A Cautionary Tale of Innovation in Refractive Surgery

George O. Waring III, MD, FRCOphth

Hyperopia is difficult to treat surgically. Nearly a dozen techniques strive toward safe, effective outcomes. All techniques are bedeviled by 3 challenges: (1) the need for accurate centration over the pupil of a steeper central optical zone approximately 5 mm in diameter, (2) the potential decreased visual acuity caused by image minification, and (3) the creation of corneal contours with physiologic characteristics able to minimize optical aberrations and regression of initial refractive effect.

Excimer laser photorefractive keratectomy and laser in situ keratomileusis (LASIK) for hyperopia are being developed with ongoing changes in ablation algorithms. Thermal keratoplasty with a pulsed holmium:YAG laser has been plagued by marked regression of effect when attempting to treat more than approximately +1.00 diopter (D) of hyperopia. An infrared continuous-wave diode laser (wavelength of 1.9 µm) is also being studied in clinical trials. Plus-power phakic intraocular lenses face the design challenge of being placed in hyperopic eyes that often have shallower anterior chambers and less surgical space for implantation than myopic eyes; continued design changes and careful clinical trials will probably yield safe and useful phakic intraocular lenses for hyperopia within the next few years. Clear lens extraction for high hyperopia with placement of 1 or 2 intraocular lenses in the capsular bag or ciliary sulcus has successfully treated these patients who otherwise have considerable visual disability. Intracorneal lenses have a 50-year history of unsuccessful clinical trials in the treatment of hyperopia and aphakia, but new materials and surgical techniques and designs, such as radially placed intracorneal polymethyl methacrylate stents and keratophakia with new synthetic lenticules, keep future possibilities interesting. Intracorneal lenses with small diameter and high index of refraction have been studied in a small number of eyes, but decreased quality of vision led to termination of the research without publication of results.

Three other methods for surgical correction of hyperopia have experienced transient popularity until the high rate of complications and lack of predictability caused them to slink quietly away: hot-needle thermal keratoplasty, which produced focal corneal necrosis and an unstable refraction; hexagonal keratotomy, which commonly produced irregular astigmatism; and hyperopic automated lamellar keratoplasty (also known as H-ALK; more properly, deep lamellar keratotomy for hyperopia), which produced progressive corneal ectasia in some eyes.

THE LIMITS OF KERATOMILEUSIS

Deep lamellar keratotomy for hyperopia (“hyperopic ALK”) attempts to create controlled steepening of the central cornea by cutting with a microkeratome a lamellar disc that is approximately 75% of corneal thickness. This disc is left in place without sutures. The remaining thinner posterior cornea displaces forward with increased curvature to reduce hyperopia. The procedure was done from approximately 1993 to 1996 on an estimated 60,000 eyes. In 1998, Lyle and Jin reported 67 consecutive eyes treated with hyperopic ALK with a 67% follow-up at 1 year. They observed that although the procedure steepened the central cornea and improved uncorrected visual acuity, instability of refraction ensued with a mean myopic shift of 0.50 D between 3 months and 1 year and of 1.00 D between 1 and 2 years. In addition, 26% of the eyes developed enough steepening and irregular astigmatism to be dubbed “iatrogenic keratoconus,” and 16.4% had enough ectasia to require penetrating keratoplasty.

From the Department of Ophthalmology, Emory University School of Medicine, Atlanta, Ga.
The concept of creating a controlled corneal ectasia in refractive surgery is not new. Radial keratotomy for myopia intends to produce a controlled ectasia in which the corneal steepening occurs para-centrically with concomitant central flattening\(^1\), hexagonal keratotomy for hyperopia attempted to create central corneal steepening\(^1\), and hyperopic ALK, with a similar biomechanical concept, aims to produce a controlled central steepening. The “control” is determined by the biomechanical properties of the individual cornea and is set by the length and depth of the incisions, whether radial, hexagonal, or lamellar. A lamellar keratotomy is also done during keratomileusis (including LASIK) to create a flap or disc that reveals the stroma for refractive correction. The changes in corneal shape after radial, hexagonal, and lamellar keratotomy occur in 3 time frames: (1) acutely, within hours, resulting in a substantial—usually desirable—change in refraction and visual acuity; (2) short-term fluctuation, such as diurnal variation after radial keratotomy\(^1\); and (3) gradually over a few years, as occurs in progressive ectasia after hyperopic ALK and in the hyperopic shift that occurs after radial keratotomy with incisions that extend to the limbus.\(^16,17\)

