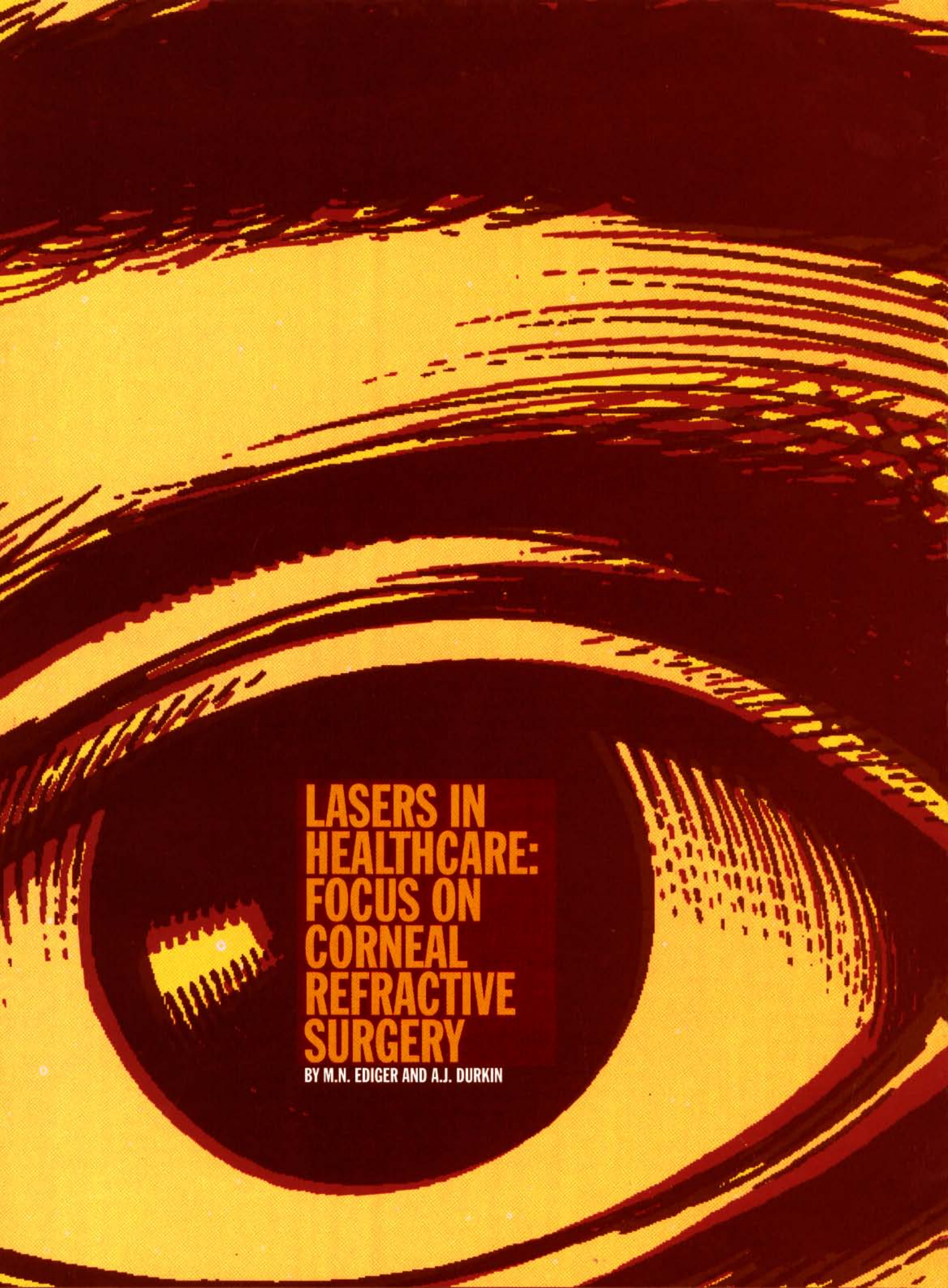

LASERS IN HEALTHCARE: FOCUS ON CORNEAL REFRACTIVE SURGERY

BY M.N. EDIGER AND A.J. DURKIN

Refractive surgery techniques allow people with vision defects to see without the use of external aids. The authors provide a comprehensive picture of state-of-the-art, corneal surgery.

