result was less correlation among refraction, central keratometry, and UDVA, presumably because the new corneal curvature created a more complex, multifocal optical system. The effect is that keratometric readings, which sample a limited number of points approximately 3.0 mm apart, might show degrees of astigmatism that differ from those detected by refraction. Similarly, UDVA might vary, particularly depending on pupil diameter: the smaller the pupil, the less the multifocal effect from postoperative corneal contour and the better the quality of vision. Also, the central corneal flattening may affect intraocular lens (IOL) power calculation for cataract surgery (discussed later in this chapter and in Chapter 11).

Stability of refraction

Most eyes were generally stable by 3 months after RK surgery. However, diurnal fluctuation of vision and a progressive flattening effect after surgery have been known to persist, resulting in refractive instability.

Diurnal fluctuation of vision occurs due to hypoxic edema of the incisions with the eyelids closed during sleep. This edema causes flattening of the cornea (and hyperopic shift) upon awakening, followed by steepening later in the day. In a subset of the PERK study at 10 years, the mean change in the spherical equivalent of refraction between the morning (waking) and evening examinations was an increase of 0.31 +- 0.58 D in minus power.

The *progressive flattening effect of surgery* was one of the major untoward results with RK. The refractive error in 43% of eyes in the PERK study changed in the hyperopic direction by 1.00 D or more between 6 months and 10 years postoperatively. The hyperopic shift was statistically associated with decreasing diameter of the central optical clear zone. Corneal lasso sutures were once advocated, but their use has become largely obsolete. The potential stabilizing effect of collagen crosslinking induced with riboflavin and ultraviolet A (UVA) light is currently being studied.

Complications

After RK surgery, 1%-3% of eyes experienced loss of 2 or more lines of Snellen visual acuity. This effect was due to induction of irregular astigmatism from hypertrophic scarring, intersecting radial and transverse incisions (Fig 3-3A, B), and central clear zones smaller than 3.0 mm.

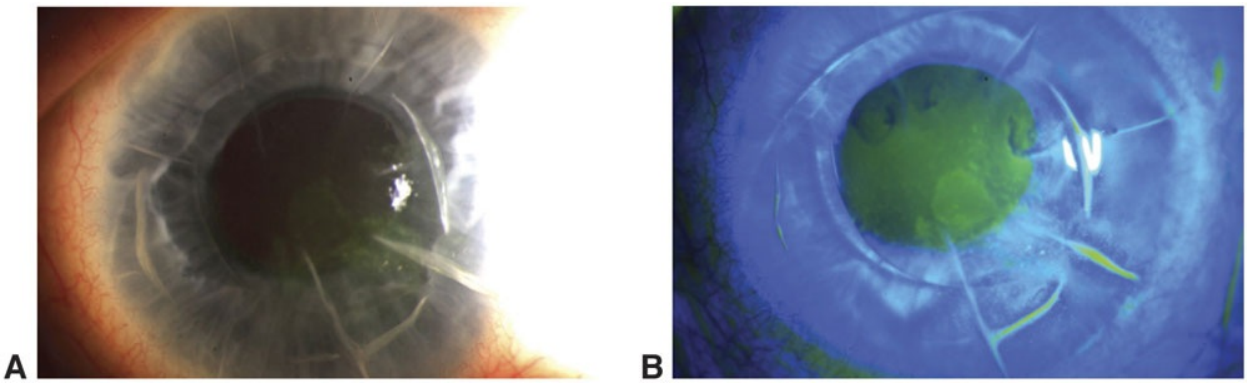

Figure 3-3 A, Crossed RK and arcuate keratotomy incisions with epithelial plugs in a patient who had intraoperative corneal perforation. **B,** Fluorescein study demonstrates gaping of the incisions, causing persistent ocular irritation. *(Courtesy of Jayne S. Weiss, MD.)*

Many patients reported the appearance of starburst, glare, or halo effects around lights at night after RK. Although most patients found the starburst effect comparable to looking through dirty spectacles or contact lenses, some patients could not drive at night because of this complication. Treatment with drugs that promote pupillary constriction,

such as brimonidine or pilocarpine, may be able to reduce symptoms. Other complications included postoperative pain, undercorrection and overcorrection, induced astigmatism due to epithelial plugs and wound gape (see Fig 3-3), vascularization of stromal scars, and nonprogressive endothelial disruption beneath the incisions.

Potentially blinding complications occurred only rarely after RK. These included perforation of the cornea, which can lead to endophthalmitis, epithelial downgrowth, and traumatic cataract. The postoperative use of contact lenses may have resulted in vascularization of the incisions, with subsequent scarring and irregular astigmatism.

Radial keratotomy incisions remain a point of weakness, and traumatic rupture of RK wounds has been reported up to 13 years after the procedure (Fig 3-4).

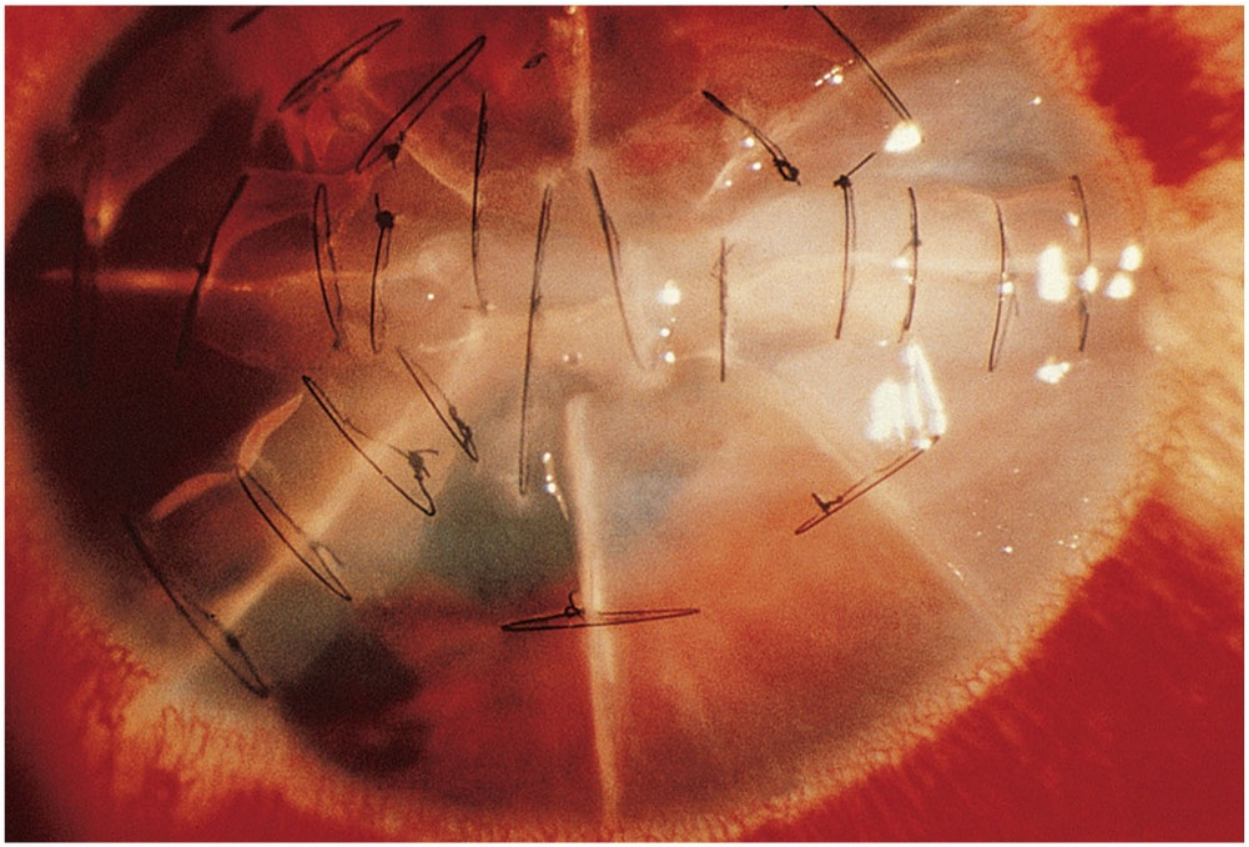

Figure 3-4 Traumatic rupture of an 8-incision RK, showing communication between 2 horizontal RK incisions. Interrupted 10-0 nylon sutures were used to close the incision. *(Reprinted with permission from* External Disease and Cornea: AMultimedia Collection. *San Francisco: American Academy of Ophthalmology; 2000.)*

Ocular surgery after radial keratotomy

It is not uncommon for RK patients to present years later with hyperopia. LASIK and surface ablation have been shown to be effective in correcting hyperopia and myopia after RK. However, surface ablation may be preferred, as creation of a LASIK flap may

result in irregular astigmatism due to splaying of the incisions and epithelial ingrowth, which can be challenging to treat. Surface ablation avoids the LASIK-related risks after RK but does increase the risk of postoperative corneal haze. The off-label use (in the United States) of mitomycin C, 0.02% (0.2 mg/mL), has dramatically reduced surface ablation haze after RK and other prior corneal surgeries (eg, corneal transplant and LASIK). The drug should be copiously irrigated from the eye so that toxic effects are reduced. The refractive correction is often reduced by 5%-15% when mitomycin C is used prophylactically.

Patients undergoing laser vision correction for refractive errors after RK should understand that laser correction will not remove scars caused by RK incisions, so glare or fluctuation symptoms may remain after the laser surgery. In addition, obtaining accurate wavefront analysis may not be possible due to complex optical irregularities associated with RK. Because of the progressive hyperopia that can occur with RK, it is prudent to aim for slight myopia with laser vision correction, as some patients may still progress to hyperopia in the future.

In patients with endothelial dystrophy, corneal infection, irregular astigmatism, severe visual fluctuations, or starburst effects, keratoplasty may be needed to restore visual functioning. It should be avoided if the patient's visual problems can be corrected with glasses or contact lenses. If keratoplasty is deemed necessary, the RK incisions may need to be sutured before trephination in order to minimize the chance of their opening and to allow adequate suturing of the donor corneal graft to the recipient bed.

Cataract extraction with IOL implantation may lead to variable results after RK. In the early postoperative period, corneal edema may result in temporary hyperopia. In addition, IOL power calculation may be problematic and may result in ametropia. Calculation of implant power for cataract surgery after RK should be done by first using a third-generation formula (eg, Haigis, Hoffer Q, Holladay 2, or SRK/T) rather than a regression formula (eg, SRK I or SRK II) and then choosing the highest resulting IOL power. Keratometric power is determined in 1 of 3 ways: direct measurement using corneal topography; application of pre-RK keratometry value minus the refractive change; or adjustment of the base curve of a plano contact lens by the overrefraction (see Chapter 11). Newer modalities such as intraoperative aberrometry may help refine IOL selection.

Incision placement and construction is vital when performing cataract surgery in the post-RK patient. Scleral tunnel incisions are often preferred, because clear corneal incisions increase the risk of the blade transecting the RK incision, which can induce irregular astigmatism. To help reduce preoperative corneal astigmatism, the surgeon may consider placing the incision in the steep astigmatic meridian of the cornea; in addition, toric IOLs can be used, but multifocal IOLs should be avoided. At the conclusion of cataract surgery, care should be taken to prevent overhydrating the

cataract incision to avoid rupture of the RK incision.

Anbar R, Malta JB, Barbosa JB, Leoratti MC, Beer S, Campos M. Photorefractive keratectomy with mitomycin-C for consecutive hyperopia after radial keratotomy. *Cornea.* 2009;28(4):371-374.

Hill WE, Byrne SF. Complex axial length measurements and unusual IOL power calculations. *Focal Points: Clinical Modules for Ophthalmologists*. San Francisco: American Academy of Ophthalmology; 2004, module 9.

Joyal H, Gregoire J, Faucher A. Photorefractive keratectomy to correct hyperopic shift after radial keratotomy. *J Cataract Refract Surg.* 2003;29(8):1502-1506.

Linebarger EJ, Hardten DR, Lindstrom RL. Laser-assisted in situ keratomileusis for correction of secondary hyperopia after radial keratotomy. *Int Ophthalmol Clin.* 2000;40(3):125-132.

Nassaralla BA, McLeod SD, Nassaralla JJ Jr. Prophylactic mitomycin C to inhibit corneal haze after photorefractive keratectomy for residual myopia following radial keratotomy. *J Refract Surg.* 2007;23(3):226-232.

Salamon SA, Hjortdal JO, Ehlers N. Refractive results of radial keratotomy: a ten-year retrospective study. *Acta Ophthalmol Scand.* 2000;78(5):566-568.

Seitz B, Langenbucher A. Intraocular lens calculations status after corneal refractive surgery. *Curr Opin Ophthalmol.* 2000;11(1):35-46.

Waring GO III. Radial keratotomy for myopia. *Focal Points: Clinical Modules for Ophthalmologists*. San Francisco: American Academy of Ophthalmology; 1992, module 5.

Incisional Correction of Astigmatism

Several techniques of incisional surgery have been used to correct astigmatism, including transverse (straight) keratotomy and arcuate (curved) keratotomy (AK), in which incisions are typically placed in the cornea at the 7-mm optical zone; and limbal relaxing incisions (LRIs), which are placed at the limbus. Transverse keratotomy was frequently used in the past in combination with RK to correct myopic astigmatism, but it is now used only seldomly. Arcuate keratotomy was also used to correct naturally occurring astigmatism, but the procedure is now used primarily to correct postkeratoplasty astigmatism. LRIs are used to help manage astigmatism during or after cataract surgery and IOL implantation and after refractive surgery procedures such as LASIK and photorefractive keratectomy.

Coupling

When 1 meridian is flattened from an astigmatic incision, an amount of steepening occurs in the meridian 90deg away (Fig 3-5). This phenomenon is known as *coupling*. When the coupling ratio (the amount of flattening in the meridian of the incision divided by the induced steepening in the opposite meridian) is 1.0, the spherical equivalent remains unchanged. When there is a positive coupling ratio (greater than 1.0), a hyperopic shift occurs. The type of incision (arcuate vs tangential) and the length and number of parallel incisions can influence the coupling ratio. Long, straight, and tangential incisions tend to induce more positive coupling (greater than 1.0), and therefore more hyperopia, than do short, arcuate incisions. When a correction is less than 2.00 D of astigmatism, the coupling ratio is typically 1.0, whereas when a correction is greater than 2.00 D of astigmatism, the ratio tends to be greater than 1.0. In general, LRIs do not change the spherical equivalent.

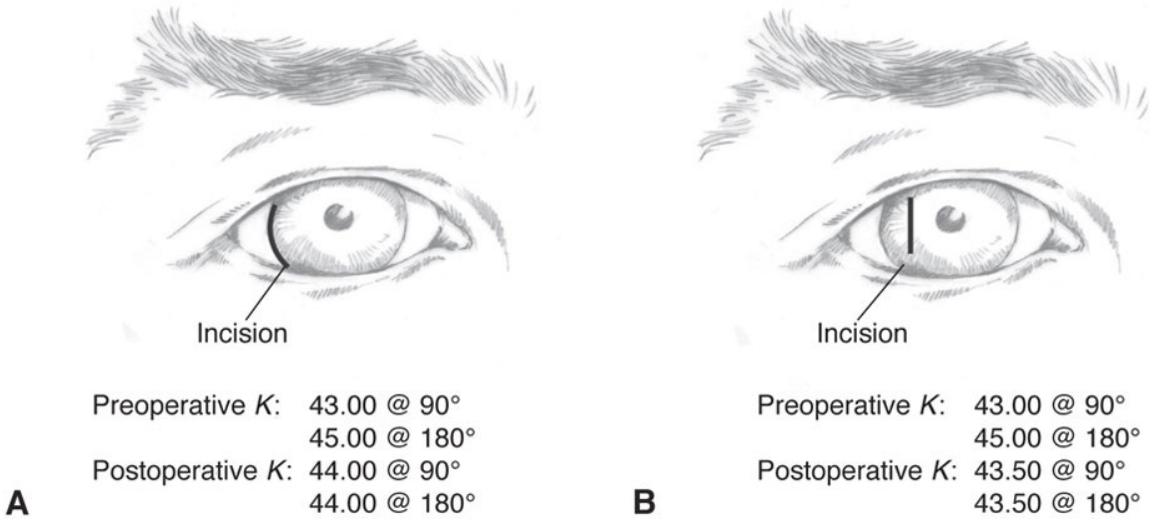

Figure 3-5 Coupling effect of astigmatic incisions. **A,** A limbal relaxing incision has a coupling ratio of 1.0, and the spherical equivalent and average corneal power are not changed. **B,** A transverse incision has a coupling ratio greater than 1.0, which causes a hyperopic change in refraction by making the average corneal power flatter. *(Illustration by Cyndie C. H. Wooley.)*

Rowsey JJ, Fouraker BD. Corneal coupling principles. *Int Ophthalmol Clin.* 1996;36(4):29-38.

Arcuate Keratotomy and Limbal Relaxing Incisions

Arcuate keratotomy is an incisional surgical procedure in which arcuate incisions of approximately 95% depth are made in the steep meridians of the midperipheral cornea at the 7-mm optical zone. LRIs are incisions set at approximately 600 mm depth, or 50 mm less than the thinnest pachymetry measurement at the limbus, and placed just anterior to the limbus (Fig 3-6). Arcuate keratotomy differs from LRIs by its midperipheral location and its greater relative depth. Due to the concomitant steepening of the orthogonal meridian (coupling), AK and LRIs correct astigmatism without inducing a substantial hyperopic shift of the spherical equivalent of the preoperative refraction. LRIs achieve increased effect primarily by increasing the length of the incision. For AK, cylindrical correction can be increased by increasing the length or depth of the incision, using multiple incisions, or reducing the optical zone (Table 3-1). The longer and deeper the incision and smaller the optical zone, the greater the astigmatic correction.

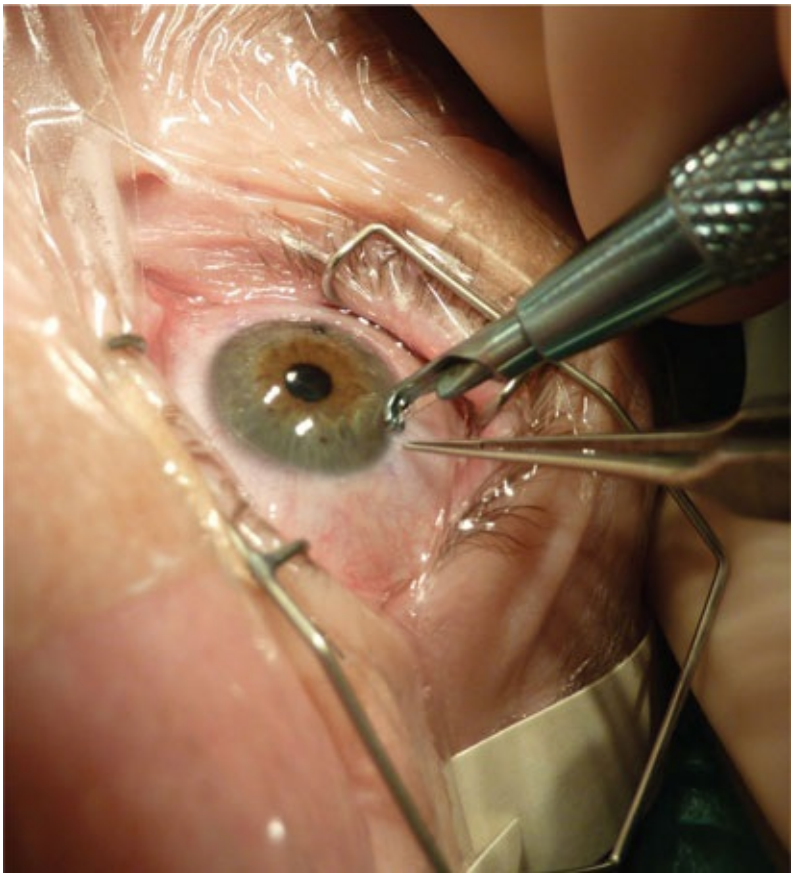

Figure 3-6 Limbal relaxing incision. A relaxing incision is made at the limbus with the use of a diamond knife. The coupling ratio is typically 1.0 and does not change the spherical equivalent. *(Courtesy of Brian S. Boxer Wachler, MD.)*

Table 3-1

Table 3-1 Sample Nomogram for Limbal Relaxing Incisions to Correct Keratometric Astigmatism During Cataract Surgery

Preoperative Astigmatism (D)	Age (Years)	Number	Length (Degrees)
With-the-rule			
0.75–1.00	<65	2	45
	≥65	1	45
1.01–1.50	<65	2	60
	≥65	2	45 (or 1 × 60)
>1.50	<65	2	80
	≥65	2	60
Against-the-rule/oblique*			
1.00–1.25†	–	1	35
1.26–2.00	–	1	45
>2.00	–	2	45

*Combined with temporal corneal incision.
†Especially if cataract incision is not directly centered on the steep meridian.

From Wang L, Misra M, Koch DD. Peripheral corneal relaxing incisions combined with cataract surgery. *J Cataract Refract Surg.* 2003;29(4):712–722.

Instrumentation

The instruments used in AK and LRIs are similar. Front-cutting diamond blades are

more often used in AK, and back-cutting diamond blades are more often used in LRI surgery. A mechanized trephine, the Hanna arcuate trephine, has been shown to make smooth, curvilinear AK incisions of specified optical zone and arc length. Recently, the femtosecond laser has been adapted to create peripheral arcuate incisions. These incisions may be titratable, as only part of the incision may be opened initially, followed by a larger area later if there is a need for greater astigmatic correction.

Surgical Techniques

With any astigmatism correction system, accurate determination of the steep meridian is essential. The plus cylinder axis of the manifest refraction is used, as this accounts for corneal and lenticular astigmatism, which are "manifest" in the refraction. If the crystalline lens is to be removed at the time of the astigmatic incisional surgery (ie, LRI), the correction should be based on the steep meridian and magnitude as measured with corneal topography or keratometry. Intraoperative keratoscopy can be helpful in determining incision location and effect. The amount of treatment for a given degree of astigmatism can be determined from a nomogram, such as the one shown in Table 3-1.

It is prudent to make horizontal reference marks using a surgical marking pen, with the patient sitting up, preferably at the slit lamp. Marking with the patient in this position avoids reference-mark error due to cyclotorsion of the eyes. Studies have demonstrated that up to 15deg of cyclotorsion can occur when patients move from an upright to a supine position. Arcuate keratotomy incisions may be placed in pairs along the steep meridian and, because of induced glare and aberrations, no closer than 3.5 mm from the center of the pupil. LRIs are placed in the peripheral cornea, near the limbus. They result in lower amounts of astigmatic correction than do AK incisions, presumably due to faster healing because of their proximity to the vascularized limbus. Arcuate keratotomy incisions used to correct post-penetrating keratoplasty astigmatism are often made in the graft or in the graft-host junction, but care must be taken to avoid perforation. When AK incisions are made in the host, the effect is significantly reduced. Arcuate keratotomy incisions in a corneal graft may require compression sutures at the meridian 90deg away, and an initial overcorrection is desired in order to compensate for wound healing.

Outcomes

The outcome of AK and LRI surgery depends on several variables, including patient age; the distance separating the incision pairs; and the length, depth, and number of incisions. Few large prospective trials have been performed. The Astigmatism Reduction Clinical Trial (ARC-T) of AK, which used a 7-mm optical zone and varying arc lengths, showed a reduction in astigmatism of 1.6 +- 1.1 D in patients with preoperative, naturally occurring astigmatism of 2.8 +- 1.2 D. Other studies of AK have

shown a final UDVA of 20/40 in 65%-80% of eyes. Overcorrections have been reported in 4%-20% of patients.

Studies of LRIs are limited, but these incisions are frequently used with seemingly good results in astigmatic patients undergoing cataract surgery. One study showed an absolute change in refractive astigmatism of 1.72 +- 0.81 D after LRIs in patients with mixed astigmatism. Astigmatism was decreased by 0.91 D, or 44%, in another series of LRIs in 22 eyes of 13 patients. Incisions in the horizontal meridian have been reported to cause approximately twice as much astigmatic correction as those in the vertical meridian (see Table 3-1).

Complications

Irregular astigmatism may occur after either AK or LRIs; however, it is more common with AK than with LRIs, probably because LRIs are farther from the corneal center, thus mitigating any effects of irregular incisions. Off-axis AK can lead to undercorrection or even worsening of preexisting astigmatism. To avoid creating an edge of cornea that swells and cannot be epithelialized, arcuate incisions and LRIs should not intersect other incisions (see Fig 3-3). Corneal infection and perforation have been reported.

Ocular Surgery After Arcuate Keratotomy and Limbal Relaxing Incisions

Arcuate keratotomy and LRIs can be combined with or performed after cataract surgery, surface ablation, or LASIK surgery. Better predictability can be obtained if astigmatic correction is performed after refractive stability is achieved. Penetrating keratoplasty can be done after extensive AK, but the wounds may have to be sutured before trephination, as discussed earlier for RK. A prerequisite for combining LRIs with cataract surgery is the use of astigmatically predictable phacoemulsification.

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Budak K, Yilmaz G, Aslan BS, Duman S. Limbal relaxing incisions in congenital astigmatism: 6 month follow-up. *J Cataract Refract Surg.* 2001;27(5):715-719.

Faktorovich EG, Maloney RK, Price FW Jr. Effect of astigmatic keratotomy on spherical equivalent: results of the Astigmatism Reduction Clinical Trial. *Am J Ophthalmol.* 1999; 127(3):260-269.

Nichamin LD. Astigmatism control. *Ophthalmol Clin North Am.* 2006;19(4):485-493.

Price FW, Grene RB, Marks RG, Gonzales JS; ARC-T Study Group. Astigmatism Reduction Clinical Trial: a multicenter prospective evaluation of the predictability of arcuate keratotomy. Evaluation of surgical nomogram predictability. *Arch Ophthalmol.* 1995;113(3):277-282.

Rubenstein JB, Raciti M. Management of astigmatism: LRIs. *Int Ophthalmol Clin.* 2012; 52(2): 31-40.

CHAPTER 4

Onlays and Inlays

Refractive error, including presbyopia, may be corrected by placing preformed tissue or synthetic material onto or into the cornea. This treatment alters the optical power of the cornea either by changing the shape of the anterior corneal surface or by creating a lens with a higher index of refraction than that of the corneal stroma. Tissue addition procedures, such as epikeratoplasty, have fallen out of favor because of the poor predictability of the refractive and visual results, loss of corrected distance visual acuity (CDVA; also called *best-corrected visual acuity, BCVA*), and difficulty of obtaining donor tissue. Compared with donor tissue, synthetic material can be shaped more precisely, and it can be mass-produced. Because of problems with re-epithelialization when synthetic material is placed on top of the cornea, synthetic material generally has to be placed within the corneal stroma. This placement requires a partial or complete lamellar dissection using specialized instruments. Early work using lenticules made of glass and plastic resulted in necrosis of the overlying stroma because glass and plastic are impermeable to water, oxygen, and nutrients. Current techniques use lenticule inlays made of more permeable substances such as hydrogel, with or without microperforations in the lenticule, to increase the transmission of nutrients. Another type of inlay indirectly alters the shape of the central cornea by using midperipheral corneal ring segments made of polymethylmethacrylate (PMMA). Because the ring segments are narrow, the overlying stroma can receive nutrients from surrounding tissue.

Keratophakia

In keratophakia, a plus-powered lens is placed intrastromally to increase the curvature of the anterior cornea to correct hyperopia and presbyopia. After a central lamellar keratectomy is performed with a microkeratome or femtosecond laser, the flap is lifted, the lenticule is placed onto the host bed, and the flap is replaced and adheres without sutures. Lenticules can be prepared from either donor cornea or synthetic material; these types are referred to as homoplastic and alloplastic lenticules, respectively.

Homoplastic Corneal Inlays

A homoplastic inlay is created from a donor cornea by a lamellar keratectomy after removal of the epithelium and Bowman layer. The lenticule (fresh or frozen) is then shaped into a lens using an automated lathe. The lens can be preserved fresh in refrigerated tissue-culture medium, frozen at subzero temperatures, or freeze-dried.

Keratophakia has been used to correct aphakia and hyperopia of up to 20.00 D, but few studies on this procedure have been published. Troutman and colleagues reported on 32 eyes treated with homoplastic keratophakia, 29 of which also underwent cataract extraction. Even for procedures done by experienced surgeons, refractive predictability was still low: the eyes of 25% of patients were more than 3.00 D from the intended correction. Complications included irregular lamellar resection, wound dehiscence, and postoperative corneal edema. Although the procedure was originally intended to be used in conjunction with cataract extraction for the correction of aphakia, the complexity of the procedure and the unpredictable refractive results could not compete--in the early 1980s--with aphakic contact lenses or the improved technology of intraocular lens (IOL) implantation. Homoplastic keratophakia is now largely obsolete.

Alloplastic Corneal Inlays

Alloplastic inlays offer several potential advantages over homoplastic inlays, such as the ability to be mass-produced in a wide range of sizes and powers that can be measured and verified. Synthetic material may have optical properties that are superior to those of tissue lenses.

For insertion of the inlay, a laser in situ keratomileusis (LASIK)-type flap or a stromal pocket dissection can be performed; such procedures are technically easier than doing a complete lamellar keratectomy. Experiments performed in the early 1980s resulted in corneal opacities, nonhealing epithelial erosions, and diurnal fluctuation in vision because fluid and nutrients were blocked from reaching the anterior cornea. Thus, to allow for the transfer of fluid and nutrients to the anterior cornea, microperforations were incorporated into the inlays. Because of work performed by Knowles and others, most subsequent studies used water-permeable hydrogel implants. Hydrogel lenses have an index of refraction similar to that of the corneal stroma, so these lenses have little intrinsic optical power when implanted. To be effective, they must change the curvature of the anterior cornea.

Currently, 3 companies are beginning to commercialize such products. A new device, the *Kamra inlay*, formerly known as the AcuFocus Corneal Inlay (AcuFocus Inc, Irvine, CA), has been available in several countries outside the United States and was recently approved by the US Food and Drug Administration (FDA) for use in the treatment of presbyopia. This device is composed of an ultrathin (5-mm), biocompatible polymer that is microperforated to allow improved nutrient flow. The

3.8-mm-diameter inlay has a central aperture of 1.6 mm and is generally implanted in the nondominant eye. A 200-mm-thick corneal flap or intrastromal pocket is created, and the inlay is placed on the stromal bed, centered on the pupil. Although the inlay has no refractive power, the central aperture functions as a pinhole to increase depth of focus and improve near vision without changing distance vision. See Chapter 12 for further discussion of corneal inlays.

Ismail MM. Correction of hyperopia with intracorneal implants. *J Cataract Refract Surg.* 2002;28(3):527-530.

Epikeratoplasty

To eliminate the complexity of the lamellar dissection and intraoperative lathing of early keratomileusis procedures--in which a corneal cap was dissected from the eye, shaped on a cryolathe, and then repositioned with sutures--Kaufman, Werblin, and colleagues developed epikeratoplasty (also called *epikeratophakia*) in the early 1980s. Epikeratoplasty involved suturing a preformed homoplastic lenticule directly onto the Bowman layer of the host cornea (Fig 4-1). Because no viable cells existed in the donor tissue, classic graft rejection did not occur. Epikeratoplasty was originally intended to create a "living contact lens" for patients with aphakia who were unable to wear contact lenses. Indications for this procedure were later expanded to include hyperopia, myopia, and keratoconus, but problems such as adherence of the grafted tissue, infection, epithelial ingrowth into the bed, poor predictability of results, and corneal edema have relegated epikeratoplasty to a historical footnote. In treating patients with these conditions, surgeons need to approach corneal refractive surgery with caution.

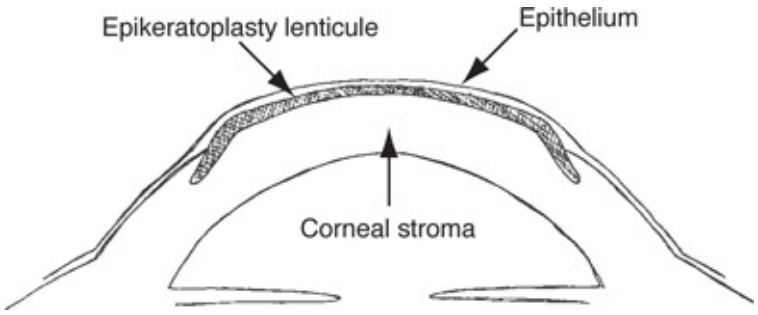

Figure 4-1 Schematic depiction of epikeratoplasty. The lenticule is sutured onto the cornea after removal of the epithelium. The edge of the lenticule is placed into a shallow lamellar dissection and tucked under the peripheral cornea.

Werblin TP, Kaufman HE, Friedlander MH, Sehon KL, McDonald MB, Granet NS. A prospective study of the use of hyperopic epikeratophakia grafts for the correction of aphakia in adults. *Ophthalmology.* 1981;88(11):1137-1140.

Intrastromal Corneal Ring Segments

Background

Intrastromal corneal ring segments (ICRS) can treat low degrees of myopia by displacing the lamellar bundles and shortening the corneal arc length. These circular arcs, made of PMMA, are placed in the midperipheral corneal stroma in a lamellar channel (Figs 4-2, 4-3). The thicker the segment is, the greater will be the flattening of the cornea and the reduction in myopia. Ferrara rings (Ferrara Ophthalmics, Belo Horizonte, Brazil) have a smaller optical zone and a greater flattening effect than do Intacs (Addition Technology, Des Plaines, IL). This section focuses on Intacs because Ferrara rings, though commonly used internationally, are not FDA approved for use in the United States.

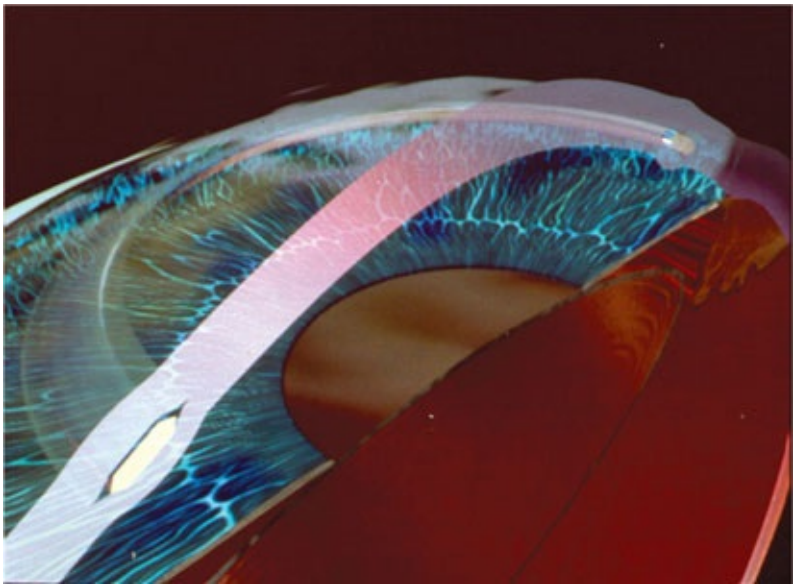

Figure 4-2 Rendering of a cross section of the cornea with an intrastromal corneal ring segment. The ring segment displaces the lamellar bundles, thereby shortening the corneal arc length and reducing the myopia. *(Courtesy of Addition Technology.)*

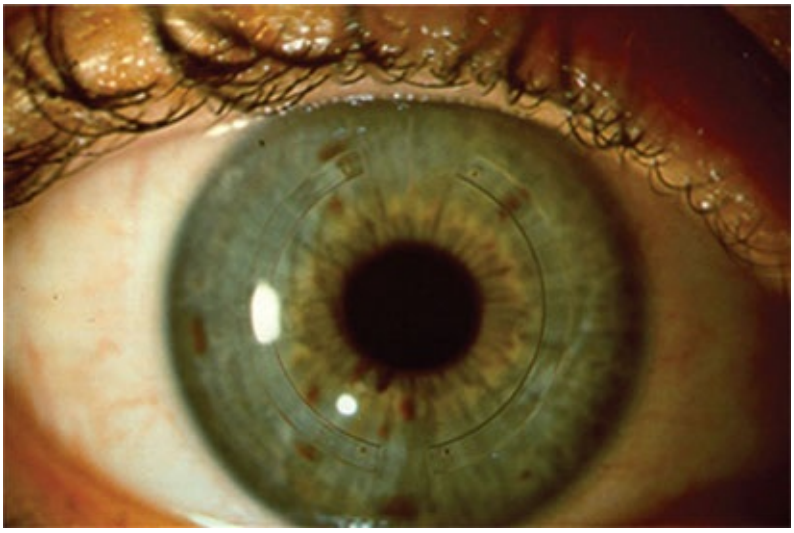

Figure 4-3 Clinical photograph showing ring segments implanted in an eye to treat low myopia. Note the vertical placement of the ring segments with a clear central zone. *(Courtesy of Steven C. Schallhorn, MD.)*

Treatment using ring segments has several potential advantages over other forms of refractive surgery. The ring segments can be explanted, making the refractive result of the procedure potentially reversible, and they can be replaced with ring segments of a different thickness to titrate the refractive result. Intacs are FDA approved to treat myopia at levels ranging from -1.00 to -3.00 D spherical equivalent; they are not approved for patients with astigmatism. However, Intacs surgery is no longer commonly performed for myopia because the results are not as predictable as are those with ablative corneal surgery.

Intacs are typically contraindicated in

- patients with collagen vascular, autoimmune, or immunodeficiency diseases
- pregnant or breastfeeding women
- patients who may be predisposed to future complications because of the presence of ocular conditions (such as herpetic keratitis, recurrent corneal erosion syndrome, and corneal dystrophy)

Instrumentation

Initially, a 1-piece 360deg Intacs ring was used in the procedure, but it proved difficult to insert. The design was later changed to 2 segments of 150deg arc. The segments have a fixed inner diameter of 6.50 mm and an outer diameter of 8.10 mm, and they are available in various thicknesses: 0.210, 0.250, 0.275, 0.300, 0.325, 0.350, 0.400, and 0.450 mm. The degree of correction achieved is related to the thickness of the ring segments; thicker ring segments are used for greater correction. Manually operated

surgical equipment or a femtosecond laser can be used to create the channels.

Technique

The procedure involves creating a lamellar channel at approximately 68%-70% stromal depth, followed by insertion of the ring segments. The geometric center of the cornea is marked with a blunt hook. An ultrasound pachymeter is used to measure the thickness of the cornea over the entry mark. A diamond knife is set to 68%-70% of the stromal depth and then used to create a 1.0-mm radial incision. Specially designed mechanical instruments are then used to create the channels for the segments by blunt separation of the collagen lamellae (Fig 4-4). Similar entry incisions and channels may be created using a femtosecond laser. The channels are created in an arc pattern at the desired inner and outer diameters. Once the channels are created, specialized forceps are used to insert the first ring segment and rotate it into position, followed by similar insertion and rotation of the second segment. Tissue glue or 1 or 2 10-0 nylon sutures may be used to close the radial incision at the corneal surface.

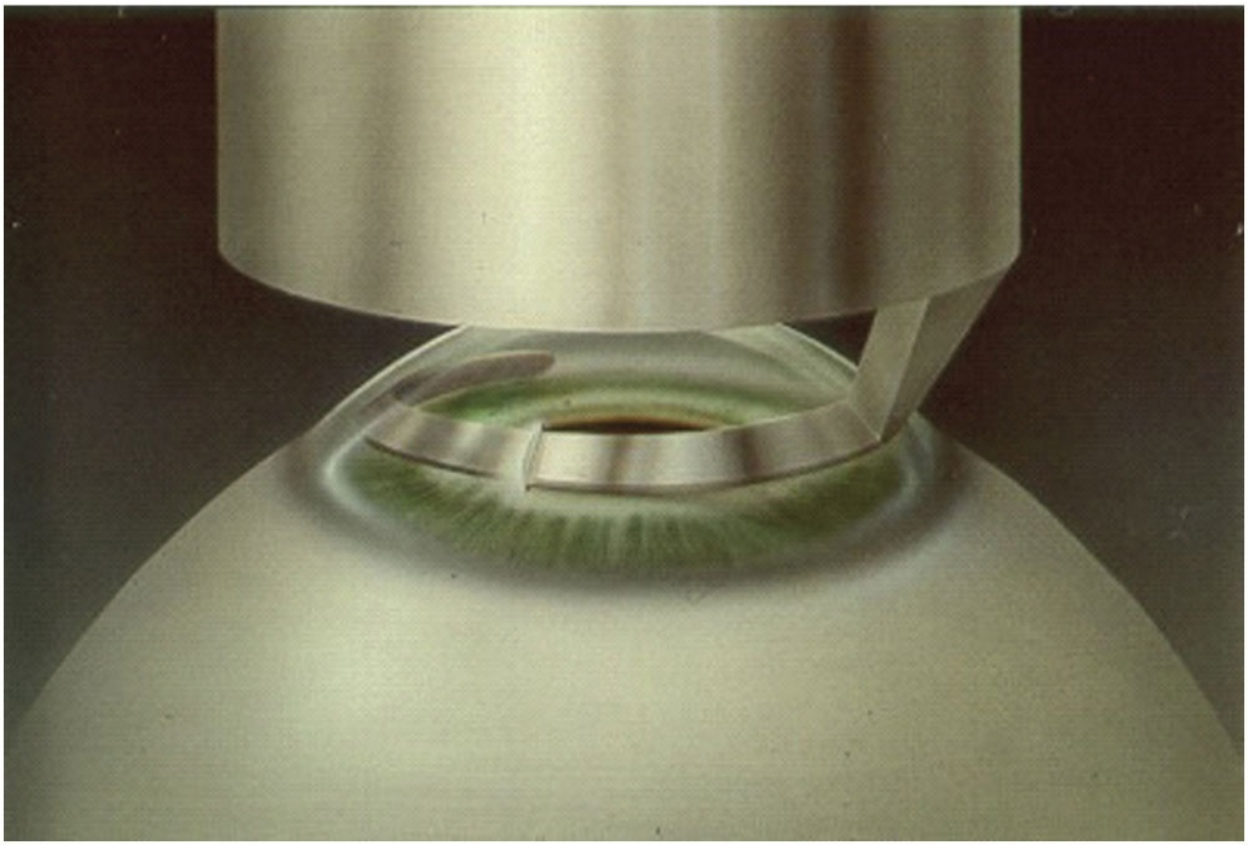

Figure 4-4 Rendering of the Intacs dissector tool as it is being rotated to create the intrastromal channel. *(Courtesy of Addition Technology.)*

Outcomes

FDA clinical trials provided the most complete outcome analysis of Intacs for myopia. A total of 452 patients enrolled in these trials. Patients received 0.25-, 0.30-, or 0.35-mm ring segments to correct an average preoperative mean spherical equivalent of -2.240 D (range, -0.750 to -4.125 D). At 12 months postoperatively, 97% of treated eyes had 20/40 or better uncorrected vision and 74% had achieved 20/20 or better. In addition, 69% and 92% of eyes were within +-0.50 and 1.00 D of emmetropia, respectively. These clinical outcomes were similar to early results with photorefractive keratectomy (PRK) and LASIK, although excimer laser studies generally treated a broader range of preoperative myopia.

Additional FDA approval was later granted to include intermediate segment sizes of 0.275 and 0.325 mm. Internationally, CE (Conformite Europeene) marking status (similar in concept to US FDA approval) was extended to thicker segment sizes. In 2000, Colin found that Intacs implantation compared favorably with PRK for treating low myopia, although it induced greater astigmatism.

The removal or exchange rate varies between 3% and 15%. The most common reason for a ring segment exchange is residual myopia. Ring segment removal is most often performed because of disabling vision symptoms such as glare, double vision, and photophobia. Few complications are associated with ring segment removal. In a series of 684 eyes that received Intacs, 46 (6.7%) underwent their removal. Most patients returned to their original preoperative myopia by 3 months postremoval (73% returned to within 0.50 D of preoperative mean spherical equivalent). No patient had a loss of CDVA of more than 2 lines. However, up to 15% of patients reported new or worsening symptoms after removal.

Intacs and Keratoconus

Until recently, very few surgical options other than penetrating and lamellar keratoplasty were available for the treatment of keratoconus. Excimer laser procedures, which correct ametropia by removing tissue, are generally not recommended for treating keratoconus because of the risk of exacerbating corneal structural weakening and ectasia.

In 2004, Intacs received a *Humanitarian Device Exemption* (*HDE;* see Appendix 1) from the FDA for use in reducing or eliminating myopia and astigmatism in certain patients with keratoconus, specifically those who can no longer achieve adequate vision with their contact lenses or spectacles. The intent is to restore functional vision and defer the need for a corneal transplant. Labeled selection criteria for patients include

- progressive deterioration in vision such that the patient can no longer achieve

adequate functional vision on a daily basis with contact lenses or spectacles
- age 21 years or older
- clear central corneas
- a corneal thickness of 450 mm or greater at the proposed incision site
- a lack of options other than corneal transplantation for improving functional vision

Although these are FDA labeling parameters, many surgeons perform Intacs insertion outside these criteria. In one study of 26 keratoconus patients, the ring segments were oriented horizontally, with a thick ring (0.450 mm) placed in the inferior cornea and a thinner one (0.250 mm) in the superior cornea. In another study of 50 patients (74 eyes), the orientation of the ring segments was adjusted according to the refractive cylinder. On the basis of the level of myopia, either the 0.300-mm ring or the 0.350-mm ring (the largest available in the United States at that time) was placed inferiorly, and the 0.250-mm ring was placed superiorly. Patients had mild to severe keratoconus with or without scarring. A superficial channel with perforation of the Bowman layer in 1 eye was the only operative complication. A total of 6 rings were explanted for segment migration and externalization (1 ring) and foreign-body sensation (5 rings).

The improvement in vision was significant. With an average follow-up period of 9 months, the mean uncorrected distance visual acuity (UDVA; also called *uncorrected visual acuity, UCVA*) improved from approximately 20/200 (1.05 logMAR [base-10 logarithm of the minimum angle of resolution]) to 20/80 (0.61 logMAR) ($P < .01$). The mean CDVA also improved, from approximately 20/50 (0.41 logMAR) to 20/32 (0.24 logMAR) ($P < .01$). Most patients still required optical correction to achieve their best-corrected vision. Eyes with corneal scarring had a similar improvement in UDVA and CDVA. Inferior steepening was reduced on topography. The dioptric power of the inferior cornea relative to the superior (I-S value) was reduced from a preoperative mean of 25.62 to 6.60 postoperatively.

A study evaluating the long-term stability of Intacs in keratoconus found that in nearly 93% of patients with documented progression of keratoconus pre-Intacs, there was no further progression of keratoconus between 1 and 5 years after Intacs implantation. Additionally, no statistically significant differences were noted in mean steep, flat, and average keratometry readings; manifest refraction spherical equivalent; and UDVA and CDVA ($P > .05$) between 1 and 5 years postimplantation.

One or Two Intacs Segments?

Although most surgeons implant 2 Intacs segments, the use of only 1 segment may be indicated. If the steep area is peripheral (similar to pellucid marginal degeneration), it may be preferable to place 1 segment instead of 2 segments because the keratoconic cornea has 2 optical areas of distortion within the pupil: a steep lower area and a flat

upper area. For peripheral keratoconus, it is better to flatten the steep area and steepen the flat area than to flatten the entire cornea. Single-segment placement can achieve that result (Fig 4-5). When a single segment is placed, it flattens the adjacent cornea but causes steepening of the cornea 180deg away--the "beanbag effect" (ie, when one sits on a beanbag, it flattens in one area and pops up in another area). This effect may yield a more physiologic improvement than would the global flattening effect from the use of double segments. Intacs treatment can also be combined with corneal collagen crosslinking (not yet FDA approved) for improved corneal strength and phakic IOL implantation to improve refractive error.

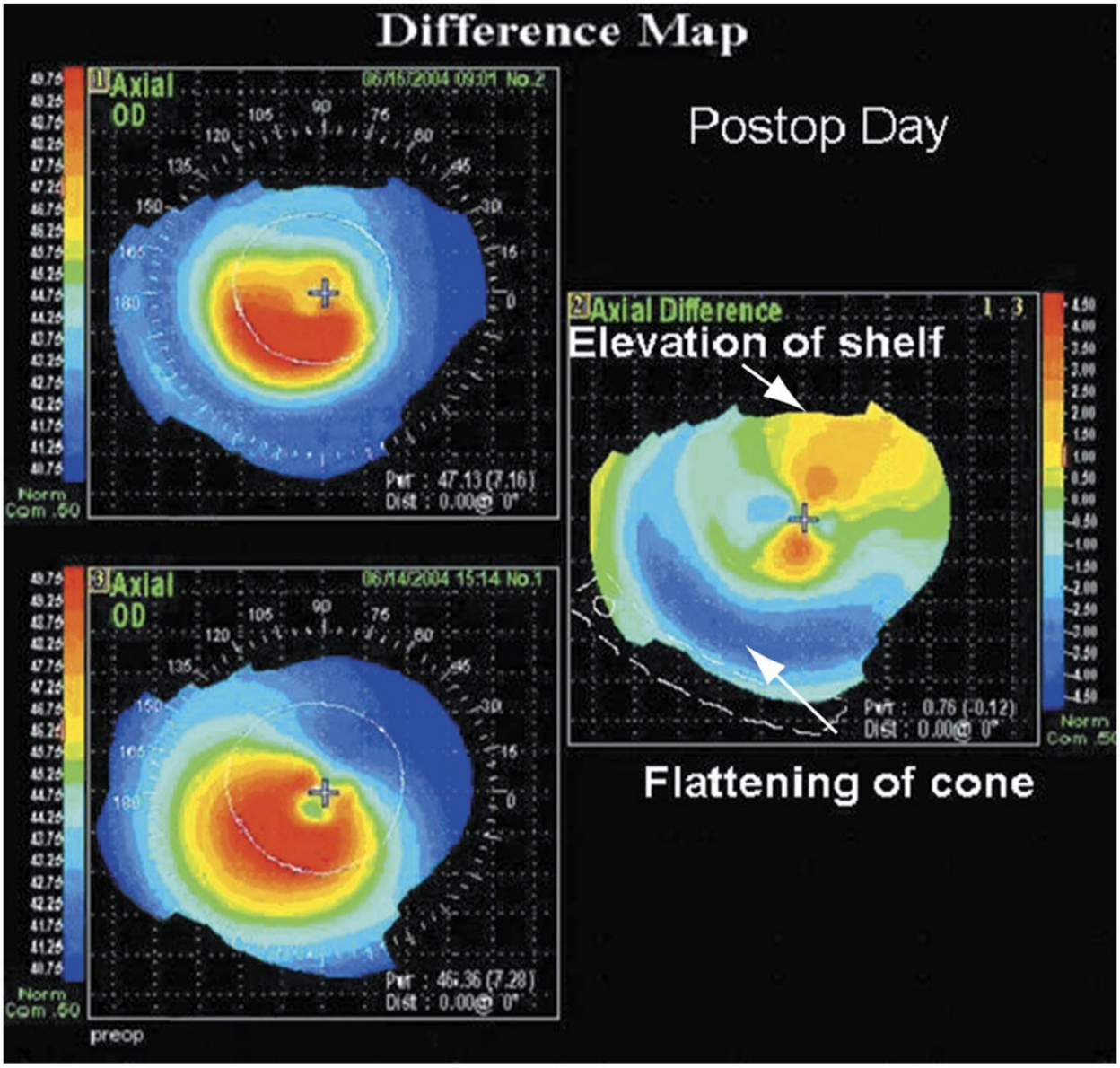

Figure 4-5 Corneal topography analysis before and after single-segment Intacs placement. The preoperative topography *(lower left)* shows oblique steepening, and the postoperative topography *(upper*

left) shows contraction of a steep cone after a single-segment Intacs was placed outside the cone. The difference map (subtraction of preoperative and postoperative topography) *(right)* shows flattening over the cone *(blue)* and steepening in the overly flat area *(red)*. The apex of the cornea has moved more centrally. *(Courtesy of Brian S. Boxer Wachler, MD.)*

Bedi R, Touboul D, Pinsard L, Colin J. Refractive and topographic stability of Intacs in eyes with progressive keratoconus: five-year follow-up. *J Refract Surg.* 2012;28(6):392-396.

Ertan A, Karacal H, Kamburoglu G. Refractive and topographic results of transepithelial cross-linking treatment in eyes with Intacs. *Cornea.* 2009;28(7):719-723.

Sharma M, Boxer Wachler BS. Comparison of single-segment and double-segment Intacs for keratoconus and post-LASIK ectasia. *Am J Ophthalmol.* 2006;141(5):891-895.

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Complications

The loss of CDVA ([?]2 lines of vision) after Intacs insertion is approximately 1% at 1 year postoperatively. Adverse events (defined as events that, if left untreated, could be serious or result in permanent sequelae) occur in approximately 1% of patients. Reported adverse events include

- anterior chamber perforation
- microbial keratitis
- implant extrusion (Fig 4-6)
- shallow ring segment placement
- corneal thinning over Intacs (Fig 4-7)

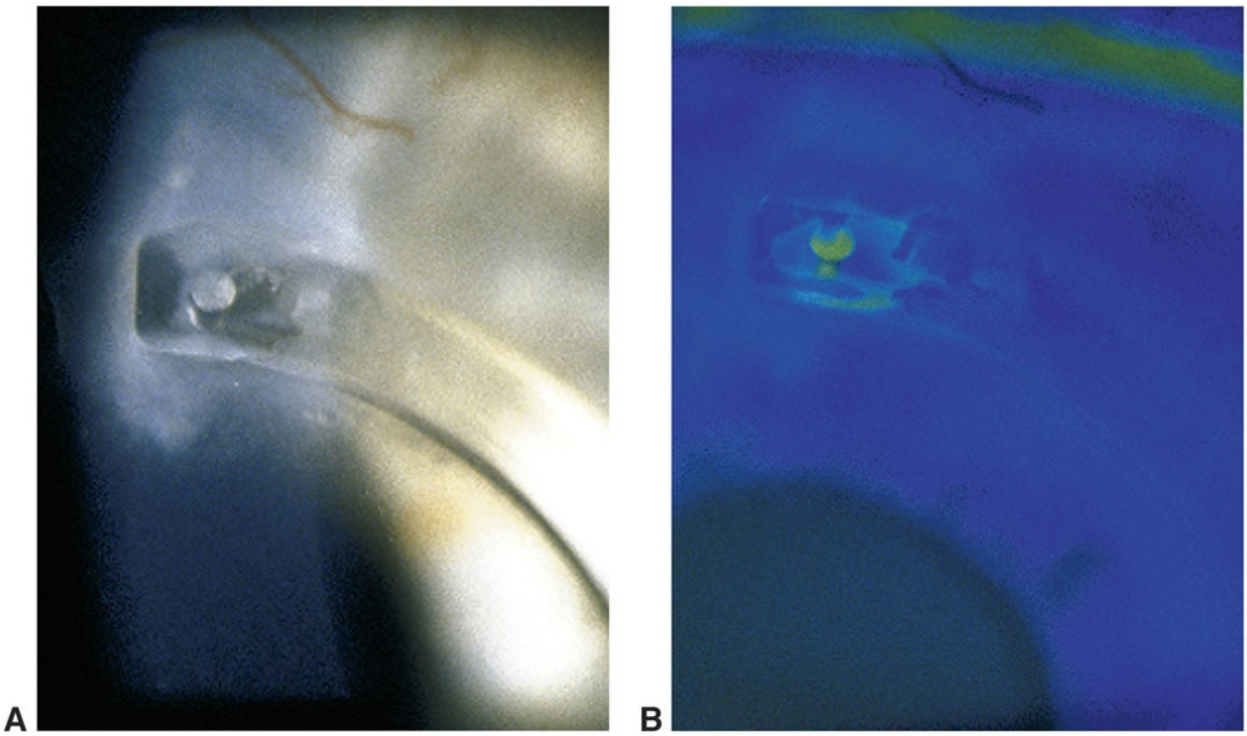

Figure 4-6 Slit-lamp images of an adverse event of Intacs placement: extrusion of the ring segment. **A,** Tip extrusion. **B,** Tip extrusion easily seen with fluorescein dye. *(Courtesy of Brian S. Boxer Wachler, MD.)*

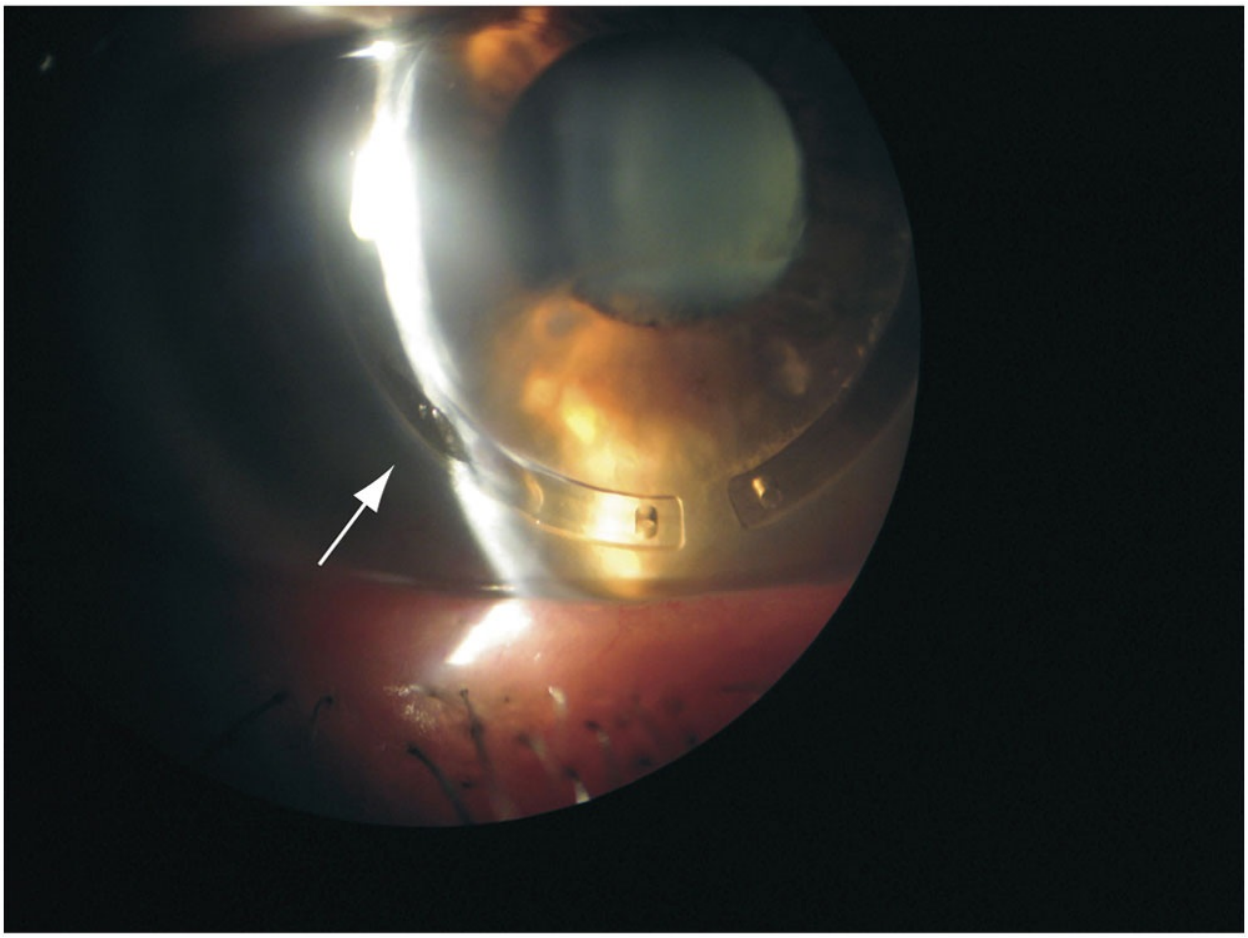

Figure 4-7 Image of an adverse event of Intacs: corneal thinning over the ring segment *(arrow)* after excessive use of a nonsteroidal anti-inflammatory drug. *(Courtesy of Brian S. Boxer Wachler, MD.)*

Ocular complications (defined as clinically significant events that do not result in permanent sequelae) have been reported in 11% of patients at 12 months postoperatively. These complications include

- reduced corneal sensitivity (5.5%)
- induced astigmatism between 1.00 and 2.00 D (3.7%)
- deep neovascularization at the incision site (1.2%)
- persistent epithelial defect (0.2%)
- iritis/uveitis (0.2%)

Visual symptoms rated as severe and always present have been reported in approximately 14% of patients and include

- difficulty with night vision (4.8%)
- blurred vision (2.9%)
- diplopia (1.6%)
- glare (1.3%)
- halos (1.3%)
- fluctuating distance vision (1.0%)
- fluctuating near vision (0.3%)
- photophobia (0.3%)

Fine white deposits occur frequently within the lamellar ring channels after Intacs placement (Fig 4-8). The incidence and density of the deposits increase with the thickness of the ring segment and the duration of implantation. Deposits do not seem to alter the optical performance of the ring segments or to cause corneal thinning or necrosis, although some patients are bothered by their appearance.

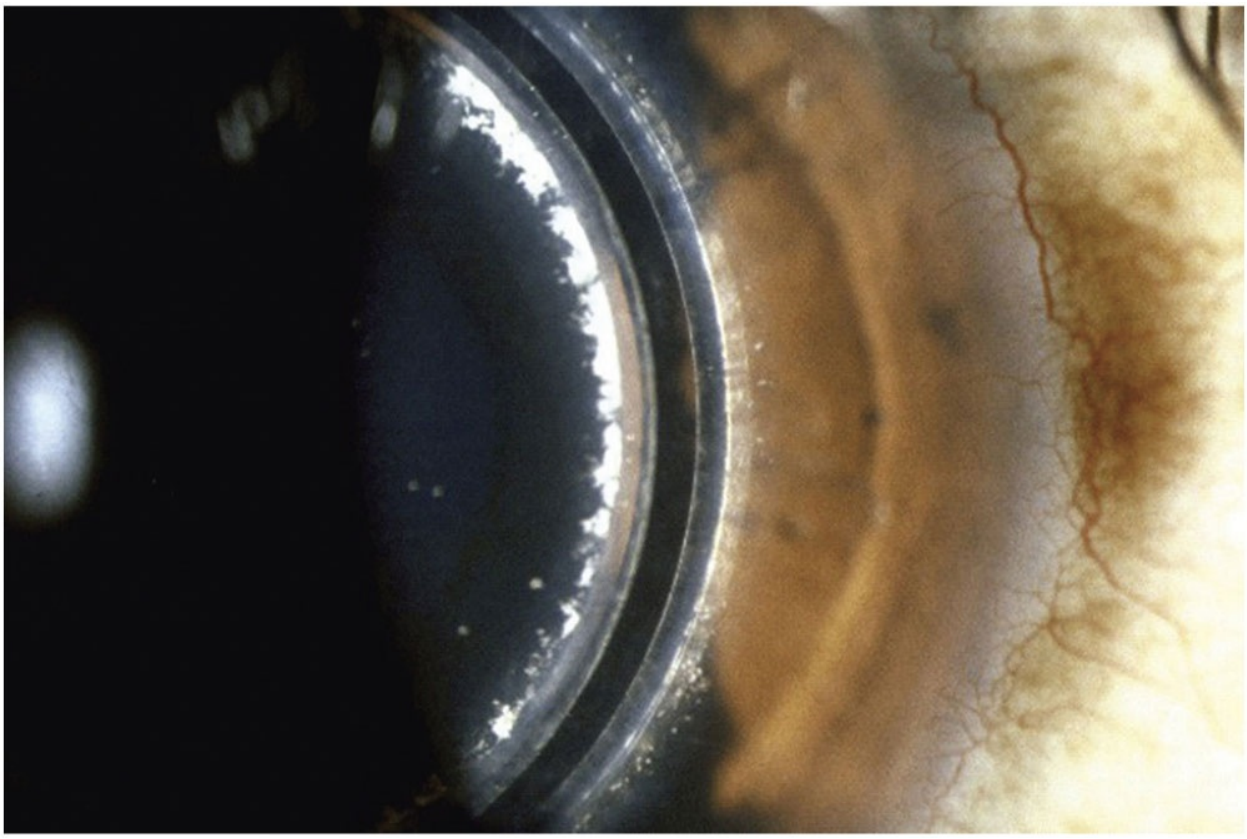

Figure 4-8 Clinical photograph showing grade 4 deposits around ring segments. The deposits can be graded on a scale from 0 (no deposits) to 4 (confluent deposits). These channel deposits are typically not apparent until weeks or months after surgery. Although the corneal opacities may cause cosmetic complaints, they usually do not cause other ocular problems. *(Courtesy of Addition Technology.)*

Intacs achieve the best results in eyes with mild to moderate keratoconus. The goals

are generally to improve vision and reduce distortions and are determined on the basis of the degree of keratoconus. For example, a patient with mild keratoconus and a corrected distance visual acuity (CDVA) of 20/30 may have the goal of improved quality of vision in glasses or soft contact lenses. However, a contact lens-intolerant patient with more advanced keratoconus and a CDVA of 20/60 may have the goal of improved ability to wear a rigid gas-permeable contact lens. For some advanced cases of keratoconus, such as eyes with keratometry values greater than 60.00 D, the likelihood of functional improvement of vision is lower than for eyes with flatter keratometry values. In such cases, despite the use of Intacs, a corneal transplant may be unavoidable. If required, penetrating or lamellar keratoplasty may be performed after Intacs placement.

Ectasia After LASIK

Ring segments have also been used for the postoperative management of corneal ectasia after LASIK. As in the treatment of keratoconus, few surgical options are available to treat corneal ectasia. Use of an excimer laser to remove additional tissue is generally considered contraindicated. A lamellar graft or penetrating keratoplasty may result in significant morbidity, such as irregular astigmatism, delayed recovery of vision, and tissue rejection. In limited early trials that used Intacs to treat post-LASIK ectasia, myopia was reduced and UDVA was improved. However, the long-term effect of such an approach for managing post-LASIK ectasia is still being evaluated. Use of Intacs for post-LASIK ectasia is an off-label treatment.

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Uses for Intrastromal Corneal Ring Segments After LASIK

Corneal ring segments have been used to correct residual myopia following LASIK with good initial results. In such cases, a nomogram adjustment is necessary to reduce the risk of overcorrection. This procedure may be useful in patients whose stromal bed is not sufficient to support a second excimer laser ablation. Conversely, after ring segments have been removed from patients whose vision did not improve satisfactorily (eg, due to undercorrection or induced astigmatism), LASIK has been performed with good success. The flap is created in a plane superficial to the previous ring segment channel.

Boxer Wachler BS, Christie JP, Chandra NS, Chou B, Korn T, Nepomuceno R. Intacs for keratoconus. *Ophthalmology.* 2003;110(5):1031-1040.

Guell JL, Velasco F, Sanchez SI, Gris O, Garcia-Rojas M. Intracorneal ring segments after laser in situ keratomileusis. *J Refract Surg.* 2004;20(4):349-355.

Kymionis GD, Siganos CS, Kounis G, Astyrakakis N, Kalyvianaki MI, Pallikaris IG. Management of post-LASIK corneal ectasia with Intacs inserts: one-year results. *Arch Ophthalmol.* 2003;121(3):322-326.