The use of lamellar keratotomy in hyperopic ALK and in keratomileusis raises a fundamental question about corneal biomechanics: What is the minimal thickness of the cornea that can preserve corneal shape for the lifetime of the patient without development of progressive corneal steepening or frank ectasia? No one knows. An unsutured corneal disc or flap that is created during keratomileusis contributes minimally to the biomechanical strength of the cornea, because its attachments to the limbus have been severed. Thus, the corneal strength and shape are determined by the biomechanical properties of the residual corneal bed, which are probably different for each individual. As Lyle and Jin\(^1\) demonstrated after hyperopic ALK and as Seiler et al\(^1\) have shown after LASIK, a bed approximately 150 µm thick will become excessively steep. Current opinion estimates the minimal thickness of the bed for long-term stability to be 200 to 250 µm. This figure is based on the observation that for some 30 years, cryolathe and nonfreeze keratomileusis were done in normal corneas that had a presumed central thickness of approximately 500 to 550 µm, by creating an approximately 300-µm thick disc that then received a refractive cut and was replaced with sutures, leaving a corneal bed 200 to 250 µm thick. Carmen Barraquer\(^19\) reported that of 1606 eyes that received cryolathe myopic keratomileusis (with a disc thickness of approximately 300 µm) and were followed up for approximately 2 decades, 45 (2.8%) developed corneal ectasia. She also reported the changes in average corneal power (and radius of curvature) over time: before surgery, 43.75 D (7.7 mm); at 30 days, 35.50 D (9.5 mm); at 90 days, 36.75 D (9.2 mm); at 3 to 12 months, 37.12 D (9.1 mm); at 5 years, 37.87 D (8.9 mm); at 10 years, 39.25 D (8.6 mm); and at 21 years, 39.25 D (8.6 mm). The causes for this mild progressive corneal steepening of approximately 2 D from 1 to 20 years after keratomileusis are unknown, but possibilities include weakened biomechanical support in the corneal bed, underlying disease such as undetected keratoconus, variations in surgical technique that created a thinner corneal bed than intended, chronic trauma to the cornea such as chronic eye rubbing, and epithelial hyperplasia. Unfortunately, there is no published long-term follow-up on a consecutive series of eyes with a thorough statistical analysis of changes in corneal curvature after keratomileusis.

José Barraquer\(^20,21\) stated that a residual corneal thickness of 300 µm should remain to prevent ectasia. Hanna and colleagues\(^22\) used finite element modeling of the cornea to demonstrate that resection of a layer of cornea approximately 50% its thickness (250 µm, 7.5-mm diameter) doubled the stresses at the center of the inner surface of the cornea and created slight anterior displacement of the bed. These simulated changes were only acute, and to date there is no mathematical model of the cornea that can simulate viscoelastic and wound healing processes that occur over time. The distribution of the stress-bearing layers of the cornea has been studied, but not definitively characterized. MacPhee and colleagues\(^23\) reported that all corneal layers equally bear stress. The finite element simulations of Hanna and colleagues\(^22\) suggested that more stress was borne by the posterior layers than the anterior layers. Seiler and colleagues\(^24\) demonstrated that Bowman layer itself does not contribute more biomechanical support to the cornea than does the cellular stroma. This theoretical information supports the concept that lamellar keratotomy made too deeply in the cornea will produce corneal ectasia.

The major reason that the minimal residual thickness required for corneal stability after keratomileusis remains unknown is that there has been no reliable way to measure the thicknesses of individual corneal layers postoperatively. The ultrasound biomicroscope that uses a 50-MHz transducer can give beautiful images of portions of the cornea (4-mm wide), but the 20-µm precision of this system\(^25\) is insufficient to adequately evaluate corneal refractive surgery. A newer digital 50-MHz high-frequency ultrasound system described by Reinstein and colleagues\(^26\) can resolve and measure the epithelium, the stromal component of the corneal flap, and the thickness of the residual stromal bed in keratomileusis with a precision of 1.3 µm (Figure). These measurements may create a better understanding of the limits of procedures that remove corneal tissue to change refractive shape, such as photorefractive keratectomy and LASIK. Such postoperative measurements in human eyes are necessary, because we do not know at the time of surgery the actual thickness of the corneal flap or the actual ablation depth within the stromal bed; manufacturers give guidance to the surgeon as to the predicted thickness of the corneal flap in LASIK based on the gap set in the microkeratore, but it is well known that flap thickness can vary greatly from one eye to another using the same instrument. Similarly, the excimer laser ablation rate of

©1999 American Medical Association. All rights reserved.
corneal stroma quoted by the manufacturer (eg, 0.25 µm per pulse) also varies because of conditions in the laser, such as variation in the quality of the optics in the delivery system; in an individual cornea, such as variation in hydration; and/or in the operating area during surgery, such as variation in the humidity and temperature. Intraoperative measurement of flap and bed thickness by ultrasound probes is very inaccurate because of the low frequency of handheld probes (20 MHz), the location and positioning of the probe, and immediate changes that occur in stromal hydration on raising the flap. Therefore, only accurate postoperative measurements of the thickness of individual corneal layers coupled with measurements of corneal radius of curvature, corneal shape, and ocular refraction followed over time will define the residual thickness of the cornea needed for stability after lamellar refractive corneal surgery.