Almost since its inception, the laser has been investigated as a tool for medicine and surgery. The first reported surgical laser application, retinal photocoagulation with a ruby laser, was performed in 1961.[1, 2] In the intervening years, clinical lasers have had a somewhat bumpy ride. There are now well-established, laser-based diagnostic or therapeutic procedures in most medical specialties. However, finding niches where laser-based instruments have a distinct benefit over conventional methods has not always been easy.

In many instances, therapeutic uses of lasers have suffered a backlash reaction by both scientists and the public when the new device or procedure didn't satisfy exaggerated expectations. A prime example of early exuberance followed by well-founded caution was the treatment of tumors in the 1960s with high-power ruby and Nd:YAG lasers. Early enthusiasm about partial and even complete eradication of certain types of tumors in animal studies was soon tempered by much less success in other kinds of tumors. Furthermore, the optical and thermal properties of the tissue were far more complex than had been initially appreciated. Worse yet, the resulting "splatter" and airborne particles from the irradiated tumor could contain viable tumor cells. Hence, there was a real risk of spreading the cancer to other tissues or organs in this mode of treatment.[3] The laser's future in this context was dubious and development was for a time hindered by the perceptions resulting from this simple "point-and-shoot" experimentation. Still, interest in possible medical and surgical laser applications continued, albeit with a great deal of caution. A more thorough understanding of the interaction of light with tissue was in order. In fact, even now research on tissue optics continues to elucidate details and break new ground. A number of resources, including the compendium compiled by Welch and van Gemert,[4] provide detailed information on this science.

Over the last 35 years, research and development in biomedical optics has become a rich and varied field. Not only have a number of therapeutic applications become commonplace, but in the past 10 years there has been a groundswell of activity in the development of diagnostic uses of lasers, including blood glucose monitoring,[5] tissue oxygenation,[6] and optical biopsy.[7] Investigations continue both to examine the details of light-tissue interaction and try to answer questions about the real-world utility of many of these applications. Because this has become an area of appreciable breadth, with each application possessing a unique and detailed basis, a thorough review of lasers in medicine and surgery would be beyond the scope of this article. There are several excellent review articles[8–10] that attempt to provide a broader view of the field. We will limit our attention to ophthalmology—the field that began laser surgery. Specifically, we will discuss the use of ultraviolet lasers for altering the shape of the cornea, *i.e.*, refractive surgery.

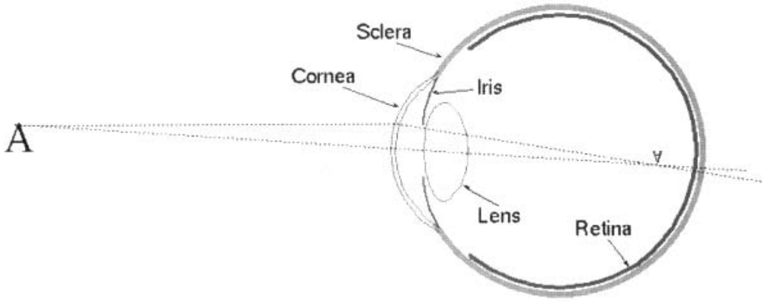

Figure 1. Basic anatomy and optics of the eye. The dashed lines depict a ray tracing of myopia where the eye is relatively too long and distant images are focused in front the retina.