Rapuano CJ, Sugar A, Koch DD, et al. Intrastromal corneal ring segments for low myopia: a report by the American Academy of Ophthalmology. *Ophthalmology.* 2001;108(10): 1922-1928.
Siganos CS, Kymionis GD, Kartakis N, Theodorakis MA, Astyrakakis N, Pallikaris IG. Management of keratoconus with Intacs. *Am J Ophthalmol.* 2003;135(1):64-70.

Orthokeratology

Orthokeratology, or corneal refractive therapy, refers to the overnight use of rigid gas-permeable contact lenses to temporarily reduce myopia. The goal of this nonsurgical method of temporary myopia reduction is to achieve functional UDVA during the day. The contact lens is fitted at a base curve that is flatter than the corneal curvature. Temporary corneal flattening results from the flattening of corneal epithelium. The 2002 FDA approval of the rigid contact lens for overnight orthokeratology was for the temporary reduction of naturally occurring myopia between -0.50 and -6.00 D of sphere, with up to 1.75 D of astigmatism.

Orthokeratology is most appropriate for highly motivated patients with low myopia who do not want refractive surgery but who want to avoid use of contact lenses and spectacles during the day. These contact lenses do not treat astigmatism or hyperopia. Prospective patients should be informed that in clinical trials, approximately one-third of patients discontinued contact lens use and most patients (75%) experienced discomfort at some point during contact lens wear. Complications of orthokeratology include induced astigmatism, induced higher-order aberrations, recurrent erosions, and infectious keratitis. Infectious keratitis--the most serious complication--can be bilateral and seems to be more common in children and teenagers. It may be caused by a number of pathogens, including *Pseudomonas*, *Acanthamoeba*, *Staphylococcus*, and *Nocardia* species.

According to the American Academy of Ophthalmology, the prevalence and incidence of complications associated with orthokeratology, such as bacterial and parasitic keratitis, have not been determined. Sufficiently large, well-designed, controlled studies are needed to provide a more reliable measure of the risks of treatment and to identify risk factors for complications. See BCSC Section 3, *Clinical Optics*, for further discussion of orthokeratology.

Berntsen DA, Barr JT, Mitchell GL. The effect of overnight contact lens corneal reshaping on higher-order aberrations and best-corrected visual acuity. *Optom Vis Sci.* 2005;82(6): 490-497.
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Saviola JF. The current FDA view on overnight orthokeratology: how we got here and where we are going. *Cornea.* 2005;24(7):770-771.
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CHAPTER 5

Photoablation: Techniques and Outcomes

The 193-nm argon-fluoride (ArF) excimer laser treats refractive error by ablating the anterior corneal stroma to create a new radius of curvature. Two major refractive surgical techniques use excimer laser ablation. In *surface ablation* techniques, including photorefractive keratectomy (PRK), laser subepithelial keratomileusis (LASEK), and epipolis laser in situ keratomileusis (epi-LASIK), the Bowman layer is exposed either by debriding the epithelium through various methods or by loosening and moving, but attempting to preserve, the epithelium. In LASIK, the excimer laser ablation is performed under a lamellar flap that is created with either a mechanical microkeratome or a femtosecond laser. Currently available excimer laser ablation algorithms can be classified generally as conventional, wavefront-optimized, or wavefront-guided.

Excimer Laser

Background

The excimer laser uses a high-voltage electrical charge to transiently combine atoms of excited argon and fluorine; when the molecule, or dimer, reverts to its separate atoms, a charged photon is emitted. The word *excimer* comes from "*exc*ited d*imer*." Srinivasan, an IBM engineer, was studying the far-ultraviolet (UV; 193-nm) ArF excimer laser for photoetching of computer chips. He and Trokel, an ophthalmologist, not only showed that the excimer laser could remove corneal tissue precisely with minimal adjacent corneal damage--*photoablation*--but they also recognized its potential use for refractive and therapeutic corneal surgery.

Photoablation, the removal of corneal tissue with minimal adjacent corneal damage, occurs because the cornea has an extremely high absorption coefficient at 193 nm. A single 193-nm photon has sufficient energy to directly break carbon-carbon and carbon-nitrogen bonds that form the peptide backbone of the corneal collagen molecules. Excimer laser radiation ruptures the collagen polymer into small fragments, expelling a

discrete volume and depth of corneal tissue from the surface with each pulse of the laser (Fig 5-1) without significantly damaging adjacent tissue.

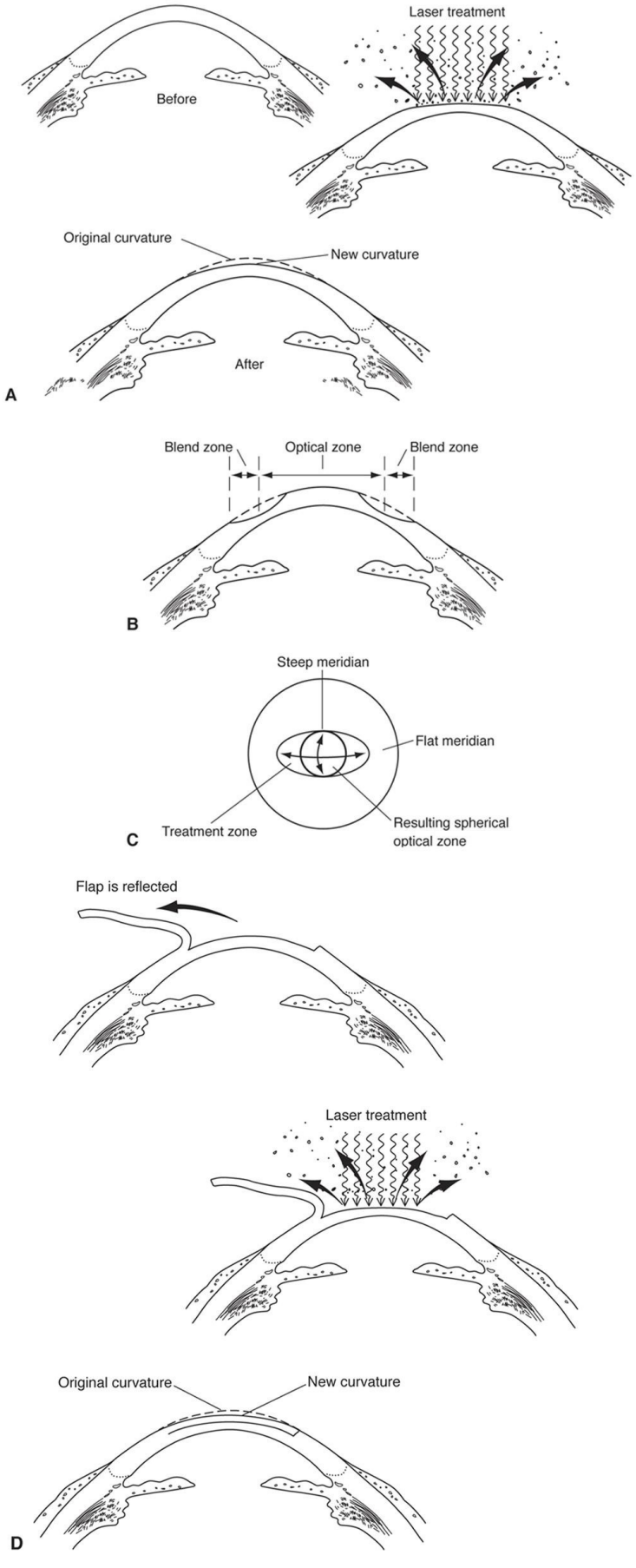
Laser treatment
Before
Original curvature
New curvature
After
A
Blend zone
Optical zone
Blend zone
B
Steep meridian
Flat meridian
Treatment zone
Resulting spherical optical zone
C
Flap is reflected
Laser treatment
Original curvature
New curvature
D

Figure 5-1 Schematic representations of corneal recontouring by the excimer laser. **A,** Correction of myopia by flattening the central cornea. **B,** Correction of hyperopia by steepening the central corneal optical zone and blending the periphery. **C,** Correction of astigmatism by differential tissue removals 90deg apart. Note that in correction of myopic astigmatism, the steeper meridian with more tissue removal corresponds to the smaller dimension of the ellipse. **D,** In LASIK, a flap is reflected back, the excimer laser ablation is performed on the exposed stromal bed, and the flap is then replaced. The altered corneal contour of the bed causes the same alteration in the anterior surface of the flap. *(Illustrations by Jeanne Koelling.)*

Surface Ablation

Surface ablation procedures were initially performed as PRK, the sculpting of the de-epithelialized corneal stroma to alter refractive power, and they underwent extensive preclinical investigation before being applied to sighted human eyes. Results of early animal studies provided evidence of relatively normal wound healing in laser-ablated corneas.

The popularity of PRK decreased in the late 1990s when LASIK began to be performed because of LASIK's faster recovery of vision and decreased postoperative discomfort. Although more LASIK than surface ablation procedures are still performed, the number of surface ablations has increased in recent years. PRK remains an especially attractive alternative for specific indications, including irregular or thin corneas; epithelial basement membrane disease (often called *map-dot-fingerprint dystrophy*); previous corneal surgery, such as penetrating keratoplasty and radial keratotomy; and treatment of some LASIK flap complications, such as incomplete or buttonholed flaps. Surface ablation eliminates the potential for stromal flap-related complications and may have a decreased incidence of postoperative dry eye. Corneal haze, the major risk of PRK, decreased markedly with the use of adjunctive mitomycin C; subsequently, the use of PRK for higher levels of myopia has increased.

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LASIK

The term *keratomileusis* comes from the Greek words for "cornea" *(kerato)* and "to carve" *(mileusis)*. *Laser in situ keratomileusis*, which combines keratomileusis with excimer laser stromal ablation, is currently the most frequently performed keratorefractive procedure because of its safety, efficacy, quick recovery of vision, and minimal patient discomfort. LASIK combines 2 refractive technologies: excimer laser stromal ablation and creation of a stromal flap.

Wavefront-Optimized and Wavefront-Guided Ablations

Conventional excimer laser ablation treats lower-order, or spherocylindrical, aberrations such as myopia, hyperopia, and astigmatism. These lower-order aberrations constitute approximately 90% of all aberrations. Higher-order aberrations make up the remainder; such aberrations cannot be treated with spectacles. Ophthalmologists are still learning about the visual impact of higher-order aberrations in the normal population. In fact, the small amounts of higher-order aberrations found in this population may not adversely affect vision. Higher-order aberrations are also a by-product of excimer laser ablation. Some higher-order aberrations can cause symptoms--such as loss of contrast sensitivity and nighttime halos and glare--that decrease the quality of vision. The aberrations most commonly associated with these visual complaints are spherical aberration and coma. See Chapter 1 for more detailed discussion of higher-order aberrations.

In an effort to reduce preexisting aberrations and minimize the induction of new aberrations, wavefront-guided ablation creates ablation profiles that are customized for individual patients. In addition to addressing higher-order aberrations, wavefront-guided treatments can correct the lower-order aberrations of spherical error and astigmatism. Wavefront-optimized lasers have changed the ablation profile of conventional treatments by adding more prolate peripheral ablation, thereby reducing spherical aberration; however, they have no effect on other higher-order aberrations.

Compared with conventional excimer laser ablation, wavefront-guided ablations and wavefront-optimized ablations appear to offer better contrast sensitivity and induce fewer postoperative higher-order aberrations. Although advances in aberrometry and registration systems have led to improved outcomes, patients who undergo photoablation may still have more higher-order aberrations postoperatively than they did preoperatively.

Wavefront-guided ablation appears to have clear-cut benefit compared with wavefront-optimized ablation only for patients with significant preoperative higher-order aberrations; thus, wavefront-guided ablation is not suitable for all patients and may not be appropriate for use after cataract surgery, particularly with multifocal intraocular lenses. In addition, wavefront data may be impossible to obtain in highly irregular corneas or in eyes with small pupils. Patients with highly irregular corneas that cannot be treated with wavefront technology may be treated with topography-based ablations. Topography-based ablations were recently approved by the US Food and Drug Administration (FDA) and have been widely used in Canada, Europe, and other countries. In general, wavefront-guided ablations remove more tissue than conventional ablations do.

Nuijts RM, Nabar VA, Hament WJ, Eggink FA. Wavefront-guided versus standard laser in situ keratomileusis to correct low to moderate myopia. *J Cataract Refract Surg.* 2002;28(11): 1907-1913.

Stonecipher KG, Kezirian GM. Wavefront-optimized versus wavefront-guided LASIK for myopic astigmatism with the ALLEGRETTO WAVE: three-month results of a prospective FDA trial. *J Refract Surg.* 2008;24(4):S424-S430.

Patient Selection for Photoablation

The preoperative evaluation of patients considering refractive surgery is presented in detail in Chapter 2. Table 5-1 lists relative contraindications to photoablation.

Table 5-1

Table 5-1 Relative Contraindications to Excimer Laser Photoablation

Connective tissue disease
Rheumatoid arthritis
Sjögren syndrome
Systemic lupus erythematosus
Wegener granulomatosis (granulomatosis with polyangiitis)
Corneal ectatic disorders
Corneal stromal dystrophies
Diabetic retinopathy
Dry eye syndrome
Fuchs corneal dystrophy
Medications
Amiodarone hydrochloride
Isotretinoin
Monocular patients
Neurotrophic corneas
Patients who are pregnant or breastfeeding
Patients with unreasonable expectations
Patients younger than 18 years
Previous herpes simplex infection
Previous herpes zoster ophthalmicus
Thyroid eye disease
Uncontrolled systemic diabetes mellitus

Special Considerations for Surface Ablation

In general, any condition that significantly delays epithelial healing is a relative contraindication to surface ablation. Although keloid scar formation was listed as a contraindication to PRK in FDA trials, 1 study found that African Americans with a history of keloid formation did well after PRK, and keloid formation is no longer considered a contraindication to surface ablation or LASIK. Historically, patients taking isotretinoin or amiodarone hydrochloride were excluded from undergoing excimer laser procedures, although there is little evidence that these drugs adversely affect laser keratorefractive outcomes.

Patients with epithelial basement membrane dystrophy (EBMD) are better candidates for surface ablation than for LASIK because surface ablation may be therapeutic, reducing epithelial irregularity and improving postoperative quality of vision while enhancing epithelial adhesion. In contrast, LASIK may cause a frank epithelial defect in eyes with EBMD, especially when performed with a mechanical microkeratome.

Any patient undergoing excimer laser photoablation should have a pachymetric and topographic evaluation (see Chapter 2). Younger patients and patients with thin corneas, low predicted residual stromal bed thickness, or irregular topography may be at increased risk for the development of ectasia with LASIK. As such, these patients may be better candidates for surface ablation. Patients with subtle topographic pattern abnormalities need to be evaluated on a case-by-case basis. In some circumstances, patients who are stable may be offered surface ablation but with a clear acknowledgment, as well as a signed informed consent form, that they understand there

may still be a risk of progression to corneal ectasia.

Special Considerations for LASIK

The preoperative evaluation of patients for LASIK is similar to that for surface ablation. A narrow palpebral fissure and a prominent brow with deep-set globes both increase the difficulty of creating a successful corneal flap, and the presence of either may lead a surgeon to consider surface ablation over LASIK.

Many reports indicate that postoperative dry eye due to corneal denervation is more common with LASIK than with surface ablation. This difference is important to remember when considering refractive surgery in a patient with known dry eye syndrome. Nevertheless, many patients undergoing PRK will also experience postoperative dry eye, but it is believed that this occurs to a lesser extent than for LASIK patients.

Corneal topography must be performed to assess corneal cylinder and rule out the presence of forme fruste keratoconus, pellucid marginal degeneration, or contact lens-induced corneal warpage. Corneas steeper than 48.00 D are more likely to have thin flaps or frank buttonholes (central perforation of the flap) with procedures using mechanical microkeratomes. Corneas flatter than 40.00 D are more likely to have smaller-diameter flaps and are at increased risk for creation of a free cap due to transection of the hinge with mechanical microkeratomes. These problems may be reduced by using a smaller or larger suction ring, which changes the flap diameter; modifying the hinge length; slowing passage of the microkeratome to create a thicker flap or using a microkeratome head designed to create thicker flaps; applying higher suction levels and creating a higher intraocular pressure (IOP); or selecting a femtosecond laser to create the lamellar flap. If a patient is having both eyes treated in a single session, the surgeon must be aware that using the same blade to create the flap in the second eye typically results in a flap that is 10-20 mm thinner than the flap in the first eye. In addition, there is some concern about transferring epithelium and/or infectious agents between eyes. These specific concerns are greatly minimized with the use of a femtosecond laser for flap creation.

Preoperative pachymetric measurement of corneal thickness is mandatory because an adequate stromal bed must remain to decrease the possibility of postoperative corneal ectasia, although the definition of what constitutes an adequate residual stromal bed (RSB) remains controversial. The following formula is used to calculate the RSB:

RSB = Central Corneal Thickness - Thickness of Flap - Depth of Ablation

Although most practitioners use a minimum RSB of 250 mm as a guideline, this figure is clinically derived rather than based on any definitive laboratory investigations or controlled prospective studies. A thicker stromal bed after ablation does not guarantee that postoperative corneal ectasia will not develop. Moreover, the actual

LASIK flap may be thicker than that noted on the label of the microkeratome head, making the stromal bed thinner than the calculated minimum of 250 mm. Consequently, an increasing number of surgeons are using intraoperative pachymetry--especially for high myopic corrections, enhancements, or thin corneas--to determine actual flap thickness.

Although many practitioners do not routinely measure intraoperative pachymetry and instead use an estimated flap thickness based on plate markings, the most accurate method for determining flap thickness and RSB is to measure the central corneal thickness at the beginning of the procedure, create the LASIK flap with the surgeon's instrument of choice, lift the flap, measure the untreated stromal bed, and subtract the intended thickness of corneal ablation from the stromal bed to ascertain whether the RSB will be 250 mm or whatever safe threshold is desired. Flap thickness is then calculated by subtracting the untreated stromal bed measurement from the initial central corneal thickness. It is important to measure the corneal bed thickness quickly after making the flap in order to avoid corneal thinning from exposure to the air.

The surgeon should preoperatively inform patients with thinner corneas or higher corrections that future LASIK enhancement may not be possible because of inadequate RSB. These patients may be better candidates for surface ablation enhancements if needed.

Many ophthalmologists believe that excessive corneal flattening or steepening after LASIK may reduce vision quality and increase aberrations. Thus, many of them avoid creating overly flat or overly steep corneas, although no established guidelines are available on the specific values to avoid. The surgeon can estimate the postoperative keratometry by calculating a flattening of 0.80 D for every diopter of myopia treated and a steepening of 1.00 D for every diopter of hyperopia treated (see Chapter 2).

If wavefront-guided laser ablation is planned, wavefront error is measured preoperatively, as discussed in Chapter 1. Although wavefront data are used to program the laser, the surgeon must still compare these data to the manifest refraction before surgery to prevent data-input errors. In general, substantial differences between the manifest refraction and the wavefront refraction should alert the surgeon to a potentially poor candidate for the procedure.

Flanagan G, Binder PS. Estimating residual stromal thickness before and after laser in situ keratomileusis. *J Cataract Refract Surg.* 2003;29(9):1674-1683.

Kim WS, Jo JM. Corneal hydration affects ablation during laser in situ keratomileusis surgery. *Cornea.* 2001;20(4):394-397.

Randleman JB, Hebson CB, Larson PM. Flap thickness in eyes with ectasia after laser in situ keratomileusis. *J Cataract Refract Surg.* 2012;38(5):752-757. Epub 2012 Mar 16.

Randleman JB, Woodward M, Lynn MJ, Stulting RD. Risk assessment for ectasia after corneal refractive surgery. *Ophthalmology.* 2008;115(1):37-50. Epub 2007 Jul 12.

Salib GM, McDonald MB, Smolek M. Safety and efficacy of cyclosporine 0.05% drops versus unpreserved artificial tears in dry-eye patients having laser in situ keratomileusis. *J Cataract Refract Surg.* 2006;32(5):772-778.

Smith RJ, Maloney RK. Laser in situ keratomileusis in patients with autoimmune diseases. *J Cataract Refract Surg.* 2006;32(8):1292-1295.

Williams LB, Dave SB, Moshirfar M. Correlation of visual outcome and patient satisfaction with preoperative keratometry after hyperopic laser in situ keratomileusis. *J Cataract Refract Surg.* 2008;34(7):1083-1088.

Surgical Technique for Photoablation

Many of the steps in keratorefractive surgery are identical for surface ablation and LASIK. These include calibration and programming of the laser and patient preparation. The major difference between surface ablation and LASIK is preparation for ablation, which is by exposure of the Bowman layer for surface ablation and the midstroma for LASIK. A list of FDA-approved lasers for refractive surgery can be found on the FDA website (www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/SurgeryandLifeSupport/LASIK/ucm168641.htm).

Calibration of the Excimer Laser

The laser should be checked at the start of each surgery day and between patients by a technician for proper homogeneous beam profile, alignment, and power output, according to the instructions of the manufacturer. Ultimately, it is the responsibility of the surgeon to ensure that the laser is functioning correctly before treating each patient.

Preoperative Planning and Laser Programming

An important part of preoperative planning is programming the laser with the appropriate refraction. Often, the patient's manifest and cycloplegic refractions differ, or the amount and axis of astigmatism differ between the topographic evaluation and refractive examination. Thus, it may be unclear which refractive data to enter into the laser. The surgeon's decision about whether to use the manifest or the cycloplegic refraction is based on his or her individual nomogram and technique. The manifest refraction is more accurate than the cycloplegic refraction in determining cylinder axis and amount. If the refractive cylinder is confirmed to differ from the topographic cylinder, lenticular astigmatism or posterior corneal curvature is assumed to be the cause. In this case, the laser is still programmed with the axis and amount of cylinder noted on refraction. The surgeon should take particular care to check the axis obtained on the refraction with the value programmed into the laser because entering an incorrect value is a potential source of error, particularly when converting between plus and minus cylinder formats. Before each surgery, the surgeon and the technician should review a checklist of information, confirming the patient's name, the refraction, and the eye on which surgery is to be performed. In wavefront procedures, the treatment should correspond to the patient's refraction, and adjustments may be required to compensate for accommodation.

For many laser models, the surgeon also must enter the size of the optical zone and indicate whether a blend of the ablation zone should be performed. The *blend zone* is an area of peripheral asphericity designed to reduce the possible undesirable effects of an abrupt transition from the optical zone to the untreated cornea (Fig 5-1B). A prolate

blend zone reduces the risk of glare and halo after excimer laser photoablation.

Special considerations for wavefront-guided techniques

Several wavefront mapping systems and wavefront-guided lasers are available commercially in the United States and worldwide. Wavefront mapping systems are unique to the specific wavefront-guided laser used. Calibration should be performed according to the manufacturer's specifications.

For wavefront-guided ablations, the wavefront maps are taken with the patient sitting up at an aberrometer under scotopic conditions; the mapping results are then applied to the cornea in the laser suite with the patient lying down under an operating microscope. Some systems require pupillary dilation to capture wavefront data, whereas others do not. The wavefront refraction indicated on wavefront analysis is then compared with the manifest refraction. If the difference between them exceeds 0.75 D, both the manifest refraction and the wavefront analysis may need to be repeated. The data are either electronically transferred to the laser or downloaded to a disk and then transferred to the laser. Unlike conventional or wavefront-optimized excimer laser treatment, in which the manifest or cycloplegic refraction is used to program the laser, wavefront-guided laser treatment uses programmed wavefront data to create a custom ablation pattern.

Preoperative Preparation of the Patient

Many surgeons administer topical antibiotic prophylaxis preoperatively. The patient's skin is prepared with povidone-iodine, 5%-10%, or alcohol wipes before or after the patient enters the laser suite, and povidone-iodine solution, 5%, is sometimes applied as drops to the ocular surface and then irrigated out for further antisepsis. There is no consensus about the utility of these measures. When preparing the patient, the surgeon should take care to avoid irritation of the conjunctiva, which could lead to swelling of the conjunctiva and difficulties with suction. In addition, before laser treatment, patients should be informed about the sounds and smells they will experience during the laser treatment. They may receive an oral antianxiety medication such as diazepam.

If substantial astigmatism is being treated, some surgeons elect to mark the cornea at the horizontal or vertical axis while the patient is sitting up to ensure accurate alignment under the laser. This step is done to compensate for the cyclotorsion that commonly occurs when the patient changes from a sitting to a lying position. A 15deg offset in the axis of treatment can decrease the effective cylinder change by 35% and can result in a significant axis shift.

After the patient is positioned under the laser, a sterile drape may be placed over the skin and eyelashes according to the surgeon's preference. Before doing so, a "time-out" should be performed during which the correct patient is identified, and the treatment and eye(s) to which treatment will be performed are confirmed. Topical

anesthetic drops are placed in the eye; for LASIK patients, care should be taken to ensure that the drops are not instilled too early, as doing so may loosen the epithelium substantially. An eyelid speculum is placed in the eye to be treated, and an opaque patch is placed over the fellow eye to avoid cross-fixation. A gauze pad may be taped over the temple between the eye to be treated and the ear to absorb any excess fluid. The patient is asked to fixate on the laser centration light while the surgeon reduces ambient illumination from the microscope, focuses on the cornea, and centers the laser. It is important for the plane of the eye to remain parallel to the plane of the laser, for the patient to maintain fixation, and for the surgeon to control centration even when using lasers with tracking systems. For most patients, voluntary fixation during photoablation produces more accurate centration than globe immobilization by the surgeon.

Preparation of the Bowman Layer or Stromal Bed for Excimer Ablation

The next surgical step for all excimer photoablation procedures is preparation of the cornea for ablation. With surface ablation procedures, such preparation consists of epithelial removal to expose the Bowman layer, whereas with LASIK, it involves the creation of a lamellar flap with either a mechanical microkeratome or a femtosecond laser to expose the central stroma.

Epithelial debridement techniques for surface ablation

The epithelium can be removed with (Fig 5-2)

- a sharp blade
- a blunt spatula
- a rotary corneal brush
- application of 20% absolute alcohol to the corneal surface for 20-45 seconds to loosen the epithelium
- a mechanical microkeratome with an epi-LASIK blade
- transepithelial ablation from the excimer laser itself

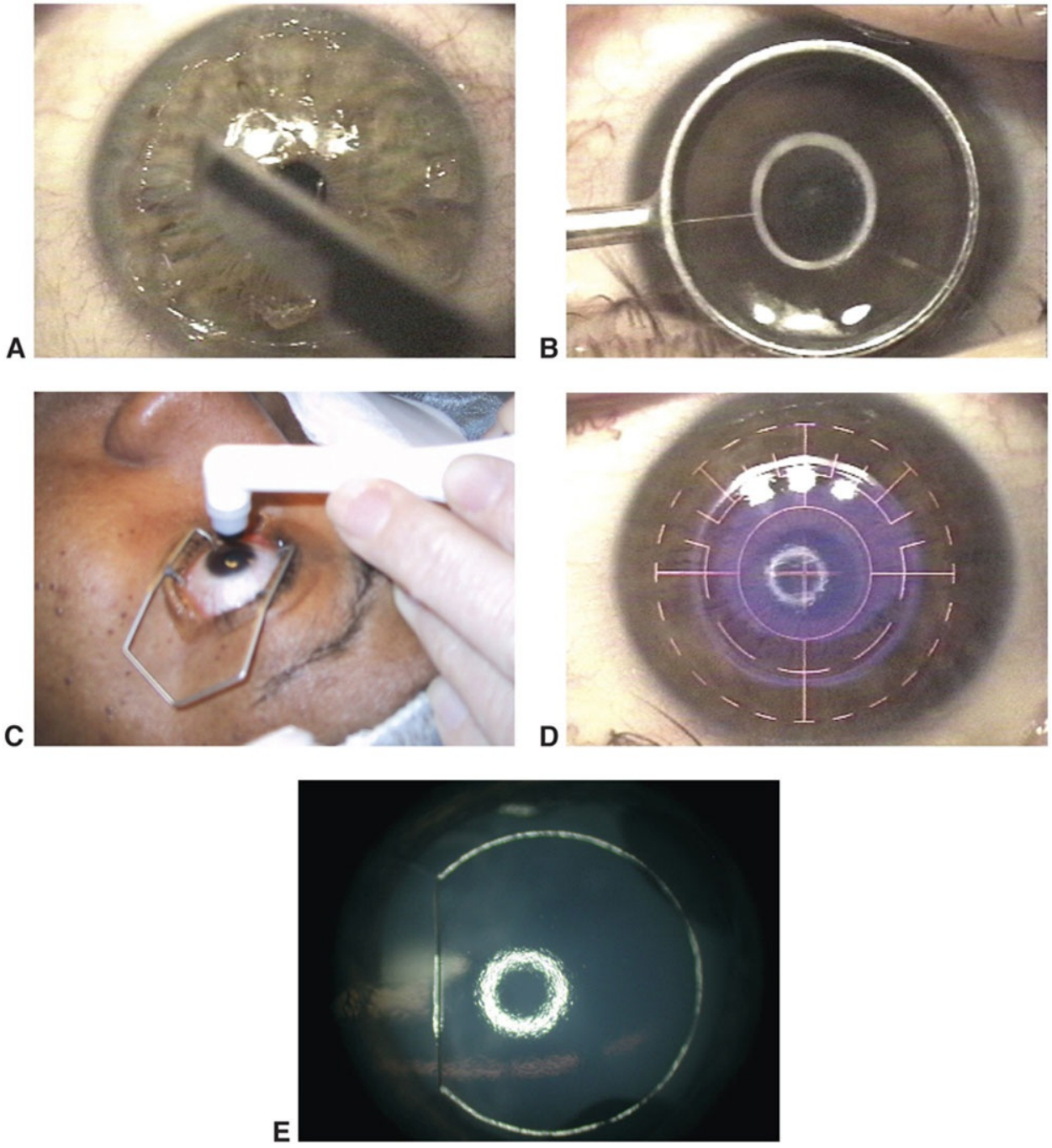

Figure 5-2 Techniques for de-epithelialization for surface ablation. **A,** Scraping with a blade. **B,** 20% dilution of absolute ethanol in an optical zone marker well. **C,** Rotary brush debridement. **D,** "Laser scrape," in which a broad-beam laser exposes the entire treatment zone to ablation pulses; these pulses remove most of the epithelium that is fluorescing brightly, after which the basal epithelial layer is removed by scraping with a blade. **E,** Epi-LASIK with a mechanical microkeratome (the epithelial flap may be removed or retained). *(Parts A, B, and D courtesy of Roger F. Steinert, MD; part C courtesy of Steven C. Schallhorn, MD; part E courtesy of Eric D. Donnenfeld, MD.)*

In both transepithelial ablation and epi-LASIK, the peripheral margin of the de-

epithelialization is defined by the laser or epi-keratome itself. For other epithelial debridement techniques, the surgeon often defines the outer limit of de-epithelialization with an optical zone marker and then debrides from the periphery toward the center. An ophthalmic surgical cellulose sponge can be brushed uniformly over the surface of the cornea to remove any residual epithelium and provide a smooth surface. The epithelium should be removed efficiently and consistently to prevent hydration changes in the stroma, because excessive corneal stromal dehydration may increase the rate of excimer laser ablation and lead to overcorrection. The laser treatment zone must be free of epithelial cells, debris, and excess fluid before ablation.

Epithelial preservation techniques

LASEK In the LASEK variant of surface ablation, the goal is to preserve the patient's epithelium. Instead of debriding and discarding the epithelium or ablating the epithelium with the excimer laser, the surgeon loosens the epithelium with 20% alcohol for 20 seconds and folds back an intact sheet of epithelium.

Epi-LASIK In epi-LASIK, an epithelial flap is fashioned with a microkeratome fitted with a blunt epikeratome and a thin applanation plate that mechanically separates the epithelium.

Although the goal of LASEK and epi-LASIK is to reduce postoperative pain, speed the recovery of visual acuity, and decrease postoperative haze formation compared with PRK, controlled studies have had mixed results. In addition, the epithelial flap may not remain viable and may slough off, actually delaying healing and vision recovery. To date, epi-LASIK and LASEK have not proved to be superior to PRK in reducing corneal haze.

Ambrosio R Jr, Wilson S. LASIK vs LASEK vs PRK: advantages and indications. *Semin Ophthalmol.* 2003;18(1):2-10.
Matsumoto JC, Chu YS. Epi-LASIK update: overview of techniques and patient management. *Int Ophthalmol Clin.* 2006;46(3):105-115.

Flap creation for LASIK

Lamellar flap creation can be performed using either a mechanical microkeratome or a femtosecond laser. Many surgeons make asymmetric sterile ink marks in the corneal periphery, away from the intended flap hinge, just before placement of the suction ring. These marks can aid in alignment of the flap at the end of surgery and in proper orientation in the rare event of a free cap.

Microkeratome Before each surgery, the microkeratome and vacuum unit are assembled, carefully inspected, and tested to ensure proper functioning. The importance of meticulously maintaining the microkeratome and carefully following the manufacturer's recommendations cannot be overemphasized.

The basic principles of the microkeratome and the role of the suction ring and cutting head are illustrated in Figure 5-3. The suction ring has 2 functions: to adhere to

the globe, providing a stable platform for the microkeratome cutting head; and to raise the IOP to a high level, which stabilizes the cornea. The dimensions of the suction ring determine the diameter of the flap and the size of the stabilizing hinge. The thicker the vertical dimension of the suction ring and the smaller the diameter of the ring opening, the less the cornea will protrude, and hence a smaller-diameter flap will be produced. The suction ring is connected to a vacuum pump, which typically is controlled by an on-off foot pedal.

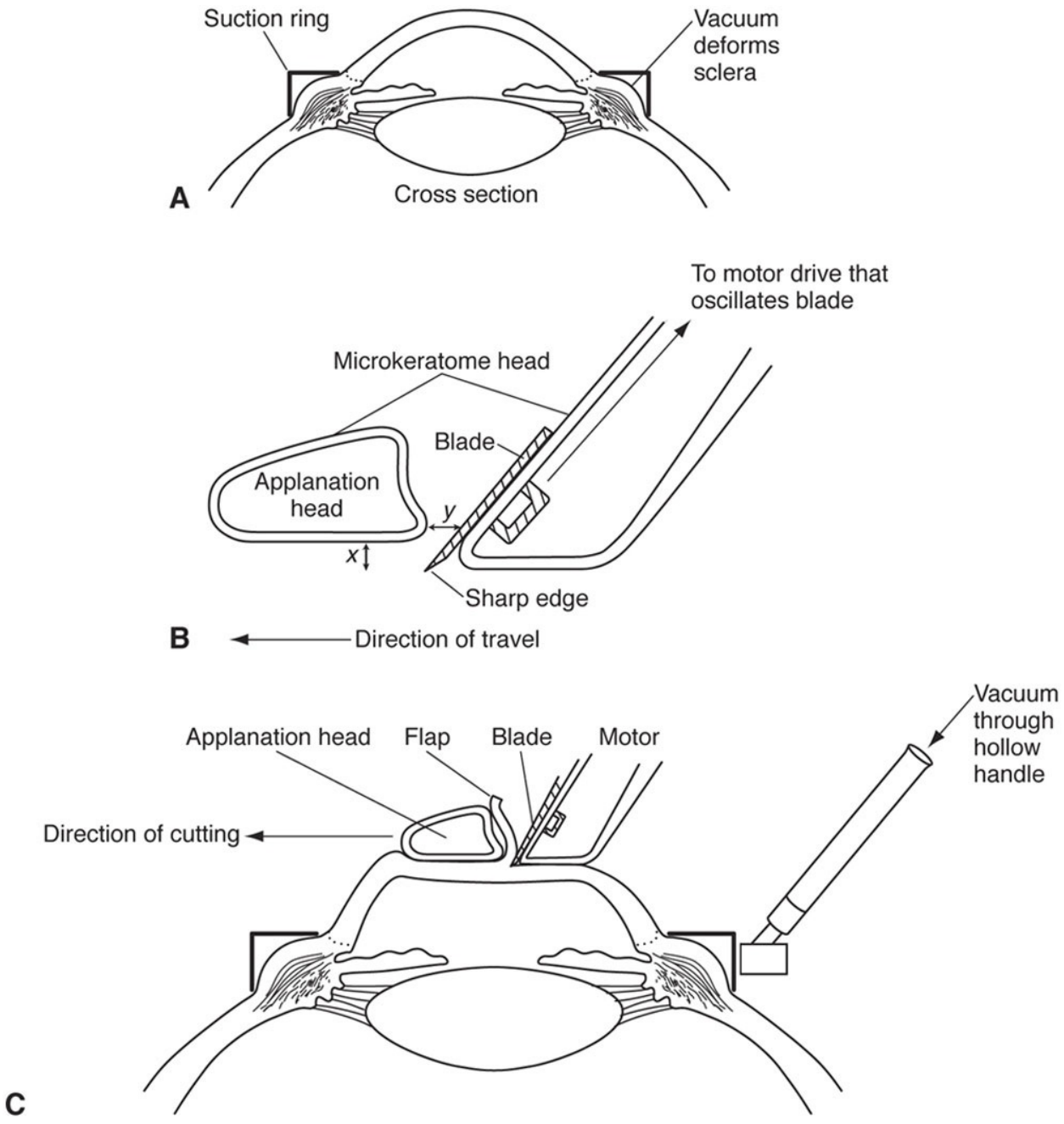

Figure 5-3 Schematic representation of the principles of a microkeratome. **A,** The suction ring serves as

a platform for the microkeratome head, gripping the conjunctiva and sclera adjacent to the limbus. **B,** Simplified cross-section schematic of a typical microkeratome head. **C,** Creation of the flap. When the microkeratome head passes across the cornea, the applanating surface of the head flattens the cornea in advance of the blade. *(Illustration by Jeanne Koelling.)*

The microkeratome cutting head has several key components. Its highly sharpened, disposable cutting blade is discarded after each patient, either after treatment of a single eye or after bilateral treatment. The applanation head, or plate, serves to flatten the cornea in advance of the cutting blade. The length of the blade that extends beyond the applanation plate and the clearance between the blade and the applanation surface are the principal determinants of flap thickness. The motor, either electrical or gas-driven turbine, oscillates the blade rapidly, typically between 6000 and 15,000 cycles per minute. The same motor or a second motor is used to mechanically advance the cutting head, which is attached to the suction ring, across the cornea, although in some models the surgeon manually controls the advance of the cutting head. Smaller and thinner flap size and longer hinge cord length may be more important than hinge location in sparing the nerves and reducing the incidence and severity of dry eyes. Regardless of hinge type, patients generally recover corneal sensation to preoperative levels within 6-12 months after surgery.

Once the ring is properly positioned, suction is activated (Fig 5-4). The patient should be notified prior to surgery that when the suction is applied, there may be some discomfort and vision may diminish temporarily. The IOP should be assessed at this point because low IOP can result in a poor-quality, thin, or incomplete flap. It is essential to have both excellent exposure of the eye, allowing free movement of the microkeratome, and proper suction ring fixation. Inadequate suction may result from blockage of the suction ports caused by eyelashes under the suction ring or redundant or scarred conjunctiva. To avoid the possibility of pseudosuction (occlusion of the suction port with conjunctiva but not sclera), the surgeon can confirm the presence of true suction by observing that the eye moves when the suction ring is gently moved, the pupil is mildly dilated, and the patient can no longer see the fixation light. Methods used to assess whether the IOP is adequately elevated include use of a hand-held Barraquer plastic applanator or a pneumotonometer and palpation of the eye by the surgeon. Surgeons without extensive experience are advised to use an objective rather than only a subjective method.

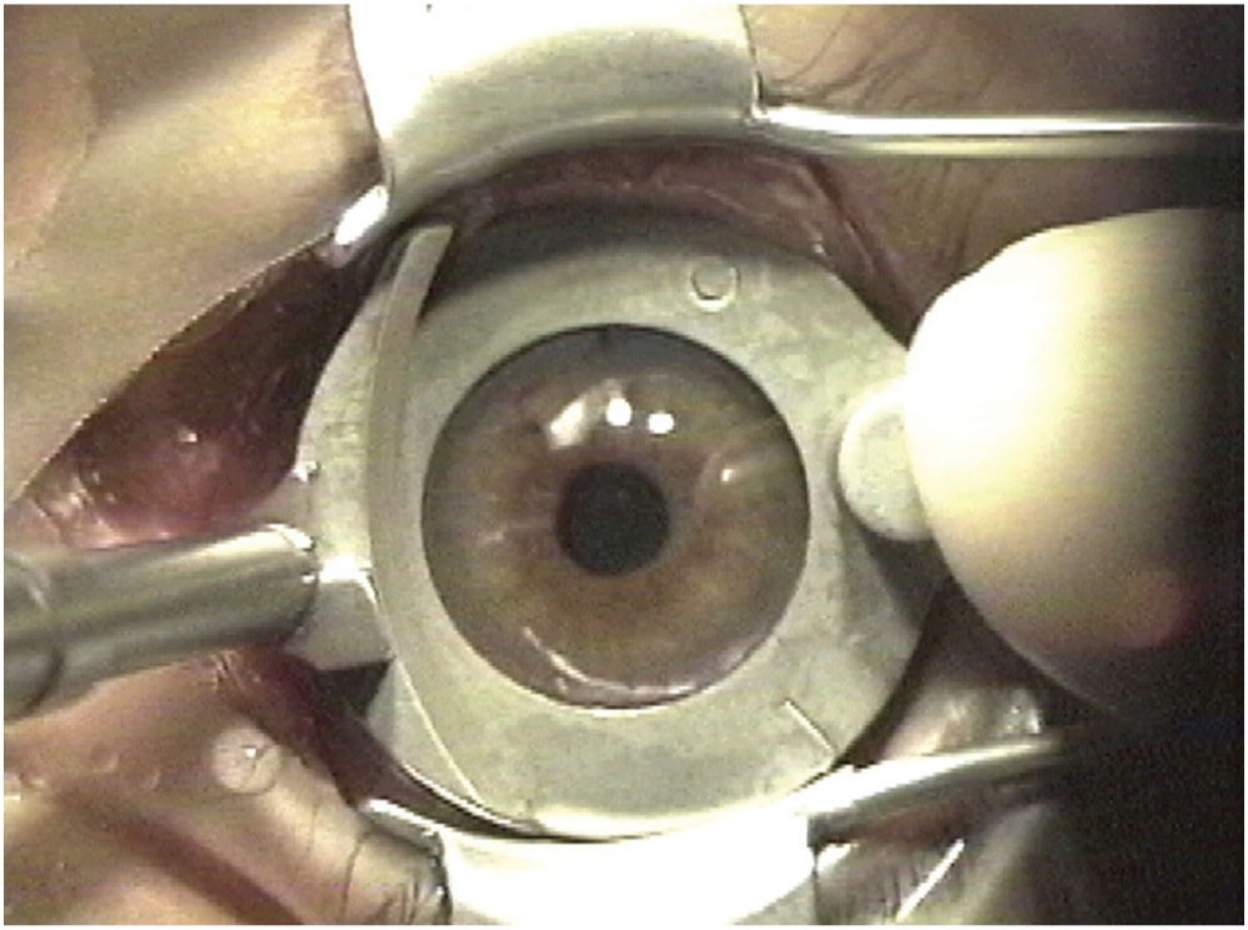

Figure 5-4 Placement of a suction ring. *(Courtesy of Roger F. Steinert, MD.)*

Before the lamellar cut is made, the surface of the cornea is moistened with proparacaine with glycerin or with nonpreserved artificial tears. Use of balanced salt solution should be avoided at this point because mineral deposits may develop within the microkeratome and interfere with its proper function. The surgeon places the microkeratome on the suction ring (if it is a 2-piece system) and checks that its path is free of obstacles such as the eyelid speculum, drape, or overhanging eyelid. The microkeratome is then activated, passed over the cornea (Fig 5-5) until it is halted by the hinge-creating stopper, and then reversed off the cornea. It is common practice to utilize the same blade on the second eye of the same patient.

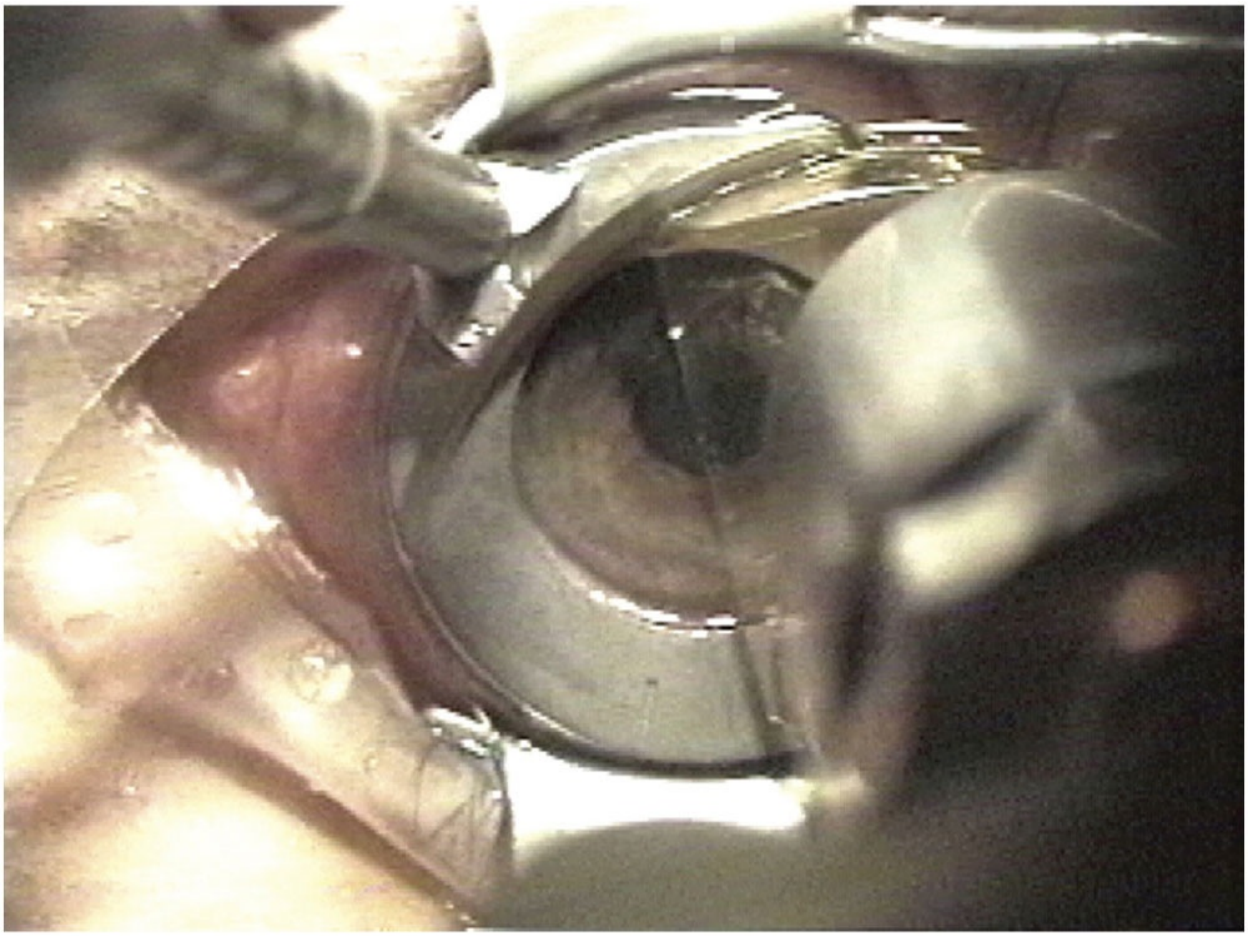

Figure 5-5 Movement of the microkeratome head across the cornea. *(Courtesy of Roger F. Steinert, MD.)*

In addition, the surgeon should be aware that, regardless of the label describing the flap thickness of a specific device, the actual flap thickness varies with the type of microkeratome, patient age, preoperative corneal thickness, preoperative keratometry reading, preoperative astigmatism, corneal diameter, and translation speed of the microkeratome pass. It is important to maintain a steady translation speed to avoid creating irregularities in the stromal bed.

Barequet IS, Hirsh A, Levinger S. Effect of thin femtosecond LASIK flaps on corneal sensitivity and tear function. *J Refract Surg.* 2008;24(9):897-902.

Bryar PJ, Hardten DR, Vrabec M. Femtosecond laser flap creation. In: Feder RS, ed. *The LASIK Handbook: A Case-Based Approach.* 2nd ed. Philadelphia: Lippincott Williams & Wilkins; 2013:chap 5.

Calvillo MP, McLaren JW, Hodge DO, Bourne WM. Corneal reinnervation after LASIK: prospective 3-year longitudinal study. *Invest Ophthalmol Vis Sci.* 2004;45(11):3991-3996.

Donnenfeld ED, Ehrenhaus M, Solomon R, Mazurek J, Rozell JC, Perry HD. Effect of hinge width on corneal sensation and dry eye after laser in situ keratomileusis. *J Cataract Refract Surg.* 2004;30(4):790-797.

Hardten DR, Feder RS, Rosenfeld SI. Mechanical microkeratomes. In: Feder RS, ed. *The LASIK Handbook: A Case-Based Approach.* 2nd ed. Philadelphia: Lippincott Williams & Wilkins; 2013:chap 4.

Kumano Y, Matsui H, Zushi I, et al. Recovery of corneal sensation after myopic correction by laser in situ keratomileusis with a nasal or superior hinge. *J Cataract Refract Surg.* 2003; 29(4):757-761.

Solomon KD, Donnenfeld E, Sandoval HP, et al; Flap Thickness Study Group. Flap thickness accuracy: comparison of 6 microkeratome models. *J Cataract Refract Surg.* 2004;30(5): 964-977.

Femtosecond laser A femtosecond laser also creates flaps by performing a lamellar dissection within the stroma. Each laser pulse creates a discrete area of photodisruption of the collagen. The greater the number of laser spots and the more the spots overlap, the more easily the tissue will separate when lifted. The femtosecond laser allows adjustments for several variables involved in making the flap, including flap thickness, flap diameter, hinge location, hinge angle, bed energy, and spot separation. Although the goal is to try to minimize the total energy used in flap creation, a certain level of power is necessary to ensure complete photodisruption. With the computer programmed for flap diameter, depth, and hinge location and size, thousands of adjacent pulses are scanned across the cornea in a controlled pattern that results in creation of a flap. Advocates cite the potential for obtaining better depth control, reducing or avoiding the occurrence of such complications as buttonhole perforations, and precisely controlling flap dimension and location. With some femtosecond laser models, the side cut of the corneal flap can be modified in a manner that may reduce the incidence of epithelial ingrowth. One study of 208 eyes that underwent femtosecond laser flap creation showed that 1.9% had a loss of suction during femtosecond laser flap creation but that all had successful flap performance after reapplanation of the eye. Occasionally, an opaque bubble layer (OBL) may form and lead to improper flap creation. To prevent such OBL formation, most lasers now create a pocket deep within the cornea to disperse the gas as much as possible.

The use of a femtosecond laser generally requires more time than does the use of a mechanical microkeratome because it involves several extra steps. Although some variation exists between femtosecond lasers, all systems require centration and vacuum adherence to the patient's cornea. Complete applanation of the cornea must be achieved, or an incomplete flap or incomplete side cut may result. Figures 5-6, 5-7 and 5-8 illustrate some of the components of the femtosecond laser.

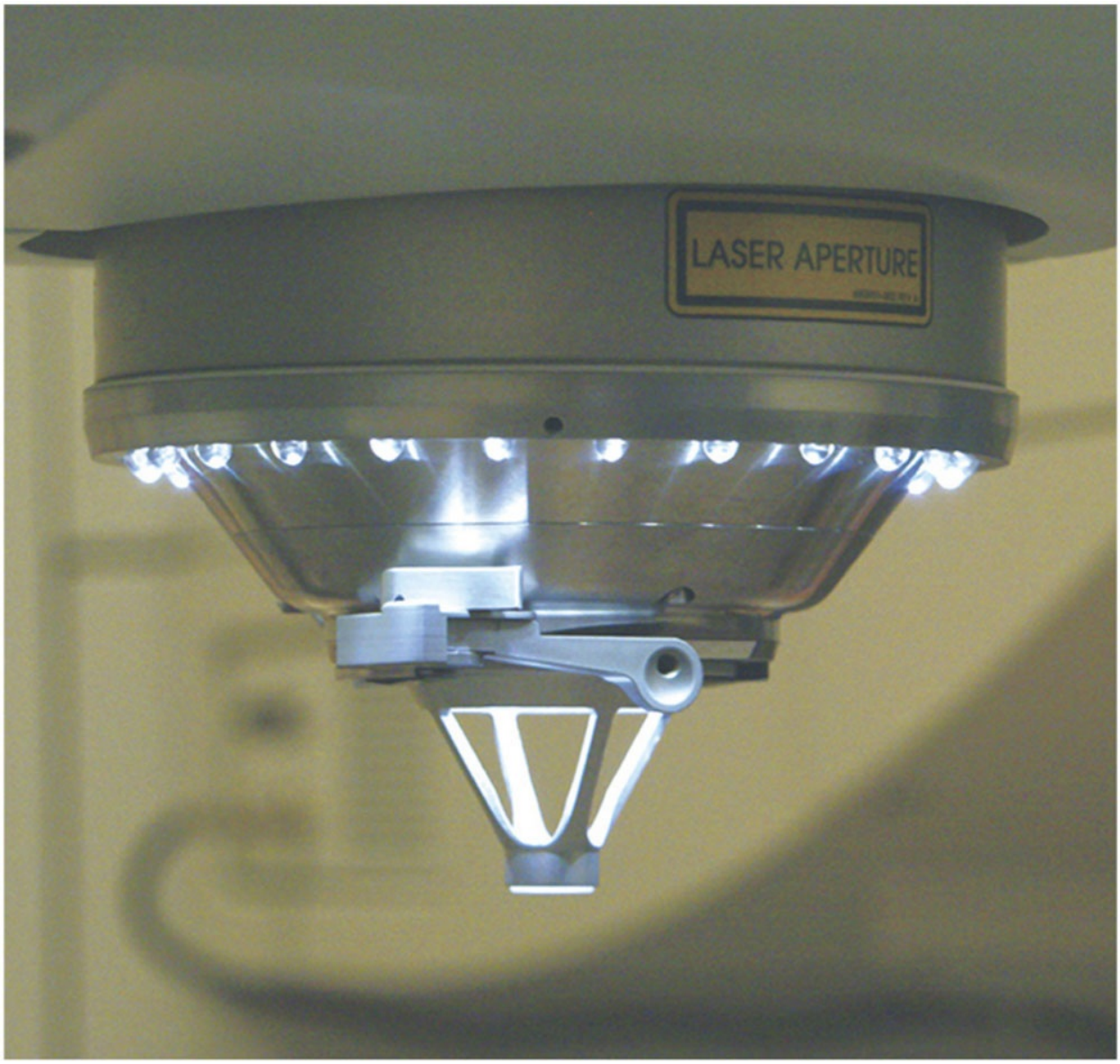

Figure 5-6 IntraLase femtosecond laser with cone attached. *(Reproduced with permission from Feder RS, Rapuano CJ.* The LASIK Handbook: A Case-Based Approach. *Philadelphia: Lippincott Williams & Wilkins; 2007:45, fig 2.7. Photograph courtesy of Robert Feder, MD.)*

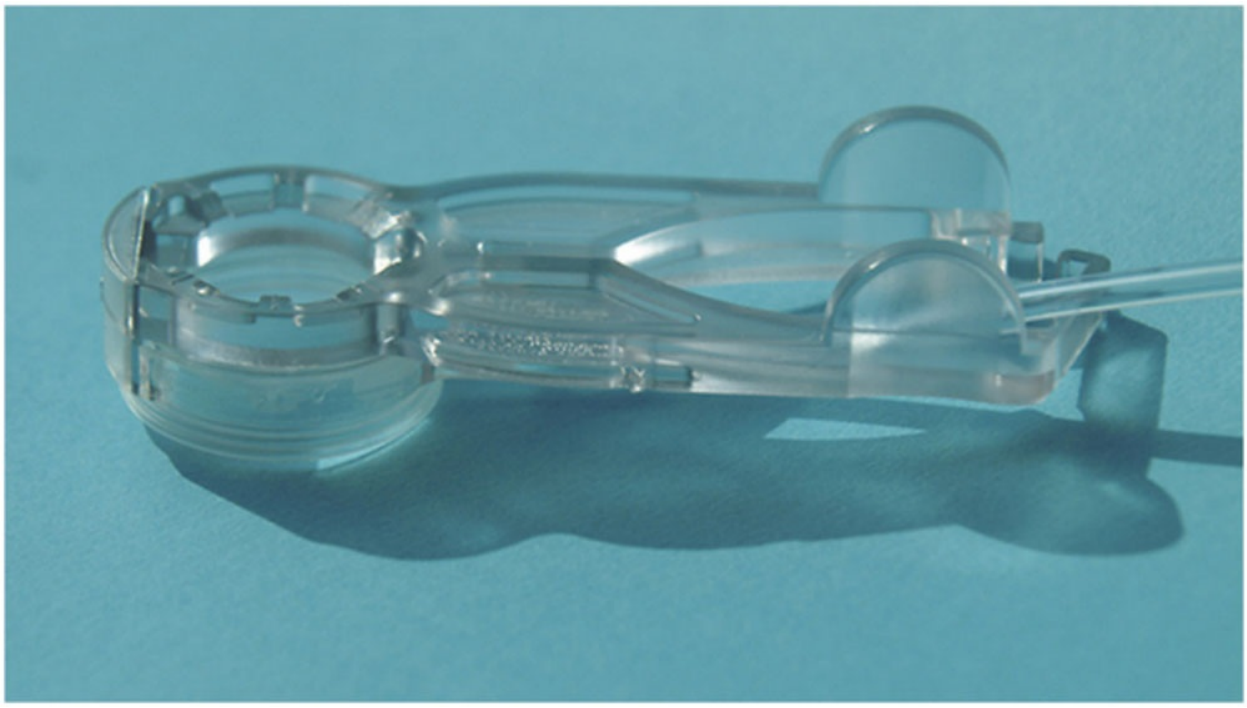

Figure 5-7 IntraLase suction ring. *(Reproduced with permission from Feder RS, Rapuano CJ.* The LASIK Handbook: A Case-Based Approach. *Philadelphia: Lippincott Williams & Wilkins; 2007:45, fig 2.8. Photograph courtesy of Robert Feder, MD.)*

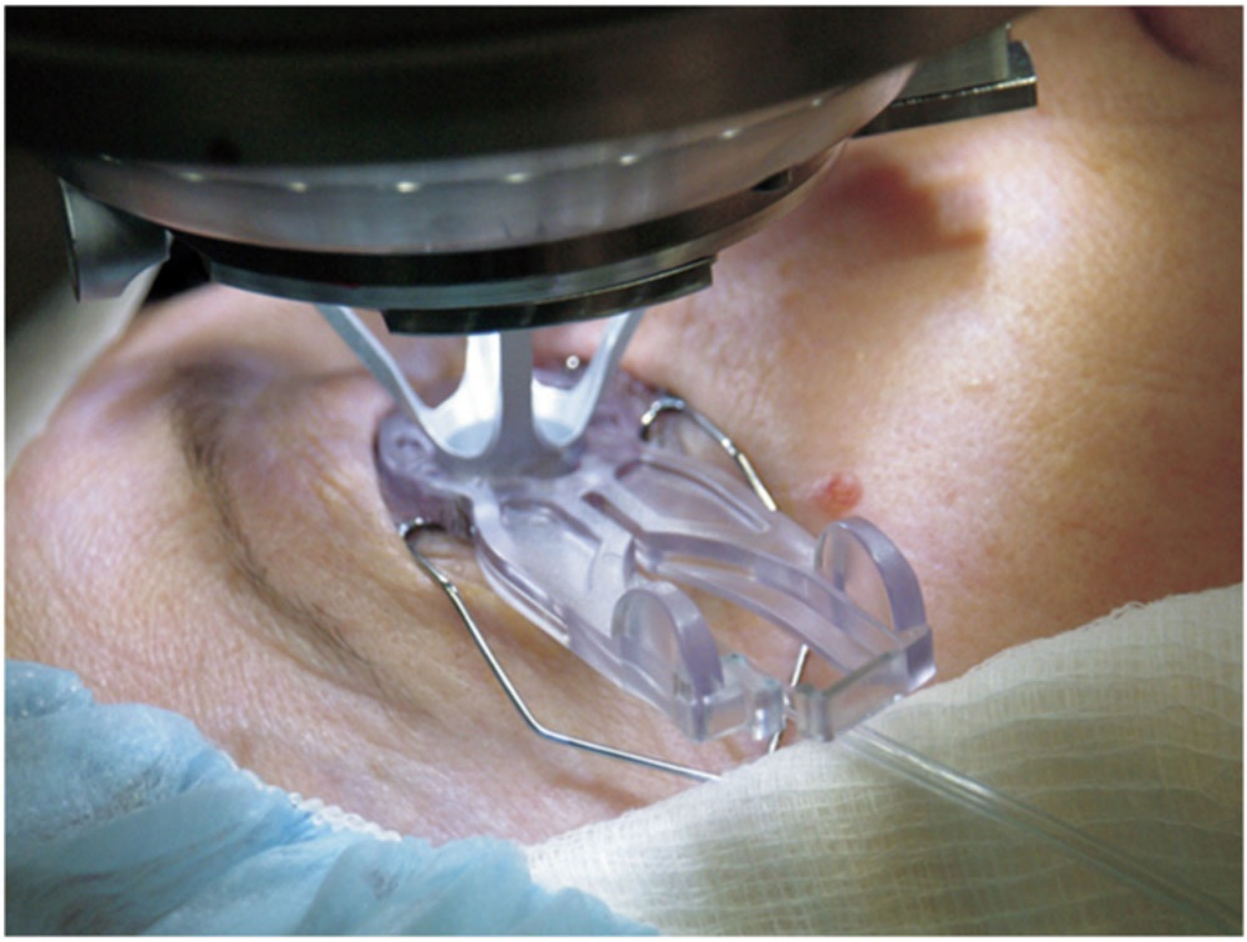

Figure 5-8 Docking of IntraLase cone with suction ring positioned on the eye. *(Reproduced with permission from Feder RS, Rapuano CJ.* The LASIK Handbook: ACase-Based Approach. *Philadelphia: Lippincott Williams & Wilkins; 2007:46, fig 2.9. Photograph courtesy of Robert Feder, MD.)*

Once centration is confirmed on the laser, the surgeon administers the femtosecond laser treatment. The vacuum is then released, the suction ring is removed, and the patient is positioned under the excimer laser. A spatula with a semisharp edge identifies and scores the flap edge near the hinge (Fig 5-9). The instrument is then passed across the flap along the base of the hinge, and the flap is lifted by sweeping inferiorly and separating the flap interface, dissecting one-third of the flap at a time and thus reducing the risk of tearing.

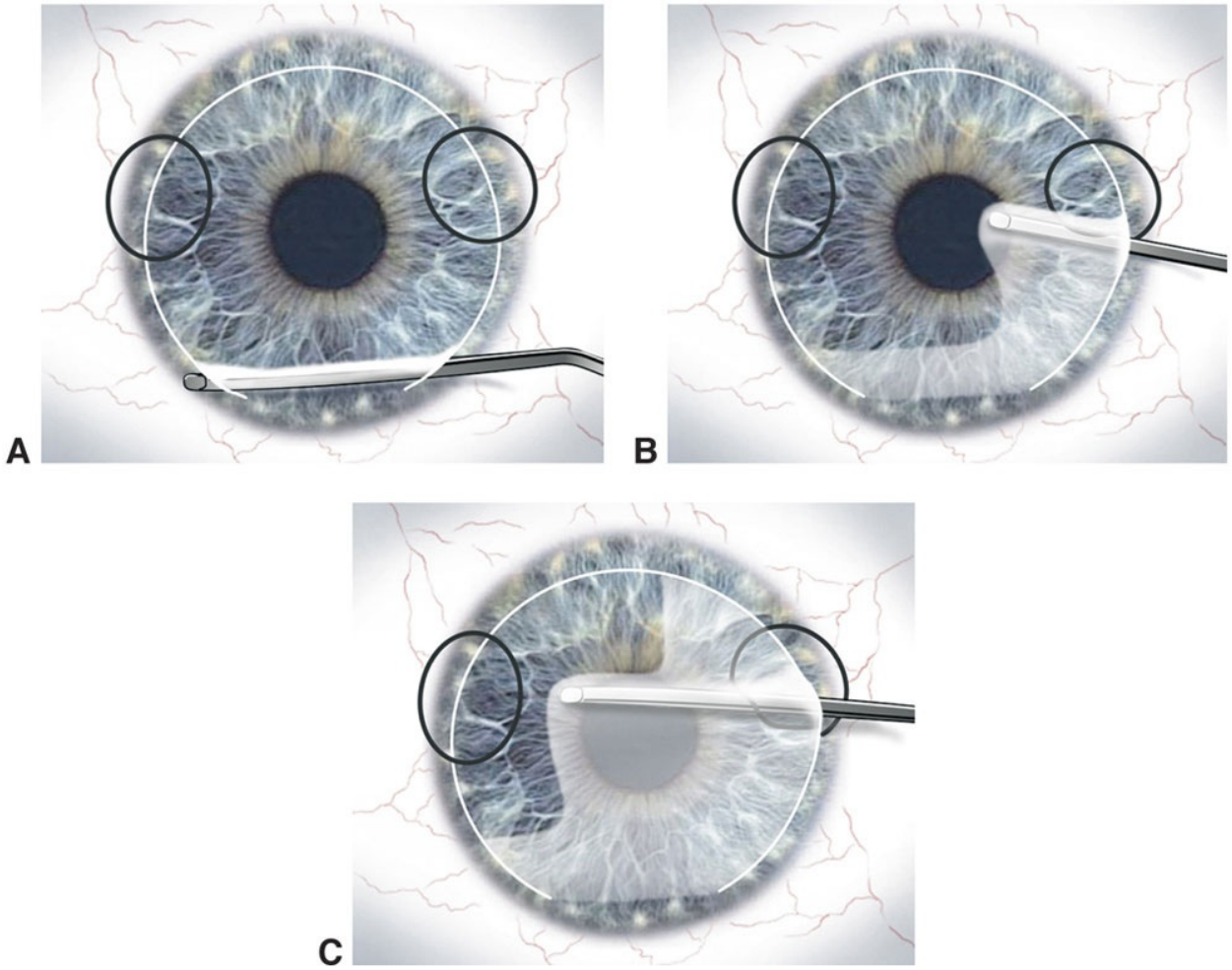

Figure 5-9 Flap lift technique following femtosecond laser application. **A,** After the flap edge is scored near the hinge on either side *(black ovals),* a spatula is passed across the flap. **B,** The interface is separated by starting at the superior hinge and sweeping inferiorly. **C,** Dissecting one-third of the flap at a time reduces the risk of tearing the hinge. *(Reproduced with permission from Feder RS, Rapuano CJ.* The LASIK Handbook: A Case-Based Approach. *Philadelphia: Lippincott Williams & Wilkins; 2007:48, fig 2.12. Photograph courtesy of Robert Feder, MD.)*

Several studies have compared the benefits of the mechanical microkeratome with those of femtosecond lasers for creating flaps and have found minimal differences between techniques for most patients (Table 5-2).

