Laser In Situ Keratomileusis for Myopia and Astigmatism: Safety and Efficacy

A Report by the American Academy of Ophthalmology

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Objective: This document describes laser in situ keratomileusis (LASIK) for myopia and astigmatism and examines the evidence to answer key questions about the efficacy and safety of the procedure.

Methods: A literature search conducted for the years 1968 to 2000 retrieved 486 citations and an update search conducted in June 2001 yielded an additional 243 articles. The panel members reviewed 160 of these articles and selected 47 for the panel methodologist to review and rate according to the strength of evidence. A Level I rating is assigned to properly conducted, well-designed, randomized clinical trials; a Level II rating is assigned to well-designed cohort and case-control studies; and a Level III rating is assigned to case series and poorly designed prospective and retrospective studies, including case-control studies.

Results: The assessment describes randomized controlled trials published in 1997 or later (Level I evidence) and more recent comparative and noncomparative case series (Level II and Level III evidence), focusing on results for safety and effectiveness. It is difficult to extrapolate results from these studies that are comparable to current practices with the most recent generation lasers because of the rapid evolution of LASIK technology and techniques. It is also difficult to compare studies because of variations in the range of preoperative myopia, follow-up periods, lasers, nomograms, microkeratomes and techniques, the time frame of the study, and the investigators' experience.

Conclusions: For low to moderate myopia, results from studies in the literature have shown that LASIK is effective and predictable in terms of obtaining very good to excellent uncorrected visual acuity and that it is safe in terms of minimal loss of visual acuity. For moderate to high myopia (>6.0 D), the results are more variable, given the wide range of preoperative myopia. The results are similar for treated eyes with mild to moderate degrees of astigmatism (<2.0 D). Serious adverse complications leading to significant permanent visual loss such as infections and corneal ectasia probably occur rarely in LASIK procedures; however, side effects such as dry eyes, night time starbursts, and reduced contrast sensitivity occur relatively frequently. There were insufficient data in prospective, comparative trials to describe the relative advantages and disadvantages of different lasers or nomograms. *Ophthalmology 2002;109:175–187 © 2002 by the American Academy of Ophthalmology.*

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Background

Laser in situ keratomileusis is commonly known as LASIK, a term used by Pallikaris et al[1,2] to describe a new technique to correct myopia and astigmatism. It is a procedure that has evolved from a variety of techniques in refractive surgery.

Keratomileusis, with both freeze and nonfreeze techniques, was first used in the United States in the 1970s. Its refractive effect is achieved on the removed disc of the anterior corneal stroma and requires resuturing it to the corneal surface. These procedures were followed by automated lamellar keratoplasty (ALK), in which a microkeratome is used to create a free, or hinged, corneal flap or cap. Tissue from the corneal bed is removed to alter the refractive error and the corneal flap is repositioned.

After the ophthalmic excimer laser was developed, it was used to reshape the surface of the cornea in a technique

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called photorefractive keratectomy (PRK). Laser keratomileusis was initially performed on an excised corneal cap, but this proved to be problematic. In LASIK a corneal flap is created using a microkeratome, after which excimer laser ablation of the stromal bed reshapes the cornea and the flap is replaced. This technique, which has been developed as an alternative to PRK, has the following potential advantages over PRK:

- Earlier postoperative stabilization of visual acuity
- Less postoperative patient discomfort
- Faster improvement in visual acuity
- Less stromal haze formation
- Possibly improved predictability, stability, and corneal clarity in higher correction groups
- Shorter duration of postoperative medications use
- Easier enhancement procedure.

Preoperative Evaluation

Preoperative evaluation of patients for myopic LASIK consists of a complete ophthalmologic examination, including a medical and ophthalmologic history.[3] It also includes informed consent and careful refraction, which is key to determining the refractive treatment. A cycloplegic refraction should be performed even if treatment may be based on the dry manifest refractive error. For patients who wear contact lenses, especially rigid lenses, any evidence of corneal warpage requires that corneal stability be confirmed by serial measurements. Rigid contact lenses should be removed for several weeks and soft lenses for several days to weeks before examination.[4] Documentation of refractive stability, usually less than 0.5 diopters (D) of change over 1 year or more, is also advised to help ensure that the correction will be appropriate in the future.

The preoperative ophthalmic examination will detect pathology that may be a contraindication to LASIK. Fuchs corneal endothelial dystrophy has been associated with poor flap adhesion and corneal decompensation. A thorough peripheral retinal examination is necessary to rule out retinal tears, especially in highly myopic eyes. The presence of systemic autoimmune disease has been associated with corneal melting after PRK and may therefore increase LASIK risks, although the peer reviewed literature on this topic is sparse. Because corneal hydration, refractive error, and wound healing may be altered during pregnancy and lactation, these conditions should delay LASIK.

The ocular surface should be evaluated carefully before surgery and patients with preexisting dry eyes should be warned about potential postoperative exacerbation, because many patients experience dry eyes with superficial punctate keratopathy for weeks to months after LASIK.[5] Corneal epithelial basement membrane dystrophic changes increase the risk of epithelial sloughing at surgery and later epithelial ingrowth and diffuse lamellar keratitis, and may be an indication for PRK rather than LASIK.[6] Significant blepharitis should be treated preoperatively to decrease the risks of infection and interface inflammation following surgery.