The eye as a camera

As a starting point for discussing refractive surgery, it's helpful to understand the basic structure of the human eye and its main components (see Fig. 1). Not surprisingly, there are strong similarities between the eye and a simple camera. The cornea and lens act as a compound lens to focus an image onto the film—the retina. The cornea, approximately 1/2-mm thick, primarily consists of randomly-oriented bundles of collagen fibers (~20%) and water (~75%). The composition of the cornea and the sclera—the white part of the eye—are actually very similar. Fortunately, the chemistry of a healthy cornea keeps the web of protein and water in the cornea remarkably clear. The cornea itself accounts for about two-thirds of the focusing power of the eye. This isn't too remarkable since the index of refraction mismatch at

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the air-cornea interface is much larger than for any of the other refractive surfaces. As a result, the focusing power of the eye can be significantly adjusted by relatively small surgical changes in the curvature of the cornea. The lens, an elastic biconvex disc, is attached to the body of the eye via a system of ligaments and muscle fibers. The eye focuses or accommodates by making minor adjustments in the tension of these muscle fibers, thereby slightly altering the shape of the lens.

The optics of vision defects

Myopia or near-sightedness occurs in approximately one-quarter of the U.S. population. For most of these people, their eyes are "too long," and distant images come to a focus in front of their retina (see Fig. 1, page 19). For people with hyperopia or far-sightedness, the point where the image would be in focus is behind the retina. In either case, the resulting image on the retina is out-of-focus and blurred. Astigmatism occurs when the cornea has an oblong rather than spherical shape. The optical equivalent of a cornea with astigmatism is a combination of spherical and cylindrical lenses. The retinal images of people with astigmatism are spatially distorted, as well as blurred due to the accompanying myopia or hyperopia. Another "opia" that affects many adults over forty is presbyopia, where over the course of a lifetime, the elastic properties of the lens degrade and the eye loses some of its ability to focus on nearby objects.

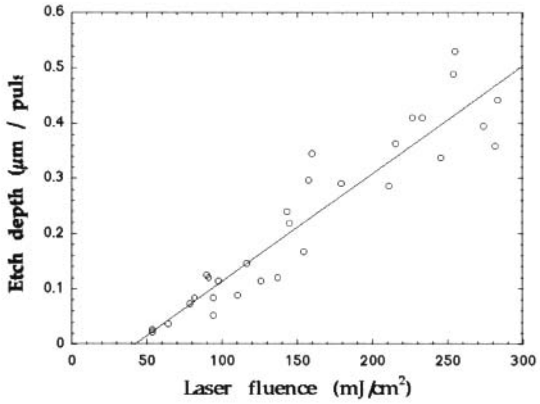

Figure 2. Etch depth, the thickness of corneal tissue removed by each laser pulse, plotted against excimer laser fluence. The open circles are values from the literature[17] for ablation of human cornea. The line represents a linear fit to the data.

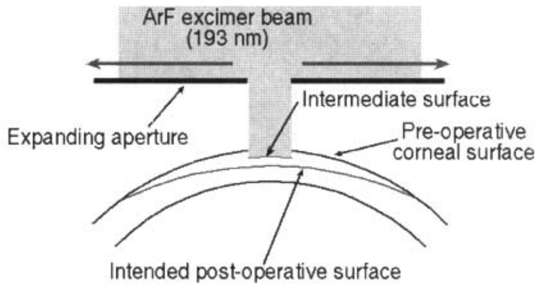

Figure 3. Correction of myopia by restricting the diameter of the laser with an iris diaphragm. Under computer control, the iris is opened as the laser is pulsed producing a near-spherical approximation of the desired surface.

