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The 25th Anniversary of Excimer Lasers in Refractive Surgery: Historical Review

Ronald R. Krueger, MD, MSE; Yaron S. Rabinowitz, MD; Perry S. Binder, MS, MD

The excimer laser as an experimental and surgical tool was first introduced into ophthalmology and refractive surgery over 25 years ago with the publication of the seminal article by Stephen Trokel, MD; Rangaswamy Srinivasan, PhD; and Bodil Braren in the *American Journal of Ophthalmology* in 1983.[1] Two and one-half decades of development in excimer laser vision correction have led to the current status of LASIK being the most frequently performed elective surgical procedure in the modern world.

How excimer laser surgery got started in ophthalmology 25 years ago, and the pathway of its development and refinement was the subject of the International Society of Refractive Surgery's scientific symposium at the American Academy of Ophthalmology (AAO) annual meeting on November 9, 2008. This review is the synopsis of the speakers' and video presentations on the history of the excimer laser. The video was produced by Yaron S. Rabinowitz, MD, in collaboration with associates Perry S. Binder, MD; James J. Salz, MD; Ronald R. Krueger, MD, MSE; Marguerite B. McDonald, MD; Stephen Klyce, PhD; and George O. Waring III, MD. Other participants in this historic symposium included Theo Seiler, MD, PhD; Charles Munnerlyn, PhD; Stephen Trokel, MD; John Marshall, PhD; Bruce Jackson, MD; Ioannis Pallikaris, MD; Jorge Alió, MD; Thomas Neuhann, MD; and moderators Paul Rosen, MD, and Jose Guell, MD, PhD. The video can be viewed and downloaded in its entirety on the Internet at www.isrs.org by clicking Resources on the navigation bar, or at www.journalofrefractivesurgery.com.

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DISCOVERY OF THE LASER'S SURGICAL POTENTIAL

In 1982, Stephen Trokel, MD, a Professor of Ophthalmology at Columbia University in New York, with a background in engineering and physics, was impressed by the remarkable way the Nd:YAG laser could precisely cut through the posterior capsule after cataract surgery. This motivated him to experiment with different lasers to reshape the cornea and possibly correct refractive errors. Although the argon fluoride excimer laser was first described by physicists at the University of Kansas in 1976,[2] it was not until 1981 that John Taboada, MS, an investigator of ocular damage for the military, described the effects of the 193-nm argon fluoride excimer laser on the cornea.[3] Taboada noted that at certain energy levels the laser would imprint an indentation of the laser beam in the corneal epithelium, but this would fill in 1 hour later. This observation suggested to Trokel that tissue was being removed without collateral damage and he sought to obtain an excimer laser to further study this phenomenon. In early 1983, Trokel was introduced to Rangaswamy Srinivasan, PhD, a photochemist who was working with the 193-nm argon flouride excimer laser to etch microprocessors at IBM. He demonstrated to Trokel how the excimer laser could precisely remove organic tissue without producing collateral thermal damage in a human hair (Fig 1)—a process he called ablative photodecomposition.[4]

The process of ablative photodecomposition involved three main components: absorption, bond breaking, and ablation (Fig 2).[4] In absorption, the high energy of a single photon of 193-nm ultraviolet light, being 6.4 eV, was sufficient to exceed the energy required to break molecular bonds (~3.6 eV) and eject the particulate debris from the eye. When the concentration of photons or energy density exceeds a critical threshold value, sufficient

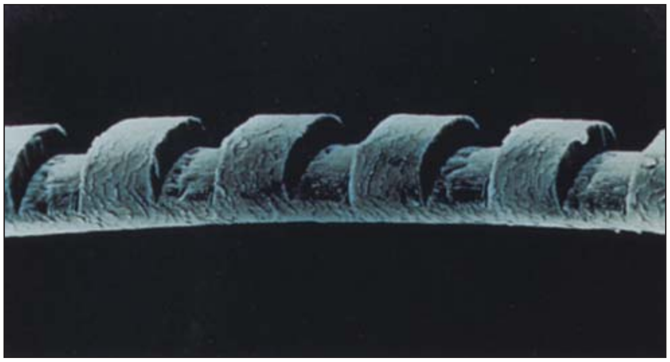

Figure 1. Excimer laser etchings in a human hair, demonstrating precision without thermal damage.

molecular bonds are broken, without recombining, to separate the tissue into microscopic fragments. These fragments then also have sufficient kinetic energy to be ejected from the surface of the tissue, signifying the onset of ablation. This convinced Trokel to experiment with a few cadaveric animal corneas in Srinivasan's laboratory. The accuracy with which this laser could be controlled and the preservation of smoothness and clarity of the cornea spurred further research. In 1983, Trokel, Srinivasan, and Bodil Braren published the first experiments on enucleated calf corneas, suggesting the use of the excimer laser for refractive corneal surgery.[1] Because IBM did not allow animal research, Trokel leased an excimer laser from Lambda Physik (Goettingen, Germany) (Fig 3), and commenced the first animal experiments at Columbia University in the fall of 1983. By early 1984, Theo Seiler, MD, PhD, also leased a Lambda Physik excimer laser as the second independent investigator in Berlin, Germany.

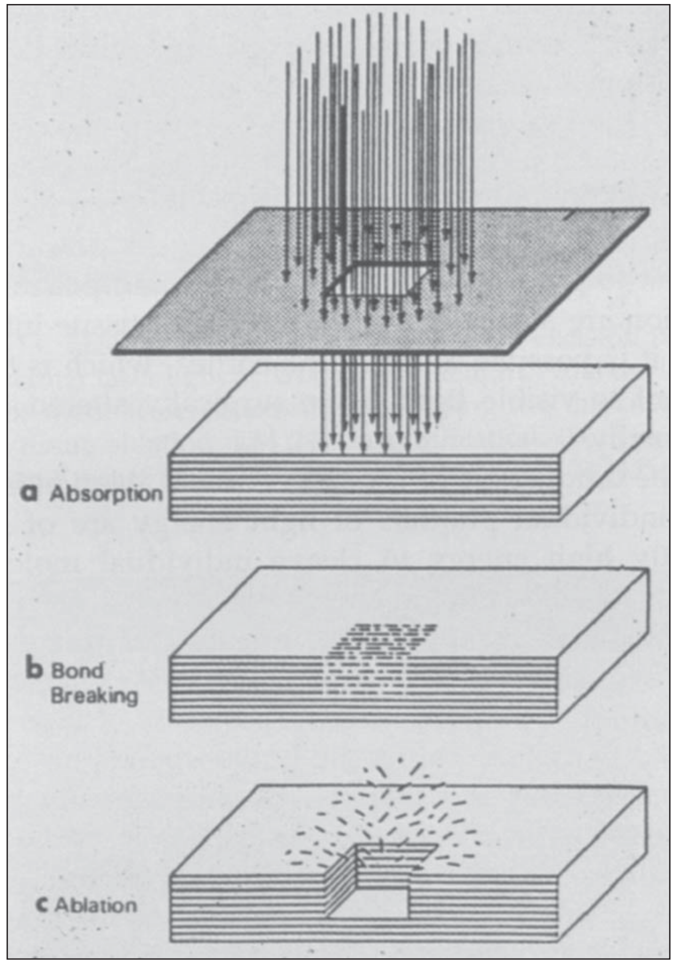

Figure 2. Three components of excimer laser photoablation: absorption, bond breaking, and ablation. (Reprinted with permission from Srinivasan R. Kinetics of the ablative photodecomposition of organic polymers in the far ultraviolet (193 nm). *Journal of Vacuum Science and Technology B*. 1983;1(4):923-926. Copyright © 1983 Rangaswamy Srinivasan, PhD.)

CHARACTERIZATION OF THE LASER'S TISSUE EFFECTS

While still a medical student, Ronald Krueger read Trokel's article, contacted him, and they jointly commenced bovine eye experiments to refine the technology. Their work from 1983 to 1985 was to determine the ablation threshold, the optimal ablation rate, and to demonstrate presence or lack of thermal tissue damage at certain wavelengths and fluences. These findings were published in two noteworthy articles in 1985, revealing 193 nm to be the superior wavelength, with negligible thermal damage (Fig 4) and lowest ablation threshold to be 50 mJ/cm^2.[5] The greatest ablation efficiency ranged from 150 to 400 mJ/cm^2 and within this range, each pulse was determined to remove a depth of 1/4 to 1/3 of a micron of corneal stroma according to the beam shape.[6]

During the same period, detailed histopathology and electron microscopy were performed by John Marshall, PhD, at the Institute of Ophthalmology in London on samples that were prepared by Trokel and Krueger, and then brought to Marshall for investigation. These histopathologic healing studies included both radial excisions and broad disk ablations on rabbit eyes, and the operated specimens were hand-delivered on a monthly basis by Trokel after an overnight flight to London. From this work, Marshall also published a 1985 article, in which he verified the clarity and precision of tissue interaction that was unique to the 193-nm wavelength.[7] Marshall's work showed that after excimer laser removal of corneal tissue, a smooth, optically acceptable anterior surface was left behind without the formation of a corneal scar. Ultrastructurally, he also demonstrated the formation of a subepithelial surface pseudomembrane of alternating hyperdense and lightly staining layers (~70 nm thickness each) bordering the treated tissue (Fig 5).[7-9] This pseudomembrane provided a template on which the epithelium could regrow and was