**FLAWED METHODS OF EVALUATING NEW SURGICAL TECHNIQUES**

The report of Lyle and Jin raises a broader question: How did hyperopic ALK become transiently popular? This procedure and 2 other transiently popular procedures for hyperopia—hot-needle thermal keratoplasty and hexagonal keratotomy—spotlight 3 errors made commonly in the evaluation of new surgical procedures.

The first error affirms the adage, “Those ignorant of history are doomed to repeat it.” Those who pursued hot-needle thermal keratoplasty could have benefited both from the unsuccessful experience of some investigators with high-temperature probes to flatten keratoconus that produced variable unstable changes in corneal shape, and from the common-sense observation that thermal necrosis of the corneal stroma would be unlikely to create a reliably predictable change in corneal shape and refraction. Hexagonal keratotomy was used by Sato and Akiyama in the 1940s with 6 to 9 overlapping incisions in the posterior cornea to steepen the central cornea of rabbits. The variable refractive results were accompanied by induction of large amounts of astigmatism; the technique was abandoned. Advocates of hyperopic ALK could have benefited from the early experience of José Barraquer with keratomileusis, which would have warned that a 350- to 400-µm deep lamellar cut in the cornea would probably produce uncontrolled steepening with progressive ectasia.

The second common error was the propagation of these 3 procedures among ophthalmologists on the basis of informal experience, newspaper communication, and authoritative endorsement by prominent surgeons. Hot-needle thermal keratoplasty emanated from Russia in 1984, with powerful promulgation by Svyatoslav Fyodorov, MD, the champion of modern refractive keratotomy. Some surgeons who had followed Fyodorov’s early lead in refractive keratotomy surgery used the Russian-manufactured thermal keratoplasty instrument in both laboratory and human trials, informally reporting favorable results. Hexagonal keratotomy reemerged from Mendez of Mexico in 1987. The procedure quickly underwent a series of modifications aimed at decreasing the complications of poor wound healing, including anterior displacement of central cornea, excessive scarring, and induced astigmatism. The modifications went from initial intersecting hexagonal pattern to nonintersecting patterns and then to nonintersecting patterns with paracentral transverse incisions. Many of these changes occurred as the procedure was promulgated in commercially sponsored refractive keratotomy skills transfer courses with the enthusiastic endorsement of refractive surgeons who had extensive clinical experience, such as Mendez, Jensen, and Casebeer and Phillips. Many of the student ophthalmologists failed to ask, “If the results reported in the presentations are so good, why are the surgical techniques changing so much?” Hyperopic ALK was pulled along in the wake of automated lamellar keratoplasty for myopia by incorporation in the Chiron-Casebeer lamellar refractive surgery courses. The use of the commercially created brand name “automated lamellar keratoplasty (ALK)” blurred the distinction between the techniques for myopia and hyperopia, which used a common surgical instrument—the microkeratome—but which achieved their results through entirely different mechanisms.

The combined phenomena of enthusiastic presentations by “pioneers” from “eye institutes” at ophthalmic meetings and happy reports of “breakthroughs” by uncritical staff writers in ophthalmic and lay newspapers propelled the 3 procedures forward. The common clichés, “In my experience,” “I have done hundreds of cases,” and “My patients are extremely happy,” peppered the oratory, often without thorough assessment of clinical data. For example, the following quotes were published in an ophthalmic newspaper (Ocular Surgery News. August 1, 1992) concerning hexagonal keratotomy: “We have not had a single case of irregular astigmatism...not a single patient who could not be refracted to 20/20...we have quite a number of happy patients in our practice.” “None of my patients have experienced irregular astigmatism.” Ophthalmologists are...
ing about things that happened 10 years ago instead of being aware of what is going on now.” Candid presentation of complications was missing, or sometimes the complications were disguised under the rubric that the technique was for “advanced surgeons.” The scenes at meetings and courses resembled the fairy-tale emperor parading in his new clothes; the voice of a lone child revealed the emperor’s nakedness. In the case of hexagonal keratotomy, the lone voice came from Nordan and Maxwell, who reported in the news media and letters to the editor that hexagonal keratotomy “has proven to be a failure” and called for a moratorium on the procedure; their challenge and subsequent reports of complications led to the disappearance of hexagonal keratotomy from active use.

