

Excimer Laser Photorefractive Keratectomy

Peter S Hersh, MD, FACS, Jonathan D Carr, MD, MA, FRCOphth

ABSTRACT

The excimer laser has developed rapidly from the laboratory to its current clinical use for refractive surgery, in a procedure known as photorefractive keratectomy (PRK). The excimer laser is able to meticulously sculpt the corneal surface, altering the surface optical architecture to correct refractive errors. Such surgery is achieved with minimal mechanical and thermal effects upon the remaining corneal tissue. Preoperative preparation is of paramount importance to the outcome of PRK. Computer-controlled application of laser energy remove a corneal tissue lens to achieve the desired refractive correction. Results to date have been encouraging. Several studies of low to moderate myopes have shown that generally 50% to 70% of patients obtain uncorrected vision of 20/20 or better and 80% to 95% obtain 20/40 or better. Ultimate correction appears stable without a progressive hyperopic shift. Epithelialization following PRK is prompt. Stromal wound healing may result in a fine stromal haze or significant scarring in rare cases. This article summarizes the principles of excimer laser PRK and reviews the procedure, results, and complications to date.

INTRODUCTION

Over the past decade, the excimer laser has evolved rapidly from the laboratory¹⁻⁴ to its current clinical use internationally for refractive surgery. Although currently an investigational device for refractive procedures in the United States, this promising modality is undergoing a number of rigorous clinical trials and is advancing through the regulatory guidelines of the U.S.

P. S. Hersh — Associate Professor; J. D. Carr — Clinical Cornea Fellow, Department of Ophthalmology, Albert Einstein College of Medicine, Bronx, New York

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Food and Drug Administration (FDA). Should the excimer laser ultimately be approved for use, this would bring a unique modality to the surgical correction of refractive errors.

OVERVIEW OF THE EXCIMER LASER

The excimer laser is based on the combination of two gases — a noble gas and halogen. Both of these are generally stable in their normal low energy state. When a high-voltage electrical discharge is delivered into the laser cavity containing these gases, however, the gases combine to form a higher energy gas state compound. The term “excimer,” indeed, is a contraction of “excited dimer.” Upon the dissociation of this high energy compound, a photon of energy is released corresponding to the bond energy of the noble gas:halogen molecule.^{5,6} This wavelength of light energy is amplified in the laser system, resulting in the production of a discrete high energy pulse of laser energy.

The specific wavelength of an excimer laser depends on the gases used. Excimer lasers in current clinical use rely on argon and fluorine gas to emit a wavelength of 193 nm, thus falling in the ultraviolet C range of the light spectrum. In contrast, the krypton fluoride excimer laser used in early laboratory studies emits a wavelength of 248 nm.^{7,8}

Laser energy at 193 nm is very well absorbed by the proteins, glycosaminoglycans, and nucleic acids comprising the cornea. Since a 193-nm photon is of higher energy than the molecular bond strength of these compounds, absorption of the laser energy results in breaking of the bonds. The resulting molecular fragments are ejected from the surface of the cornea at supersonic speeds.^{9,10}

The excimer laser tissue removal process is termed “ablative photodecomposition.”³ It is important to understand that the excimer laser does not cut tissue like a scalpel; rather it ablates or removes tissue from the corneal surface. The ablated material appears as an effluent plume that upon analysis has been shown to consist of a variety of high-molecular-weight hydrocarbons.¹¹

Unlike other lasers used in ophthalmic surgery, the excimer laser pulse can be delivered as a relatively broad beam. Current excimer lasers have beam diam-

eters up to 6.5 mm. Over the entire area upon which the laser beam impinges, molecular bonds are broken and tissue removed. Hence, relatively large areas of the cornea can be treated with each pulse. The excimer laser technique is thus qualitatively different from refractive surgical techniques such as radial keratotomy (RK), which achieves corneal reshaping through biomechanical changes mediated through thin knife incisions.