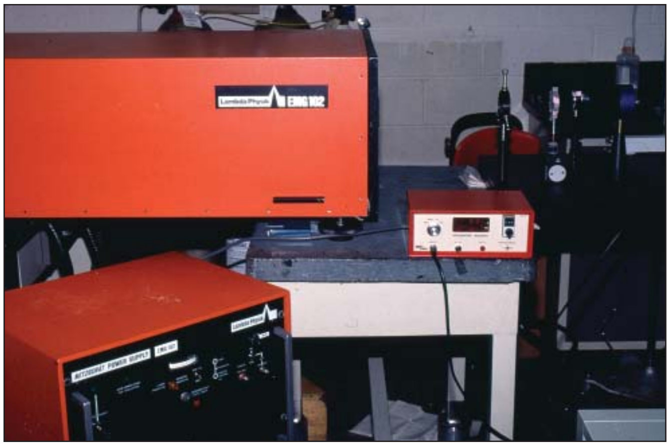

Figure 3. The first experimental excimer laser used in performing cadaver eye and animal experiments at Columbia University 25 years ago. Note the power supply (lower device) and laser cavity (upper device).

so named because it exhibited membrane-like properties that could support the contents of an epithelial cell cleaved by the laser.[7] Marshall's histopathology work played a key role in the acceptance of this technology for refractive surgery.

DEFINING THE SHAPE AND HEALING OF SURFACE LASER ABLATION (PRK)

In the summer of 1984, Trokel and Krueger also treated rabbit corneas with large-area circular ablations at the suggestion of Charles Munnerlyn, PhD, an optical engineer. Removing tissue from the optical center of the cornea was controversial at the time because of concern about scarring. The sculpting potential of the excimer laser, however, was quickly realized for removing large areas or graded circular disks of tissue. This was practically applied in the first excimer laser phototherapeutic keratectomy (PTK) procedure at Columbia University, where fungal keratitis was successfully removed using the laser in rabbits.[10] Also, the circular disks of tissue, created with a circular masking aperture, were found to flatten the corneal surface, producing a refractive effect of increased plus power, which was demonstrated using photokeratography in monkeys at both Columbia University (Fig 6) and Louisiana State University (LSU), New Orleans, Louisiana. In both the rabbit and monkey experiments, the corneal tissue was removed and later healed with good optical clarity and without a scar in the treated central area.[9] In the monkeys, this was the first clinical demonstration that Bowman layer could be penetrated and removed without scarring and represented a significant paradigm shift in corneal surgery.

In 1985, Munnerlyn provided the formula for accurately calculating the central depth of tissue removal required to achieve a specific refractive change using

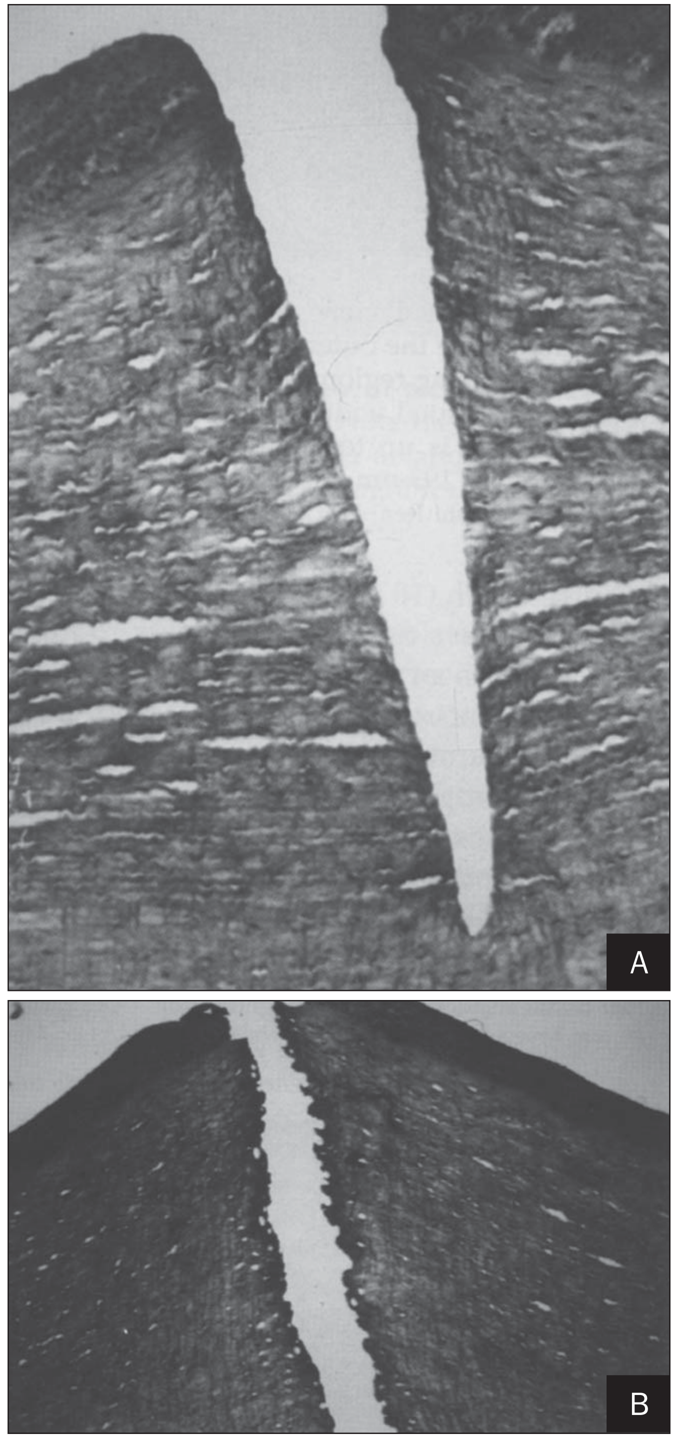

Figure 4. A) 193-nm excimer laser ablation in corneal tissue is nonthermal (straight, sharp border), but not so with longer ultraviolet wavelengths of **B)** 248 nm and beyond (jagged, thermal border). (Reprinted with permission from Krueger RR, Trokel SL, Schubert HD. Interaction of ultraviolet laser light with the cornea. *Invest Ophthalmol Vis Sci*. 1985;26(11):1455-1464. Copyright © 1985 Association for Research in Vision and Ophthalmology.)

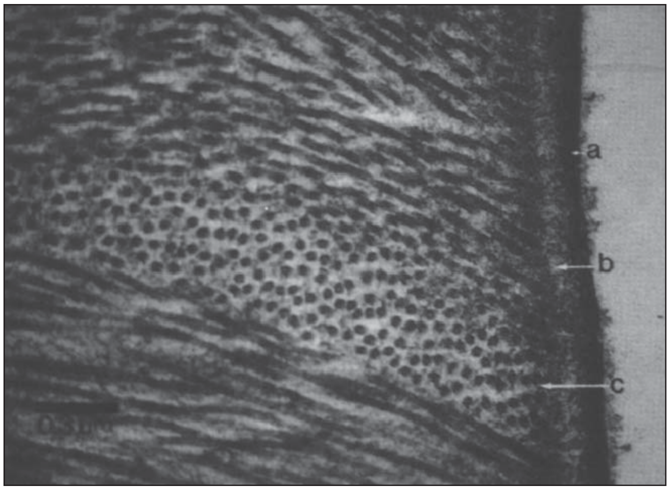

Figure 5. Pseudomembrane bordering the edge of excimer laser ablated cornea with hyperdense and light staining layer each 70-nm thick. (Reprinted with permission from Marshall J, Trokel S, Rothery S, Schubert H. An ultrastructural study of corneal incisions induced by an excimer laser at 193 nm. *Ophthalmology*. 1985;92(6):749-758. Copyright © 1985 Elsevier.)

