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Striving for Perfect Vision: Insights from Refractive Surgery

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Overview

Refractive surgery involves the surgical correction of the refractive errors of the eye such as myopia, hyperopia, astigmatism, presbyopia, and cataracts. As one of the rapidly evolving fields in ophthalmology, it has come along a long way since 1948 when Father Waclaw Szuniewicz pioneered the concept of refractive surgery by experimenting to change the shape of the corneal curvature. Today, femtosecond lasers have revolutionized the surgical procedure by providing precision, safety, and reproducibility like never before. The major milestones of refractive surgery include the introduction of keratomileusis in 1964, the invention of radial keratotomy in 1970, the invention of the excimer laser between 1973 and 1983, the first excimer laser use for corneal ablation in 1987, the first LASIK use in the 1990s, the approval of PRK and LASIK by the FDA in 1995 and 1996, respectively, the approval of wavefront technology in 2003, and the evolution of the femtosecond laser for refractive surgery in 2001 [1].

Optics

The human eye as an optical system is very similar to a camera, where the cornea (diameter:12 mm, central thickness: 0.55 mm, refractive index: 1.3771) and lens (actively accommodating) refract light. However, the eye is a much simpler optical instrument compared to many artificial optical instruments in terms of its design and complexity. Only two positive lenses, the cornea and the crystalline lens, comprise the optical instrument of the eye, and these initiate the visual process by projecting the images into the retina. Still, the usual field of the view of the eye is relatively large as compared to most optical instruments, at least 160 × 130° [2]. The wave-like nature of light governs the quality of the retinal images under most normal viewing conditions. Wavefront aberration and point-spread function (PSF, the image of a point source) are used to describe the optical quality under such conditions. To form a perfect retinal image, the wavefront aberrations would have to be null or constant; an eye without any aberrations would do just that, where the retinal image would depend only on the pupil diameter [2]. In conditions of very low luminance after dark adaptations, the particle nature of light plays a role in the

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vision. In these conditions, photoreceptors absorb photons in discrete quanta, the probability of a photon being absorbed imposes a fundamental limit to the vision related to the photon statistics.

Wound Healing

The cornea accounts for approximately 70% of its refractive power; hence, the way a cornea heals after keratorefractive surgery is of paramount interest and importance. The healing process of the corneal wound affects the efficacy and the safety of the refractive procedure. Corneal wound healing involves complex and coordinated cascades of molecular and cellular pathways, involving cytokines and growth factors that result in a highly variable biologic response. Epithelial, stromal, and endothelial cells are the three main types of cells involved in corneal wound healing. Epithelial and stromal cells interact with each other during wound healing, while endothelial cells are relatively less affected. Roughly, the wound healing process follows inflammation (latent phase), myofibroblast differentiation (migration), extracellular matrix (ECM) deposition (proliferation), and fibrosis development (epithelial reattachment) (Fig. 14.1) [3].

Epithelial Wound Healing

Epithelial wound healing involves limbal stem cells and their progeny under the action of growth factors and cytokines from tears and cells, as well as the basement membrane proteolytic remodeling, with no actual cell transformation [4]. The therapies to facilitate epithelial wound healing include limbal stem cell transplantation, gene therapy, miRNA, and nanocarriers. Limbal stem cell transplantation significantly improves corneal reepithelialization. Gene therapy, miRNA, and nanocarriers are emerging therapies. The miRNAs are considered to play important roles in many phases of corneal epithelial wound healing, with some miRNAs promoting and others inhibiting healing [5–9]. The inhibitors of miRNA (antagomir), specifically miR-146a, have been reported to enhance wound healing in human diabetic organ-cultured corneas [8]. Further investigations of the miRNA targets and affected pathways are still needed to understand normal epithelial healing, and its dysregulation in chronic wounds and diseased corneas. Gene therapy has a good potential for normalizing epithelial wound healing. Viral- and nanocarrier-based gene therapies are the two kinds of available gene therapies. Viral-based therapies (recombinant adenoviruses, rAV; adeno-associated viruses, rAAV; and lentiviruses) have been successfully used to deliver specific genes into the cornea to produce high-level expression of the target gene rapidly. The viral vectors are chosen depending upon the desired level of expression and desired target cell; rAV transduction has been reported to produce considerably higher expression of the green fluorescent protein (GFP) reporter than with rAAV transduction [10]; however, the transduction appears to reach only the epithelial and endothelial cells. rAAV transduction is seen on all layers of corneal cells: the epithelial, stromal, and endothelial cells [11]. Nanocarrier-based therapies include metal-, lipid-, and polymer-based systems, and they allow several different plasmids to combine in one particle to increase the desired gene expression [12] and effective drug delivery [13]. Nanoparticles coated with all-trans retinoic acid, lactide-co-glycolide and loaded with antifibrotic drug pirfenidone, and elastin-like polypeptides loaded with mitogenic protein lacritin, have been reported to promote corneal epithelial wound healing [14–15].