Several attributes of the argon fluoride excimer laser ablation process make it particularly appropriate for corneal sculpting. The laser energy is very well absorbed near the corneal surface and thus theoretically should produce few deep direct or secondary mechanical (shockwave) effects upon the corneal tissue. The ablation process is rapid and excess energy is ejected with the effluent plume.¹² Thus there appears to be minimal thermal damage to the tissue as well. These attributes allow the excimer laser to meticulously etch the corneal surface while minimizing damage to the remaining tissue,^{7,13} and first suggested its use for refractive surgery via the strategy of corneal sculpting.

Although there appears to be relatively little "collateral" damage to the corneal tissue produced by excimer laser treatment, corneal wound healing remains a major variable affecting clinical outcomes. Although significant scarring does not seem to be a problem with current excimer laser clinical protocols, there is, indeed, documentable corneal wound healing after treatment. This includes epithelial healing over the ablated area.¹⁴ Moreover, new collagen synthesis is found in the superficial stroma in the area of photoablation.¹⁵ Such wound healing, as we shall see, likely accounts for variations in treatment results. To date, however, the wound healing that does occur appears to result in acceptable clinical outcomes.

Finally, with any laser radiation, particularly in the ultraviolet spectrum, there is always concern of the potential for mutagenesis or carcinogenesis. A number of studies has demonstrated that the 193-nm excimer laser is neither mutagenic nor carcinogenic.^{16,17} This may in part be due to shielding of the nucleus by the cell's cytoplasm.

LASER CONFIGURATION FOR REFRACTIVE SURGICAL PROCEDURES

Current manufacturers of excimer lasers in clinical use include Summit Technology, VisX, Chiron Technolas, Nidek, Meditec, Schwind, LaserSight, and Novatec. Until recently, only the Summit and VisX excimer lasers have been undergoing clinical trials in the United States. Now others are in the early phases of clinical investigation.

As of this writing, the Summit excimer laser has received full FDA approval for phototherapeutic keratectomy (PTK) for the treatment of a variety of corneal disorders. In addition, the FDA advisory panel has recommended that the Summit excimer laser be conditionally approved for myopic refractive procedures. The FDA advisory panel has also recommended conditional approval of the VisX excimer laser for therapeutic procedures.

The clinical excimer laser is comprised of the following components: (1) gases, (2) a power source, (3) a laser cavity, (4) beam forming optics, (5) a delivery system, (6) an aiming system, and (7) a surgical microscope.

In most current excimer laser systems, the initial pulse delivered from the laser cavity is a broad rectangular beam of irregular energy level. For clinical use, this beam needs to be homogenized to yield a consistent energy over the entire delivery area. In the absence of a smooth and consistent beam energy, ablation rates could vary over the treatment area, resulting in irregular tissue removal. In addition, the beam needs to be masked in two dimensions to the appropriate size and shape. Such beam homogenization and shaping are accomplished through beam-shaping optics in the optical train of the laser. Moreover, a diaphragm¹⁸ interposed within this optical train masks the beam, causing it to be delivered as a circular spot of chosen diameter.

The energy level and homogeneity of the laser beam must be verified prior to treatment. This is accomplished through energy level monitors within the laser units. In addition, controlled test ablations on polymethylmethacrylate (PMMA) disks can then be measured to verify the appropriate ablation depth as well as surface smoothness. Current excimer lasers in clinical use operate at energy levels of approximately 160 to 180 mJ, a pulse rate of 5 to 10 pulses Hz, and a pulse duration of approximately 10 nanoseconds. The expected ablation rate of corneal tissue averages approximately 0.25 μm per pulse.¹⁹⁻²¹

To achieve refractive correction, the excimer laser energy is applied to the patient's cornea in a controlled fashion in order to sculpt the appropriate tissue lens from the corneal surface. In most excimer laser units this is accomplished by a diaphragm interposed within the optical rail of the system which expands as the treatment proceeds. Consecutively less tissue is thus removed from the center to the periphery of the ablation zone, with consequent flattening of the corneal surface; the excimer laser thus corrects myopic refractive errors by removing a plus spherical lens tissue from the corneal surface through the process of tissue ablation. The pace of diaphragm opening and duration of the procedure, and consequently the refractive correction, are determined by parameters programmed into the excimer laser's computer control.