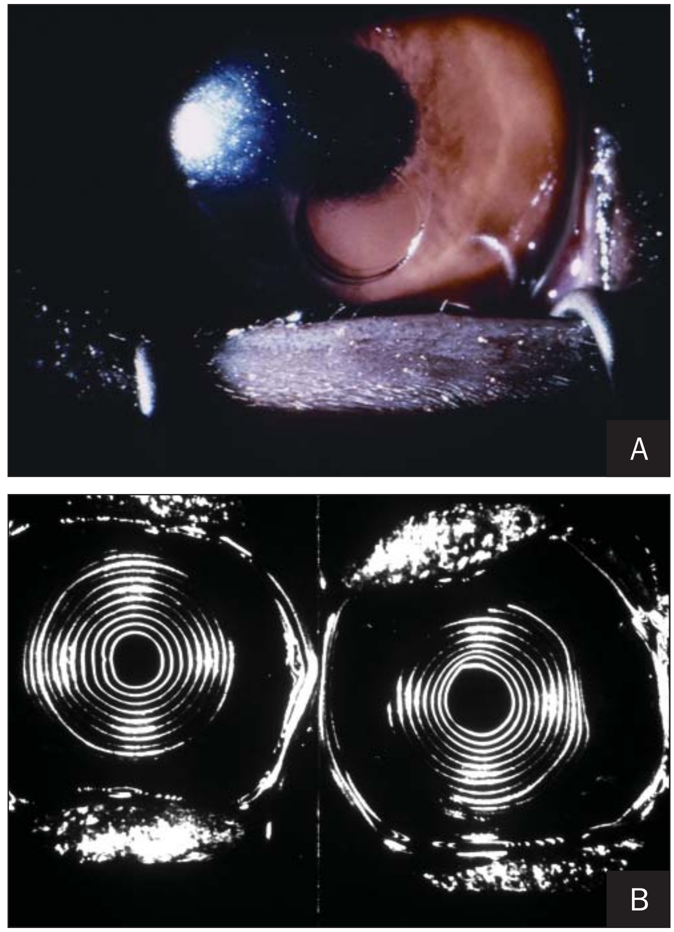

Figure 6. A) Monkey cornea immediately following a paracentral disk-like ablation. **B)** When viewed with photokeratoscopy, the treated cornea flattens over the area of ablation.

a myopic ablation profile of progressive disks expanding or constricting in diameter. In this profile, the central depth of tissue removal (t_o) was found to be mathematically proportional to the square of the outer diameter (S) and the diopters of refractive correction (D) embodied in the equation $t_o = S^2D/3$ (Fig 7).[11] Marshall also independently began work on graded large area ablations with Anthony Raven in Oxford (Fig 8). This graded refractive profile, when applied to the anterior surface of the cornea, would change its radius of curvature and was given the name "photorefractive keratectomy" (PRK) by Munnerlyn with his coauthors Stephen Koons and Marshall in 1985, when they first submitted their manuscript (personal communication, Charles Munnerlyn, PhD, March 2010, with letter dated November 1985 from Marshall to Munnerlyn acknowledging submission), even though it was not published until 1988.[11] Based on his communications with Munnerlyn, Marshall also published the naming and histopathology of "photorefractive keratectomy" in an earlier manuscript in 1986,[9] and then continued with long-term healing studies of PRK.[12]

Meanwhile, Munnerlyn and Terry Clapham, BS, began the development of a commercial laser system to perform this procedure after speaking with Trokel about the concept in 1983, and had three clinical prototypes completed by 1986. Marshall and Raven met with David Muller in 1985 to begin their own development of a clinical system for vision correction. Marguerite McDonald, MD, working with Herbert Kaufman, MD, at LSU in New Orleans, read Trokel's article and contacted him because she knew he had limited access to a primate vivarium. Following this, a long distance collaboration began, with Trokel in New York, Munnerlyn in California, and McDonald in Louisiana.

Beginning in 1985, the team of Trokel, Munnerlyn, and McDonald began the work to prove that PRK was a clinically useful and viable procedure, with McDonald as the surgeon, performing PRK on hundreds of porcine, human cadaver, and living rabbit eyes. In 1986, McDonald treated living monkey corneas with circular central ablations at the Delta Primate Center in Covington, Louisiana, and like Trokel, used a photokeratoscope to show that the corneas were flattened in the area of the treatment. These monkey experiments further validated the potential for commercial application of the laser.[13,14] McDonald and others demonstrated that the excimer laser beam did not produce significant anterior corneal haze or endothelial damage, and that the epithelium grew back over the ablated cornea in a smooth manner.[13-15]

Other animal work included that of Roger Steinert, MD, and Carmen Puliafito, MD, at Harvard University,

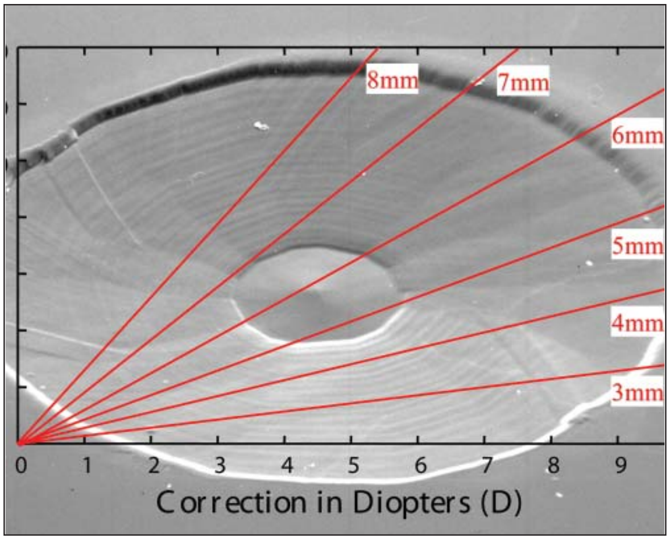

Figure 7. Graphical relationship of the central ablation depth in association with dioptric power and ablation diameter according to the Munnerlyn formula.

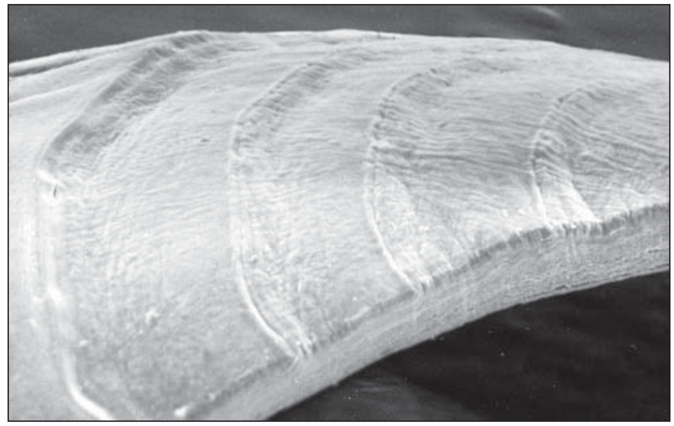

Figure 8. Scanning electron micrograph of an experimental cornea showing the change in radius of curvature with a stepwise graded ablation using an iris aperture. (Reprinted with permission from Marshall J, Trokel S, Rothery S, Krueger RR. Long-term healing of the central cornea after photorefractive keratectomy using an exicmer laser. *Ophthalmology*. 1988;95(10):1411-1421. Copyright © 1988 Elsevier.)

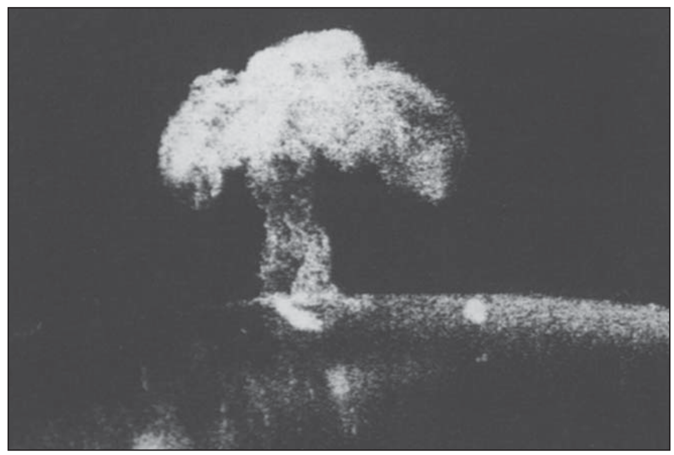

Figure 9. High speed photography of the excimer laser ablation plume when treating the cornea. (Reprinted with permission from Puliafito CA, Stern D, Krueger RR, Mandel ER. High-speed photography of excimer laser ablation of the cornea. *Arch Ophthalmol*. 1987;105(9):1255-1259. Copyright © 1987 American Medical Association. All rights reserved.).

Cambridge, Massachusetts.[16-18] Together with Krueger, they also performed time lapse photography showing the excimer plume coming off the cornea's surface with no surrounding tissue destruction (Fig 9).[19] Khalil Hanna, MD, and Yves Pouliquen, MD, at Hotel Dieu in Paris, France, developed a rotating-slit delivery system and demonstrated its utility for surface ablation in rabbits.[20,21] George O. Waring III, MD, funded by a National Eye Institute grant, established an excimer laser research laboratory at the Emory University Primate Center, Atlanta, Georgia, with Hanna and Keith Thompson, MD, and numerous corneal fellows. They used both Lambda Physik and Summit Technologies Inc (Waltham, Massachusetts) prototype excimer lasers to demonstrate the refractive changes and the histopathologic, ultrastructural, and immunohistochemical wound healing within the first 18 months after PRK.[21-25]

Seiler and colleagues in Germany independently began their own experimental animal studies that further characterized the technical parameters and healing process of excimer laser photoablation just shortly after Trokel first began his early investigation in 1983.[26-29] As the number of scientific investigators and interest in this new technology began to increase, Seiler, Trokel, and Marshall, as the leading scientific pioneers of this new technology, hosted the first Corneal Laser Surgery Congress in Berlin, Germany during the fall of 1986.

