LASIK and Surface Ablation in the Modern Era: Trends and Novel Applications

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Abstract Refractive laser surgery has become one of the most successful and commonly performed elective ophthalmic procedures. Since the introduction of photorefractive keratectomy, followed closely by the advent of laser in situ keratomileusis, the field of laser refractive surgery has continued to rapidly evolve. Surgical techniques are constantly refined to improve patient outcomes and minimize complications, and technology continues to advance to provide more precise and customizable treatment options. New applications of refractive procedures continually emerge in the literature. Breakthroughs in the field have led to novel applications of refractive procedures that may offer options to patients that previously had been considered poor surgical candidates. It is important for the clinician to maintain awareness of the current trends and new developments in refractive surgery to provide appropriate counseling and treatment for their patients.

Keywords LASIK · Photorefractive keratectomy · Surface ablation · Treatment · Refractive error

Introduction

Permanent correction of myopic, hyperopic, and astigmatic refractive errors has long been a goal of ophthalmic care. Spectacles and contact lenses provide effective temporary correction. Both have functional limitations, such as problems encountered when engaging in sports, the inconvenience of carrying contact lens solutions and storage

containers, and the significant disability that results in the event of loss or damage to these vision aids. Contact lens use is not without danger and can lead to increased risk of vision-threatening corneal infections [1, 2]. The advent of refractive laser surgery has offered solutions for patients interested in decreasing dependence on glasses and contact lenses.

Laser refractive surgery was first introduced in the late 1980s with the development and refinement of the ophthalmic excimer laser [3, 4]. Photorefractive keratectomy (PRK) was the first laser technique used to treat myopia with a high degree of success [4]. In response to the perceived shortcomings of PRK, including post-operative pain and extended recovery time, laser in situ keratomileusis (LASIK) was introduced [5]. LASIK quickly increased in popularity and surpassed PRK as the predominant form of refractive surgery in the late 1990s, a trend that continues to this day [6]. Other forms of surface ablation have been developed in subsequent years, including laser-assisted subepithelial keratectomy (LASEK) and epipolis-LASIK (epi-LASIK) among other variations [7]. Each technique has its own advantages and disadvantages.

The goal of all laser refractive procedures is the correction of refractive errors, including myopia, hyperopia, and astigmatism. Myopia is the most common form of refractive error and is generally caused by either an increase in the eye's axial length or too much refractive power in the cornea and lens apparatus. The end result is light from the object of interest focused anterior to the retina. Hyperopia results from decreased axial length or too little refractive power, causing focus of light rays at a point posterior to the retina. Astigmatism is due to irregularity in the curvature of the cornea or lens and causes image blur. Refractive laser surgery utilizing surface ablation or LASIK seeks to correct these deficiencies by either flattening or steepening certain meridians of the cornea. Surface ablation techniques such as

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PRK utilize the excimer laser to remove portions of the surface of the cornea through a process called ablative photodecomposition, wherein high-energy photons from the laser break molecular bonds causing ejection of material [8]. The same process is used to reshape the cornea in LASIK, but ablation occurs deeper in the stroma after a flap creation and mobilization.

Both surface ablation and LASIK have a high degree of safety and efficacy, but few extensive randomized controlled studies have been conducted comparing their use [9, 10]. Accurate comparisons are often difficult because rapidly evolving technology and techniques create widespread fragmentation in performance of the procedures among practitioners. It is the objective of this review to provide an overview of recent literature comparing the safety and efficacy of LASIK and surface ablation techniques. It also seems appropriate to examine evolving technologies and surgical techniques along with novel applications and uses of refractive surgery.

Surface Ablation

Photorefractive Keratectomy (PRK)

Photorefractive keratectomy has the longest history and is for many the most familiar of the surface ablation procedures. In photorefractive keratectomy, mechanical removal of the corneal epithelium precedes ablation of Bowman's layer and the anterior corneal stroma using an excimer laser. Complications such as refractive regression and corneal haze are a consequence of epithelial and stromal regeneration [11, 12]. Indications for PRK include low to moderately high myopia and hyperopia with and without astigmatism. Due the rising popularity of LASIK, PRK is more often reserved for patients with thin corneas, irregular astigmatism, dry eye syndrome, or increased likelihood of eye trauma [13]. Absolute contraindications typically include unstable refraction, keratoconus, active infection, intraocular inflammation and uncontrolled glaucoma [14]. Unique to PRK are concerns about postoperative pain and slower visual recovery [9].