A third error occurred during the clinical spread of these 3 techniques: there was a paucity of detailed reports of consecutive series of eyes with a high percentage of follow-up in the peer-reviewed literature—or anywhere. Concerning hot-needle thermal keratoplasty, Neumann and colleagues gathered and published data from an informal Russian series and then embarked on clinical trials to try to determine the optimal variables for the procedure, but the opening sentence of their final publication in a non–peer-reviewed periodical reflected considerable bias: “Hyperopic thermokeratoplasty (HTK), a recently developed procedure, may offer the best combination of safety, predictability, stability, and cost effectiveness for correcting hyperopia.” Publications concerning hexagonal keratotomy by Neumann and McCarty, Grady, Jensen, and Casebeer and Phillips presented useful clinical information from a cumulative group of more than 400 eyes and concluded that the technique was effective and safe but required more study; however, at no point did the authors call for or conduct a formally structured clinical trial or suggest a moratorium on the expansion of the surgery until more trial-and-error refinement and informal testing could define its safety and efficacy. The paucity of articles on hyperopic ALK in the peer-reviewed literature is relieved somewhat by the observations of Lyle and Jin, who recommended cessation of the use of the procedure. Unfortunately, this recommendation in 1998 arrived years after hyperopic ALK had disappeared from clinical use.

SOCIAL ENGINEERING IN REFRACTIVE SURGERY

Social engineering is a marketing technique in which proponents of a subject devise a strategy to overcome a target group’s traditional aversion to an idea. It can be used for good cause, such as finding ways to introduce birth control in traditionally male-dominated societies with overpopulation problems, or for the more dubious cause of creating rapid profits by promulgating sales of surgical equipment and adoption of new surgical techniques that bypass professional and scientific safeguards. Commonly, a company will create a “surgeon expert” who may trivialize the importance of scientific work and the systematic evaluation of new techniques by the ophthalmic community and by formal prospective clinical trials. The company and the expert create a series of courses, exploit enthusiastic articles in ophthalmic newspapers, and spread word-of-mouth hype. Many ophthalmic surgeons—including respected academics who want to be in the forefront of refractive surgery—jump on the bandwagon, increasing sales of new instruments and increasing the number of cases done with new techniques. The result is that a large amount of this innovative work is poorly documented, because the techniques and results are not reported in the peer-reviewed literature. This is a pattern that occurred with hot-needle thermal keratoplasty, hexagonal keratotomy for hyperopia, and hyperopic ALK, to the detriment of many patients. Some have claimed that a similar path was followed by LASIK, but I believe that is not correct, because the early descriptions of LASIK were scientific, were published in the peer-reviewed literature, and the technique was based on the principles of keratome, which had been practiced clinically since 1963. A considerable number of articles rapidly appeared in the peer-reviewed literature substantiating the safety and effectiveness of LASIK.

SUGGESTIONS FOR TESTING NEW SURGICAL TECHNIQUES

These modern cautionary tales of new refractive surgical techniques gone awry raise a serious question for ophthalmic surgeons: How can new surgical techniques be developed and refined for general clinical use—or abandoned—without creating the widespread clinical morbidity that resulted from these 3 procedures? The answer is easy, as I have suggested elsewhere.

1. Maintain an attitude of professional restraint that places the interest of the patient before the interest of the surgeon and that resists the mindless rush to be the first physician to do the latest procedure on the most patients for the greatest gain.

2. Insist on a staged evaluation of new techniques with a limited number of eyes being treated and reported in the peer-reviewed literature in the earlier stages of development, with later expansion, follow-up, and reporting of larger numbers.

3. Disclose the weaknesses, drawbacks, and complications of a procedure, in spite of attempts to conceal them by industry sponsors or surgeon progenitors, while extolling its virtues and advantages, so that more impressionable colleagues will have a balanced understanding. Evaluate it—don’t sell it.

4. Avoid premature dissemination of evolving and unproved procedures so that student surgeons do not operate on large numbers of patients using partially developed or inadequate techniques.

5. Invest the money, time, and energy to do simple prospective trials: train office staff, ensure 90% or more patient follow-up, contract with skilled individuals who can help compile and analyze the results, write and publish an article that reports all cases and complications.

6. Publish communications in peer-reviewed journals—not just ophthalmic newspapers. All peer-reviewed journals publish letters to
the editor, brief reports, case studies, and preliminary results—in addition to detailed original articles.

7. Publish negative results and reasons why a technique should be or has been abandoned, as wisely done by Lyle and Jin concerning hyperopic ALK. This helps reduce repetition of the same problems in the future. Indeed, those who fail to heed prior mistakes are doomed to repeat them—to the detriment of our patients and our professional reputations.

Accepted for publication April 22, 1999.

Reprints: George O. Waring III, MD, FACS, FRCOphth, Department of Ophthalmology, Emory University School of Medicine, 1365 Clifton Rd, Atlanta, GA 30322 (e-mail: ophgtgw@emory.edu).

REFERENCES