Options for vision correction/motivation for refractive surgery

Glasses and contact lenses are popular solutions for many individuals with a vision "defect." Since glasses and contacts can be bothersome and obtrusive, eliminating the need for them has broad appeal. Today there are a variety of non-laser, surgical techniques to correct refractive errors. Probably the most well-known and widely practiced is radial keratotomy (RK), which is used primarily to treat myopia. A variation, astigmatic keratotomy (AK), is used to treat astigmatism. In an RK procedure, an ophthalmologist uses a diamond knife to create a series of spoke-like, radial incisions. In the spoke-wheel analogy, the hub is the pupil of the eye. The incisions extend outward from this hub and thus do not overlap the visually important center of the cornea. The incisions are relatively deep, cutting through approximately 90% of the thickness of the cornea. The result is to relax the cornea and flatten it slightly. Practicing RK and AK is somewhat of an art. The results of the surgery depend on the technique and the skill of the surgeon, and are somewhat mitigated by the healing response of the eye. Data from an early study indicated that there is a hyperopic shift in some patients,[11] and there is speculation that the cornea may be weakened by the RK incisions and, thus, be more susceptible to traumatic injury. Given these RK characteristics, there has been considerable interest in developing tools for refractive surgery that are more automated and not so dependent on the experience and skill of a surgeon. Other sought-after features in a refractive tool are a long-term stable result and the preservation of the integrity of the cornea. In many respects, refractive surgery using excimer lasers attempts to meet these challenges and has received considerable attention.

Ultraviolet laser ablation

The use of excimer lasers in ophthalmology is an outgrowth of work by a number of groups, notably Srinivasan and co-workers, who studied the effects of excimer lasers on polymers in the early 1980s. They found that these relatively new sources of ultraviolet radiation could remove thin layers of plastics via "photoablative decomposition" with relatively little thermal damage to the remaining material.[12] They also found that laser ablation was similarly effective at machining biologic tissue. (The term laser ablation has come to mean laser-induced material removal, regardless of the specific laser-material interaction.) A collaboration between ophthalmologist Steve Trokel and Srinivasan's group at IBM produced the first reported work on excimer laser corneal ablation in 1983.[13] At about the same time, another ophthalmologist, Francis L'Esperance, independently filed the first patent application covering laser reprofiling of the cornea.[14]

Early investigations determined that the argon-fluoride (ArF) excimer laser, which emits deep-ultraviolet radiation at 193 nm, was the laser of choice for corneal ablation. Compared to other readily available excimer wavelengths, like krypton-fluoride (KrF; 248 nm), xenon-chloride (XeCl; 308 nm), or xenon-fluoride (XeF; 351 nm), ablation with the ArF laser produced significantly less damage to the adjacent tissue and the least risk of DNA damage to or cataract formation in the eye. Also, the etch depth of the ArF laser—the thickness of material removed with each laser pulse—was less than with the other laser candidates. This shallow penetration depth—the ability to remove a sub-micron thickness of tissue—governs the precision of corneal laser surgery.

The precise physical mechanisms of corneal ablation are still under investigation and are the subject of some debate. It is known that the peptide bonds linking adjacent amino acids in the collagen molecules are strong absorbers of ultraviolet energy.[15] The general paradigm has been that cleaving of these chemical bonds by the laser radiation weakens the ablated region and thus leads to its decomposition. Because of this, ultraviolet ablation is often referred to as a photochemical process. Also, because relatively little thermal energy is imparted to the remaining tissue, the excimer laser is sometimes called a "cold" laser in the popular press. However, the ablation mechanism is complex and likely involves thermal (and other) processes as well.[16]

Although our understanding of ultraviolet laser ablation is still incomplete, an empirical picture of the ablation can be constructed. Because the optical absorption of cornea at 193 nm is large,[17] and the laser pulse is brief (approximately 15 nsec), the laser energy of a single pulse is deposited into a very small volume in a very brief time. The volumetric energy density can easily exceed a few kilojoules per cubic centimeter.[18] The result is a near-explosive expansion of the irradiated material producing an audible "pop." Velocities of the ejected material are initially very high (supersonic at some laser intensities), but the plume slows rapidly and takes on the appearance of a mini-mushroom cloud.[19] While the ablation plume is predominantly composed of water droplets,[20] recent studies indicate that particles—fragments of the collagen—may fall from the ablation cloud and redeposit in the crater.[21] This ablation debris may partially absorb subsequent laser pulses. The recoil from the ejected ablation products also induces an acoustic wave in the eye.[22] Despite early concerns, there seems to be little risk to the eye from these ablation-initiated pressure transients.