One of the most influential factors on the decreased utilization of PRK is concern for post-operative corneal haze. The introduction of mitomycin c (MMC) 0.2 % has gone a long way in alleviating this concern. MMC is a DNA-cross-linking agent that inhibits DNA synthesis and induces apoptosis. Originally introduced as a chemotherapy agent, its ophthalmic applications include glaucoma and refractive procedures. The proposed mechanism by which MMC reduces haze is inhibition of myofibroblast transformation [15]. A meta-analysis comparing surface ablation for myopia with mitomycin c 0.2 % and without

found significantly less haze in PRK patients treated with intraoperative MMC [16•]. Though MMC has been found to be effective in decreasing the incidence of corneal haze, optimal treatment protocols and long term safety still need to be addressed [17•].

LASEK

A drive for improvement in existing surface ablation techniques led to the development of laser subepithelial keratomileusis [18]. The technique uses dilute alcohol and a trephine to loosen and then remove a replaceable flap of epithelium. Ablation is performed and the flap is returned and centered over the cornea. In theory, the use of LASEK leads to less pain, less haze, and faster visual recovery when judged against traditional PRK [16]. The validity of these advantages has since been brought into question [19–22].

Epi-LASIK

Due to concerns about the toxicity of alcohol to the corneal endothelium, a hybrid technique called epithelial laser-assisted in situ keratomileusis was introduced by Pallikaris in 2003 [23]. It involves the use of an epikeratome to separate the epithelium from the underlying stroma and create a flap before ablation. Ideally, Epi-LASIK produces less pain, less endothelial toxicity, and increased protection of the underlying corneal stroma when the flap is replaced.

Laser In Situ Keratomileusis (LASIK)

Theorizing that many of the complications surrounding PRK had to do with destruction and consequent healing of corneal epithelium, the search for an alternative to surface ablation lead to the introduction of LASIK [3]. The primary difference between PRK and LASIK is the creation of a partial thickness lamellar corneal flap cut with a microkeratome or femtosecond laser. Traditionally, the depth of the cut has been down to mid-stroma below Bowman's layer with a thickness between 130 μ m and 160 μ m. The excimer laser is applied to the stroma after lifting the flap. The flap is then replaced and stabilizes due to natural adherence caused by endothelial pump dehydration. Although refractive regression can occur in a similar method to PRK, it is usually to a lesser extent [24]. LASIK trials began in the United States in 1996, and the procedure gained approval in 1999. Indications for LASIK include low to high myopia and hyperopia with and without astigmatism. Contraindications for the procedure are similar to PRK, with greater attention paid to corneal thickness, evidence of ectatic disease, and increased potential for eye trauma.

Femtosecond LASIK

When LASIK was first introduced, one of the most critical steps, flap creation, was performed with a mechanical microkeratome. More recently, femtosecond laser technology has become an increasingly popular alternative. A focused infrared laser delivers ultrafast pulses of 100-femtosecond duration, generating microplasma and forming microscopic gas bubbles to create a flap. The first femtosecond laser for refractive surgery was introduced in 2001. The growth in its use has led to the development of multiple laser platforms for LASIK flap creation. A meta-analysis by Chen et al. evaluated safety, efficacy, and predictability of the IntraLase (Abbott Medical Optics) versus the mechanical microkeratome in myopic LASIK. The authors found no significant differences in safety or efficacy between the two methods, but did find that the femtosecond laser produced a more predictable flap thickness than the microkeratome [25••].

LASIK versus Surface Ablation: Safety, Efficacy, Complications

One of the greatest difficulties in comparing surface ablation and LASIK arises from the constant of evolution of techniques and technology in the field of laser refractive surgery. Though there exist a plethora of studies comparing surface ablation and LASIK, there are a limited number of randomized controlled trials comparing these techniques. The utility of these available studies is limited by the use of older laser technologies and techniques.

A Cochrane review of visual outcomes and complications analyzed available randomized controlled trials comparing PRK and LASIK in the treatment of myopia and myopic astigmatism. The reviewers found that: (1) final uncorrected visual acuity was comparable between procedures, (2) visual recovery with LASIK was faster than PRK, (3) the accuracy of each procedure was comparable (no-differences in post-operative refractions), (4) the risk of loss of two or more lines of best corrected visual acuity in LASIK may be less than PRK [26]. Several studies have evaluated wavefront-guided ablations in LASIK and PRK. These studies again revealed faster visual recovery with LASIK than PRK, but at later follow up visits there were no significant differences in efficacy, safety, or predictability between LASIK and PRK [27–29].

A recent Cochrane review of visual outcomes and complications analyzed available randomized controlled trials comparing PRK and LASIK in the treatment of hyperopia and hyperopic astigmatism [10]. The authors found no randomized clinical trials for analysis. Analysis of the excluded studies revealed a general agreement that PRK and LASIK

had similar efficacy, safety, and stability of post-operative refractions but concluded additional well-planned, large, high-quality randomized controlled trials were needed.