Stromal Wound Healing

Stromal wound healing involves keratocyte transformation from inactive keratocytes into activated fibroblasts and subsequently into myofibroblasts. The myofibroblasts, expressing α-SMA, contribute to wound contraction. The keratocyte transformation is influenced by cytokines and growth factors derived from the epithelial cells, immigrating immune cells, and stromal cells themselves [4]. The process of wound healing after refractive surgery involves epithelial-mesenchymal interactions, stepwise transformation of corneal cells during healing, and the involvement of TGF-β signaling. Antifibrotic agents appear to be promising

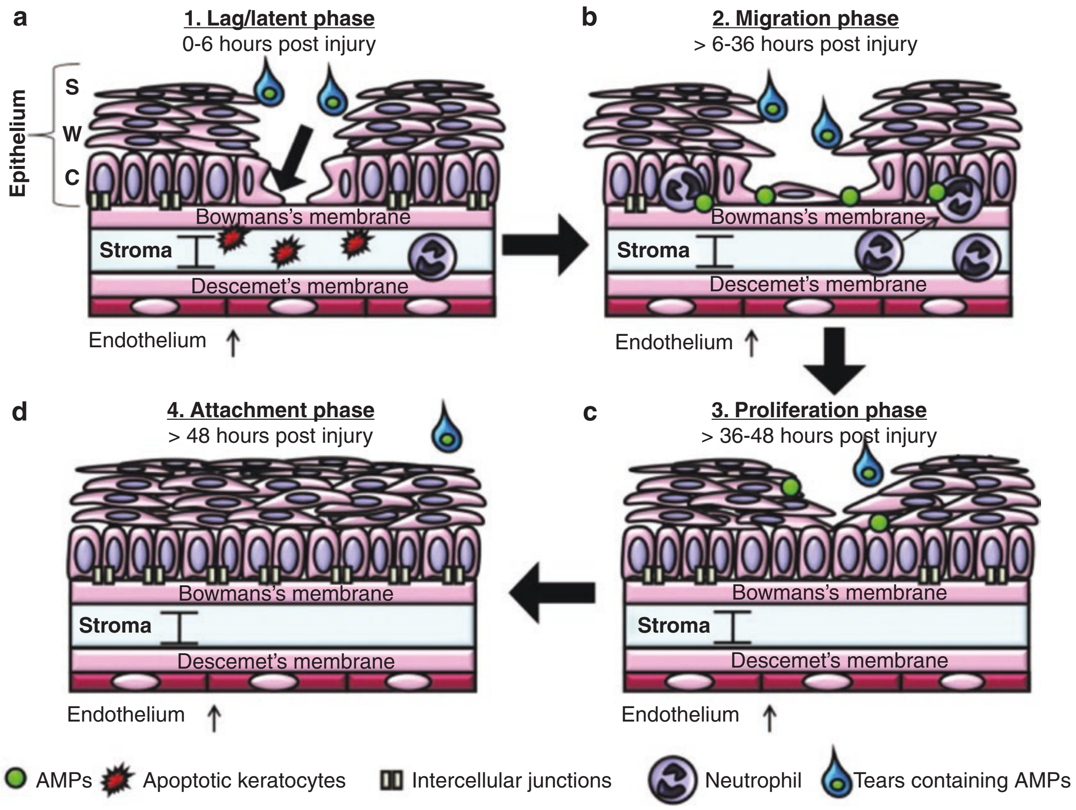

Fig. 14.1 Four main stages of corneal epithelial wound healing. Corneal epithelial wound healing can be described to occur in four main phases (**a**–**d**). The initial lag or latent phase (**a**) of the wound-healing process takes place during the first 6 h after injury. The lag or latent phase can be marked with a reduction in the number of intercellular junctions, the apoptosis of anterior keratocytes and the beginning of some neutrophil infiltration into the cornea. During this phase, the basal epithelial cells (*arrow*) forming the columnar layer also prepare to migrate. During the migration phase (**b**) occurring 6–36 h postinjury, the epithelial cells continue to migrate to close the gap and begin to adhere to the basement membrane. A primary wave (at 18 h) and a secondary wave (at 30 h) of neutrophils containing AMPs infiltrate into the stroma. The corneal epithelial cells produce AMPs such as CAP37 during this time. During the proliferation phase (**c**) occurring between 36 and 48 h postinjury, the basal epithelial cells from the columnar layer begin to proliferate before differentiating into wing and stratified corneal epithelial cells. The last phase in the process, the attachment phase (**d**), occurs 48 h postinjury as the cells firmly adhere back to the basement membrane and the number of intercellular junctions increase. The tear film is present throughout this process and is a known source of AMPs that may modulate the wound healing process. AMP antimicrobial peptide, CAP37 cationic antimicrobial protein of molecular weight 37 kDa [3]

treatments for stromal haze and scarring. Emerging TGF-β inhibition–based new interventions using gene therapy, introduction of specific ECM components, implantation of stromal equivalents, and nanotechnology for drug delivery are being investigated for stromal wound healing. Stem cell therapy is a promising approach to deal with fibrosis and haze. Treatment with femtosecond lasers for LASIK and keratectomy is thought to lead to better refractive outcomes, potentially due to less damage to the stromal cells [16–18].

Endothelial Wound Healing