PROTOTYPE LASERS AND EARLY STUDIES

The earliest clinical refractive application was performed by Seiler in the summer of 1985, when he used a prototype system to correct astigmatism with a contact lens that contained an arcuate slit that was aligned across the steep corneal meridian during treatment. He created these laser arcuate transverse (arcT) relaxing incisions (actually excisions) in patients and reduced a high degree of astigmatism. He also performed the first slit-beam PRK, shaped using three concentric mask apertures, for myopia correction with a Meditec (Jena, Germany) laser in 1986. Seiler was also the first to show that patient fixation was adequate for achieving alignment and centration of the laser treatment.

The first excimer laser prototype (Meditec) intended for clinical use was shown in 1985 at the AAO annual meeting in San Francisco, California. It was designed by Reinhardt Thyzel to make incisions to duplicate radial keratotomy (RK) as a potentially safer alternative to diamond knife incisions. Unfortunately, the laser's radial excisions did not work as well as the radial incisions with a diamond knife,[30] and future investigations progressed toward central large area PRK. This early excimer laser design explains why both Meditec and Japanese manufacturer, NIDEK Co Ltd (Gamagori, Japan), had early prototype lasers that were designed to place slits on the cornea, a design anticipated by Hanna's rotating slit in 1987.[21,31,32] Both companies eventually converted their lasers to scanning slits for use in PRK.

The first excimer laser prototype that used a broad area ablation was shown by Munnerlyn and Clapham as part of CooperVision Inc at the AAO annual meeting in New Orleans, Louisiana, in 1986. They designed a laser delivery system that would homogenize the beam of a standard commercial excimer laser (which intrinsically had hotter spots and colder areas) and deliver it as a preprogrammed, circularly shaped pattern on the cornea. This later gave rise to the development of the first prototype VISX laser after VISX was incorporated (Santa Clara, California) in August 1987. McDonald worked with this prototype VISX laser. She performed the first human broad-beam PRK using the prototype system in early 1988 on an eye that was going to be enucleated for malignant melanoma.[33] After the cornea healed it remained transparent. The eye was enucleated and histopathology revealed uniform removal of Bowman layer and the anterior stroma with an intact overlying epithelium (personal communication, Stephen Trokel, MD, March 2010). In late 1988, McDonald performed the first successful PRK in a non-sighted myopic eye with optic neuropathy. After surgery, the patient was found to have hysterical blindness and an unexpected recovery with an uncorrected distance visual acuity of 20/20 (similar to many serendipitous advances that occur during research).

The first Summit excimer laser prototype using broad-area ablation was shown at the AAO meeting in Dallas, Texas, in 1987, after which Summit Technologies began collaborating with Seiler on their initial clinical investigations. Seiler, working at the Frei University of Berlin, Germany had previously worked with an experimental excimer laser and the early Meditec clinical prototype. He recognized that the excimer laser would have important therapeutic as well as refractive applications. He performed the first human excimer laser PTK procedure in 1985, showing that one could remove enough opacified corneal tissue to eliminate a visually significant corneal scar. Using prototypes of the Meditec and Summit excimer lasers, he also showed clinically that one could remove tissue from a clear central cornea without forming a scar, ultimately leading the way to widespread acceptance of PRK and PTK throughout the rest of the world.[34]

Subsequently, US clinical trials on PTK were begun with both the Summit and VISX excimer lasers, validating Seiler's early work.[35] Both companies carried out clinical trials of PTK under Food and Drug Administration (FDA) Investigational Device Exemptions (IDE), and in an unusual FDA hearing where both companies presented their findings back-to-back, premarket approval for clinical use of PTK was granted to Summit first in early 1995 and then VISX in late 1995.

CORPORATE STRUCTURES

In response to the earliest work of Trokel and Srinivasan, Francis L'Esperance, Jr, MD, also at Columbia University, filed a patent application for a scanning excimer laser to correct refractive errors a few weeks prior to Trokel's filing in 1983. Trokel's first manuscript, however, was submitted for publication before L'Esperance submitted his related patent, and Trokel's claims later prevailed. In 1986, both parties filed for IDEs with the FDA. In mid 1986, L'Esperance formed Taunton Technologies Inc (Monroe, Connecticut), and began clinical investigations with his company's laser.[36-38] VISX was incorporated in August 1987, with Munnerlyn, Clapham, and Trokel as the founders. The existence of VISX depended on obtaining patent rights, and interferences were filed between the VISX patents and the corresponding L'Esperance patents. After a year of discovery, Taunton acquired VISX, keeping the VISX name, management, and system. Summit Technologies Inc was formed initially to develop an excimer laser angioplasty system. Marshall, however, convinced David Muller, Chief Executive Officer, to switch their effort to corneal surgery.

Summit Technologies Inc had their own excimer laser patents, so instead of initiating patent litigation, VISX and Summit Technologies Inc reached an agreement whereby both companies could continue to exist, but with an obligatory, procedure-based royalty payment being made to a separate patent holding firm, called Pillar Point Partners. Summit Technologies was the first to install clinical broad-beam, surface ablating lasers internationally, with one of the first lasers going to Seiler in Berlin, Germany in 1988. VISX's first international system was shipped to the El Maghraby Eye Hospital in Jeddah, Saudi Arabia, in 1989, followed by the installation of other VISX excimer laser systems in Italy, Canada, and Korea. During the period from 1989 to 1995, however, Summit led the worldwide market in sales of excimer laser systems.

US FDA CLINICAL TRIALS

Following the first excimer PRK on a "normally sighted eye" at LSU in 1988, Phase 1 FDA studies of

PRK were performed at LSU in 9 legally blind eyes[39] followed by 10 partially sighted eyes.[40]

After June 1989, 40 normally sighted eyes were enrolled in Phase IIA studies by McDonald and Kaufman at LSU and Michael Dietz, MD, and Larry Peibenga, MD, at the University of Missouri, Kansas City, Missouri.[40]

The first Summit PRK was performed by Michael Gordon, MD, in San Diego, California in 1989. In 1990, Phase IIB studies were started at 5 investigational sites with 80 patients.[41] The last phase (III) of the US FDA PRK study began in the spring of 1991: 3 US ophthalmic excimer laser manufacturers—Summit, VISX, and Taunton Technologies Inc—were allowed to enter 700 eyes each for a total of 2100 eyes with follow-up of at least 2 years. Both VISX and Summit actually enrolled more than 700 eyes because of the negative effects of blowing nitrogen across the surface to evacuate the plume in the VISX, and the need for an additional subset with a larger, more desirable 6.0-mm zone in the Summit. The efficacy and safety of PRK were validated by these trials. Waring and Steinert presented the Summit data to the FDA Ophthalmic Devices Panel, which led to the approval of PRK for the Summit device in October 1995. Shortly thereafter in early 1996, PRK was approved for the VISX laser, while the Taunton laser never gained approval because the two companies (VISX and Taunton Technologies Inc) merged.

INTRODUCTION AND GROWTH OF LASIK

While the US FDA trials were occurring in the United States, patients were already being successfully treated in many other countries.[42,43] Although PRK led to good outcomes for low and moderate levels of myopia, those with higher myopia experienced a greater incidence of corneal haze and night glare symptoms, with loss of corrected visual acuity.[44,45] Also, postoperative pain and delayed visual recovery became an impediment to the widespread acceptance of PRK. Laser in situ keratomileusis (LASIK) overcame issues of pain and delayed healing, while safely expanding the range to include higher myopic corrections. Being created as a modification of keratomileusis introduced by José I. Barraquer, MD, in the mid 1950s,[46] LASIK stimulated a surge in the popularity of excimer laser vision correction in the early 1990s. Building on the concepts of in situ keratomileusis[47] and automated lamellar keratoplasty (ALK),[48] LASIK, as a concept, was first filed by Gholam Peyman, MD, in 1985 and later patented in 1989.[49] However, as a retinal specialist, Peyman was not experimentally involved in the development of the procedure. The practical experimental development was independently proposed along two major lines. The first, described by Lucio Buratto, MD, from Milan, Italy, involved the creation of a disk (free cap) of cornea made by a microkeratome, followed by refractive excimer laser ablation performed on the back surface of the disk (instead of the cryolathing carried out by Barraquer); the disk was then sutured back onto the cornea.[50]

Only a handful of cases were attempted with this approach (including a series in Jeddah, Saudi Arabia by Waring, Osama Ibrahim, MD, and Tarek Salah, MD, as well as investigations initiated by Stephen F. Brint, MD, in the United States) because of the difficulties in centration of the optics on the back of the disk. The second direction, developed by Ioannis G. Pallikaris, MD, in Crete, Greece in 1988, involved the creation of a lamellar corneal flap with a microkeratome of his own design, using the excimer laser to recontour the host stromal bed under the flap.[51,52] He coined the term, "laser in situ keratomileusis (LASIK)" (not laser-assisted in situ keratomileusis, as sometimes incorrectly used).