Pupil size measurement in low light conditions should be performed, because increasing pupil size may be correlated with increased postoperative vision disturbances such as halos and glare.[7] Many surgeons consider that a pupil size greater than 7 mm in dim illumination increases the risk of corneal refractive surgery, especially in highly myopic or astigmatic eyes, although the allowable size may vary with the diameter of the treatment and blend zones of the laser ablation. The goal is to have an effective treatment zone at least as large as the scotopic pupil.

Corneal topography measurement to assess corneal shape is a critical feature of the pre-LASIK evaluation. It can detect irregular astigmatism, whether from contact lens warpage or other causes, which, if significant, is a contraindication to LASIK. Additionally, corneal topography is used to screen for keratoconus or asymmetrical steepening, which may be associated with unpredictable refractive outcomes and progressive ectasia after LASIK.[8] Inferior corneal steepening, sometimes designated as forme fruste keratoconus, is a frequent finding in corneas that appear normal on slit-lamp biomicroscopy, and mathematical indices to detect subtle keratoconus topographically have been developed.[9] Flat corneas are important to note preoperatively, because they are associated with small microkeratome flaps and free caps, and steep corneas are associated with flap buttonholes.[10] Corneal topography is also useful in predicting the final keratometry after LASIK. Central keratometry flatter than 35 or 36 D or steeper than 50 D after LASIK is said to be associated with a decrease in quality of vision.

Measurement of corneal thickness is also critical in the preoperative assessment for LASIK. While corneal thinness may be an indication of subtle keratoconus, it also indicates a need for caution in tissue removal. The safety goal is to leave a central bed beneath the microkeratome flap that will allow corneal stability and prevent bulging or ectasia. Apparently the flap itself does not contribute to stability of central corneal curvature. While the minimum safe bed thickness is not known with certainty, it is thought to be at least 250 μm, and many surgeons recommend leaving 275 or 300 μm.[11,12] The surgeon and patient need to take into account whether the corneal bed will be thick enough for an enhancement after LASIK. The amount of tissue removed varies with laser algorithms but is a function of treatment diameter and dioptric correction. The depth of ablation is determined using the Munnerlyn formula[13]:

$$\text{Ablation depth in microns} = \frac{\text{D}}{3} \times (\text{ablation diameter in mm}^2)$$

Microkeratome Issues

Ideally, the microkeratome should cut flaps within a narrow range of acceptable thickness. A microkeratome that tends to cut thin flaps is more likely to produce buttonholes. Conversely, thick flaps leave a thinner corneal bed and limit the amount of ablation that can be safely performed. Based on case reports and biomechanical considerations, a residual posterior stromal thickness of at least 250 μm is recommended to reduce the risk of post-LASIK keratectasia.[14–16] In addition to this minimum stromal bed thickness, Joo and Kim[17] indicate that the stromal bed should be at least over half of the original corneal thickness. In calculating expected residual thickness, the average flap thickness and its

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range of variation as well as the estimated ablation depth should be considered. To help ensure an acceptable final postoperative residual stromal thickness, flap thickness is most often measured by intraoperative subtractive pachymetry, taking the difference between ultrasound pachymetry measurements of the intact cornea and the posterior stromal thickness after the microkeratome cut.[18–24]

Review of the literature suggests that the average flap thickness does not predictably follow the manufacturer's label due to instrument variability and other operative factors.[18–24] The standard deviation of flap thickness by subtractive pachymetry ranges from 16 to 30 μm in these studies. Presumably some of the variability is due to inconsistency in the positioning of the ultrasound probe. Mapping of the flap thickness using very-high-frequency ultrasound B-scan[25] or imaging with optical coherence tomography[26] may yield more accurate flap thickness measurements by reducing the positioning problem. The flap thickness standard deviation with optical coherence tomography was 19 μm in one report.[26] Preoperative corneal thickness was positively correlated with flap thickness in some studies,[20,21,23] but not in another.[22] A study with enucleated pig eyes reported thicker flap measurements with slower microkeratome translation speed,[27] indicating that translation speed may introduce additional variability with manually advanced microkeratomes. The suction ring pressure was found to influence flap thickness in another study.[28] Repeat blade (metallic) use was associated with progressively thinner flaps in enucleated eye studies, likely due to dulling of the microkeratome blade.[29,30]

The diameters of flaps are typically reproducible within a standard deviation of less than 0.4 mm.[18,23] Steeper corneas are associated with larger flaps.[23] Manufacturers designate predicted flap diameters for each suction ring, provide nomograms for predicting flap diameters given keratometry and suction ring designation (eg, Moria's Carriazo-Barraquer and M2 [Doylestown, PA]), or provide intraoperative flap diameter estimation (eg, Alcon's Summit Krumeich-Barraquer [Fort Worth, TX]). The flap size should adequately accommodate the laser ablation zone.

In a number of studies the scanning electron microscope has examined the smoothness of the stromal surface after the microkeratome cut.[29–32] Rougher cuts have been associated with higher translation speed relative to blade oscillation rate[32] and with repeat blade use.[29,30] The clinical significance of these findings has not been demonstrated.