Endothelial wounds are relatively rare, however, they do occur, usually as a consequence of burns or surgeries meant to replace dysfunctional endothelial cells, such as DSEK or DMEK [19–21]. The process of endothelial wound healing is substantially different from that of epithelial and stromal cells; they involve cell migration and spreading. The emerging progress in endothelial wound healing treatment include ROCK inhibitors (in the form of eye drops) to facilitate cell migration, and SMAD 7 gene therapy to suppress fibrotic changes [4].

Instrumentation

The major instrumentation in refractive surgery includes excimer lasers, laser (femtosecond) and mechanical microkeratomes, eye trackers, and instruments for collagen crosslinking. Excimer lasers and microkeratomes are crucial to LASIK, LASEK, epi-LASIK, and PRK procedures. With the development of wavefront and topography-guided excimer laser platforms, LASIK procedures have become more precise, safer, customizable to patient needs, and more widely applicable to refractive correction of all kinds of ammetropia. Intralase (60 kHz, 150 kHz, 500 kHz) and VisuMax are the two kinds of femtosecond laser platforms that are in routine use as laser microkeratomes. Nd:glass (amplification glass matrix mixed with neodymium) is used to create laser energy, and the delivery system comprises of two perpendicular galvanometers to allow the three-dimensional scanning of the laser. Comparative studies of both femtosecond lasers have shown similar safety, efficacy, and predictability, and both produce excellent visual results [22], although different levels of tear proteins are reported to arise with these different laser platforms due to induction of distinct biological responses in the cornea and ocular surface [23]. The FDA has approved the use of VisuMax femtosecond laser for correction of myopia through the new, increasingly popular SMILE procedure. The collagen crosslinking instrumentation is possible through UV LEDs and optical beam delivery system. Proper wavelength selection with consideration of temperature influence on the wavelength and the power output is important when choosing the appropriate UV-light source. Appropriate output shaping and control of the optical beam are key factors of crosslinking equipment, and the factors to consider include optical beam spot size, optical output power density distribution, optical beam aiming and positioning, as well as auxiliary beam aiming. The LED UV emitters in the crosslinking equipment system must comply with the IE 60825 safety regulation [24]. IEC 60601-1-11:2015 contains the most common regulations adopted by several countries. Opto X-Link, Avedro, Avedro KXL system, Kestrel-Intacs-XL, CSO Vega, and CCL Vario SwissMed are some representative crosslinking models that are available in the market.