Table 5-2

Table 5-2 Advantages and Disadvantages of the Femtosecond Laser

Advantages	Disadvantages
More customizable flap parameters	Longer suction time
Size and thickness of flap less dependent on corneal contour	More flap manipulation
Centration easier to control	Opaque bubble layer may interfere with excimer ablation
Epithelial defects on flap are rare	Bubbles in the anterior chamber may interfere with tracking and registration
Less risk of free cap and buttonhole	Increased overall treatment time
More reliable flap thickness	Difficulty lifting flap after 6 months
Hemorrhage from limbal vessels less likely	Increased risk of transient light sensitivity
Ability to re-treat immediately if incomplete femtosecond laser ablation	Increased cost
	Delayed photosensitivity or good acuity plus photosensitivity, which may require prolonged topical corticosteroid therapy

Modified with permission from Feder RS, Rapuano CJ. *The LASIK Handbook: A Case-Based Approach.* Philadelphia: Lippincott Williams & Wilkins; 2007.

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Slade SG, Durrie DS, Binder PS. A prospective, contralateral eye study comparing thin-flap LASIK (sub-Bowman keratomileusis) with photorefractive keratectomy. *Ophthalmology.* 2009;116(6):1075-1082.

Tran DB, Sarayba MA, Bor Z, et al. Randomized prospective clinical study comparing induced aberrations with IntraLase and Hansatome flap creation in fellow eyes: potential impact on wavefront-guided laser in situ keratomileusis. *J Cataract Refract Surg.* 2005;31(1):97-105.

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Application of Laser Treatment

Tracking, centration, and ablation

For surface ablation, the exposed Bowman layer should be inspected and found to be smooth, uniformly dry, and free of debris and residual epithelial islands. For LASIK, the flap must be lifted and reflected, and the stromal bed must be uniformly dry before treatment. Fluid or blood accumulation on the stromal bed should be avoided, as it can lead to an irregular ablation.

All excimer lasers in current use employ tracking systems, which have improved clinical outcomes. The tracker used is an open-loop system, which employs video technology to monitor the location of an infrared image of the pupil and to shift the laser beam accordingly.

The laser is centered and focused according to the manufacturer's recommendations. Tracking systems, although effective, do not lessen the importance of keeping the reticule centered on the patient's entrance pupil. If the patient is unable to maintain fixation, the illumination of the operating microscope should be reduced. If decentration occurs and the ablation does not stop automatically, the surgeon should immediately stop the treatment until adequate refixation is achieved. It is still important for the

surgeon to monitor for excessive eye movement, which can result in decentration despite the tracking device.

The change in illumination and in patient position (ie, from sitting to lying down) can cause pupil centroid shift and cyclotorsion. In most patients, the pupil moves nasally and superiorly when it is constricted. *Registration* is a technique in which a fixed landmark is used at the time of aberrometry and treatment to apply the ablation to the correct area of the cornea; it relies on iris landmarks and not on the pupil for laser centration (Fig 5-10). Once the patient confirms that the fixation light of the excimer laser is still visible and that he or she is looking directly at it, ablation begins. Neither tracking nor iris registration is a substitute for accurate patient fixation. It is important to initiate stromal ablation promptly, before excessive stromal dehydration takes place. During larger-diameter ablations, a flap protector may be needed to shield the underside of the LASIK flap near the hinge from the laser pulses.

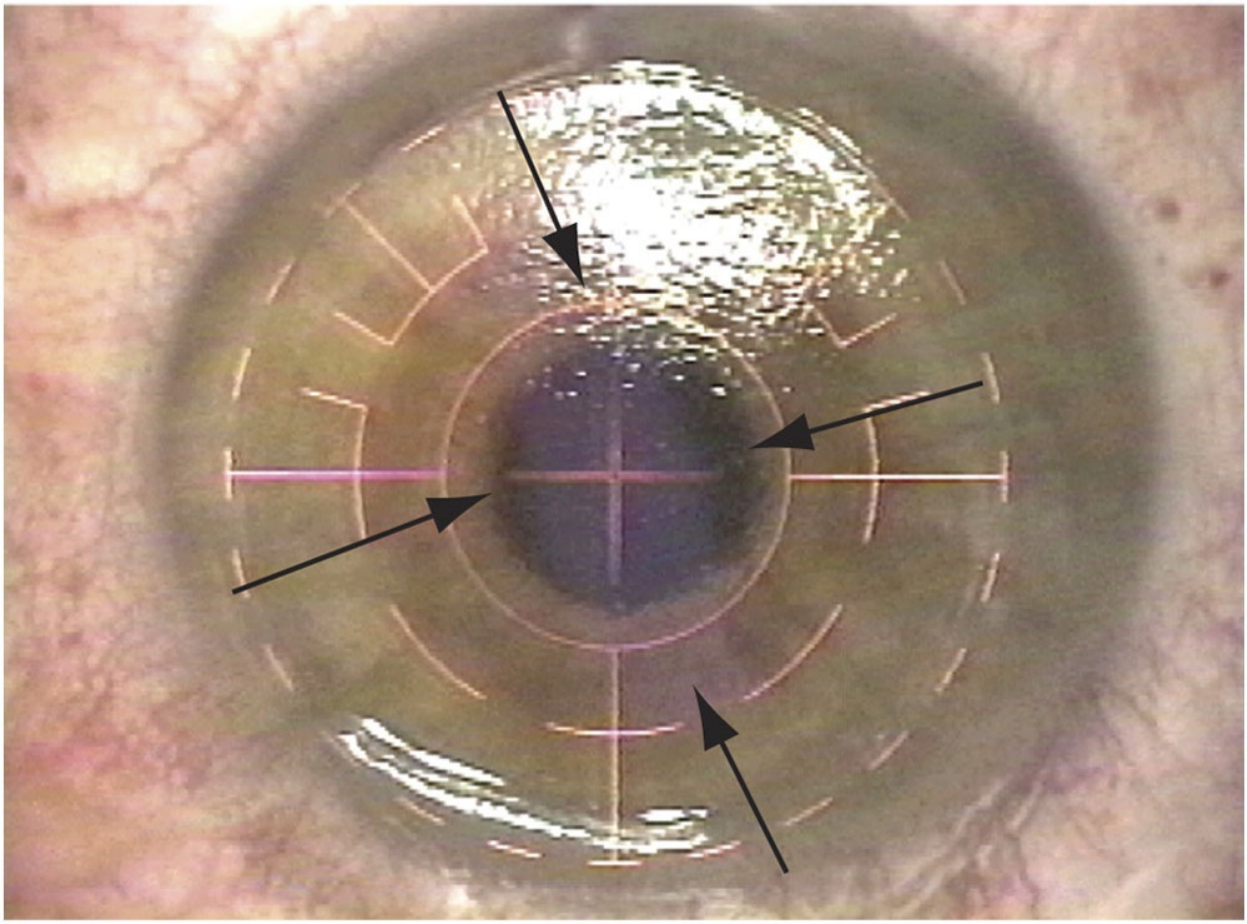

Figure 5-10 Excimer laser ablation of the stromal bed. Note the faint blue fluorescence of the stromal bed from the laser pulse *(arrows).* The rectangular shape of the exposure by this broad-beam laser indicates that the laser is correcting the cylindrical portion of the treatment. (Photograph is enhanced to visualize fluorescence; the surgeon usually sees minimal or no fluorescence through the operating microscope.) *(Courtesy of Roger F. Steinert, MD.)*

Donnenfeld E. The pupil is a moving target: centration, repeatability, and registration. *J Refract Surg.* 2004;20(5):S593-S596.
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Immediate Postablation Measures

Surface ablation

One of the major potential complications of surface ablation is corneal haze. To decrease the chance of post-surface ablation corneal haze, especially for eyes with previous corneal surgery such as PRK, LASIK, penetrating keratoplasty, or radial keratotomy, a pledget soaked in mitomycin C (usually 0.02% or 0.2 mg/mL) can be placed on the ablated surface for approximately 12 seconds to 2 minutes at the end of the laser exposure. The concentration and duration of mitomycin C application may vary by diagnosis and surgeon preference; however, most surgeons are tending toward use of a shorter duration of mitomycin C exposure. Application of mitomycin C for 12 seconds appears to be as efficacious for prophylaxis as prolonged times. Many surgeons also employ mitomycin C in primary surface ablation for moderate to high treatments or deeper ablation depths. Some surgeons reduce the amount of treatment when applying mitomycin C in surface ablation due to reports of potential endothelial cell toxicity. The cornea is then copiously irrigated with balanced salt solution to remove excess mitomycin C. To avoid damage to limbal stem cells, care should be taken not to expose the limbus or conjunctiva to mitomycin C. Human confocal microscopy studies have shown a reduced keratocyte population and less haze in eyes that received mitomycin C.

Some surgeons apply sterile, chilled, balanced salt solution or a frozen cellulose sponge before and/or after the surface ablation procedure in the belief that cooling reduces pain and haze formation. However, the advantage of this practice has not been substantiated in a controlled study. Care should be taken to not expose the eye to tap water, which may result in infectious contamination.

If the LASEK or epi-LASIK variant has been performed, the surgeon carefully floats and moves the epithelial sheet back into position with balanced salt solution. Antibiotic, corticosteroid, and, sometimes, nonsteroidal anti-inflammatory drugs (NSAIDs) are then placed on the eye, followed by a bandage soft contact lens. Some NSAIDs and antibiotics can be placed directly on the corneal bed, whereas others should be placed only on the surface of the contact lens, as they have been associated with poor corneal healing. If the patient cannot tolerate a bandage soft contact lens, a pressure patch may be used. Of note, the American Society of Cataract and Refractive Surgery released a clinical alert on February 14, 2013, discussing the postoperative risks posed by certain medications used topically prior to or during LASIK or PRK. The medications listed in this statement have the potential to cause flap slippage and/or diffuse lamellar keratitis (DLK) following LASIK surgery and poor epithelial healing

following PRK. This statement is available at www.eyeworld.org/article-medication-alert-for-lasik-and-prk.

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Virasch VV, Majmudar PA, Epstein RJ, Vaidya NS, Dennis RF. Reduced application time for prophylactic mitomycin C in photorefractive keratectomy. *Ophthalmology.* 2010;117(5): 885-889. Epub 2010 Feb 16.

LASIK

After the ablation is completed, the flap is replaced onto the stromal bed. The interface is irrigated until all interface debris is eliminated (which is apparent more readily with oblique than with coaxial illumination). The surface of the flap is gently stroked using a smooth instrument, such as an irrigation cannula or a moistened microsurgical spear sponge, from the hinge, or center, to the periphery to ensure that wrinkles are eliminated and that the flap settles back into its original position, as indicated by realignment of the corneal marks made earlier. The peripheral gutters should be symmetric and even. The physiologic dehydration of the stroma by the endothelial pump will begin to secure the flap in position within several minutes. If a significant epithelial defect or a large, loose sheet of epithelium is present, a bandage contact lens should be put in place. Once the flap is adherent, the eyelid speculum is removed carefully so as not to disturb the flap. Most surgeons place varying combinations of antibiotic, NSAID, and corticosteroid drops on the eye at the conclusion of the procedure. The flap is usually rechecked at the slit lamp before the patient leaves to make sure it has remained in proper alignment. A clear shield or protective goggles are often placed to guard against accidental trauma that could displace the flap. Patients are instructed not to rub or squeeze their eyes.

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Postoperative Care

Surface ablation

After surface ablation, patients may experience variable degrees of pain, from minimal to severe, and some may need oral NSAID, narcotic, or neuropathic pain medications. Studies have shown that topical NSAID drops reduce postoperative pain, although they may also slow the rate of re-epithelialization and promote sterile infiltrates (see Chapter 6). Corneal melting and stromal scarring have been described after the use of some topical NSAIDs. For patients who are not healing normally after surface ablation, use of any topical NSAID should be discontinued.

Patients should be monitored closely until the epithelium is completely healed, which usually occurs within 4-7 days. As long as the bandage soft contact lens is in place, patients are treated with topical broad-spectrum antibiotics and corticosteroids, usually 4 times daily. Once the epithelium is healed, the bandage soft contact lens, antibiotic drops, and NSAID drops (if used) may be discontinued.

The use of topical corticosteroids to modulate postoperative wound healing, reduce anterior stromal haze, and decrease regression of the refractive effect remains controversial. Although some studies have demonstrated that corticosteroids have no significant long-term effect on corneal haze or visual outcome after PRK, other studies have shown that corticosteroids are effective in limiting haze and myopic regression after PRK, particularly after higher myopic corrections. Some surgeons who advocate use of topical corticosteroids after the removal of the bandage soft contact lens restrict their use to patients with higher levels of myopia (eg, myopia greater than -4.00 or -5.00 D). When used after removal of the bandage lens, corticosteroid drops are typically tapered over a 1- to 4-month period, depending on the patient's corneal haze and refractive outcome. Patients who received mitomycin C at the time of surgery have a reduced risk of haze formation and thus may have a shorter duration of corticosteroid use. Patients who had PRK for hyperopia may experience prolonged epithelial healing because of the larger epithelial defect resulting from the larger ablation zone, as well as a temporary reduction in best-corrected distance visual acuity in the first week to month, which usually improves with time. Many patients with hyperopia also experience a temporary myopic overcorrection, which regresses over several weeks to months. In the absence of complications, routine follow-up examinations are typically scheduled at approximately 2-4 weeks, 2-3 months, 6 months, and 12 months postoperatively and perhaps more frequently, depending on the steroid taper used.

LASIK

Many surgeons instruct their patients to use topical antibiotics and corticosteroids postoperatively for 3-7 days. With femtosecond laser procedures, some surgeons prescribe more frequent applications of corticosteroid eye drops or a longer period of use. In addition, it is very important for the surface of the flap to be kept well lubricated in the early postoperative period. Patients may be told to use the protective shield for 1 day to 1 week when they shower or sleep and to avoid swimming and use of hot tubs for 2 weeks. Patients are examined 1 day after surgery to ensure that the flap has remained in proper alignment and that there is no evidence of infection or excessive inflammation. In the absence of complications, the next examinations are typically scheduled at approximately 1 week, 1 month, 3 months, 6 months, and 12 months postoperatively.

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Solomon KD, Donnenfeld ED, Raizman M, et al; Ketorolac Reformulation Study Groups 1 and 2. Safety and efficacy of

ketorolac tromethamine 0.4% ophthalmic solution in post-photorefractive keratectomy patients. *J Cataract Refract Surg.* 2004;30(8):1653-1660.

Refractive Outcomes

As the early broad-beam excimer laser systems improved and surgeons gained experience, the results achieved with surface ablation and LASIK improved markedly. The ablation zone diameter was enlarged because it was found that small ablation zones, originally selected to limit depth of tissue removal, produced more haze and regression in surface ablation treatments and complaints of subjective glare and halos for both surface ablation and LASIK. The larger treatment diameters currently used, including for optical zones and gradual aspheric peripheral blend zones, improve optical quality and refractive stability in both myopic and hyperopic treatments. Central island elevations have become less common with improvements in beam quality, vacuums to remove the ablation plume, and the development of scanning and variable-spot-size excimer lasers.

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Outcomes for Myopia

Initial FDA clinical trials of conventional excimer laser treatments limited to low myopia (generally less than -6.00 D) revealed that 56%-86% of eyes treated with either PRK or LASIK achieved uncorrected distance visual acuity (UDVA; also called *uncorrected visual acuity, UCVA*) of at least 20/20, 88%-100% achieved UDVA of at least 20/40, and 82%-100% were within 1.00 D of emmetropia. Up to 2.1% of eyes lost [?]2 lines of corrected distance visual acuity (CDVA; also called *best-corrected visual acuity, BCVA*). Reports since 2000 have demonstrated significantly improved outcomes and safety profiles, with <0.6% of eyes losing 2 or more lines of CDVA.

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Watson SL, Bunce C, Alan BD. Improved safety in contemporary LASIK. *Ophthalmology.* 2005;112(8):1375-1380.

Outcomes for Hyperopia

In myopic ablations, the central cornea is flattened, whereas in hyperopic ablations, more tissue is removed from the midperiphery than from the central cornea, resulting in an effective steepening (Fig 5-1B). To ensure that the size of the central hyperopic treatment zone is adequate, a large ablation area is required for hyperopic treatments. Most studies have employed hyperopic treatment zones with transition zones out to 9.0-9.5 mm. FDA clinical trials of PRK and LASIK for hyperopia up to +6.00 D reported that 46%-59% of eyes had postoperative UDVA of 20/20 or better, 92%-96% had UDVA of 20/40 or better, and 84%-91% were within 1.00 D of emmetropia; loss of >2 lines of CDVA occurred in 1%-3.5%. The VISX FDA clinical trial of hyperopic astigmatic PRK up to +6.00 D sphere and +4.00 D cylinder reported an approximate postoperative UDVA of 20/20 or better in 50% of eyes, UDVA of 20/40 or better in 97%, and 87% within +-1.00 D of emmetropia, with loss of >2 lines of CDVA in 1.5%. For the same amount of correction, the period from surgery to postoperative stabilization is longer for hyperopic than for myopic corrections. Overall, studies with larger ablation zones have demonstrated good results for refractive errors up to +4.00 D for conventional treatments, but predictability and stability are markedly reduced with LASIK treatments for hyperopia above this level. Consequently, most refractive surgeons do not treat up to the highest levels of hyperopia that have been approved by the FDA for conventional treatments.

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Wavefront-Guided and Wavefront-Optimized Treatment Outcomes for Myopia and Hyperopia

Wavefront-guided or wavefront-optimized LASIK coupled with sophisticated eye-tracking systems has greatly improved the accuracy and reproducibility of results, allowing even higher percentages of patients to obtain UDVA of 20/20 and 20/40. In

wavefront-guided LASIK for myopic astigmatism, for example, up to about -10.00 to -12.00 D, 79%-95% of patients obtained 20/20 UDVA, and 96%-100% obtained 20/40 UDVA. In wavefront-guided LASIK for hyperopic astigmatism up to +6.00 D, 55%-59% of patients obtained 20/20 UDVA, and 93%-97% obtained 20/40 UDVA. In wavefront-guided LASIK for mixed astigmatism with up to +5.00 D of cylinder, 56%-61% of patients obtained 20/20 UDVA, and 95% obtained 20/40 UDVA. A recent study found that the visual acuity results for the vast majority of patients were equivalent between wavefront-guided and wavefront-optimized LASIK.

Fares U, Otri AM, Al-Aqaba MA, Faraj L, Dua HS. Wavefront-optimized excimer laser in situ keratomileusis for myopia and myopic astigmatism: refractive outcomes and corneal densitometry. *J Cataract Refract Surg.* 2012;38(12):2131-2138. Epub 2012 Oct 18.

Keir NJ, Simpson T, Jones LW, Fonn D. Wavefront-guided LASIK for myopia: effect on visual acuity, contrast sensitivity, and higher order aberrations. *J Refract Surg.* 2009;25(6): 524-533.

Rajan MS, Jaycock P, O'Brart D, Nystrom HH, Marshall J. A long-term study of photorefractive keratectomy: 12-year follow-up. *Ophthalmology.* 2004;111(10):1813-1824.

Randleman JB, Perez-Straziota CE, Hu MH, White AJ, Loft ES, Stulting RD. Higher-order aberrations after wavefront-optimized photorefractive keratectomy and laser in situ keratom ileusis. *J Cataract Refract Surg.* 2009;35(2):260-264.

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Re-treatment (Enhancements)

Although excimer laser ablation reduces refractive error and improves UDVA in almost all cases, some patients have residual refractive errors and would benefit from re-treatment. The degree of refractive error that warrants re-treatment varies depending on the patient's lifestyle and expectations. Re-treatment rates also vary, depending on the degree of refractive error being treated, the laser and nomograms used, and the expectations of the patient. One advantage of LASIK over surface ablation is that refractive stability generally occurs earlier, allowing earlier enhancements, typically within the first 3 months after LASIK. With surface ablation, the ongoing activation of keratocytes and the risk of haze after enhancement usually require a wait of 3-6 months before an enhancement surface ablation is undertaken. Typically, re-treatment rates are higher for hyperopia and for high astigmatism than for other indications.

Studies showed that rates of re-treatment are higher for higher initial correction, for residual astigmatism, and for patients older than 40 years. Re-treatment rates vary from 1% to 11%, based on surgeon experience, patient demands, and the other factors just described. Surface ablation re-treatment is nearly identical to primary surface ablation treatment, whereas LASIK re-treatment can be performed either by lifting the preexisting lamellar flap and applying additional ablation to the stromal bed or by performing surface ablation on the LASIK flap. In most cases, the flap can be lifted many years after the original procedure. However, because of the safety of surface ablation after LASIK and the increased risk of epithelial ingrowth with flap lifts, many

surgeons now prefer to perform surface ablation re-treatment if the primary LASIK was performed more than 2-3 years earlier. Creating a new flap with a mechanical microkeratome should be avoided because free slivers of tissue, irregular stromal beds, and irregular astigmatism may be produced. Using the femtosecond laser to create a new side cut within the boundaries of the previous flap may facilitate flap-lift enhancements; however, it is important to have an adequate exposed diameter for ablation. When attempting to lift or manipulate a femtosecond laser-created flap, the surgeon must take care to avoid tearing it, because the femtosecond laser usually creates a thinner flap than traditional microkeratomes do.

When a preexisting flap is lifted, it is important to minimize epithelial disruption. A jeweler's forceps, Sinskey hook, or 27-gauge needle can be used to localize the edge of the previous flap. Because the edge of the flap can be seen more easily with the slit lamp than with the diffuse illumination of the operating microscope of the laser, some surgeons find it easier to begin a flap lift at the slit lamp and complete it at the excimer laser. Alternatively, the surgeon can often visualize the edge of the flap under the diffuse illumination of the operating microscope by applying pressure with a small Sinskey hook or similar device; the edge of the flap will dimple and disrupt the light reflex (Fig 5-11). A careful circumferential epithelial dissection is performed so that the flap can then be lifted without tearing the epithelial edges. Smooth forceps, iris spatulas, and several instruments specifically designed for dissecting the flap edge can be used to lift the original flap.

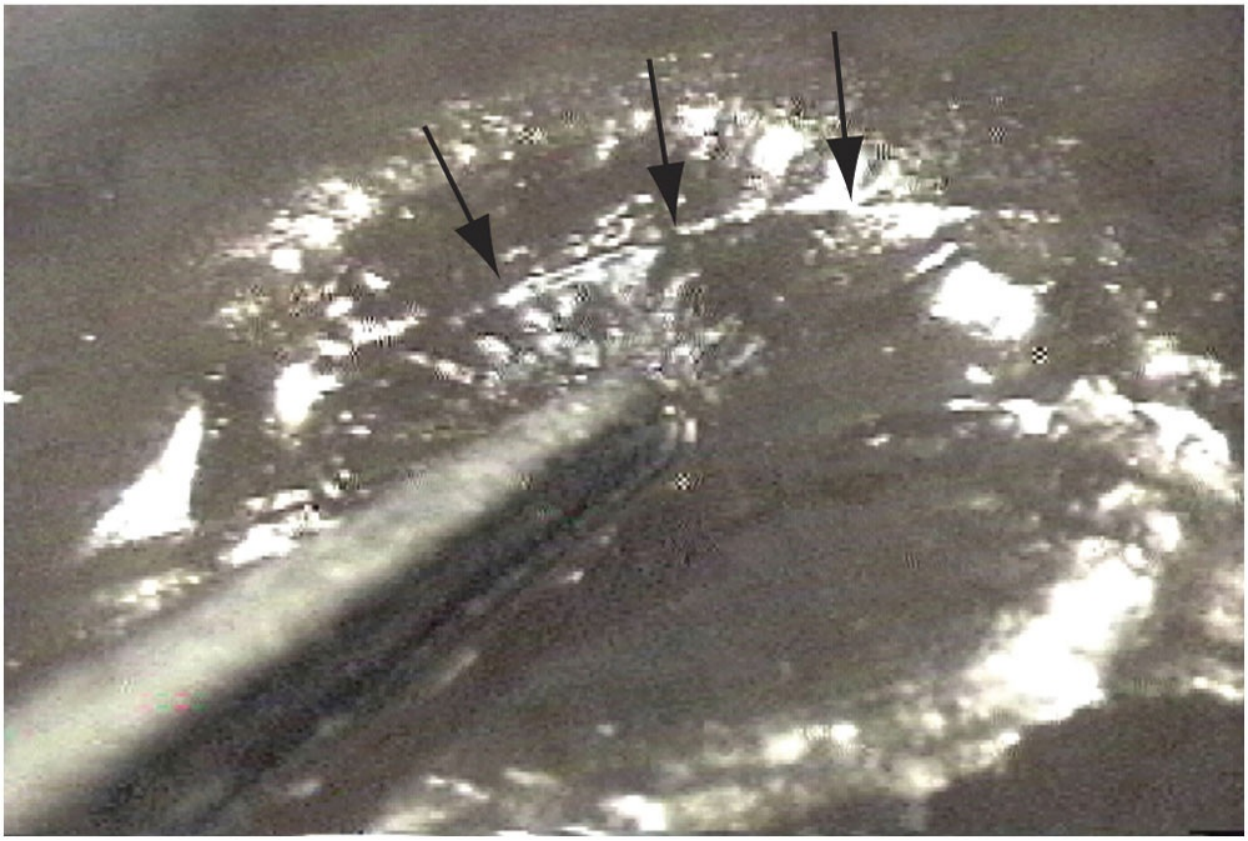

Figure 5-11 Indenting the cornea with forceps to visualize the edge of the flap *(arrows)* through an operating microscope prior to an enhancement procedure. *(Courtesy of Roger F. Steinert, MD.)*

Once the ablation has been performed, the flap is repositioned and the interface is irrigated, as in the initial LASIK procedure. Special care must be taken to ensure that no loose epithelium is trapped beneath the edge of the flap that could lead to epithelial ingrowth; the risk of epithelial ingrowth is greater after re-treatment than after primary treatment.

Surface ablation may be considered to enhance a previous primary LASIK treatment. Surface ablation performed on a LASIK flap carries an increased risk of haze formation and irregular astigmatism, but it is an appealing alternative when the residual stromal bed is insufficient for further ablation; when the LASIK was performed by another surgeon and the flap thickness, or RSB, is not known; or with conditions such as a buttonhole or incomplete flap. Care must be taken when removing the epithelium over a flap to avoid inadvertently lifting or dislocating the flap. Applying 20% ethanol for 20-30 seconds inside a corneal well will loosen the epithelium, after which scraping motions are applied that extend from the hinge toward the periphery. A rotating brush should not be used to remove the epithelium from a LASIK flap. The risk of postoperative haze due to surface ablation over a previous LASIK flap may be avoided or reduced by administering topical corticosteroids and

topical mitomycin C, 0.02%.

The appropriate choice between conventional and wavefront-guided treatment for enhancing the vision of patients who have previously undergone conventional LASIK is not yet established. Some studies report better results in both safety and efficacy with conventional LASIK re-treatment. With wavefront-guided re-treatments, particularly in patients with high spherical aberrations, the risk of overcorrection may be greater. Caution should be exercised in evaluating the degree of higher-order aberrations and the planned depth of the ablation when deciding between conventional and wavefront-guided treatments.

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Hiatt JA, Grant CN, Boxer Wachler BS. Complex wavefront-guided retreatments with the Alcon CustomCornea platform after prior LASIK. *J Refract Surg.* 2006;22(1):48-53.

Jin GJ, Merkley KH. Conventional and wavefront-guided myopic LASIK retreatment. *Am J Ophthalmol.* 2006;141(4):660-668.

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CHAPTER 6

Photoablation: Complications and Adverse Effects

Surface ablation techniques, including photorefractive keratectomy (PRK) and laser in situ keratomileusis (LASIK), are relatively safe and effective surgical procedures. As with all types of surgery, there are potential risks and complications. It is important to understand how to avoid, diagnose, and treat many of the complications of refractive surgery. Comprehensive ophthalmologists, as well as refractive surgeons, should be knowledgeable about these postoperative problems, given the increasing number of patients who undergo refractive surgery each year.

General Complications Related to Laser Ablation

Overcorrection

Myopic or hyperopic surface ablation typically undergoes some degree of refractive regression for at least 3-6 months. In general, patients with higher degrees of myopia and any degree of hyperopia require more time to attain refractive stability, which must be achieved before any decision is made regarding possible re-treatment of the overcorrection.

Overcorrection may occur if substantial stromal dehydration develops before the laser treatment is initiated because more stromal tissue will be ablated per pulse. A long delay before beginning the ablation after removing the epithelium in surface ablation or after lifting the flap in LASIK allows for excessive dehydration of the stroma and increases the risk of overcorrection. Controlling the humidity and temperature in the laser suite within the recommended guidelines should standardize the surgery and ideally improve refractive outcomes. Overcorrection tends to occur more often in older individuals because their wound-healing response is less vigorous and their corneas ablate more rapidly for reasons not fully understood. Studies reveal that

older patients with moderate to high myopia have a greater response to the same amount of dioptric correction than younger patients do.

Various modalities are available for treating small amounts of overcorrection. Myopic regression can be induced after surface ablation by abrupt discontinuation of corticosteroids. Patients with consecutive hyperopia--that is, hyperopia that occurs when originally myopic eyes are overcorrected--and patients with myopia due to overcorrection of hyperopia require less treatment to achieve emmetropia than do patients with previously untreated eyes, as both are considered to have over-responded to the initial treatment. When re-treating such patients, the surgeon should take care not to overcorrect a second time. With conventional ablation, most surgeons will reduce the ablation by 20%-25% for consecutive treatments. For wavefront procedures, review of the depth of the ablation and the amount of higher-order aberration helps titrate the re-treatment.

Undercorrection

Undercorrection occurs much more commonly at higher degrees of ametropia because of greater severity and more frequent occurrence of regression. Patients with regression after treatment of their first eye have an increased likelihood of regression in their second eye. Sometimes the regression may be reversed with aggressive use of topical corticosteroids. Topical mitomycin C, administered at the time of initial surface ablation, can be used to modulate the response, especially in patients with higher levels of ametropia. The patient may undergo a re-treatment after the refraction has remained stable for at least 3 months postoperatively. A patient with significant corneal haze and regression after surface ablation is at higher risk after re-treatment for further regression, recurrence of visually significant corneal haze, and loss of corrected distance visual acuity (CDVA; also called *best-corrected visual acuity, BCVA*). It is recommended that the surgeon wait at least 6-12 months for the haze to improve spontaneously before repeating surface ablation. In patients with significant haze and myopic regression, removal of the haze with adjunctive use of mitomycin C should not be coupled with a refractive treatment, as the resolution of the haze commonly improves the refractive outcome. Undercorrection after LASIK typically requires flap lift and laser treatment of the residual refractive error after the refraction has remained stable for at least 3 months. Higher levels of residual myopia or hyperopia may be managed with phakic intraocular lenses or refractive lens exchange, respectively.

Optical Aberrations

After undergoing surface ablation or LASIK, some patients report symptoms related to optical aberrations, including glare, ghost images, and halos. These symptoms are most prevalent after treatment with smaller ablation zones (<6.0 mm in diameter), after

attempted higher spherical and cylindrical correction, and in patients with symptoms prior to refractive surgery. These vision problems seem to be exacerbated in dim-light conditions when mydriasis occurs, although no correlation has been found between pupil size and optical aberrations. Wavefront mapping can reveal higher-order aberrations associated with these subjective complaints. In general, a larger, well-centered optical zone provides a better quality of vision, especially at night.

Night-vision complaints are often the result of spherical aberration, although other higher-order aberrations also contribute. The cornea and lens have inherent spherical aberration. In addition, excimer laser ablation increases spherical aberration in the midperipheral cornea. Customized wavefront-guided corneal treatment patterns are designed to reduce existing aberrations and to help prevent the creation of new aberrations, with the goal of achieving a better quality of vision after laser ablation.

Several studies have demonstrated that although the excimer laser photoablation causes the majority of post-LASIK change in lower-order and higher-order aberrations, the creation of the flap itself can also change lower-order and higher-order aberrations (Fig 6-1). Some studies have demonstrated that femtosecond lasers cause little or no change in higher-order aberrations, in contrast to mechanical microkeratomes. Pallikaris showed that LASIK flap creation alone, without lifting, caused no significant change in refractive error or visual acuity but did cause a significant increase in total higher-order wavefront aberrations.

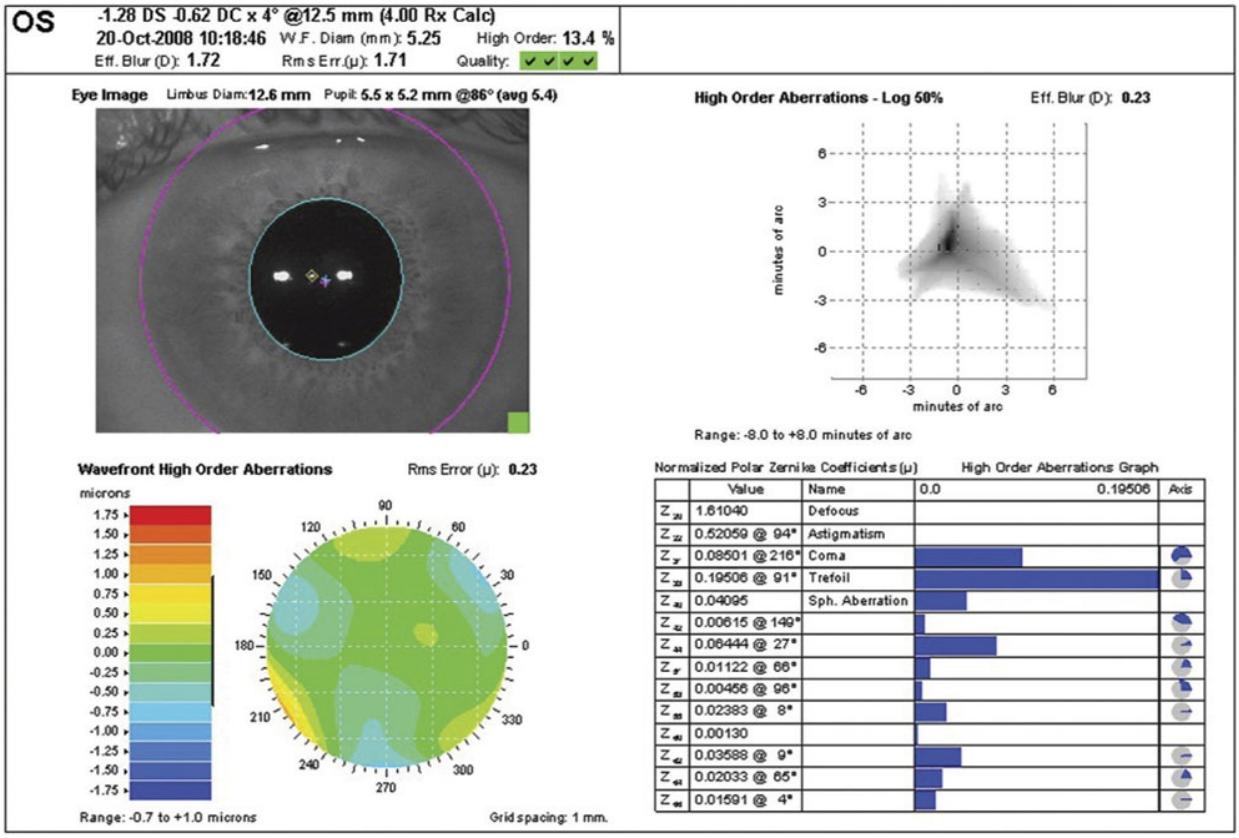

Figure 6-1 Wavefront analysis depicting higher-order aberrations after laser in situ keratomileusis (LASIK), including coma and trefoil. *(Courtesy of Steven I. Rosenfeld, MD.)*

Pallikaris IG, Kymionis GD, Panagopoulou SI, Siganos CS, Theodorakis MA, Pellikaris AI. Induced optical aberrations following formation of a laser in situ keratomileusis flap. *J Cataract Refract Surg.* 2002;28(10):1737-1741.

Tran DB, Sarayba MA, Bor Z, et al. Randomized prospective clinical study comparing induced aberrations with IntraLase and Hansatome flap creation in fellow eyes: potential impact on wavefront-guided laser in situ keratomileusis. *J Cataract Refract Surg.* 2005; 31(1):97-105.

Waheed S, Chalita MR, Xu M, Krueger RR. Flap-induced and laser-induced ocular aberrations in a two-step LASIK procedure. *J Refract Surg.* 2005;21(3):346-352.

Central Islands

A central island appears on computerized corneal topography as an area of central corneal steepening surrounded by an area of flattening that corresponds to the myopic treatment zone in the paracentral region (Fig 6-2). A central island is defined as a steepening of at least 1.00 D with a diameter of >1 mm compared with the paracentral flattened area. Central islands may be associated with decreased visual acuity, monocular diplopia and multiplopia, ghost images, and decreased contrast sensitivity.

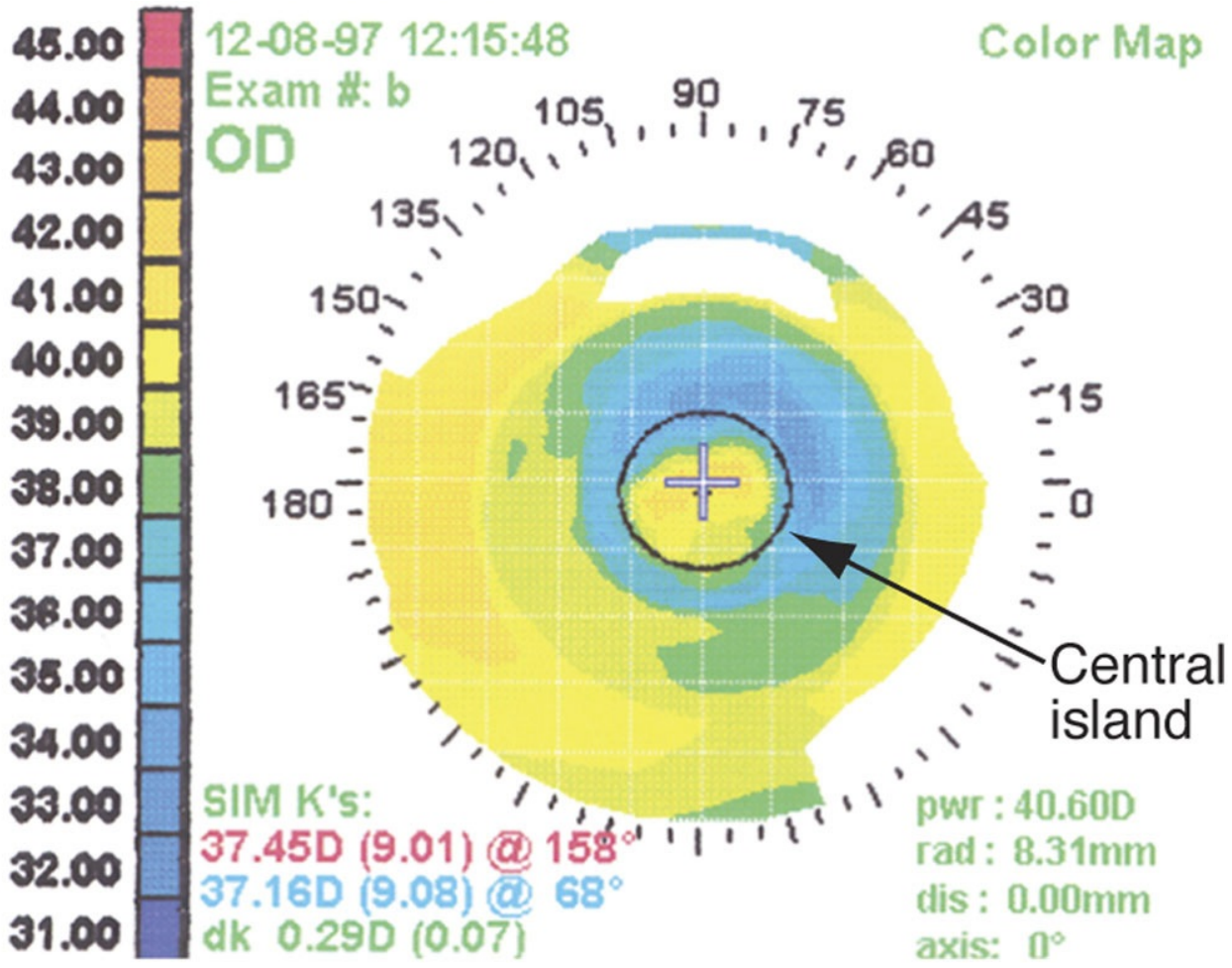

Figure 6-2 Corneal topography findings of a myopic ablation *(blue)* with a central island *(yellow)* in the visual axis. *(Courtesy of Roger F. Steinert, MD.)*

The occurrence of central islands has been reduced significantly through the use of scanning and variable-spot-size lasers and is now rarely encountered with modern laser technology. Fortunately, most central islands diminish over time, especially after surface ablation, although resolution may take 6-12 months. Treatment options such as topography-guided ablations may be helpful in treating persistent central islands.

Decentered Ablations

Accurate centration during the excimer laser procedure is important in optimizing the visual results. Centration is even more crucial for hyperopic than myopic treatments. A decentered ablation may occur if the patient's eye slowly begins to drift and loses fixation or if the surgeon initially positions the patient's head improperly; if the patient's eye is not perpendicular to the laser treatment, parallax can result (Fig 6-3). The incidence of decentration increases with slow eye tracking, hyperopic ablations, and higher refractive correction, due to longer ablation times. Decentration may be reduced by ensuring that the patient's head remains in the correct plane throughout the treatment--that is, perpendicular to the laser (parallel to the ground)--and that there is no head tilt. Treatment of decentration with topography-guided technology may be effective.

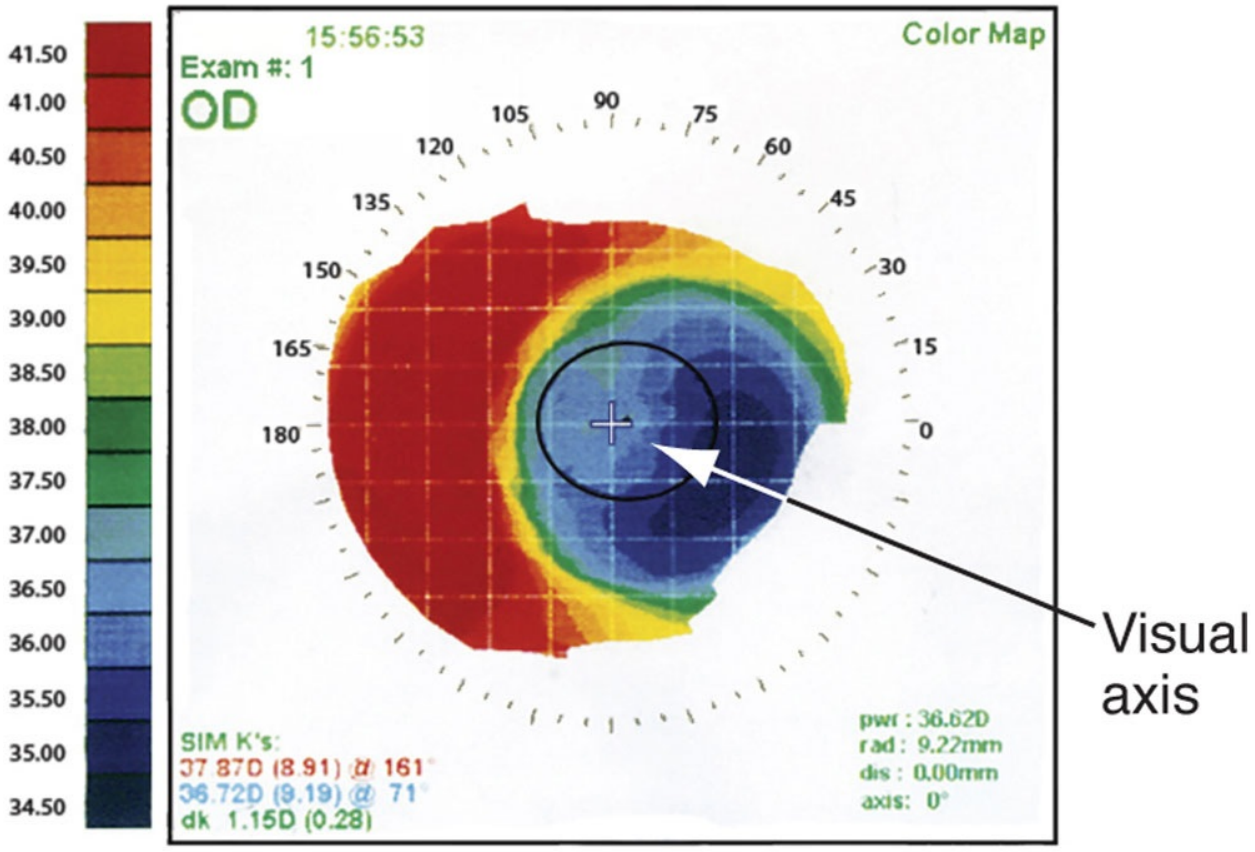

Figure 6-3 Corneal topography findings of a decentered ablation. *(Courtesy of Roger F. Steinert, MD.)*

Corticosteroid-Induced Complications

The incidence of increased intraocular pressure (IOP) after surface ablation has been reported to range from 11% to 25%. Occasionally, the IOP may be quite high. In 1 study, 2% of patients had IOP greater than 40 mm Hg. The majority of cases of elevated IOP are associated with prolonged topical corticosteroid therapy. Accordingly, postoperative steroid-associated IOP elevations are more likely to occur after surface ablation (after which steroid therapy may be used 2-4 months to prevent postoperative corneal haze) or after complicated LASIK cases. Corticosteroid-induced elevated IOP occurs in 1.5%-3.0% of patients using fluorometholone but in up to 25% of patients using dexamethasone. The increase in IOP is usually controlled with topical IOP-lowering medications and typically normalizes after the corticosteroids are decreased or discontinued. Because of the changes in corneal curvature and/or corneal thickness, Goldmann tonometry readings after myopic surface ablation and LASIK are artifactually reduced (see Glaucoma After Refractive Surgery in Chapter 11). Several alternative techniques of measuring IOP have been suggested, but dynamic contour

tonometry is the only technique shown to have sufficient reproducible accuracy in eyes after refractive ablation. Other corticosteroid-associated complications that have been reported after surface ablation are herpes simplex virus keratitis, ptosis, and cataracts.

Central Toxic Keratopathy

Central toxic keratopathy is a rare, acute, noninflammatory central corneal opacification that can occur within days after uneventful LASIK or PRK (Fig 6-4). The etiology is unknown but may be related to enzymatic degradation of keratocytes.

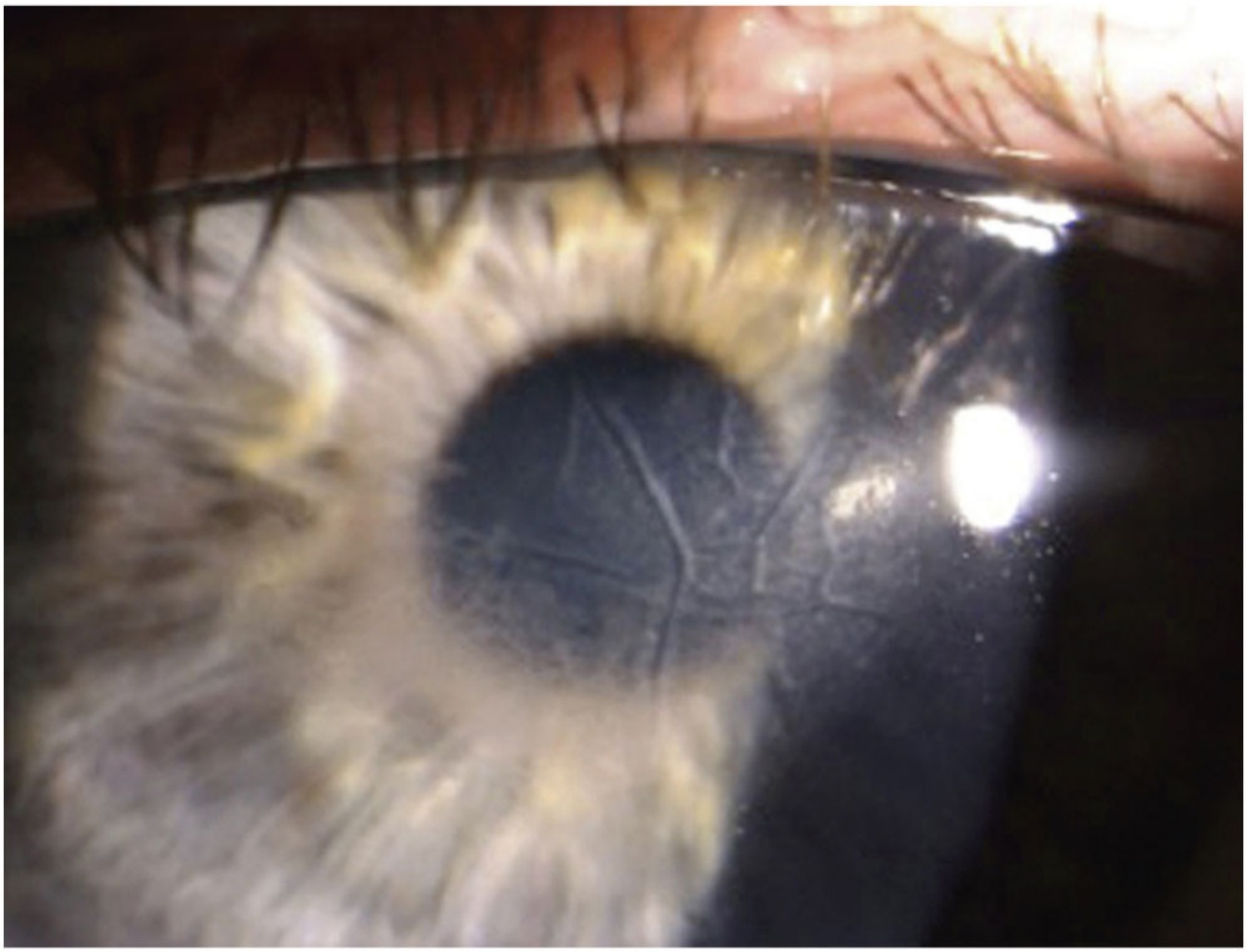

Figure 6-4 Clinical photograph of central toxic keratopathy, a rare, acute, noninflammatory central corneal opacification that can occur within days after uneventful LASIK or photorefractive keratectomy (PRK). *(Courtesy of Parag Majmudar, MD.)*

Confocal microscopy has demonstrated activated keratocytes without inflammatory cells, with initial keratocyte loss from the stromal bed and gradual repopulation over time. Central toxic keratopathy has been reported to demonstrate anterior curvature flattening without alteration of posterior curvature in anterior segment tomography;

however, some cases do appear to alter all tomographic findings, likely as measurement artifact. The onset is acute without worsening over time, unlike in most other interface entities.

Moshirfar M, Hazin R, Khalifa YM. Central toxic keratopathy. *Curr Opin Ophthalmol.* 2010; 21(4):274-279.
Thornton IL, Foulks GN, Eiferman RA. Confocal microscopy of central toxic keratopathy. *Cornea.* 2012;31(8):934-936.

Infectious Keratitis

Infectious keratitis may occur after surface ablation procedures or LASIK, as both types of surgery involve disturbance of the ocular surface, although infections are significantly more common after surface ablation. The risk of infection varies depending on the specific technique. The most common etiologic agents for these infections are gram-positive organisms, including *Staphylococcus aureus*, methicillin-resistant *Staphylococcus aureus (MRSA), Streptococcus pneumoniae,* and *Streptococcus viridans.* Although health care workers and others exposed in hospital and nursing home settings may be at greatest risk for MRSA infection, MRSA infections have been diagnosed in increasing numbers of cases without known risk factors. Atypical mycobacteria, *Nocardia asteroides*, and fungi have also been reported to cause infectious keratitis after surface ablation and LASIK (Fig 6-5).

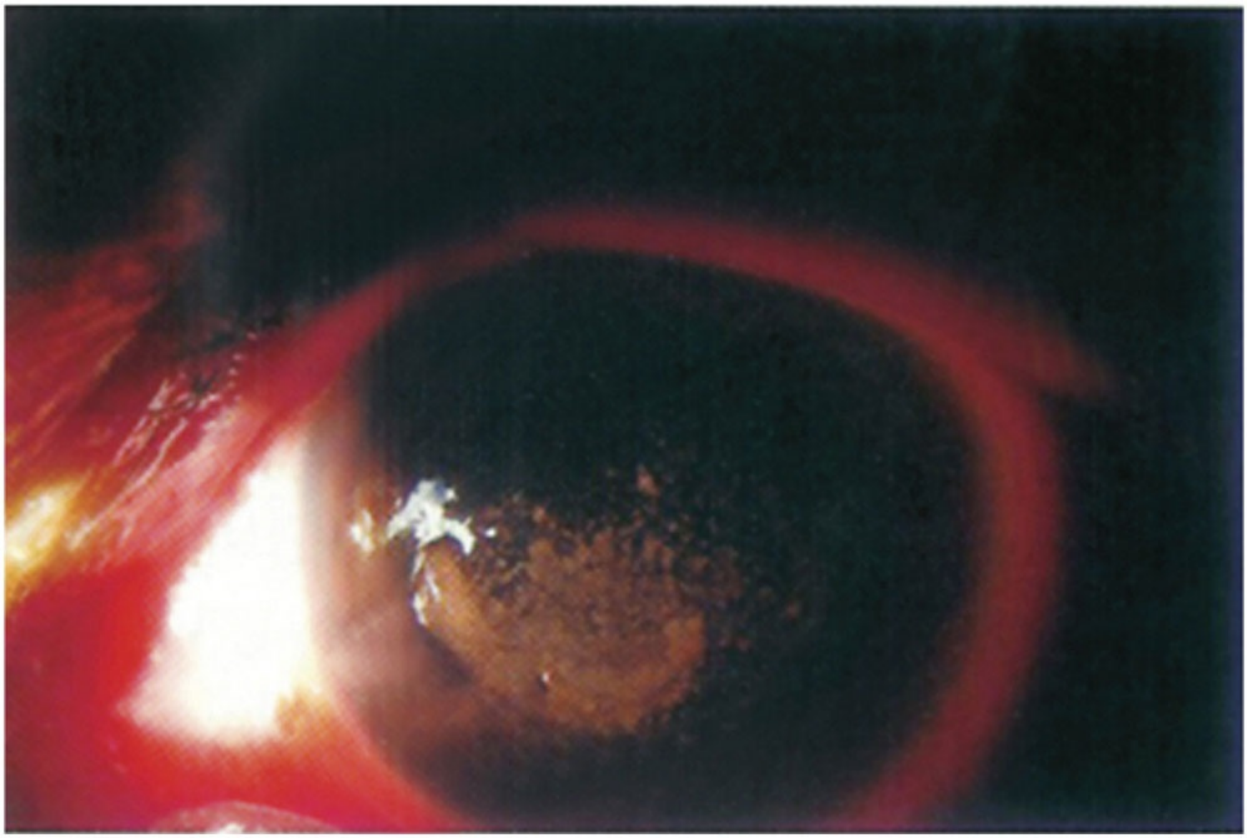

Figure 6-5 Slit-beam image of *Mycobacterium chelonae* interface infection presenting 3 weeks after LASIK; this infection was initially treated as diffuse lamellar keratitis with topical corticosteroids. *(Courtesy of Christopher J. Rapuano, MD.)*

PRK and other surface ablation techniques involve creation of an iatrogenic corneal epithelial defect that may take 3-5 days to heal. During this time, the risk of postoperative infectious keratitis is greatest because of exposure of the stroma, use of a bandage contact lens, and administration of topical steroid drops, all of which increase the opportunity for eyelid and conjunctival bacterial flora to gain access to the stroma. Treatment of postoperative infectious keratitis consists of culture and sensitivity testing of contact lens and corneal scrapings and institution of appropriate intensive, topical, broad-spectrum antibiotic coverage, being cognizant of the higher prevalence of keratitis secondary to gram-positive organisms. Antibiotics may include a combination of the following: fourth-generation fluoroquinolones, polymyxin B-trimethoprim, fortified vancomycin or cefazolin, and for tified tobramycin or gentamicin. Fungal keratitis can also occur, especially with concomitant corticosteroid use. With that in mind, cultures should include fungal assays, and treatment for keratitis should include antifungals in suspected cases.

During or shortly after LASIK, which involves creation of a corneal flap, eyelid and conjunctival flora may enter and remain sequestered under the flap. The antimicrobial components in the tears and in topically applied antibiotic drops have difficulty penetrating into the deep stroma to reach the organisms (Fig 6-6). If a post-LASIK infection is suspected, the flap should be lifted and the stromal bed scraped for culture and sensitivity testing. Intensive treatment with topical antibiotic drops, as described previously, should be started pending culture results. If there is lack of clinical progress, additional scrapings may be obtained, the flap may be amputated, and the antibiotic regimen altered.

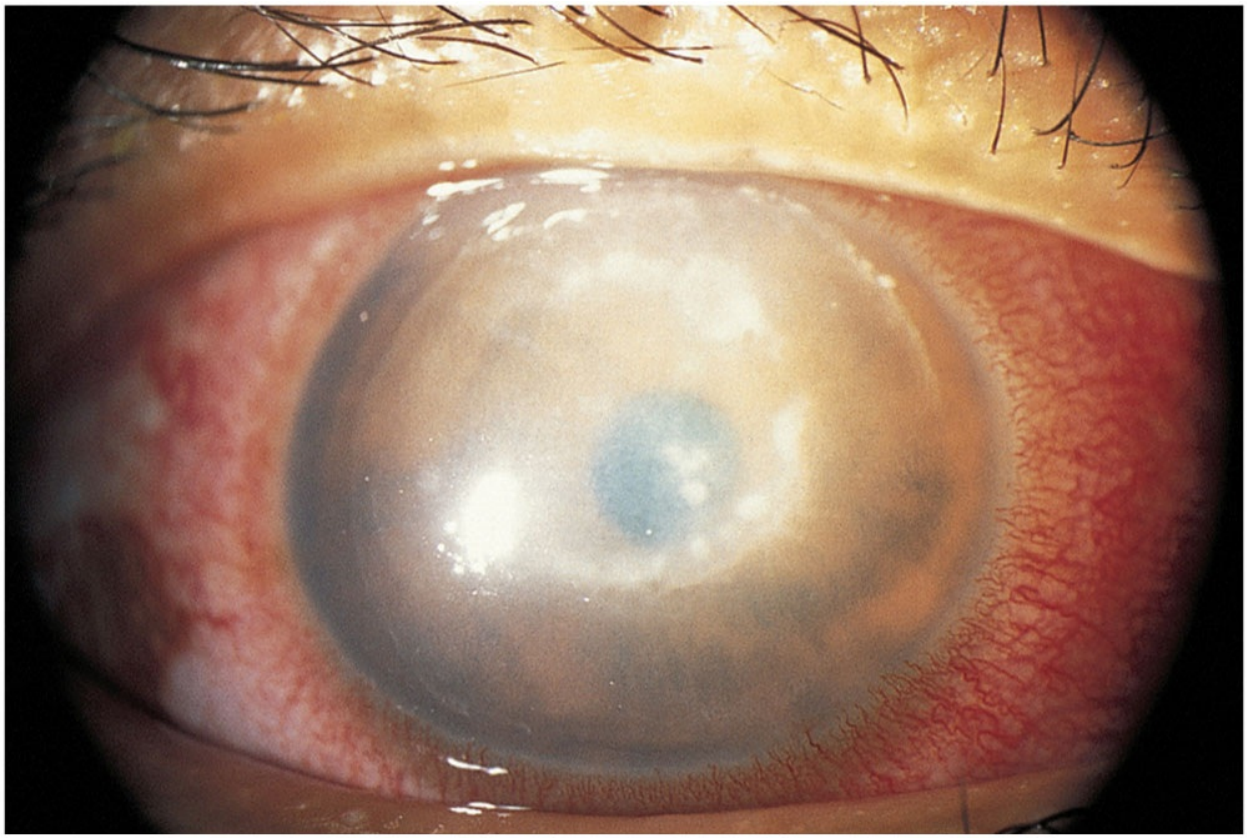

Figure 6-6 Infectious keratitis in a LASIK flap after recurrent epithelial abrasion. *(Courtesy of Jayne S. Weiss, MD.)*

Llovet F, de Rojas V, Interlandi E, et al. Infectious keratitis in 204,586 LASIK procedures. *Ophthalmology.* 2010;117(3):232-238. Epub 2009 Dec 14.

Moshirfar M, Welling JD, Feiz V, Holz H, Clinch TE. Infectious and noninfectious keratitis after laser in situ keratomileusis: occurrence, management, and visual outcomes. *J Cataract Refract Surg.* 2007;33(3):474-483.

Mozayan A, Madu A, Channa P. Laser in-situ keratomileusis infection: review and update of current practices. *Curr Opin Ophthalmol.* 2011;22(4):233-237.

Solomon R, Donnenfeld ED, Perry HD, et al. Methicillin-resistant *Staphylococcus aureus* infectious keratitis following refractive surgery. *Am J Ophthalmol.* 2007;143(4):629-634. Epub 2007 Feb 23.

Wroblewski KJ, Pasternak JF, Bower KS, et al. Infectious keratitis after photorefractive keratectomy in the United States Army and Navy. *Ophthalmology.* 2006;113(4):520-525. Epub 2006 Feb 17.

Complications Unique to Surface Ablation

Persistent Epithelial Defects

Usually, the epithelial defect created during surface ablation heals within 3-5 days with the aid of a bandage soft contact lens. A frequent cause of delayed re-epithelialization is keratoconjunctivitis sicca, which may be treated with increased lubrication, cyclosporine, and/or temporary punctal occlusion. Patients who have undiagnosed

autoimmune connective tissue disease or diabetes mellitus or who smoke may also have poor epithelial healing. Topical nonsteroidal anti-inflammatory drugs (NSAIDs) should be discontinued in patients with delayed re-epithelialization. Gentle epithelial debridement and oral tetracyclines may be beneficial for persistent epithelial defects. Temporary discontinuation of other potentially toxic topical drugs, such as glaucoma drops, may also help in re-epithelialization. The importance of closely monitoring patients until re-epithelialization occurs cannot be overemphasized, as a persistent epithelial defect increases the risk of corneal haze, irregular astigmatism, refractive instability, delayed visual recovery, and infectious keratitis.

Sterile Infiltrates

The use of bandage contact lenses to aid epithelial healing is associated with sterile infiltrates, which may occur more frequently in patients using topical NSAIDs for longer than 24 hours without concomitant topical corticosteroids. The infiltrates, which have been reported in approximately 1 in 300 cases, are secondary to an immune reaction (Fig 6-7). They are treated with institution of topical steroids, tapering and discontinuation of topical NSAIDs, and close follow-up. It must be kept in mind that any infiltrate may be infectious and should be managed appropriately. If infectious keratitis is suspected, the cornea should be scraped and cultured for suspected organisms.

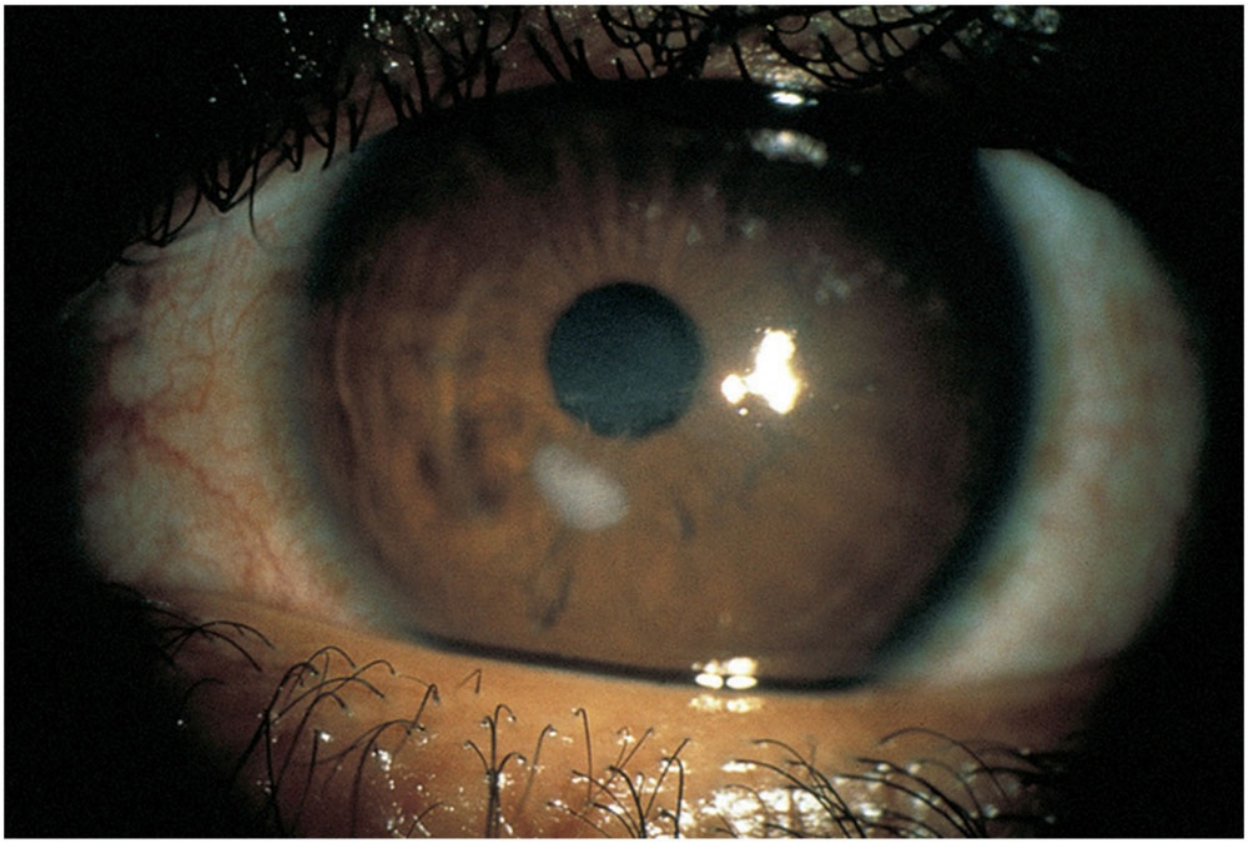

Figure 6-7 Stromal infiltrates after use of a bandage soft contact lens following PRK. *(Courtesy of Jayne S. Weiss, MD.)*

Corneal Haze

The manner of wound healing after surface ablation is important in determining postoperative topical corticosteroid management. Eyes that have haze and are undercorrected may benefit from increased corticosteroid use. Eyes with clear corneas following surface ablation and that are overcorrected may benefit from a reduction in topical corticosteroids, which may lead to regression of the overcorrection.