Operative Technique

Before surgery the excimer laser, suction ring, microkeratome, and blade should be checked by the technician and the surgeon. The surgeon should also confirm that the correct treatment data were entered into the laser computer. An eyelid speculum is inserted in the operative eye, which has been anesthetized topically, and the fellow eye is covered. The cornea is marked with an instrument and dye to aid in postoperative flap or free cap alignment. A suction ring is placed on the eye to achieve an intraocular pressure (IOP) of greater than 65 to 70 mmHg. The elevation in IOP is verified using a combination of techniques that include noting pupil dilatation; using finger tension, a contact applanation device, or pneumotonometer; and by the patient's report of dimming of vision. The microkeratome is used to perform a lamellar keratotomy and create a hinged corneal flap with adequate central clearance for the treatment zone of the excimer laser ablation. Depending on the microkeratome used, the flap hinge may be superior, nasal, or oblique. Depending on total corneal thickness, the flap thickness chosen for a particular microkeratome may be between 130 and 180 μm.

After the flap has been created, it is reflected above and away from the cut exposed surface, and the stromal bed is examined for regularity. If it is regular, the excimer laser ablation is performed, centered on the pupil, in a similar fashion to PRK. Following ablation, the flap is repositioned with some irrigation of the interface bed. Once flap alignment is verified and the peripheral gutters are inspected and found to be minimal and symmetric, the flap is allowed sufficient time to adhere. The eyelid speculum is carefully removed without disturbing the flap. The eye is examined at a slit-lamp biomicroscope 5 to 30 minutes later to verify flap alignment.

If the flap created during the LASIK procedure is irregular, incomplete, or buttonholed, laser treatment often cannot safely be performed in the same session. However, after a healing period, a recut and ablation may subsequently be performed successfully in some cases.[33]

Postoperative Management

Patients may have mild postoperative discomfort for 4 to 6 hours following LASIK treatment, during which time they should keep their eyes closed and rest or take a nap. Patients should not rub their eyes for at least several days and preferably several weeks after surgery. They are usually given steroid drops and antibiotic drops to use for 4 to 10 days after surgery, and they are generally seen 1 day, 1 week, 1 month, 3 months, 6 months and 12 months postoperatively. Patients are usually told to use preservative-free or minimally preserved tears at least four times a day starting the day after surgery for a duration of weeks to months depending on the amount of dryness symptoms and corneal punctate staining.

Refractive stabilization for myopes may require up to 3 months and usually longer for hyperopes, depending on the amount of treatment performed. Reoperations, also called enhancements, can be performed once the refraction is stable for at least 1 month after surgery, but generally is not performed before 3 months.

FDA Status

The Food and Drug Administration (FDA) premarket approval process for LASIK began in the mid-1990s. Currently seven excimer lasers are approved by the FDA for myopia with or without astigmatism (see Table 1).

Microkeratome manufacturers are required to submit a 510(k) premarket notification to the FDA to demonstrate that the device to be marketed is as safe and effective as (that is, substantially equivalent to) a legally marketed de-

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Table 1. FDA-Approved Lasers for LASIK for Myopia and Astigmatism

Company and Model	Approval Number and Date	Approved Indications
Autonomous Technology (LADARVision)	P970043/S5 5/9/00	Myopia less than −9.0 D with or without astigmatism from −0.5 to −3.0 D
Bausch & Lomb Surgical (Technolas 217a)	P990027 2/23/00	Myopia from −1.0 to −7.0 D with or without astigmatism less than −3.0 D
CRS/VISX (Star S2/S3)	P990010 11/19/99	Myopia less than −14.0 D with or without astigmatism between −0.5 and −5.0 D
Dishler	P970049 12/16/99	Myopia from −0.5 to −13.0 D with or without astigmatism between −0.5 to −4.0 D
Kremer	P970005 7/30/98	Myopia from −1.0 to −15.0 D with or without astigmatism less than −5.0 D
Nidek (EC5000)	P970053/S2 4/14/00	Myopia from −1.0 to −14.0 D with or without astigmatism less than 4.0 D
Summit (Apex Plus)	P930034/S13 10/21/99	Myopia less than −14.0 D with or without astigmatism from 0.5 to 5.0 D

Source: Food and Drug Administration Center for Devices and Radiological Health. Available at http://www.fda.gov/cdrh/lasik/lasers.htm. Accessed 8/21/01.

D = diopters

vice that is not subject to premarket approval. Premarket notification is required at least 90 days before marketing unless the device is exempt from 510(k) requirements.

The FDA deemed that the microkeratome device is "substantially equivalent (for the indications for use stated in the enclosure) to devices marketed in interstate commerce before May 28, 1976, the enactment date of the Medical Devices Amendments, or to devices that have been reclassified in accordance with the provisions of the Food, Drug, and Cosmetics Act (Act)." As a consequence the microkeratome manufacturers were given the FDA clearance to "market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration."

Resource Requirements

To perform LASIK a surgeon needs to be trained in the use of both a microkeratome (or, most recently, a laser) to create a corneal flap and an excimer laser to perform the refractive ablation. Each laser company requires successful completion of a course specific to each particular excimer laser. These courses may be given for free or for a fee of upwards of $1000 each.

Most surgeons who perform LASIK do not own a microkeratome or excimer laser. The equipment is typically owned by a corporate laser center or a hospital. In some cases a company will deliver a microkeratome set, mobile excimer laser, and technical staff to the surgeon so the surgery can be performed in his or her office. In these cases the surgeon has minimal start-up costs to perform LASIK. Surgeons who wish to have more control over the global fee the patient is charged can lease or buy their own equipment. A microkeratome set costs approximately $40,000 to 60,000, and an excimer laser costs $250,000 to 550,000.

The cost of LASIK surgery to the patient varies greatly, between approximately $500/eye and $3000/eye. Depending on the cost, this fee may or may not include follow-up care, initial medications, and enhancements.