Incisional Surgery (AK, RK, LRI, FEMTO-AK; FEMTO Wedge Resection)

Incisional corneal surgery has been employed in a variety of refractive procedures. Radial keratotomy (RK) was first attempted by Sato in the 1930s and was popularized by Fyodorov in the 1970s [25]. This technique was used to treat myopia by using radial incisions to flatten the central cornea (Fig. 14.2). The method developed by Fyodorov involved a series of paired radial incisions made through the epithelium and into the deep stroma. While relatively effective in reducing myopia overall, there was significant refractive fluctuation in the first 3 months, partly caused by varying degrees of stromal hydration [25].

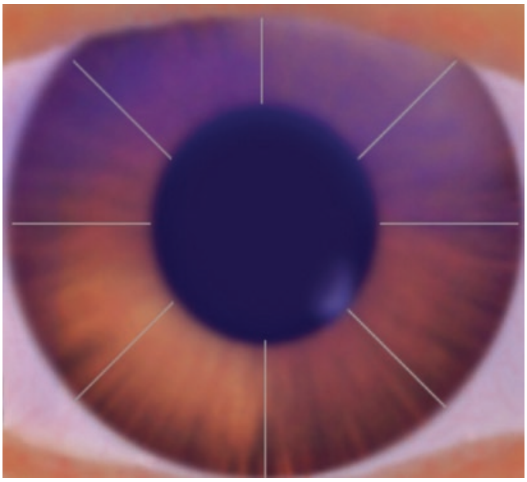

Fig. 14.2 Radial keratotomy

This procedure was ultimately replaced with newer refractive surgery techniques, such as photorefractive keratectomy (PRK), which was also studied as a method of treating residual refractive error after RK, and laser-assisted in situ keratomileusis (LASIK) [26].

Astigmatic keratotomy (AK), also known as arcuate keratotomy (when made in an arcuate configuration), was described by Binder in 1984 [27]. Using a blade, an incision, or a pair of opposing incisions, is made centered on the steep meridian of the cornea, thereby reducing corneal astigmatism; initially, this was at times paired with RK, although now it is often performed at the time of cataract surgery, or as an independent procedure (Fig. 14.3). The length and depth of the incisions, as well as the distance from the limbus, may be varied based on the amount of astigmatism and degree of effect desired. A number of nomograms were developed to guide the surgeon in AK placement [28]. A subset of AK, limbal relaxing incisions (LRIs) are made in the peripheral cornea near the limbus in an arcuate configuration. While AK causes flattening in the meridian of the incision, it tends to cause steepening in the opposite meridian as would be predicted by Gauss' law of inelastic domes, leading to a negligible effect on the spherical equivalent [29].

Femtosecond laser arcuate wedge-shaped resection was described by Ghanem and Azar in 2006 (Fig. 14.4) [30]. This technique utilized intersecting arcuate incisions created by a femtosecond laser to perform a wedge resection for the correction of high corneal astigmatism. After the development of a formula to calculate the relative decentration of arcuate cuts, the technique was tested in porcine corneas, and then carried out in a postpenetrating keratoplasty patient with 20 diopters of astigmatism. The procedure resulted in a nearly 15 diopter reduction of astigmatism, which was significantly greater than what had been demonstrated with AK alone.

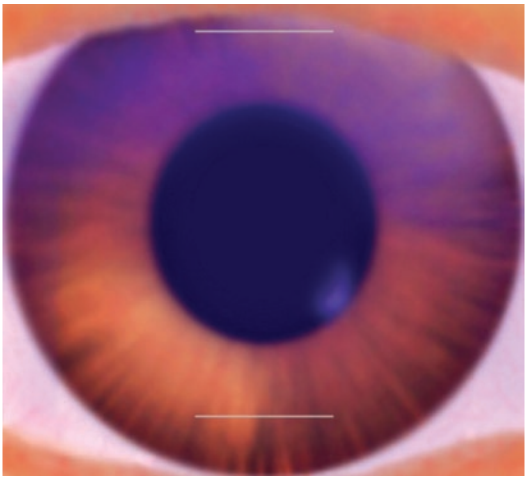

Fig. 14.3 Astigmatic keratotomy.