New Developments and Novel Applications

Wavefront-Guided and Wavefront-Optimized Laser Refractive Surgery

The introduction of wavefront technology has enabled refractive surgeons to address not only lower-order aberrations (sphere and cylinder) but also higher-order aberrations (coma, trefoil, spherical aberration). In a normal eye, higher-order aberrations have minimal impact on the quality of vision. However, in special cases (such as after refractive surgery) higher-order aberrations can significantly alter visual quality. Wavefront sensors allow evaluation of the scattering of light rays as they pass from the fovea outward through the cornea and crystalline lens or from a distant point source of light inward through the optical elements of the eye [30]. Wavefront-guided ablations attempt to decrease the induction of additional wavefront errors, resulting in a potential increase in contrast sensitivity compared to conventional treatments [31, 32]. Wavefront-optimized ablations attempt to minimize the induction of higher-order aberrations, specifically spherical aberration, by maintaining a more prolate corneal shape with an aspheric ablation profile [33•]. Further investigations are necessary to determine the overall effect of correcting higher-order aberrations on visual quality and criteria for selection of patients who would most benefit from such treatments.

Corneal Collagen Cross-Linking

Corneal collagen cross-linking (CXL) has recently been proposed as a treatment for patients with keratoconus and as a method to stabilize the cornea in refractive surgery. CXL is based on the theory that exposing materials and chemicals to UV light can often strengthen them through the induction of cross-linking [34]. The exact mechanism by which the cross-linking and subsequent strengthening of the cornea is not well understood; it appears to be facilitated, at least to some extent, by oxidative mechanisms associated with hydroxyl radical release. It is interesting to note that a similar process using glycosylation-mediated cross-linking occurs naturally with aging and in individuals diagnosed with diabetes [35, 36]. Researchers at the Technical University of Dresden in Germany developed the first procedure using riboflavin and 370-nm UVA irradiation to induce cross-linking in the stroma of corneas [37].

Collagen cross-linking treatment of the cornea is performed after mechanical epithelial debridement so that the

riboflavin is able to penetrate the stroma to an acceptable depth [38]. The riboflavin is important not only to help modify the collagen, but also to protect the sensitive endothelial cells at the back of the cornea from damaging UVA radiation [39]. Preoperative topical anesthetic is applied and followed by the instillation of 0.1 % riboflavin solution every 2–5 min for 30 min. Depth of penetration is verified, and an area 9.0 mm in diameter at the center of the cornea is irradiated with 370 nm wavelength UVA light for 30 min, while riboflavin continues to be administered every 2–3 min. Postoperative treatment includes topical steroids, antibiotic drops, and a bandage contact lens application [40].

Recent interest is directed at modifying and improving upon the methods mentioned above. Protocols in which the epithelial layer is left intact are attracting great interest, since this would hopefully facilitate a faster recovery, reduce pain, and decrease chances for infection and corneal haze [41, 42]. A recent case study and case series have been conducted testing the effectiveness of CXL combined with topography-guided PRK on patients with post-LASIK keratectasia, with mostly positive results that seem to demonstrate a halting or even reversal of the disease process [43, 44]. A different trial studied 20 eyes treated with CXL after diagnosis of post-LASIK corneal ectasia [45]. The patients were followed at intervals for 1 year, and the study concluded that CXL does show long-term stability of LASIK-related ectasia with very few side effects.

Work is also being done by Kanellopoulos to look at the effect of prophylactic CXL treatment conducted at the same time as LASIK in high-myopic eyes [46]. The 23 patients in this study have shown stable visual acuity and no signs of ectasia at a mean follow up of 3.5 years. At the same time, it was noted in a recent review by Suri [40] that CXL is not without possible adverse effects including corneal haze, keratitis, loss of visual acuity, and most importantly endothelial damage. Recent case reports have reinforced these concerns with links between CXL and endothelial failure and corneal edema [47, 48].

Given the novel nature of this process and the difficulty of judging the effectiveness by means other than clinical progression, a method to directly measure the physical changes on the cornea would be very useful. Researchers in France have used supersonic shear wave imaging in ex vivo and in vivo porcine eyes to measure corneal stiffness after treatment with CXL [49]. The results thus far are promising and could provide a way to not only monitor the effect of CXL but also give important information preoperatively for refractive procedures in general. Another technology that shows promise in gauging the effect of CXL on corneal biomechanics is the ocular response analyzer (Reichert Inc.)

The ocular response analyzer measures several biomechanical properties of the cornea including corneal

hysteresis (CR) and corneal resistance factor (CRF). Studies attempting to gauge the effects of CXL on CH and CRF have been inconclusive, but further investigations are necessary [50, 51].

Corneal collagen cross-linking continues to be an exciting area of both research and development, with much work being done domestically and internationally to refine and test its use. It may eventually not only offer a therapy for post-LASIK ectasia, but may also broaden the patient base that is currently ineligible for refractive surgery due to thin corneas.