Questions for Assessment

The focus of this assessment is to address the following questions:

- What is the efficacy (predictability, stability) of LASIK for myopia and astigmatism?
- What are the complications of LASIK?

Description of Evidence

The peer-reviewed literature was analyzed and all possible relevant articles were selected. The literature search was conducted in March 2000 in MEDLINE for 1968 to 2000 and was limited to articles published in English. The Cochrane Library of clinical trials was also investigated. The search text words were LASIK or laser in situ keratomileusis. This search selected 486 citations, and an update search conducted in June 2001 yielded 243 additional articles. Abstracts of meeting presentations were not subject to peer review and were not included in the analysis.

The authors selected 160 articles of possible clinical relevance for review by the panel. Of these, 47 were considered sufficiently clinically relevant for review by the panel methodologist, who assigned one of the following ratings of level of evidence to each of the selected articles. A Level I rating is assigned to properly conducted, well-designed randomized clinical trials; a Level II rating is assigned to well-designed cohort and case-control studies; and a Level III rating is assigned to case series. Members of the Ophthalmic Technology Assessment Committee, other AAO committees, and relevant subspecialty societies re-

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viewed drafts of this document before formal approval by the Board of Trustees.

The published peer-reviewed literature through May 2001 contained seven randomized clinical trials that were assigned Level I ratings [34–40] and 10 additional articles that received Level II ratings.[41–50] Four Level I trials were from a comparison of LASIK and PRK using the Summit laser and were carefully designed studies, although follow-up was relatively short.[37 to 40] Two Level I trials compared LASIK and PRK for low to moderate myopia,[34,35] and there was one randomized controlled trial comparing single-zone and multizone LASIK with a follow-up period of 3 months.[36] Five nonrandomized comparative trials[41,43–45,47] and five longitudinal cohort studies[6,42,46,48,51] were assigned Level II ratings. The study by Casebeer and Kezerian[52] included large numbers but had only a 3-month follow-up. The "preliminary trial" of Pallikaris and Siganos[43] had 100% one-year follow-up, but it evaluated only 20 eyes. Perez-Santonja et al[51] also had a very small sample size. Most of the studies reviewed were clinical case series and were considered to be Level III evidence. The methodologist considered the overall quality of the literature reviewed to be significantly better than that of the literature reviewed for the similar assessment of PRK published in 1999.[53]

Published Results

This assessment describes randomized controlled trials published in 1997 or later (Level I evidence) and more recent comparative and noncomparative case series (Level II and Level III evidence), focusing on results for safety and effectiveness. Tables 2A and 2B list the results for LASIK patients for different ranges of myopia, Table 3 lists the results for LASIK patients for different types of laser, and Table 4 compares the results for LASIK and PRK.

Outcomes of LASIK Surgery

In reviewing the literature, it is difficult to compare studies because of variations in the range of preoperative myopia, follow-up periods, lasers, nomograms, microkeratomes and techniques, the time frame of the study, and the investigators' experience. Compliance to follow-up also varies in many of these studies. Because of the rapid evolution of LASIK technology and techniques, it is also difficult to extrapolate results in the literature that are comparable to current practices that use the most recent generation lasers.

For low to moderate myopia, results from studies in the literature have shown that LASIK is effective and predictable in terms of obtaining very good to excellent uncorrected visual acuity and that it is safe in terms of minimal loss of visual acuity. For moderate to high myopia (>6.0 D), the results are more variable, given the wide range of preoperative myopia. The results are similar for treated eyes with low to moderate degrees of astigmatism (<2.0 D). One prospective, multicenter study shows that outcomes were similar among eyes with spherical myopia and eyes with myopia and astigmatism (≤5.0 D).[54]

Comparing PRK and LASIK, two randomized controlled clinical trials for moderate to high myopia (−6 to −15 D),[37,38] two randomized bilateral studies for low myopia (−2 to −8 D),[34,35] and other nonrandomized comparative studies have shown that visual acuity and refractive outcomes are similar at 6 months to 1 year after surgery. More rapid recovery of uncorrected visual acuity to 20/20 or better is seen with LASIK at 1 day and before 1 month after surgery. One randomized clinical trial did not find statistically significant differences in surgically induced astigmatism, although PRK tended to have more induced with-the-rule astigmatism.[40] This same trial did find that LASIK eyes had significantly more regular corneal topography than PRK eyes at 1 and 3 months after surgery.[40]

There were insufficient data in prospective, comparative trials to describe the relative advantages and disadvantages of different lasers or nomograms. One prospective, comparative trial did not find significant differences in predictability between multizone and single-zone ablation.[36]

Oshika et al[47] compared corneal wavefront aberrations in 22 patients who received PRK in one eye and LASIK in the other eye. The sequence of surgery and treatment was randomly assigned to each eye. Wavefront aberrations of the cornea were calculated based on corneal topography. The findings suggested that both PRK and LASIK increase the wavefront aberrations of the cornea. No significant differences were seen in a 3-mm pupil at 12 months, but significant differences were seen for a 7-mm pupil with LASIK having more induced wavefront aberrations (1.826 for the PRK group, and 2.724 for the LASIK group, $P < 0.001$).