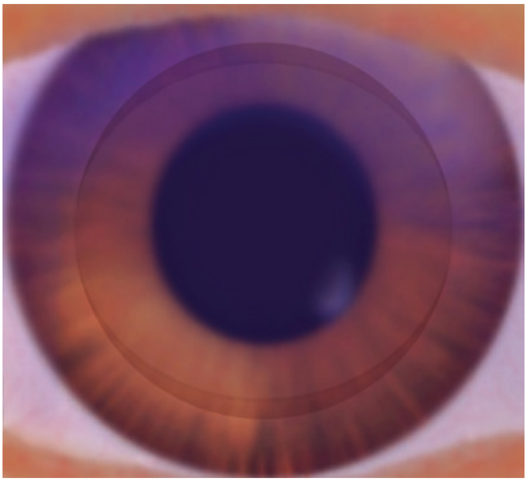

Fig. 14.4 Femtosecond laser arcuate wedge-shaped resection.

Soon thereafter, femtosecond laser-assisted AK (FLAK) was described by Harissi-Dagher and Azar [31]. Two patients with high corneal astigmatism after penetrating keratoplasty underwent FLAK comprised of paired arcuate incisions within the donor cornea [31]. The corneal astigmatism improved from 8.5 to 4.9 diopters in the first case, and from 7.0 to 4.3 diopters in the second case, with improvements in best corrected visual acuity of 20/100 to 20/30, and 20/200 to 20/60, respectively. FLAK has subsequently been found to be a reliable and effective procedure to address corneal astigmatism [32].

The relatively recent advent of femtosecond laser-assisted cataract surgery (FLACS) has popularized FLAK, which may be performed in the same session as wound creation, capsulotomy, and lens fragmentation. Similar to manual AK, the location, length, and depth of FLAK incisions may be varied, and a nomogram may be used to guide placement. FLAK incisions may include the anterior corneal surface or start within the anterior stroma, and typically end within the deep stroma (e.g., at 90% depth). The biomechanical properties of the cornea (i.e., corneal hysteresis and corneal resistance factor), as well as astigmatism type, may influence the efficacy of FLAK [33].

PRK, LASEK, and EPI-LASIK

Photorefractive keratectomy (PRK) was first performed in the USA by Dr. Stephen Trokel in the 1980s after collaborating with research scientists at IBM to modify an excimer laser for ophthalmic use [34]. The procedure involved the removal of corneal epithelium, followed by the use of an excimer laser to ablate and reshape the anterior corneal stroma (Fig. 14.5). The following year, Munnerlyn et al. published a study describing the use of the excimer laser to reshape rabbit corneas [35]. The authors also described a theoretical formula (subsequently known as the Munnerlyn formula) that estimated the depth of corneal ablation required in excimer refractive surgery: the depth per diopter of intended treatment equaled the square of the treatment zone diameter in millimeters divided by three.

The surface-based excimer refractive procedures also include laser epithelial keratomileusis (LASEK) and epi-LASIK. LASEK was first performed at the Massachusetts Eye and Ear Infirmary by Dr. Dimitri Azar in 1996. This procedure involved the use of a semisharp circular instrument that was placed on the cornea and filled with alcohol for approximately 30 seconds, after which modified Vannas scissors were used to create a hinged epithelial flap. An excimer laser was then applied to the stroma, followed by replacement of the epithelium [36]. Epi-LASIK was described by Dr. Ioannis Pallikaris and colleagues at the University of Crete [37]. This procedure was similar to LASEK, except that instead using alcohol, a microkeratome was used to create an epithelial flap. Subsequent work revealed that LASEK and epi-LASIK had similar visual outcomes, epithelial closure time, pain, and haze formation, regardless of whether the epithelial flap was retained or discarded [38]. Similar visual outcomes between PRK, LASEK, and epi-LASIK, as well as other factors (including the challenge of successfully replacing the epithelial flap), led many surgeons to favor PRK among the surface-based refractive procedures.

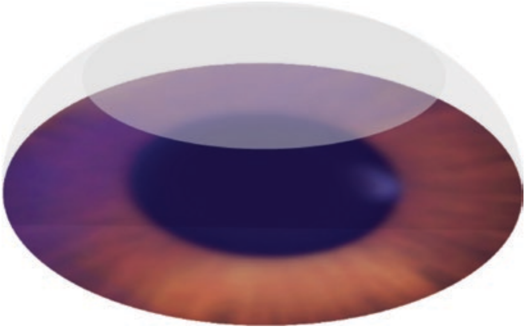

Fig. 14.5 Photorefractive keratectomy.