Ablation in practice

As we noted earlier, an attractive feature of the excimer laser, as it applies to corneal ablation, is its ability to precisely remove tissue with minimal damage to the remaining cornea. The amount of tissue removed with each laser pulse, the etch depth, is plotted in Figure 2 as a function of laser fluence. The data points represent values of etch depths reported in the literature for ablation of human corneas. Even though the data is somewhat noisy, a linear-fit, as indicated by the solid line, does a reasonably good job of describing the data. Clearly, the objective in any refractive surgery is to reshape the curvature of the cornea. In order to do this with a laser, there must be a way to precisely control the beam that is incident on the cornea. This may include regulating spatial size, shape, and position of the beam, as well as the number of pulses delivered. In the case of a myopic patient, the cornea needs to be slightly flattened to reduce the refractive power of the cornea and to place the image in focus on the retina. From the perspective of reshaping the cornea, more tissue needs to be removed from the center of the cornea than from the edge. A simple approach, as depicted in Figure 3, is to restrict the size of the laser beam with an automated iris diaphragm or a series of apertures, gradually enlarging the size of the beam as the laser is fired. In this manner, a new surface can be machined by the laser that approximates the desired spherical surface. This is the general concept at work in the first generation of lasers used to perform photorefractive keratectomy (PRK) to correct myopia.

Although the acronyms are somewhat alike, RK (radial kera*totomy*) and PRK (photorefractive kera*tectomy*) are actually quite different. In RK, the surgeon manually creates a radial pattern of relatively deep incisions in the cornea. In PRK, a relatively thin sliver of tissue is vaporized by a computer-controlled laser. The thickness of the tissue removed, the difference between the pre- and post-op surfaces in Figure 3 at the center, is approximately 10 μm per diopter (D) of correction. Thus for a person with –5 D myopia, PRK will reduce their central corneal thickness by about 10% (the thickness of a human cornea is typically ~500 μm).

Astigmatism can be corrected by applying the general idea shown in Figure 3, except that an expanding slit replaces the iris diaphragm. Again, the laser removes more tissue from the center than from the edge, but with cylindrical instead of circular symmetry. Consequently, the cylindrical lens nature of the astigmatism is eliminated. Of course, a means to align the axis of the slit with the axis of the patient's astigmatism is needed as well.

Treatment for hyperopia requires that the curvature of the cornea be steepened. Thus, more tissue needs to be removed from the periphery than from the center. This can be accomplished by inserting a variety of masks into the beam that convert the laser beam into annular rings of varying widths.

Glossary

Myopia: Near-sightedness.

Hyperopia: Far-sightedness.

Excimer laser: "Excimer" is derived from "excited dimer," an excited diatomic molecule; excimer lasers commonly refer to ultraviolet, rare-gas/halide lasers (*e.g.*, argon-fluoride/ArF).

Ablation: Laser vaporization of tissue; the mechanisms are varied and complex and depend upon wavelength, pulse length, and tissue type.

Photorefractive keratectomy (PRK): Reshaping the surface of the cornea by laser ablation to correct vision defects.

Laser (assisted) *In-situ* keratomileusis (LASIK): A flap of cornea is folded back prior to PRK-type treatment of the exposed corneal tissue.

In a typical PRK procedure, topical anesthetic eye drops are applied to the cornea. The surgeon then manually scrapes away the epithelium—the top layer of proliferative cells on the cornea—using a blade. The laser ablation is then performed on the exposed stromal layer of the cornea. While the epithelium regrows in a few days to a week, reaching a stable refraction may take a few months, as shown in Figure 4.[23] This plot shows the average refraction of 126 myopic patients from their preoperative condition (average myopia = –4.07 D) out to two years after PRK. This data shows no statistically significant shift or regression after the third month.