Other strategies have been and are currently being developed to sculpt the corneal surface for refractive computer control. Summit Technology has developed an ablatable mask that is a PMMA lens interposed between the laser and the patient.²²⁻²⁴ This mask is progressively ablated by the incoming laser beam. Thus a concave mask is completely ablated centrally before peripherally. As the mask shield to the incoming beam is progressively ablated away, the optical power of the mask is transferred to the corneal surface. Theoretically, toric as well as spherical surfaces can be achieved.

Other laser strategies include a small scanning beam (e.g., LaserSight) or a scanning slit (e.g., Nidek) that can be programmed to properly ablate the desired tissue.

Strategies for the correction of astigmatism include the ablatable mask, expandable slits (for correcting cylindrical errors), and elliptical diaphragms for toric ablations. In all astigmatism strategies using the excimer laser, the goal is to remove a spherocylindrical tissue lens from the corneal surface.

Laser-Eye Coupling

Another important component of the clinical excimer laser system is the modality of laser-eye coupling. Initially, some investigators used a variety of handheld fixation devices and suction rings to stabilize the patient's eye. Most ophthalmic surgeons, however, have switched to simple patient fixation; the patient is directed to fixate on a target coaxial with the incoming laser beam. This seems to allow for better centration of the procedure than does actual physical fixation.²⁵ In the future, laser-eye coupling may be achieved by a variety of eye-tracking devices that currently are in the developmental stage. Optimally, the laser will follow the eye in real time, thus minimizing the effects of eye movements during the procedure.

Nitrogen Blowing System

In early clinical work with some laser systems, nitrogen was blown over the corneal surface while suction was also applied to the treatment area. This technique was devised to remove the effluent plume between each laser pulse, preventing masking of the incoming beam by the plume of the preceding pulse. Laboratory work has shown the cornea to be less smooth after this technique and clinical results were found to be somewhat worse using these interventions.²⁵⁻²⁷ Therefore, most procedures now do not incorporate the nitrogen blowing system.

PREOPERATIVE PATIENT EVALUATION

Preoperative patient evaluation and other procedures are of utmost importance in PRK. Patient evaluation should include multiple refractions and a complete re-

fractive history. Both subjective and cycloplegic refractions should be obtained and the surgeon must be assured that the refraction is stable. This can be ascertained by a review of the patient's chart, inspection of old glasses, or with serial examinations.

A complete eye history and examination are mandatory. Generally, patients eligible for PRK are those with healthy eyes and with no contraindicating factors. Patients with evidence of any disease processes that could conceivably affect subsequent wound healing should not undergo the procedure. These include patients with collagen vascular disease, ocular surface inflammatory diseases, severe dry eye, and uncontrolled diabetes.

Examination should focus on careful observation of the conjunctiva, tear film, and corneal surface integrity. PRK for patients with keratoconus is contraindicated. Patients with endothelial disease should also be excluded. Further investigation (see below) will help identify those patients whose postoperative outcomes likely will be good or poor.

Keratometry and computerized corneal topographic analysis²⁸ should be performed, especially to exclude patients with irregular astigmatism and incipient keratoconus.^{29,30} In current clinical studies, contrast sensitivity and glare testing are also performed.

Informed consent is required. The patient must be informed of both the potential optical (e.g., glare, halo) and physical (e.g., scarring) complications of the procedure.

PREOPERATIVE PROTOCOL

Preoperatively, the target eye is labelled and the contralateral eye is patched. The refractive correction is confirmed. It is important that the surgeon make the patient feel comfortable, confident, and cooperative. A mild sedative may be administered. In general, the patient is positioned on the excimer laser chair. Several drops of a topical anesthetic are applied and then a lid speculum is placed.

The patient is then properly aligned under the laser downtube. This procedure differs with the various laser systems. Generally, the patient is asked to fixate on a light that is coaxial with the incoming laser beam. While the patient is fixating, the eye is moved into position such that the incoming beam is centered around the patient's entrance pupil. Theoretical analysis has shown that refractive surgical procedures should be centered on the patient's entrance pupil while the patient is coaxially fixating; this should lead to fewer optical aberrations postoperatively.³¹

The patient is then explained what sensations he or she may expect to experience; these include the laser snapping sounds and effluent smell.