When present, subepithelial corneal haze typically appears several weeks after surface ablation, peaks in intensity at 1-2 months, and gradually diminishes or disappears over the following 6-12 months (Fig 6-8). Late-onset corneal haze may occur several months or even a year or more postoperatively after a period in which the patient had a relatively clear cornea. Histologic studies in animals with corneal haze after PRK demonstrate abnormal glycosaminoglycans and/or nonlamellar collagen deposited in the anterior stroma as a consequence of epithelial-stromal wound healing. Most histologic studies from animals and humans show an increase in the number and activity of stromal keratocytes, which suggests that increased keratocyte activity may be the source of the extracellular deposits.

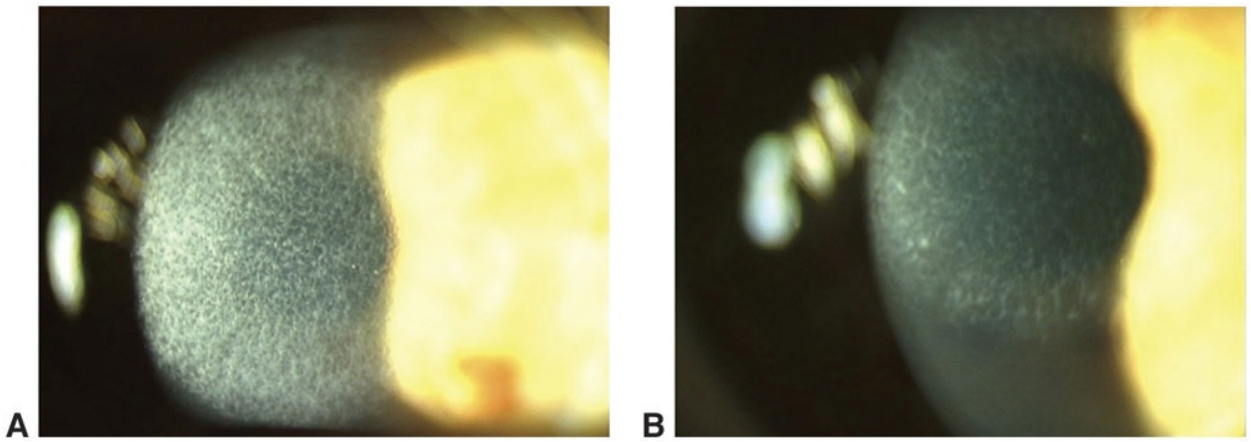

Figure 6-8 Corneal haze after PRK. **A,** Severe haze 5 months after PRK. The reticular pattern is characteristic of PRK-induced haze. **B,** Haze has improved to a moderate level by 13 months postoperatively. *(Courtesy of Roger F. Steinert, MD.)*

Persistent severe haze is usually associated with greater amounts of correction or smaller ablation zones. Animal studies have demonstrated that ultraviolet (UV) B exposure after PRK prolongs the stromal healing process, with an increase in

subepithelial haze. Clinical cases of haze after high UV exposure (such as at high altitude) corroborate these studies.

If clinically unacceptable haze persists, a superficial keratectomy or phototherapeutic keratectomy (PTK) may be performed. In addition, topical mitomycin C (0.02%), with PTK or debridement, may be used to prevent recurrence of subepithelial fibrosis. Because haze is known to resolve spontaneously with normal wound remodeling, re-ablation should be delayed for at least 6-12 months. The clinician should be aware that, in the presence of haze, refraction is often inaccurate, typically with an overestimation of the amount of myopia.

Ayres BD, Hammersmith KM, Laibson PR, Rapuano CJ. Phototherapeutic keratectomy with intraoperative mitocmycin C to prevent recurrent anterior corneal pathology. *Am J Ophthalmol.* 2006;142:490-492.

Donnenfeld ED, O'Brien TP, Solomon R, Perry HD, Speaker MG, Wittpenn J. Infectious keratitis after photorefractive keratectomy. *Ophthalmology.* 2003;110(4):743-747.

Hofmeister EM, Bishop FM, Kaupp SE, Schallborn SC. Randomized dose-response analysis of mitomycin-C to prevent haze after photorefractive keratectomy for high myopia [published online ahead of print July 3, 2013]. *J Cataract Refract Surg.* doi:10.1016/j.jcrs.2013.03.029.

Krueger RR, Saedy NF, McDonnell PJ. Clinical analysis of steep central islands after excimer laser photorefractive keratectomy. *Arch Ophthalmol.* 1996;114(4):377-381.

Moller-Pedersen T, Cavanagh HD, Petroll WM, Jester JV. Stromal wound healing explains refractive instability and haze development after photorefractive keratectomy: a 1-year confocal microscopic study. *Ophthalmology.* 2000;107(7):1235-1245.

Complications Unique to LASIK

The complications associated with LASIK are primarily related to flap creation, postoperative flap positioning, or interface problems.

Microkeratome Complications

In the past, the more severe complications associated with LASIK were related to problems with the microkeratome, which caused the planned LASIK procedure to be abandoned in 0.6%-1.6% of cases. In current practice, advances in microkeratome technology and the advent of femtosecond laser use for creating the LASIK flap have substantially reduced the incidence of severe, sight-threatening complications.

When using the microkeratome, meticulous care must still be taken in the cleaning and assembly of the microkeratome to ensure a smooth, uninterrupted keratectomy. Defects in the blade, poor suction, or uneven progression of the microkeratome across the cornea can produce an irregular, thin, or buttonhole flap (Fig 6-9), which can result in irregular astigmatism with loss of CDVA. Steep corneal curvature is a risk factor for the development of some intraoperative flap complications. If a thin or buttonhole flap is created, or if an incomplete flap does not provide a sufficiently large corneal stromal surface to perform the laser ablation, the flap should be replaced and the ablation should not be performed. Substantial loss of vision can be prevented if, under such circumstances, the ablation is not performed and the flap is allowed to heal before another refractive procedure is attempted months later. In such cases, a bandage soft

contact lens is applied to stabilize the flap, typically for several days to a week. Although a new flap can usually be cut safely using a deeper cut after at least 3 months of healing, most surgeons prefer to use a surface ablation technique.

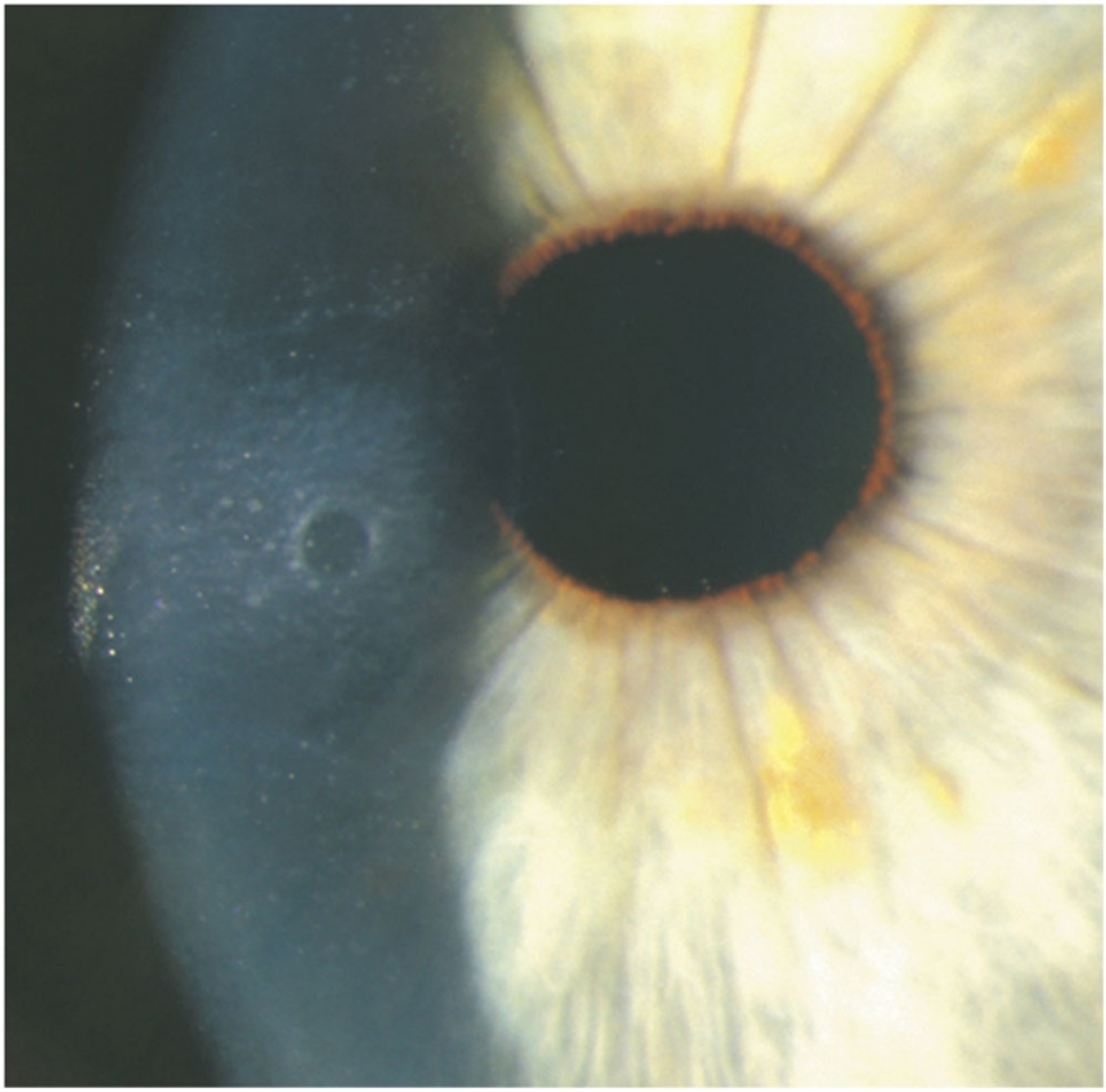

Figure 6-9 LASIK flap with buttonhole. *(Reproduced with permission from Feder RS, Rapuano CJ.* The LASIK Handbook: A Case-Based Approach. *Philadelphia: Lippincott Williams & Wilkins; 2007:95, fig 5.1. Photograph courtesy of Christopher J. Rapuano, MD.)*

Occasionally, a free cap is created instead of a hinged flap (Fig 6-10). In these cases, if the stromal bed is large enough to accommodate the laser treatment, the corneal cap is placed in a moist chamber while the ablation is performed. It is important to replace the cap with the epithelial side up and to position it properly using

the previously placed radial marks. A temporary 10-0 nylon suture can be placed to create an artificial hinge, but the physiologic dehydration of the stroma by the endothelial pump will generally keep the cap secured in proper position. A bandage soft contact lens can help protect the cap. A flat corneal curvature (<40.00 D) is a risk factor for creating a free cap because the flap diameter is often smaller than average in flat corneas.

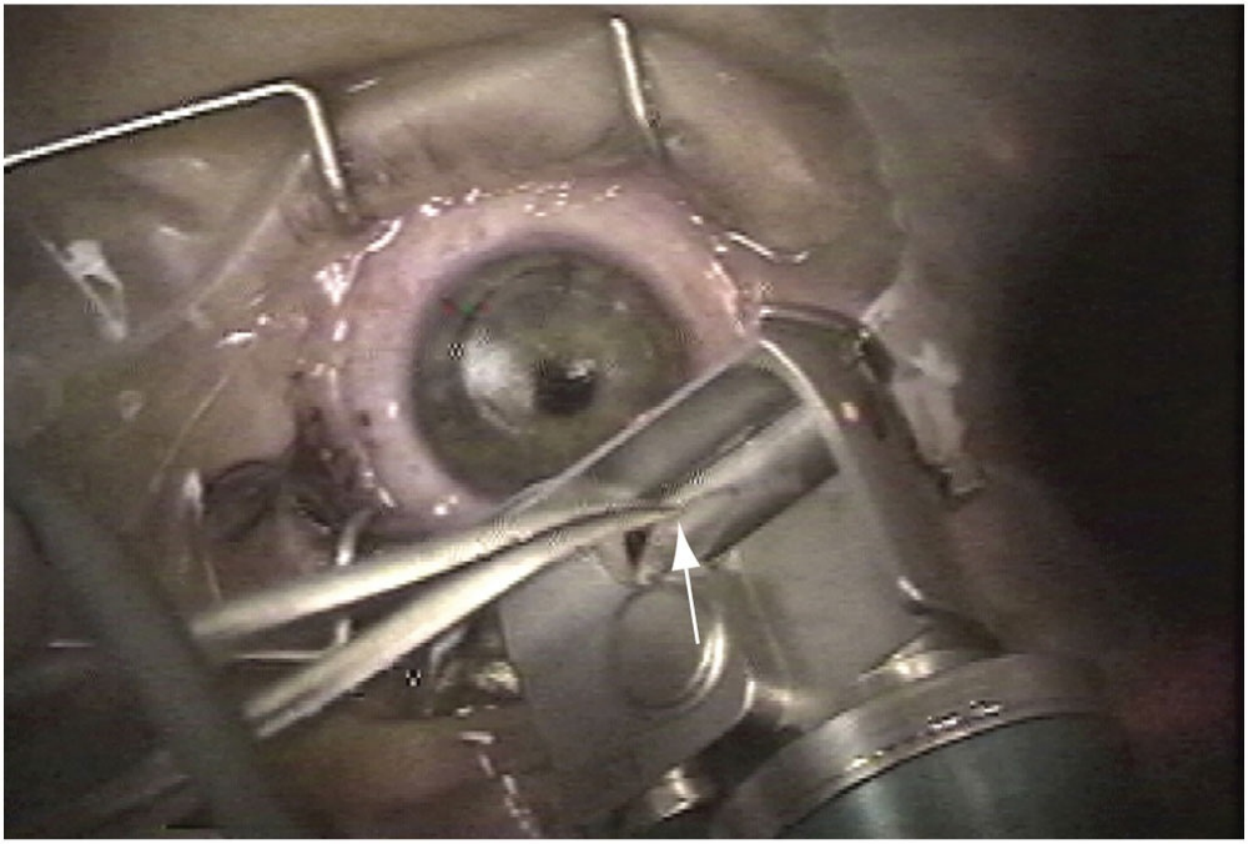

Figure 6-10 A free cap resulting from transection of the hinge. The cap is being lifted from the microkeratome with forceps *(arrow),* and care is being taken to maintain the orientation of the epithelial external layer to prevent accidental inversion of the cap when it is replaced. *(Courtesy of Roger F. Steinert, MD.)*

Corneal perforation is a rare but devastating intraoperative complication that can occur if the microkeratome is not properly assembled or if the depth plate in an older-model microkeratome is not properly placed. It is imperative for the surgeon to double-check that the microkeratome has been properly assembled before beginning the procedure. All microkeratomes made after the 1990s are constructed with a prefixed depth plate, which eliminates this source of error. Corneal perforation can also occur when LASIK is performed on an excessively thin cornea. Corneal thickness must be measured with pachymetry prior to the LASIK procedure, especially in patients who are undergoing re-treatment.

Jacobs JM, Taravella MJ. Incidence of intraoperative flap complications in laser in situ keratomileusis. *J Cataract Refract Surg.* 2002;28(1):23-28.

Lee JK, Nkyekyer EW, Chuck RS. Microkeratome complications. *Curr Opin Ophthalmol.* 2009; 20(4):260-263.

Nakano K, Nakano E, Oliveira M, Portellinha W, Alvarenga L. Intraoperative microkeratome complications in 47,094 laser in situ keratomileusis surgeries. *J Refract Surg.* 2004; 20(Suppl 5):S723-726.

Epithelial Sloughing or Defects

The friction of microkeratome passage across the pressurized cornea may loosen a sheet of epithelium (termed *epithelial slough*) or cause a frank epithelial defect. Although patients with epithelial basement membrane dystrophy are at particular risk--in which case surface ablation rather than LASIK is advisable--other patients show no preoperative epithelial abnormalities. The risk of epithelial abnormality during LASIK correlates with older age. Also, in bilateral LASIK procedures with mechanical microkeratomes, the second eye has a greater likelihood of sustaining an epithelial defect (57%) if the first eye developed an intraoperative epithelial defect. Techniques suggested to decrease the rate of epithelial defects include limiting medications to avoid toxicity, using chilled proparacaine, minimizing use of topical anesthetic, using nonpreserved drops until just before performing the skin prep or starting the procedure, having patients keep their eyes closed after topical anesthetic is administered, frequent use of corneal lubricating drops, meticulous microkeratome maintenance, and shutting off suction on the microkeratome reverse pass. The femtosecond laser is associated with a reduced incidence of epithelial defects because there is no microkeratome movement across the epithelium.

In cases of significant epithelial defects, a bandage soft contact lens is often applied immediately postoperatively and retained until stable re-epithelialization occurs, with subsequent use of intensive lubricants and, occasionally, punctal occlusion. Persistent abnormal epithelium with recurrent erosions or loss of CDVA may require debridement and even superficial PTK using the technique employed for treatment of recurrent erosions (see BCSC Section 8, *External Disease and Cornea*). Epithelial defects are associated with an increased incidence of postoperative diffuse lamellar keratitis, infectious keratitis, flap striae, and epithelial ingrowth, and surgeons should watch closely for these conditions.

Chen S, Feng Y, Stojanovic A, Jankov MR II, Wang Q. IntraLase femtosecond laser vs mechanical microkeratomes in LASIK for myopia: a systematic review and meta-analysis. *J Refract Surg.* 2012;28(1):15-24.

Tekwani NH, Huang D. Risk factors for intraoperative epithelial defect in laser in-situ keratomileusis. *Am J Ophthalmol.* 2002;134(3):311-316.

Flap Striae

Flap folds, or striae, are a potential cause of decreased visual acuity after LASIK. When present, most (56%) flap folds are noted on the first postoperative day, and 95% are noted within the first week. Risk factors for development of folds include excessive irrigation under the flap during LASIK, thin flaps, and deep ablations with flap-bed

mismatch. Recognition of visually significant folds is important. Early intervention is often crucial in treating folds that cause loss of CDVA or visual distortion.

The first step in evaluating a patient with corneal folds is determining the CDVA. Folds are not treated if the CDVA and the subjective visual acuity are excellent. Folds are examined with a slit lamp using direct illumination, retroillumination, and fluorescein staining. Circumferential folds may be associated with high myopia and typically resolve with time. Folds that are parallel and emanate from the flap hinge grouped in the same direction indicate flap slippage, which requires prompt intervention. Corneal topography is usually not helpful in diagnosing folds.

Folds are often categorized as either macrostriae or microstriae, although there is significant overlap between these types (Table 6-1). *Macrostriae* represent full-thickness, undulating stromal folds. These folds invariably occur because of initial flap malposition or postoperative flap slippage (Fig 6-11A). Current approaches to smoothing the flap and avoiding striae at the end of the LASIK procedure vary widely. No matter which technique is used, however, the surgeon must carefully examine for the presence of striae once the flap is repositioned. Coaxial and oblique illumination should be used at the operating microscope for this purpose. Macrostriae may occur as patients attempt to squeeze their eyelids shut when the eyelid speculum is removed at the end of surgery. Accordingly, before removing the speculum, the surgeon can apply momentary compressed air and instruct the patient not to overly squeeze the lids upon removal of the speculum. Checking the patient in the early postoperative period is important to detect flap slippage. A protective plastic shield is often used for the first 24 hours to discourage the patient from touching the eyelids and inadvertently disrupting the flap.

Table 6-1

Table 6-1 **Differentiation Between Macrostriae and Microstriae in LASIK Flaps**

Characteristic		Macrostriae	Microstriae
Pathology		Large folds involving entire flap thickness	Fine folds, principally in Bowman layer
Cause		Flap slippage	Mismatch of flap to new bed; contracture of flap
Slit-lamp appearance	Direct illumination	Broad undulations as parallel or radial converging lines; widened flap gutter may be present	Fine folds, principally in Bowman layer; gutter usually symmetric
	Retroillumination	Same as above	Folds more obvious on retroillumination
	Fluorescein	Same as above, with negative staining pattern	Often has normal fluorescein pattern
Analogy		Wrinkles in skewed carpet	Dried, cracked mud
Topography		Possible disruption over striae	Color map may be normal or slightly disrupted; Placido disk mires show fine irregularity
Vision		Decreased CDVA and/or multiplopia if central	Subtle decreased CDVA or multiplopia if clinically significant; microstriae masked by epithelium are universal and asymptomatic
Treatment options	Acute	Refloat/reposition flap immediately	Observe; support surface with aggressive lubrication
	Established	Refloat, de-epithelialize over striae, hydrate and stroke, apply traction, or suture Phototherapeutic keratectomy	If visually significant, refloat; try hydration, stroking, suturing Phototherapeutic keratectomy

CDVA = corrected distance visual acuity; LASIK = laser in situ keratomileusis.

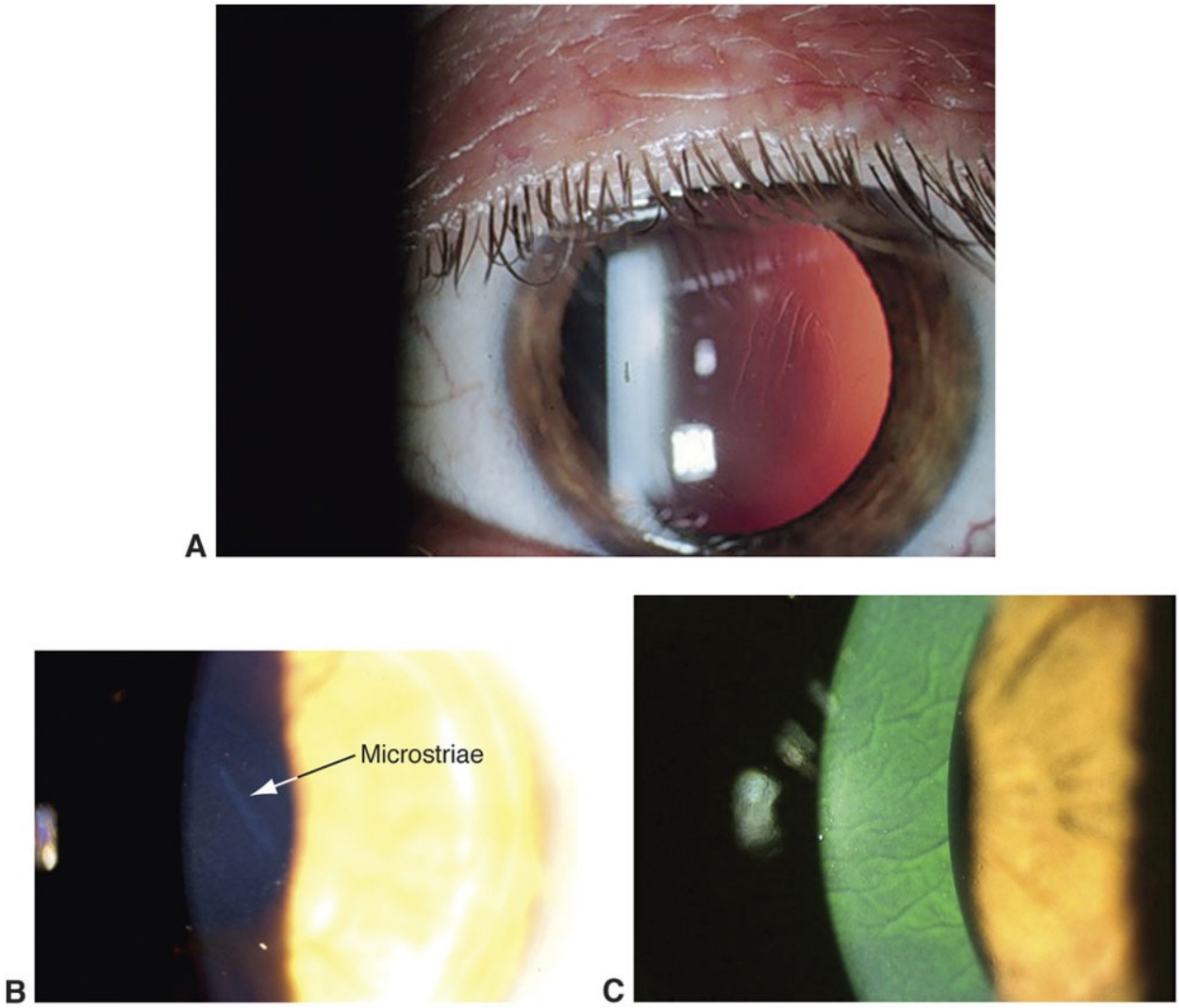

Figure 6-11 Post-LASIK striae. **A,** Retroillumination of multiple horizontal parallel macrostriae in the visual axis from mild flap dislocation. **B,** Diffuse illumination of visually insignificant microstriae in the visual axis after LASIK. **C,** Numerous randomly directed microstriae on fluorescein staining. These striae resemble multiple cracks in a piece of ice, are apparent on the first postoperative day after LASIK, and usually resolve without intervention. *(Part A courtesy of Parag Majmudar, MD; part B courtesy of Jayne S. Weiss, MD; part C courtesy of Steven C. Schallhorn, MD.)*

Flap dislocation has been reported to occur in up to 1.4% of eyes. Careful examination should disclose a wider gutter on the side where the folds are most prominent. Flap slippage should be rectified as soon as it is recognized because the folds rapidly become fixed. Under the operating microscope or at the slit lamp, an eyelid speculum is placed, the flap is lifted and repositioned, copious irrigation with sterile balanced salt solution is used in the interface, and the flap is repeatedly stroked perpendicular to the fold until the striae resolve or improve. Using hypotonic saline or sterile distilled water as the interface-irrigating solution swells the flap and may initially reduce the striae, but swelling also reduces the flap diameter, which widens

the gutter, delays flap adhesion because of prolonged endothelial dehydration time, and may worsen the striae after the flap dehydrates. If the macrostriae have been present for more than 24 hours, reactive epithelial hyperplasia in the valleys and hypoplasia over the elevations of the macrostriae tend to fix the folds into position. In such a case, in addition to refloating of the flap, the central 6 mm of the flap over the macrostriae may be de-epithelialized to remove this impediment to smoothing the wrinkles. A bandage soft contact lens should be used to stabilize the flap and to protect the surface until full re-epithelialization occurs. In cases of intractable macrostriae, a tight 360deg antitorque running suture or multiple interrupted sutures using 10-0 nylon may be placed and retained for several weeks, but irregular astigmatism may still be present after suture removal.

Microstriae are fine, hairlike optical irregularities that are best viewed on red reflex illumination or by light reflected off the iris (Fig 6-11B, C). They are fine folds in the Bowman layer, and this anterior location accounts for the disruption of CDVA in some eyes. Computer topographic color maps do not usually show these fine irregularities. However, disruption of the surface contour may result in irregularity of the Placido disk image. In addition, application of dilute fluorescein often reveals so-called *negative staining*, in which the elevated striae disrupt the tear film and fluorescence is lost over them.

If optically significant microstriae persist, the flap may be sutured in an attempt to reduce the striae by means of tension. As with macrostriae, however, suturing has the potential to induce new irregular astigmatism. An alternative procedure is PTK. Pulses from a broad-beam laser, set to a maximal diameter of 6.5 mm, are initially applied to penetrate the epithelium in about 200 pulses. The epithelium acts as a masking agent, exposing the elevated striae before the valleys between the striae. After the transepithelial ablation, additional pulses are applied, and a thin film of medium-viscosity artificial tears is administered every 5-10 pulses, up to a maximum of 100 additional pulses. If these guidelines are followed, little to no haze results, and an average hyperopic shift of less than +1.00 D occurs as a result of the minimal tissue removal.

Ashrafzadeh A, Steinert RF. Results of phototherapeutic keratectomy in the management of flap striae after LASIK before and after developing a standardized protocol: long-term follow-up of an expanded patient population. *Ophthalmology.* 2007;114(6):1118-1123. Epub 2007 Jan 29.

Jackson DW, Hamill MB, Koch DD. Laser in situ keratomileusis flap suturing to treat recalcitrant flap striae. *J Cataract Refract Surg.* 2003;29(2):264-269.

Traumatic Flap Dislocation

Flap dislocation has been reported to occur in up to 1.4% of eyes. Dislocation of the LASIK flap is not uncommon on the first postoperative day, when dryness and adhesion of the flap to the upper tarsal conjunctiva are sufficient to cause the flap to slip. After the first day, however, the re-epithelialization of the gutter begins the process of

increasing flap stability. Within several weeks, keratocytes begin to lay down new collagen at the cut edge of the Bowman layer, and eventually a fine scar is established at the edge of the flap. Minimal healing occurs across the stromal interface for several years, however, allowing flap lifting for enhancement procedures. Late dislocation from blunt trauma has been reported many years after LASIK; late dislocation can also occur if the shearing force exceeds the strength of the peripheral Bowman layer-level healing. Flap dislocation requires urgent treatment to replace the flap in its proper anatomical position. The surgeon should make sure that there is no epithelium on the underside of the flap covering the stromal bed, a situation that significantly increases the chances of epithelial ingrowth.

LASIK-Interface Complications

Diffuse lamellar keratitis

The effects of diffuse lamellar keratitis (DLK) (Fig 6-12) can range from asymptomatic interface haze near the edge of the flap to marked diffuse haze under the center of the flap with diminished CDVA. The condition represents a nonspecific sterile inflammatory response to a variety of mechanical and toxic insults. The interface under the flap is a potential space; any cause of anterior stromal inflammation may trigger the accumulation of white blood cells therein. DLK has been reported in association with epithelial defects that occur during primary LASIK or during enhancement, or even months after the LASIK procedure from corneal abrasions or infectious keratitis. Other reported inciting factors include foreign material on the surface of the microkeratome blade or motor, meibomian gland secretions, povidone-iodine solution (from the preoperative skin preparation), marking ink, substances produced by laser ablation, contamination of the sterilizer with gram-negative endotoxin, and red blood cells in the interface. The inflammation generally resolves with topical steroid treatment alone without sequelae, but severe cases can lead to scarring or flap melting.

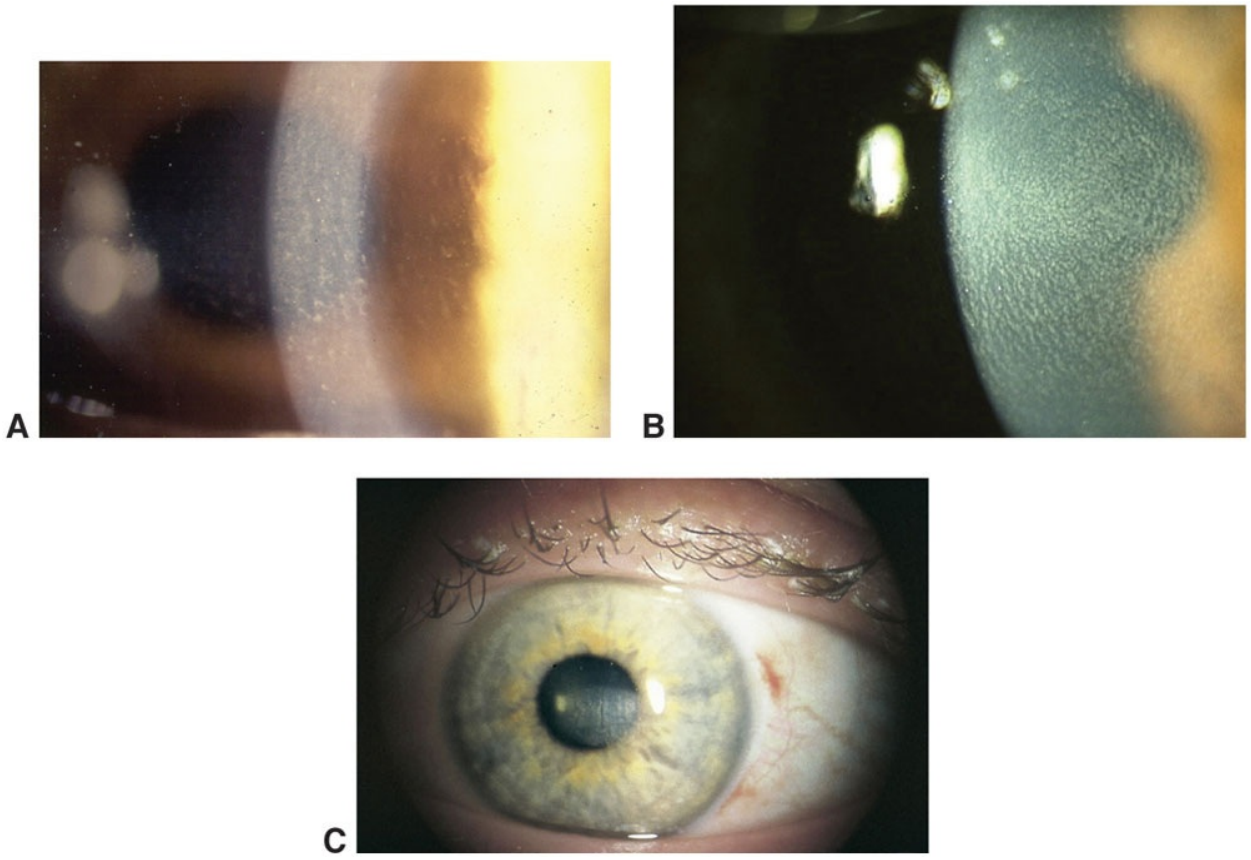

Figure 6-12 Diffuse lamellar keratitis (DLK). **A,** High magnification image of stage 2 DLK. Note accumulation of inflammatory cells in the fine ridges created by the oscillating microkeratome blade. **B,** Stage 3 DLK showing dense accumulation of inflammatory cells centrally. **C,** Stage 4 DLK with central scar and folds. *(Parts A and B courtesy of Roger F. Steinert, MD; part C courtesy of Jayne S. Weiss, MD.)*

DLK is typically classified by the stages described in Table 6-2. Although stages 1 and 2 usually respond to frequent topical corticosteroid application, stages 3 and 4 usually require lifting the flap and irrigating, followed by intensive topical corticosteroid treatment. Systemic corticosteroids may be used adjunctively in severe cases. Some surgeons use topical and systemic corticosteroids in stage 3 DLK instead of, or in addition to, lifting the flap. Recovery of vision in DLK is usually excellent if the condition is detected and treated promptly.

Table 6-2

Table 6-2 Staging of Diffuse Lamellar Keratitis

Stage	Findings
1	Peripheral faint white blood cells; granular appearance
2	Central scattered white blood cells; granular appearance
3	Central dense white blood cells in visual axis
4	Permanent scarring or stromal melting

A surgeon should have a low threshold for selecting treatment by lifting or irrigating underneath the flap in suspected cases of DLK. Lifting the flap allows removal of

inflammatory mediators from the interface and direct placement of corticosteroids and NSAIDs to suppress inflammation and collagen necrosis. If there is any suspicion that the inflammation is due to infection, lifting the flap and obtaining samples for corneal cultures of the interface should be considered. Topical antibiotics can also be placed in the flap interface at the same time. In cases of suspected DLK not responsive to steroids within 7-10 days of initiation, the diagnosis should be reconsidered, as infectious keratitis or pressure-induced stromal keratopathy (PISK, discussed later) can mimic DLK and requires steroid cessation for resolution.

Haft P, Yoo SH, Kymionis GD, Ide T, O'Brien TP, Culbertson WW. Complications of LASIK flaps made by the IntraLase 15- and 30-kHz femtosecond lasers. *J Refract Surg.* 2009; 25(11):979-984. Epub 2009 Nov 13.

Holland SP, Mathias RG, Morck DW, Chiu J, Slade SG. Diffuse lamellar keratitis related to endotoxins released from sterilizer reservoir biofilms. *Ophthalmology.* 2000;107(7): 1227-1233.

Randleman JB, Shah RD. LASIK interface complications: etiology, management, and outcomes. *J Refract Surg.* 2012;28(8):575-586.

LASIK infectious keratitis

It is important to differentiate sterile interface inflammation from potentially devastating infectious inflammation. Increased pain and decreased vision are the primary indicators of infection. However, postoperative eye discomfort is common, so it is difficult for patients to distinguish between normal and abnormal eye pain. Moreover, because corneal nerves are severed during flap creation, corneal sensation may be reduced, along with the subjective symptom of pain that usually accompanies infection. Infection after LASIK is usually associated with redness, photophobia, and decreased vision. Several distinct features can help distinguish between DLK and infectious keratitis (Table 6-3). DLK is usually visible within 24 hours of surgery and typically begins at the periphery of the flap. There is usually a gradient of inflammation, with the inflammation being most intense at the periphery and diminishing toward the center of the cornea. In general, the inflammatory reaction in DLK is diffusely distributed but localized and confined to the area of the flap interface; it does not extend far beyond the edge of the flap (Fig 6-13). In contrast, post-LASIK infectious keratitis usually begins 2-3 days after surgery and involves a more focal inflammatory reaction that is not confined to the lamellar interface. An anterior chamber reaction may further help differentiate between an infectious and a sterile process. The inflammatory reaction can extend up into the flap, deeper into the stromal bed, and even beyond the confines of the flap.

Table 6-3

Table 6-3 Diffuse Lamellar Keratitis vs Infectious Keratitis

Diffuse Lamellar Keratitis	Infectious Keratitis
Usually visible within first 24 hours	Usual onset at least 2–3 days postoperatively
Typically begins at flap periphery	Can occur anywhere under flap
More intense inflammation at periphery decreasing toward center	
Inflammation primarily confined to interface	Inflammation extends above and below interface, and beyond flap edge
Diffuse inflammation	Focal inflammation around infection
Minimal to no anterior chamber reaction	Mild to moderate anterior chamber reaction
Flap melts can occur	Flap melts can occur

Modified with permission from Culbertson WW. Surface ablation and LASIK patients share similar infection potential. *Refractive Eyecare.* September 2006:12.

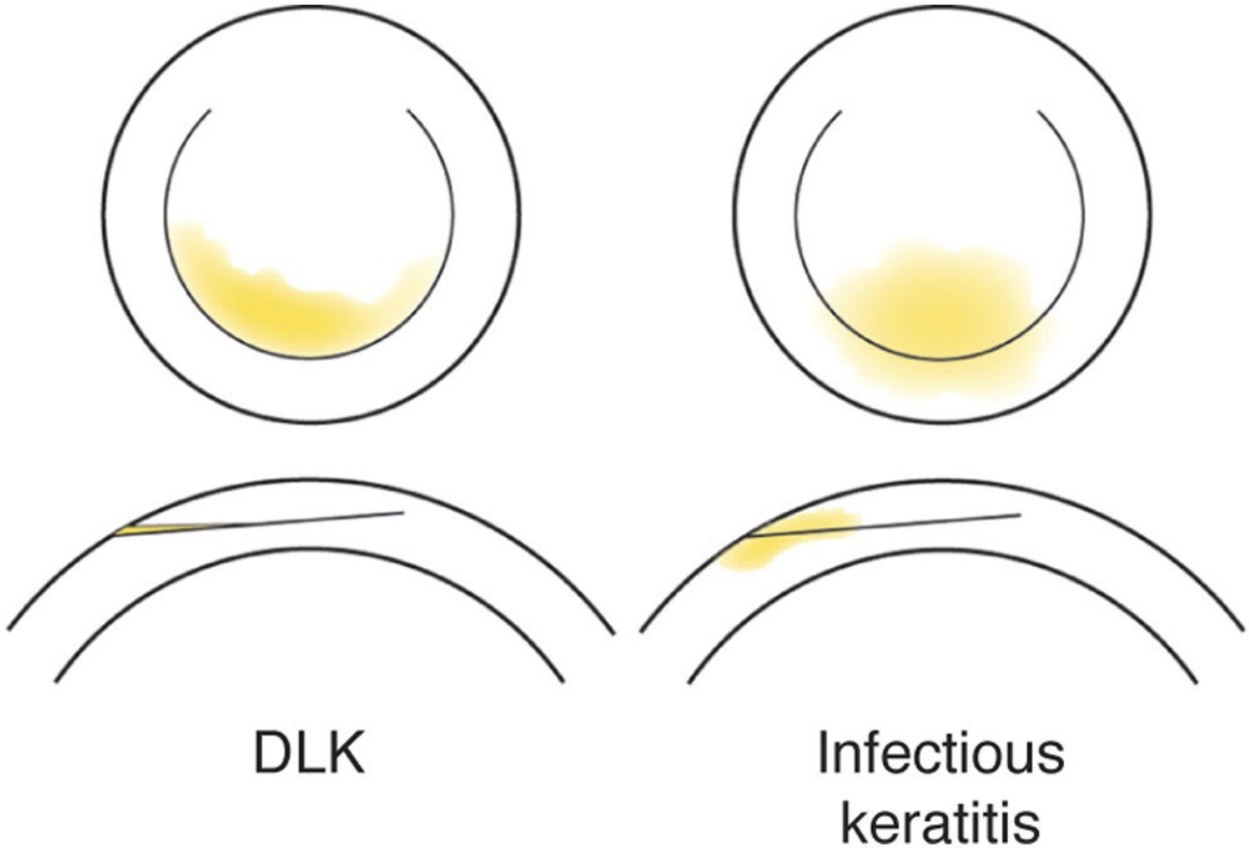

Figure 6-13 DLK is differentiated from infectious keratitis by the confinement of the infiltrate to the interface alone in DLK. *(Reproduced with permission from Culbertson WW. Surface ablation and LASIK patients share similar infection potential.* Refractive Eyecare. *September 2006:12.)*

Infection within the interface can lead to flap melting, severe irregular astigmatism, and corneal scarring that may require corneal transplantation. If infection is suspected, the flap should be lifted and the interface cultured and irrigated with antibiotics. The most common infections are from gram-positive organisms, followed in frequency by those caused by atypical mycobacteria. Mycobacteria infection can be diagnosed more rapidly by using acid-fast and fluorochrome stains rather than by waiting for culture results (see Fig 6-5).

In general, the timing of the onset of symptoms provides a clue as to the etiology of

the infection. Infections occurring within 10 days of surgery are typically bacterial, with the preponderance being from gram-positive organisms. Suggested empirical treatment for broad coverage may include fortified vancomycin (10-50 mg/mL) and tobramycin (14 mg/mL) or a fourth-generation fluoroquinolone and cefazolin (50 mg/mL). Infections presenting more than 10 days after surgery are more likely caused by atypical mycobacteria and fungi. Topical clarithromycin (10 mg/mL), oral clarithromycin (500 mg bid), and topical amikacin (8 mg/mL) are recommended for treatment of mycobacterial infections. If a filamentous fungus is identified, natamycin (50 mg/mL) is recommended; amphotericin (1.5 mg/mL) is recommended for yeast infections. Voriconazole (10 mg/mL) may be used for both yeasts and filamentous fungi and is often supplemented with voriconazole tablets (400 mg bid). If the infection does not respond to treatment, amputation of the flap may be necessary to improve antimicrobial penetration. The fourth-generation fluoroquinolones gatifloxacin and moxifloxacin have excellent efficacy against the more common bacteria that cause post-LASIK infections, including some atypical mycobacteria; however, monotherapy with these drugs may not be sufficient. A LASIK flap infection may occur after a recurrent erosion (see Fig 6-6).

Freitas D, Alvarenga L, Sampaio J, et al. An outbreak of *Mycobacterium chelonae* infection after LASIK. *Ophthalmology.* 2003;110(2):276-285.

Llovet F, de Rojas V, Interlandi E, Martin C, Cobo-Soriano R, Ortega-Usobiaga J, Baviera J. Infectious keratitis in 204,586 LASIK procedures. *Ophthalmology.* 2010;117(2):232-238.

Moshirfar M, Welling JD, Feiz V, Holz H, Clinch TE. Infectious and noninfectious keratitis after laser in situ keratomileusis: occurrence, management, and visual outcomes. *J Cataract Refract Surg.* 2007;33(3):474-483.

Pressure-induced stromal keratopathy

A diffuse stromal and interface opacity termed pressure-induced stromal keratopathy (PISK) has been reported as a result of elevated IOP; it can be mistaken for DLK and is sometimes associated with a visible fluid cleft in the interface (Fig 6-14). The surgeon must be aware of this rare condition in order to properly diagnose and treat it. The pressure-induced haze from PISK is associated with prolonged corticosteroid treatment and usually presents after 10 days to 2 weeks. Key differentiators between DLK and PISK are that with DLK, the onset is earlier and the IOP is not elevated. IOP should be measured both centrally and peripherally in suspected cases, possibly with a pneumotonometer or Tono-Pen, because applanation pressure may be falsely lowered centrally in PISK by fluid accumulation in the lamellar interface. Several alternative techniques of measuring IOP have been suggested, but dynamic contour tonometry is the only technique shown to have sufficient reproducible accuracy in eyes that have undergone refractive ablation. Treatment for PISK involves rapid cessation of corticosteroid drops and the use of glaucoma medications to lower IOP. Severe glaucomatous vision loss has been reported in cases with delayed diagnosis.

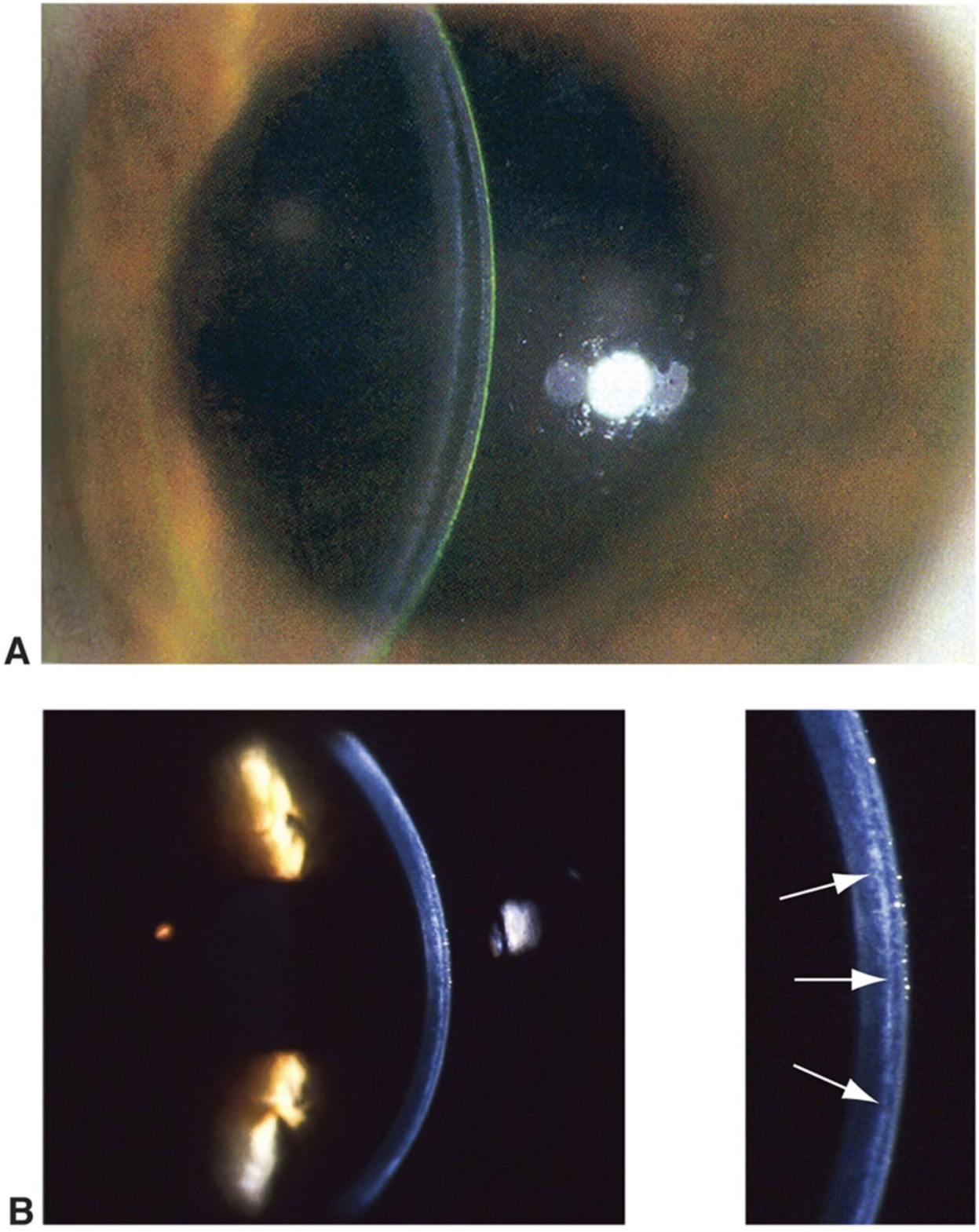

Figure 6-14 Pressure-induced stromal keratopathy (PISK) after LASIK. **A,** An optically clear, fluid-filled space between the flap and stromal bed. This condition is hypothesized to be caused by transudation of fluid across the endothelium as a result of steroid-induced elevation of intraocular pressure (IOP). **B,**

PISK without interface gap. A diffuse stromal and interface opacity without an interface fluid cleft can also result from elevated IOP with prolonged corticosteroid use *(left panel).* Close-up *(right panel, arrows)* further demonstrates the opacification of the stroma and interface. *(Part A reproduced with permission from Hamilton DR, Manche EE, Rich LF, Maloney RK. Steroid-induced glaucoma after laser in situ keratomileusis associated with interface fluid.* Ophthalmology. *2002;109(4):659-665; part B reprinted with permission from Randleman JB, Shah RD. Lasik interface complications: etiology, management, and outcomes.* J Refract Surg. *2012;28(8):575-586.)*

Belin MW, Hannush SB, Yau CW, Schultze RL. Elevated intraocular pressure-induced interlamellar stromal keratitis. *Ophthalmology.* 2002;109(10):1929-1933.

Dawson DG, Schmack I, Holley GP, Waring GO III, Grossniklaus HE, Edelhauser HF. Interface fluid syndrome in human eye bank corneas after LASIK: causes and pathogenesis. *Ophthalmology.* 2007;114(10):1848-1859.

Hamilton DR, Manche EE, Rich LF, Maloney RK. Steroid-induced glaucoma after laser in situ keratomileusis associated with interface fluid. *Ophthalmology.* 2002;109(4):659-665.

Moya Calleja T, Iribarne Ferrer Y, Sanz Jorge A, Sedo Fernandez S. Steroid-induced interface fluid syndrome after LASIK. *J Refract Surg.* 2009;25(2):235-239.

Epithelial ingrowth

Epithelial ingrowth occurs in less than 3% of eyes (Fig 6-15). There is no need to treat isolated nests of epithelial cells in the peripheral lamellar interface that are not advancing and are not affecting vision. However, if the epithelium is advancing toward the visual axis, is associated with decreased vision from irregular astigmatism (Fig 6-16), or triggers overlying flap melting, it should be removed by lifting the flap, scraping the epithelium from both the underside of the flap and the stromal bed, and then repositioning the flap. After scraping the under-flap surface and stromal bed, some surgeons also remove epithelium from the peripheral cornea to allow for flap adherence before the epithelial edge advances to the flap edge. Recurrent epithelial ingrowth can be treated with repeated lifting and scraping, with or without flap suturing or using fibrin glue at the flap edge.

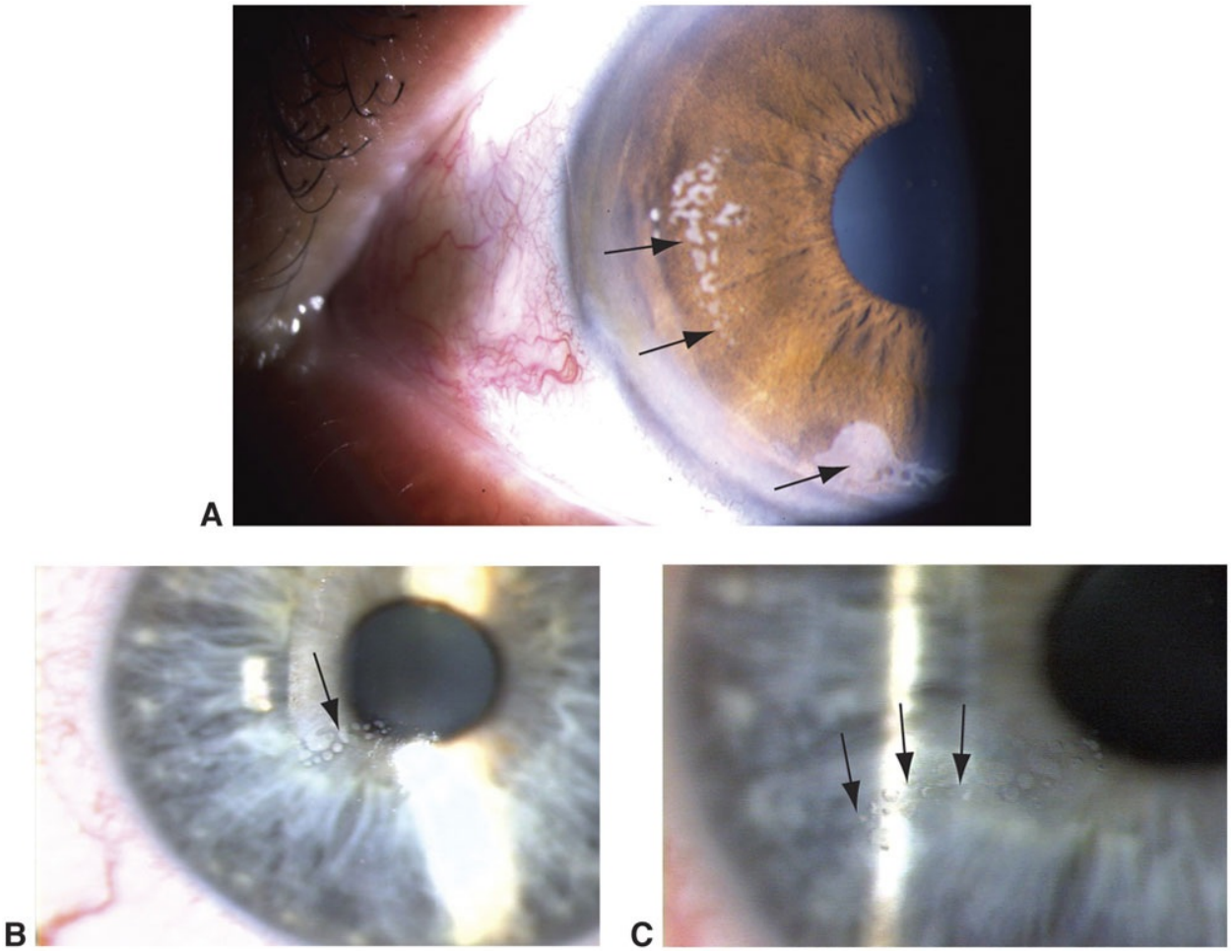

Figure 6-15 Epithelial ingrowth in the interface under a LASIK flap. **A,** Peripheral ingrowth of 1-2 mm *(arrows)* is common and inconsequential and does not require intervention unless it induces melting of the overlying flap. **B,** Central nests of epithelial cells *(arrow)* disrupt the patient's vision by elevating and distorting the flap. The flap must be lifted and the epithelium debrided. **C,** Inspection of the midperiphery shows the track followed by the invading epithelium from the periphery toward the center *(arrows).*
(Courtesy of Roger F. Steinert, MD.)

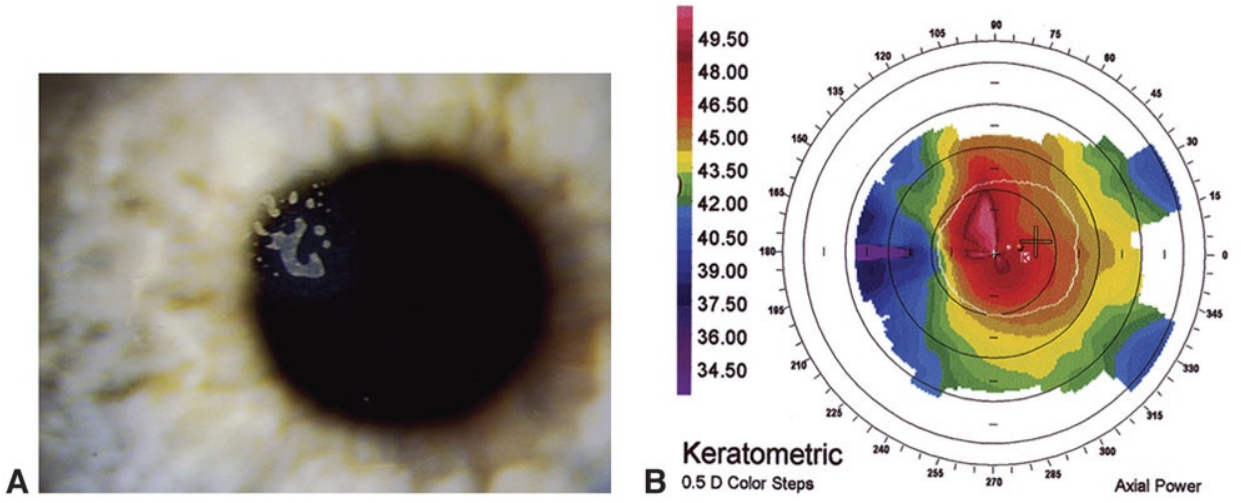

Figure 6-16 A, Epithelial ingrowth in visual axis. **B,** Corresponding topographic steepening and irregularity. *(Courtesy of J. Bradley Randleman, MD.)*

The incidence of epithelial ingrowth is greater in eyes that develop an epithelial defect at the time of the procedure, undergo a re-treatment with lifting of a preexisting flap, or have traumatic flap dehiscence. In such cases, special care should be taken to ensure that no epithelium is caught under the edge of the flap when it is repositioned. Placement of a bandage contact lens at the conclusion of the procedure may also decrease the incidence of epithelial ingrowth for patients at higher risk of developing this complication.

Asano-Kato N, Toda I, Hori-Komai Y, Takano Y, Tsubota K. Epithelial ingrowth after laser in situ keratomileusis: clinical features and possible mechanisms. *Am J Ophthalmol.* 2002; 134(6):801-807.

Caster AI, Friess DW, Schwendeman FJ. Incidence of epithelial ingrowth in primary and retreatment laser in situ keratomileusis. *J Cataract Refract Surg.* 2010;36(1):97-101.

Henry CR, Canto AP, Galor A, Vaddavalli PK, Culbertson WW, Yoo SH. Epithelial ingrowth after LASIK: clinical characteristics, risk factors, and visual outcomes in patients requiring flap lift. *J Refract Surg.* 2012;28(7):488-492.

Rapuano CJ. Management of epithelial ingrowth after laser in situ keratomileusis in a tertiary care cornea service. *Cornea.* 2010;29(3):307-313.

Interface debris

Debris in the interface is occasionally observed postoperatively. The principal indication for intervention by flap lifting, irrigation, and manual removal of debris is an inflammatory reaction elicited by the foreign material. Small amounts of lint, nondescript particles, or tiny metal particles from stainless steel surgical instruments are usually well tolerated. A small amount of blood that may have oozed into the interface from transected peripheral vessels may also be tolerated and typically resolves spontaneously with time; however, a significant amount of blood usually elicits an inflammatory cell response and should be irrigated from the interface at the time of the LASIK procedure (Fig 6-17). Use of a topical vasoconstrictor such as epinephrine to facilitate coagulation when the flap is being replaced helps minimize

this problem. The surgeon should be aware that applying epinephrine prior to laser ablation can result in pupillary dilation and treatment decentration.

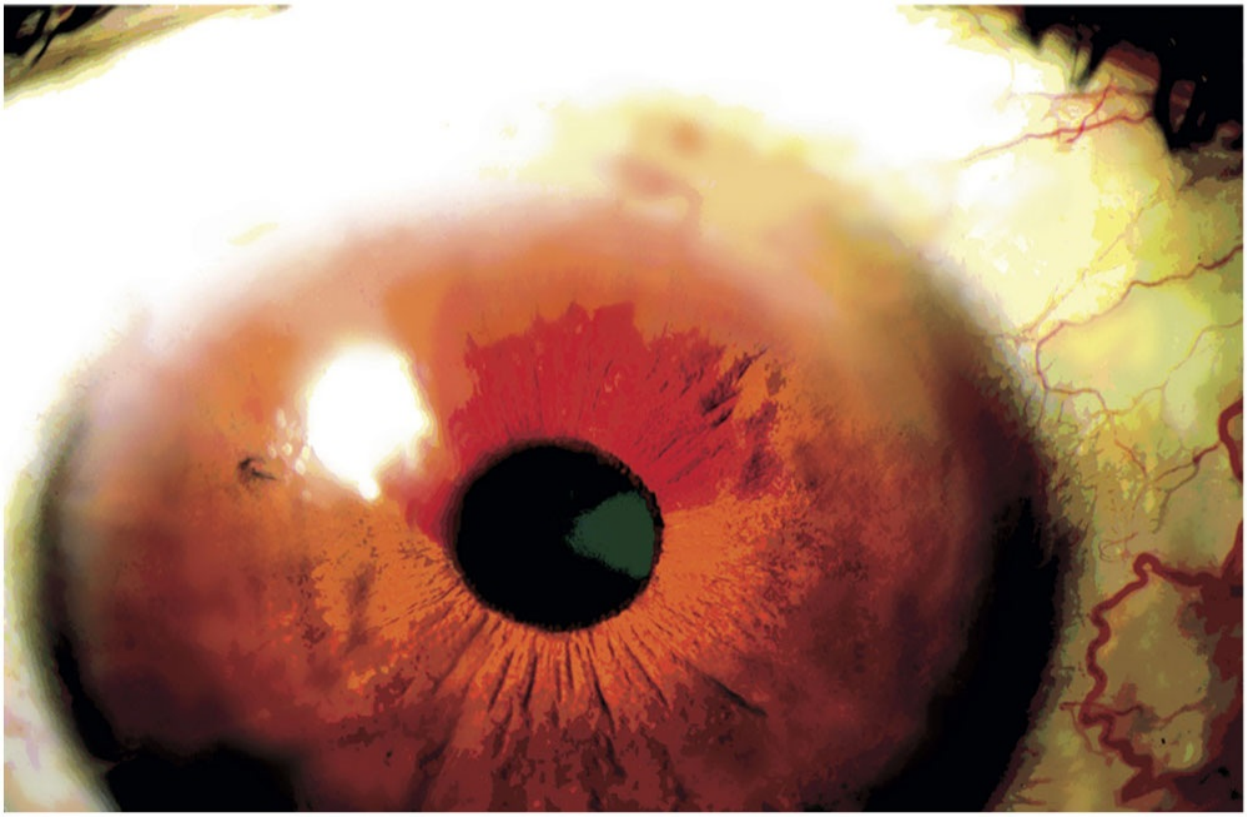

Figure 6-17 Blood in the LASIK interface. *(Courtesy of Jayne S. Weiss, MD.)*

Visual Disturbances Related to Femtosecond Laser LASIK Flaps

Transient light sensitivity

Several weeks to months after LASIK with femtosecond laser flaps, some patients experience acute onset of pain, photophobia, and light sensitivity in an otherwise white and quiet eye with excellent uncorrected distance visual acuity (UDVA; also called *uncorrected visual acuity, UCVA*). The cornea and flap interface appear normal. It has been speculated that an acute onset of ocular inflammation or dry eyes is somehow related to use of the femtosecond laser. Treatment consists of frequent administration of topical corticosteroids (eg, prednisolone acetate, 1%, every 2 hours) and topical cyclosporine A, titrated to the clinical condition. Almost all cases respond to treatment and resolve in weeks to months.

Rainbow glare

Rainbow glare, a new optical adverse effect of treatment with the femtosecond laser, is

described as bands of color around white lights at night. This complication seems to be related to higher raster energy levels and increased length of time between service calls for the laser.

Farjo AA, Sugar A, Schallhorn SC, et al. Femtosecond lasers for LASIK flap creation: a report by the American Academy of Ophthalmology. *Ophthalmology.* 2013;120(3):e5-e20. Epub 2012 Nov 20.

Ectasia

Corneal ectasia develops after excimer laser ablation when the corneal biomechanical integrity is reduced beyond its functional threshold; this complication results from performing surgery in patients who either are otherwise predisposed to developing corneal ectatic disorders or have a significantly reduced postablation residual stromal bed (RSB). The importance of an adequate RSB to prevent structural instability and postoperative corneal ectasia is discussed in Chapter 2. Ectasia has been reported far more frequently after LASIK than after surface ablation. Cumulative analysis of more than 200 eyes with postoperative ectasia found that ectasia is usually associated with LASIK performed in patients with preoperative topographic abnormalities. Other risk factors include younger patient age, thinner corneas, higher myopic corrections, and patients who have undergone several laser ablations. However, cases of ectasia without any demonstrable risk factors have also been reported.

For postoperative ectasia, corneal collagen crosslinking (CXL) is becoming the first-line treatment worldwide; in the United States, however, this treatment is under investigation but not yet approved by the Food and Drug Administration. Often, functional visual acuity can be restored with rigid gas-permeable or hybrid contact lens wear. The implantation of symmetric or asymmetric intrastromal ring segments to reduce the irregular astigmatism has been successful in select cases. In extreme cases, corneal transplantation may be required.

In 2005, a joint statement was issued by the American Academy of Ophthalmology, the International Society for Refractive Surgery, and the American Society of Cataract and Refractive Surgery summarizing current knowledge of corneal ectatic disorders and ectasia after LASIK. Their 8 conclusions at the time were

1. No specific test or measurement is diagnostic of a corneal ectatic disorder.
2. A decision to perform LASIK should take into account the entire clinical picture, not just the corneal topography.
3. Although some risk factors have been suggested for ectasia after LASIK, none is an absolute predictor of its occurrence.
4. Because keratoconus may develop in the absence of refractive surgery, the occurrence of ectasia after LASIK does not necessarily mean that LASIK was a causative or contributing factor for its development.
5. Risk factors for ectasia after LASIK may not also predict ectasia after surface

ablation.

6. Ectasia is a known risk of laser vision correction.
7. Forme fruste keratoconus is a topographic diagnosis rather than a clinical one. It is not a variant of keratoconus. Rather, forme fruste implies subclinical disease with the potential for progression to clinically evident keratoconus.
8. Although to date no formal guidelines exist and good scientific data for future guidelines are presently lacking, in order to reduce some of the risks of ectasia after LASIK, the groups recommended that surgeons review topographic findings prior to surgery. Intraoperative pachymetry should be used to measure flap thickness and calculate the RSB after ablation to ascertain if the RSB is near the safe lower limits for the procedure, for that patient.

Current screening strategies that include a combination of these risk factors in a weighted fashion have been found to improve screening sensitivity and specificity.

Ambrosio R Jr, Randleman JB. Screening for ectasia risk: what are we screening for and how should we screen for it? *J Refract Surg.* 2013:29(4):230-232.

Binder PS, Lindstrom RL, Stulting RD, et al. Keratoconus and corneal ectasia after LASIK. *J Cataract Refract Surg.* 2005;31(11):2035-2038.

Ou RJ, Shaw EL, Glasgow BJ. Keratectasia after laser in situ keratomileusis (LASIK): evaluation of the calculated residual stromal bed thickness. *Am J Ophthalmol.* 2002;134(5):771-773.

Randleman JB, Woodward M, Lynn MJ, Stulting RD. Risk assessment of ectasia after corneal refractive surgery. *Ophthalmology.* 2008;115(1):37-50.