Pediatrics

Traditionally, pediatric patients are thought of as poor candidates for refractive surgery. Not only do many of them require general anesthetic for the procedure, but the outcomes are greatly influenced by difficulty with follow-up care and natural changes in refractive error with growth and development [52]. The majority of children are effectively treated with spectacles or contact lenses when severe anisometropia or isoametropia threatens to cause refractive amblyopia. These methods of treatment are not always possible though, especially when patients suffer from social or behavioral complications. When all other options have been exhausted, refractive surgery may be the only solution.

In a recent article published in the Journal of American Association for Pediatric Ophthalmology and Strabismus, Dr. Paysse [53] and his colleagues offer an excellent overview of recent advances in pediatric refractive surgery, indications, and treatment protocols. The three groups that they single out as special candidates for treatment include children with severe isoametropia and neurobehavioral problems that result in intolerance to traditional care, children with significant anisometropia who are also non-compliant, and finally children with either of the previous disorders whose anatomical abnormalities prevent correction with spectacles or contact lenses. Despite the results of several literature reviews indicating relatively little difference in the effectiveness between surface ablation and LASIK [52, 54, 55, 56], Paysse indicates a preference for PRK due to its “lower risk profile.” It makes sense that in young children there would be an increased theoretical risk of flap complications due to eye rubbing and trauma. Paysse also believes that the corneal haze previously reported as the main complication of refractive surgery can be managed with proper follow-up care [57].

It is interesting to consider that research now being done on adults to utilize the novel advantages of corneal cross-linking might someday be used to help stabilize refractive surgery done on children. Work that has been done using CXL in patients with keratoconus seems to support this

idea since younger patients, including those of pediatric age, had a better “functional response” [58]. Controversies involving which method of refractive surgery is best along with how early these treatments should be initiated certainly demands more long term prospective multicenter studies. The exciting aspect of this work with children is that the improvement of visual acuity has far reaching effects on both social and intellectual development.

Pregnancy

A well-known consequence of pregnancy is the myriad of physiological alterations that occur throughout the body, including changes to the eyes. These changes have been well documented and include refractive fluctuations, contact lens intolerance, and deterioration of chronic eye conditions such as diabetic retinopathy [59, 60]. Increased corneal haze and myopic regression have been reported in patients who have recently undergone PRK [61]. Recent work has demonstrated significant changes in the cylinder and spherical equivalents in women through their first two trimesters of pregnancy [62]. This research group then went on to theorize that the hormonally caused changes may biomechanically weaken the LASIK-treated cornea, leading to refractive regression. Cases of post-LASIK ectasia exacerbated or caused by pregnancy have also been reported [63, 64]. It is therefore strongly recommend that patients who may become pregnant are well informed about the effect it might have on their surgery and are encouraged to wait several months after pregnancy before considering refractive treatment.

Laser Refractive Surgery Following Corneal Transplantation

Penetrating Keratoplasty (PKP)

Penetrating keratoplasty involves the replacement of the host cornea with a full-thickness donor. Due to the nature of the procedure, unpredictable refractive results are common. High spherocylindrical refractive errors commonly result in significant ametropia and aniseikonia. Though some patients are able to tolerate hard contact lenses and glasses, in many cases a more definitive and permanent solution is desired.

The role of PRK and LASIK in the treatment of refractive errors following PKP has been evaluated. There have been reports of increased incidence of stromal haze, unpredictable refractive results, and photoablation-induced graft rejection with PRK [65–69]. Recent interest has focused on the role of LASIK in the management of refractive errors in the PKP patient.

Descemet Stripping Automated Endothelial Keratoplasty (DSEK/DSAEK)

Descemet stripping automated endothelial keratoplasty has become the treatment of choice for corneal endothelial diseases. The procedure allows the selective replacement of diseased host epithelium and provides more rapid visual rehabilitation, minimizes surgically induced astigmatism, allows for greater structural integrity, and more predictable refractive outcomes when compared to traditional penetrating keratoplasty [70–72].

The addition of a lamellar graft to the posterior surface of the cornea has been shown to affect optical characteristics post-operatively, resulting in significant hyperopic shift. Following in the footsteps of surgeons who utilized refractive laser surgery for the treatment of refractive error in PK patients, clinicians have employed LASIK in the treatment of hyperopic shift following DSAEK [73–76]. A study by Ratanasit and Gorovoy evaluated outcomes of LASIK and PRK in 5 pseudophakic patients following DSEK [77]. All patients experienced an improvement in uncorrected visual acuity following laser refractive surgery without complications. Fung et al. reported a case of femtosecond LASIK in the treatment of hyperopia subsequent to DSAEK in a 66-year-old female. Uncorrected visual acuity (UCVA) improved from 20/120 prior to wavefront guided LASIK to UCVA of 20/20 post procedure.