Suiter et al[48] matched 82 eyes implanted with intrastromal corneal ring segments (INTACS, Addition Technology Inc., Fremont, CA) inserts to 133 eyes treated with LASIK, based on the following factors: age, preoperative myopia (−1.00 to −3.5 D), astigmatism (≤1.00 D), and single treatment for full correction. Visual acuity and predictability were evaluated at 3 months. At 1 day following surgery, uncorrected visual acuity was 20/20 or better in 24% of INTACS eyes compared with 55% of LASIK eyes. At 3 months 75% of INTACS eyes and 67% of LASIK eyes achieved an uncorrected visual acuity of 20/20 or better. Seventy percent of INTACS eyes were within 0.50 D of intended correction compared with 82% of LASIK eyes. Seven of the INTACS eyes lost two or more lines of BCVA compared with one LASIK eye.

Variables Affecting Outcomes

Excimer lasers marketed for laser vision correction provide internal nomograms that prescribe the amount of laser treatment given the target refractive correction. These nomograms are typically calibrated on the basis of premarket clinical trials. To improve the accuracy of refractive correction, individual surgeons and laser centers may customize nomograms based on their own results. Developing a nomogram requires analyzing a database containing laser settings, preoperative and postoperative refraction, laser parameters, surgical techniques, and patient characteristics. Software programs are commercially available to help develop nomograms.

Larger laser transition zones increase treatment effects.[55]

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Table 2A. Results of LASIK for Low to Moderate Myopia (−1 to −6 D)

First Author, Year Study was Performed	No. of Eyes	Follow-up in Months (% Who Completed)	Level of Evidence	Range of Preop Myopia (D) (Astigmatism)	Preop Refraction (D, Mean Spherical Equivalent)	Postop Refraction (D, Mean Spherical Equivalent)	Percent Within ± 0.50 D/ 1.0 D	Postop UCVA ≥20/20 (%)	Postop UCVA ≥20/40 (%)	Loss of ≥2 Lines BCVA (%)
El Danasoury,[35] 1999	26	12 (92.3)	I	−2 to −5.5	−3.44 ± 0.72	−0.14 ± 0.32	83.3/100	79.2	100	0
El Maghraby,[34] 1993–1994	33	12 (91)	I	−2 to −8 (±1.0 D)	−4.80 ± 1.6	0.0 ± 0.60	73/90	61		7
		24 (85)					71/87.5	63	100	0
Casebeer,[52] 1996–1997	911	3 (100)	II	−1 to −4	NR	NR	75/90		92	0
				−4 to −7			52/73		86	0
Mrochen[101] Published 2001	35	3 (88)	III	−1.0 to −9.5 (<3.5 D)	−4.8 ± 2.3	−0.22 ± 0.59	68/93.5	93.5	100	0
Reviglio[41] 1998–1999	74		III	−1.0 to −4	−2.21 ± 0.88	−0.09 ± 0.41		60.8	100	0
		6 (100)					90.44/ 96.32			
	62			−4.0 to −6	−4.59 ± 0.60	−0.26 ± 0.74		45.2	95.2	0

BCVA = best corrected visual acuity; D = diopter; NR = not reported; UCVA = uncorrected visual acuity.

Multizone and single-zone ablation profiles require separate nomogram adjustments.[36] Hyperopic correction requires ablation profiles that contain sharper transitions and it results in greater postoperative regression of effect.[56] This requires greater nomogram compensation with increased laser treatment.[57]

Depending on the laser, LASIK and PRK may achieve different amounts of correction. Two studies found that myopic LASIK with the Nidek EC-5000 required 19% to 20% reductions relative to the internal nomogram developed for PRK,[55,58] while one study with the Summit Apex-Plus laser found that the LASIK nomogram should be adjusted upward.[37] For LASIK, the hinge position may affect outcome. In one study, an average 0.24 D of induced with-the-rule astigmatism was associated with superiorly hinged flaps.[59] Age has been found to affect refractive outcome in several studies.[60–62] Prior refractive surgery was found to affect the outcome of hyperopic LASIK.[60] One study with neural network[62] found that sex, keratometry, and intraocular pressure also affect outcome. Another study suggests that hormone-replacement therapy for menopause may decrease the effectiveness of PRK.[63]

Nomogram development for astigmatic correction requires the use of vector analysis.[58,64,65] Some lasers may also require analysis of the linkage between cylindrical

Table 2B. Results of LASIK for Moderate to High Myopia: (−6 to −25 D)