Richoz O, Mavrakanas N, Pajic B, Hafezi F. Corneal collagen cross-linking for ectasia after LASIK and photorefractive keratectomy: long-term results. *Ophthalmology.* 2013;120(7): 1354-1359.

Rare Complications

Rare, sometimes coincidental, complications of LASIK include optic nerve ischemia, premacular subhyaloid hemorrhage, macular hemorrhage associated with preexisting lacquer cracks or choroidal neovascularization, choroidal infarcts, postoperative corneal edema associated with preoperative cornea guttata, and ring scotoma. Diplopia is another rare complication that may occur in patients whose refractive error has been corrected and who have iatrogenic monovision, improper control of accommodation (in patients with strabismus), or decompensated phorias.

Gimbel HV, Penno EE, van Westenbrugge JA, Ferensowicz M, Furlong MT. Incidence and management of intraoperative and early postoperative complications in 1000 consecutive laser in situ keratomileusis cases. *Ophthalmology.* 1998;105(10):1839-1848.

Gunton KB, Armstrong B. Diplopia in adult patients following cataract extraction and refractive surgery. *Curr Opin Ophthalmol.* 2010;21(5):341-344.

Netto MV, Dupps W Jr, Wilson SE. Wavefront-guided ablation: evidence for efficacy compared to traditional ablation. *Am J Ophthalmol.* 2006;141(2):360-368.

Stulting RD, Carr JD, Thompson KP, Waring GO III, Wiley WM, Walker JG. Complications of laser in situ keratomileusis for the correction of myopia. *Ophthalmology.* 1999;106(1): 13-20.

Sugar A, Rapuano CJ, Culbertson WW, et al. Laser in situ keratomileusis for myopia and astigmatism: safety and efficacy: a report by the American Academy of Ophthalmology. *Ophthalmology.* 2002;109(1):175-187.

CHAPTER 7

Collagen Shrinkage and Crosslinking Procedures

Keratorefractive surgical procedures aim to alter the refractive power of the cornea by changing its shape. Various methods are used to alter corneal curvature, including incising or removing corneal tissue or implanting artificial material into the cornea. Procedures that change the character of the corneal collagen have also been developed. This chapter focuses on 2 such procedures: corneal collagen shrinkage and corneal collagen crosslinking.

Collagen Shrinkage

History

The idea of using heat to alter the shape of the cornea was first proposed by Lans, a Dutch medical student, in 1898. When Lans used electrocautery to heat the corneal stroma, he noticed astigmatic changes in the cornea. In 1975, Gasset and Kaufman proposed a modified technique known as *thermokeratoplasty* to treat keratoconus. In 1984, Fyodorov introduced a technique of radial thermokeratoplasty that used a handheld, heated Nichrome needle designed for deeper thermokeratoplasty. The handheld probe contained a retractable 34-gauge wire heated to 600degC. For a duration of 0.3 second, a motor advanced the wire to a preset depth of 95% of the corneal thickness. Fyodorov used different patterns to treat hyperopia and astigmatism.

However, excessive heating of the cornea resulted in necrosis and corneal remodeling, and regression and unpredictability of treatment limited the success of this technique. It is now known that the optimal temperature for avoiding stromal necrosis while still obtaining corneal collagen shrinkage is approximately 58deg-76degC. Human collagen fibrils can shrink by almost two-thirds when exposed to temperatures in this range, as the heat disrupts the hydrogen bonds in the supercoiled structure of

collagen. In the cornea, the maximal shrinkage is approximately 7%. When higher temperatures are reached (>78degC), tissue necrosis occurs.

Neumann AC, Fyodorov S, Sanders DR. Radial thermokeratoplasty for the correction of hyperopia. *Refract Corneal Surg.* 1990;6(6):404-412.

Laser Thermokeratoplasty

In the 1990s, numerous lasers were tested for use in laser thermokeratoplasty (LTK). Only the holmium:yttrium-aluminum-garnet (Ho:YAG) laser reached commercial production and received US Food and Drug Administration (FDA) approval. The Ho:YAG laser produces light in the infrared region at a wavelength of 2100 nm and has corneal tissue penetration to approximately 480-530 mm.

Two different delivery systems were investigated: a contact system and a noncontact version. One noncontact system approved by the FDA in 2000 used a slit-lamp delivery system to apply 8 simultaneous spots at a wavelength of 2.1 mm at a frequency of 5 Hz and a pulse duration of 250 msec. The system was approved for the temporary correction of 0.75-2.50 D of hyperopia with less than 1.00 D of astigmatism. The initial interest in LTK later waned, primarily because of the significant refractive regression that frequently occurred. Few LTK units, if any, remain in clinical use.

Conductive Keratoplasty

In the past decade, radiofrequency has reemerged as a method of heating the cornea. In 2002, the FDA approved the ViewPoint CK system (Refractec, Irvine, CA) for the temporary treatment of mild to moderate hyperopia with minimal astigmatism. In 2004, conductive keratoplasty (CK) received FDA approval for treatment of presbyopia in the nondominant eye of a patient with an endpoint of -1.00 to -2.00 D.

The nonablative, collagen-shrinking effect of CK is based on the delivery of radiofrequency energy through a fine conducting tip that is inserted into the peripheral corneal stroma (Fig 7-1). As the current flows through the tissue surrounding the tip, resistance to the current creates localized heat. Collagen lamellae in the area surrounding the tip shrink in a controlled fashion and form a column of denatured collagen. The shortening of the collagen fibrils creates a band of tightening that increases the curvature of the central cornea.

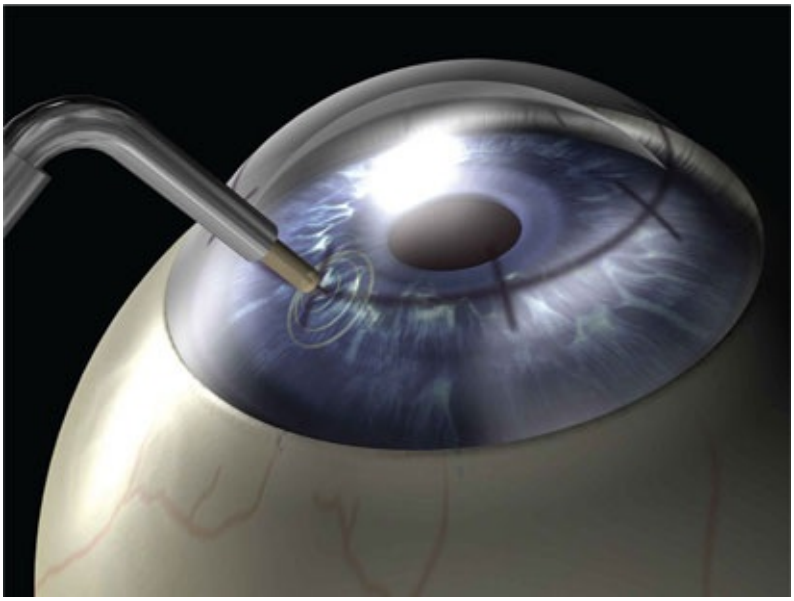

Figure 7-1 Schematic representation of an eye undergoing conductive keratoplasty, which delivers radiofrequency energy to the cornea through a handheld probe inserted into the peripheral cornea. *(Courtesy of Refractec, Inc.)*

For the treatment of hyperopia, the surgeon inserts the tip into the stroma in a ring pattern around the peripheral cornea. The number and location of spots determine the amount of refractive change, with an increasing number of spots and rings used for higher amounts of hyperopia. The CK procedure is performed using topical anesthesia and typically takes less than 5 minutes. The collagen shrinkage leads to visible striae between the treated spots, which fade with time (Fig 7-2).

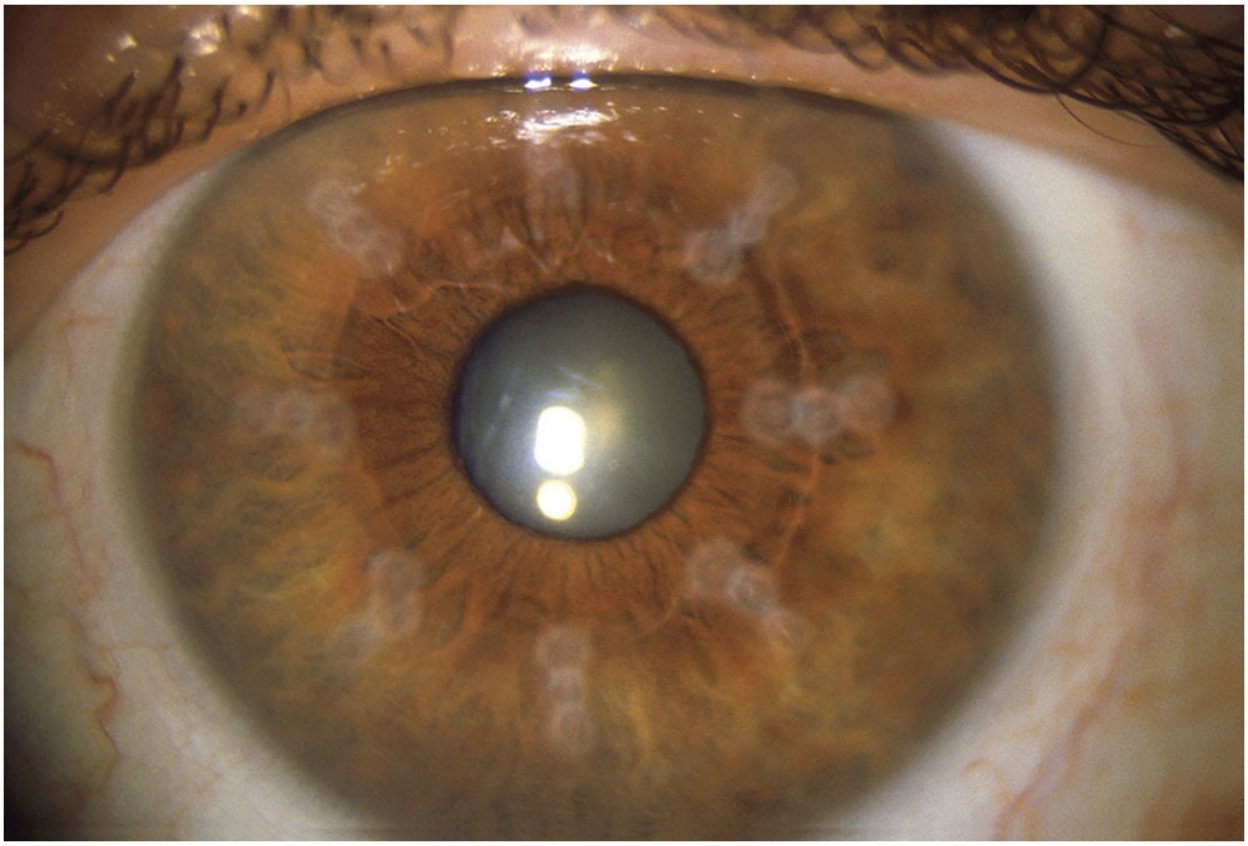

Figure 7-2 One month after a 24-spot conductive keratoplasty treatment in a patient with +2.00 D hyperopia, the spots are beginning to fade. Three sets of 8 spots each were applied at a 6.0-, 7.0-, and 8.0-mm optical zones. *(Courtesy of Refractec, Inc.)*

Patient selection

The Refractec system is FDA approved for the temporary reduction of spherical hyperopia in patients 40 years or older with a spherical equivalent of +0.75 to +3.25 D and [?]0.75 D of astigmatism. The treatment is not advised for use in patients who have undergone radial keratotomy, and it is not FDA approved for use in patients with keratoconus, ectatic disorders, or significant irregular astigmatism. An upper limit of +1.50 D (spherical equivalent) appears to be the current treatment ceiling for this technology, and repeat applications over time or increased number of spots does not seem to enhance or increase that limit.

Safety

In the principal FDA clinical trial to date, no patient had a worse outcome than 20/40 visual acuity, and none lost more than 2 lines of vision. One patient of a total of 391 had >2.00 D of induced cylinder, and no patient with a preoperative corrected distance visual acuity (CDVA; also called *best-corrected visual acuity*, *BCVA*) of [?]20/20 had

<20/25 at 1 year. Although induced cylinder of >2.00 D is an FDA safety variable, smaller amounts of induced cylinder were apparent. At 1 year, 6% of patients had >1.00 D of induced cylinder. The magnitude of the induced cylinder decreased with time. No central corneal haze was noted at 12 months, and endothelial cell counts were similar before and after the study.

Results

The clinical trial included 12-month data for 401 eyes; mean cohort age was 55.3 years (range, 40.2-73.9 years). The mean cycloplegic spherical equivalent was +1.86 +- 0.63 D. By 12 months postoperatively, 92% of study patients had achieved uncorrected distance visual acuity (UDVA; also called *uncorrected visual acuity, UCVA*) of 20/40 or better, 74% achieved 20/25 or better, and 54% had 20/20 or better. By 24 months postoperatively, 93% of study patients had achieved UDVA of 20/40 or better, 76% achieved 20/25 or better, and 52% had 20/20 or better. There was a slow, continued drift toward increasing hyperopia, with regression of +0.21 D and +0.48 D at 12 and 24 months, respectively. Overall, there was a 20% loss of effect after 2 years. This loss of effect is probably a combination of true regression and the normal hyperopic drift that occurs as people age. The results in the FDA CK trial for presbyopia were similar.

Despite initial reports of refractive stability, long-term follow-up has revealed regression and/or lack of adequate effect with CK. In a long-term (mean, 73.1 months; range, 44-90 months) follow-up of patients enrolled in the phase 3 multicenter trial of CK, Ehrlich and Manche found nearly complete regression of treatment effect in the 16 eyes (of the original 25 eyes) available for follow-up.

Ehrlich JS, Manche EE. Regression of effect over long-term follow-up of conductive keratoplasty to correct mild to moderate hyperopia. *J Cataract Refract Surg.* 2009;35(9): 1591-1596.

Hersh PS. Optics of conductive keratoplasty: implications for presbyopia management. *Trans Am Ophthalmol Soc.* 2005;103:412-456.

Kymionis GD, Kontadakis GA, Naoumidi TL, Kazakos DC, Giapitzakis I, Pallikaris IG. Conductive keratoplasty followed by collagen cross-linking with riboflavin-UV-A in patients with keratoconus. *Cornea.* 2010;29(2):239-243.

McDonald MB. Conductive keratoplasty: a radiofrequency-based technique for the correction of hyperopia. *Trans Am Ophthalmol Soc.* 2005;103:512-536.

Other applications

Other potential off-label uses also exist for CK. In cases of overcorrected myopic LASIK and myopic photorefractive keratectomy (PRK), CK can be used to correct hyperopia. In these procedures, CK obviates the need to lift or cut another flap. In one report, CK was used to treat both keratoconus and post-LASIK ectasia. Although corneal irregularities improved immediately, with some improvement in visual acuity, some cases showed regression of effect at 1 month. Larger studies with additional follow-up are needed.

In postcataract or postkeratoplasty patients with astigmatism, CK can be used to steepen the flat axis, because each spot is individually placed. The overall effect is still a myopic shift, so CK is particularly useful when the spherical equivalent is hyperopic.

In a study of 16 patients who had CK for hyperopia after cataract surgery, 1-year follow-up data showed that CK for low to moderate postcataract hyperopia was effective and safe.

Some surgeons have also used CK in combination with collagen crosslinking in an attempt to correct the corneal curvature abnormalities in keratoconus.

Conductive keratoplasty appears to have advantages both in cost and in allowing flexible (off-label) treatment patterns because the tip can be placed anywhere on the cornea. More experience and long-term data will be required to determine how important CK will be in the refractive surgeon's armamentarium. Currently, however, its use remains fairly limited because of the high rate of refractive regression.

Alio JL, Ramzy MI, Galal A, Claramonte PJ. Conductive keratoplasty for the correction of residual hyperopia after LASIK. *J Refract Surg*. 2005;21(6):698-704.

Claramonte PJ, Alio JL, Ramzy MI. Conductive keratoplasty to correct residual hyperopia after cataract surgery. *J Cataract Refract Surg*. 2006;32(9):1445-1451.

Kolahdouz-Isfahani AH, McDonnell PJ. Thermal keratoplasty. In: Brightbill FS, ed. *Corneal Surgery: Theory, Technique, and Tissue*. 3rd ed. St Louis: CV Mosby; 1999.

Kymionis GD, Kontadakis GA, Naoumidi TL, Kazakos DC, Giapitzakis I, Pallikaris IG. Conductive keratoplasty followed by collagen cross-linking with riboflavin-UV-A in patients with keratoconus. *Cornea*. 2010;29(2):239-243.

Collagen Crosslinking

The corneal collagen crosslinking procedure combines riboflavin (vitamin B_2), which is a naturally occurring photosensitizer found in all human cells, with ultraviolet A (UVA) light to strengthen the biomechanical properties of the cornea. Riboflavin alone has no crosslinking effect. Its function as a photosensitizer is to serve as a source for the generation of singlet oxygen and superoxide anion free radicals, which are split from its ring structure after excitation by the UVA irradiation and which then lead to physical crosslinking of the corneal collagen fibers. In the presence of riboflavin, approximately 95% of the UVA light irradiance is absorbed in the anterior 300 mm of the corneal stroma. Therefore, most studies require a minimal corneal thickness of 400 mm after epithelial removal in order to prevent corneal endothelial damage by the UVA irradiation. Thinner corneas may be thickened temporarily with application of a hypotonic riboflavin formulation prior to UVA treatment.

Although there may also be a slight flattening of the cornea, the most important effect of collagen crosslinking is that it appears to stabilize the corneal curvature and prevent further steepening and bulging of the corneal stroma. There is no significant change in the refractive index or the clarity of the cornea. The primary clinical application of collagen crosslinking is as a treatment to prevent the progression of keratoconus and post-corneal refractive surgery ectasia.

Corneal collagen crosslinking was first described by Sporl and colleagues in 1997. In the performance of this procedure, riboflavin solution is continually applied to the eye for 30 minutes (in most studies), and the riboflavin is then activated by illumination of the cornea with UVA light for 30 minutes, during which time application of the

riboflavin solution continues. The corneal epithelium is generally removed before application of the riboflavin so that riboflavin penetration is increased. Alternative riboflavin formulations and crosslinking techniques that avoid epithelial removal are being evaluated and seem promising.

Corneal collagen crosslinking is approved for use in many countries but not currently in the United States. An FDA clinical trial evaluating collagen crosslinking for the treatment of keratoconus and corneal ectasia is ongoing. In one US clinical trial, all patients with either keratoconus or post-LASIK ectasia had their corneal epithelium removed, which was followed by a 30-minute application of riboflavin (0.1% diluted in 20% dextran) every 2 minutes, and a subsequent 30-minute UVA treatment (365 nm; 3 mW/cm^2 irradiation), with concomitant administration of topical riboflavin as a photosensitizer (Fig 7-3). Two control groups--sham and fellow eye--were included in the study, and all patients were monitored for 1 year. Treated eyes initially showed a slight steepening of the cornea with a decrease in CDVA, followed by corneal flattening of approximately 1.00-2.00 D, which peaked at between 1 and 3 months after crosslinking. In addition to a reduction in corneal cylinder, a transient compaction of the cornea and an increase in CDVA were observed. There appears to be stabilization in most treated eyes. Some eyes may require re-treatment, and there have been rare cases of loss of 2 or more lines of best-corrected distance visual acuity in these studies, however.

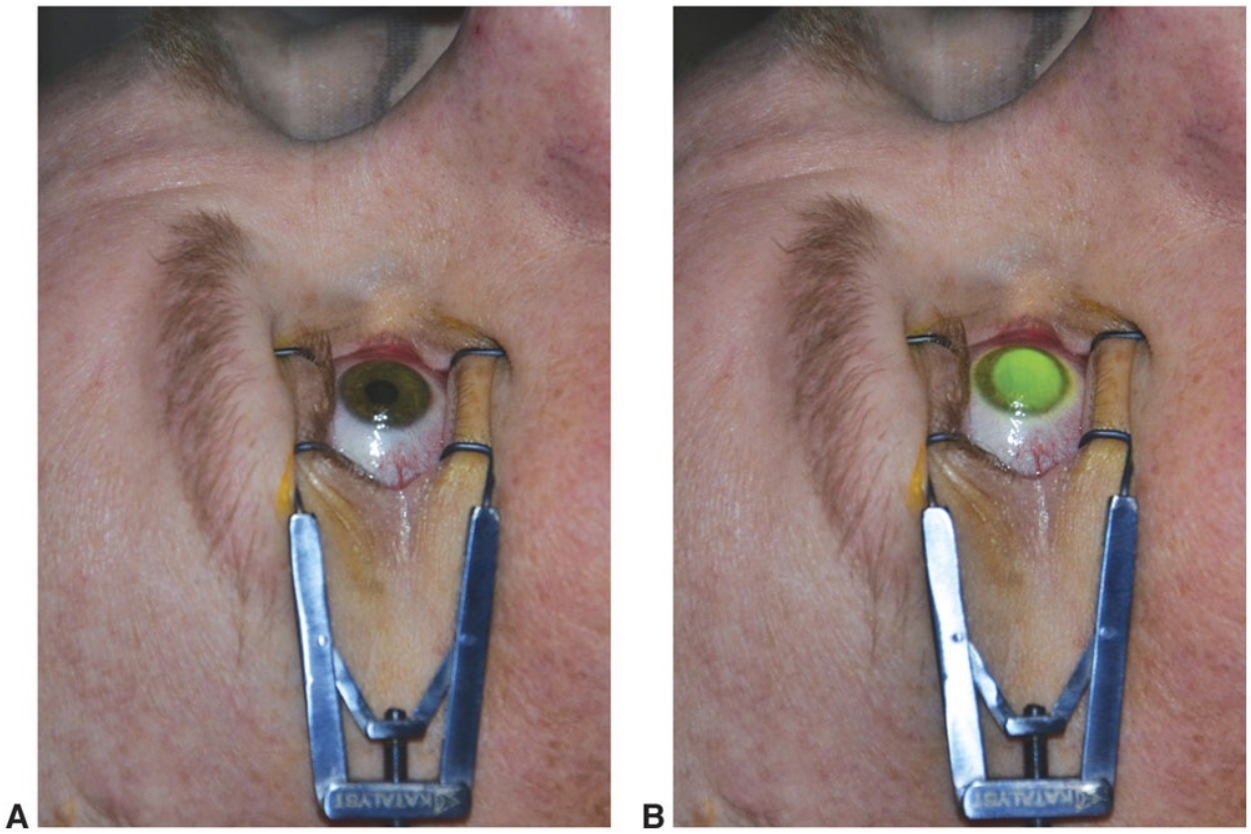

Figure 7-3 Patient undergoing corneal collagen crosslinking. **A,** Patient preparing to undergo crosslinking of the cornea immediately prior to riboflavin application. **B,** After topical administration, the riboflavin fluoresces during application of UV irradiation to the cornea. *(Courtesy of Gregg J. Berdy, MD.)*

Complications of corneal collagen crosslinking vary by the technique used for the procedure. They include delayed epithelial healing, corneal haze (which may be visually significant), decreased corneal sensitivity, infectious keratitis, persistent corneal edema, and endothelial cell damage.

Although crosslinking alone seems to be effective in stabilizing corneal ectatic conditions, vision rehabilitation may require additional intervention. Corneal collagen crosslinking has been used successfully in combination with other treatment methods, such as intrastromal corneal ring segments and/or excimer laser photoablation (simultaneously or sequentially) to improve the best-corrected vision in these disorders. Whereas this treatment modality has proved beneficial in the treatment of naturally occurring and laser keratorefractive ectasias, it probably should not be employed to treat ectasia resulting from incisional keratorefractive surgery; cases have been reported of incisional gaping requiring surgical repair after crosslinking of cornea that has undergone prior incisional surgery.

Collagen crosslinking is a very promising treatment modality, and studies are evaluating its place among the options for corneal therapy. In addition to conducting studies employing denuded epithelium for crosslinking, investigators are examining riboflavin penetration across intact epithelium for crosslinking. Additionally, there have been reports of collagen crosslinking employed successfully to treat fungal and bacterial infections of the cornea. This use may represent a potential new application of this technology.

Abad JC, Vargas A. Gaping of radial and transverse corneal incisions occurring early after CXL. *J Cataract Refract Surg.* 2011;37(12):2214-2217.

Anwar HM, El-Danasoury AM, Hashem AN. Corneal collagen crosslinking in the treatment of infectious keratitis. *Clin Ophthalmol.* 2011;5:1277-1280.

Filippello M, Stagni E, O'Brart D. Transepithelial corneal collagen crosslinking: bilateral study. *J Cataract Refract Surg.* 2012;38:283-291.

Greenstein SA, Shah VP, Fry KL, Hersh PS. Corneal thickness changes after corneal collagen crosslinking for keratoconus and corneal ectasia: one-year results. *J Cataract Refract Surg.* 2011;37(4):691-700.

Hersch PS, Greenstein SA, Fry KL. Corneal collagen crosslinking for keratoconus and corneal ectasia: one-year results. *J Cataract Refract Surg.* 2011;37(1):149-160.

Kremer I, Aizenman I, Lichter H, Shayer S, Levinger S. Simultaneous wavefront-guided photorefractive keratectomy and corneal collagen crosslinking after intrastromal corneal ring segment implantation for keratoconus. *J Cataract Refract Surg.* 2012;38(10):1802-1807.

Makdoumi K, Mortensen J, Sorkhabi O, Malmvall BE, Crafoord S. UVA-riboflavin photochemical therapy of bacterial keratitis: a pilot study. *Graefes Arch Clin Exp Ophthalmol.* 2012;250(1): 95-102. Epub 2011 Aug 27.

Raiskup-Wolf F, Hoyer A, Spoerl E, Pillunat LE. Collagen crosslinking with riboflavin and ultraviolet-A light in keratoconus: long-term results. *J Cataract Refract Surg.* 2008;34(5): 796-801.

Spoerl E, Wollensak G, Dittert DD, Seiler T. Thermomechanical behavior of collagen-cross-linked porcine cornea. *Ophthalmologica.* 2004;218(2):136-140.

Wollensak G, Spoerl E, Seiler T. Riboflavin/ultraviolet-A-induced collagen crosslinking for the treatment of keratoconus. *Am J Ophthalmol.* 2003;135(5):620-627.

CHAPTER 8

Intraocular Refractive Surgery

In its first 2 decades, *refractive surgery* was synonymous with *corneal refractive (keratorefractive) surgery;* however, several factors have expanded the scope of refractive surgery to include lens-based intraocular surgical techniques for primarily refractive outcomes.

In lens-sparing procedures, termed *phakic intraocular lens implantation*, phakic intraocular lenses (PIOLs) allow treatment of more extreme refractive errors, especially high myopia. Available PIOLs in the United States include iris-fixated and posterior chamber (sulcus) lenses for myopia; outside the United States, angle-supported, iris-fixated, and posterior chamber lenses are available for hyperopia and myopia, and some phakic toric intraocular lenses are available to correct both myopia and astigmatism.

In lens-extraction procedures, termed *refractive lens exchange,* advances in surgical technique (small, predictable wounds), biometry, and IOL power calculation formulas have greatly improved outcomes. Additionally, expanded choices of intraocular lenses (IOLs) have afforded more accurate refractive outcomes, with available lenses now including a wide variety of IOLs: spherical and aspheric monofocal, toric, light-adjustable, multifocal, combined toric and multifocal, and accommodating lenses.

The combination of corneal and intraocular refractive surgery, termed *bioptics,* allows patients at the extremes of refractive error, both spherical (myopia, hyperopia) and cylindrical (astigmatism), to attain good, predictable outcomes by combining the advantages of the intraocular refractive surgery in treating large corrections with the adjustability of keratorefractive techniques. In addition, the optical quality may be improved by dividing the refractive correction between the 2 surgical procedures.

This chapter discusses the intraocular surgical techniques that are now, or are soon expected to be, available to the refractive surgeon.

Phakic Intraocular Lenses

Background

The history of the PIOL in correcting refractive error began in Europe in the 1950s, but manufacturing-quality limitations precluded these IOLs from achieving widespread use until the 1990s. Refinements in IOL design have reduced the incidence of complications and, consequently, increased the popularity of these PIOLs both inside and outside the United States. Within the United States, 4 PIOLs are currently approved by the US Food and Drug Administration (FDA) for myopia: 3 that are nonfoldable polymethylmethacrylate (PMMA) iris-fixated PIOLs, and 1 that is a foldable collamer posterior chamber PIOL. The 3 nonfoldable PMMA lenses are identical in design but have different dioptric ranges. Outside the United States, available models include foldable versions of the PMMA PIOLs, hyperopic and toric versions of all of the above PIOLs, and an angle-fixated PIOL. Representative lenses in each category (Table 8-1) are discussed in the following sections.

Table 8-1

Table 8-1 Phakic Intraocular Lenses

Position	Model	Available Power (D)	Optic Size/ Effective Diameter (mm)	Length (mm)	Material	Manufacturer	FDA Approval
Angle-supported	AcrySof Cachet	–8.00 to –16.00	5.5	12.5, 13.0, 13.5	Acrylic	Alcon Laboratories	
	Phakic 6 H2	–4.00 to –20.00 +2.00 to +10.00	5.5–6.0	11.5–14.0	PMMA	Ophthalmic Innovations International (Ontario, CA)	
	Kelman Duet	–6.00 to –20.00	6.3/5.5	12.0, 12.5, 13.0, 13.5	Silicone optic PMMA haptics	Tekia (Irvine, CA)	
Iris-supported	Verisyse model* VRSM5US	–5.00 to –20.00	5.0	8.5	PMMA	Abbott Medical Optics (Santa Ana, CA)	Approved
	Verisyse model* VRSM6US	–5.00 to –15.00	6.0	8.5	PMMA	Abbott Medical Optics (Santa Ana, CA)	Approved
	Artisan model 203	+3.00 to +12.00	5.0 or 6.0	8.5	PMMA	Ophtec (Groningen, The Netherlands; USA, Boca Raton, FL)	
	Artisan toric IOL	Custom	5.0 or 6.0	8.5	PMMA	Ophtec (Groningen, The Netherlands; USA, Boca Raton, FL)	
	Artiflex/ Veriflex	–3.00 to –23.50	5.0 or 6.0	8.5	Polysiloxane	Ophtec (Groningen, The Netherlands; USA, Boca Raton, FL)	
Sulcus-supported	Visian ICL†	–3.00 to –20.00	4.9–5.8	12.1, 12.6, 13.2, 13.7	Collamer	STAAR (Monrovia, CA)	Approved
	Visian ICL	+3.00 to +12.00		11.5–13.2	Collamer	STAAR (Monrovia, CA)	
	Visian Toric ICL	Up to +2.50 Custom to +4.00	4.75–5.50	11.5–13.2	Collamer	STAAR (Monrovia, CA)	

FDA = US Food and Drug Administration; ICL = implantable collamer lens; IOL = intraocular lens; PMMA = polymethylmethacrylate.
*The Artisan lens (Ophtec), marketed as the Verisyse lens (Abbott Medical Optics), has been FDA approved for use in the lens power range of –5.00 to –20.00 D.
†The Visian ICL (STAAR) posterior chamber phakic IOL has received FDA approval to correct myopia in the range of –3.00 to –20.00 D.

Huang D, Schallhorn SC, Sugar A, et al. Phakic intraocular lens implantation for the correction of myopia: a report by the American Academy of Ophthalmology. *Ophthalmology.* 2009; 116(11):2244-2258.

Advantages

PIOLs have the advantage of treating a much larger range of refractive errors than can be treated safely and effectively with corneal refractive surgery. The skills required for insertion are, with a few exceptions, similar to those used in cataract surgery. The equipment needed for IOL implantation is substantially less expensive than an excimer laser and is similar to that used for cataract surgery. In addition, the PIOL is removable; therefore, the refractive effect should theoretically be reversible. However, any intervening damage caused by the PIOL implantation is often permanent. Compared with refractive lens exchange (discussed later in this chapter), PIOL implantation has the advantage of preserving natural accommodation; it also has a lower risk of endophthalmitis and postoperative retinal detachment because the crystalline lens barrier is preserved and there is minimal vitreous destabilization.

Disadvantages

PIOL insertion is an intraocular procedure, with all the potential risks associated with intraocular surgery. In addition, each PIOL style has its own set of associated risks. Lenses with PMMA optics are not foldable, so their insertion requires a larger wound, which may result in postoperative astigmatism. Posterior chamber PIOLs have a higher incidence of cataract formation. For patients with PIOLs in whom a visually significant cataract eventually develops, the PIOL will have to be explanted at the time of cataract surgery, possibly through a larger-than-usual wound. Although PIOLs to correct hyperopia are available outside the United States, indications for their implantation are narrower because the anterior chamber tends to be shallower than in patients with myopia, causing the IOL to sit too close to the endothelium and resulting in increased endothelial cell loss.

Patient Selection

Indications

PIOLs can be offered as the primary surgical option for anyone who has refractive errors within the available treatment range and meets other screening criteria (discussed later). However, most surgeons reserve PIOL use for patients whose refractive limits are near or beyond the FDA-approved limits for laser vision correction, or who are otherwise not good candidates for keratorefractive surgery. Although excimer lasers can be used to treat high degrees of myopia, many surgeons have reduced the upper limits for laser in situ keratomileusis (LASIK) and surface ablation in their refractive practices because of the decreased predictability, high rate of regression, large amount of stromal tissue removed, increased incidence of microstriae, and night-vision problems that can occur with treatment of a patient with high myopia. Similarly, LASIK and surface ablation for correction of hyperopia greater than +4.00 D and astigmatism greater than 4.00 D of cylinder are less accurate than they are for lower corrections. If surgeons become comfortable with the use of PIOLs, they may also choose to implant them for refractive powers significantly lower than the maximal limits for programmable excimer laser treatments.

PIOLs are available in powers between -3.00 D and -20.00 D in the United States (see Table 8-1). Outside the United States, PIOLs are available for correcting hyperopia up to +10.00 D. PIOLs may be considered off-label treatment for eyes with irregular topographies from forme fruste keratoconus and even frank keratoconus.

Contraindications

PIOLs have specific contraindications. These include preexisting intraocular disease such as a compromised corneal endothelium, iritis, significant iris abnormality, rubeosis iridis, cataract, or glaucoma. The anterior chamber diameter, anterior chamber

depth, and pupil size must be appropriate for the specific PIOL being considered. (The anatomical requirements for the placement of each style of IOL are discussed in the next section.)

Patient evaluation

A thorough preoperative evaluation is necessary, as detailed in Chapter 2. Phakic IOLs are not approved in the United States for patients younger than 21 years.

Informed consent

As with any refractive procedure, an informed consent specifically for this procedure should be obtained before surgery. The patient should be informed of the potential short-term and long-term risks of the procedure and of available alternatives; he or she should also be counseled about the importance of long-term follow-up because of the potential for endothelial cell loss over time. The surgeon must also ensure that the patient has realistic expectations about the visual outcomes of the procedure.

Ancillary tests

Specular microscopy or confocal microscopy should be performed to evaluate endothelial cell count and morphology. Anterior chamber depth must also be assessed because adequate depth is required for safe implantation of a PIOL. If the anterior chamber depth is <3.2 mm, the risk of endothelial and iris or angle trauma from placement of an anterior chamber, iris-fixated, or posterior chamber PIOL is increased. Anterior chamber depth can be measured by ultrasound, anterior segment optical coherence tomography (OCT), partial coherence interferometry, slit-beam topography, or Scheimpflug imaging. In the United States, PIOL implantation is contraindicated in individuals who do not meet the minimum endothelial cell count specified for each PIOL and who do not have a minimum anterior chamber depth of 3.2 mm. Methods for IOL power selection are specific to each PIOL and manufacturer, and some manufacturers provide software for use in IOL power calculation.

Surgical Technique

Topical anesthesia with an intracameral supplement is appropriate if the patient is able to cooperate and the PIOL can be inserted through a small incision. If the patient cannot cooperate for the use of topical anesthesia or if a large incision is required, peribulbar or general anesthesia is preferable. Retrobulbar anesthesia should be used with caution in patients whose eyes have a high axial length because of the increased risk of globe perforation.

A peripheral iridotomy is recommended for all currently FDA-approved PIOLs to reduce the risk of pupillary block and angle closure; however, this recommendation may soon change, and iridotomy is not required for angle-supported PIOLs. One or

more laser iridotomies can be performed before the PIOL surgery, or an iridectomy can be performed as part of the implant procedure. Viscoelastic material should be meticulously removed at the conclusion of surgery to prevent postoperative elevation of IOP.

Iris-fixated phakic intraocular lens

Most surgeons induce pupillary miosis before they initiate iris-fixated PIOL implantation, both to protect the crystalline lens and to make the iris easier to manipulate. The lens is generally inserted through a superior limbal incision but can be implanted with the wound placed at the steep meridian to minimize postoperative astigmatism. The long axis of the PIOL is ultimately oriented perpendicular to the axis of the incision. A side port incision is made approximately 2-3 clock-hours on either side of the center of the incision; thus, a 12 o'clock incision requires side port incisions near the 10 and 2 o'clock meridians. The "claw" haptics are fixated to the iris in a process called *enclavation*. After the PIOL has been carefully centered over the pupil, it is stabilized with a forceps while a specially designed enclavation needle is introduced through one of the side port incisions, and a small amount of iris is brought up into the claw haptic. This procedure is repeated on the other side. If adjustment of the PIOL position becomes necessary after fixation, the iris must be released before the PIOL is moved. Careful wound closure helps minimize surgically induced astigmatism. PMMA PIOLs require a 6-mm wound and thus generally require sutures for proper closure, whereas iris-fixated PIOLs made of flexible materials can be inserted through a small, self-sealing wound of approximately 3 mm.

Sizing the iris-fixated PIOL Because this PIOL is fixated to the midperipheral iris, not the angle or sulcus, it has the advantage of having a "one-size-fits-all" length. It is 8.5 mm in length, with a 5.0- or 6.0-mm PMMA optic (Fig 8-1).

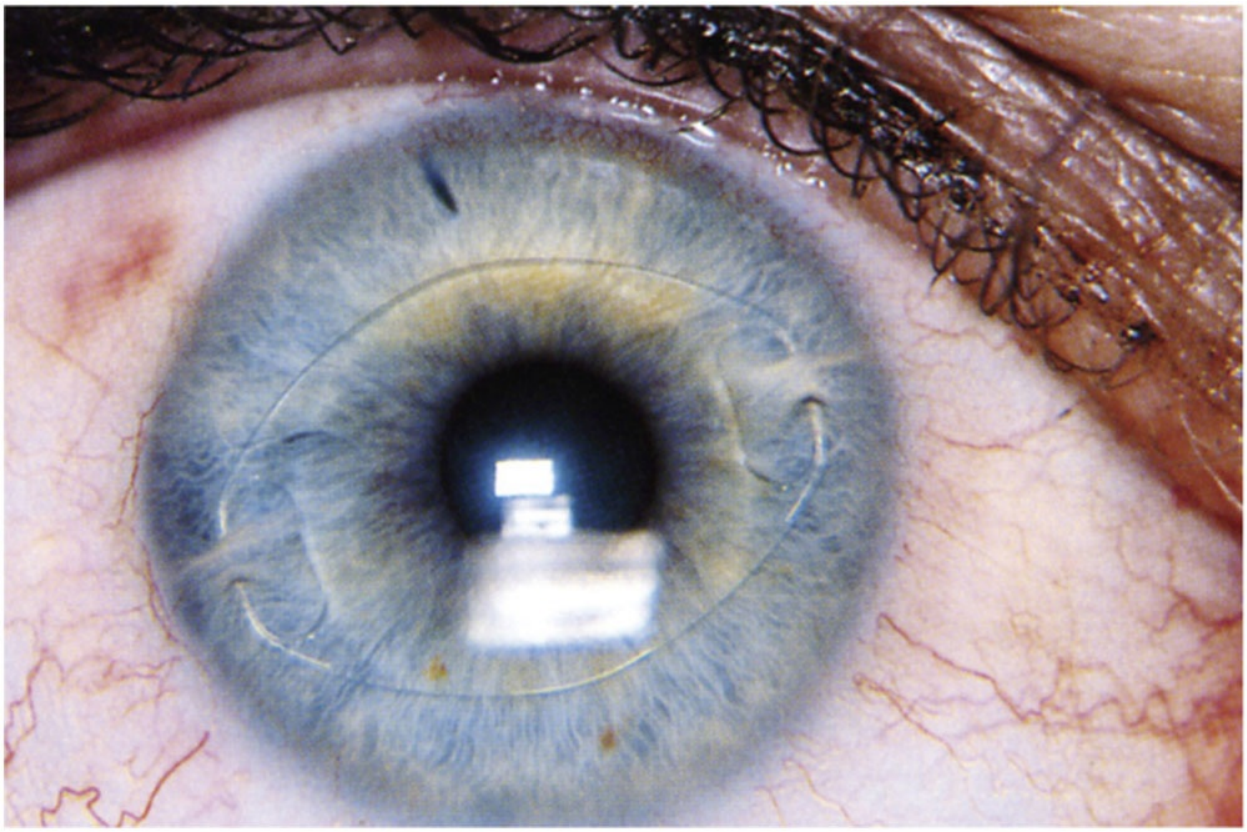

Figure 8-1 An iris-fixated phakic intraocular lens (PIOL) for myopic correction. *(Courtesy of Abbott Medical Optics.)*

Posterior chamber phakic intraocular lens

Posterior chamber PIOLs require pupillary dilation prior to implantation. These PIOLs are made of a flexible collamer material and are implanted through a small wound approximately 3 mm in length (Fig 8-2). The optic of the PIOL is vaulted to avoid contact with the crystalline lens and to allow aqueous to flow over the crystalline lens. This vaulting can be viewed at the slit lamp as well as with ultrasound biomicroscopy or Scheimpflug imaging (Fig 8-3). The lens manufacturers suggest that an acceptable amount of vaulting of the lens optic over the crystalline lens is 1.0 +- 0.5 corneal thicknesses. Using the appropriate vault is crucial for reducing complications (discussed later in the chapter).

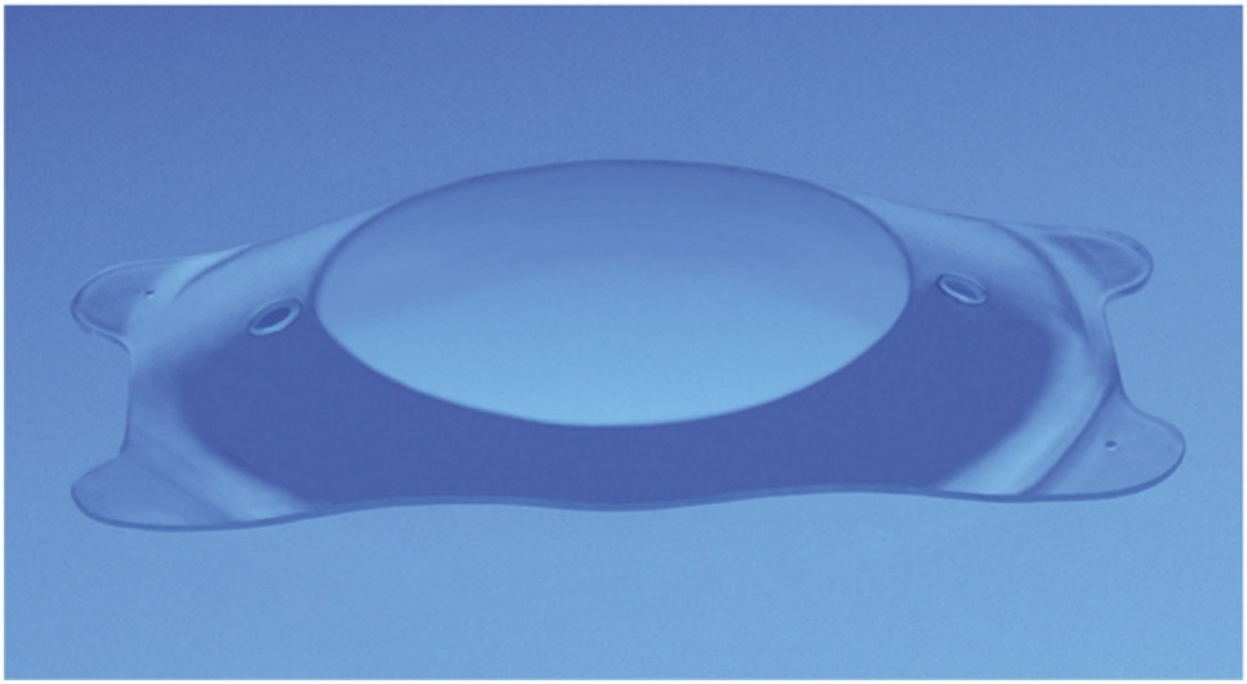

Figure 8-2 Side view of an implantable collamer posterior chamber PIOL. *(Courtesy of STAAR Surgical Company.)*

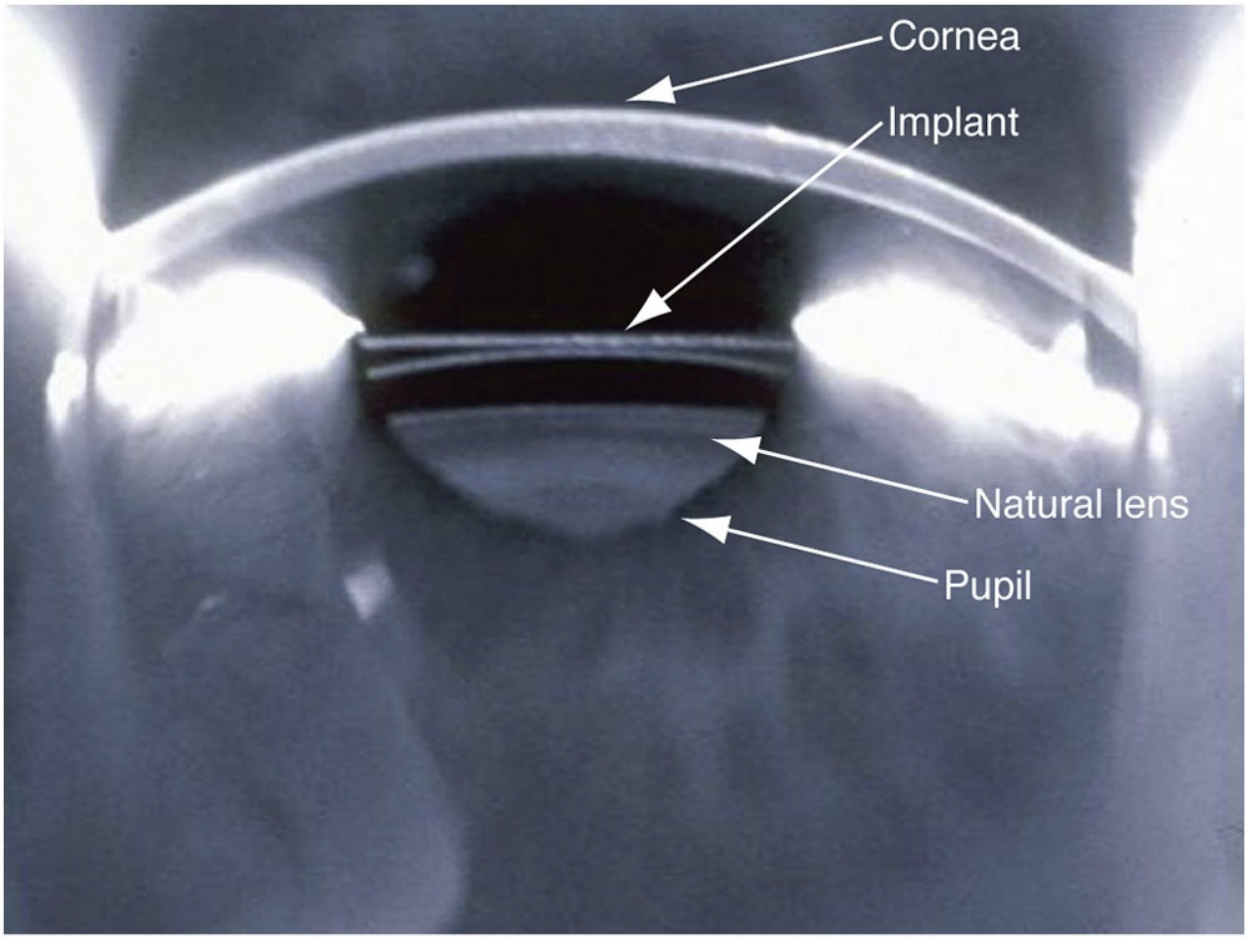

Figure 8-3 Scheimpflug image of a posterior chamber PIOL in place within the ciliary sulcus. *(Courtesy of STAAR Surgical Company.)*

For lens implantation, following pupil dilation, a 3.0- to 3.2-mm temporal clear corneal incision is made, and 1-2 additional paracentesis incisions are created, usually superiorly and inferiorly, to facilitate lens positioning. The lens is inserted using a cohesive viscoelastic material; after the lens unfolds, the footplates are positioned under the iris (Fig 8-4). The leading footplate is marked for identification and must be confirmed to be in the correct location once the lens exits the injector in order to ensure appropriate lens orientation. The surgeon should avoid contact with the central 6.0 mm of the lens, as any contact might damage the thin lens optic. Care should be taken to avoid touching the PIOL to minimize the risk of cataract. Positioning instruments should be inserted through the paracenteses and should be kept peripheral to this central area. The pupil is then constricted. It is crucial to remove all viscoelastic material at the conclusion of the procedure to reduce the risk of a postoperative spike in intraocular pressure (IOP).

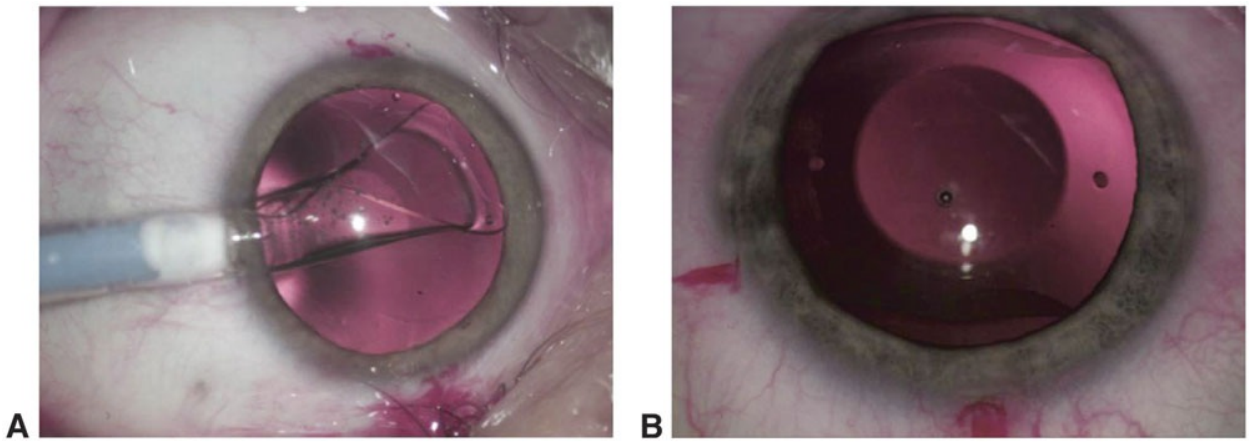

Figure 8-4 A, After placement with an IOL inserter, the posterior chamber PIOL unfolds in the anterior chamber. **B,** A posterior chamber PIOL shown unfolded and in position anterior to the crystalline lens in the posterior chamber. *(Courtesy of STAAR Surgical Company.)*

Sizing the posterior chamber PIOL The correct IOL length is selected by using the white-to-white measurement between the 3 and 9 o'clock meridians or by direct sulcus measurements made by a variety of techniques, including high-frequency ultrasound, anterior segment OCT, slit-beam or Scheimpflug imaging, and laser interferometry. Although the FDA-approved technique for measurement remains white-to-white measurement, there is growing evidence that direct sulcus measurement using any of these methods is superior and minimizes the risk of incorrect PIOL sizing.

For more information on PIOLs, please see the FDA website at www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/ImplantsandProsthetics/PhakicIntraocularLenses/default.htm.

Angle-supported phakic intraocular lens

No angle-supported PIOLs are currently approved by the FDA. Outside the United States, several commercial angle-supported PIOLs are available. The most widely used lens is made of flexible acrylic material and can be inserted through a small incision without the need for pupil dilation.

Outcomes

With better methods for determining PIOL power, outcomes have steadily improved. The significant postoperative gains in lines of corrected distance visual acuity (CDVA; historically referred to as *best-corrected visual acuity, BCVA*) over preoperative values are likely the result of a reduction in the image minification present with spectacle correction of high myopia. Loss of CDVA is rare. Moreover, the loss of

contrast sensitivity noted after LASIK for high myopia does not occur after PIOL surgery. In fact, in all spatial frequencies, contrast sensitivity increases from preoperative levels with best spectacle correction.

Barsam A, Allan BD. Excimer laser refractive surgery versus phakic intraocular lenses for the correction of moderate to high myopia. *Cochrane Database Syst Rev.* 2012;1:CD007679. Epub 2012 Jan 18.

Boxer Wachler BS, Scruggs RT, Yuen LH, Jalali S. Comparison of the Visian ICL and Verisyse phakic intraocular lenses for myopia from 6.00 to 20.00 diopters. *J Refract Surg.* 2009;25(9): 765-770. Epub 2009 Sep 11.

Dick HB, Budo C, Malecaze F, et al. Foldable Artiflex phakic intraocular lens for the correction of myopia: two-year follow-up results of a prospective European multicenter study. *Ophthalmology.* 2009;116(4):671-677.

Hassaballa MA, Macky TA. Phakic intraocular lenses outcomes and complications: Artisan vs. Visian ICL. *Eye (Lond).* 2011;25(10):1365-1370. Epub 2011 Aug 5.

Kamiya K, Shimizu K, Igarashi A, Hikita F, Komatsu M. Four-year follow-up of posterior chamber phakic intraocular lens implantation for moderate to high myopia. *Arch Ophthalmol.* 2009;127(7):845-850.

Kohnen T, Kook D, Morral M, Guell JL. Phakic intraocular lenses: part 2: results and complications. *J Cataract Refract Surg.* 2010;36(12):2168-2194.

Lovisolo CF, Reinstein DZ. Phakic intraocular lenses. *Surv Ophthalmol.* 2005;50(6):549-587.

Parkhurst GD, Psolka M, Kezirian GM. Phakic intraocular lens implantation in United States military warfighters: a retrospective analysis of early clinical outcomes of the Visian ICL. *J Refract Surg.* 2011;27(7):473-481. Epub 2011 Jan 17.

Perez-Cambrodi RJ, Pinero DP, Ferrer-Blasco T, Cervino A, Brautaset R. The posterior chamber phakic refractive lens (PRL): a review. *Eye (Lond).* 2013;27:14-21. Epub 2012 Dec 7.

US Food and Drug Administration. Summary of Safety and Effectiveness Data. Artisan phakic lens. PMA No. P030028. www.accessdata.fda.gov/cdrh_docs/pdf3/P030028b.pdf. Approval September 10, 2004. Accessed July 3, 2013.

US Food and Drug Administration. Summary of Safety and Effectiveness Data. STAAR Visian ICL (Implantable Collamer Lens). PMA No. P030016. www.accessdata.fda.gov/cdrh_docs/pdf3/P030016b.pdf. Approval December 22, 2005. Accessed July 3, 2013.

Complications

PIOL surgery shares the same possible risks and complications as other forms of IOL surgery. However, the most relevant potential complications include raised IOP, persistent anterior chamber inflammation, traumatic PIOL dislocation, cataract formation, and endothelial cell loss. Some of these complications do not manifest for years, thus necessitating long-term follow-up.

Iris-fixated phakic intraocular lens

At 1-year follow-up in FDA clinical trials of 662 patients who had an iris-fixated PIOL implanted for myopia, 1 patient had a hyphema, 5 had IOL dislocations, and 3 had iritis. Preoperative to postoperative change, as assessed by questionnaire, in glare, starbursts, and halos was 13.5%, 11.8%, and 18.2%, respectively. However, improvement in these symptoms from preoperative to postoperative status occurred in 12.9%, 9.7%, and 9.8%, respectively. In general, nighttime symptoms were worse in patients with larger pupil diameters.

Stulting and colleagues reported a 3-year follow-up study on 232 eyes of the 662 eyes enrolled in the FDA study. A total of 5 lenses dislocated and required reattachment, and an additional 20 lenses required surgery for insufficient lens fixation. No eyes required IOP-lowering medications after the first month. The mean decrease in endothelial cell density from baseline to 3 years was 4.8%. Six eyes required retinal detachment repair (rate, 0.3% per year), and 3 eyes underwent cataract surgery.

Pop M, Payette Y. Initial results of endothelial cell counts after Artisan lens for phakic eyes: an evaluation of the United States Food and Drug Administration Ophtec Study. *Ophthalmology.* 2004;111(2):309-311.

Stulting RD, John ME, Maloney RK, Assil KK, Arrowsmith PN, Thompson VM; U.S. Verisyse Study Group. Three-year results of Artisan/Verisyse phakic intraocular lens implantation. Results of the United States Food and Drug Administration clinical trial. *Ophthalmology.* 2008;115(3):464-472. Epub 2007 Nov 26.

Posterior chamber phakic intraocular lens

In addition to the potential risks associated with implantation of other types of PIOLs, implantation of posterior chamber PIOLs increases the risk of cataract formation and pigmentary dispersion. If the posterior chamber PIOL is too large, vaulting increases, and iris chafing with pigmentary dispersion could result. If the PIOL is too small, the vaulting is reduced, decreasing the chance of chafing but increasing the risk of cataract. Incorrect PIOL vault can necessitate exchange of the implanted lens for one with a better fit.

In an FDA clinical trial for one posterior chamber PIOL model, the incidence of nighttime visual symptoms was approximately 10%, but a similar percentage showed improvement in these symptoms after surgery. The incidence of visually significant cataract in the FDA clinical trial as reported by Sanders and colleagues was 0.4% for anterior subcapsular cataracts and 1% for nuclear sclerotic cataracts.

Kamiya and colleagues reported 4-year follow-up results on 56 eyes of 34 patients with implanted posterior chamber PIOLs. No eyes developed pupillary block or a significant increase in IOP. The mean central endothelial cell loss from baseline to 4 years was 3.7%. Two eyes developed symptomatic cataracts requiring surgery, and 6 other eyes developed asymptomatic anterior subcapsular cataracts. In a study of more than 500 eyes monitored for an average of 4.7 years, Sanders reported that 6%-7% of eyes developed anterior subcapsular opacities and 1%-2% developed visually significant cataracts.

The incidence of retinal detachment after posterior chamber PIOL insertion is very low. In a series of 16 eyes, surgical reattachment was achieved in 100%, with a mean follow-up of 35.25 months (range, 12-67 months) and a mean postoperative best spectacle-corrected visual acuity of 20/28.

Kohnen T, Knorz MC, Cochener B, et al. AcrySof phakic angle-supported intraocular lens for the correction of moderate-to-high myopia: one-year results of a multicenter European study. *Ophthalmology.* 2009;116(7):1314-1321. Epub 2009 May 30.

Martinez-Castillo V, Boixadera A, Verdugo A, Elies D, Coret A, Garcia-Arumi J. Rhegmatogenous retinal detachment in phakic eyes after posterior chamber phakic intraocular lens implantation for severe myopia. *Ophthalmology.* 2005;112(4):580-585.

Sanders DR. Anterior subcapsular opacities and cataracts 5 years after surgery in the Visian Implantable Collamer Lens FDA trial. *J Refract Surg.* 2008;24(6):566-570.

Sanders DR, Vukich JA, Doney K, Gaston M; Implantable Contact Lens in Treatment of Myopia Study Group. U.S. Food and Drug Administration clinical trial of the Implantable Contact Lens for moderate to high myopia. *Ophthalmology.* 2003;110(2):255-266.

Angle-supported phakic intraocular lens

The complications reported most frequently for angle-supported PIOLs are nighttime glare and halos, pupil ovalization, and endothelial cell loss. The risk of pupillary block is low with the use of modern PIOL designs and of iridotomies when needed.

Glare and halos, the most commonly reported symptoms after angle-supported PIOL insertion, occurred in 18.8%-20.0% of patients, but these symptoms appear to decrease by as much as 50% over a postoperative period of 7 years. Endothelial cell loss occurring 1-7 years after angle-supported PIOL insertion ranges from 4.6% to 8.4%. Pupil ovalization can occur because of iris tuck during insertion, or it can occur over time as a result of chronic inflammation and fibrosis around the haptics within the anterior chamber angle. The incidence of pupil ovalization ranges from 5.9% to 27.5% and is directly related to the postoperative interval studied. Ovalization is more likely when the implant is too large. In contrast, endothelial damage and decentration are most often associated with movement of a lens that is too small.

Knorz and colleagues reported on the 6-month to 3-year results of an angle-supported PIOL in 360 eyes with moderate to high myopia. No eyes experienced pupillary block, pupil ovalization, or retinal detachment. The annualized percentage loss in central and peripheral endothelial cell density from 6 months to 3 years was 0.41% and 1.11%, respectively.

Knorz MC, Lane SS, Holland SP. Angle-supported phakic intraocular lens for correction of moderate to high myopia: Three-year interim results in international multicenter studies. *J Cataract Refract Surg*. 2011;37(3):469-480.

Refractive Lens Exchange

Patient Selection

Indications

The indications for refractive lens exchange (RLE)--that is, removal of the crystalline lens with IOL implantation for the primary purpose of correcting refractive error--are evolving. Refractive lens exchange is usually considered only if alternative refractive procedures are not feasible and there is a strong reason that spectacles or contact lenses are unacceptable alternatives. RLE may be preferable to a PIOL in older patients who no longer have adequate accommodation and in patients with lens opacity that may progress in the relatively near future. RLE is generally not considered medically necessary and is usually not covered by the patient's insurance. As all FDA-approved IOLs are approved specifically for implantation at the time of cataract surgery, implantation for RLE is considered an off-label use in the United States.

Informed consent

Refractive lens exchange carries risks and complications identical to those for routine cataract extraction with IOL implantation. Potential candidates must be capable of understanding the short-term and long-term risks of the procedure. Patients should be informed that unless they are targeted for residual myopia with monofocal, toric, or accommodating IOLs, or have a multifocal IOL implanted, they will not have functional

near vision without correction. A consent form should be given to the patient prior to surgery to allow ample time for review and signature. A sample consent form for RLE for the correction of hyperopia and myopia is available from the Ophthalmic Mutual Insurance Company (OMIC) at www.omic.com.

Myopia

Refractive lens exchange can be considered in patients with myopia; however, in addition to the risks associated with cataract surgery, the surgeon must specifically inform the patient about the risk of retinal detachment associated with removal of the crystalline lens. Myopia is a significant risk factor for retinal detachment in the absence of lens surgery, and this risk rises with increased axial length. The risk of retinal detachment in eyes with up to 3.00 D of myopia may be as much as 4 times greater than it is in emmetropic eyes, whereas in eyes with >3.00 D of myopia, the risk may be as high as 10 times that in emmetropia. In the absence of trauma, more than 50% of retinal detachments occur in myopic eyes.

American Academy of Ophthalmology Retina/Vitreous Panel. Preferred Practice Patterns Guidelines. *Posterior Vitreous Detachment, Retinal Breaks, and Lattice Degeneration.* San Francisco: American Academy of Ophthalmology; 2008. Available at: www.aao.org/ppp.

Hyperopia

If the amount of hyperopia is beyond the range of alternative refractive procedures, RLE might be the only available surgical option. As with correction for myopia, the patient must be informed about the risks of intraocular surgery. A patient with a shallow anterior chamber from a thickened crystalline lens or small anterior segment would not be a candidate for a PIOL and could benefit from the reduced risk of angle-closure glaucoma after RLE. Patients with hyperopia have a lower risk of retinal detachment than do patients with myopia.

Nanavaty MA, Daya SM. Refractive lens exchange versus phakic intraocular lenses. *Curr Opin Ophthalmol.* 2012;23(1):54-61.

Astigmatism

Patients with significant astigmatism are also candidates for RLE with the advent of toric IOLs that cover an expanded range. In the United States, there are currently no FDA-approved combined toric multifocal IOLs. Thus, US patients planning to undergo implantation of a toric IOL must understand the lack of uncorrected near acuity if targeted for distance; patients considering multifocal IOL implantation should understand that these IOLs will not sufficiently reduce astigmatism. Also, patients need to understand that an additional surgical procedure, usually LASIK or photorefractive keratectomy, may be necessary to maximize spectacle independence and that laser vision correction candidacy should be determined prior to lens-based surgery if it is being considered. Smaller amounts of astigmatism may be managed with corneal incisional surgery.

Surgical Planning and Technique

Although RLE is similar to cataract surgery, there are some additional considerations for planning and performing the procedure because the primary surgical goal is refractive rather than merely reduction of vision loss due to cataract. First, in contrast to keratorefractive procedures, which are usually performed as immediately sequential procedures in the same surgical session, RLE is usually performed as sequential surgery on separate days to minimize the potential for bilateral endophthalmitis. However, this standard continues to evolve, and some surgeons are performing bilateral RLE in the same surgical session.

Preoperative corneal topography is essential to determine the degree of irregular astigmatism present and identify patients with borderline corneal ectatic disorders such as keratoconus and pellucid marginal degeneration. Patients with these conditions may still have RLE performed; however, they must understand the limits of vision correction obtainable, and if there is suspicion of ectatic corneal disease, patients must understand that they are not good candidates for postoperative treatment with LASIK or photorefractive keratectomy to refine the refractive correction.

Surgeons must identify the degree of corneal versus lenticular astigmatism present, as only the corneal astigmatism will remain postoperatively. The patient should be informed if substantial astigmatism is expected to remain after surgery, and a plan should be devised to correct it in order to optimize the visual outcome. Small amounts of corneal astigmatism (<1.00 D) may be reduced if the incision is placed in the steep meridian.

Limbal relaxing incisions with either blade or femtosecond laser may be used to correct residual corneal astigmatism of less than 2.00 D (see Chapter 3). Supplemental surface ablation or LASIK could also be considered (see the following discussion on bioptics). Although glasses or contact lenses are an alternative for managing residual astigmatism, refractive surgery patients frequently reject this option.

Some surgeons obtain preoperative retinal OCT to identify potential macular pathology. Careful attention should be paid to the peripheral retinal examination, especially in patients with higher myopia. If relevant pathology is discovered, appropriate treatment or referral to a retina specialist is warranted. In patients with high axial myopia, retrobulbar injections should be performed with caution because of the risk of perforating the globe. Peribulbar, sub-Tenon, topical, and intracameral anesthesia are alternative options. In a highly hyperopic eye with an axial length <18 mm, nanophthalmos should be considered. Eyes with these characteristics have a higher risk of uveal effusion syndrome and postoperative choroidal detachment.

Many surgeons believe that an IOL should be implanted after RLE in a patient with high myopia rather than leaving the patient with aphakia, even when little or no optical power correction is required. Plano power IOLs are available if indicated. The IOL acts as a barrier to anterior prolapse of the vitreous, maintaining the integrity of the

aqueous-vitreous barrier, in the event that Nd:YAG laser posterior capsulotomy is required. Some IOL models also reduce the rate of posterior capsule opacification.