The excimer laser is programmed by the surgeon's assistant

THE PRK PROCEDURE

Once the patient is relaxed, comfortable, and ready to proceed, the surgeon uses a round optical zone marker to mark the border of epithelium to be debrided. The epithelium is then carefully removed with a scarifier blade and cellulose sponges. Care is taken not to damage Bowman's layer. Moreover, the basal epithelial cells must be meticulously removed, as any residual epithelium would block the incoming beam and lead to uneven ablation.

Upon epithelium removal (approximately 7 mm in diameter to accommodate a 6.0-mm laser optical zone size), centration is assured and the foot pedal of the laser is depressed. A typical treatment may take approximately 200 laser pulses: 20 sec at 10 Hz or 40 sec at 5 Hz.

POSTOPERATIVE MANAGEMENT

At the end of the procedure, a combination antibiotic/steroid ointment is applied and the eye is patched. Studies of PRK procedures that use topical nonsteroidal anti-inflammatory drugs (NSAIDs) and soft contact lenses have suggested that these may be useful in decreasing postoperative pain,³² but conclusive results are not as yet available. The patient may be given oral nonsteroidal agents or narcotics as well as sleeping medications to make the first postoperative night a comfortable one.

The patient is followed closely until the epithelium is healed, generally by 72 hours. Upon epithelial healing, a tapering regimen of corticosteroids is generally used for the first several months. Corticosteroid dosage may be modified depending on the patient's wound healing response. It has been suggested that increasing steroids may ameliorate regression and haze while decreasing steroids may accelerate regression in patients who are overcorrected.³³

The necessity and appropriate use of corticosteroids remain controversial. Some investigators have suggested that steroids are not necessary,^{34,36} while others recommend they be used to prevent the formation of significant postoperative corneal haze and regression.³³

CLINICAL RESULTS OF PRK

The excimer laser has been undergoing clinical studies in the United States for approximately the past five years. Most studies have focused on the correction of myopia in the range of 1.5 D to 6.0 D.^{25,37,38} Other investigations have focused on the use of the excimer

laser for the correction of higher degrees of myopia³⁹ and of astigmatism.^{22,24,40-42} Many of these latter investigations have been carried out outside of the United States.⁴³⁻⁴⁵ The literature reports that uncorrected visual acuity (VA) following PRK is 20/40 or better in 80% to 95% of low-degree myopes, and 20/20 or better in 50% to 70% of such patients.^{25,37,38}

Recent studies have reported better results than those obtained in investigations in the earlier phases of clinical excimer development, suggesting improvement of the PRK procedure. In Phase III clinical trials, for instance, both Summit and VisX report uncorrected visual acuity of 20/40 in over 90% of eyes.^{25,37,38}

An important predictor of PRK outcomes is the predictability of the procedure, i.e., are we achieving the refractive correction which we are attempting? Although results of studies vary widely, in general they have shown that approximately 50% of patients fall within 0.5 D of the attempted correction; approximately 75% fall within 1.0 D, and approximately 95% fall within 2 D. Studies of patients with higher degrees of myopia show somewhat less predictability and postoperative uncorrected vision.³⁹

Another major outcome of importance in any refractive surgical procedure is the stability of the refractive correction. RK recently has been called into question because of the finding of progressive hyperopia over many years in one study.⁴⁶ To date, studies of PRK have not reported this progressive hyperopia effect.

In the early wound-healing phases, many excimer-treated eyes regress somewhat, and appear to plateau at a relatively stable correction after approximately six months. Such stabilization may take longer in patients with higher refractive corrections.

Stability and ultimate outcome may be affected by the individual patient's wound-healing pattern. Most patients follow the typical pattern of slight regression early in the postoperative course with subsequent stabilization. Others show minimal regression corresponding to little wound healing, while still others show excessive wound healing with regression and significant haze formation (Daniel Durrie, MD, personal communication). A better understanding of the individual post-PRK wound-healing response may suggest pharmacologic interventions to modulate the outcome. For instance, increased corticosteroid use may decrease regression in aggressive healers, while omission of corticosteroids may encourage stromal healing in those with overcorrection.^{33,47,48}

Excimer laser PRK has also been used following other refractive surgery procedures such as RK. If effective, patients who have been undercorrected following RK might achieve a better correction with PRK.