First Author, Year Study was Performed	No. of Eyes	Follow-up in Months (% Who Completed)	Level of Evidence	Range of Preop Myopia (D) (Astigmatism)	Preop Refraction (D, Mean)	Postop Refraction (D, Mean)	Percent Within ±0.50 D/ 1.0 D	Postop UCVA ≥20/20 (%)	Postop UCVA ≥20/40 (%)	Loss of ≥2 Lines BCVA (%)
Hersh[37] Published 1998	115	6 (58)	I	−6 to −15 (≥2.0 D)	−9.3 ± 1.7	NR	27.1/40.7	26.2	55.7	3.2
Steinert[38] Published 1998	76	12 (68)	I	−6 to −12 (<1.5 D)	−9.2 ± 1.2	NR	23/54	36	85	2
Casebeer,[52] 1996–1997	911	3 (100)	II	−7 to −10	NR	NR	40/54	NR	68	0
Perez-Santonja[42] 1995	143	6 (NR)	II	Total group:				NR		
				−8 to −20 (≥1.5 D)	−13.19 ± 2.89	+0.181 ± 1.66	/60.0		46.4	1.4
				Subgroups:						
	59			−8 to −12	−10.48 ± 1.08	+0.30 ± 1.23	/72.4			
	54			−12 to −16	−13.73 ± 1.04	+0.25 ± 2.09	/46.0			
	30			−16 to −20	−17.54 ± 1.35	−0.20 ± 1.58	/50.0			
McDonald[54] 1998–1999	347	6 (94.4)	III	−1 to −11 (≤ 5.0 D)	NR	−0.29 ± 0.45	75.2/95.2	57.0	94.0	0.9
Pallikaris,[43] 1994	20	12 (100)	II	−8.80 to −19 (≤5.0 D)	−10.62 ± 25.87	NR	/66.6	NR	NR	0
Kawesch[102] 1996–1998	290	9 (67.6)	III	−9 to −22	NR	−0.46 ± 1.12	/75.9	NR	85.1	3.6
Reviglio[41] 1998–1999	126	6 (100)	III	−6.0 to −10	−7.63 ± 1.09	−0.37 ± 0.92		25.4	87.2	0
							68.42/85.08			
				−10 to −25	−12.70 ± 2.81	−0.64 ± 1.23		9.8	78.4	0

BCVA = best corrected visual acuity; D = diopter; NR = not reported; UCVA = uncorrected visual acuity.

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Table 3. Comparison of Summit and VISX Lasers for LASIK

First Author, Year Study was Performed	No. of Eyes	Follow-up in Months (% Who Completed)	Level of Evidence	Range of Preop Myopia (D) (Astigmatism)	Summit Percent Within 0.50 D/1.0 D	VISX Percent Within 0.50 D/1.0 D	Summit Postop UCVA >20/20 (%)	VISX Postop UCVA ≥20/20 (%)	Summit Loss of >2 Lines (%)	VISX Loss of ≥2 2 Lines (%)
Casebeer[52] 1988	486 Summit	3 (100)	II	Total −1 to −10			27.4	27.0	0	0
	425 VISX			Subgroups:						
				−1 to −4	78/91	73/89			0	0
				−4 to −7	50/72	55/74			0	0
				−7 to −10	29/53	56/56			0	0

D = diopter; UCVA = uncorrected visual acuity.

ablation and spherical refractive outcome. In particular, the Nidek EC-5000 has been found to produce an unexpectedly large coupling between negative cylinder ablation and hyperopic shift.[58]

Complications

Complications occur in LASIK as in any other surgical procedure. There is no accurate estimate of the incidence of complications because of the difficulty in defining what constitutes a complication compared to a minor nuisance or annoying side effect. However, serious adverse complications leading to significant permanent visual loss such as infections and corneal ectasia probably occur rarely in LASIK procedures.[66–68] In contrast, annoying side effects such as dry eyes, night time starbursts, and/or reduced contrast sensitivity occur relatively frequently.[7,69] Usually patients consider these symptoms minor nuisances but in rare situations they may be so severe that they cause optical handicap. Furthermore, patients usually perceive serious complications more critically because their corrected visual acuity was most likely excellent before the procedure and because they elected to have surgery.

The most common complication/side effect following LASIK is the induction of a relative dry eye state.[70,71] Multiple factors have been implicated in this problem, including aqueous tear deficiency, poor tear film coverage of an altered (flatter or steeper) corneal shape, and neurotrophic epitheliopathy. Fluorescein, lissamine green, and/or rose bengal staining of superficial epithelial keratopathy occurs in the exposure area of the cornea in both the flap and the surrounding cornea. Patients experience a foreign body sensation and decreased or fluctuating vision. Symptoms tend to improve with time, but decreased Schirmer's tests (from preoperative levels) are recordable 1 year postoperatively. Treatment has consisted of nonpreserved lubricating drops and temporary or permanent punctal occlusion.[5]

Complications from LASIK surgery can occur in the flap, interface, stromal bed, and fundus of the eye. Complications involving the LASIK flap have been reported to occur in approximately four percent of primary LASIK cases.[6,66,67] Intraoperatively these events include free, incomplete, or buttonholed flaps and postoperatively they include striae/folds or slipped/displaced flaps. Free caps are usually replaced after laser ablation with good visual results. Incomplete and buttonholed flaps are managed by replacing the flap without performing the laser treatment. Postoperative striae and/or folds may adversely affect visual acuity and contrast sensitivity, and treatment has included refloating the flap at the earliest possible time. If prolonged time has elapsed, options for treatment include lifting the flap combined with removing the flap epithelium; warming the flap; or treating the flap with hypotonic saline and replacing the treated flap by stretching and/or suturing it back into position.[68,72] The relative efficacy of these techniques is uncertain.

Flaps may become displaced during the early or late postoperative period.[73,74] Early displacement is usually observed on the first postoperative day and may occur either spontaneously or as a result of minor manipulation of the eye. The incidence of early flap postoperative displacement has been reported to be approximately 1.5%.[6] The flap is replaced immediately and visual acuity is generally not affected. Late flap displacement (more than one month postoperatively) is rare and typically results from direct trauma to the eye.[74–76] The incidence of late displacement of the flap is unknown.