Though these findings are promising, care should continue to be exercised in the selection of patients for refractive laser surgery following DSAEK. Screening these patients for ectasia and determining safety may be confused by decreased reliability in the measurement of corneal parameters following DSAEK. Cornea thickness may be affected by variable graft thickness due to preparation techniques, a non-uniform thickness gradient from graft center to periphery, decentration of the lenticule during cutting, and failure to center the graft on the visual axis [78]. These factors may limit evaluation to the anterior corneal surface which may be insufficient to rule out potential risk for ectasia.

Conclusions

The field of laser refractive surgery continues to develop at a rapid pace. The last decade has witnessed the introduction of the femtosecond laser, wavefront-guided ablation, and mitomycin c, among others. Millions of individuals have enjoyed decreased dependence on glasses and contacts lenses as a result of surface ablation and LASIK procedures. New techniques and technologies will continue to drive advances, resulting in safer and more effective procedures, and opening these treatments to patient populations

previously deemed ineligible. Laser refractive procedures are already being implemented in the treatment of keratoconus, following endothelial and penetrating keratoplasty, and even in the pediatric population. As technologies and techniques continue to improve, laser refractive surgery will see even wider implementation to meet the broad range of visual requirements specific to individual patients.

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References

Papers of particular interest, published recently, have been highlighted as:

- Of importance
- Of major importance

1. Buehler PO, Schein OD, Stamler JF, et al. The increased risk of ulcerative keratitis among disposable soft contact lens users. *Arch Ophthalmol*. 1992;110(11):1555–8.
2. Mah-Sadorra JH, Yavuz SG, Najjar DM, Laibson PR, Rapuano CJ, Cohen EJ. Trends in contact lens-related corneal ulcers. *Cornea*. 2005;24(1):51–8.
3. Trokel SL, Srinivasan R, Braren B. Excimer laser surgery of the cornea. *Am J Ophthalmol*. 1983;96:710–5.
4. Munnerlyn CR, Koons SJ, Marshall J. Photorefractive keratectomy: a technique for laser refractive surgery. *J Cataract Refract Surg*. 1988;14:46–52.
5. Pallikaris IG, Papatzanaki ME, Stathi EZ, Frenschok O, Georgiadis A. Laser in situ keratomileusis. *Lasers Surg Med*. 1990;10:463–8.
6. Duffey RJ, Leaming D. Trends in refractive surgery in the United States. *J Cataract Refract Surg*. 2004;30(8):1781–5.
7. Kieval JZ. Techniques in surface ablation: a comparison of visual outcomes and complications. *Int Ophthalmol Clin*. 2011;51(2):1–10.
8. Pellin MJ, Williams GA, Young CE, Gruen DM, Peters MA. Endoexcimer laser intraocular ablative photodecomposition. *Am J Ophthalmol*. 1985;99:483–4.
9. Shortt AJ, Allan BD. Photorefractive keratectomy (PRK) versus laser-assisted in situ keratomileusis (LASIK) for myopia. *Cochrane Database Syst Rev*. 2006;19(2):CD005135.
10. Settas G, Settas C, Minos E, Yeung IY. Photorefractive keratectomy (PRK) versus laser assisted in situ keratomileusis (LASIK) for hyperopia correction. *Cochrane Database Syst Rev*. 2012;6:CD007112.
11. Marshall J, Trokel SL, Rothery S, Krueger RR. Long-term healing of the central cornea after photorefractive keratectomy using an excimer laser. *Ophthalmology*. 1988;95:1411–21.
12. Moller-Pedersen T, Cavanagh HD, Petroll WM, Jester JV. Stromal wound healing explains refractive instability and haze development after photorefractive keratectomy: a 1-year confocal microscopic study. *Ophthalmology*. 2000;107(7):1235–45.
13. Taneri S, Weisberg M, Azar DT. Surface ablation techniques. *J Cataract Refract Surg*. 2011;37(2):392–408.
14. Bastawrous A, Silvestro A, Batterbury M. Laser refractive eye surgery. *BMJ*. 2011;342:d2345.
15. Kim TI, Tchah H, Lee SA, Sung K, Cho BJ, Kook MS. Apoptosis in keratocytes caused by mitomycin C. *Invest Ophthalmol Vis Sci*. 2003;44(5):1912–7.
16. •• Chen SH, Feng YF, Stojanovic A, Wang QM. Meta-analysis of clinical outcomes comparing surface ablation for correction of myopia with and without 0.02% mitomycin C. *J Refract Surg*. 2011;27(7):530–4. *A recent meta-analysis comparing outcomes of surface ablation for myopia with and without mitomycin-C found decreased haze and improved visual acuity with topical application of mitomycin-C during surgery.*
17. • Santhiago MR, Netto MV, Wilson SE. Mitomycin C: biological effects and use in refractive surgery. *Cornea*. 2012;31(3):311–21. *This is a detailed review of the safety and efficacy of mitomycin C and its role in refractive surgery procedures.*
18. Azar DT, Ang RT, Lee JB, et al. Laser subepithelial keratomileusis: electron microscopy and visual outcomes of flap photorefractive keratectomy. *Curr Opin Ophthalmol*. 2001;12:323–8.
19. Lee JB, Seong GJ, Lee JH, Seo KY, Lee YG, Kim EK. Comparison of laser epithelial keratomileusis and photorefractive keratectomy for low to moderate myopia. *J Cataract Refract Surg*. 2001;27(4):565–70.
20. Litwak S, Zadok D, Garcia-de Quevedo V, Robledo N, Chayet AS. Laser-assisted subepithelial keratectomy versus photorefractive keratectomy for the correction of myopia. A prospective comparative study. *J Cataract Refract Surg*. 2002;28(8):1330–3.
21. Zhao LQ, Wei RL, Cheng JW, Li Y, Cai JP, Ma XY. Meta-analysis: clinical outcomes of laser-assisted subepithelial keratectomy and photorefractive keratectomy in myopia. *Ophthalmology*. 2010;117(10):1912–22.
22. Ghanem VC, Kara-Jose N, Ghanem RC, Coral SA. Photorefractive keratectomy and butterfly laser epithelial keratomileusis: a prospective, contralateral study. *J Refract Surg*. 2008;24:671–84.
23. Pallikaris IG, Katsanevaki VJ, Kalyvianaki MI, Naoumidi II. Advances in subepithelial excimer refractive surgery techniques: epi-LASIK. *Curr Opin Ophthalmol*. 2003;14:207–12.
24. Chayet AS, Assil KK, Montes M, Espinosa-Lagana M, Castellanos A, Tsioulas G. Regression and its mechanisms after laser in situ keratomileusis in moderate and high myopia. *Ophthalmology*. 1998;105(7):1194–9.
25. •• Chen S, Feng Y, Stojanovic A, Mirko R, Jankov M. IntraLase Femtosecond Laser vs Mechanical Microkeratomes in LASIK for Myopia: A Systematic Review and Meta-analysis. *J Refractive Surg*. 2012;28(1):15–24. *A recent meta-analysis comparing femtosecond laser created flaps versus microkeratome flaps showed no significant differences in safety or efficacy but did suggest a potential advantage in predictability with laser created flaps.*
26. Shortt AJ, Allan BD. Photorefractive keratectomy (PRK) versus laser-assisted in situ keratomileusis (LASIK) for myopia. *Cochrane Database Syst Rev*. 2006;2:CD005135.
27. Manchee EE, Haw WW. Wavefront-guided laser in situ keratomileusis (LASIK) versus wavefront-guided photorefractive keratectomy (PRK): a prospective randomized eye-to-eye comparison (an American Ophthalmological Society thesis). *Trans Am Ophthalmol Soc*. 2011;109:201–20.
28. Randleman JB, Perez-Stratziota CE, Hu MH, White AJ, Loft ES, Stulting RD. Higher-order aberrations after wavefront-optimized photorefractive keratectomy and laser in situ keratomileusis. *J Cataract Refract Surg*. 2009;35(2):260–4.
29. Moshirfar M, Schliesser JA, Chang JC, Oberg TJ, Mifflin MD, Townley R, Livingston CJ, Kurz MK. Visual outcomes after wavefront-guided photorefractive keratectomy and wavefront-guided laser in situ keratomileusis: prospective comparison. *J Cataract Refract Surg*. 2010;36(8):1336–43.
30. Feng Y, Yu J, Wang Q. Meta-analysis of wavefront-guided vs. wavefront-optimized LASIK for myopia. *Optom Vis Sci*. 2011;88(12):1463–9.
31. Maeda N. Clinical applications of wavefront aberrometry—a review. *Clin Exp Ophthalmol*. 2009;37:118–29.