IOL Power Calculations in Refractive Lens Exchange

High patient expectations for excellent uncorrected distance visual acuity (UDVA; also called *uncorrected visual acuity, UCVA*) after RLE make accurate IOL power determination crucial. However, IOL power formulas are less accurate at higher levels of myopia and hyperopia. In addition, in high myopia, a posterior staphyloma can make the axial length measurements less reliable. Careful fundus examination and B-scan ultrasound imaging can identify the position and extent of staphylomas. The subject of IOL power determination is covered in greater detail in BCSC Section 3, *Clinical Optics,* and Section 11, *Lens and Cataract*.

In the case of a patient with high hyperopia, biometry may suggest an IOL power beyond what is commercially available. The upper limit of commercially available IOL power is now +40.00 D. A special-order IOL of a higher power may be available or may be designed, but acquiring or designing such a lens usually requires the approval of the institutional review board at the hospital or surgical center, which delays the surgery. Another option is to use a "piggyback" IOL system, in which 2 posterior chamber IOLs are inserted. One IOL is placed in the capsular bag, and the other is placed in the ciliary sulcus. When piggyback IOLs are used, the combined power may need to be increased +1.50 to +2.00 D to compensate for the posterior shift of the posterior IOL. One serious complication of piggyback IOLs is the potential for developing an interlenticular opaque membrane. These membranes cannot be mechanically removed or cleared with the Nd:YAG laser; the IOLs must be removed. Interlenticular membranes have occurred most commonly between 2 acrylic IOLs, especially when both IOLs are placed in the capsular bag. When piggyback lenses are used, they should be of different materials and the fixation should be split between the bag and the sulcus. Piggyback IOLs may also shallow the anterior chamber and increase the risk of iris chafing, especially in smaller eyes.

Hill WE, Byrne SF. Complex axial length measurements and unusual IOL power calculations. *Focal Points: Clinical Modules for Ophthalmologists*. San Francisco: American Academy of Ophthalmology; 2004, module 9.

Shammas HJ. IOL power calculation in patients with prior corneal refractive surgery. *Focal Points: Clinical Modules for Ophthalmologists*. San Francisco: American Academy of Ophthalmology; 2013, module 6.

Complications

At more than 2 years postoperatively, the incidence of retinal detachment in 1519 consecutive patients (2356 eyes) with an axial length greater than 27.0 mm was reported to be 1.5%-2.2%, a level that corresponds to the incidence of idiopathic retinal detachment in myopia.

Horgan N, Condon PI, Beatty S. Refractive lens exchange in high myopia: long term follow up. *Br J Ophthalmol.* 2005;89(6):670-

672.
Neuhann IM, Neuhann TF, Heimann H, Schmickler S, Gerl RH, Foerster MH. Retinal detachment after phacoemulsification in high myopia: analysis of 2356 cases. *J Cataract Refract Surg.* 2008;34(10):1644-1657.

Advantages

Refractive lens exchange has the advantage of greatly expanding the range of refractive surgery beyond what can be achieved with other available methods. The procedure retains the normal contour of the cornea, which may enhance the quality of vision, and it may be used to treat presbyopia as well as refractive error with incorporation of multifocal and/or accommodating IOLs.

Disadvantages

Quality of vision may not be as good with current multifocal IOLs as with other forms of vision correction. Patient expectations for excellent uncorrected visual acuity may be higher for RLE than for cataract surgery, underscoring the need for thorough preoperative discussion, close attention to detail preoperatively and intraoperatively, and postoperative treatment of residual refractive error.

Monofocal Intraocular Lenses

For some patients, the best IOL choice for implantation at the time of RLE is a monofocal IOL. There are a variety of IOL choices and styles available, and all are utilized in routine cataract surgery as well (see BCSC Section 11, *Lens and Cataract*, for more detail). Patients without significant corneal astigmatism who desire best distance vision only, or individuals who have tolerated monovision well in the past and want it re-created after cataract surgery, are generally the best candidates for monofocal IOL implantation.

Toric Intraocular Lenses

Recent studies have concluded what many surgeons have long believed, namely, that 0.75 D or more of residual astigmatism impacts visual function and patient satisfaction. Large population analyses indicate that more than 50% of patients have 0.75 D or more corneal astigmatism at presentation for cataract surgery, and 15%-29% have 1.50 D or more corneal astigmatism. Thus, toric IOLs can address a major need for vision correction after crystalline lens removal. Current toric IOLs in the United States generally come in powers that can correct from 1.00 to 4.00 D of astigmatism at the spectacle plane, and wider power ranges are available outside the United States; however, this range is continually evolving.

Patient Selection

A toric IOL is appropriate for patients with regular corneal astigmatism, currently up to 4.00 D in the United States. Patients with astigmatism in amounts exceeding the upper correction limits of these lenses require additional measures to obtain full correction. In addition to understanding the risks associated with intraocular surgery, patients must be capable of understanding the limitations of a toric IOL. Not all patients with toric IOL implantation achieve spectacle independence for distance vision. Further, patients should be informed that toric IOL implantation will not eliminate the need for reading glasses (unless monovision is planned). The patient also needs to be informed that the IOL may rotate in the capsular bag shortly after surgery and that a secondary intraocular surgery may be required to reposition it. A silicone toric IOL may be less appropriate for patients who may carry a significant potential of requiring silicone oil for retinal detachment repair in the future; thus, acrylic IOLs are more appropriate choices for these patients.

Planning and Surgical Technique

The amount, axis, and regularity of the astigmatism should be measured accurately with a keratometer and confirmed if possible with corneal topography. The axis of astigmatism from the refraction should not be used because it may be influenced by lenticular astigmatism, which will be eliminated with cataract surgery.

The manufacturers of toric IOLs have online applications available to aid in surgical planning. After the surgeon enters data such as keratometry measurements, axes, IOL spherical power generated by A-scan, average surgeon-induced astigmatism, and axis of astigmatism, these programs will generate the correct power and model lens as well as orientation of the lens alignment markers.

There are many ways that surgeons mark the cornea prior to surgery. The surgeon should establish and mark the vertical and/or horizontal meridians with the patient in an upright position to avoid potential misalignment resulting from torsional globe rotation, which sometimes occurs in the supine position. Cataract surgery with a wound that induces a predictable amount of astigmatism is necessary to achieve the intended benefit of a toric lens. All online toric IOL software requires input of the expected surgically induced astigmatism for lens power calculations.

After the IOL is injected into the capsular bag, the viscoelastic material behind the IOL is aspirated and the IOL is rotated into position on the steep meridian. Some surgeons prefer to leave the toric IOL purposely underrotated by 10deg-20deg and then rotate it into position after all viscoelastic substance has been removed; others position the IOL in its planned orientation and then hold it in place with a variety of techniques while removing the viscoelastic material. If the IOL rotates beyond its appropriate position, it will need to be fully rotated around again, as the 1-piece IOLs tend not to

rotate well against their haptics. This maneuver should be performed using viscoelastic material to prevent capsule rupture during rotation.

Outcomes

In clinical trials of a plate-haptic toric IOL, 48%-84% of patients achieved a UDVA of >20/40. Data provided by the FDA indicated uncorrected acuity of >20/40 in 93.8% of 198 patients implanted with a 1-piece acrylic toric IOL (all sizes combined). With the plate-haptic IOL, postoperative astigmatism was <0.50 D in 48% of patients and <1.00 D in 75%-81% of patients; results were 61.6% and 87.7%, respectively, for the 1-piece acrylic toric IOL.

In patients with corneal astigmatism greater than that correctable by toric IOLs, surgeons may opt to simultaneously or sequentially correct residual astigmatism with incisional procedures such as astigmatic keratotomy or limbal relaxing incisions.

Complications Specific to Toric IOLs

The primary complication of toric IOLs is the possibility of IOL rotation resulting in a misalignment of the astigmatic correction. Full correction is not achieved unless the IOL is properly aligned in the axis of astigmatism. Astigmatism calculations have shown that every 10deg off-axis rotation of the lens reduces the correction by approximately one-third. Thus, at 30deg the lens is functionally astigmatically neutral, and IOL misalignment greater than 30deg can increase the cylindrical refractive error. In the FDA clinical trials for a plate-haptic toric IOL, 76% of lenses were within 10deg of preoperative alignment, and 95% were within 30deg. In the FDA clinical trials for the 1-piece acrylic toric IOL, the degree of postoperative rotation in 242 implanted eyes was 5deg or less in 81.1% and 10deg or less in 97.1%. None of the eyes exhibited postoperative rotation greater than 15deg.

Typically, a misaligned IOL is recognized within days of the surgery; it should be repositioned before permanent fibrosis occurs within the capsular bag. However, waiting 1 week for some capsule contraction to occur may ultimately help stabilize this IOL. A new online calculator is available to help determine the exact amount of IOL rotation necessary to optimize visual outcome (www.astigmatismfix.com).

Lane SS, Ernest P, Miller KM, Hileman KS, Harris B, Waycaster CR. Comparison of clinical and patient-reported outcomes with bilateral AcrySof toric or spherical control intraocular lenses. *J Refract Surg.* 2009;25(10):899-901. Epub 2009 Oct 12.

Visser N, Ruiz-Mesa R, Pastor F, Bauer NJ, Nuijts RM, Montes-Mico R. Cataract surgery with toric intraocular lens implantation in patients with high corneal astigmatism. *J Cataract Refract Surg.* 2011;37(8):1403-1410.

Light-Adjustable Intraocular Lenses

The light-adjustable IOL is a 3-piece silicone-optic posterior chamber IOL that can be irradiated with ultraviolet light through a slit-lamp delivery system 1-2 weeks after

implantation to induce a change in the shape, and thus the power, of the IOL (Fig 8-5). This lens is not currently FDA approved but is available for use outside the United States. Specific irradiation patterns can be applied to the lens to induce myopic, hyperopic, and astigmatic shifts. In initial work, results indicate that up to 5.00 D of spherical and up to 2.00 D of astigmatic change can be induced. Once final irradiation is performed, the effect is "locked in" and no further adjustments can be made.

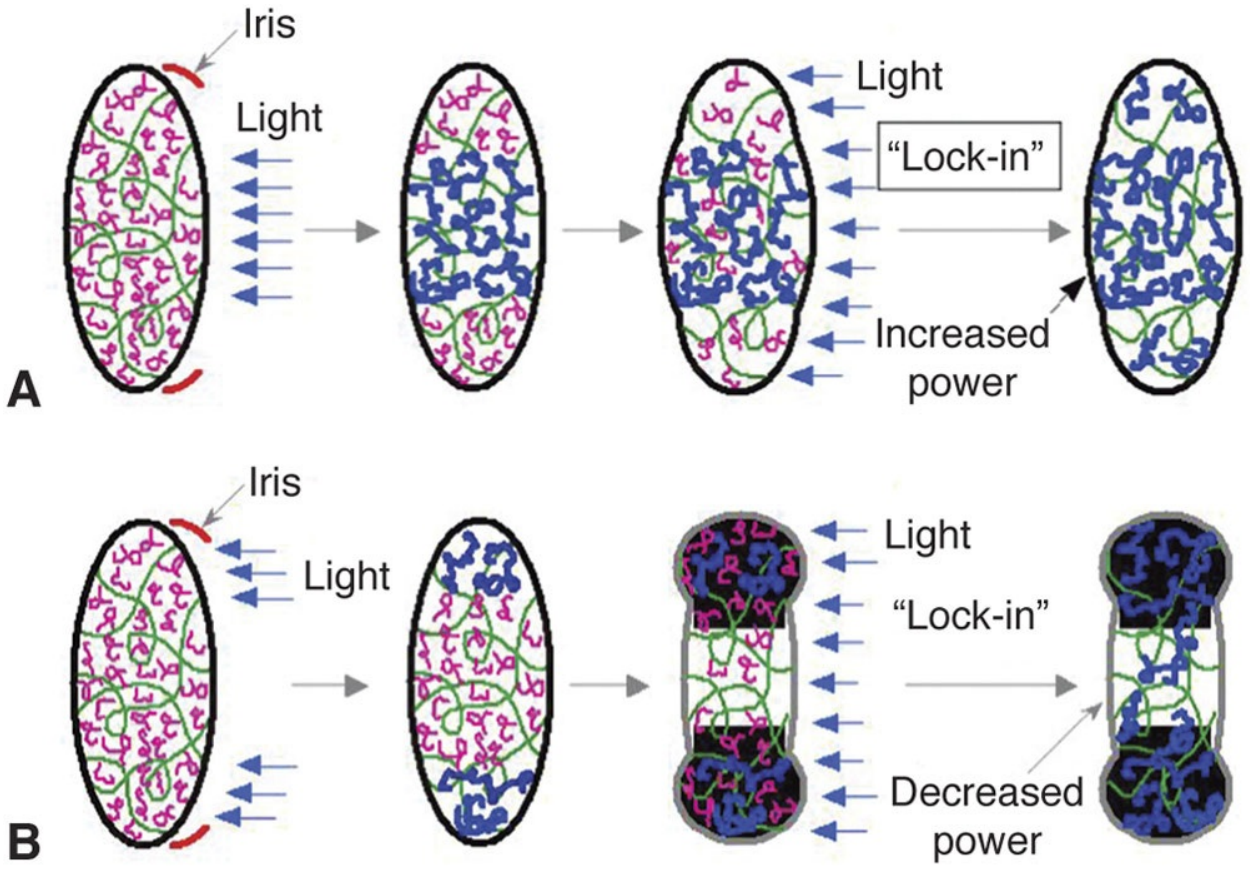

Figure 8-5 Schematic representation of the light-adjustable IOL. **A,** When the IOL is treated with UV light in the center, polymerization occurs and macromers move to the center, increasing the IOL power. **B,** When the IOL is treated with light in the periphery, macromers move to the periphery, decreasing the IOL power. *(Courtesy of Calhoun Vision.)*

Prior to postoperative irradiation, the lens must be protected from sunlight exposure. Further, it seems possible that an error in the irradiation treatment related to centration or improper data entry could cause irreversible changes in the IOL's visual properties and require IOL exchange surgery. Despite the refractive alterations available initially, after irradiation, the lens is functionally a monofocal IOL with all the limitations that come from that implantation strategy. See also Chapter 9 for more details.

Accommodating Intraocular Lenses

Accommodating lenses are another alternative for implantation during refractive lens exchange. Currently, only one model of accommodating IOL is approved by the FDA, although others are being investigated. Development is also currently under way for dual-optic IOLs and deformable IOLs. Additional investigational IOLs are discussed in Chapter 9.

Although the accommodating lens was designed to improve distance, intermediate, and near acuity through movement of its hinged haptics during the accommodative process, recent studies have found limited IOL movement and limited improvement in near acuity for most patients targeted for best distance acuity. Thus, many surgeons are utilizing a "mini-monovision" strategy when implanting the accommodating IOL, leaving the nondominant eye targeted for slight myopia (-0.50 to -0.75 D).

Hoffman RS, Fine IH, Packer M. Accommodating IOLs: current technology, limitations, and future designs. *Current Insight.* San Francisco: American Academy of Ophthalmology. Available at http://aao.org/current-insight/accommodating-iols-current-technology-limitations-.

Wallace BR III. Multifocal and accommodating lens implantation. *Focal Points: Clinical Modules for Ophthalmologists*. San Francisco: American Academy of Ophthalmology; 2004, module 11.

Multifocal Intraocular Lenses

Multifocal IOLs have the ability to provide appropriate patients with functional vision at near, intermediate, and far distances in each eye. This ability is due to lens multifocality that causes light rays to be split such that different focal points are created where objects will be clearest. However, all multifocal IOLs have potential trade-offs in vision quality and adverse effects, especially at night, and careful patient selection and counseling are necessary to achieve optimal outcomes. These types of lenses and their outcomes are discussed further in Chapter 9.

Patient Selection

Patients likely to be successful with a multifocal IOL implant after lens surgery are adaptable, less visually demanding individuals who place a high value on reduced spectacle dependence at all distances postoperatively. They should have good potential vision without significant pathology at any other location along the visual axis. Specific preoperative evaluation of macular function and anatomy may be warranted to exclude patients with epiretinal membrane or other conditions leading to suboptimal retinal function. Careful attention should be paid to evaluation of the corneal endothelium, as patients with any sign of Fuchs dystrophy are not ideal candidates for multifocal IOLs. Patients with more than 0.75 D residual astigmatism after multifocal IOL implantation frequently have suboptimal vision quality, and if this result is expected, strategies to reduce postoperative astigmatism should be evaluated and discussed before IOL

implantation. Evidence has shown that patients generally have better visual outcomes if multifocal IOLs are implanted bilaterally.

Surgical Technique

The surgical technique for multifocal IOL insertion is the same as that used in standard small-incision cataract surgery with a foldable acrylic IOL. Multifocal IOLs are much more sensitive than are monofocal IOLs to minor optic decentration. If the posterior capsule is not intact, IOL decentration is more likely to occur, and adequate fixation for a multifocal IOL should be determined before implantation.

Outcomes

Patients are most likely to achieve independence from glasses after bilateral implantation of multifocal IOLs. Recent meta-analyses found bilateral multifocal IOL implantation associated with significant improvement in both distance and near visual acuity with each type of implant studied.

As patients age, the pupillary diameter may decrease. If the pupillary diameter decreases to less than 2.0 mm, unaided reading ability may diminish. Gentle dilation with topical mydriatic drugs or laser photomydriasis may restore near acuity. Photomydriasis may be performed with an argon or dye photocoagulator, by placing green laser burns circumferentially outside the iris sphincter, or with a Nd:YAG photodisruptor, by creating approximately 4 partial sphincterotomies.

Adverse Effects, Complications, and Patient Dissatisfaction with Multifocal IOLs

Patient complaints after multifocal IOL implantation can generally be divided into 2 categories: blurred vision and photic phenomena (glare, halos). Patients may experience both groups of symptoms. These symptoms can occur even after uneventful surgery with a well-centered multifocal IOL.

Patients with multifocal IOLs are more likely to have significant glare, halos, and ghosting than are patients with monofocal, toric, or accommodating IOLs. These issues stem from a variety of different etiologies, including intrinsic IOL problems. The reports of halos tend to subside over several months, perhaps from the patient's neural adaptation, but they may be persistent. Because of a reduction in contrast sensitivity, the subjective quality of vision after multifocal IOL insertion may not be as good as after monofocal IOL implantation. The trade-off of decreased quality of vision in return for reduced dependence on glasses must be discussed fully with the patient preoperatively. With multifocal IOLs, intermediate vision may be weaker than distance or near acuity. Some surgeons implant different models of multifocal IOLs, called *mixing and*

matching, in the 2 eyes of a patient to maximize the range of visual function.

A small percentage of patients never adapt to multifocal IOLs and require IOL explantation and exchange to recover vision. All patients should be counseled as to this possibility before surgery. Patients with multifocal IOLs appear to be much more sensitive to lesser extents of posterior capsule opacification (PCO) than are individuals with monofocal IOLs. These patients benefit from Nd:YAG capsulotomy; however, tolerance of the multifocal IOL must be determined before undergoing the Nd:YAG capsulotomy, as an open posterior capsule significantly complicates IOL explantation and exchange. Intrinsic IOL symptoms usually appear very early if not immediately in the postoperative course and do not generally worsen over time. In contrast, symptoms from PCO are not present initially but gradually worsen over the first few weeks to months after surgery.

Agresta B, Knorz MC, Kohnen T, Donatti C, Jackson D. Distance and near visual acuity improvement after implantation of multifocal intraocular lenses in cataract patients with presbyopia: a systematic review. *J Refract Surg*. 2012;28:426-435.

Cillino S, Casuccio A, Di Pace F, et al. One-year outcomes with new-generation multifocal intraocular lenses. *Ophthalmology*. 2008;115(9):1508-1516. Epub 2008 Jun 5.

Cionni RJ, Osher RH, Snyder ME, Nordlund ML. Visual outcome comparison of unilateral versus bilateral implantation of apodized diffractive multifocal intraocular lenses after cataract extraction: prospective 6-month study. *J Cataract Refract Surg*. 2009;35(6): 1033-1039.

Packer M, Chu YR, Waltz KL, et al. Evaluation of the aspheric Tecnis multifocal intraocular lens: one-year results from the first cohort of the Food and Drug Administration clinical trial. *Am J Ophthalmol*. 2010;149(4):577-584. Epub 2010 Feb 6.

Rosenfeld SI, O'Brien TP. The dissatisfied presbyopia-correcting IOL patient. *Focal Points: Clinical Modules for Ophthalmologists*. San Francisco: American Academy of Ophthalmology; 2011, module 8.

Woodward MA, Randleman JB, Stulting RD. Dissatisfaction after multifocal intraocular lens implantation. *J Cataract Refract Surg*. 2009;35(6):992-997.

Bioptics

The term *bioptics* was suggested by Zaldivar in the late 1990s and is now used to describe the combination of 2 refractive procedures--one intraocular and one corneal--to treat patients with refractive errors that are suboptimally treated with a single procedure. Examples include extreme myopia, high myopia or hyperopia with significant astigmatism, and multifocal IOL implantation in patients with significant astigmatism. In these cases, the intraocular procedure is performed first, with keratorefractive surgery performed after both anatomical and refractive stability are achieved, usually 1-3 months after the initial surgery.

Bioptics with LASIK or surface ablation are reasonable alternatives, depending on patient parameters. As new treatment options are developed, the possibilities for other combinations of refractive surgery will increase.

The ability to successfully combine refractive procedures further expands the limits of refractive surgery. The predictability, stability, and safety of LASIK increase when smaller refractive errors are treated. In addition, there is usually sufficient corneal tissue to maximize the treatment zone diameter without exceeding the limits of ablation depth. The LASIK procedure provides the feature of adjustability in the overall refractive operation. These benefits must be balanced against the combined risks of

performing 2 surgeries rather than 1 surgery.

Alfonso JF, Fernandez-Vega L, Montes-Mico R, Valcarcel B. Femtosecond laser for residual refractive error correction after refractive lens exchange with multifocal intraocular lens implantation. *Am J Ophthalmol.* 2008;146(2):244-250. Epub 2008 May 23.

Guell JL, Vazquez M, Gris O. Adjustable refractive surgery: 6-mm Artisan lens plus laser in situ keratomileusis for the correction of high myopia. *Ophthalmology.* 2001;108(5): 945-952.

CHAPTER 9

Accommodative and Nonaccommodative Treatment of Presbyopia

Introduction

Presbyopia, the normal progressive loss of accommodation, affects all individuals beginning in middle age, regardless of any underlying refractive error. This relentless loss of near vision and dependency on glasses may be particularly distressing for individuals with emmetropic vision who have previously enjoyed excellent uncorrected vision. The possibility of "curing" or reducing the effects of presbyopia remains the "Holy Grail" of refractive surgery.

A number of procedures intended to increase the amplitude of accommodation are being investigated. Some of these techniques rely on various types of so-called scleral expansion. Others involve implantation of intraocular lenses (IOLs) capable of anteroposterior movement, with a subsequent change in effective lens power. Still others involve the creation of a multifocal cornea or use of a multifocal IOL. Some procedures were initially developed partly on the basis of rejection of the long-accepted Helmholtz theory of accommodation. As several proposed types of surgery for presbyopia stem from new theories of accommodation, the discussion begins by examining the different theories of accommodation.

Theories of Accommodation

Vision scientists do not yet have a complete understanding of the relationship between the effect of ciliary muscle contraction and zonular tension on the equatorial lens. In addition, a few markedly different anatomical relationships have been described between the origin of the zonular fibers and the insertion of these fibers into the lens.

The *Helmholtz hypothesis*, or *capsular theory*, of accommodation states that during distance vision, the ciliary muscle is relaxed and the zonular fibers that cross the circumlental space between the ciliary body and the lens equator are at a "resting"

tension. With accommodative effort, circumferential ciliary muscle contraction releases this tension on the zonules. An anterior movement of the ciliary muscle annular ring also occurs during accommodation. The reduced zonular tension allows the elastic capsule of the lens to contract, causing a decrease in equatorial lens diameter and an increase in the curvatures of the anterior and posterior lens surfaces. This "rounding up" of the lens yields a corresponding increase in its dioptric power, as is necessary for near vision (Fig 9-1). When the accommodative effort ceases, the ciliary muscle relaxes and the zonular tension on the lens equator rises to its resting state. This increased tension on the lens equator causes a flattening of the lens, a decrease in the curvature of the anterior and posterior lens surfaces, and a decrease in the dioptric power of the unaccommodated eye.

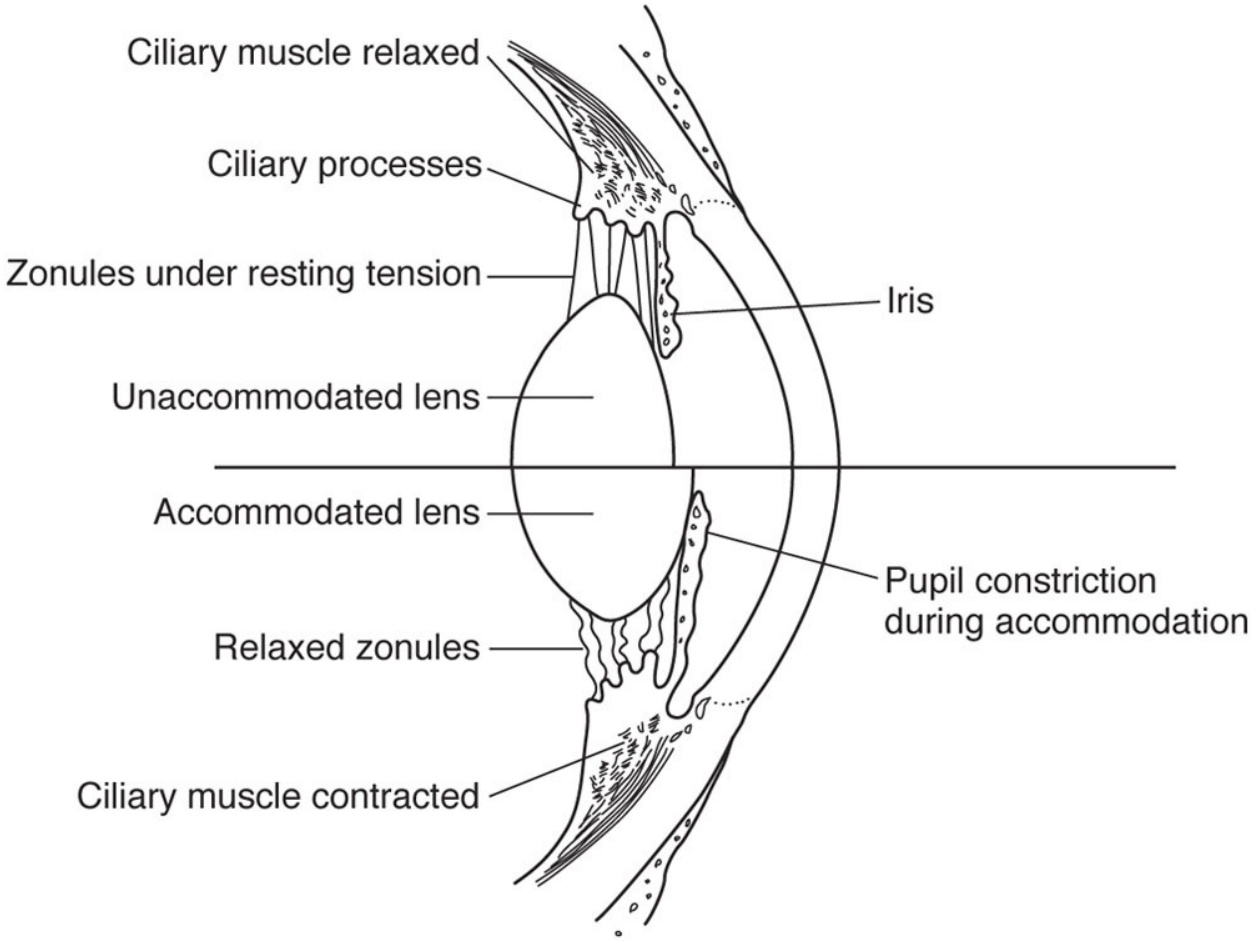

Figure 9-1 Schematic representation of the Helmholtz theory of accommodation, in which contraction of the ciliary muscle during accommodation *(bottom)* leads to relaxation of the zonular fibers. The reduced zonular tension allows the elastic capsule of the lens to contract, causing an increase in the anterior and posterior lens curvature. *(Illustration by Jeanne Koelling.)*

In the Helmholtz theory, the equatorial edge of the lens moves away from the sclera during accommodation and toward the sclera when accommodation ends. In this theory,

all zonular fibers are relaxed during accommodation and all are under tension when the accommodative effort ends. According to Helmholtz, presbyopia results from the loss of lens elasticity with age. When the zonules are relaxed, the older lens does not change its shape to the same degree as the young lens does; therefore, presbyopia is an aging process that can be reversed only by changing the elasticity of the lens or its capsule.

Diametrically opposed to the Helmholtz hypothesis is the *Schachar theory* of accommodation. Schachar suggests that during accommodation, ciliary muscle contraction leads to a selective increase in equatorial zonular tension--rather than to the uniform decrease (anterior, equatorial, and posterior) proposed by the Helmholtz theory--with a subsequent pulling of the equatorial lens outward toward the sclera (Fig 9-2). Schachar postulates that accommodation occurs through the direct effect of zonular tension (as opposed to the passive effect proposed by Helmholtz), causing an increase in lens curvature. In this theory, the loss of accommodation with age is a result of the continued growth of the lens, leading to increasing lens diameter and a decrease in the lens-ciliary body distance, which results in a loss of zonular tension. Anything that increases resting zonular tension (eg, scleral expansion) should restore accommodation.

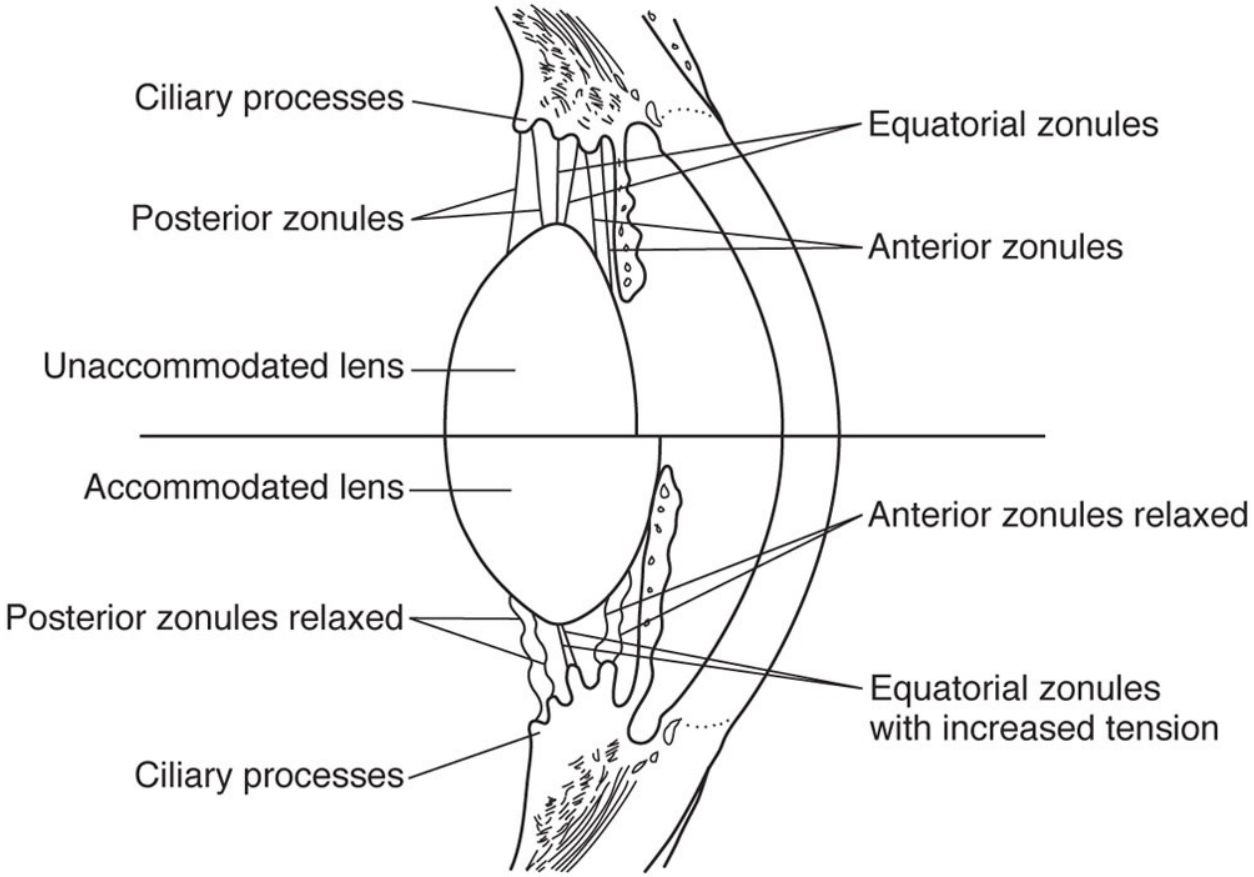

Figure 9-2 Schematic depiction of the Schachar theory, which proposes that only the equatorial zonules

are under tension during accommodation and that the anterior and posterior zonular fibers serve solely as passive support structures for the lens. *(Illustration by Jeanne Koelling.)*

Schachar proposed that the mechanism for functional lens shape change is equatorial stretching by the zonules, which would decrease the peripheral lens volume and increase the central volume, thus producing central steepening of the anterior central lens capsule (Fig 9-3). During accommodation and ciliary muscle contraction, tension on the equatorial zonular fibers increases, whereas tension on the anterior and posterior zonules is reduced. These actions would allow the lens to maintain a stable position at all times, even as it undergoes changes in shape. Schachar theorized that the anterior and posterior zonules serve as passive support structures for the lens, whereas the equatorial zonules are the active components in determining the optical power of the lens.

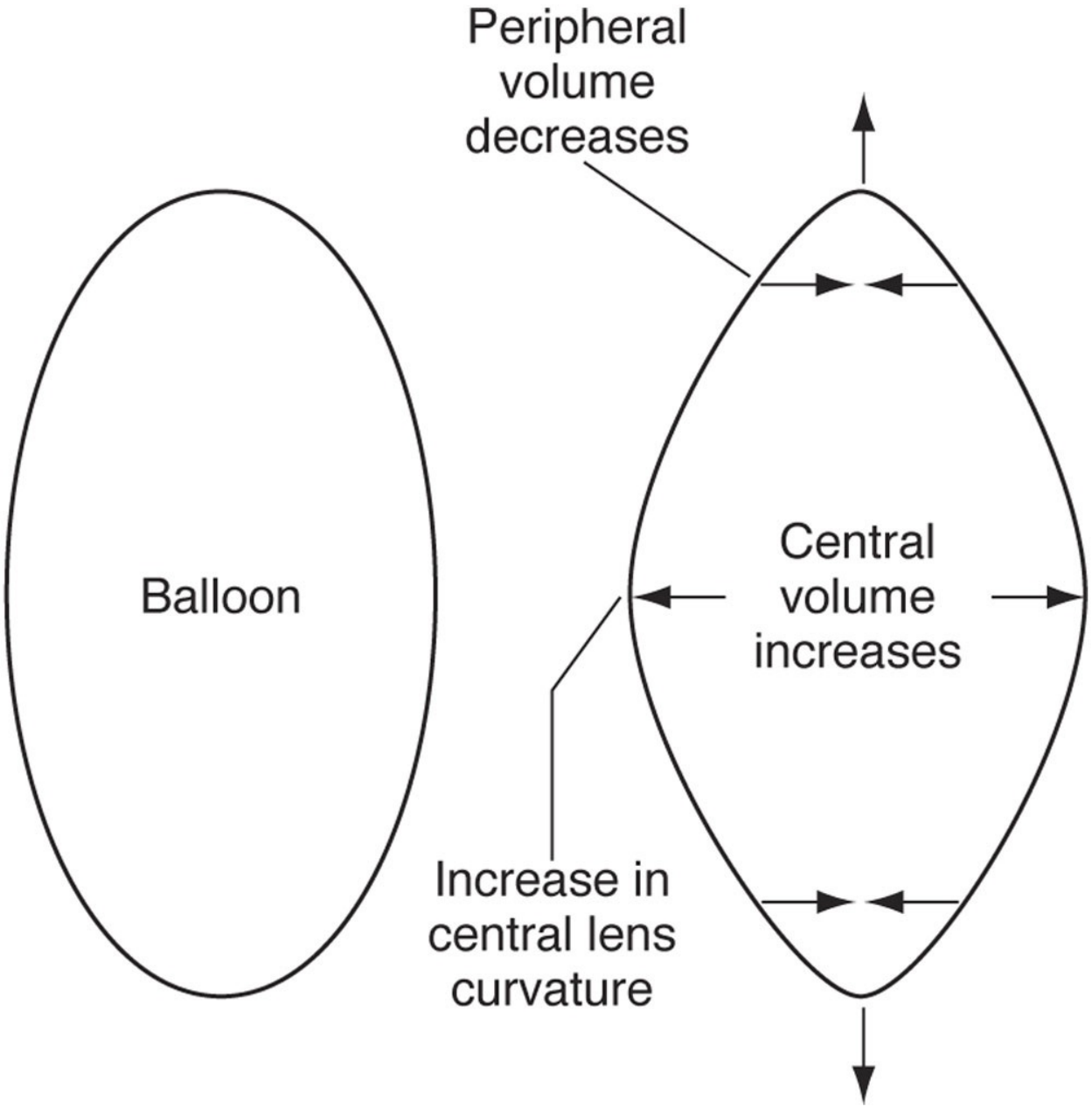

Figure 9-3 The Schachar theory proposes that the increase in equatorial zonular tension causes a decrease in peripheral lens volume and, thus, an increase in central lens volume and central lens curvature. *(Illustration by Jeanne Koelling.)*

Evidence from recent studies on human and nonhuman primates contest Schachar's theories on accommodation and presbyopia. Investigations in human tissues and with scanning electron microscopy reveal no zonular insertions (equatorial or otherwise) at the iris root or anterior ciliary muscle. Various imaging techniques consistently indicate that the diameter of the crystalline lens *decreases* with accommodation so that the equator moves away from the ciliary body. In vitro laser scanning imaging shows that

the crystalline lens does not change focal length when increasing and decreasing radial stretching forces are applied. This evidence thus runs contrary to Schachar's proposal that the lens remains pliable with age and that presbyopia is due solely to lens growth and crowding that prevents optimum ciliary muscle action.

Glasser A, Kaufman PL. The mechanism of accommodation in primates. *Ophthalmology.* 1999; 106(5):863-872.

Schachar RA. Cause and treatment of presbyopia with a method for increasing the amplitude of accommodation. *Ann Ophthalmol.* 1992;24(12):445-447, 452.

Strenk SA, Strenk LM, Koretz JF. The mechanism of presbyopia. *Prog Retin Eye Res.* 2005; 24(3):379-393. Epub 2004 Dec 19.

Nonaccommodative Treatment of Presbyopia

Monovision

Currently in the United States, monovision is the technique used most frequently for modifying presbyopia in individuals with phakic eyes. In this approach, the refractive power of 1 eye is adjusted to improve near vision. Monovision may be achieved with contact lenses, laser in situ keratomileusis (LASIK), surface ablation, conductive keratoplasty, or even lens surgery. The process involves intentionally undercorrecting a patient with myopia, overcorrecting a patient with hyperopia, or inducing mild myopia in an individual with emmetropic vision. Historically, the term *monovision* typically referred to the use of a distance contact lens in 1 eye and a near contact lens in the other. A power difference between the 2 eyes of 1.25-2.50 D was targeted on the basis of near acuity demands. Currently, many refractive surgeons target mild myopia (-0.50 to -1.50 D) for the near-vision eye in the presbyopic and prepresbyopic population. The term *modified,* or *mini-, monovision* is more appropriate for this lower level of myopia for the near-vision eye. Mini-monovision is associated with only a mild decrease in distance vision, retention of good stereopsis, and a significant increase in the intermediate zone of functional vision. The intermediate zone is where many visual functions used for activities of daily life occur (eg, looking at a computer screen, store shelves, or a car dashboard). For many patients, this compromise is an attractive alternative to constantly reaching for reading glasses. Selected patients who want better near vision may prefer higher amounts of monovision correction (-1.50 to -2.50 D) despite the accompanying decrease in distance vision and stereopsis. Future directions in monovision may involve modification of corneal asphericity to improve depth of focus.

Patient selection

Appropriate patient selection and education are fundamental to the overall success of monovision treatment. Although monovision can be demonstrated with trial lenses in the examination room, a contact lens trial period at home is often more useful. Patients whose vision is neither presbyopic nor approaching presbyopia are typically not good

candidates for monovision, as they are usually seeking optimal bilateral distance acuity. However, patients in their mid- to late 30s should be counseled about impending presbyopia and the option of monovision.

The best candidates for monovision are patients with myopia who are over the age of 40 years and who, because of their current refractive error, retain some useful uncorrected near vision. These patients have always experienced adequate near vision simply by removing their glasses and therefore understand the importance of near vision. Patients who do not have useful uncorrected near vision (myopia worse than -4.50 D, high astigmatism, hyperopia, or contact lens wearers) may be more accepting of the need for reading glasses after refractive surgery. For some patients, refractive surgeons routinely aim for mild myopia (-0.50 to -0.75 D, occasionally up to -1.50 D) in the nondominant eye. It is prudent to give the patient a trial with contact lenses to ascertain patient acceptance and the exact degree of near vision desired. Patients should understand that loss of accommodation is progressive, so that monovision may not remain fully effective over time, and corrective glasses may eventually be required.

Reinstein DZ, Carp GI, Archer TJ, Gobbe M. LASIK for presbyopia correction in emmetropic patients using aspheric ablation profiles and a micro-monovision protocol with the Carl Zeiss Meditec MEL 80 and VisuMax. *J Refract Surg.* 2012;28(8):531-541.

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;35:1885-1892.

Conductive Keratoplasty

As discussed in Chapter 7, conductive keratoplasty (CK) is a nonablative, collagen-shrinking procedure approved for the correction of low levels of hyperopia (+0.75 to +3.25 D). The procedure is approved by the US Food and Drug Administration (FDA) for the treatment of presbyopia in individuals with hyperopic or emmetropic vision.

Multifocal IOL Implants

The IOL options for patients undergoing cataract surgery have increased in recent years. Patients may select a traditional monofocal IOL with a refractive target of emmetropia, mild myopia, or monovision; or they may opt for a multifocal or an accommodating IOL for greater range of focus.

The first multifocal IOL to be granted FDA approval in the United States has since been replaced by other lens designs originally including zonal *refractive* and apodized *diffractive* IOLs. The zonal refractive lens design utilizes refractive power changes from the center of the lens to the periphery to provide distance and near correction. In contrast, diffractive lens designs employ a series of concentric rings to form a diffraction grating (see BCSC Section 3, *Clinical Optics*) to create 2 separate focal points for distance and near vision (Fig 9-4). Some diffractive lenses are apodized, meaning that the diffractive step heights are gradually tapered to allow a more even

distribution of light, which theoretically makes for a smoother transition among images from distance, intermediate, and near targets. Currently there are no zonal refractive IOLs available in the United States. Zonal refractive lenses, however, are available in a variety of styles in Europe. Examples of this type of lens include the Rayner M-flex T (Rayner Intraocular Lenses Ltd, East Sussex, United Kingdom) and the Lentis Mplus intraocular lens (Oculentis GmbH, Berlin, Germany) (Fig 9-5). In addition, IOLs with trifocal optics are available in Europe; examples are the FineVision (PhysIOL, Liege, Belgium) and the AT Lisa tri (Carl Zeiss Meditec, Jena, Germany).

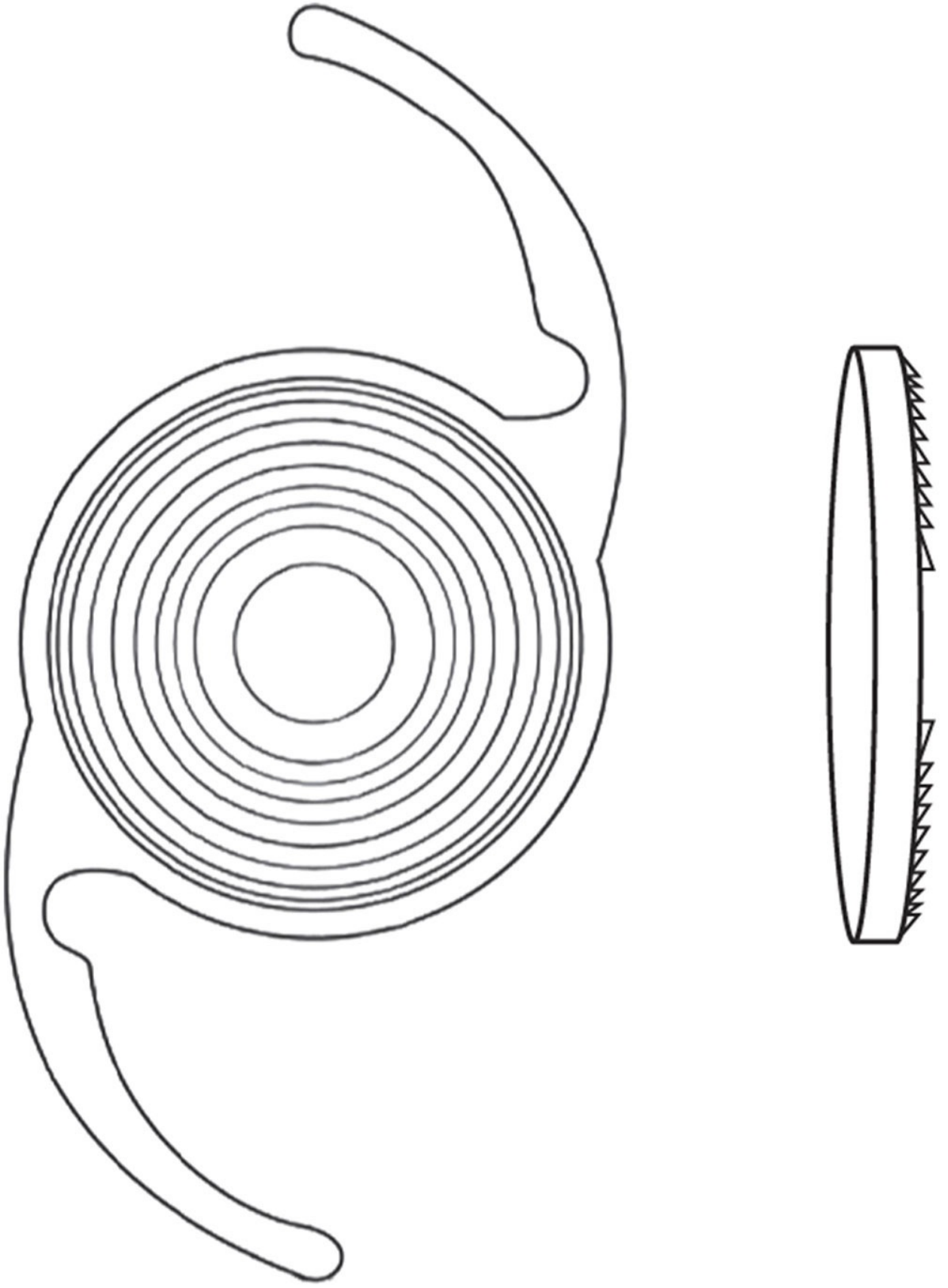

Figure 9-4 Example of a diffractive multifocal IOL. *Left,* schematic of the frontal view. *Right,* schematic of the side view. *(Left image courtesy of Abbott Medical Optics Inc.)*

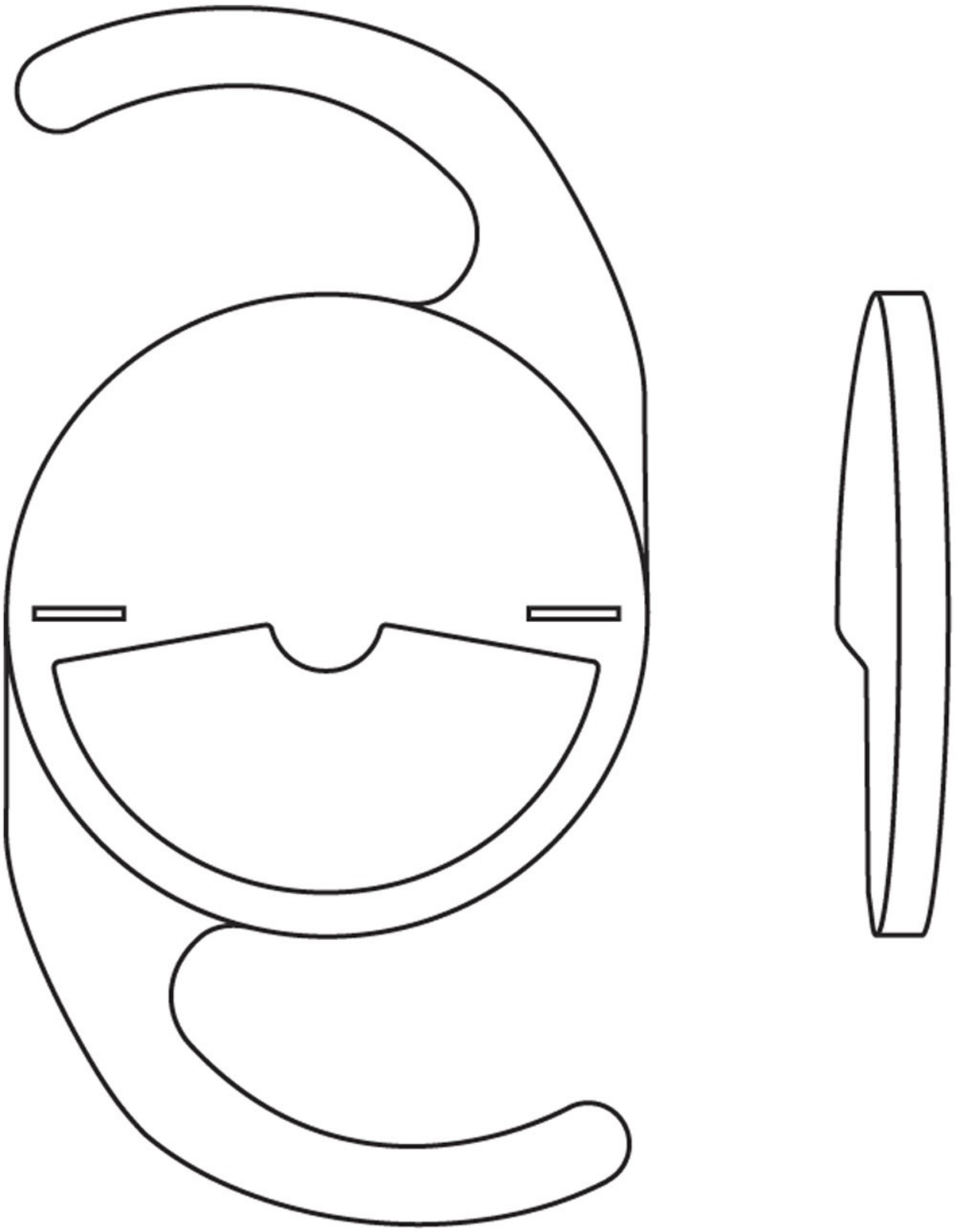

Figure 9-5 Example of a zonal refractive multifocal IOL. *Left,* schematic frontal view. *Right,* schematic lateral view of the rotationally asymmetric, multifocal sector lens, which is made from a combination of 2 spherical surfaces of differing radii. *(Illustration by Mark Miller from information courtesy of Oculentis GmbH.)*

Complications

Patient dissatisfaction with the quality of vision after multifocal IOL implantation should be addressed carefully. These patients should undergo a comprehensive evaluation of the ocular surface to the macula. Possible causes of visual disturbance should be excluded, such as dry eye, irregular astigmatism, vitreous opacities, cystoid macular edema or epiretinal membrane. Postoperative capsular opacification is of greater concern with multifocal IOLs because minimal changes in the capsule can cause early deterioration in vision. To achieve optimal vision, Nd:YAG capsulotomy may be required earlier or more frequently in patients with multifocal IOLs than in patients with monofocal IOLs. However, if IOL exchange is being contemplated, Nd:YAG capsulotomy should be deferred. Other possible causes of vision disturbance (eg, dry eye, irregular astigmatism, cystoid macular edema, or epiretinal membrane) should be excluded before an IOL exchange is considered. Multifocal IOLs may result in glare and halos around lights at night, although newer multifocal IOLs incorporate technology that substantially reduces these optical phenomena. Symptoms may be reduced through the use of nighttime driving glasses or instillation of topical brimonidine drops to reduce mesopic pupil size. In addition, most of these symptoms will decrease over time through neuroadaptation. Nevertheless, careful selection of motivated, well-informed patients is mandatory.

Custom or Multifocal Ablations

The excimer laser may be used to create a multifocal cornea. The potential for improving near vision without significantly compromising distance vision was investigated after it was noted that, following excimer ablation, the uncorrected near vision of many patients improved more than expected (Fig 9-6).

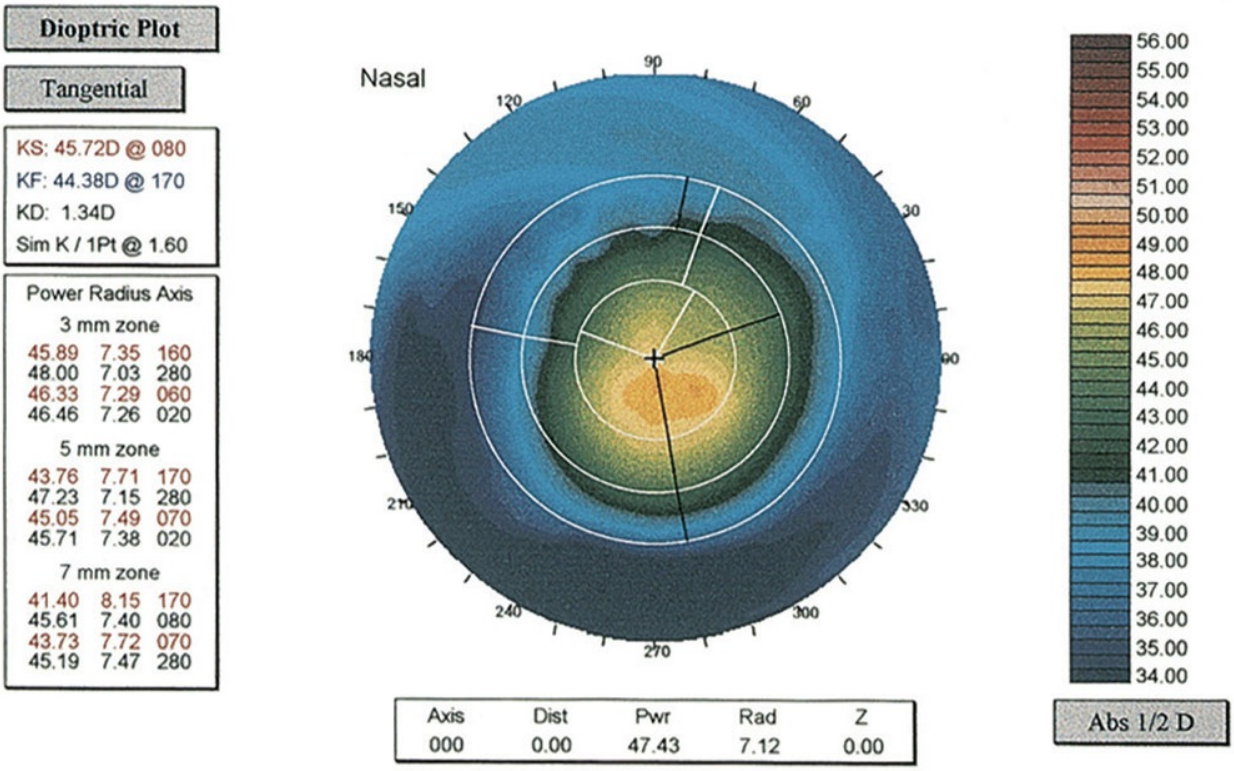

Figure 9-6 Multifocal ablation. Corneal topographic map showing a multifocal pattern after hyperopic laser in situ keratomileusis in a 62-year-old with preoperative hyperopia of +4.00 D. Postoperatively, the uncorrected visual acuity at distance is $20/25^{-2}$ and at near is Jaeger score J1. Manifest refraction of -0.25 +0.75 x 20 yields 20/20. Corneal topography demonstrates central hyperopic ablation *(green)* with relative steepening in the lower portion of the pupillary axis *(orange),* which provides the near add for reading vision. *(Courtesy of Jayne S. Weiss, MD.)*

A number of ablation patterns are being evaluated, including the following:

- a small, central steep zone ablation, in which the central portion of the cornea is used for near and the midperiphery is used for distance vision
- an inferior near-zone ablation
- an inferiorly decentered hyperopic ablation
- a central distance ablation with an intermediate/near midperipheral ablation

Some of these patterns generate simultaneous near and distance images, whereas others rely on pupillary constriction (accommodative convergence) to concentrate light rays through the steeper central ablation.

Although the excimer laser offers some potential advantages, results of multifocal corneal ablations have been disappointing to date.

Alarcon A, Anera RG, del Barco LJ, Jimenez JR. Designing multifocal corneal models to correct presbyopia by laser ablation. *J Biomed Opt.* 2012;17(1):018001.

Corneal Intrastromal Femtosecond Laser Treatment

Femtosecond lasers may now also be used to treat presbyopia. This minimally invasive approach is available in several countries outside the United States (but is not currently FDA approved) and does not involve incisions or flap creation. In this procedure, known as IntraCor, the femtosecond laser makes 5 concentric rings within the stroma, starting in the center with a ring diameter of 1.8 mm, and proceeding with subsequent rings toward the periphery. The formation of these rings produces a localized biomechanical change that reshapes the cornea to correct presbyopia. The procedure is normally performed only in the nondominant eye. Studies have demonstrated that this procedure has the potential to provide a solution for patients with hyperopic presbyopia (+0.50 D to +1.25 D), with a potential gain of 4-5 lines of near vision. However, to date, some studies have shown that 7%-15% of treated eyes have lost 2 or more lines of corrected distance visual acuity (CDVA; also known as *best-corrected visual acuity, BCVA*).

Holzer MP, Knorz MC, Tomalla M, Neuhann TM, Auffarth GU. Intrastromal femtosecond laser presbyopia correction: 1-year results of a multicenter study. *J Refract Surg.* 2012;28(3): 182-188.

Menassa N, Fitting A, Auffarth GU, Holzer MP. Visual outcomes and corneal changes after intrastromal femtosecond laser correction of presbyopia. *J Cataract Refract Surg.* 2012; 38(5):765-773.

Ruiz LA, Cepeda LM, Fuentes VC. Intrastromal correction of presbyopia using a femtosecond laser system. *J Refract Surg.* 2009;25(10):847-854.

Thomas BC, Fitting A, Auffarth GU, Holzer MP. Femtosecond laser correction of presbyopia (INTRACOR) in emmetropes using a modified pattern. *J Refract Surg.* 2012;28(12):872-878.

Corneal Inlays

Corneal inlays have been available outside the United States and in 2015, the Kamra inlay (AcuFocus Inc, Irvine, CA) received FDA approval. Corneal inlays improve near vision by changing corneal curvature, increasing depth of field via a small central aperture, or changing the refractive index of the cornea. Because the procedure is performed only in the nondominant eye, some adverse visual effects (night halos) may be less perceptible in binocular viewing conditions. These devices can be removed or combined with other refractive procedures, such as LASIK. (See Chapter 4 for more details.)

Bouzoukis DI, Kymionis GD, Limnopoulou AN, Kounis GA, Pallikaris IG. Femtosecond laser-assisted corneal pocket creation using a mask for inlay implantation. *J Refract Surg.* 2011;27(11):818-820. Epub 2011 Jul 18.

Garza EB, Gomez S, Chayet A, Dishler J. One-year safety and efficacy results of a hydrogel inlay to improve near vision in patients with emmetropic presbyopia. *J Refract Surg.* 2013; 29(3):166-172.

Limnopoulou AN, Bouzoukis DI, Kymionis GD, et al. Visual outcomes and safety of a refractive corneal inlay for presbyopia using femtosecond laser. *J Refract Surg.* 2013;29(1):12-19.

Tomita M, Kanamori T, Waring GO IV, et al. Simultaneous corneal inlay implantation and laser in situ keratomileusis for presbyopia in patients with hyperopia, myopia, or emmetropia: six-month results. *J Cataract Refract Surg.* 2012;38(3):495-506.

Waring GO IV. Correction of presbyopia with a small aperture corneal inlay. *J Refract Surg.* 2011;27(11):842-845.

Accommodative Treatment of Presbyopia

Scleral Surgery

Several scleral surgical procedures have been evaluated for use in the reduction of presbyopia. They share the objective of attempting to increase zonular tension by weakening or altering the sclera over the ciliary body to allow for its passive expansion. Thornton first proposed weakening the sclera by creating 8 or more scleral incisions over the ciliary body (anterior ciliary sclerotomy, or ACS). Results were mixed, and any positive effect appeared short-lived. A prospective study of ACS using a 4-incision technique was discontinued because of significant adverse events, including anterior segment ischemia. In 2001, the American Academy of Ophthalmology stated that ACS was ineffective and a potentially dangerous treatment for presbyopia. Another method involves the placement of scleral expansion bands, but this surgical option has had mixed results for safety, efficacy, and patient satisfaction (Fig 9-7).

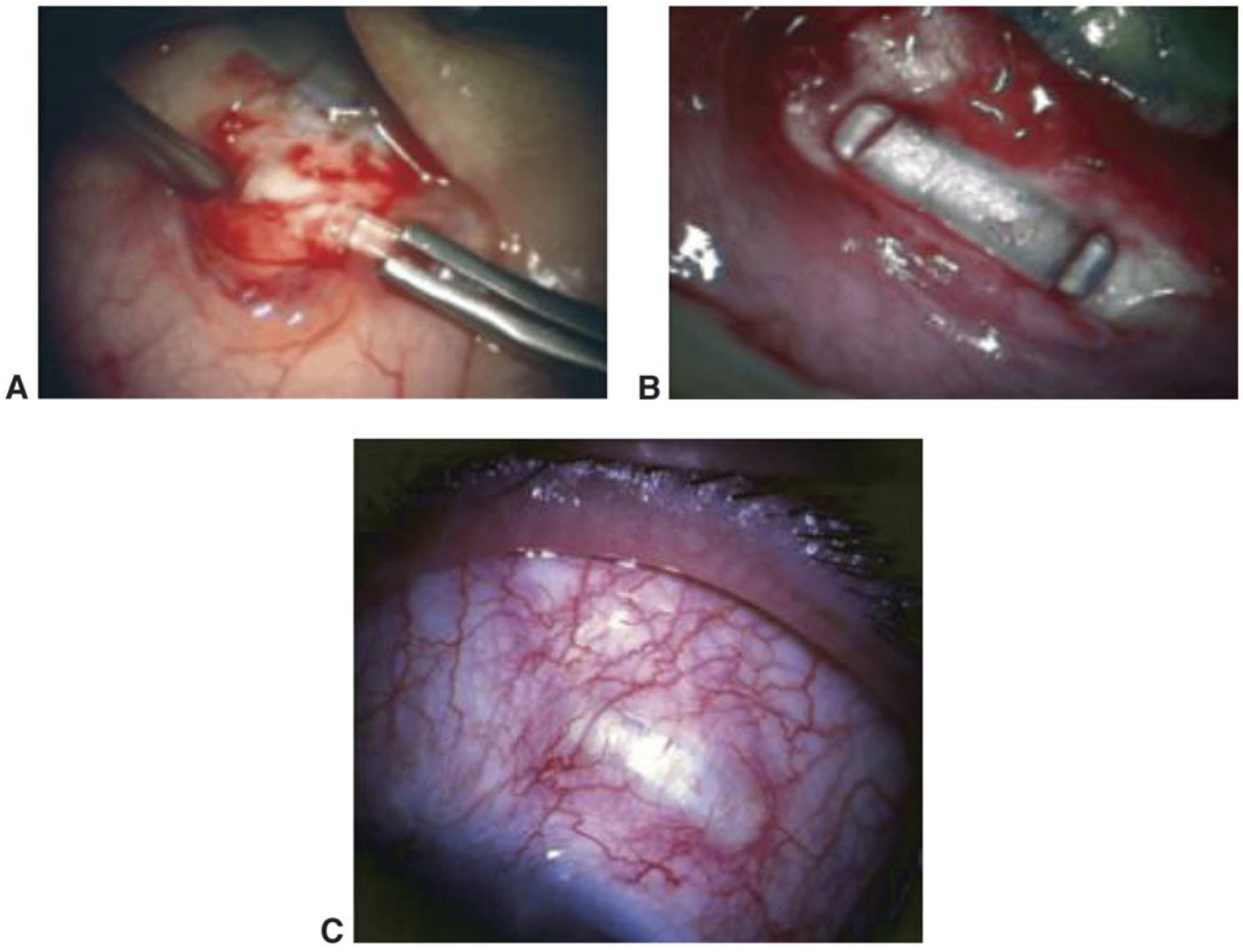

Figure 9-7 A, The scleral expansion band is inserted in a scleral tunnel over the ciliary body parallel to the limbus. **B,** The appearance of the band after placement, prior to conjunctival closure. **C,** The appearance of the well-healed band. *(Courtesy of Refocus Group.)*

Despite some initial encouraging results in recent FDA trials of scleral expansion, it remains unclear whether any of these procedures produces real and lasting results with an acceptable safety profile.

Hamilton DR, Davidorf JM, Maloney RK. Anterior ciliary sclerotomy for treatment of presbyopia: a prospective controlled study. *Ophthalmology.* 2002;109(11):1970-1977.

Kleinmann G, Kim HJ, Yee RW. Scleral expansion procedure for the correction of presbyopia. *Int Ophthalmol Clin.* 2006;46(3):1-12.

Femtosecond Lens Relaxation

Accommodation restoration through photodisruption of the crystalline lens using an ultra-short-pulse femtosecond laser has been proposed. This procedure was proven relatively safe and theoretically possible.

Reggiani Mello GH, Krueger RR. Femtosecond laser photodisruption of the crystalline lens for restoring accommodation. *Int Ophthalmol Clin.* 2011;51(2):87-95.

Accommodating IOLs

Accommodating IOLs attempt to restore a significant amount of true accommodation to patients with surgically induced pseudophakia. Accommodating IOLs were designed after it was observed that some patients who received silicone-plate IOLs reported near vision beyond that expected from their refractive result. Investigations revealed that, during ciliary muscle contraction, forward displacement of the IOL led to an increase in the IOL's effective power and thus an improvement in near vision. However, some studies have questioned the amplitude of true accommodation that can be expected solely on the basis of anterior displacement of the IOL optic. Other factors, such as pupil size, with-the-rule astigmatism, and mild myopia, may also contribute to unaided near visual acuity.