Some success with this procedure has been reported,⁴⁹ but there also are reports of outcomes that are less successful than those obtained with the standard PRK procedure. These poorer outcomes may be the result of increased corneal scarring which has been seen in some patients treated with PRK following RK. It has been hypothesized that the reservoir of keratocytes within the RK wounds may act as a nidus for increased haze formation following PRK. A large-scale study with a long follow-up period is required to clarify the safety and efficacy of PRK as a post-RK enhancement procedure.

POTENTIAL COMPLICATIONS OF EXCIMER LASER PRK

Any refractive surgical procedure carries potential complications. In most studies of excimer laser PRK procedures, re-epithelialization has been prompt and recurrent erosion syndromes have not been found. Some degree of stromal wound healing does occur, of course, and this may manifest clinically as a superficial corneal haze. A fine haze is probably indicative of anticipated corneal wound healing and likely is of minor clinical consequence. More substantial haze and scarring indicates aggressive wound healing and may lead to regression of effect and loss of best corrected VA, as well as optical side effects such as decreased contrast sensitivity, binocular diplopia, glare, and halo. Most studies³⁶ have shown corneal haze to decrease over the first year following PRK (Fig 1).

Some post-PRK patients report subjective complaints such as glare and halo, and also of effects upon night driving even in the absence of haze. These complaints may possibly be a result of optical zone edge effects, especially when the pupil is dilated.⁵⁰

Many PRK patients complain of postoperative discomfort. This discomfort may be secondary to a combination of the epithelial defect, damage to corneal nerves, and ultraviolet keratitis. To help ameliorate this problem, several modalities are currently under trial with encouraging results, such as the use of topical NSAIDs and bandage soft contact lenses.³² However, sterile corneal infiltrates have been reported in patients using bandage soft contact lenses. Patients must therefore be closely followed until re-epithelialization is complete. Further studies are required to elucidate the safety and efficacy of these potential postoperative regimens.³²

CORNEAL TOPOGRAPHY FOLLOWING PRK

The goal of PRK is to optimize the patient's uncorrected VA as well as other objective and subjective measures of visual function. This is accomplished, as we have seen, by reshaping the cornea's anterior optical surface. The development of computer-assisted

videokeratography has aided in the understanding of both visual function and wound healing following excimer laser procedures.⁵¹⁻⁵³

The general topographic theory underlying PRK is the reshaping of the normal prolate optical configuration of the central cornea to a flatter, oblate configuration postoperatively (Fig 2). Such reconfigurations have been verified in studies using current computer-assisted videokeratography units. In addition, a more thorough understanding of the various qualitative and quantitative optical patterns following PRK is providing insight into both the effects of PRK on the cornea and the effects of these different patterns on the patient's ultimate visual outcome.

Investigators using the VisX excimer laser have described postoperative homogeneous, semicircular, keyhole, and central island patterns.⁵¹ Investigators using the Summit excimer laser have described a seven-category grading system of qualitative corneal topography patterns following excimer laser PRK.⁵³

Central Islands

The central island pattern, in particular, has recently been a subject of concern in some laser systems. This pattern is typified by the finding of relatively less power decrease in the central area compared to the more peripheral areas of the optical zone.⁵¹ The exact definition of the central island varies with the clinical study but, in general, a central island comprises areas of central relative steepening measuring greater than 1 mm and greater than 1 D in power. Central islands have been implicated in undercorrection as well as in objective optical symptomology such as glare, halo, and monocular diplopia.

Further in-depth analysis of corneal topography will assist both the diagnosis of optical problems following PRK and the future development of PRK.

EXCIMER LASER RETREATMENT

There are relatively few studies in the literature regarding retreatment following excimer laser PRK.⁵⁴⁻⁵⁶ Theoretically, retreatment could obtain additional correction in patients who have been undercorrected. A retreatment could also be used for patients who have significant corneal haze or scarring as well as regression of the refractive effect, and for those with central island formation.