32. Lee HK, Choe CM, Ma KT, Kim EK. Measurement of contrast sensitivity and glare under mesopic and photopic conditions following wavefront-guided and conventional LASIK surgery. *J Refract Surg.* 2006;22:647–55.
33. • Mello GR, Rocha KM, Santhiago MR, Smadja D, Krueger RR. Applications of wavefront technology. *J Cataract Refract Surg* 2012 Sep;38(9):1671–83. *This article reviews the basic principles of the optics of the eye, the effects of optical aberrations on visual acuity, the operation of wavefront sensors, and the applications of wavefront technology in refractive surgery.*
34. Dahl BJ, Spotts E, Truong JQ. Corneal collagen cross-linking: an introduction and literature review. *Optometry.* 2012;83(1):33–42.
35. Daxer A, Misof K, Grabner B, Ettl A, Fratzl P. Collagen fibrils in the human corneal stroma: structure and aging. *Invest Ophthalmol Vis Sci.* 1998;39:644–8.
36. Sady C, Khosrof S, Nagaraj R. Advanced Maillard reaction and crosslinking of corneal collagen in diabetes. *Biochem Biophys Res Commun.* 1995;214(3):793–7.
37. Seiler T, Hafezi F. Corneal cross-linking-induced stromal demarcation line. *Cornea.* 2006;25(9):1057–9.
38. Goldich Y, Marcovich AL, Barkana Y, Avni I, Zadok D. Safety of corneal collagen cross-linking with UV-A and riboflavin in progressive keratoconus. *Cornea.* 2010;29:409–11.
39. Spoerl E, Mrochen M, Sliney D, Trokel S, Seiler T. Safety of UVA-riboflavin cross-linking of the cornea. *Cornea.* 2007;26(4):385–9.
40. Suri K, Hammersmith KM, Nagra PK. Corneal collagen cross-linking: ectasia and beyond. *Curr Opin Ophthalmol.* 2012;23:280–7.
41. Filippello M, Stagni E, O'Brart D. Transepithelial corneal collagen crosslinking: bilateral study. *J Cataract Refract Surg.* 2012;38(8):283–91.
42. Stojanovic A, Chen X, Jin N, Zhang T, Stojanovic F, Raeder S, Utheim TP. Safety and efficacy of epithelium-on corneal collagen cross-linking using a multifactorial approach to achieve proper stromal riboflavin saturation. *J Ophthalmol.* 2012;2012:498435.
43. Kymionis GD, Portaliou DM, Diakonis VF, et al. Management of post laser in situ keratomileusis ectasia with simultaneous topography guided photorefractive keratectomy and collagen cross-linking. *Open Ophthalmol J.* 2011;5:11–3.
44. Kanellopoulos AJ, Binder PS. Management of corneal ectasia after LASIK with combined, same-day, topography-guided partial transepithelial PRK and collagen cross-linking: the athens protocol. *J Refract Surg.* 2011;27:323–31.
45. Li G, Fan ZJ, Peng XJ. Corneal collagen crosslinking for corneal ectasia of post-LASIK: one-year results. *Int J Ophthalmol.* 2012;5(2):190–5.
46. Kanellopoulos AJ. Long-term safety and efficacy follow-up of prophylactic higher fluence collagen cross-linking in high myopic laser-assisted in situ keratomileusis. *Clin Ophthalmol.* 2012;6:1125–30.
47. Bagga B, Pahuja S, Murthy S, Sangwan VS. Endothelial failure after collagen cross-linking with riboflavin and UV-A: case report with literature review. *Cornea.* 2012;31(10):1197–200.
48. Sharma A, Nottage JM, Mirchia K, Sharma R, Mohan K, Nirankari VS. Persistent corneal edema after collagen cross-linking for keratoconus. *Am J Ophthalmol.* 2012;154(6):922–926.e1.
49. Nguyen TM, Aubry JF, Touboul D, Fink M, Gennisson JL, Bercoff J, Tanter M. Monitoring of cornea elastic properties changes during UV-A/Riboflavin-induced corneal collagen cross-linking using supersonic shear wave imaging: a pilot study. *Invest Ophthalmol Vis Sci.* 2012;53(9):5948–54.
50. Sedaghat M, Naderi M, Zarei-Ghanavati M. Biomechanical parameters of the cornea after collagen crosslinking measured by waveform analysis. *J Cataract Refract Surg.* 2010;36(10):1728–31.
51. Goldich Y, Marcovich AL, Barkana Y, Mandel Y, Hirsh A, Morad Y, Avni I, Zadok D. Clinical and corneal biomechanical changes after collagen cross-linking with riboflavin and UV irradiation in patients with progressive keratoconus: results after 2 years of follow-up. *Cornea.* 2012;31(6):609–14.
52. Daoud YJ, Hutchinson A, Wallace DK, Song J, Kim T. Refractive surgery in children: treatment options, outcomes, and controversies. *Am J Ophthalmol.* 2009;147(4):573–582 e2.
53. Paysse EA, Tychsen L, Stahl E. Pediatric refractive surgery: corneal and intraocular techniques and beyond. *J AAPOS.* 2012;16(3):291–7.
54. •• Alio JL, Wolter NV, Pinero DP, et al. Pediatric refractive surgery and its role in the treatment of amblyopia: meta-analysis of the peer-reviewed literature. *J Refract Surg* 2011;27:364–74. *This is a recent meta-analysis of visual outcomes following pediatric refractive surgery for anisometropic amblyopia.*
55. Qian Y, Pineda R. Safety and efficacy of PRK and LASIK in pediatric patients. *Int Ophthalmol Clin.* 2008;48(2):193–208.
56. Song J, Al-Ghamdi I, Awad A. Pediatric refractive surgery in evolution. *Middle East Afr J Ophthalmol.* 2012;19(1):22–3.
57. Astle WF, Fawcett SL, Huang PT, Alewenah O, Ingram A. Long-term outcomes of photorefractive keratectomy and laser-assisted subepithelial keratectomy in children. *J Cataract Refract Surg.* 2008;34(3):411–6.
58. Caporossi A, Mazzotta C, Baiocchi S, Caporossi T, Denaro R, Balestrazzi A. Riboflavin-UVA-induced corneal collagen cross-linking in pediatric patients. *Cornea.* 2012;31:227–31.
59. Ness T, Paulus W. Eye and pregnancy. *Ophthalmologe.* 2010;107:863–72.
60. Dinn RB, Harris A, Marcus PS. Ocular changes in pregnancy. *Obstet Gynecol Surv.* 2003;58:137–44.
61. Hafezi F, Iseli HP. Pregnancy-related exacerbation of iatrogenic keratectasia despite corneal collagen crosslinking. *J Cataract Refract Surg.* 2008;34(7):1219–21.
62. Lopez-Prats MJ, Hidalgo-Mora JJ, Sanz-Marco E, Pellicer A, Perales A, Diaz-Llopis M. Influence of pregnancy on refractive parameters after LASIK surgery. *Arch Soc Esp Oftalmol.* 2012;87(6):173–8.
63. Padmanabhan P, Radhakrishnan A, Natarajan R. Pregnancy-triggered iatrogenic (post-laser in situ keratomileusis) corneal ectasia—a case report. *Cornea.* 2010;29:569–72.
64. Hafezi F, Koller T, Derhartunian V, Seiler T. Pregnancy may trigger late onset of keratectasia after LASIK. *J Refract Surg.* 2012;28:242–3.
65. Chan WK, Hunt KE, Glasgow BJ, Mondino BJ. Corneal scarring after photorefractive keratectomy in a penetrating keratoplasty. *Am J Ophthalmol.* 1996;121:570–1.
66. Yoshida K, Tazawa Y, Demong TT. Refractive results of post penetrating keratoplasty photorefractive keratectomy. *Ophthalmic Surg Lasers.* 1999;30:354–9.
67. Bansal AK. Photo astigmatic refractive keratectomy for correction of astigmatism after keratoplasty. *J Refract Surg.* 1999;15:S243–5.
68. Fraenkel G, Sutton G, Rogers C, Lawless M. Paradoxical response to photorefractive treatment for post-keratoplasty astigmatism. *J Cataract Refract Surg.* 1998;24:861–5.
69. Leccisotti A. Photorefractive keratectomy with mitomycin C after deep anterior lamellar keratoplasty for keratoconus. *Cornea.* 2008;27:417–20.
70. Lee WB, Jacobs DS, Musch DC, et al. Descemet's stripping endothelial keratoplasty: safety and outcomes. *Ophthalmology.* 2009;116:1818–30.
71. Ghaznawi N, Chen ES. Descemet's stripping automated endothelial keratoplasty: innovations in surgical technique. *Curr Opin Ophthalmol.* 2010;21:283–7.