Complications that occur at the level of the interface between the flap and the stromal bed include diffuse lamellar keratitis, infection, and epithelial ingrowth. Diffuse lamellar keratitis is an inflammatory disorder characterized by a sterile diffuse cellular infiltrate in the LASIK interface typically beginning 1 to 3 days after surgery.[77–79] Although many cases are sporadic, some occur in clusters and the reported incidence has varied from nonexistent to 5% of cases. Treatment consists of topical corticosteroids combined with lifting the flap and irrigating beneath it in the most severe cases. Some surgeons also find a short course of oral corticosteroid helpful. The etiology has been variously ascribed to bacterial endotoxin, residual cleaning solution on the instruments, epithelial abrasions, or infections. In cases of mild or moderate intensity, visual acuity is not permanently affected. In severe cases persistent stromal haze, loss of stromal tissue, and irregular topographic changes are common, with resultant adverse effects on visual function.

Epithelium may grow into the interface between the LASIK flap and the stromal bed.[80–82] This complication,

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Table 4. Comparison of LASIK

First Author, Year Study was Performed	No. of Eyes	Follow-up in Months (% Who Completed)	Level of Evidence	Preop Myopia (D) (Astigmatism)	Preop Mean Spherical Equivalent PRK (D)	Mean Preop Spherical Equivalent LASIK (D)	PRK Mean Postop Spherical Equivalent (D)
Hersh[37]	105 PRK	6 (58)	I	−6 to −15	NR	NR	NR
Published in 1998	115 LASIK			(≤2.0 D)			
Steinert[38]	76 PRK	12 (68)	I	−6 to −12	NR	NR	NR
Published in 1998	76 LASIK			(<1.5 D)			
El Danasoury[35]	26 PRK	12 (92)	I	−2 to −5.5	−3.23 ± 0.63	−3.44 ± 0.72	−0.08 ± 0.38
1999	25 LASIK						
El Maghraby[34]	33 PRK	12 (91)	I	−2 to −8	−4.70 ± 1.50	−4.80 ± 1.60	−0.10 ± 0.60
1993–1994	33 LASIK			(±1.0 D)			
		24 (85)					
Tole[44]	308 PRK	6 (55)	II	−0.5 to −6.0	NR	NR	NR
Published in 2000	314 LASIK						
Pop[45]	107 PRK	12 (70)	II	−1 to −9.5	NR	NR	NR
Published in 1998	107 LASIK			(<4.5 D)			
Fernández[46]	75 PRK	12 (NR)	II	−1 to −3	−3.28 (range: −1.00 to −6.00)	−3.86 (range: −1.00 to −6.00)	−0.18 ± 0.61
Published in 2000	133 LASIK			−3 to −6			−0.44 ± 0.87

D = diopter; NR = not reported; PRK = photorefractive keratectomy; UCVA = uncorrected visual acuity.

called epithelial ingrowth, occurs in 0.2% to 2.2% of cases. It appears to be more common following primary hyperopic treatments, enhancements, corneal abrasions, and displaced flaps. Surgical intervention to remove the epithelium is required for progressive ingrowth greater than 1.0 to 2.0 mm from the flap margin in approximately 1.4% of LASIK cases.[83] Epithelial ingrowth may result in melting of the overlying LASIK flap as well as irregular astigmatism.[80] Surgical removal requires lifting the involved portion of the flap and debriding epithelium from the stromal surface of the flap and the stromal bed.[82]

Infection following LASIK is very uncommon and has been estimated to occur in approximately 1 in 5000 cases. [Suarez E, personal communication, 2001] Early postoperative infections have been reported from staphylococcus and streptococcal species, and delayed onset infection has been reported from mycobacterium species.[84–91] Early acute infection may result in corneal opacification, melting, and irregularity. Late presenting infections due to mycobacteria are difficult to cure and occasionally require amputation of the flap to facilitate antibiotic access.

Many patients report difficulty in night driving after LASIK surgery. Factors contributing to night driving problems include a postoperative decrease in contrast sensitivity and starburst and halos around lights at night.[7,69] The origin of these symptoms is multifactorial and includes aberrations at the edge of the ablation zone, irregular astigmatism, decentered ablations, and flap striae.

LASIK has the potential to disrupt fusion, causing strabismus and diplopia in susceptible patients.[92,93] Patients with a history of strabismus or with abnormal ocular motility preoperatively may benefit from more extensive ocular motility testing before undergoing LASIK.

The corneal surface may become progressively distorted after LASIK.[12,14,15] This induced ectasia, called keratectasia, may occur spontaneously as a result of a residual stromal bed that is too thin or from an inherent predisposition of the cornea to distortion. Rapid corneal steepening, distortion, and thinning develops, which requires penetrating keratoplasty. It has been advocated that the corneal bed be left with no less than 250 μm and 50% of residual stroma after LASIK. This recommendation is based on the finding that that a reduction in corneal thickness by less than 50% leaves a normal cornea with approximately the same distortability as a keratoconus cornea.[94]

It is uncertain if there is any relationship between LASIK and an increased incidence of postoperative retinal detachment.[95,96] No prospective study has been performed, and retrospective analysis has demonstrated no clear evidence of a relationship. Ischemic optic neuropathy has been reported following LASIK, and while the mechanism is unclear, it may be related to the high intraoperative pressure occurring during the microkeratome pass.[97,98]

Future Developments in LASIK

Developments in the LASIK procedure have occurred very quickly since the first FDA approval of the excimer laser. Nevertheless, future developments are still required to move this procedure to the next level of safety and efficacy.