The Transepithelial Approach

Some investigators have suggested that retreatments be undertaken using a transepithelial approach.^{55,57} In such cases, rather than mechanically removing the epithelium as is done for the initial PRK procedure, the



Fig. 1 Top: Corneal haze one month following excimer laser PRK for 6.0 D of myopia. **Bottom:** Three months following surgery, the corneal haze has diminished.

excimer laser is used to remove the epithelium. The logic behind transepithelial treatment is two-fold: (1) Since Bowman's layer has been removed in the previous procedure, subsequent removal of the epithelium over the stromal bed might be more difficult, resulting in greater trauma as well as a less efficient epithelial removal; and (2) excimer laser removal of the epithelium may possibly minimize trauma and have a lesser likelihood of producing corneal haze and scarring after the procedure.

In the transepithelial approach, the laser is set for a plano ablation, i.e., the diaphragm remains fixed and open while the beam ablates the epithelial tissue. Usually, the stroma is first reached in the periphery of the optical zone, leaving an island of central epithelium.⁵⁵ This can be observed by a decrease in fluorescence in the areas where the epithelium has been removed. The laser is then set for a refractive PRK and applied. Care is taken to not to overcorrect.

Mechanical Superficial Keratectomy

In addition to excimer laser retreatments, some investigators have advocated mechanical superficial kerate-

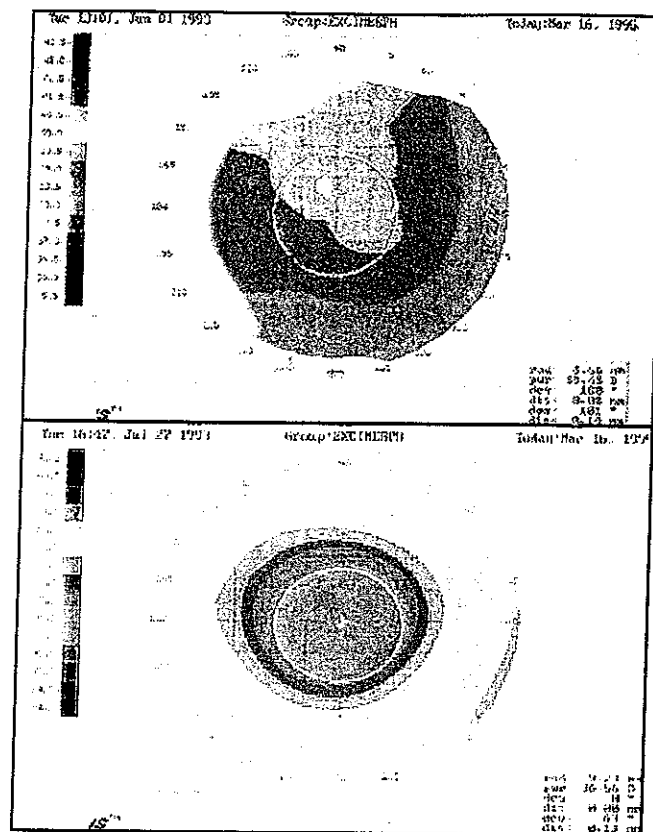


Fig. 2 Top: Preoperative corneal topography of a patient with 6.0 D of myopia. **Bottom:** Postoperative corneal topography of same patient. Note the central decrease in corneal power (blue zone).

ctomy techniques to remove scar tissue in selected patients.^{58,59} Such patients include those with a plaque-like scar interposed between the epithelium and the stroma. Such fibrous tissue can be meticulously peeled and stripped, leaving a clear and smooth ablation zone in some cases.^{58,59}

Results using such retreatment techniques are as yet limited in scope and follow-up.⁵⁴⁻⁵⁶ Further experience should clarify the use of PRK retreatment either as an optical enhancement procedure or as a therapeutic procedure for removing corneal haze.

CONCLUSION

The ability of the excimer laser to optically sculpt the corneal surface makes it a unique and potentially powerful tool for the surgical correction of refractive errors. Patients, to date, are enjoying good outcomes with few side effects. Further understanding of the laser-tissue interaction, individual wound healing responses, and the optics and topography of the postsurgical cornea should suggest changes in treatment strategies and postoperative interventions to improve upon present

results Advances in technique and treatment should also allow for the correction of higher degrees of myopia, astigmatism, and hyperopia in the future □

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