72. Ratanasit A, Gorovoy MS. Long-term results of Descemet stripping automated endothelial keratoplasty. *Cornea*. 2011;30:1414–8.
73. Ghaznawi N, Chen ES. Descemet's stripping automated endothelial keratoplasty: innovations in surgical technique. *Curr Opin Ophthalmol*. 2010;21:283–7.
74. Van der Meulen IJ, Patel SV, Lapid-Gortzak R, et al. Quality of vision in patients with Fuchs endothelial dystrophy and after Descemet stripping endothelial keratoplasty. *Arch Ophthalmol*. 2011;129:1537–42.
75. Price MO, Price FW. Descemet's stripping endothelial keratoplasty. *Curr Opin Ophthalmol*. 2007;18:290–4.
76. Yamaguchi T, Negishi K, Yamaguchi K, et al. Comparison of anterior and posterior corneal surface irregularity in Descemet stripping automated endothelial keratoplasty and penetrating keratoplasty. *Cornea*. 2010;29:1086–90.
77. Ratanasit A, Gorovoy MS. Laser-assisted in situ keratomileusis or photorefractivekeratectomy after Descemet stripping automated endothelial keratoplasty. *Cornea*. 2011;30:787–9.
78. Price FW, Price MO, Guerra F. Is excimer laser corneal surgery appropriate after resolution of corneal edema in fuchs dystrophy by descemet membrane endothelial keratoplasty. *J Refractive Surgery* 2011; 27(4):299–302.