The subsequent combination using a commercially available automated mechanical microkeratome (Automatic Corneal Shaper [ACS], Chiron and Bausch & Lomb, Rochester, New York) and excimer laser for in situ keratomileusis under a flap was first performed in the United States by Stephen G. Slade, MD, in Houston, Texas, in 1993. He colloquially dubbed the technique "flap and zap." Further developments of the technique were carried out by Brint in New Orleans, Louisiana; Luis Antonio Ruiz, MD, in Bogota, Columbia; Michiel Kritzinger, MD, in Johannesburg, South Africa; and Akef El Maghraby, MD, and colleagues in Jeddah, Saudi Arabia.[53] Waring, Thompson, and R. Doyle Stulting, MD, PhD, at Emory University in Atlanta, Georgia, used the NIDEK EC-5000 excimer laser system to conduct the first physician-sponsored FDA study for LASIK.[54,55]

Because LASIK allowed rapid clinical recovery—compared to PRK—the issue of surgery on both eyes in the same session (simultaneous) versus sequential (days to weeks apart) sparked vigorous discussion in the ophthalmology trade journals and at meetings. The issue was settled by Waring and colleagues through a prospective, randomized trial—in favor of same-session surgery.[55]

Further development and US FDA approvals of LASIK progressed over the next decade.[54,56,57] Mechanical microkeratome technology improved with the development of automated advancement, superior hinge "down–up" LASIK,[58] dual motors for oscillation and advancement,[59] and disposable microkeratome heads.[60] Eventually, femtosecond lasers were introduced as an alternative tool for flap creation.[61]

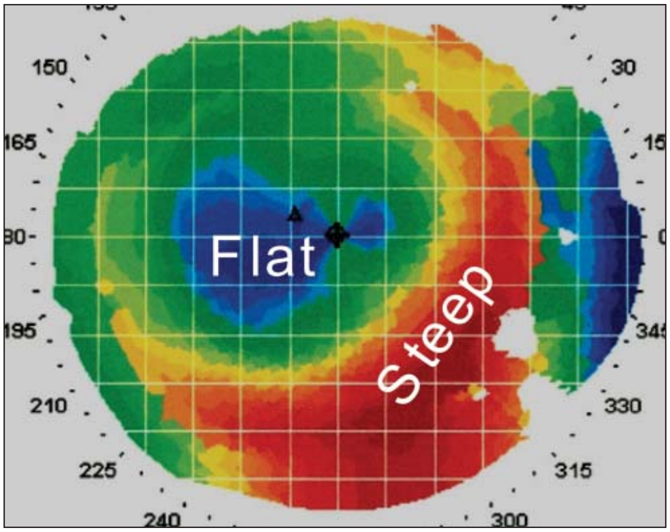

Figure 10. Postoperative topography of decentered ablation after excimer laser photorefractive keratectomy.

DIAGNOSTIC TOOLS IN SUPPORT OF EXCIMER LASER SURGERY

One of the most significant developments alongside the development of the excimer laser was the development of videokeratography. This was preceded by qualitative and numerical assessment of corneal topography by Rowsey et al in 1981.[62] This allowed examination of the corneal topography in exquisite detail, revealing the effects of the excimer laser on corneal curvature and shape to help explain optical problems, such as decentered ablations[63] and the development of steep central islands (Fig 10).[64] Stephen Klyce, PhD, developed color-coding of videokeratography and published the first article in 1984.[65] An important application of videokeratography is the screening of candidates for refractive surgery, particularly for the detection of "early" or forme fruste keratoconus, a subject explored in detail for many years by Yaron S. Rabinowitz, MD, at Cedars-Sinai in Los Angeles, California.[66] Together with Steven E. Wilson, MD, Klyce and Rabinowitz wrote one of the first textbooks on corneal topography and independently developed indices to characterize corneal abnormalities.[67-73] Rabinowitz et al wrote the first article warning about the dangers of performing LASIK on forme fruste keratoconus, followed later by Seiler's publication of the first article on corneal ectasia after LASIK.[68,74]

Another tool essential in the preoperative screening of patients for excimer laser surgery was ultrasonic corneal thickness measurement, or pachymetry, developed initially by Fredrick Kremer in 1980.[75] Corneas with a central thickness less than 2 standard deviations from the normal corneal thickness mean were considered suspicious and greater attention was given to the symmetry and indices with videokeratography.[70] Eventually, scanning slit tomography (Orbscan, Bausch & Lomb) was introduced to give a profile of corneal thickness in addition to corneal shape.[76] Both rotating Scheimpflug tomography and optical coherence tomography (OCT) have enhanced the imaging of corneal thickness and anterior and posterior surface profiles.[77,78]

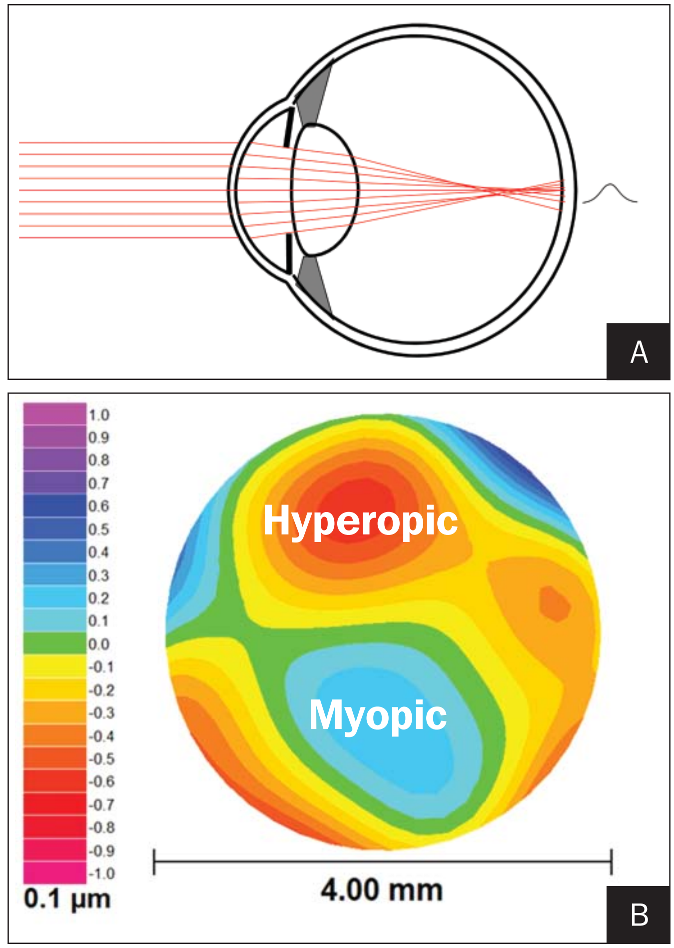

Figure 11. A) Pathway of light in the eye representative of a wavefront with aberrations. **B)** Color-coded wavefront representation (two-dimensional map) with a micron scale of deviation from the ideal planar wavefront.

Yet another key tool in support of excimer laser refractive surgery is the ocular wavefront sensor or aberrometer. This tool was introduced in 1994 by Junzhong Liang, PhD, and became commercially available in the late 1990s as a refractive optical profile map, which paralleled the mapping of surface shape with corneal topography.[79-81] The wavefront sensor detects and displays the refractive pattern of light within the entrance pupil (Fig 11A) and expresses optical detail beyond just sphere, cylinder, and axis by measuring the higher order optical aberrations such as coma and spherical

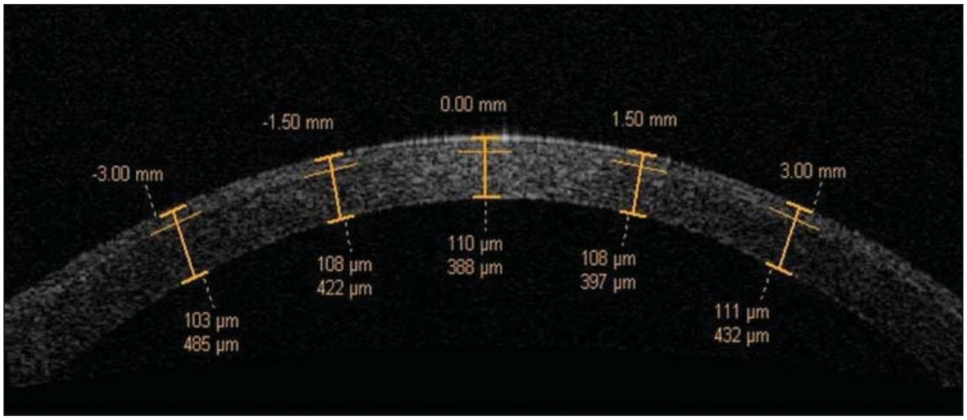

Figure 12. Uniform profile of femtosecond laser flap as measured with optical coherence tomography.

aberration. These measurements—also displayed as color-coded maps—gave much greater detail about the refractive status, and this, like topography, was useful in prescreening of eyes for refractive surgery and in diagnosing optical distortions following both corneal and intraocular lens (IOL) surgery (Fig 11B).[82-85]