Some IOLs that use this accommodative approach are modified silicone, plate-haptic lenses (Fig 9-8). Potentially, these lenses allow anterior movement of the lens during accommodation. Another possibility is that ciliary body contraction causes a steepening of the anterior optic surface, allowing for better near vision. Although the exact cause of the movement is unclear, it appears to be a combination of posterior chamber pressure on the back surface of the IOL and ciliary body pressure on the IOL that vaults the optic forward. The anterior displacement is postulated to result in an effective increase in optical power and near vision.

Figure 9-8 Example of an IOL with a flexible hinge in the haptic at the proximal end and a polyamide footplate at the distal end. The footplate functions to maximize contact with the capsule and ciliary body, and the hinge transfers the horizontal force into an anteroposterior movement of the optic. *(Courtesy of Eyeonics.)*

Findl O, Kiss B, Petternel V, et al. Intraocular lens movement caused by ciliary muscle contraction. *J Cataract Refract Surg.* 2003;29(4):669-676.

Langenbucher A, Huber S, Nguyen NX, Seitz B, Gusek-Schneider GC, Kuchle M. Measurement of accommodation after implantation of an accommodating posterior chamber intraocular lens. *J Cataract Refract Surg.* 2003;29(4):677-685.

Other IOL Innovations on the Horizon

In contrast to single-plate accommodating IOLs, which are thought to work via lens effectivity secondary to a change in the position of the optic in the eye, lenses with dual-optic elements connected by a system of springlike struts are undergoing clinical investigation (eg, Synchrony lens [Visiogen, Irvine, CA]; Fig 9-9). During accommodation, the lens system confined within the capsular bag undergoes a change in the separation of the 2 optics, resulting in increased effective lens power. The lens can be implanted into the eye through a 3.5-mm incision.

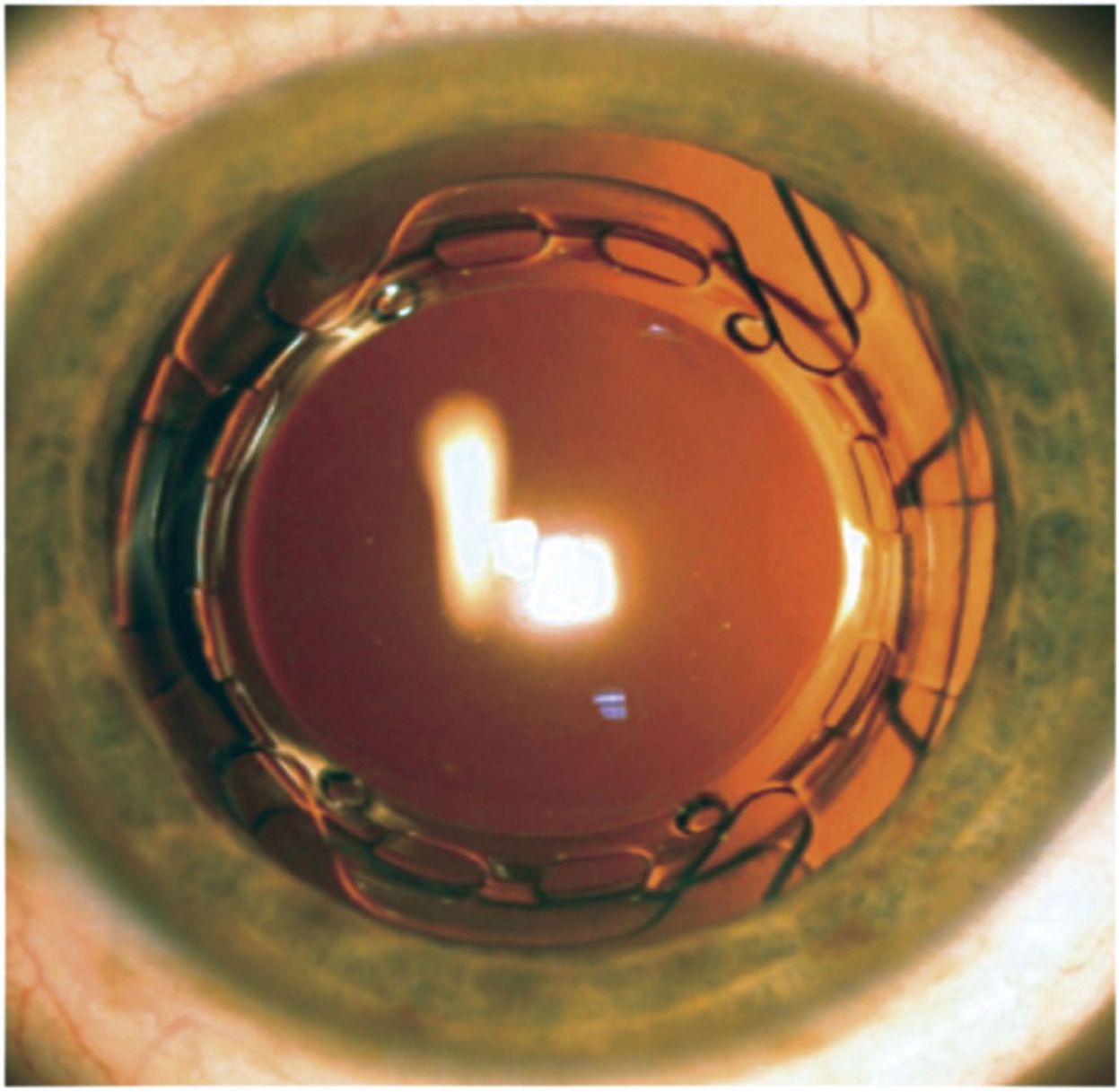

Figure 9-9 Clinical photograph of implanted dual-optic accommodating IOL, which has a high-plus anterior optic connected by spring haptics to a posterior optic with variable negative power. The three-dimensional design mimics the natural lens, and its response to the contraction and relaxation of the ciliary muscle increases paraxial power and provides accommodation. *(Courtesy of Ivan Ossma, MD)*

Another type of lens is made from a thermoplastic acrylic gel that can be customized to any size, shape, or power specified by the physician (eg, SmartLens; Medennium, Irvine, CA). The hydrophobic acrylic material is chemically bonded to wax, which melts inside the eye at body temperature and allows the predetermined shape and power of the material to emerge. Theoretically, compression of this pliable lens by the capsular bag would allow adjustment of its effective power in a manner similar to the way the crystalline lens adjusts. Other examples of deformable IOLs in

preliminary stages of development are the FlexOptic (Abbott Medical Optics, Santa Ana, CA), FluidVision IOL (PowerVision, Belmont, CA), and NuLens Accommodating IOL (NuLens, Herzliya Pituach, Israel). The NuLens changes its power rather than its position in the eye. It incorporates a small chamber of silicone gel and a posterior piston with an aperture.

In addition, flexible polymers are being designed for injection into a nearly intact capsular bag after extraction of the crystalline lens through a tiny, laterally placed capsulorrhexis.

The Light Adjustable Lens (LAL; Calhoun Vision, Pasadena, CA) is made from a macromer silicone matrix with smaller, embedded photosensitive molecules that allow for postoperative customization of the power via tunable ultraviolet light treatment (see Chapter 8 for more detail).

CHAPTER 10

Refractive Surgery in Ocular and Systemic Disease

Introduction

Over the past 2 decades, the field of refractive surgery has evolved from one involving controversial procedures into a subspecialty with finely tuned, computer-assisted procedures that play an important role in the surgical armamentarium of today's ophthalmologists. As the spectrum of indications for refractive surgery has grown so, too, has the prevalence of patients with concomitant known ocular or systemic diseases who wish to undergo these procedures.

During this period, many patients excluded from the original US Food and Drug Administration (FDA) clinical trials have been successfully treated with refractive surgery, and some formerly absolute contraindications have been changed to relative contraindications. Surgeons must always remember that refractive surgery is elective and involves risks. However, over time indications have changed, and refractive surgery is now being successfully performed in patients who were previously considered less than ideal candidates. With increased experience, laser in situ keratomileusis (LASIK), photorefractive keratectomy (PRK), and advanced surface ablation (ASA) have been performed safely and effectively in patients with ocular or systemic diseases. Nevertheless, the use of these procedures on patients whose conditions would have excluded them from participation in the original FDA protocols is considered off-label. In truth, performing off-label surgery is neither illegal nor medically incorrect if, in the judgment of the surgeon, the benefit of a surgical procedure outweighs the potential risk to a patient. However, it is the surgeon's ethical, legal, and medical responsibility to explain the concept of off-label surgery to the patient and to determine whether the procedure meets the standard of care in the community.

As with other surgeries, ophthalmologists should never go beyond their comfort zone when performing refractive surgery. The surgeon may seek a second opinion for a

difficult case or refer certain patients to more experienced colleagues. In higher-risk patients, unilateral surgery may offer the advantage of providing assurance that 1 eye is doing well before surgery is performed on the second eye. In addition, when deciding whether a patient with connective tissue disease or immunosuppression is an appropriate candidate for refractive surgery, the surgeon may find that consultation with the patient's primary physician or rheumatologist provides important information about the patient's systemic health.

The process of consent should be altered, not only to inform the patient, but also to document the patient's understanding of the additional risks and limitations of postoperative results associated with any coexisting ocular or systemic diseases. The refractive surgeon may choose to supplement the standard written consent with additional points to highlight specific concerns. The ophthalmologist should assiduously avoid the high-risk refractive surgery patient who volunteers to sign any preoperative consent because "I know these complications won't happen to me." Such patients have not heard or understood the informed consent discussion.

American Academy of Ophthalmology Refractive Management/Intervention Panel. Preferred Practice Pattern Guidelines. *Refractive Errors and Refractive Surgery.* San Francisco: American Academy of Ophthalmology; 2012. Available at: http://www.aao.org/guidelines-browse?filter=preferredpracticepatternsguideline.

Ocular Conditions

Ocular Surface Disease

Dry eye symptoms after LASIK are the most common adverse effects of refractive surgery. During creation of the flap, corneal nerves are severed, causing significant epithelial anesthesia that lasts 3-6 months and may persist for years. As a result, most patients experience a decrease in tear production. Patients who had dry eyes prior to surgery, or whose eyes were marginally compensated before surgery, may experience more severe symptoms postoperatively. In addition, these individuals demonstrate tear-film and ocular surface disruption and often report fluctuating vision between blinks episodically throughout the day. In a review of 109 patients who had undergone LASIK surgery, Levinson and colleagues found that dry eye symptoms and blepharitis were the most common diagnoses leading to patient dissatisfaction with the procedure, even for patients with relatively good postoperative vision outcomes. Among patients with dry eye or blepharitis, 42% had postoperative uncorrected distance visual acuity (UDVA, also called *uncorrected visual acuity, UCVA*) of 20/15-20/20, and 53% had UDVA of 20/25-20/40. Patients with persistent dry eye were among the least satisfied in this series. Fortunately, in the great majority of these patients, symptoms resolve 3-6 months after surgery. To optimize outcomes, it is imperative that dry eye disease be diagnosed and treated before surgery.

Ophthalmologists may take several steps to reduce the incidence and severity of dry

eye symptoms after refractive surgery. One of the most important is to screen patients carefully for dry eye and tear-film abnormalities before surgery. Many patients seeking refractive surgery are actually dry eye patients who are intolerant of contact lens wear because of their preexisting dry eye disease. Any history of contact lens intolerance should suggest the possibility of underlying dry eye.

Refractive surgery may be problematic in patients with dry eye because a normal tear-film layer is important to the healing of the corneal stroma and epithelium. Epidermal growth factor, vitamin A, and immunoglobulin A (IgA), which are present in tears, help prevent postoperative infection and promote wound healing. Consequently, severe dry eye syndrome was previously thought to be a relative contraindication to refractive surgery. However, studies of 543 eyes in 290 patients who had undergone LASIK showed no significant differences in UDVA or corrected distance visual acuity (CDVA, also called *best-corrected visual acuity, BCVA*) among eyes with or without preoperative dry eye. Additionally, there was no increased incidence of epithelial defects in the patients with preoperative dry eye. However, the group of patients with dry eye demonstrated slower recovery of corneal sensation, increased vital dye staining of the ocular surface, lower tear production, and more severe dry eye symptoms until 1 year after LASIK.

Any refractive surgery candidate with signs or symptoms of dry eye should be thoroughly evaluated. Patient history should include questions about collagen vascular diseases and conjunctival cicatrizing disorders; these conditions are relative contraindications to refractive procedures and should be addressed prior to any surgical consideration (see Chapter 2).

External examination should include evaluation of eyelid closure for such conditions as incomplete blink, lagophthalmos, entropion, ectropion, and eyelid notching. On slit-lamp examination, the ophthalmologist should note blepharitis, meibomitis, tear-film quantity and quality, and the presence of subconjunctival fibrosis or symblepharon. Ancillary testing for dry eyes, such as Schirmer testing, tear breakup time, fluorescein corneal staining, and lissamine green or rose bengal conjunctival staining, should be performed.

Preexisting abnormalities should be addressed and treated. Treatment of ocular surface disease with aqueous deficiency may include topical tear replacement, punctal occlusion, and use of topical anti-inflammatory drugs such as corticosteroids or cyclosporine (see BCSC Section 8, *External Disease and Cornea*). Topical cyclosporine improves dry eye and refractive outcomes in patients with dry eye who are undergoing LASIK and surface ablation. Patients with ocular surface disease and blepharitis or meibomitis should be instructed in methods of lid hygiene utilizing lid scrubs and in the use of dietary supplements such as flaxseed or omega-3 fish oils to improve the tear film.

Although excimer laser ablation may be performed in selected patients with dry

eye, these patients must be cautioned about the increased risk of their dry eye condition becoming worse postoperatively. The worsening of dry eye may result in additional discomfort or decreased vision and may be permanent.

American Academy of Ophthalmology Cornea/External Disease Panel. Preferred Practice Pattern Guidelines. *Blepharitis. Limited Revision.* San Francisco: American Academy of Ophthalmology; 2011. Available at: www.aao.org/ppp.

American Academy of Ophthalmology Cornea/External Disease Panel. Preferred Practice Pattern Guidelines. *Dry Eye Syndrome. Limited Revision.* San Francisco: American Academy of Ophthalmology; 2011. Available at: www.aao.org/ppp.

Levinson BA, Rapuano CJ, Cohen EJ, Hammersmith KM, Ayres BD, Laibson PR. Referrals to the Wills Eye Institute Cornea Service after laser in situ keratomileusis: reasons for patient dissatisfaction. *J Cataract Refract Surg.* 2008;34(1):32-39.

Salib GM, McDonald MB, Smolek M. Safety and efficacy of cyclosporine 0.05% drops versus unpreserved artificial tears in dry-eye patients having laser in situ keratomileusis. *J Cataract Refract Surg.* 2006;32(5):772-778.

Toda I, Asano-Kato N, Hori-Komai Y, Tsubota K. Laser-assisted in situ keratomileusis for patients with dry eye. *Arch Ophthalmol.* 2002;120(8):1024-1028.

Toda I, Yagi Y, Hata S, Itoh S, Tsubota K. Excimer laser photorefractive keratectomy for patients with contact lens intolerance caused by dry eye. *Br J Ophthalmol.* 1996;80(7):604-609.

Herpesvirus Infection

Many surgeons avoid laser vision correction in patients with a history of herpes simplex virus (HSV) keratitis because of the risk of recurrent disease induced by the surgery. Trauma from the lamellar dissection or exposure to the excimer laser may reactivate the virus and cause recurrent HSV keratitis. However, some authors have concluded that the recurrence reflects simply the natural course of the disease rather than reactivation due to excimer laser ablation.

The role of excimer laser ablation in inciting recurrence of HSV keratitis has been investigated in the laboratory. Rabbits infected with HSV type 1 demonstrated viral reactivation after exposure of the corneal stroma to 193-nm ultraviolet radiation during PRK and LASIK. Pretreatment with systemic valacyclovir before the laser treatment decreased the rate of recurrence in the rabbit model. In another study, a rabbit latency model demonstrated that systemic valacyclovir reduced ocular shedding of HSV after LASIK.

Reactivation of HSV keratitis has been reported in humans after radial keratotomy (RK), phototherapeutic keratectomy (PTK), PRK, and LASIK. Fagerholm and colleagues reported a 25% incidence of postoperative HSV keratitis 17 months after PTK for surface irregularities from prior HSV infections, compared with an 18% recurrence rate in an equivalent time period prior to PTK. The authors concluded that the procedure does not seem to significantly increase the incidence of recurrences.

A retrospective review of 13,200 PRK-treated eyes with no history of corneal HSV revealed a 0.14% incidence of HSV keratitis. Of these cases, 16.5% occurred within 10 days of the procedure; the authors postulated that this finding may indicate a direct effect of the excimer ultraviolet laser. In 78% of cases, HSV keratitis occurred within 15 weeks, which could be related to the corticosteroid therapy.

Reactivation of herpes zoster ophthalmicus was also reported in 1 case after LASIK, in association with vesiculoulcerative lesions on the tip of the nose. The few cases in which herpes zoster ophthalmicus was reactivated responded to topical and

oral antiviral treatment with excellent recovery of vision. There are anecdotal reports of flap interface inflammation resembling diffuse lamellar keratitis after LASIK in patients with herpes simplex or herpes zoster keratitis. In these cases, topical corticosteroids may also be required.

Because of the potential for loss of vision from recurrence of HSV keratitis, some refractive surgeons consider prior herpetic keratitis a contraindication to refractive surgery. Surgeons should exercise caution in deciding whether to perform PRK, PTK, or LASIK in a patient with a history of prior ocular herpetic infection. Results of the Herpetic Eye Disease Study (HEDS) showed only a 50% reduction in the risk of recurrence with a prophylactic dose of oral acyclovir over the course of 1 year in patients with latent HSV and no inciting factors, such as treatment with an excimer laser. Patients with pronounced corneal hypoesthesia or anesthesia, vascularization, thinning and scarring, or recent herpetic attacks should not be considered candidates for refractive surgery.

Some surgeons will consider performing LASIK in a patient with a history of HSV keratitis who has not had any recent recurrences and who has good corneal sensation, minimal or no corneal vascularization or scarring, and normal CDVA, although the use of LASIK in such patients is controversial. However, note that the use of LASIK in patients with prior HSV keratitis is an extremely rare occurrence. Preoperative and postoperative prophylaxis with systemic antiviral drugs should be strongly considered. Any patient with a history of herpes simplex or herpes zoster keratitis must be counseled about the continued risk of recurrence and its concomitant potential for loss of vision after excimer laser vision correction.

Asbell PA. Valacyclovir for the prevention of recurrent herpes simplex virus eye disease after excimer laser photokeratectomy. *Trans Am Ophthalmol Soc.* 2000;98:285-303.

de Rojas Silva V, Rodriguez-Conde R, Cobo-Soriano R, Beltran J, Llovet F, Baviera J. Laser in situ keratomileusis in patients with a history of ocular herpes. *J Cataract Refract Surg.* 2007;33(11):1855-1859.

Dhaliwal DK, Romanowski EG, Yates KA, et al. Valacyclovir inhibition of recovery of ocular herpes simplex virus type 1 after experimental reactivation by laser in situ keratomileusis. *J Cataract Refract Surg.* 2001;27(8):1288-1293.

Jain V, Pineda R. Reactivated herpetic keratitis following laser in situ keratomileusis. *J Cataract Refract Surg.* 2009;35(5):946-948.

Levy J, Lapid-Gortzak R, Klemperer I, Lifshitz T. Herpes simplex virus keratitis after laser in situ keratomileusis. *J Refract Surg.* 2005;21(4):400-402.

Nagy ZZ, Keleman E, Kovacs A. Herpes simplex keratitis after photorefractive keratectomy. *J Cataract Refract Surg.* 2003;29(1):222-223.

Keratoconus

Keratoconus is generally considered a contraindication to LASIK and surface ablation. Weakening of the cornea, as a result of the loss of structural integrity involved in creating the LASIK flap, and removal of tissue significantly increase the risk of progressive ectasia, which may occur even if the keratoconus was stable prior to treatment. Although advanced stages of keratoconus can be diagnosed by slit-lamp examination and manual keratometry, more sensitive analyses using corneal topography and corneal pachymetry can reveal findings early in the disease process. No specific

agreed-upon test or measurement is diagnostic of a corneal ectatic disorder, but both corneal topography and corneal pachymetry should be part of the evaluation because subtle corneal thinning or curvature changes can be overlooked on slit-lamp evaluation.

The existing literature on ectasia and longitudinal studies of the fellow eye of patients with unilateral keratoconus indicate that asymmetric inferior corneal steepening or asymmetric bow-tie topographic patterns with skewed steep radial axes above and below the horizontal meridian (Fig 10-1) are risk factors for progression to keratoconus and post-LASIK ectasia. LASIK using current technology should not be considered in such patients. Patients with an inferior "crab-claw" pattern accompanied by central flattening are at risk of developing pellucid marginal degeneration (PMD) or a "low-sagging cone" variety of keratoconus, even in the absence of clinical signs (Fig 10-2). This pattern may be designated "pellucid suspect," and LASIK should be avoided in eyes that exhibit it.

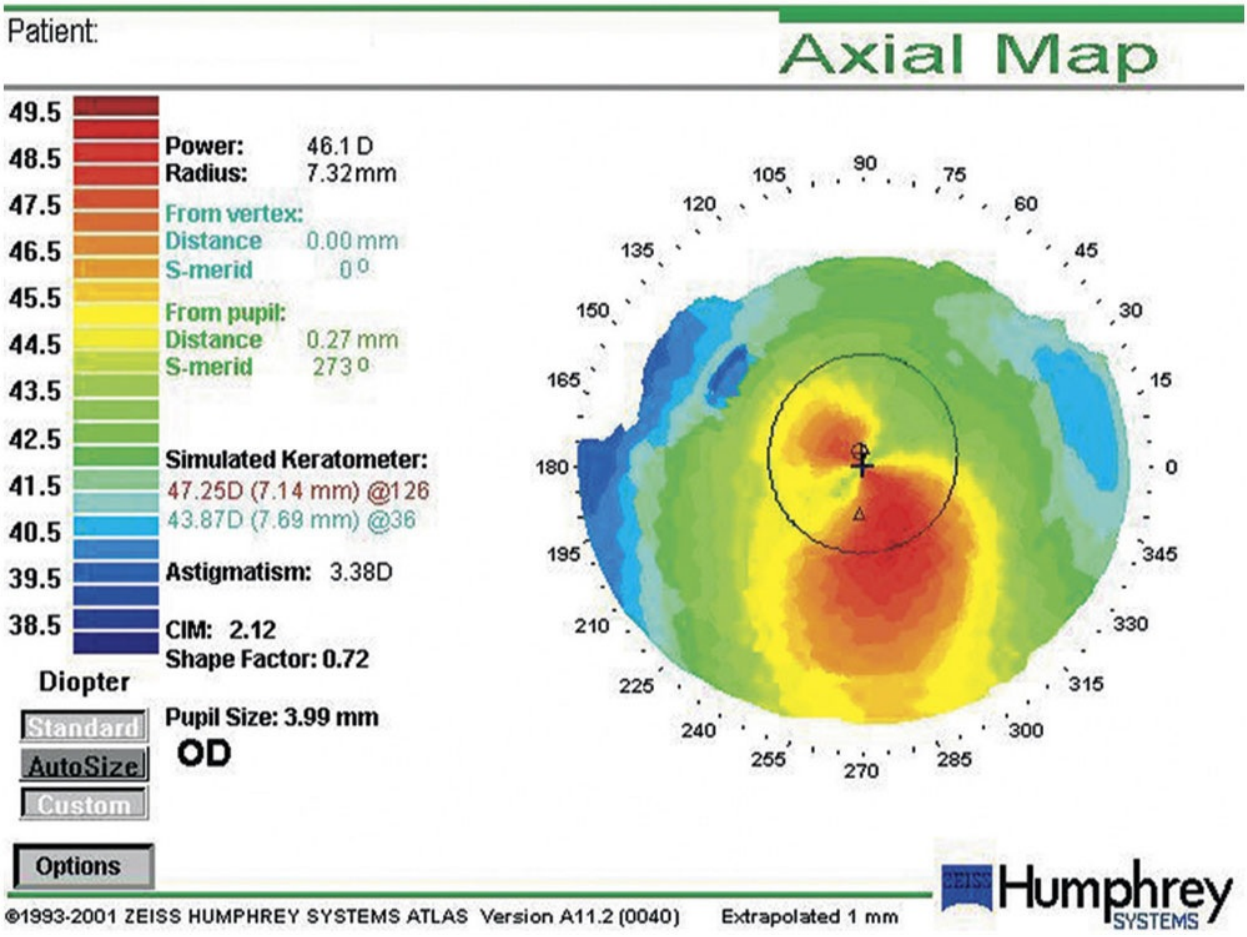

Figure 10-1 Corneal topographic map indicating forme fruste keratoconus with asymmetric irregular steepening. *(Courtesy of Eric D. Donnenfeld, MD.)*

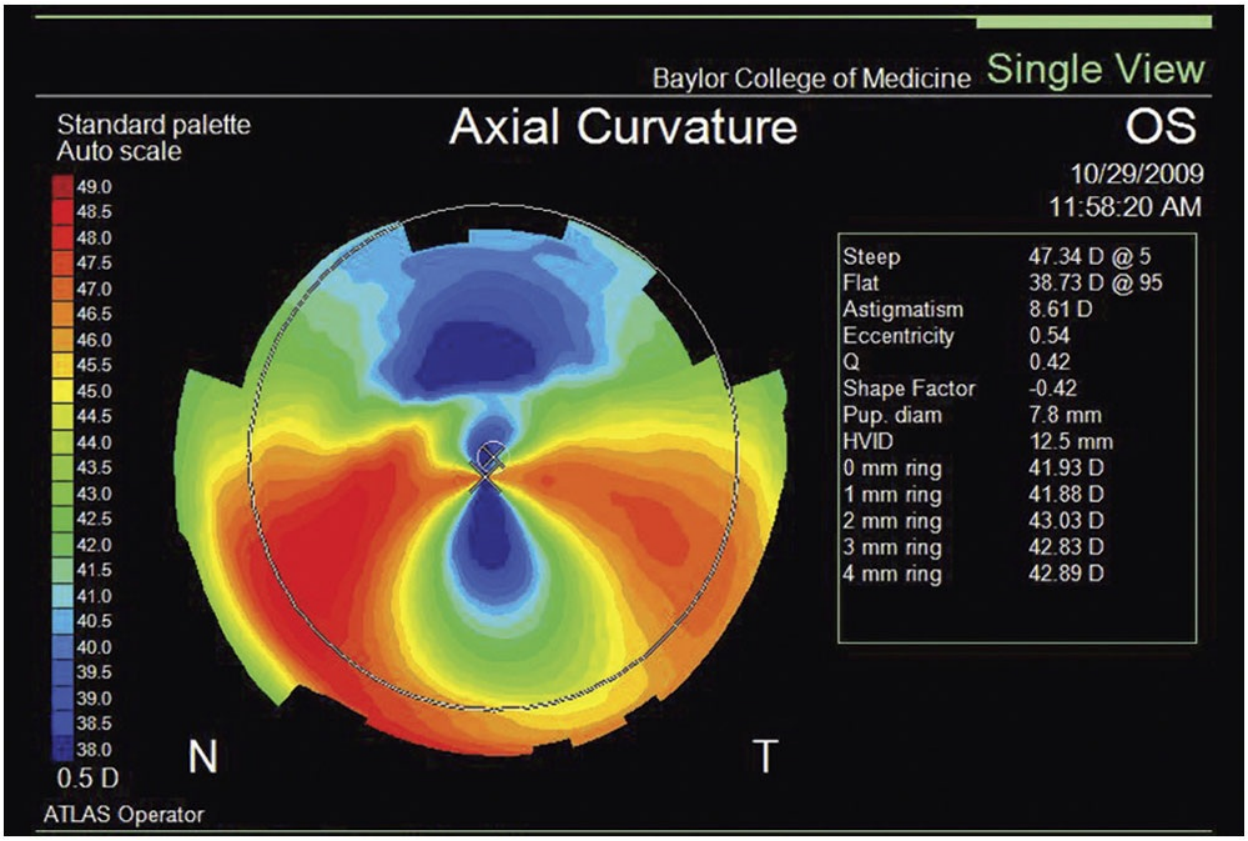

Figure 10-2 Topography of pellucid marginal degeneration showing the "crab-claw" appearance. N = nasal; T = temporal. *(Courtesy of M. Bowes Hamill, MD.)*

Global pachymetry measurements may be important to help rule out forme fruste keratoconus. Posterior curvature evaluation with new corneal imaging technology may also prove significant (Fig 10-3). Often, the refractive surgeon is the first physician to inform a refractive surgery candidate that she or he has corneal ectatic disease. The patient may have excellent vision with glasses or contact lenses and may be seeking the convenience of a more permanent correction through LASIK. It is important that the ophthalmologist clearly convey that, although the presence of forme fruste keratoconus does not necessarily indicate the presence of a progressive disease, refractive surgery should not be performed because of the potential for unpredictable results and loss of vision.

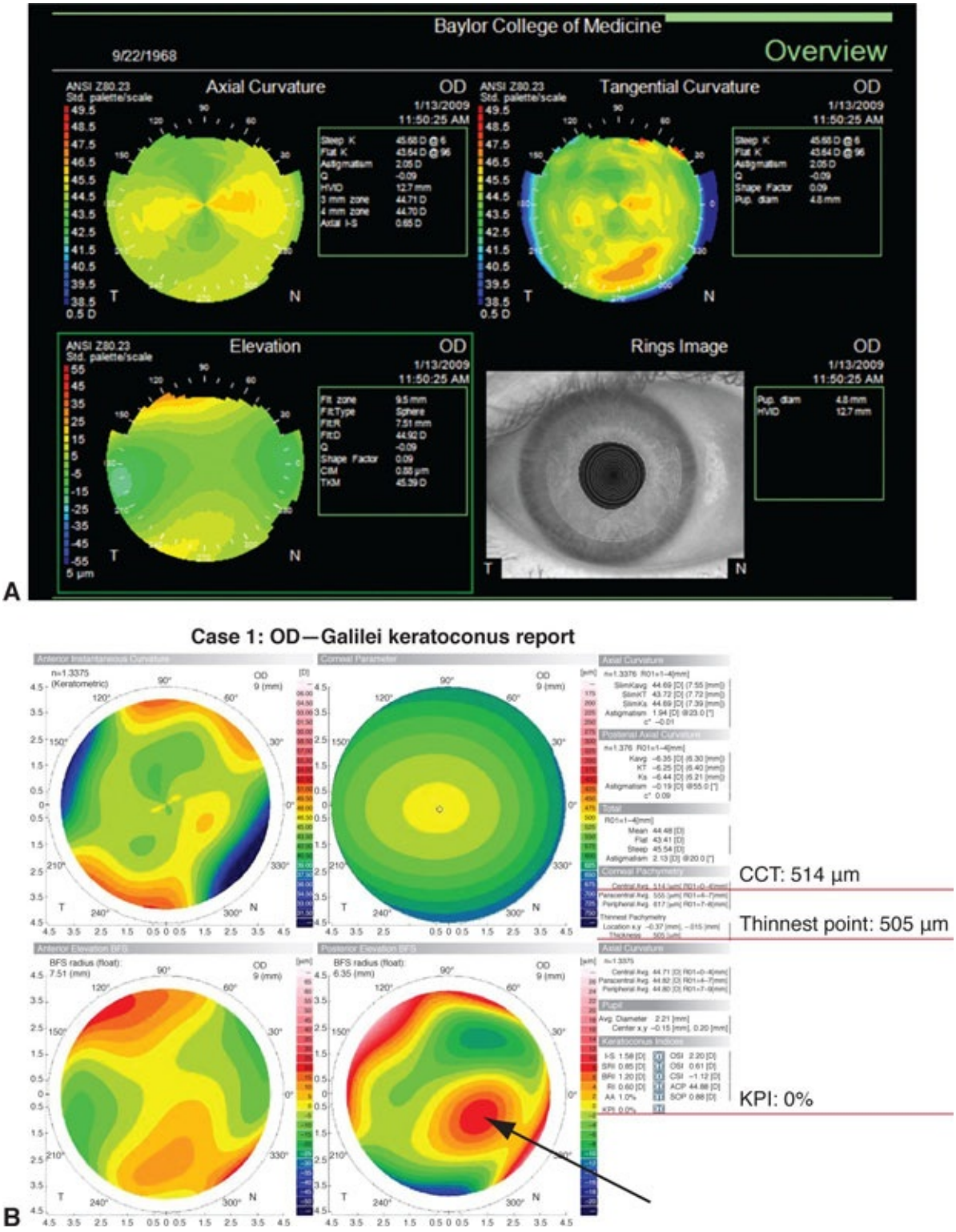

Figure 10-3 A 40-year-old man wishes to correct his myopia and high astigmatism. He does not wear contact lenses. His manifest refraction is -4.00 +3.00 x 4 OD and -3.75 +3.00 x 168 OS; corrected distance visual acuity is 20/20 OU. Both eyes appear normal on slit-lamp examination. **A,** Although the topographic examination appears normal on first glance, there is subtle inferior steepening that requires

close inspection to appreciate. **B,** A clearly abnormal hot spot *(arrow)* is apparent on the Galilei dual Scheimpflug analyzer posterior elevation map, which may indicate forme fruste keratoconus. Technologies that evaluate regional corneal thickness and posterior corneal elevation in addition to anterior curvature may improve the identification of patients with early keratoconus. CCT = central corneal thickness; KPI = keratoconus prediction index. *(Courtesy of Douglas D. Koch, MD.)*

Intrastromal corneal ring segments are FDA approved for keratoconus (see Chapter 4). Corneal collagen crosslinking (CXL) with riboflavin administration and ultraviolet A exposure shows promising early results and may prove effective in preventing and treating corneal ectasia (see Chapter 7 and BCSC Section 8, *External Disease and Cornea*). Although some early case reports have suggested that combining CXL treatments with PRK may offer some benefit to keratoconus patients, the clinical experience remains very preliminary.

Alessio G, L'Abbate M, Sborgia C, La Tegola MG. Photorefractive keratectomy followed by cross-linking versus cross-linking alone for management of progressive keratoconus: two-year follow-up. *Am J Ophthalmol.* 2013;155(1):54-65. Epub 2012 Sep 27.

Ambrosio R Jr, Alonso RS, Luz A, Coca Velarde LG. Corneal-thickness spatial profile and corneal-volume distribution: tomographic indices to detect keratoconus. *J Cataract Refract Surg.* 2006;32(11):1851-1859.

Belin MW, Asota IM, Ambrosio R, Khachikian SS. What's in a name: keratoconus, pellucid marginal degeneration, and related thinning disorders. *Am J Ophthalmol.* 2011;152(2): 157-162. Epub 2011 Jun 25.

Binder PS, Lindstrom RL, Stulting RD, et al. Keratoconus and corneal ectasia after LASIK. *J Cataract Refract Surg.* 2005;31(11):2035-2038.

Kilic A, Colin J. Advances in the surgical treatment of keratoconus. *Focal Points: Clinical Modules for Ophthalmologists*. San Francisco: American Academy of Ophthalmology; 2012: module 2.

Randleman JB, Russell B, Ward MA, Thompson KP, Stulting RD. Risk factors and prognosis for corneal ectasia after LASIK. *Ophthalmology.* 2003;110(2):267-275.

Saad A, Gatinel D. Topographic and tomographic properties of forme fruste keratoconus corneas. *Invest Ophthalmol Vis Sci.* 2010;51(11):5546-5555. Epub 2010 Jun 16.

Post-Penetrating Keratoplasty

Refractive unpredictability after penetrating keratoplasty (PKP) is extremely common owing to the inherent imprecision of the operation. Most series document a mean postoperative astigmatism of 4.00-5.00 D. In many cases, these refractive errors are not amenable to spectacle correction, and between 10% and 30% of patients require contact lens correction to achieve good vision after PKP. However, contact lens fitting may not be successful in this patient population because of either the abnormal corneal curvature or the patient's inability to tolerate or manipulate a contact lens.

Surgical alternatives for the correction of post-PKP astigmatism include corneal relaxing incisions, compression sutures, and wedge resections. In a series of 201 corneal transplants for keratoconus, 18% of patients required refractive surgery to correct the astigmatism. Although these procedures can significantly decrease corneal cylinder and are highly effective, they have minimal effect on spherical equivalent. In addition, they can be unpredictable and may destabilize the graft-host wound.

Patients with pseudophakia who have significant anisometropia after PKP surgery may be candidates for intraocular lens (IOL) exchange or piggyback IOL implantation; new options include toric IOLs (see Chapter 8). These alternatives require another intraocular procedure, which increases the risk of endothelial decompensation,

glaucoma, and cystoid macular edema and may incite graft rejection.

Given the successful use of the excimer laser in treating myopia and astigmatism, PRK has been studied and used to treat post-PKP refractive errors. PRK has the disadvantages associated with epithelial removal in a corneal transplant and may result in corneal haze when high refractive errors are treated. With the use of prophylactic topical mitomycin C, PRK has become a more common treatment option for refractive errors after PKP. Although the refractive results are often good, PRK in post-PKP patients is generally less predictable and less effective than it is for naturally occurring astigmatism and myopia.

LASIK after PKP is subject to the same patient-selection constraints as conventional LASIK is. Without extenuating circumstances, monocular patients or patients with limited vision potential in the fellow eye are not candidates. In addition, patients with a wound-healing disorder, significant dry eye syndrome, or a collagen-vascular disease should be offered other options. Finally, patients should have realistic expectations for their rehabilitation after post-PKP LASIK. The goal of LASIK following PKP is to return the patient to spectacle-corrected binocularity or to enable the patient to wear contact lenses successfully, as the accuracy of the procedure is less predictable than that of conventional LASIK. Also, note that there are no FDA-approved procedures to treat irregular astigmatism. Pre-operative evaluation of the post-PKP patient who is considering refractive surgery should include the original indications for the PKP. Patients with low endothelial cell counts may be at increased risk of flap dislocation after LASIK because of impairment of the endothelial cell pump function.

Optimal timing of refractive surgery after PKP is controversial. All sutures should be removed, and the refraction should be stable. To avoid wound dehiscence, many surgeons wait at least 1 year after PKP, and an additional 4 months after all sutures are removed, before performing the refractive surgery. An interval of at least 18-24 months after PKP provides sufficient wound healing in most cases. No matter how much time has elapsed since the PKP surgery, the graft-host wound should be carefully inspected to make sure it appears strong enough to undergo a LASIK procedure, as there is a small but significant risk of keratoplasty wound dehiscence during application of the vacuum ring used to create the LASIK flap.

Refraction and corneal topography should be stable, as documented by 2 consecutive readings on separate visits at least 1 month apart. Areas of suspected ectasia should be confirmed with pachymetry to avoid perforation. Refractive surgery should be avoided if the corneal graft shows evidence of inflammation, diffuse vascularization, ectasia, inadequate healing of the graft-host interface, or refractive instability or if there are signs of rejection or decompensation.

Because eye alignment under the laser is crucial for accurate treatment of astigmatism, some surgeons mark the vertical or horizontal axis of the cornea at the slit

lamp before placing the patient under the laser. Suction time should be minimized to decrease stress on the corneal wound and to lessen the potential for the devastating complication of wound dehiscence. If the corneal curvature is very steep, cutting a thicker flap during the microkeratome pass may decrease the risk of buttonhole formation. PRK should also be considered in steep corneas to avoid flap complications.

Another potential problem specific to post-PKP LASIK is that the creation of a lamellar flap may itself cause a change in the amount and axis of the astigmatism. Therefore, some surgeons perform LASIK in 2 stages. First, the flap is cut and laid back down. Second, several weeks later, after the curvature and refraction have stabilized, the flap is lifted and laser ablation is performed. Some reports describe minimal refractive changes after flap creation, and some surgeons prefer to perform LASIK in 1 step to avoid increasing the potential for the complications associated with performing 2 separate procedures, including infection, graft rejection, and epithelial ingrowth. Flap retraction and necrosis have been reported in patients undergoing LASIK after keratoplasty.

The mean percentage reduction of astigmatism after LASIK following PKP ranges from 54.0% to 87.9%. Although most series report improvement in UDVA, up to 42.9% of patients require enhancement because of cylindrical undercorrection. In addition, up to 35% of patients lose 1 line of CDVA. Corneal graft rejection has been described after PRK; thus, higher and more prolonged dosing with topical corticosteroids should be prescribed for post-PKP refractive surgery patients to decrease this risk.

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Sharma N, Sinha R, Vajpayee RB. Corneal lamellar flap retraction after LASIK following penetrating keratoplasty. *Cornea*. 2006;25(4):496.

Ocular Hypertension and Glaucoma

An estimated 9%-28% of patients with myopia have primary open-angle glaucoma (POAG). Consequently, it is likely that some patients with glaucoma will request refractive surgery.

Of particular concern in patients with ocular hypertension or POAG is the effect of the acute rise in intraocular pressure (IOP) to more than 65 mm Hg when suction is applied while the stromal flap is cut for LASIK or the epithelial flap for epipolis LASIK (epi-LASIK). Although healthy optic nerves seem to tolerate this degree of IOP elevation, ophthalmologists do not yet entirely understand the effect on compromised

optic nerves. There have been reports of new visual field defects arising immediately after LASIK that are attributed to mechanical compression or ischemia of the optic nerve head from the temporary increase in IOP.

Evaluation of a patient with ocular hypertension or POAG includes a complete history and ocular examination with peripheral visual field testing and corneal pachymetry. A history of poor IOP control, nonadherence to treatment, maximal medical therapy, or prior surgical interventions may suggest progressive disease, which may contraindicate refractive surgery. The surgeon should also note the status of the angle, the presence and amount of optic nerve cupping, and the degree of visual field loss.

Several reports have confirmed that central corneal thickness affects the Goldmann applanation tonometry (GAT) measurement of IOP (see the section Glaucoma After Refractive Surgery in Chapter 11). The principle of applanation tonometry assumes a corneal thickness of 520 mm. Studies have demonstrated that thinner-than-normal corneas give falsely low IOP readings, whereas thicker corneas give falsely high readings. For example, IOP is underestimated by approximately 5.2 mm Hg in a cornea with a central thickness of 450 mm. Although all reports agree that central corneal thickness affects GAT IOP measurement, there is no consensus on a specific formula to compensate for this effect in clinical practice.

In the treatment of myopia, LASIK and surface ablation procedures remove tissue to reduce the steepness of the cornea; this sculpting process creates a thinner central cornea, which leads to artifactually low IOP measurements postoperatively. Such inaccurately low central applanation tonometry measurements hinder the diagnosis of corticosteroid-induced glaucoma after keratorefractive procedures, resulting in optic nerve cupping, visual field loss, and decreased visual acuity (Fig 10-4).

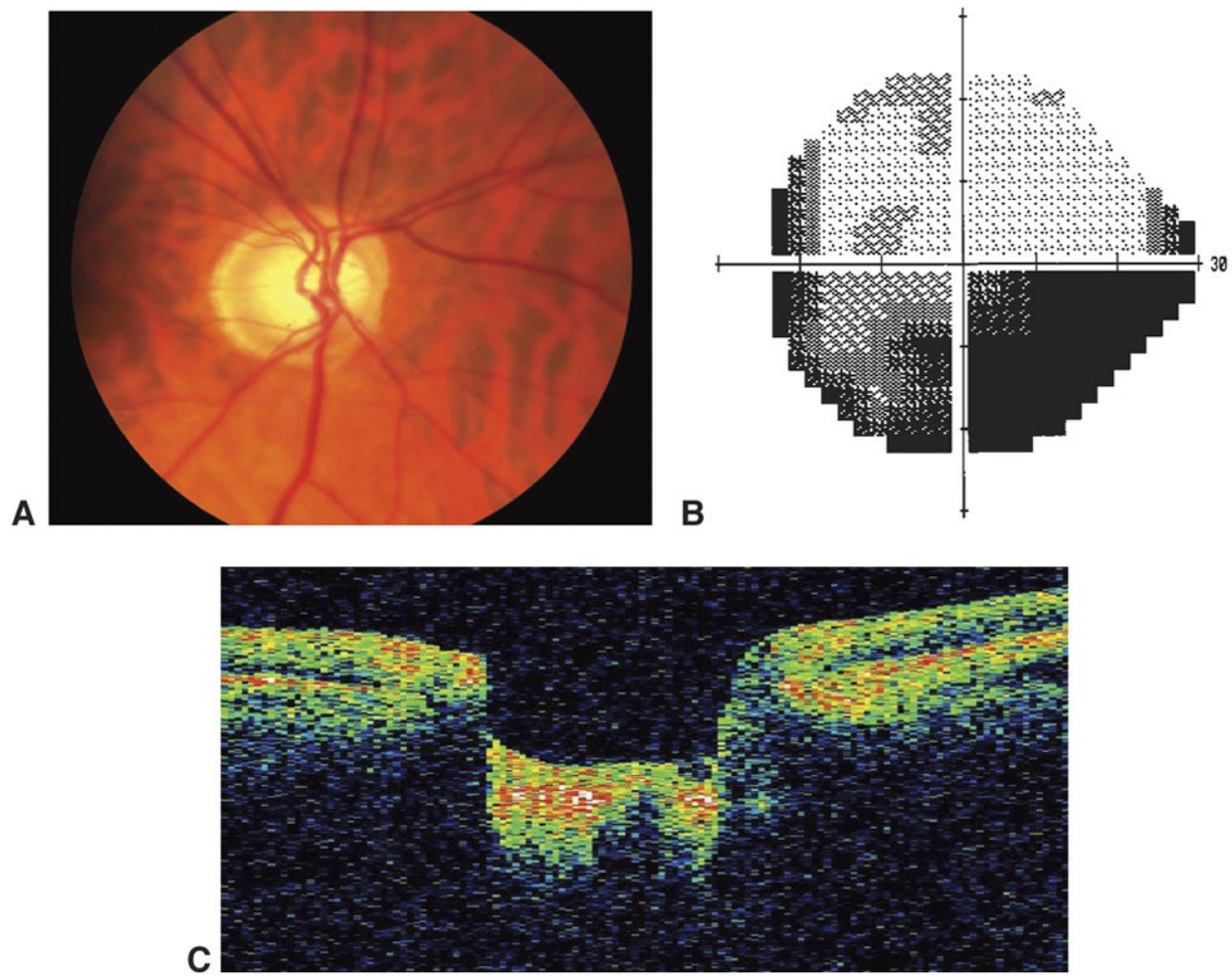

Figure 10-4 Glaucomatous optic nerve atrophy in a patient with "normal" intraocular pressure (IOP) after laser in situ keratomileusis (LASIK). **A,** Fundus photograph demonstrating increased cup-disc ratio in a patient who received a diagnosis of glaucoma 1 year after LASIK. The patient had decreased vision, with corrected distance visual acuity of 20/40 and IOP of 21 mm Hg. **B,** Humphrey 24-2 visual field with extensive inferior arcuate visual field loss corresponding to thinning of the superior optic nerve rim. **C,** Optical coherence tomography image demonstrates marked optic nerve cupping. *(Parts A and B courtesy of Jayne S. Weiss, MD; part C courtesy of Steven I. Rosenfeld, MD.)*

Because of the difficulty that PRK and LASIK cause in the accurate measurement of IOP, these refractive procedures should not be considered for a patient whose IOP is poorly controlled. Furthermore, patients should be advised of the effect of refractive surgery on their IOP measurements and urged to inform future ophthalmologists about their surgery. Patients should be referred to a glaucoma specialist when indicated.

Patients with ocular hypertension can often safely undergo refractive surgery. Such patients must be counseled preoperatively that refractive surgery treats only the refractive error and not the natural history of the ocular hypertension, which can sometimes progress to glaucoma, accompanied by optic nerve cupping and visual field loss. The ophthalmologist should pay particular attention to the risk factors for

progression to glaucoma, including older age, reduced corneal thickness, increased cup-disc ratio, and elevated IOP. Each patient needs to understand that after excimer laser ablation, it is more difficult to accurately assess IOP.

The decision about whether to perform refractive surgery in a patient with glaucoma is controversial. There are no long-term studies on refractive surgery in this population. LASIK is contraindicated in any patient with marked optic nerve cupping, visual field loss, or visual acuity loss. The refractive surgeon may ask the patient to sign an ancillary consent form that documents the patient's understanding that POAG may cause progressive loss of vision independent of any refractive surgery and that IOP elevation during a LASIK or epi-LASIK procedure, or following LASIK or surface ablation (often due to a corticosteroid response), can cause glaucoma progression.

The surgeon should be aware that placement of a suction ring may not be possible if there is a functioning filtering bleb. In rare cases in which both filtering surgery and LASIK are being planned, it is preferable to perform LASIK before the filter is placed. Suction time should be minimized to decrease the chance of optic nerve damage from the transient increase in IOP. Alternatively, PRK or laser subepithelial keratomileusis (LASEK) may be preferable because each avoids the IOP rise associated with LASIK flap creation. The surgeon must exercise caution when using postoperative corticosteroids because of their potential for elevating IOP. The patient should be informed as to when to resume postoperative topical medications for glaucoma. Finally, to avoid trauma to the flap, IOP should generally not be checked for at least 72 hours.

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Retinal Disease

High myopia

Patients with high myopia are at increased risk of retinal tears and detachment. A thorough, dilated retinal examination (including scleral depression, if indicated) should be performed on all patients with high myopia, and a referral to a retina specialist

should be considered for patients with predisposing retinal pathology. One study of 4800 consecutive patients in a private refractive surgery practice found that 52 (1.1%) had posterior segment pathology that required intervention. Another study of 29,916 myopic and hyperopic eyes undergoing LASIK demonstrated that 1.5% of patients required preoperative treatment of retinal pathology.

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Retinal detachment

Patients with high myopia should be counseled that refractive surgery corrects only the refractive aspect of the myopia and not the natural history of the highly myopic eye with its known complications. Such patients remain at risk of retinal tears and detachment throughout their lives, despite refractive surgery.

Although no causal link has been established between retinal detachment and excimer laser refractive surgery, the potential adverse effects should be considered. The rapid increase and then decrease in IOP could theoretically stretch the vitreous base, and the acoustic shock waves from the laser could play a role in the development of a posterior vitreous detachment. Although the actual risk to eyes with high myopia or preexisting retinal pathology has not been determined through well-controlled, long-term studies, current data suggest that radial keratotomy, surface ablation, and LASIK do not appear to increase the incidence of retinal detachment. The occurrence of retinal detachment after LASIK ranges from 0.034% to 0.250%. In a series of 1554 eyes that underwent LASIK for myopia with a mean refractive error of -13.52 +- 3.38 D, 4 eyes (0.25%) developed retinal detachments at 11.25 +- 8.53 months after the procedure. Three of the eyes had retinal flap tears, and 1 eye had an atrophic hole. There was no statistically significant difference in CDVA before and after conventional retinal reattachment surgery. A myopic shift did result from the scleral buckle, however.

In a study of 38,823 eyes with a mean myopia of -6.00 D, the frequency of rhegmatogenous retinal detachments at a mean of 16.3 months after LASIK was 0.8%. The eyes that developed retinal detachments had a mean preoperative myopia of -8.75 D. In a retrospective review, Blumenkranz reported that the frequency of retinal detachment after excimer laser treatment was similar to the frequency in the general population, averaging 0.034% over 2 years. The operating retinal surgeon must be informed that LASIK has previously been performed because of the potential for flap dehiscence during retinal detachment surgery, especially during corneal epithelial scraping.

Highly myopic eyes undergoing phakic IOL procedures are at risk of retinal detachment from the underlying high myopia, as well as from the intraocular surgery. A retinal detachment rate of 4.8% was reported in a study of phakic IOLs used to correct high myopia.

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Previous retinal detachment surgery

Patients who have had prior scleral buckle surgery or vitrectomy may seek refractive surgery because of resultant myopia. Prior retinal detachment surgery can result in a myopic shift because of axial elongation of the eye from indentation of the scleral buckle. Refractive surgery can be considered in selected cases that have symptomatic anisometropia with good CDVA. The surgeon should determine whether the scleral buckle or conjunctival scarring will interfere with placement of the suction ring in preparation for creation of the LASIK flap. If it will, PRK or LASEK may be considered instead of LASIK. Preoperative pathology, including preexisting macular pathology, will continue to limit UDVA and CDVA after refractive surgery. There are no published long-term series of the results of excimer laser vision correction in patients with prior retinal detachment surgery. Both the patient and the surgeon should realize that the final visual results may not be as predictable as after other refractive surgeries. Patients should also be aware that if the scleral buckle needs to be removed, the refractive error could change dramatically. Unexpected corneal steepening has been reported in patients undergoing LASIK with previously placed scleral buckles.

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Amblyopia and Strabismus in Adults and Children

Amblyopia and anisometropic amblyopia

Amblyopia is defined as a decrease in visual acuity without evidence of organic eye disease, typically resulting from unequal visual stimulation during the period of visual development. The prevalence of amblyopia is 2%-4% of the US population; up to half of these cases represent anisometropic amblyopia. Patients with anisometropia of >3.00 D between the 2 eyes are likely to develop amblyopia that may be more resistant to traditional amblyopia therapy, such as glasses, contact lenses, patching, or atropine penalization therapy, partly because of the large aniseikonia induced.

Evaluation of a patient with amblyopia should include a thorough medical history to identify any known cause of amblyopia, a history of ocular disease or surgery, assessment of ocular alignment and motility, and a comprehensive anterior segment and retinal examination. Patients should be referred to a strabismus specialist when indicated. Preoperative counseling of a patient with amblyopia must emphasize that, even after refractive surgery, the vision in the amblyopic eye will not be as good as that

in the nonamblyopic eye. The patient should also understand that CDVA will be the same, or nearly so, with or without refractive surgery.

Typically, refractive surgery is performed in this group of patients to treat high anisometropia or astigmatism in 1 eye or high refractive error in both eyes. Laser vision correction and phakic IOL implantation have been successfully performed in the more myopic, amblyopic eye in adult patients with anisometropic amblyopia. Some studies suggest that postoperative CDVA may even improve modestly compared with preoperative levels in a subset of adults who undergo refractive surgery. In a study examining phakic IOL implantation in patients with >3.00 D of anisometropia, an average of 3 lines of vision were gained; 91% of eyes gained >1 line, and no eyes lost best-corrected vision. This improvement in vision was attributed to an increase in magnification and a decrease in optical aberrations, rather than an actual improvement in the amblyopia.

Performing refractive surgery in the normal eye of the adult patient with amblyopia, however, is controversial. The decision to do so depends on many factors, including the level of CDVA in the amblyopic eye and the normal eye as well as the ocular alignment. To increase safety, unilateral surgery in the amblyopic eye followed by surgery in the nonamblyopic eye can be considered. However, ocular alignment deviation has been reported after unilateral LASIK for high myopia because of focus disparity causing esodeviation and impairment of fusion. In some cases, a preoperative contact lens trial may help in assessing this potential risk.

Consider a patient with anisometropic amblyopia whose vision is corrected to 20/40 with -7.00 D in the right eye and to 20/20 with -1.00 D in the left eye. This patient may be an excellent candidate for refractive surgery in the amblyopic right eye because he or she probably cannot tolerate glasses to correct the anisometropic amblyopia and may not tolerate contact lenses. Even if the post-LASIK UDVA were worse than 20/40 in the amblyopic eye, it would be better than the pre-LASIK UDVA of counting fingers.

If the postoperative UDVA in the amblyopic right eye improved to 20/40, the patient could be considered for laser vision correction in the left eye for -1.00 D. However, if the patient had presbyopia, some surgeons would discourage further intervention and discuss potential advantages of the low myopia. In a younger patient with accommodation, some surgeons would inform the patient of the potential risks associated with treating the better eye but would perform the excimer laser vision correction.

If CDVA in the amblyopic eye were 20/200 or worse, the patient would be considered legally blind if he or she were to lose significant vision after laser refractive surgery in the normal eye. In such cases, refractive surgery in the amblyopic eye may or may not offer much benefit, and refractive surgery in the nonamblyopic eye should be regarded as contraindicated in most cases. In the extenuating circumstances

for which such surgery might be considered, the physician and patient should have an extensive discussion about the potential risks. Generally, if the patient would not be happy with the vision in the amblyopic eye alone in the event that something adverse happened to the better eye, then refractive surgery should not be performed on the better eye.

Persistent diplopia has been reported after bilateral LASIK in a patient with anisometropic amblyopia and a history of intermittent diplopia in childhood. Preoperatively, this type of patient can adjust to the disparity of the retinal image sizes with spectacle correction. Refractive surgery, however, can result in a dissimilar retinal image size that the patient cannot fuse, resulting in diplopia. This type of diplopia cannot be treated by prisms or muscle surgery.

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Refractive surgery in children

In children, refractive surgery is controversial because their eyes and refractive status continue to change. Additional studies on the growing eye and the long-term effect of excimer laser treatment and phakic IOLs on the corneal endothelium and lens are needed to better assess the outcome of refractive surgery in children. Consequently, these procedures are typically regarded as investigational.

However, the literature is replete with reports of the successful performance of PRK, LASEK, LASIK, and phakic IOL implantation in children, mostly 8 years and older, when conventional therapies have failed. Most of these children underwent treatment for anisometropic amblyopia in the more myopic eye. In these studies, refractive error was decreased and visual acuity was maintained or improved in moderately amblyopic eyes. Refractive surgery did not improve CDVA or stereopsis in older children with densely amblyopic eyes. The limited effect on visual acuity was generally attributed to the fact that the children were beyond amblyogenic age. In one study, general anesthesia was used during performance of PRK in 40 children, ages 1-6 years, who were unable to wear glasses or contact lenses for high myopia or anisometropic amblyopia from myopia. Patients were treated for existing amblyopia, and mean CDVA improved from 20/70 to 20/40. The study found that 60% of eyes developed posttreatment corneal haze. Most patients demonstrated "increasing corneal clarity" within 1 year, although 2 of 27 patients required PTK for the corneal haze. Regression of effect was attributed to a vigorous healing response and the axial myopic shift associated with growth.

Several studies have reported successful implantation of phakic IOLs in children with high anisometropia and amblyopia. This technique eliminates the previously

mentioned corneal-wound-healing problems associated with keratorefractive procedures and may be considered when the refractive error is high and other traditional methods of amblyopia therapy have failed. Depending on the type of phakic IOL, however, other potentially serious complications may ensue, including progressive corneal endothelial cell loss, cataract formation, pupillary block glaucoma, and persistent inflammation, as well as the usual risks associated with intraocular surgery. Thus, phakic IOLs should be considered investigational in children, and larger clinical trials are necessary to adequately evaluate the safety and efficacy of this technique in this age group.

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Accommodative esotropia

Uncorrected hyperopia can stimulate an increase in accommodation, leading to accommodative convergence. Esotropia arises from insufficient fusional divergence. Traditional treatment includes correction of hyperopia with glasses or contact lenses and muscle surgery for any residual esotropia (see BCSC Section 6, *Pediatric Ophthalmology and Strabismus*). While glasses or contact lenses are being worn, the esotropia is usually not manifest. As a child ages, the hyperopia typically decreases, with concomitant resolution of the accommodative esotropia. If significant hyperopia persists, glasses or contact lenses continue to be needed to control the esotropia.

Before refractive surgery, it is important to perform an adequate cycloplegic refraction (using cyclopentylate, 1%) on patients younger than 35 years who have intermittent strabismus or phoria. Accurate refraction is necessary to avoid inducing postoperative hyperopia. Otherwise, the postoperative hyperopia may result in a new onset of esotropia with an accommodative element.

Several studies performed outside the United States report the use of PRK and LASIK for adults with accommodative esotropia. In one of the studies, orthophoria or microesotropia was achieved after LASIK for hyperopia in accommodative esotropia in a series of 9 patients older than 18 years. A second study demonstrated a reduction in the mean esotropia of 21 prism diopters (D) prior to LASIK to 3.7D after surgery. However, another study of LASIK in accommodative esotropia in patients 10-52 years of age found that 42% of these patients had no reduction in their esotropia.

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Systemic Conditions

Human Immunodeficiency Virus Infection

Little has been written about refractive surgery in patients with known human immunodeficiency virus (HIV) infection, and individual opinions vary. Note that the FDA recommends that patients with an immunodeficiency disease not undergo LASIK, regardless of the excimer platform, because the risk outweighs the benefit.

In a recent survey of members of the International Society of Refractive Surgery, 51% of respondents considered HIV-seropositive patients who did not have definite acquired immune deficiency syndrome (AIDS) to be acceptable refractive surgery candidates. Only 13% thought that patients with definite AIDS were candidates for refractive surgery, whereas 44% believed that the presence of AIDS was an absolute contraindication to refractive surgery. Some surgeons advise such patients against undergoing refractive surgery because of concerns about postoperative complications, including the increased risk of infection associated with immunosuppression. However, only 1 case of keratitis (a bilateral infection with *Staphylococcus aureus*) following LASIK in an HIV-seropositive patient has been reported.

An additional concern is the potential for aerosolizing live virus during laser ablation, which could pose a risk to laser-suite personnel. Because refractive surgeons may operate on patients who do not know they are infected with viruses such as HIV or one of the hepatitis viruses, universal precautions must be followed with all patients.

In 1 study, excimer laser ablation of a cornea infected with pseudorabies virus, a porcine-enveloped herpesvirus similar to HIV and herpes simplex virus (HSV), did not appear capable of causing infection by transmission through the air. The authors concluded that excimer laser ablation of the cornea in a patient infected with HIV is unlikely to pose a health hazard to the surgeon or assistants. Another study demonstrated that, after excimer laser ablation of infected corneal stroma, polymerase chain reaction did not detect viable varicella virus (200 nm in diameter) but did detect viable polio particles (70 nm in diameter).

Inhaled particles [?]5 mm in diameter are deposited in the bronchial, tracheal, nasopharyngeal, and nasal walls, and particles <2 mm in diameter are deposited in the bronchioles and alveoli. Even if viral particles are not viable, the excimer laser plume produces particles with a mean diameter of 0.22 mm. Although the health effects of inhaled particles from the plume have not yet been determined, there have been anecdotal reports of respiratory ailments such as chronic bronchitis in high-volume excimer laser refractive surgeons. Canister filter masks can exclude particles down to a

diameter of 0.1 mm and may be more protective than conventional surgical masks. In addition, evacuation of the laser plume potentially decreases the amount of breathable debris.

If a surgeon is considering performing excimer laser ablation in an HIV-infected patient who is not immunocompromised and has normal results on eye examination, extra precautions are warranted. The surgeon should counsel the patient about the visual risks of HIV infection and the lack of long-term follow-up results for refractive surgery in this population. The surgeon may also consider consulting with the physicians managing the patient's underlying disease, including specialists in infectious diseases. The surgeon may choose to treat 1 eye at a time on separate days and schedule the patient as the last patient of the day. In addition, the surgeon may consider implementing additional precautions for the operating room staff, such as wearing filter masks during the procedure and evacuating the laser plume.

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Diabetes Mellitus

In January 2009, the US National Institutes of Health reported a prevalence of 13% for diabetes mellitus in US adults aged 20 years and older. As the incidence of diabetes mellitus increases, so will the number of diabetic patients requesting refractive surgery. A patient with diabetes mellitus who is considering refractive surgery should have a thorough preoperative history and examination, and the surgeon should pay special attention to the presence of active diabetic ocular disease. The blood sugar of a diabetic patient must be well controlled at the time of examination to ensure an accurate refraction. A history of laser treatment for proliferative diabetic retinopathy or cystoid macular edema indicates visually significant diabetic complications that typically contraindicate refractive surgery. Ocular examination should include inspection of the corneal epithelium to check the health of the ocular surface, identification of cataract if present, and detailed retinal examination. Preoperative corneal sensation should be assessed because corneal anesthesia can impede epithelial healing.

A retrospective review 6 months after LASIK in 30 eyes of patients with diabetes mellitus revealed a complication rate of 47%, compared with a complication rate of 6.9% in the control group. The most common problems in this study were related to epithelial healing and included epithelial loosening and defects. A loss of [?]2 lines of CDVA was reported in <1% of both the diabetes mellitus and control groups. However, 6 of the 30 eyes in the diabetes mellitus group required a mean of 4.3 months to heal because of persistent epithelial defects. The authors concluded that the high complication rate in these patients was explained by unmasking subclinical diabetic keratopathy.

Another retrospective review of 24 patients with diabetes mellitus who underwent LASIK demonstrated that 63% achieved UDVA of 20/25 or better. Three of the 24 eyes had an epithelial defect after surgery, and epithelial ingrowth developed in 2 of these eyes. No eye lost CDVA. In contrast, Cobo-Soriano and colleagues evaluated 44 diabetic patients (both insulin-dependent and non-insulin-dependent) who underwent LASIK in a retrospective, observational, case-controlled study and reported no significant difference in perioperative and postoperative complications, including epithelial defects, epithelial ingrowth, and flap complications between diabetic patients and control subjects.

In light of these contradictory reports, refractive surgeons should exercise caution in the selection of patients with diabetes mellitus for refractive surgery. Intraoperative technique should be adjusted to ensure maximal epithelial health. To reduce corneal toxicity, the surgeon should use the minimal amount of topical anesthetic (preferably in the form of nonpreserved drops) immediately before performing the procedure. Patients with diabetes mellitus should be counseled preoperatively about the increased risk of postoperative complications and the possibility of a prolonged healing time after LASIK. They should also be informed that the procedure treats only the refractive error and not the natural history of the diabetes mellitus, which can lead to future diabetic ocular complications and associated loss of vision.

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Connective Tissue and Autoimmune Diseases

Most surgeons consider active, uncontrolled connective tissue diseases, such as rheumatoid arthritis, systemic lupus erythematosus, and polyarteritis nodosa, to be contraindications to refractive surgery. Reports in the literature have discussed corneal melting and perforation following cataract extraction in patients with these conditions, as well as corneal scarring after PRK in a patient with systemic lupus erythematosus.

However, 2 retrospective series suggest that refractive surgery may be considered in patients with well-controlled connective tissue or autoimmune disease. One retrospective study of 49 eyes in 26 patients with inactive or stable autoimmune disease who underwent LASIK revealed no postoperative corneal melting or persistent epithelial defects. Another retrospective study of 62 eyes of patients with autoimmune or connective tissue disorders who had undergone LASIK revealed that these eyes had a somewhat worse refractive outcome than eyes of control subjects but did not sustain

any severe complications such as corneal melting, laceration, or interface alterations.

Because the risk from an underlying disease cannot be quantified, increased caution should be exercised if refractive surgery is considered in patients with well-controlled autoimmune or connective tissue disease. Consultation with the treating physician, unilateral surgery, and ancillary informed consent should be considered.

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CHAPTER 11

Considerations After Refractive Surgery

The number of patients who have had refractive surgery continues to grow, and ophthalmologists are increasingly confronted with the management of post-refractive surgery patients with other ocular conditions, such as cataract, glaucoma, retinal detachment, corneal opacities, and irregular astigmatism. Calculation of the intraocular lens (IOL) power presents a particular challenge in this population.