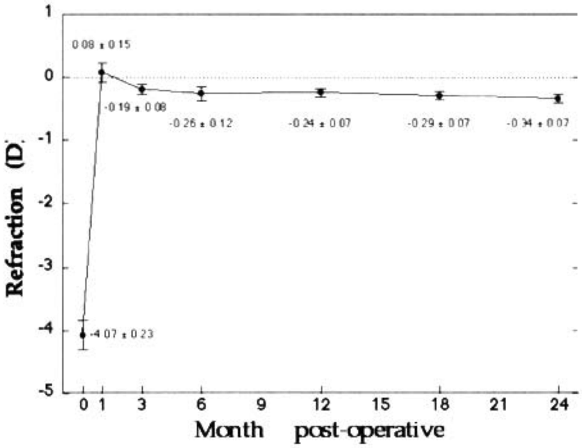

Figure 4. The average refraction of 126 myopic patients followed for two years after PRK.[23]

Status of PRK in the U.S.

There are currently two companies that have obtained FDA approval for their excimer laser devices for refractive surgery. In October 1995, Summit Technology received approval for its SVS Apex system. The following March (1996), the FDA approved the VISX Excimer Laser System. While specific indications for use were slightly different, the devices from both companies were approved for the treatment of mild to moderate myopia if the accompanying astigmatism is minimal.[24] Subsequently, in April 1997, a VISX system for treating myopia with astigmatism (PRKa) received FDA approval.[25] As of yet, no lasers have been approved for the treatment of hyperopia.

Future developments

Trying to predict the future is not without hazards. However, since the number of potential patients for this type of surgery is large, it's safe to assume that development and improvement of lasers for this type of surgery will continue. Besides the currently approved manufacturers, there are a number of other companies that are in various development and testing stages of their devices. Several of these devices use relatively small lasers with commensurately small beams that are opto-mechanically scanned over the eye. Naturally, a smaller laser head could reduce the bulk and cost of a laser system. Also, a scanned beam can machine irregular or asymmetric profiles with relative ease. Perhaps the most conspicuous current activity in refractive surgery is not in the development of new hardware but in how it is used, namely the LASIK technique.

In laser (assisted) *in situ* keratomileusis (LASIK), the surgeon cuts a cap of corneal tissue using a microkeratome. The cap is not completely cut away, but is left attached at one edge and is folded back like a flap. The thickness of the cap is approximately one-third the thickness of the cornea. The laser ablation is then applied to the revealed interior corneal tissue (the stromal bed) and then the flap is unfolded into its original position. One potential advantage of LASIK over PRK is that it may be effective for correcting higher degrees of myopia (up to –15 D). Also, patients treated with LASIK may experience less post-operative discomfort and may achieve refractive stability earlier. Various corneal implants and long-wear contact lenses are also being studied and may provide competition for laser-based treatments.

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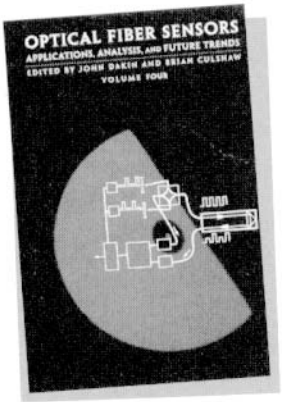

niques used for multiplexing several "point" fiber sensors, including time, frequency, code, wavelength, and coherence-based addressing techniques. The systems described include simple serial arrays of sensors based on OTDR processing concepts to more sophisticated interferometric fiber sensors;

- An overview on how optical fiber sensors will complement other new technologies; and
- A discussion on some optical fiber sensors that have matured since becoming commercially available, and also provides some market insight.

This volume doesn't cover current and voltage sensing, nor the important area of sensing in telecommunications—the principle of which was already described in volume two.

Overall, the authors present a very broad view of the application areas by introducing brief performance principles for each sector and combining detail device layouts. I found this book to be particularly interesting and a valuable reference on the subject, with an excellent overview of the state-of-the-art of fiber optical sensor technology.

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Editor's Note: Optical Sensors will be the focus of OSA's 1998 Annual Meeting in Baltimore, Md. Look also for a series of articles on optical sensors beginning in the January 1998 issue of OPN.

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