CUSTOMIZED LASER VISION CORRECTION

As excimer laser vision correction grew in popularity, so did the number of patients reporting dissatisfaction with the quality of their vision after surgery, despite having 20/20 high contrast Snellen uncorrected visual acuity. At the same time, optical scientists began adopting the technology of aberrometry and adaptive optics from astronomy into the measurement and wavefront-customized refinement of the eye's optics for vision correction. By the time aberrometers were introduced into clinical ophthalmology, refinements in excimer laser delivery had evolved from broad beam to scanning-spot ablation,[86] which necessitated the application of eye tracking systems.[87,88] The accurate localized placement of scanning spots, as directed by eye tracking, made it possible to link the complex aberration pattern, measured by wavefront sensing, together with the excimer laser to customize the ablation outcome for the individual eye.[89]

By 1999, a new paradigm was introduced when the first wavefront-customized excimer laser ablation was performed in July by Seiler in Germany[90] and in October by McDonald in the United States. This complex new development was explored during the first International Wavefront Congress in Sante Fe, New Mexico in 2000.[91] The first book devoted to customized corneal ablation was published by Scott MacRae, MD; Raymond A. Applegate, PhD; and Krueger in 2001.[92] The following year saw the first US FDA approval of wavefront-customized LASIK with the CustomCornea platform using the LADARVision laser (Alcon Laboratories Inc, Ft Worth, Texas), which was later followed by the approval of multiple excimer laser commercial platforms, with market penetration of customized LASIK growing to more than 50% of cases in the United States (2007 Market Scope Annual Refractive Surgeon Survey). In 2004, Seiler observed that "wavefront optimized treatments" (aspheric treatments that peripherally compensate for reduced effective pulse energy in the outer part of the ablation and maintain the prolate cornea shape) may be sufficient to improve the quality of vision in many individuals who did not have a sufficient degree of higher order aberrations to warrant wavefront-guided treatments.[93]

Topography-guided LASIK and PRK were also introduced in the late 1990s and then again in mid 2000 outside the United States for complex retreatments of highly aberrated eyes.[94,95] The first US FDA trial in normal myopic eyes was NIDEK's CXII topographically guided custom aspheric treatment zone (CATz) trial.[96] In addition to the improved outcomes achieved with wavefront and topographic customized and optimized corrections, the clinical introduction of femtosecond lasers in 2003 also enhanced the quality of outcomes by improving the reproducibility and profile uniformity of the LASIK flap (Fig 12).[97-99] Thin-flap femtosecond laser LASIK, with a uniform profile of less than 110 µm, was sometimes dubbed "sub-Bowman's keratomileusis (SBK)" because of its close proximity beneath Bowman layer.[100] These uniformly thinner flaps reduce the biomechanical weakening caused by thicker flaps in LASIK, approaching the stability of surface ablation with the goal of minimizing postoperative corneal ectasia.[101,102] Improvement in PRK has also been achieved with the application of topical mitomycin C on the stromal bed at the end of the ablation to prevent corneal haze. The standard dose is 0.02%, topically applied in a soaked sponge for 12 seconds to 2 minutes.[103,104] Proper management of the ocular surface with the treatment of blepharitis and tear dysfunction before and after surgery has also enhanced the healing and outcomes of both LASIK and PRK.[105]

CONCLUSION

From Trokel's initial surgical application of Taboada's work and his subsequent animal experiments with the excimer laser over 25 years ago, together with that of other pioneers, excimer laser vision correction is now performed clinically, with over a million procedures performed annually in the United States, and several million each year around the world. The technology has become so excellent and safe that it has been approved by the US military for use in soldiers, navy pilots, and most recently in NASA astronaut candidates.[106] Quality of life studies have demonstrated that it has transformed and improved the quality of life of millions of people.[107,108]

AUTHOR CONTRIBUTIONS

Study concept and design (R.R.K., Y.S.R.); data collection (R.R.K., Y.S.R.); analysis and interpretation of data (Y.S.R., P.S.B.); drafting of the manuscript (R.R.K., Y.S.R., P.S.B.); critical revision of the manuscript (R.R.K.); administrative, technical, or material support (Y.S.R.); supervision (R.R.K., P.S.B.)

REFERENCES

1. Trokel SL, Srinivasan R, Braren B. Excimer laser surgery of the cornea. *Am J Ophthalmol*. 1983;96(6):710-715.
2. Hoffman JM, Hays AK, Tisone GC. High-powered UV noble-gas halide lasers. *Appl Phys Lett*. 1976;28(10):538-539.
3. Taboada J, Archibald CJ. An extreme sensitivity in the corneal epithelium to far UV ArF excimer laser pulses. Proceedings of the Scientific Program of the Aerospace Medical Association; May 4, 1981; San Antonio, Texas.
4. Srinivasan R. Kinetics of the ablative photodecomposition of organic polymers in the far ultraviolet (193 nm). *Journal of Vacuum Science and Technology B*. 1983;1(4):923-926.
5. Krueger RR, Trokel SL, Schubert HD. Interaction of ultraviolet laser light with the cornea. *Invest Ophthalmol Vis Sci*. 1985;26(11):1455-1464.
6. Krueger RR, Trokel SL. Quantitation of corneal ablation by ultraviolet laser light. *Arch Ophthalmol*. 1985;103(11):1741-1742.
7. Marshall J, Trokel S, Rothery S, Schubert H. An ultrastructural study of corneal incisions induced by an excimer laser at 193 nm. *Ophthalmology*. 1985;92(6):749-758.
8. Marshall J, Trokel S, Rothery S, Krueger R. A comparative study of corneal incisions induced by diamond and steel knives and two ultraviolet radiations from an excimer laser. *Br J Ophthalmol*. 1986;70(7):482-501.
9. Marshall J, Trokel S, Rothery S, Krueger R. Photoablative reprofiling of the cornea using an excimer laser: photorefractive keratectomy. *Lasers Ophthalmol*. 1986;1(1):21-48.
10. Serdarevic O, Darrell RW, Krueger RR, Trokel SL. Excimer laser therapy for experimental Candida keratitis. *Am J Ophthalmol*. 1985;99(5):534-538.
11. Munnerlyn CR, Koons SJ, Marshall J. Photorefractive keratectomy: a technique for laser refractive surgery. *J Cataract Refract Surg*. 1988;14(1):46-52.
12. Marshall J, Trokel SL, Rothery S, Krueger RR. Long-term healing of the central cornea after photorefractive keratectomy using an excimer laser. *Ophthalmology*. 1988;95(10):1411-1421.
13. McDonald MB, Beuerman R, Falzoni W, Rivera L, Kaufman HE. Refractive surgery with the excimer laser. *Am J Ophthalmol*. 1987;103(3 Pt 2):469.
14. McDonald MB, Frantz JM, Klyce SD, Salmeron B, Beuerman RW, Munnerlyn CR, Clapham TN, Koons SJ, Kaufman HE. One-year refractive results of central photorefractive keratectomy for myopia in the nonhuman primate cornea. *Arch Ophthalmol*. 1990;108(1):40-47.
15. Gaster RN, Binder PS, Coalwell K, Berns M, McCord RC, Burstein NL. Corneal surface ablation by 193 nm excimer laser and wound healing in rabbits. *Invest Ophthalmol Vis Sci*. 1989;30(1):90-98.
16. Puliafito CA, Steinert RF, Deutsch TF, Hillenkamp F, Dehm EJ, Adler CM. Excimer laser ablation of the cornea and lens: experimental studies. *Ophthalmology*. 1985;92(6):749-758.
17. Puliafito CA, Wong K, Steinert RF. Quantitative and ultrastructural studies of excimer laser ablation of the cornea at 193 and 248 nanometers. *Lasers Surg Med*. 1987;7(2):155-159.
18. Nuss RC, Puliafito CA, Dehm E. Unscheduled DNA synthesis following excimer laser ablation of the cornea in vivo. *Invest Ophthalmol Vis Sci*. 1987;28(2):287-294.
19. Puliafito CA, Stern D, Krueger RR, Mandel ER. High-speed photography of excimer laser ablation of the cornea. *Arch Ophthalmol*. 1987;105(9):1255-1259.
20. Hanna KD, Pouliquen Y, Waring GO III, Savoldelli M, Cotter J, Morton K, Menasche M. Corneal stromal wound healing in rabbits after 193-nm excimer laser surface ablation. *Arch Ophthalmol*. 1989;107(6):895-901.
21. Hanna KD, Chastang JC, Pouliquen Y, Renard G, Asfar L, Waring GO III. Excimer laser keratectomy for myopia with a rotating-slit delivery system. *Arch Ophthalmol*. 1988;106(2):245-250.
22. Fantes FE, Hanna KD, Waring GO III, Pouliquen Y, Thompson KP, Savoldelli M. Wound healing after excimer laser keratomileusis (photorefractive keratectomy) in monkeys. *Arch Ophthalmol*. 1990;108(5):665-675.
23. Hanna KD, Pouliquen YM, Savoldelli M, Fantes F, Thompson KP, Waring GO III, Samson J. Corneal wound healing in monkeys 18 months after excimer laser photorefractive keratectomy. *Refract Corneal Surg*. 1990;6(5):340-345.
24. SundarRaj N, Geiss MJ III, Fantes F, Hanna K, Anderson SC, Thompson KP, Thoft RA, Waring GO III. Healing of excimer laser ablated monkey corneas. An immunohistochemical evaluation. *Arch Ophthalmol*. 1990;108(11):1604-1610.
25. Hanna KD, Pouliquen YM, Waring GO III, Savoldelli M, Fantes F, Thompson KP. Corneal wound healing in monkeys after repeated excimer laser photorefractive keratectomy. *Arch Ophthalmol*. 1992;110(9):1286-1291.
26. Seiler T, Wollensak J. In vivo experiments with excimer laser—technical parameters and healing processes. *Ophthalmologica*. 1986;192(2):65-70.
27. Seiler T, Bende T, Winckler K, Wollensak J. Side effects in excimer corneal surgery. DNA damage as a result of 193 nm excimer laser radiation. *Graefes Arch Clin Exp Ophthalmol*. 1988;226(3):273-276.
28. Bende T, Seiler T, Wollensak J. Side effects in excimer corneal surgery. Corneal thermal gradients. *Graefes Arch Clin Exp Ophthalmol*. 1988;226(3):277-280.
29. Seiler T, Kriegerowski M, Schnoy N, Bende T. Ablation rate of human corneal epithelium and Bowman's layer with the excimer laser (193 nm). *Refract Corneal Surg*. 1990;6(2):99-102.
30. Cotliar AM, Schubert HD, Mandel ER, Trokel SL. Excimer laser radial keratotomy. *Ophthalmology*. 1985;92(2):206-208.
31. Schroder E, Dardenne MU, Neuhann T, Tenner A. An oph-