At this time, our ability to refract a patient for the preoperative assessment is limited by the patients' ability to notice small refractive changes ("better 1 or 2"). With the development of wavefront technology, it may be possible to obtain refractive data without subjective patient responses,[99,100] and a new assessment of visual aberrations will be available. Time and experience will determine if some of these aberrations will alter our treatments or patient selection.

New advances in existing microkeratomes as well as the introduction of new microkeratomes will improve the abil-

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and PRK Results

LASIK Mean Postop Spherical Equivalent (D)	PRK Percent Within 0.50 D/1.0 D	LASIK Percent Within 0.50 D/1.0 D	PRK Postop UCVA >20/20 (%)	LASIK Postop UCVA ≥20/20 (%)	PRK Loss of ≥2 Lines (%)	LASIK Loss of ≥2 Lines (%)
NR	29.4/57.4	27.1/40.7	19.1	26.2	11.8	3.2
NR	44/65	23/54	26	36	11	2
−0.14 ± 0.31	83.3/100	87.5/100	62.5	79.2	0	0
0.0 ± 0.60	67/87	73/90		61	6	6
		71/87.5	27	63		
NR	82	78	65	80	1.0	1.4
NR	82.9/93.9	77.9/98.7	85.4	83.1	0	0
−0.08 ± 61	69/87	68/86	53	72		
					8	7.5
−0.09 ± 0.83	63/87	70/88	36	58.5		

ity to make consistent corneal flaps with a very low risk of complications. The use of lasers or water jet technology may allow for safer and more reproducible flap creation.

Laser technology today is already very different from the technology of 3 years ago. Recent advances include scanning lasers, eye-tracking systems, and larger ablation zones with even larger blend zones. Wavefront custom ablation is a promising laser development in the near future. Several laser companies are conducting clinical studies on treating higher order aberrations with customized ablations. These new advances may provide higher quality of vision to a larger percentage of LASIK patients.

The following issues need to be addressed in future research:

- How do we prevent iatrogenic keratectasia following LASIK?
  - Is a 250-μm posterior stromal bed sufficiently strong to prevent ectasia?
  - Does preoperative corneal thickness or the percentage of corneal tissue removed affect the required posterior stromal bed needed to prevent keratectasia?
  - What are the criteria for diagnosing forme fruste keratoconus as a contraindication to LASIK?
- What is the relationship between pupil size, treatment size, treatment depth, and glare or scotopic visual complaints following LASIK? What are the optimal optical and transition zones to prevent glare while minimizing tissue removal?
- Are there identifiable limits of corneal flattening (eg, $<$ 35–36 D) and corneal steepening (eg, $>$ 50 D) after which quality of vision decreases?
- Does lamellar surgery (required for LASIK) induce higher order aberrations that limit our ability to treat these abnormalities?
- How can a surgeon prevent epithelial defects when creating the lamellar flap?
- Does utilizing an active "eyetracker" improve visual outcomes? Does an eyetracker improve treatment centration? Can an eyetracker reduce glare complaints?
- Does excessive postoperative superficial punctate epitheliopathy induce regression?
- Is there a predictive test to determine which patients will have significant problems with superficial punctate epitheliopathy following LASIK?
- Are there pharmacologic ways to induce or prevent regression?
- Can flap complications such as buttonholes, free caps, irregular stromal beds, and macrostriae be prevented?
- Does LASIK improve quality of life for patients?

Conclusions

LASIK is an excellent procedure for many, but not all, patients. Some patients are not good candidates for a wide variety of reasons, and these patients should be counseled to not have surgery. Appropriate informed consent should be given to all patients preoperatively. The best results are obtained by surgeons who pay attention to checking the microkeratome and laser before surgery and maintain excellent surgical technique. Surgical complications, while rare, certainly occur. Newer microkeratomes and advances in excimer laser technology, including tracking systems, may help to decrease the number of surgical problems. Untoward postoperative effects, such as glare and halos, dry-eye-type symptoms, and decreased quality of vision are more difficult to address. Larger laser treatment zones, newer topical medications, and wavefront analysis may help ameliorate these issues in the future. Additionally, the importance of good postoperative care should not be over-

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Category	Abbreviation	Specific Financial Interests
Product	P	Financial interest in equipment, process, or product presented.
	Pc	Such interest in potentially *competing* equipment, process, or product.
Investor	I	Financial interest in a company or companies supplying the equipment, process, or product presented.
	Ic	Such interest in a potentially *competing* company.
Consultant	C__	Compensation received within the past 3 years for consulting services regarding the equipment, process, or product presented.
	Cc__	Such compensation received for consulting services regarding potentially *competing* equipment, process, or product.
		Examples of compensation received include:
	C1 or Cc1	1. Retainer
	C2 or Cc2	2. Contract payments for research performed
	C3 or Cc3	3. Ad hoc consulting fees
	C4 or Cc4	4. Substantial nonmonetary perquisites
	C5 or Cc5	5. Contribution to research or research funds
	C6 or Cc6	6. Contribution to travel funds
	C7 or Cc7	7. Reimbursement of travel expenses for presentation at meetings or courses
	C8 or Cc8	8. Reimbursement of travel expenses for periods of direct consultation
None	N	No financial interest. May be stated when such interests might falsely be suspected.

looked. While most patients require very little intervention by the doctor after surgery, when a question or problem does arise, the doctor needs to be available. Failure to promptly address postsurgical complications can have severe consequences. Some of the most satisfied eye care patients are LASIK patients, and the goal is to continue to increase the percent of patients who are happy with this surgery.

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