IOL Calculations After Refractive Surgery

Although numerous formulas have been developed to calculate IOL power prior to cataract surgery for eyes that have undergone refractive surgery, these cases are still prone to refractive surprises. Currently, there is no infallible way to calculate IOL power for a patient who has undergone refractive surgery. Although the measurement of axial length should remain accurate after refractive surgery, determining the keratometric power of the post-refractive surgery cornea is problematic. The difficulty arises from several factors. Small, effective central optical zones after refractive surgery (especially after radial keratotomy [RK]) can lead to inaccurate measurements because keratometers and Placido disk-based corneal topography units measure the corneal curvature several millimeters away from the center of the cornea. In addition, the relationship between the anterior and posterior corneal curvatures may be considerably altered after refractive surgery (especially after laser ablative procedures), leading to inaccurate results. Generally, if standard keratometry readings are used to calculate IOL power for a previously myopic, post-refractive surgery eye, the postoperative refractive error will be hyperopic, because the keratometry readings are erroneously steeper than the true corneal power.

A variety of methods have been developed to better estimate the central corneal power after refractive surgery. None is perfectly accurate, and different methods can lead to disparate values. As many methods as possible should be used to calculate corneal power, and these estimates should be compared with each other, with standard keratometric readings, and with corneal topographic central power and simulated K

readings.

Newer corneal topography and tomography systems not based on the Placido disk claim to directly measure the central corneal curvature; such technology may make direct calculation of IOL power after refractive surgery more accurate. In addition, intraoperative wavefront aberrometer systems use Talbot-Moire-based interferometry to obtain real-time aphakic IOL calculations--an approach that has been shown to increase accuracy and improve refractive outcomes in cataract surgery.

Prior to cataract surgery, patients need to be informed that IOL power calculations are less accurate when performed after refractive surgery and that, despite maximum preoperative effort by the surgeon, additional surgery, such as surface ablation, laser in situ keratomileusis (LASIK), IOL exchange, or implantation of a piggyback IOL, may be required to attain a better refractive result. Cataract surgery done after RK frequently induces short-term corneal swelling with flattening and hyperopic shift. For this reason, in the event of a refractive "surprise," an IOL exchange should not be performed in post-RK eyes until the cornea and refraction stabilize, which may take several weeks to months. Corneal curvature does not tend to change as much when cataract surgery is performed after photorefractive keratectomy (PRK) or LASIK; thus, it may be possible to perform an IOL exchange earlier in these patients.

Eyes With Known Pre- and Post-Refractive Surgery Data

It is important for ophthalmologists to understand the *clinical history method*, in which pre-refractive surgery refraction and keratometry values, if available, combined with the current refraction and keratometry readings, are used to approximate the true post-refractive keratometry values for the central cornea. Unfortunately, even with these measurements, this approach has not been proven to be accurate. Pre-refractive surgery information should be kept by both the patient and the surgeon. To assist in retaining these data, the American Academy of Ophthalmology (AAO) has developed the K Card with its partner, the International Society of Refractive Surgery (ISRS); the card is accessible to ISRS members at the following URL: http://isrs.aao.org/resources.

The key concept is to understand what changes occur on the corneal surface with refractive surgery. To use the historical method, the ophthalmologist should have the pre-refractive surgery refraction and keratometry readings, and the change in spherical equivalent can be calculated at the spectacle plane or, better yet, at the corneal plane. The post-refractive surgery refraction must be stable and obtained several months after the refractive surgery but before the onset of induced myopia from the developing nuclear sclerotic cataract. For example:

Preoperative average keratometry: 44.00 D
Preoperative spherical equivalent refraction (vertex distance 12 mm): -8.00 D
Preoperative refraction at the corneal plane: -8.00 D/(1 - [0.012 x -8.00 D]) = -7.30

D
Postoperative spherical equivalent refraction (vertex distance 12 mm): -1.00 D
Postoperative refraction at the corneal plane: -1.00 D/(1 - [0.012 x -1.00 D]) = -0.98 D
Change in manifest refraction at the corneal plane: -7.30 D - (-0.98 D) = -6.32 D
Postoperative estimated keratometry: 44.00 - 6.32 D = 37.68 D

Eyes With No Preoperative Information

When no preoperative information is available, the *hard contact lens method* can be used to calculate corneal power. This method is quite accurate in theory but, unfortunately, not very useful in clinical practice. The corrected distance visual acuity (CDVA, also called *best-corrected visual acuity, BCVA*) needs to be at least 20/80 for this approach to work. First, a baseline manifest refraction is performed and then a plano hard contact lens of known base curve (power) is placed on the eye, and another manifest refraction is performed. If the manifest refraction does not change, then the cornea has the same power as the contact lens. If the refraction is more myopic, the contact lens is steeper (more powerful) than the cornea by the amount of change in the refraction; the reverse holds true if the refraction is more hyperopic. For example:

Current spherical equivalent manifest refraction: -1.00 D
A hard contact lens of known base curve (8.7 mm) and power (37.00 D) is placed
Overrefraction: +2.00 D
Change in refraction: +2.00 D - (-1.00 D) = +3.00 D
Calculation of corneal power: 37.00 D + 3.00 D = 40.00 D

The ASCRS Online Post-Refractive IOL Power Calculator

A particularly useful resource for calculating IOL power in a post-refractive surgery patient has been developed by Warren Hill, MD; Li Wang, MD, PhD; and Douglas D. Koch, MD. It is available on the website of the American Society of Cataract and Refractive Surgery (ASCRS) and directly at http://iolcalc.org.

To use this IOL calculator, the surgeon selects the appropriate prior refractive surgical procedure and enters the patient data, if known (Fig 11-1). The IOL powers, calculated by a variety of formulas, are displayed at the bottom of the form, and the surgeon can compare the results to select the best IOL power for the individual situation. This spreadsheet is updated with new formulas and information as they become available and, at this time, probably represents the best option for calculation of IOL powers in post-refractive surgery patients. For more detailed IOL power calculation information, see BCSC Section 3, *Clinical Optics*.

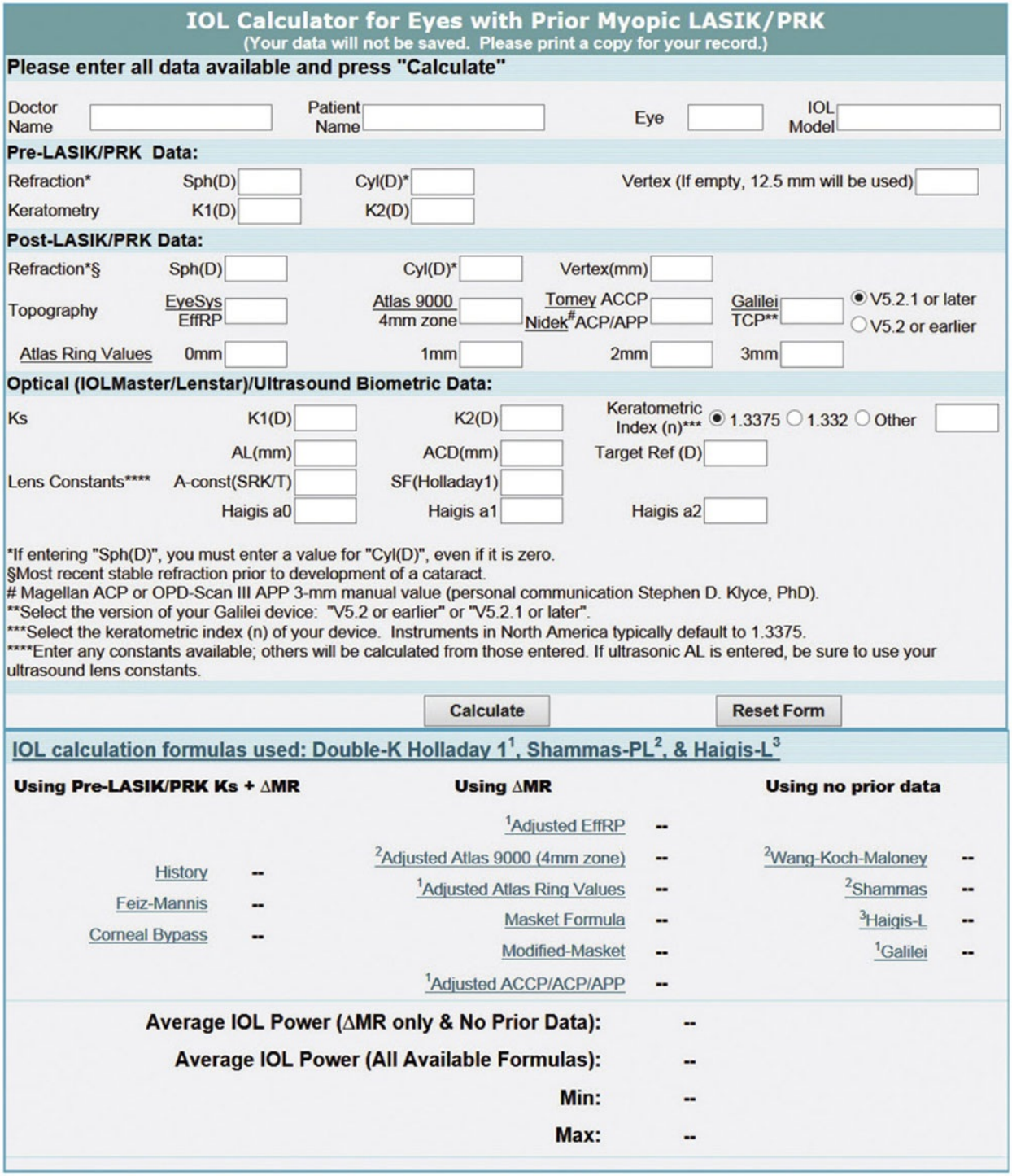

Figure 11-1 The data screen of the post-keratorefractive IOL power calculator of the ASCRS. The surgeon enters the patient's pre-refractive surgery data (if known) and the current data into the data form. After the "calculate" button at the bottom of the form is clicked, the IOL power calculated by a variety of formulas is displayed. (Note: In this illustration, accessed August 23, 2013, the "calculate" button was activated with no patient data entered so as to show the final appearance of the screen; the form itself is updated periodically and available at http://iolcalc.org/.) *(Used with permission from the American Society of Cataract and Refractive Surgery.)*

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Retinal Detachment Repair After LASIK

Even if the eyes of patients with high myopia become emmetropic as a result of refractive surgery, these patients need to be informed that their eyes remain at increased risk of retinal detachment. For this reason, the vitreoretinal surgeon should ask about prior refractive surgery. Eyes undergoing retinal detachment repair after LASIK are prone to flap problems, including flap dehiscence, microstriae, and macrostriae. The surgeon may find it helpful to mark the edge of the flap prior to surgery to aid in flap replacement in case the flap is dislodged. The risk of flap problems increases dramatically if the epithelium is debrided during the retinal detachment repair. If flap dehiscence occurs, the flap should be carefully repositioned and the interface irrigated. A bandage soft contact lens may be placed at the end of the procedure.

Postoperatively, the patient should be observed closely for signs of flap problems such as epithelial ingrowth and diffuse lamellar keratitis, especially if an epithelial defect was present on the flap. After retinal detachment repair, the intraocular pressure (IOP) needs to be monitored, especially when an intraocular gas bubble is used, keeping in mind that IOP measurements may read falsely low after refractive surgery because of corneal thinning. Additionally, elevated IOP can cause a diffuse lamellar keratitis-like picture or even a fluid cleft between the flap and the stroma, resulting in a misleading, extremely low IOP measurement. These problems are discussed in greater detail later in the chapter in the section Glaucoma After Refractive Surgery.

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Corneal Transplantation After Refractive Surgery

Corneal transplantation is occasionally required after refractive surgery. Reasons for needing a corneal graft after refractive surgery include significant corneal scarring, irregular astigmatism, corneal ectasia, and corneal edema. Issues unrelated to refractive surgery, such as trauma or corneal edema after cataract surgery, can also necessitate corneal transplant surgery. Each type of refractive surgical procedure is unique in the reasons a graft may be required and in ways to avoid problems with the corneal transplant. Corneal transplantation is discussed in greater detail in BCSC Section 8, *External Disease and Cornea.*

After RK, a graft may be required because of trauma resulting in incisional rupture; central scarring not responsive to phototherapeutic keratectomy; irregular astigmatism; contact lens intolerance; or progressive hyperopia. The RK incisions can gape or dehisce during penetrating keratoplasty trephination, preventing creation of an even, uniform, and deep trephination. One method for avoiding RK wound gape or dehiscence during keratoplasty is to mark the cornea with the trephine and then reinforce the RK incisions with interrupted sutures outside the trephine mark prior to trephination. If the RK incisions open during the corneal transplant surgery, then X, mattress, or lasso sutures may be required to close these stellate wounds.

Corneal transplantation may also be required after excimer laser surface ablation. However, because of the 6- to 8-mm ablation zones typically used, the corneal periphery is generally not thinned, and transplantation in this situation is usually straightforward.

After LASIK, corneal transplantation may be required to treat central scarring (eg, after infection or with a buttonhole) or corneal ectasia. A significant challenge in this scenario is that most LASIK flaps are larger than a typical trephine size (8 mm). Trephination through the flap increases the risk that the flap peripheral to the corneal transplant wound may separate. This complication may be avoidable through careful trephination and use of a gentle suture technique that incorporates the LASIK flap under the corneal transplant suture. Femtosecond laser trephination theoretically may decrease the risk of flap separation during trephination.

A few cases have been reported of inadvertent use of donor tissue that had undergone prior LASIK. The risk of this untoward event will increase as the donor pool includes more individuals who have undergone LASIK or surface ablation. Eye banks need to develop better methods to screen out such donor corneas. If a post-LASIK eye is inadvertently used for corneal transplantation, the patient should be informed. A regraft may be required to address significant anisometropia or irregular astigmatism.

Corneal transplantation is occasionally required in a patient with intrastromal corneal ring segments. The polymethylmethacrylate ring segments are typically placed near the edge of a standard corneal transplant, so the ring segments may be removed

prior to grafting, or--because the ring segments lie within the central 7 mm of the cornea--they may also be left in place and removed in toto with the host tissue or removed at the time of trephination.

Though rare, corneal transplantation after laser thermokeratoplasty or conductive keratoplasty may be required. Trephination should be straightforward in such cases, and the thermal scars should generally be incorporated into the corneal button. Even if the scars are not incorporated and remain peripheral to the new cornea, they should not significantly affect wound architecture, graft healing, or corneal curvature.

Contact Lens Use After Refractive Surgery

Indications

Contact lenses can be used before and after refractive surgery. For example, a patient with presbyopia can use a temporary trial with soft contact lenses to experience monovision before undergoing surgery, thus reducing the risk of postoperative dissatisfaction. Contact lenses can also be used preoperatively in a patient with a motility abnormality (eg, esotropia or exotropia) to simulate expected vision after refractive surgery and to ensure that diplopia does not become manifest.

In the perioperative period, hydrophilic soft contact lenses can help promote epithelialization and reduce discomfort after surface ablation; they may also reduce the risk of flap dehiscence in the case of a free cap or help decrease epithelial ingrowth following a flap refloat. Rigid gas-permeable (RGP) contact lenses are more effective than are soft lenses to correct reduced vision due to residual irregular astigmatism, and they can be a useful adjunct after RK and LASIK. Night-vision problems caused by a persistent, uncorrected refractive error or irregular astigmatism may also be reduced by using contact lenses. However, if the symptoms are related to higher-order aberrations, they may persist despite contact lens use.

General Principles

Contact lenses for refractive purposes should not be fitted until surgical wounds and serial refractions are stable. The most practical approach to fitting an RGP lens after refractive surgery is to do a trial fitting with overrefraction.

The clinician needs to discuss with the patient in understandable terms the challenges of contact lens fitting after refractive surgery and align the patient's expectations with reality. A patient who successfully wore contact lenses before refractive surgery is more likely to be a successful contact lens wearer postoperatively than is one who never wore contact lenses.

Contact Lenses After Radial Keratotomy

Centration is a challenge in fitting contact lenses after RK because the corneal apex is displaced to the midperiphery (Fig 11-2). Frequently used fitting techniques involve referring to the preoperative keratometry readings and basing the initial lens trial on the average keratometry values. Contact lens stability is achieved by adjusting the lens diameter. In general, larger-diameter lenses take advantage of the eyelid to achieve stability. However, they also increase the effective steepness of the lens due to increased sagittal depth. If the preoperative keratometry reading is not available, the ophthalmologist can use a paracentral or midperipheral curve, as measured with postoperative corneal topography, as a starting point.

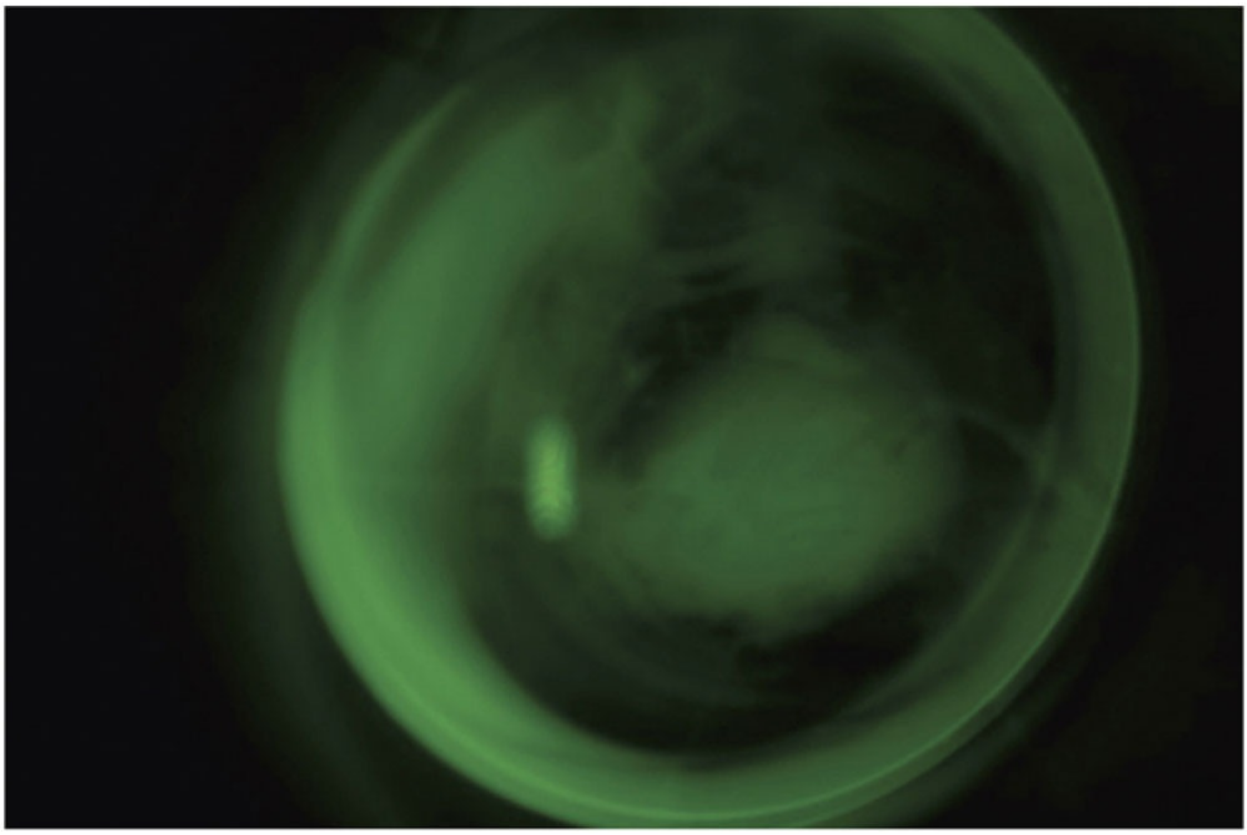

Figure 11-2 Fluorescein staining pattern in a contact lens patient who had undergone RK and LASIK shows pooling centrally and touch in the midperiphery. This pattern is the result of central corneal flattening and steepening in the midperiphery. *(Courtesy of Robert S. Feder, MD.)*

When a successful fit cannot be obtained with a standard RGP lens, a reverse-geometry lens can be used. The secondary curves can be designed to be as steep as necessary to achieve a stable fit. The larger the optical zone, the flatter the fit.

Hydrophilic soft lenses can also be used after RK. Toric soft lenses can be helpful when regular astigmatism is present. Soft lenses are less helpful in eyes with irregular

astigmatism because they are less able to mask an irregular surface. Newer lens designs such as hybrid contacts, which consist of an RGP center surrounded by a soft contact lens skirt, and scleral RGP lenses, which vault the cornea and contact the perilimbal conjunctiva/sclera, may be helpful for patients with significant irregular astigmatism who are intolerant of conventional RGP lenses.

Whenever contact lenses are prescribed for post-RK eyes, as in the preceding scenarios, the ophthalmologist should continue to monitor the cornea to check for neovascularization of the wounds. Should neovascularization occur, contact lens wear should cease. Once the vessels have regressed, refitting can commence.

Contact Lenses After Surface Ablation

Immediately after surface ablation, a soft contact lens is placed on the cornea as a bandage to help promote epithelialization and reduce discomfort. The lens is worn until the corneal epithelium has healed. Healing time depends on the size of the epithelial defect but in general takes between 4 and 7 days. A tight-fitting lens should be removed if there is evidence of corneal hypoxia (eg, corneal edema, folds in the Descemet membrane, or iritis).

Contact Lenses After LASIK

The indications for contact lens fitting after LASIK are similar to those following other types of refractive surgery. The corneal contour is usually stable by 3 months after LASIK for myopia; however, it may take up to 6 months for the cornea to stabilize after LASIK for hyperopia.

A soft contact lens may be used immediately after LASIK surgery to promote epithelialization and to prevent epithelial ingrowth. It is generally used for several days on an extended-wear basis and then removed by the surgeon. Daily-wear contact lenses for refractive purposes should not be considered until the surgeon believes the risk of flap displacement is low.

Glaucoma After Refractive Surgery

The force required for applanation of a Goldmann tonometer is proportional to the central corneal thickness. As a result, an eye that has a thin central cornea may have an artifactually low IOP as measured by Goldmann applanation tonometry (GAT). Patients with normal-tension glaucoma have significantly thinner corneas than do patients with primary open-angle glaucoma. When a correction factor based on corneal thickness is applied, more than 30% of glaucoma patients demonstrate abnormally high IOP. The correction factor needed may be lower for measurements taken with the Tono-Pen (Reichert Ophthalmic Instruments, Depew, NY) and the pneumotonometer.

For IOP measured with GAT, an artifactual IOP reduction occurs following surface ablation and LASIK for myopia, both of which reduce central corneal thickness. Similar inaccuracies in IOP measurement can occur after surface ablation and LASIK for hyperopia. After excimer laser refractive surgery, the mean reduction in IOP measurement is 0.63 mm Hg per diopter of correction, with a fairly wide variation. Postoperatively, some patients may demonstrate no change in IOP measurement, whereas others may exhibit an increase. In general, the reduction of measured IOP is greater after LASIK than after surface ablation. Surface ablation patients with a preoperative refractive error of <5.00 D may have a negligible decrease in IOP measurements.

Topical corticosteroids that are used after refractive surgery pose a serious risk of corticosteroid-induced IOP elevation, particularly because accurate IOP measurement is difficult to obtain. By 3 months postoperatively, up to 15% of surface ablation patients may have IOP above 22 mm Hg. If the elevated IOP is not recognized early enough, optic nerve damage and visual field loss can occur.

If topical corticosteroids are used postoperatively for an extended time, periodic, careful disc evaluation is essential. Optic nerve and nerve fiber layer imaging may facilitate the evaluation. Periodic visual field assessment may be more effective than IOP measurement for identifying at-risk patients before severe visual field loss occurs (see Chapter 10, Fig 10-4).

Refractive surgery patients who develop glaucoma are initially treated with IOP-lowering medications, and their IOP is carefully measured. If medication or laser treatment does not adequately reduce the IOP, glaucoma surgery may be recommended. Patients who have had refractive surgery should be warned prior to glaucoma surgery of the potential for transient vision loss from inflammation, hypotony, or change in refractive error. The glaucoma surgeon should be made aware of the patient's previous LASIK in order to avoid trauma to the corneal flap. For additional information on glaucoma management, see BCSC Section 10, *Glaucoma*.

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CHAPTER 12

International Perspectives in Refractive Surgery

Introduction

Refractive surgery has been the fastest-growing ophthalmic subspecialty, exhibiting strong growth rates in both the United States and the rest of the world. Even though that pattern changed recently as a result of the global economic downturn, global demand for refractive surgery is now expected to resume its pattern of growth, with annual procedure volume increasing steadily. This growth is due in part to an increase in demand from emerging markets in Asia and Latin America.

Global practice trends differ significantly according to ethnic and regional variance in the prevalence of refractive errors, socioeconomic factors, and regulatory practices. This chapter presents information on international trends and perspectives in refractive surgery and summarizes medical device regulation in refractive surgery in different countries. In addition, this chapter reviews new clinical studies and refractive surgery therapies currently performed outside the United States.

Global Estimates of Refractive Surgery

It is estimated that more than 3.5 million refractive surgery procedures were performed worldwide in 2012. Of these, approximately 15% were performed in the United States (Fig 12-1). Surgical volumes resumed improving in 2010 after experiencing a period of decline that stemmed from the global economic downturn in the previous decade. Outside the United States, the recent picture is mixed. Economic burdens in western Europe significantly affected some countries, while others continued to have stable growth patterns. Meanwhile, in Asia and Latin America, demand continued to grow for refractive surgery, particularly in China, India, Japan, Brazil, Russia, and Mexico.

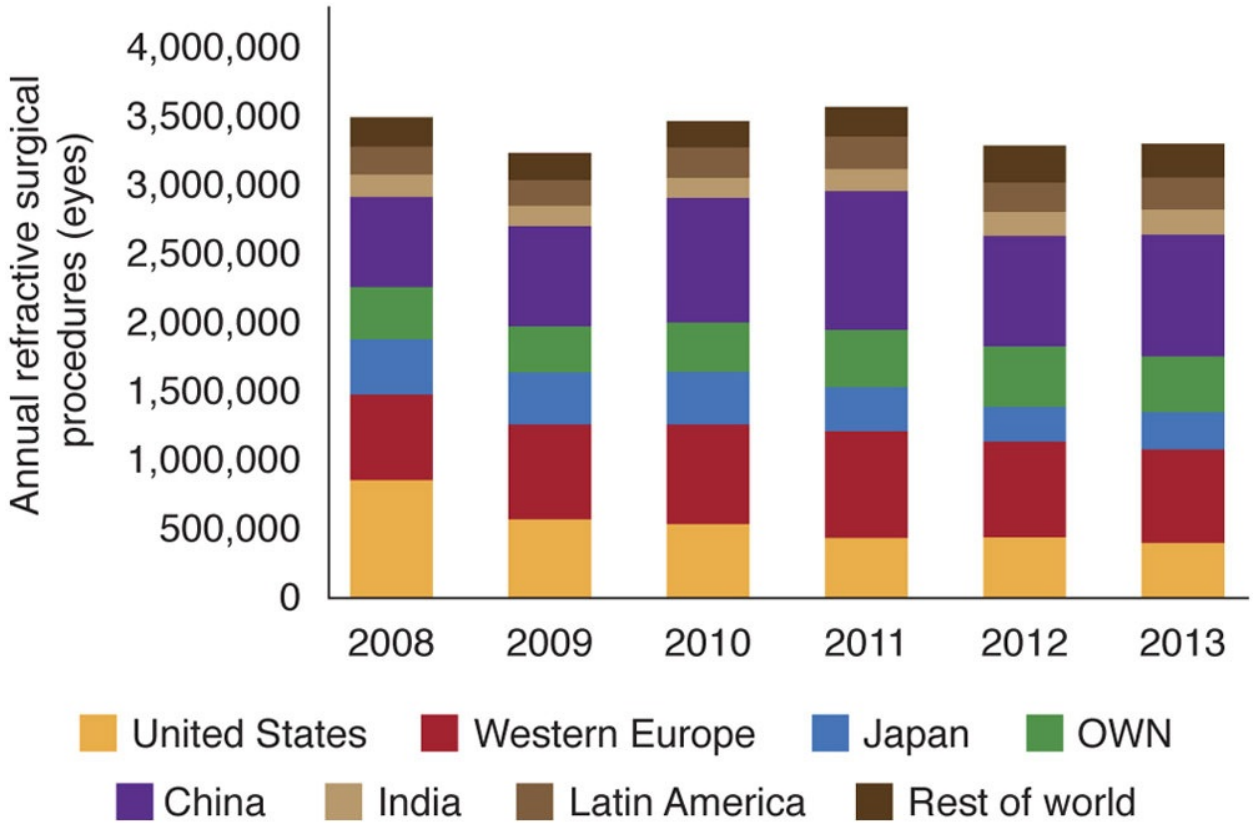

Figure 12-1 Global refractive surgical procedures by region for the years 2008-2013. OWN = other wealthy nations. *(Redrawn with permission from* Market Scope. 2012 Comprehensive Report on the Global Refractive Market. *Market Scope, LLC. Available at: www.market-scope.com/refractive-report/.)*

Global demand for laser refractive surgery is expected to grow at a compounded annual rate of approximately 5.2% until 2017, with the number of procedures increasing from 3.4 million to 5.4 million. Since 2010, growth has occurred in emerging Asian and Latin American economies and in the United States, China, Japan, India, and Brazil. China remains one of the fastest-growing laser refractive markets, with an estimated 1128 laser centers, accounting for 24% globally, fueled by a growing middle class and a highly myopic population. Rates for refractive surgery in India are also rapidly growing, with approximately 148,550 procedures performed per year.

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International Trends in Refractive Surgery

Although international trends in refractive surgery are influenced by those in the United States and in the more-developed nations in Europe and Asia, there are some distinct regional differences. For example, overall refractive surgery market statistics suggest that outside the United States, emerging lens-based refractive technologies are expected to make up approximately 10% of refractive procedures, whereas within the United States, the percentages for such procedures remain in the single digits.

The inclusion of cataract surgery as a refractive surgery procedure has been an important trend globally. This change has been reflected in the organization of scientific societies, such as that occurring in Brazil, where the Brazilian Society of Refractive Surgery and the Brazilian Society of Cataract and Intraocular Implants are expected to merge in 2014. The advent of femtosecond laser-assisted cataract surgery will enhance this trend.

Preferences among the different types of excimer lasers used for laser in situ keratomileusis (LASIK) vary internationally. In the United States, with a total of 1266 excimer lasers in use in 2012, the 3 major laser systems consisted of AMO/VISX (62%; Abbott Medical Optics, Abbott Park, IL), Alcon WaveLight (31%; Alcon, Fort Worth, TX), and TECHNOLAS (6%; Bausch + Lomb, Rochester, NY) lasers. In contrast, outside the United States, Alcon WaveLight lasers hold the largest market share (27%), followed by AMO/VISX and TECHNOLAS (both 15%), and AMARIS (15%; Schwind, Kleinostheim, Germany) lasers.

In the United States, wavefront-guided customized ablation has been the most frequently performed type of procedure since the second half of the prior decade. More recently, such customized ablations are being performed in increasing numbers internationally as well. However, the higher cost of wavefront-guided customized ablation, compared with conventional procedures, has been a major factor limiting its growth.

The increasing shift to choosing femtosecond lasers over microkeratomes for LASIK flap creation has continued. In the United States, femtosecond lasers have been used in the majority of LASIK procedures since 2008, whereas outside the United States, the market share is not expected to reach 50% until 2017 (from its current level of 32%). The use of femtosecond lasers is expected to grow internationally because of the perceived clinical advantages, the potential for increased surgeon revenue, and patient perceptions of a bladeless, "no-touch" procedure.

Surface ablation procedures are expected to remain stable, accounting for about 15% of refractive procedures. There is an increasing use of mitomycin C for higher degrees of correction in Asia and Latin America, which may also explain the global resurgence in interest in photorefractive keratectomy (PRK). In Asian countries and other countries with relatively high rates of high myopia, PRK was extensively used in the mid- to late 1990s until the significant risk of corneal haze with greater amounts of ablation was recognized, and LASIK largely replaced PRK for treatment of high

myopia. Laser subepithelial keratomileusis (LASEK) and epipolis laser in situ keratomileusis (epi-LASIK) procedures are becoming increasingly popular in some European countries, such as Italy, and in the Middle East, which has a high prevalence of keratoconus. The combination of collagen crosslinking procedures with surface ablation has also been observed for treating ectasia and keratoconus, as described in the technique named the *Athens protocol*. As of this time, collagen crosslinking is an experimental procedure in the United States, and thus any procedure combined with crosslinking should also be considered experimental in the United States.

The other major trend in the refractive market is expected to be the further development of lasers to treat presbyopia. The global presbyopic patient population is estimated to be more than 2 billion, and these patients represent an underserved market. Research is continuing in the use of excimer lasers for multifocal LASIK, or presbyLASIK, corneal inlays, and other procedures to reverse accommodation. All excimer laser platforms have procedures in development, with clinical trials currently ongoing outside the United States.

Advances with femtosecond lasers may also offer possible presbyopia treatments. LENSAR (Orlando, FL) is developing a treatment modality to restore compliance and elasticity to the crystalline lens by cutting tissue planes within the lens. A similar approach is being pursued separately in Germany. Data are still emerging on this technique.

A femtosecond laser-based presbyopic treatment, IntraCor (Technolas Perfect Vision, Munich, Germany), received European approval in 2009. With this technique, the femtosecond laser is used to create concentric ring-shaped cuts within the cornea. The theory is that these cuts change the corneal curvature in a way that leads to improvement in near vision without a trade-off in distance vision. The 18-month results showed that vision outcomes were stable; however, previous experience with incisional keratotomy from radial keratotomy (RK) may indicate a longer follow-up is necessary. Also, clinical understanding of the corneal biomechanics underlying the IntraCor procedure seems essential for selecting appropriate candidates as well as for preoperative planning and postoperative evaluation, especially if the range of IntraCor treatments is going to be expanded to include myopia, hyperopia, and astigmatism.

A third treatment area for presbyopia remains on the horizon: corneal inlays. Two companies in the United States and a global company based in the Netherlands are currently beginning to commercialize products. One inlay product design uses the small-aperture, or pinhole, effect to enhance depth of focus for the correction of emmetropic presbyopia; use of this inlay can also be combined with bilateral LASIK and simultaneous implantation in ametropic presbyopia. Implanted only in the nondominant eye, and using either a femtosecond LASIK-type flap or a femtosecond laser-generated pocket incision, the inlay is 5 mm thick and 3.8 mm in diameter, with a 1.6-mm opening. Data presented at the 2009 meeting of the European Society of

Cataract and Refractive Surgeons (ESCRS) showed an average improvement in near vision of 4 lines of vision and a mean near acuity Jaeger score of J1. The inlay has been available outside the United States since 2010 and is now available in Singapore, Japan, and Europe. Clinical studies are ongoing at 17 sites in the United States in a Food and Drug Administration (FDA) study and at 9 international sites (Europe and Asia-Pacific). Further international trials are under way to perform implantation in post-LASIK and pseudophakic patients.

Another product is a 2-mm-diameter hydrogel inlay, which is centered on the cornea under a flap or through a pocket incision. In clinical studies, the inlay showed an average improvement of 4 lines in uncorrected near vision. The company received clearance to market this device in Europe and began a phase 3 clinical study in the United States in 2010.

The third inlay under development measures 3 mm in diameter. Results have demonstrated that patients achieved less of an improvement in near vision compared with that gained using other inlays, and there was a trade-off in distance vision. For additional information on corneal inlays, see Chapter 4.

Phakic intraocular lenses (PIOLs) are widely used in Europe and Asia, mainly for the treatment of high or extreme myopia, but there is a trend toward increasing their usage for lower levels of myopia. Intrastromal corneal ring segment (ICRS) surgery remains limited to treating keratoconus and post-refractive surgery keratectasia. Intacs rings (Addition Technology, Sunnyvale, CA) have been the most commonly used ICRS model in the United States, Europe, and Asia. The use of Ferrara-type rings (eg, Ferrara, Mediphacos, Belo Horizonte, Brazil; Bisantis, Opticon 2000 spA Soleko spA, Rome, Italy; and MyoRing, Dioptex GmbH, Linz, Austria) has demonstrated continued growth in Latin America as well as increasing growth elsewhere internationally.

In Europe, as in the United States, there is strong interest in the convergence of refractive and cataract surgery, with implantation of PIOLs and presbyopia-correcting intraocular lenses (IOLs) bridging the gap between cataract and refractive technologies. Over the past several years, there has been growing interest in lens-related refractive surgery as an alternative to the established forms of keratorefractive laser surgery. In the United States, only 2 PIOLs have received FDA approval (discussed in Chapter 8). In Scandinavia (Norway, Sweden) and Spain, posterior chamber IOLs (implantable collamer lenses [ICLs] and toric ICLs) are the most commonly used PIOLs. In contrast, anterior chamber phakic IOLs are most frequently used in Germany and France, whereas approximately equal usage of anterior chamber and posterior chamber PIOLs is the trend in Italy.

In Asia, LASIK continues to be the most common refractive procedure. In South Korea, arguably a major developed Asian country with the highest penetration of refractive surgery, a 2004 survey (unpublished data, Kyung Hwan Shin) conducted by the Korean Society of Cataract and Refractive Surgery revealed that for myopia of

<12.00 D, LASIK surgery accounted for 82% of all forms of refractive surgery, followed by surface ablation procedures (18%). For myopia >12.00 D, phakic IOLs were the preferred surgical option. In China, reports suggest that more LASIK is performed annually than cataract surgery, which is thought to be related to higher incomes in its major cities.

Kanellopoulos AJ, Binder PS. Management of corneal ectasia after LASIK with combined, same-day, topography-guided partial transepithelial PRK and collagen cross-linking: the Athens protocol. *J Refract Surg.* 2011;27(5):323-331.

International Regulation of Refractive Surgery Practices and Devices

Standards and levels of regulation differ among various countries, but many developing nations accept or conform to regulatory standards from established administrations such as the US FDA and the regulatory framework of the European Union (EU).

The concept of globalization has been adopted by medical device regulation with the development of the International Harmonized System for control of medical devices, established by the Global Harmonization Task Force (GHTF) in 1992. The 5 founding members are the European Union, the United States, Canada, Australia, and Japan.

The EU began medical regulation in 1990 and has adopted a risk-based classification system comparable to that of the US FDA and consisting of 4 classes (I, II, III, and IV). Regulatory controls focus primarily on safety, with less emphasis on efficacy than is applied by the FDA.

In Asia, regulatory controls vary considerably. Some countries use existing drug and food control legislation to regulate a limited range of medical devices. However, many countries (including China and South Korea) recognize or have adopted regulatory standards set by the EU or US FDA within their respective internal regulatory frameworks. In India, medical device regulation is still undergoing reorganization, and in Japan, strict internal regulatory controls have limited the importation of refractive surgical devices and procedures. Some Asian countries have adopted, or are in the process of adopting, a harmonized approach to device regulation through the Asian Harmonization Working Party (AHWP), a nongovernmental agency formed in 1996 with direct links to the GHTF.

APPENDIX 1

The Role of the FDA in Refractive Surgery

The field of refractive surgery is highly dependent on rapidly changing technology that dictates surgical technique. Some of the investigational devices discussed in the preceding chapters will receive US Food and Drug Administration (FDA) approval by the time this book is published. Other "promising" devices or techniques may have already fallen out of favor.

Because of the continual introduction of new devices to the US market, the FDA approval process has particular influence in refractive surgery. Therefore, we have included this brief appendix to review the FDA approval process. A list of FDA-approved lasers for refractive surgery can be found on the FDA website (www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/SurgeryandLifeSupport/LASIK/ucm168641.htm).

The FDA

The scope of the FDA's work is established by legislation. The Food, Drug, and Cosmetic Act, passed by Congress in 1938, required for the first time that companies prove the safety of new drugs before placing them on the market and required regulation of cosmetics and therapeutic devices. The Medical Device Amendments of 1976 authorized the FDA to ensure that medical devices are safe and effective before they come to market in the United States. This amendment also provided for classification of medical devices into 3 categories, depending on potential risk of the device; established 3 pathways to market; and established advisory panels to assist the FDA in the review of devices. The Ophthalmic Devices Panel, for example, evaluates and advises on marketing and device applications for ophthalmic devices (see discussion later in this appendix).

Device Classification

All manufacturers of medical devices distributed in the United States must comply with

basic regulations, or general controls, including

- establishment (company) registration
- medical device listing
- quality systems regulation
- labeling requirements
- medical device reporting (of problems)

In addition, devices are classified into 1 of 3 regulatory control groups (I, II, III). This classification of medical devices identifies any regulatory control specific to the class that is necessary to ensure the safety and effectiveness of a device.

Class I devices (eg, refractometers, perimeters, sunglasses, visual acuity charts) are usually considered minimal-risk devices. Although these devices are subject to general controls, most of them are exempt from premarket review by the FDA. With few exceptions, manufacturers can go directly to market with a class I device.

Class II devices (eg, phacoemulsification units, tonometers, vitrectomy machines, daily-wear contact lenses) are usually considered moderate-risk devices. Class II devices are those for which general controls alone are insufficient to ensure safety and effectiveness and for which methods exist to provide such assurances. These devices, in addition to general controls, are subject to special controls, which may include special labeling requirements, mandatory performance standards, and postmarket surveillance. With few exceptions, class II devices require premarket review by the FDA.

Class III devices (eg, excimer lasers, intraocular lenses, extended-wear contact lenses, intraocular fluids) are considered significant-risk devices that present a potential unreasonable risk of illness or injury. Class III devices are those for which insufficient information exists to ensure safety and effectiveness solely through general or special controls. Class III devices cannot be marketed in the United States until the FDA determines that there is a reasonable assurance of safety and effectiveness when used according to the approved indications for use. Most class III devices come to market through the *premarket approval (PMA)* process and require an extensive review by the FDA before approval is granted for marketing.

Collection of Clinical Data for an Unapproved Device

For all class III devices and many class II devices, clinical performance data are required to be included in the regulatory marketing submissions. An *investigational device exemption (IDE)* allows the investigational device to be shipped and used in a clinical trial to collect the safety and effectiveness data required to support an application to the FDA requesting clearance to market. The FDA has 30 days to review and grant approval of an IDE application. Applications containing deficiencies in such

areas as bench testing, study design, or informed consent documents are denied or conditionally approved. The sponsor may begin enrollment and treatment of subjects for IDE applications that are conditionally approved, but the sponsor must respond to the deficiencies within 45 days of the date of the conditional approval letter. During the IDE process, the sponsor often meets with the FDA to discuss the details of the clinical trial in order to facilitate effective data collection for eventual review.

Pathways to Market

Premarket Notification 510(k)

Manufacturers of class I and class II devices that are not otherwise exempt from premarket review must submit a *premarket notification*, commonly referred to as a *510(k) application*, to the FDA before going to market. In the 510(k) application, a manufacturer must demonstrate that its device is substantially equivalent to a legally marketed device (commonly referred to as the "predicate device") of the same type and for the same intended use. The FDA must make its determination of substantial equivalence within 90 days. If a device is not found to be substantially equivalent, it is placed into class III, or alternatively, if the device is not of high risk, the sponsor may submit a de novo request stating that the device defines a new 510(k) device regulatory classification.

Humanitarian Device Exemption

Devices marketed under a *humanitarian device exemption (HDE)* are intended to treat or diagnose diseases or conditions that affect or are manifested in fewer than 4000 individuals per year in the United States. The sponsor is required to provide an HDE application to the FDA containing a reasonable assurance of safety. Efficacy information is limited to a demonstration of "probable benefits to health" rather than the higher standard of "reasonable assurance of effectiveness," as would be required for a PMA. These devices must be used in a facility with an institutional review board (IRB). The FDA has 75 days to review and make a decision on an HDE application.

Premarket Approval

The PMA process is the primary pathway to market for class III devices. Clinical data from the IDE study, along with manufacturing information, preclinical bench testing, animal data (if needed), and labeling, are submitted to the FDA as a PMA application. The FDA must decide within 180 days whether the information submitted in the application demonstrates the safety and effectiveness of the device in question. The time for making the decision is extended when the application lacks the required information or contains information that is incomplete or insufficient.

Ophthalmic Devices Panel

The Ophthalmic Devices Panel consists of 6 voting members, the chair (who votes in case of a tie), 1 nonvoting consumer representative, and 1 nonvoting industry representative. The panel includes ophthalmologists as well as other experts, such as vision scientists, biostatisticians, and optometrists. Consultants are included on the panel as the need for their expertise dictates. All panel members are considered "special government employees" and are subject to the conflict-of-interest rules and ethics requirements for government employees.

The Ophthalmic Devices Panel meets in open public session to evaluate and advise on marketing applications for first-of-a-kind devices and for previously approved devices for which a firm is seeking a new indication for use, as well as on device applications that raise significant issues of safety and effectiveness. The panel also provides clinical input in the development of FDA and industry guidelines for the study of new devices.

During a panel meeting scheduled to review a specific device, panel deliberations focus on the clinical study data and the proposed physician and patient labeling (if applicable). After deliberation, the panel members must determine their recommendation regarding whether the information in the PMA application demonstrates a reasonable assurance of safety and effectiveness. At the conclusion of the meeting, the panel votes on its recommendation. However, because the committee is advisory in nature, the FDA is not bound to follow its recommendation.

Labeling

The sponsor defines the inclusion and exclusion criteria for the clinical trial. Prior to approval, the FDA reviews and makes recommendations for changes in the device labeling using the data from the population studied. For example, if dry eyes are an exclusion criterion for the PMA study, there will be no data on subjects with dry eyes. Consequently, the device is not approved in this subset of patients, and the labeling will indicate that dry eyes are an exclusion criterion. This means not that the device is contraindicated in dry eye patients but that the safety and effectiveness of the device cannot be evaluated in this population because there are no data. Some exclusion criteria may be contraindications to treatment. For example, keratoconus could be an exclusion criterion as well as a contraindication to laser in situ keratomileusis (LASIK).

The clinical trial is performed for a limited range of refractive errors. Safety and effectiveness data guide the range of refractive error that is approved for use in the PMA labeling.

If a treating clinician does not follow the labeling recommendations for the device, he or she is using the device "off-label." Some off-label uses reflect the PMA's lack of

data on safety and effectiveness--for example, use of the device in a patient listed within the exclusion criterion; other off-label uses reflect decreased or unknown safety or effectiveness--for example, use of the device beyond the refractive range of the labeling. Any modifications to the device to enable an off-label use, such as the addition of unapproved software, adulterate the device and cause it to be unapproved.

In the United States, ophthalmologists very commonly use devices off-label because the FDA does not control the practice of medicine. In some cases, off-label use has actually become the standard of care. For example, topical fluoroquinolones are FDA approved to treat bacterial conjunctivitis; however, these medications are commonly used to treat corneal ulcers as well, even though they are not FDA approved for this indication. Consequently, although use of fluoroquinolones for corneal ulcer treatment may be off-label, in some situations it may also be the community standard of care.

Conversely, use of an FDA-approved device in an off-label fashion that deviates from the community standard of care may place an ophthalmologist at increased risk of legal scrutiny, particularly if there is a poor result. In such a situation, the physician should seriously consider both informing the patient and having the patient sign an ancillary consent form.

Delays in FDA Approval

At times, deficiencies in the clinical trials of a PMA application may delay its presentation to the Ophthalmic Devices Panel. Sometimes a PMA application may be recommended for approval by the panel, but the manufacturer must wait for final FDA approval before marketing the device. Usually, a panel recommendation for approval is granted with conditions that must be met before final FDA approval is granted. For example, the panel may request that data obtained on study subjects with certain ophthalmic characteristics be submitted to the FDA to determine whether visual results in this subset of patients demonstrate efficacy.

When delays occur, the public naturally wants to know why. The FDA and the Ophthalmic Devices Panel are legally bound to keep the result of the PMA application process confidential and are prohibited by law from revealing any information about the PMA, favorable or unfavorable. However, the company is not bound by these same rules and is not restricted in what it chooses to tell the public. The company's dissemination of information about the PMA often has financial motivation because such information may affect the company's stock price and the public's perception of the product. The FDA does not comment on statements made by the company; however, this does not indicate an FDA endorsement of any statement by the company. Even if a company releases incorrect or misleading information about the reasons for delay in FDA approval, the FDA is still prohibited from discussing details of the PMA application, which could include evidence contrary to statements made by the company.

Only in the public sessions of the Ophthalmic Devices Panel is information about the PMA process legally allowed to be released to the public before a final decision on the application is made by the FDA. All other deliberations regarding the application, before and after the panel meeting, remain subject to FDA confidentiality rules. Consequently, before the FDA reaches its decision, the panel meeting is the best forum for the public to actually observe the true data from the PMA clinical trial. The executive summary minutes and a complete transcript of the panel meetings are placed on the FDA public website once the chair approves the minutes.

Reporting of Medical Device-Related Adverse Events

The FDA's involvement in medical devices is not limited to the premarket process. The FDA monitors postmarket reports of device-related adverse events (AEs), or product problems, through both voluntary and mandatory reporting. This monitoring is done to detect "signals" of potential public health safety issues.

Since 1984, device manufacturers and importers have been required to report device-related deaths, serious injuries, and malfunctions to the FDA. User facilities (hospitals, nursing homes, ambulatory surgical facilities, outpatient diagnostic and treatment facilities, ambulance services, and health care entities) are required to report deaths to the FDA and deaths and serious injuries to the manufacturer.

Voluntary reporting to the FDA of device-related problems is a critical professional and public health responsibility. Currently, voluntary reporting takes place under MedWatch, an FDA product-reporting program. MedWatch allows health care professionals and consumers to report serious problems that they suspect are associated with the medical devices they prescribe, dispense, or use. Reporting can be done online at www.fda.gov/medwatch/getforms.htm, by phone (1-800-FDA-1088), or by submitting the Med-Watch 3500 form by mail or fax. Voluntary reporting to the FDA is an easy, minimally time-consuming task that has an enormous impact on public health.

The FDA relies on AE reports to maintain a safety surveillance of all FDA-regulated devices. Physician reports may be the critical factor that prompts a modification in the use or design of a product, improves the safety profile of a device, and leads to increased patient safety.

APPENDIX 2

Sample Informed Consent Forms

Example Informed Consent Form for PRK
(Courtesy of Ophthalmic Mutual Insurance Company, www.OMIC.com)

NOTE: THIS FORM IS INTENDED AS A SAMPLE FORM. IT CONTAINS THE INFORMATION OMIC RECOMMENDS YOU AS THE SURGEON PERSONALLY DISCUSS WITH THE PATIENT. IT DOES NOT CONTAIN INFORMATION ABOUT LIMBAL RELAXING INCISION (LRI). PLEASE REVIEW IT AND MODIFY TO FIT YOUR ACTUAL PRACTICE. GIVE THE PATIENT A COPY AND SEND THIS FORM TO THE HOSPITAL OR SURGERY CENTER AS VERIFICATION THAT YOU HAVE OBTAINED INFORMED CONSENT. (Version 04/09/07)

INFORMED CONSENT FOR PHOTOREFRACTIVE KERATECTOMY (PRK)

This information and the Patient Information *booklet must be reviewed so you can make an informed decision regarding Photorefractive Keratectomy (PRK) surgery to reduce your nearsightedness, farsightedness, or astigmatism. Only you and your doctor can determine if you should have PRK surgery based upon your own visual needs and medical considerations. Any questions you have regarding PRK or other alternative therapies for your case should be directed to your doctor.*

Alternatives to PRK Surgery

The alternatives to PRK include, among others, eyeglasses, contact lenses, and other refractive surgical procedures. Each of these alternatives to PRK has been explained to me.

Complications and Side Effects

I have been informed, and I understand, that certain complications and side effects have been reported in the post-treatment period by patients who have had PRK, including the following:

- **Possible short-term effects of PRK surgery:** The following have been reported in the short-term post-treatment period and are associated with the normal post-treatment healing process: *mild discomfort or pain (first 72 to 96 hours),* corneal swelling, double vision, feeling something is in the eye, ghost images, light sensitivity, and tearing.
- **Possible long-term complications of PRK surgery:**
  - *Haze:* Loss of perfect clarity of the cornea, usually not affecting vision, which usually resolves over time.
  - *Starbursting:* After refractive surgery, a certain number of patients experience glare, a "starbursting" or halo effect around lights, or other low-light vision problems that may interfere with the ability to drive at night or see well in dim light. Although there are several possible causes for these difficulties, the risk may be increased in patients with large pupils or high degrees of correction. For most patients, this is a temporary condition that diminishes with time or is correctable by wearing glasses at night or taking eye drops. For some patients, however, these visual problems are permanent. I understand that my vision may not seem as sharp at night as during the day and that I may need to wear glasses at night or take eye drops. I understand that it is not possible to predict whether I will experience these night vision or low-light problems, and that I may permanently lose the ability to drive at night or function in dim light because of them. I understand that I should not drive unless my vision is adequate. These risks in relation to my particular pupil size and amount of correction have been discussed with me.
  - *Loss of best vision:* A decrease in my best vision even with glasses or contacts.
  - *IOP elevation:* An increase in the inner eye pressure due to post-treatment medications, which is usually resolved by drug therapy or discontinuation of post-treatment medications.
  - *Mild or severe infection:* Mild infection can usually be treated with antibiotics and usually does not lead to permanent visual loss. Severe infection, even if successfully treated with antibiotics, could lead to permanent scarring and loss of vision that may require corrective laser surgery or, if very severe, corneal transplantation.
  - *Keratoconus:* Some patients develop keratoconus, a degenerative corneal disease affecting vision that occurs in approximately 1/2000 in the general population. While there are several tests that suggest which patients might be at risk, this condition can develop in patients who have normal preoperative topography (a map of the cornea obtained before surgery) and pachymetry (corneal thickness measurement). Since keratoconus may occur on its own, there is no absolute test that will ensure a patient will not develop keratoconus

following laser vision correction. Severe keratoconus may need to be treated with a corneal transplant, while mild keratoconus can be corrected by glasses or contact lenses.

- **Infrequent complications.** The following complications have been reported infrequently by those who have had PRK surgery: itching, dryness of the eye, or foreign body feeling in the eye; double or ghost images; patient discomfort; inflammation of the cornea or iris; persistent corneal surface defect; persistent corneal scarring severe enough to affect vision; ulceration/infection; irregular astigmatism (warped corneal surface which causes distorted images); cataract; drooping of the eyelid; loss of bandage contact lens with increased pain (usually corrected by replacing with another contact lens); and a slight increase of possible infection due to use of a bandage contact lens in the immediate post-operative period.

In giving my permission for PRK surgery, I declare that I understand the following information:

The long-term risks and effects of PRK surgery are unknown. The goal of PRK with the excimer laser is to reduce dependence upon or need for contact lenses and/or eyeglasses; however, I understand that as with all forms of treatment, the results in my case cannot be guaranteed. For example:

1. I understand that an overcorrection or undercorrection could occur, causing me to become farsighted or nearsighted or increase my astigmatism and that this could be either permanent or treatable. I understand an overcorrection or undercorrection is more likely in people over the age of 40 years and may require the use of glasses for reading or for distance vision some or all of the time.
2. If I currently need reading glasses, I will likely still need *reading glasses* after this treatment. It is possible that dependence on reading glasses may increase or that reading glasses may be required at an earlier age if I have PRK surgery.
3. *Further treatment may be necessary,* including a variety of eye drops, the wearing of eyeglasses or contact lenses (hard or soft), or additional PRK or other refractive surgery.
4. My *best vision, even with glasses or contacts, may become worse.*
5. There may be a *difference in spectacle correction between eyes,* making the wearing of glasses difficult or impossible. Fitting and wearing *contact lenses* may be more difficult.

I understand there is a remote chance of partial or complete loss of vision in the eye that has had PRK surgery.

I understand that it is not possible to state every complication that may occur as a result

of PRK surgery. I also understand that complications or a poor outcome may manifest weeks, months, or even years after PRK surgery.

I understand this is an elective procedure and that PRK surgery is not reversible.

FOR WOMEN ONLY: I am not pregnant or nursing. I understand that pregnancy could adversely affect my treatment result.

My personal reasons for choosing to have PRK surgery are as follows:

I have spoken with my physician, who has explained PRK, its risks and alternatives, and answered my questions about PRK surgery. I therefore consent to having PRK surgery on:

_____ **Right eye** _____ **Left eye** _____ **Both eyes**

_____ _____

Patient Signature Date

I have been offered a copy of this consent form. _____

Example Informed Consent Form for LASIK
(Courtesy of Ophthalmic Mutual Insurance Company, www.OMIC.com)

NOTE: THIS FORM IS INTENDED AS A SAMPLE FORM. IT CONTAINS THE INFORMATION OMIC RECOMMENDS YOU AS THE SURGEON PERSONALLY DISCUSS WITH THE PATIENT. IT DOES NOT CONTAIN INFORMATION ABOUT LIMBAL RELAXING INCISION (LRI). PLEASE REVIEW IT AND MODIFY TO FIT YOUR ACTUAL PRACTICE. GIVE THE PATIENT A COPY AND SEND THIS FORM TO THE HOSPITAL OR SURGERY CENTER AS VERIFICATION THAT YOU HAVE OBTAINED INFORMED CONSENT. (Version 07/19/06)

INFORMED CONSENT FOR LASER IN-SITU KERATOMILEUSIS (LASIK)

Introduction

This information is being provided to you so that you can make an informed decision about the use of a device known as a microkeratome, combined with the use of a device known as an excimer laser, to perform LASIK. LASIK is one of a number of alternatives for correcting nearsightedness, farsightedness, and astigmatism. In LASIK, the microkeratome is used to shave the cornea to create a flap. The flap then is opened like the page of a book to expose tissue just below the cornea's surface. Next, the excimer laser is used to remove ultra-thin layers from the cornea to reshape it to reduce nearsightedness. Finally, the flap is returned to its original position, without sutures.

LASIK is an elective procedure: There is no emergency condition or other reason that requires or demands that you have it performed. You could continue wearing contact lenses or glasses and have adequate visual acuity. This procedure, like all surgery, presents some risks, many of which are listed below. You should also understand that there may be other risks not known to your doctor, which may become known later. Despite the best of care, complications and side effects may occur; should this happen in your case, the result might be affected even to the extent of making your vision worse.

Alternatives to LASIK

If you decide not to have LASIK, there are other methods of correcting your nearsightedness, farsightedness, or astigmatism. These alternatives include, among others, eyeglasses, contact lenses, and other refractive surgical procedures.

Patient Consent

In giving my permission for LASIK, I understand the following: The long-term risks and effects of LASIK are unknown. I have received no guarantee as to the success of my particular case. I understand that the following risks are associated with the procedure:

Vision Threatening Complications

1. I understand that the microkeratome or the excimer laser could malfunction, requiring the procedure to be stopped before completion. Depending on the type of malfunction, this may or may not be accompanied by visual loss.
2. I understand that, in using the microkeratome, instead of making a flap, an entire portion of the central cornea could be cut off, and very rarely could be lost. If preserved, I understand that my doctor would put this tissue back on the eye after the laser treatment, using sutures, according to the ALK procedure method. It is also possible that the flap incision could result in an incomplete flap, or a flap that is too thin. If this happens, it is likely that the laser part of the procedure will have to be postponed until the cornea has a chance to heal sufficiently to try to create the flap again.
3. I understand that irregular healing of the flap could result in a distorted cornea. This would mean that glasses or contact lenses may not correct my vision to the level possible before undergoing LASIK. If this distortion in vision is severe, a partial or complete corneal transplant might be necessary to repair the cornea.
4. I understand that it is possible a perforation of the cornea could occur, causing devastating complications, including loss of some or all of my vision. This could also be caused by an internal or external eye infection that could not be controlled with antibiotics or other means.
5. I understand that mild or severe infection is possible. Mild infection can usually be treated with antibiotics and usually does not lead to permanent visual loss. Severe infection, even if successfully treated with antibiotics, could lead to permanent scarring and loss of vision that may require corrective laser surgery or, if very severe, corneal transplantation or even loss of the eye.
6. I understand that I could develop keratoconus. Keratoconus is a degenerative corneal disease affecting vision that occurs in approximately 1/2000 in the general population. While there are several tests that suggest which patients might be at risk, this condition can develop in patients who have normal preoperative topography (a map of the cornea obtained before surgery) and pachymetry (corneal thickness measurement). Since keratoconus may occur on its own, there is no absolute test that will ensure a patient will not develop keratoconus following laser vision correction. Severe keratoconus may need to be treated with a corneal transplant, while mild keratoconus can be corrected by glasses or contact lenses.
7. I understand that other very rare complications threatening vision include, but are

not limited to, corneal swelling, corneal thinning (ectasia), appearance of "floaters" and retinal detachment, hemorrhage, venous and arterial blockage, cataract formation, total blindness, and even loss of my eye.

Patient Initials: _____

Non-Vision Threatening Side Effects

1. I understand that there may be increased sensitivity to light, glare, and fluctuations in the sharpness of vision. I understand these conditions usually occur during the normal stabilization period of from one to three months, but they may also be permanent.
2. I understand that there is an increased risk of eye irritation related to drying of the corneal surface following the LASIK procedure. These symptoms may be temporary or, on rare occasions, permanent, and may require frequent application of artificial tears and/or closure of the tear duct openings in the eyelid.
3. I understand that an overcorrection or undercorrection could occur, causing me to become farsighted or nearsighted or increase my astigmatism and that this could be either permanent or treatable. I understand an overcorrection or under-correction is more likely in people over the age of 40 years and may require the use of glasses for reading or for distance vision some or all of the time.
4. After refractive surgery, a certain number of patients experience glare, a "star-bursting" or halo effect around lights, or other low-light vision problems that may interfere with the ability to drive at night or see well in dim light. The exact cause of these visual problems is not currently known; some ophthalmologists theorize that the risk may be increased in patients with large pupils or high degrees of correction. For most patients, this is a temporary condition that diminishes with time or is correctable by wearing glasses at night or taking eye drops. For some patients, however, these visual problems are permanent. I understand that my vision may not seem as sharp at night as during the day and that I may need to wear glasses at night or take eye drops. I understand that it is not possible to predict whether I will experience these night vision or low-light problems, and that I may permanently lose the ability to drive at night or function in dim light because of them. I understand that I should not drive unless my vision is adequate.
5. I understand that I may not get a full correction from my LASIK procedure and this may require future enhancement procedures, such as more laser treatment or the use of glasses or contact lenses.
6. I understand that there may be a "balance" problem between my two eyes after LASIK has been performed on one eye, but not the other. This phenomenon is called anisometropia. I understand this would cause eyestrain and make judging

distance or depth perception more difficult. I understand that my first eye may take longer to heal than is usual, prolonging the time I could experience anisometropia.

7. I understand that, after LASIK, the eye may be more fragile to trauma from impact. Evidence has shown that, as with any scar, the corneal incision will not be as strong as the cornea originally was at that site. I understand that the treated eye, therefore, is somewhat more vulnerable to all varieties of injuries, at least for the first year following LASIK. I understand it would be advisable for me to wear protective eyewear when engaging in sports or other activities in which the possibility of a ball, projectile, elbow, fist, or other traumatizing object contacting the eye may be high.
8. I understand that there is a natural tendency of the eyelids to droop with age and that eye surgery may hasten this process.
9. I understand that there may be pain or a foreign body sensation, particularly during the first 48 hours after surgery.
10. I understand that temporary glasses either for distance or reading may be necessary while healing occurs and that more than one pair of glasses may be needed.
11. I understand that the long-term effects of LASIK are unknown and that unforeseen complications or side effects could possibly occur.
12. I understand that visual acuity I initially gain from LASIK could regress, and that my vision may go partially back to a level that may require glasses or contact lens use to see clearly.
13. I understand that the correction that I can expect to gain from LASIK may not be perfect. I understand that it is not realistic to expect that this procedure will result in perfect vision, at all times, under all circumstances, for the rest of my life. I understand I may need glasses to refine my vision for some purposes requiring fine detailed vision after some point in my life, and that this might occur soon after surgery or years later.
14. I understand that I may be given medication in conjunction with the procedure and that my eye may be patched afterward. I therefore understand that I must not drive the day of surgery and not until I am certain that my vision is adequate for driving.
15. I understand that if I currently need reading glasses, I will still likely need reading glasses after this treatment. It is possible that dependence on reading glasses may increase or that reading glasses may be required at an earlier age if I have this surgery.
16. Even 90% clarity of vision is still slightly blurry. Enhancement surgeries can be performed when vision is stable UNLESS it is unwise or unsafe. If the enhancement is performed within the first six months following surgery, there

generally is no need to make another cut with the microkeratome. The original flap can usually be lifted with specialized techniques. After 6 months of healing, a new LASIK incision may be required, incurring greater risk. In order to perform an enhancement surgery, there must be adequate tissue remaining. If there is inadequate tissue, it may not be possible to perform an enhancement. An assessment and consultation will be held with the surgeon, at which time the benefits and risks of an enhancement surgery will be discussed.

17. I understand that, as with all types of surgery, there is a possibility of complications due to anesthesia, drug reactions, or other factors that may involve other parts of my body. I understand that, since it is impossible to state every complication that may occur as a result of any surgery, the list of complications in this form may not be complete.

Patient Initials: _____

For Presbyopic Patients (those requiring a separate prescription for reading)
The option of monovision has been discussed with my ophthalmologist.

Patient Initials: _____

Patient's Statement of Acceptance and Understanding
The details of the procedure known as LASIK have been presented to me in detail in this document and explained to me by my ophthalmologist. My ophthalmologist has answered all my questions to my satisfaction. I therefore consent to LASIK surgery on:

_____ **Right eye** _____ **Left eye** _____ **Both eyes**

I give permission for my ophthalmologist to record on video or photographic equipment my procedure, for purposes of education, research, or training of other health care professionals. I also give my permission for my ophthalmologist to use data about my procedure and subsequent treatment to further understand LASIK. I understand that my name will remain confidential, unless I give subsequent written permission for it to be disclosed outside my ophthalmologist's office or the center where my LASIK procedure will be performed.

_____ _____
Patient Name Date

_____ _____
Witness Name Date

I have been offered a copy of this consent form (please initial). _____

Basic Texts

Refractive Surgery

Azar DT, Gatinel D, Hoang-Xuan T, eds. *Refractive Surgery*. 2nd ed. Philadelphia: Elsevier/Mosby; 2007.

Boyd BF, Agarwal S, Agarwal A, Agarwal A, eds. *LASIK and Beyond LASIK: Wavefront Analysis and Customized Ablations*. Thorofare, NJ: Slack; 2001.

Feder R. *The LASIK Handbook: A Case-Based Approach.* 2nd ed. Philadelphia: Lippincott Williams & Wilkins; 2013.

Garg A, Rosen E, Lin JT, et al, eds. *Mastering the Techniques of Customized LASIK*. New Delhi: Jaypee Brothers; 2007.

Hardten DR, Lindstrom RL, Davis EA, eds. *Phakic Intraocular Lenses: Principles and Practice*. Thorofare, NJ: Slack; 2003.

Probst LE, ed. *LASIK: Advances, Controversies, and Custom.* Thorofare, NJ: Slack; 2003.

Troutman RC, Buzard KA. *Corneal Astigmatism: Etiology, Prevention, and Management*. St Louis: Mosby; 1992.

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