thalmic excimer laser for corneal surgery. *Am J Ophthalmol*. 1987;103(3 Pt 2):472-473.

32. Hanna K, Chastang JC, Pouliquen Y, Renard G, Asfar L, Waring GO III. A rotating slit delivery system for excimer laser refractive keratoplasty. *Am J Ophthalmol*. 1987;103(3 Pt 2):474.
33. McDonald MB, Kaufman HE, Frantz JM, Shofner S, Salmeron B, Klyce SD. Excimer laser ablation in a human eye. Case report. *Arch Ophthalmol*. 1990;107(5):641-642.
34. Seiler T, Kahle G, Kriegerowski M. Excimer laser (193 nm) myopic keratomileusis in sighted and blind human eyes. *Refract Corneal Surg*. 1990;6(3):165-173.
35. Stark WJ, Chamon W, Kamp MT, Enger CL, Rencs EV, Gottsch JD. Clinical follow-up of 193- nm ArF excimer laser photokeratectomy. *Ophthalmology.* 1992;99(5):805-811.
36. L'Esperance FA Jr, Taylor DM, Warner JW. Human excimer laser keratectomy. Short-term histopathology. *Bulletin of the New York Academy of Medicine*. 1989;65(5):551-573.
37. L'Esperance FA, Warner JW, Telfair WB, Yoder PR Jr, Martin CA. Excimer laser instrumentation and technique for human corneal surgery. *Arch Ophthalmol*. 1988;107(1):131-139.
38. Taylor DM, L'Esperance FA Jr, Del Pero RA, Roberts A, Gigstad J, Stokes MT, Warner JW, Telfair WB, Martin CA, Yoder PR Jr, et al. Human excimer laser lamellar keratectomy. A clinical study. *Ophthalmology*. 1989;96(5):654-664.
39. McDonald MB, Frantz JM, Klyce SD, Beuerman RW, Varnell R, Munnerlyn CR, Clapham TN, Salmeron B, Kaufman HE. Central photorefractive keratectomy for myopia: the blind eye study. *Arch Ophthalmol*. 1990;108(6):799-808.
40. McDonald MB, Liu JC, Byrd TJ, Abdelmegeed M, Andrade HA, Klyce SD, Varnell R, Munnerlyn CR, Clapham TN, Kaufman HE. Central photorefractive keratectomy for myopia. Partially sighted and normally sighted eyes. *Ophthalmology*. 1991;98(9):1327-1337.
41. McDonald MB, Talamo JH. Myopic photorefractive keratectomy: the experience in the United States with the VISX excimer laser. In: Salz JJ, ed. *Corneal Laser Surgery*. St Louis, MO: Mosby; 1995:45-55.
42. Seiler T, Wollensak J. Myopic photorefractive keratectomy with the excimer laser. One year follow-up. *Ophthalmology*. 1991;98(8):1156-1163.
43. Gartry DS, Kerr Muir MG, Marshall J. Excimer laser photorefractive keratectomy. 18 months follow-up. *Ophthalmology*. 1992;99(8):1209-1219.
44. Seiler T, Holschbach A, Derse M, Jean B, Genth U. Complications of myopic photorefractive keratectomy with the excimer laser. *Ophthalmology*. 1994;101(1):153-160.
45. Gartry DS, Muir MG, Lohmann CP, Marshall J. The effect of topical corticosteroids on refractive outcome and corneal haze after photorefractive keratectomy. A prospective, randomized, double-blind study. *Arch Ophthalmol*. 1992;110(7):944-952.
46. Barraquer J. Queratomileusis para la correccion de la myopia. *Arch Soc Am Oftalmol Optom*. 1964;5:27-48.
47. Ruiz L, Rowsey J. In situ keratomileusis. *Invest Ophthalmol Vis Sci*. 1988;29(Suppl):392.
48. Lyle WA, Jin GJ. Initial results of automated lamellar keratoplasty for correction of myopia: one year follow-up. *J Cataract Refract Surg*. 1996;22(1):31-43.
49. Peyman GA, inventor. Method for modifying corneal curvature. US patent 4,840,175. June 20, 1989.
50. Buratto L, Ferrari M, Rama P. Excimer laser intrastromal keratomileusis. *Am J Ophthalmol*. 1992;113(3):291-295.
51. Pallikaris I, Papatsanaki M, Stathi E, Frenschock O, Georgiadis A. Laser in situ keratomileusis. *Lasers Surg Med*. 1990;10(5):463-468.
52. Pallikaris I, Papatzanaki M, Siganos D, Tsilimbaris MK. A corneal flap technique for laser in situ keratomileusis. Human studies. *Arch Ophthalmol*. 1991;109(12)1699-1702.
53. Salah T, Waring GO III, el Maghraby A, Moadel K, Grimm SB. Excimer laser in situ keratomileusis under a corneal flap for myopia of 2 to 20 diopters. *Am J Ophthalmol*. 1996;121(2):143-155.
54. Waring GO III, Stulting, RD, Wiley WM, Carr JD, Thompson KP. LASIK in 3946 eyes with the Nidek EC-5000 excimer laser. *J Refract Surg*. 2001;17(2):S277.
55. Waring GO III, Carr JD, Stulting RD, Thompson KP, Wiley W. Prospective randomized comparison of simultaneous and sequential bilateral laser in situ keratomileusis for the correction of myopia. *Ophthalmology*. 1999;106(4):732-738.
56. Brint SF, Ostrick DM, Fisher C, Slade SG, Maloney RK, Epstein R, Stulting RD, Thompson KP. Six-month results of the multicenter phase I study of excimer laser myopic keratomileusis. *J Cataract Refract Surg*. 1994;20(6):610-615.
57. Kezirian G, Casebeer JC. The CRS LASIK study. In: Machat JJ, Slade SG, Probst LE, eds. *The Art of LASIK*. Thorofare, NJ: SLACK Inc; 1999:293-302.
58. Burrato L. Down-up LASIK with the Hansatome: personal technique. In: Burrato L, Brint S, eds. *Custom LASIK*. Thorofare, NJ: SLACK Inc; 2003:119-149.
59. Miranda D, Iacobucci M, Krueger RR. Flap reproducibility and complication rate using the B&L Hansatome, Moria CB and Alcon SKBM microkeratomes. *Ophthalmic Practice*. 2002;20(3):96-99.
60. Pietilä J, Mäkinen P, Suominen S, Huhtala A, Uusitalo H. Bilateral comparison of corneal flap dimensions with the Moria M2 reusable head and single use head microkeratomes. *J Refract Surg*. 2006;22(4):354-357.
61. Ratkay-Traub I, Ferincz IE, Juhasz T, Kurtz RM, Krueger RR. First clinical results with the femtosecond neodynium-glass laser in refractive surgery. *J Refract Surg*. 2003;19(2):94-103.
62. Rowsey JJ, Reynolds AE, Brown R. Corneal topography. Corneascope. *Acta Ophthalmol*. 1981;99(6):1093-1100.
63. Webber SK, McGhee CN, Bryce IG. Decentration of photorefractive keratectomy ablation zones after excimer laser surgery for myopia. *J Cataract Refract Surg*. 1996;22(3):299-303.
64. Krueger RR, Saedy NF, McDonnell PJ. Clinical analysis of steep central islands after excimer laser photorefractive keratectomy. *Arch Ophthalmol*. 1996;114(4):377-381.
65. Klyce SD. Computer-assisted corneal topography. High-resolution graphic presentation and analysis of keratoscopy. *Invest Ophthalmol Vis Sci*. 1984;25(12):1426-1435.
66. Rabinowitz YS, Garbus J, McDonnell PJ. Computer-assisted corneal topography in family members of patients with keratoconus. *Arch Ophthalmol*. 1990;108(3):365-371.
67. Rabinowitz YS, Wilson SE, Klyce SD. *Color Atlas of Corneal Topography: Interpreting Videokeratography*. New York, NY: Igaku-Shoin Medical Publishers; 1993.
68. Rabinowitz YS, Klyce S, Krachmer J, Nordan L, Rowsey J, Sugar J, Wilson S, Binder P, Damiano R, McDonald M, Neuman A, Seiler T, Thompson K, Wyzinski P. Keratoconus, videokeratography, and refractive surgery. *Refract Corneal Surg*. 1992;5(8):403-407.
69. Maeda N, Klyce SD, Smolek MK, Thompson HW. Automated keratoconus screening with corneal topography analysis. *Invest Ophthalmol Vis Sci*. 1994;35(6):2749-2757.
70. Rabinowitz Y. Videokeratographic indices to aid in screening for keratoconus. *J Refract Surg*. 1995;11(5):371-379.