PRK was ultimately approved by the Food and Drug Administration (FDA) in 1995. Early studies revealed the development of anterior stromal haze after PRK, and its incidence and duration appeared to correlate with stromal ablation depth [39–40]. Majmudar et al. [41] described the use of mitomycin C (MMC) in the treatment of corneal haze postrefractive surgery (including cases of RK and PRK). In 2005, Gambato et al. [42] reported the results of a prospective, randomized clinical trial that showed intraoperative MMC was effective in the prevention of anterior stromal haze after PRK.

Despite the wide adoption of LASIK, in part due to faster visual recovery and less postoperative pain, there remains an important role for the surface-based excimer refractive procedures. For example, due to the decreased ablation depth of surface-based procedures in comparison to LASIK, there is a decreased risk of postrefractive surgery ectasia. The surface-based procedures also do not carry a long-term risk of flap-related complications, such as epithelial ingrowth, traumatic flap dehiscence, and flap-related infections.

Indications and Contraindications

The primary indication for surface-based refractive surgery is the correction of refractive error, including myopia, hyperopia, and corneal astigmatism. Importantly, surface-based refractive surgery may be considered as an alternative in eyes that, with LASIK, would have a thin residual stromal bed (e.g., less than 250 microns), leading to an unacceptable risk of postrefractive surgery ectasia. There are other indications (and subindications) that have also been described. For example, phototherapeutic keratectomy (PTK) followed by PRK has been reported in the treatment of conditions such as epithelial basement membrane dystrophy with concurrent refractive error. Recent technological advancements, including the advent of topography-guided custom PRK, have facilitated the reduction of irregular astigmatism in postpenetrating keratoplasty eyes [43].

There are several contraindications to surface-based refractive surgery, some of which are considered absolute. These include pregnancy, corneal inflammation or infection (including herpes simplex virus or herpes zoster virus keratitis), neurotrophic keratopathy, and autoimmune disorders such as rheumatoid arthritis. Patients with a visually significant cataract should also be excluded, as well as those who would have a thin residual stromal bed after surface-based refractive surgery. Other contraindications include an unstable refraction (e.g., progressive myopia), moderate to severe dry eye syndrome, and the use of certain medications including isotretinoin. Patients with topographic signs of corneal ectasia (including forme fruste keratoconus) should also be excluded from surface-based refractive surgery alone; it should be noted that good outcomes have been reported with corneal collagen crosslinking followed by topography-guided PRK, and this technique may become more widely adopted [44].

Surgical Techniques

PRK involves the instillation of a topical anesthetic, antisepsis (e.g., using povidone-iodine), and the placement of an eyelid speculum. This is followed by the removal of the corneal epithelium overlying the treatment zone. This step may be performed with the assistance of alcohol, mechanically, or with a transepithelial laser; however, alcohol-assisted epithelium removal is most common and appears to provide a smooth underlying surface for subsequent ablation. Alcohol-assisted epithelium removal involves the use of a circular instrument that is placed over the cornea and filled with 18–20% ethanol for approximately 30 seconds at which time the alcohol is absorbed using a small sponge. The instrument is removed, and the epithelium within the alcohol exposure zone is gently debrided using another small sponge. The excimer laser is then applied. MMC may then be applied to prevent haze formation (e.g., a 6 mm round sponge soaked in MMC 0.02%, placed over the ablation zone for 30 seconds), after which the eye is copiously irrigated. Finally, a steroid drop, antibiotic drop, and bandage contact lens are placed.

The initial steps in LASEK are similar to PRK. Once the eyelid speculum is placed, the cornea is marked with overlapping 3 mm circles in the periphery. A semisharp circular instrument is then placed centrally into which 18–20% ethanol is placed. After approximately 30 seconds, the alcohol is absorbed using dry sponges, and if needed alcohol is placed (and absorbed) again. Next, the semisharp circular instrument is removed, and a modified Vannas scissor is used to create a hinged epithelial flap. Once the excimer laser and MMC have been applied to the stroma, the epithelium is gently floated back over the treatment zone using a balanced salt solution on an anterior chamber cannula (e.g., 27 gauge). The flap is carefully realigned using intermittent irrigation, after which it is allowed to dry for at least 2 minutes. A steroid, antibiotic, and bandage contact lens are then placed.