71. Smolek MK, Klyce SD. Current keratoconus detection methods compared with a neural network approach. *Invest Ophthalmol Vis Sci*. 1997;38(11):2290-2299.
72. Rabinowitz YS, Rasheed K. KISA% index: a quantitative algorithm embodying minimal topographic criteria for diagnosing keratoconus. *J Cataract Refract Surg*. 1999;25(10):1327-1336.
73. Klyce SD, Karon MD, Smolek MK. Screening patients with the corneal navigator. *J Refract Surg*. 2005;21(5 Suppl):S617-S622.
74. Seiler T, Quurke AW. Iatrogenic keratoectasia after LASIK in a case of forme fruste keratoconus. *J Cataract Refract Surg*. 1998;24(7):1007-1009.
75. Kremer FB. A new instrument for clinical pachymetry. In: Schachar RA, Levy NS, Schachar L, eds. *Radial Keratotomy*. Dennison, TX: LAL Publishers; 1980:201-212.
76. Yaylali V, Kaufman SC, Thompson HW. Corneal thickness measurements with the Orbscan Topography System and ultrasonic pachymetry. *J Cataract Refract Surg*. 1997;23(9):1345-1350.
77. Lackner B, Schmidinger G, Pieh S, Funovics MA, Skorpik C. Repeatability and reproducibility of central corneal thickness measurement with Pentacam, Orbscan, and ultrasound. *Optom Vis Sci*. 2005;82(10):892-899.
78. Li Y, Shekhar R, Huang D. Corneal pachymetry mapping with high-speed optical coherence tomography. *Ophthalmology*. 2006;113(5):792-799.e2.
79. Liang J, Grimm B, Goelz S, Bille JF. Objective measurement of wave aberrations of the human eye with the use of a Hartmann-Shack Wave-front sensor. *J Opt Soc Am A Opt Image Sci Vis*. 1994;11(7):1949-1957.
80. Moreno-Barriuso E, Marcos S, Navarro R, Burns SA. Comparing laser ray tracing, the spatially resolved refractometer, and the Hartmann-Shack sensor to measure the ocular wave aberration. *Optom Vis Sci*. 2001;78(3):152-156.
81. Kaemmerer M, Mrochen M, Mierdel P, Krinke HE, Seiler T. Clinical experience with the Tscherning aberrometer. *J Refract Surg*. 2000;16(5):S584-S587.
82. Seiler T, Kaemmerer M, Mierdel P, Krinke HE. Ocular optical aberrations after photorefractive keratectomy for myopia and myopic astigmatism. *Arch Ophthalmol*. 2000;118(1):17-21.
83. Marcos S. Aberrations and visual performance following standard laser vision correction. *J Refract Surg*. 2001;17(5):S596-S601.
84. Chalita MR, Xu M, Krueger RR. Correlation of aberrations with visual symptoms using wavefront analysis in eyes after laser in situ keratomileusis. *J Refract Surg*. 2003;19(6):S682-S686.
85. Maeda N, Fujikado T, Kuroda T, Mihashi T, Hirohara Y, Nishida K, Watanabe H, Tano Y. Wavefront aberrations measured with Hartmann-Shack sensor in patients with keratoconus. *Ophthalmology*. 2002;109(11):1996-2003.
86. Huang D, Arif M. Spot size and quality of scanning laser correction of higher-order wavefront aberrations. *J Cataract Refract Surg*. 2002;28(3):407-416.
87. Krueger RR. In perspective: eye tracking and autonomous laser radar. *J Refract Surg*. 1999;15(2):145-149.
88. Bueeler M, Mrochen M. Simulation of eye-tracker latency, spot size, and ablation pulse depth on the correction of higher order wavefront aberrations with scanning spot laser systems. *J Refract Surg*. 2005;21(1):28-36.
89. Krueger RR. Technology requirements for Summit-Autonomous CustomCornea. *J Refract Surg*. 2000;16(5):S592-S601.
90. Mrochen M, Kaemmerer M, Seiler T. Wavefront-guided laser in situ keratomileusis: early results in three eyes. *J Refract Surg*. 2000;16(2):116-121.
91. Miranda D, Krueger RR. Highlights of the 1st international congress of wavefront sensing and aberration-free refractive correction. *J Refract Surg*. 2001;17(5):S566-S572.
92. MacRae S, Krueger R, Applegate RA. *Customized Corneal Ablation: The Quest for Supervision*. Thorofare, NJ: SLACK Inc; 2001.
93. Koller T, Iseli HP, Hafezi F, Mrochen M, Seiler T. Q-factor customized ablation profile for the correction of myopic astigmatism. *J Cataract Refract Surg*. 2006;32(4):584-589.
94. Toda I, Yamamoto T, Ito M, Hori-Komai Y, Tsubota K. Topography-guided ablation for treatment of patients with irregular astigmatism. *J Refract Surg*. 2007;23(2):118-125.
95. Lin DT, Holland SR, Rocha KM, Krueger RR. Method for optimizing topography-guided ablation of highly aberrated eyes with the ALLEGRETTO WAVE excimer laser. *J Refract Surg*. 2008;24(4):S439-S445.
96. Dougherty PJ, Waring GO III, Chayet A, Fischer J, Fant B, Bains HS. Topographically guided laser in situ keratomileusis for myopia using a customized aspherical treatment zone. *J Cataract Refract Surg*. 2008;34(11):1862-1871.
97. Nordan LT, Slade SG, Baker RN, Suarez C, Juhasz T, Kurtz R. Femtosecond laser flap creation for laser in situ keratomileusis: six month follow-up of initial U.S. clinical series. *J Refract Surg*. 2003;19(1):8-14.
98. Slade SG. The use of the femtosecond laser in the customization of corneal flaps in laser in situ keratomileusis. *Curr Opin Ophthalmol*. 2007;18(4):314-317.
99. Stahl JE, Durrie DS, Schwendeman FJ, Boghossian AJ. Anterior segment OCT analysis of thin IntraLase femtosecond flaps. *J Refract Surg*. 2007;23(6):555-558.
100. Azar DT, Ghanem RC, de la Cruz J, Hallak JA, Kojima T, Al-Tobaigy FM, Jain S. Thin-flap (sub-Bowman keratomileusis) versus thick-flap laser in situ keratomileusis for moderate to high myopia: case-control analysis. *J Cataract Refract Surg*. 2008;34(12):2073-2078.
101. Krueger RR, Dupps WJ Jr. Biomechanical effects of femtosecond and microkeratome-based flap creation: prospective contralateral examination of two patients. *J Refract Surg*. 2007;23(8):800-807.
102. Durrie DS, Slade SG, Marshall J. Wavefront-guided excimer laser ablation using photorefractive keratectomy and sub-Bowman's keratomileusis: a contralateral eye study. *J Refract Surg*. 2008;24(1):S77-S84.
103. Lacayo GO III, Majmudar PA. How and when to use mitomycin-C in refractive surgery. *Curr Opin Ophthalmol*. 2005;16(4):256-259.
104. Thornton I, Xu M, Krueger RR. Comparison of standard (0.02%) and low dose (0.002%) mitomycin C in the prevention of corneal haze following surface ablation for myopia. *J Refract Surg*. 2008;24(1):S68-S76.
105. Albietz JM, Lenton LM. Management of the ocular surface and tear film before, during, and after laser in situ keratomileusis. *J Refract Surg*. 2004;20(1):62-71.
106. Stanley PF, Tanzer DJ, Schallhorn SC. Laser refractive surgery in the United States Navy. *Curr Opin Ophthalmol*. 2008;19(4):321-324.
107. Chen CY, Keeffe JE, Garoufalis P, Islam FM, Dirani M, Couper TA, Taylor HR, Baird PN. Vision-related quality of life comparison for emmetropes, myopes after refractive surgery, and myopes wearing spectacles or contact lenses. *J Refract Surg*. 2007;23(8):752-759.
108. Solomon KD, Fernández de Castro LE, Sandoval HP, Biber JM, Groat B, Neff KD, Ying MS, French JW, Donnenfeld ED, Lindstrom RL; Joint LASIK Study Task Force. LASIK world literature review: quality of life and patient satisfaction. *Ophthalmology*. 2009;116(4):691-701.