Epi-LASIK also involves the creation of an epithelial flap, but instead of alcohol (as in LASEK), it is created using a microkeratome; Pallikaris et al. first described the use of a modified microkeratome with an oscillating blade for this purpose. After placement of the eyelid speculum and irrigation of the corneal surface using an anterior segment cannula, the surface is dried with a sponge, and the cornea is marked using a LASIK marker. Next, the microkeratome is applied to eye, and once suction is achieved, the oscillating blade is advanced, causing epithelial separation and creating a 2–3 mm nasal hinge. The suction is then released, and the microkeratome is removed from the eye. The epithelial sheet is then reflected nasally. The remaining steps are similar to LASEK.

Conclusion

Continued developments are likely to improve visual outcomes and patient satisfaction from this category of refractive surgery. For example, topography-guided custom PRK is now available in the USA, and the results thus far are promising [44]. Corneal collagen crosslinking (CXL) followed by topography-guided custom PRK in eyes with keratoconus appears to improve both uncorrected and best corrected visual acuity compared to CXL alone and appears to have a low risk of worsening ectasia [45]. Transepithelial PRK has also been the subject of recent investigations [46]. Further research is required to determine the long-term safety and efficacy of these techniques.

LASIK and SMILE

LASIK is a well-established and commonly used refractive procedure worldwide. SMILE, on the other hand is a newer technique, but rapidly gaining popularity since its availability in 2011. SMILE is gaining increasing popularity primarily because of the noninvasive nature of the procedure while producing comparable refractive and visual outcomes to that of LASIK. The noninvasive nature comes from the absence of flap in SMILE, instead involving the direct extraction of a stromal lenticule through a 2 mm keyhole incision. The flap absence contributes to better corneal biomechanical integrity during wound healing. The corneal biomechanical integrity is maintained better in a flapless procedure theoretically because both the stromal cohesive and tangential tensile strength are stronger in the anterior portion of the cornea than in the posterior portion. In fact, the cohesive tensile strength at the anterior 40% of the corneal stroma is thought to be at least 50% stronger than at the posterior 60%. Flap-based procedures such as LASIK sever the stronger anterior corneal lamellae, leaving the cornea with the weaker cohesive tensile strength [47–52]. Severing the anterior corneal lamellae also contributes to stromal thickening during the postwound healing phase as the peripheral anterior lamellae are no longer under tension, and they relax and spread out.

The corneal biomechanical integrity has been studied using conceptual and computational modeling studies. A study comparing the contralateral eye after SMILE and flap-based corneal refractive surgery resulted in a 49% (of 10 eyes, range: 2% to 87%) greater mean reduction of effective stromal collagen fiber stiffness within the flap region compared to the SMILE eyes [53]. Mechanical strain is linked to higher chances of corneal ectasia. Another study comparing posterior corneal elevation showed backward shift of central posterior surface in both LASIK and SMILE at postoperative 3 months, while at postoperative 3 years, SMILE showed stable posterior mean elevation (PME), and LASIK showed more posterior shift of PME [54].

Patient Evaluation for LASIK and SMILE

LASIK

When evaluating patients for LASIK, patient history, physical examination, and LASIK testing are important. Patient history includes past ocular/medical history – systemic diseases (diabetes, autoimmune diseases), ocular conditions (ocular herpes, peripheral keratitis), previous history of strabismus, and patients with thin corneas. The ocular conditions are likely to resurface after LASIK surgery, and the systemic diseases may alter the normal wound healing process. Medications such as ImitrexTM (for migraine), AccutaneTM (for severe acne), and other over the counter antihistamines can alter the wound healing process and can cause dryness of the ocular surface. Other patient history to consider are patient lifestyle, family history of corneal transplant, and patient expectation of the visual outcomes after surgery. LASIK testing includes dry eye, contrast sensitivity, and pupil testing, as well as pachymetry, keratometry, corneal topography, and wavefront analysis. Other general physical examination such as visual acuity, refraction, and complete eye examination, including posterior dilated exam and tonometry, are also done.

SMILE

The important parameters to consider when performing the procedure are the desired refractive correction, the optical zone, lenticule side cut angle, minimum lenticule thickness, cap diameter and thickness, cap side cut angle, and fluence levels. Other parameters to consider are the patient age, refractive error, residual stromal bed thickness, and scotopic pupil size. In this respect, the SMILE patient evaluation parameters are similar to the LASIK procedure.

For SMILE patient evaluation, it is ensured that the patient has myopia of 1.00 D to −8.00 D and astigmatism of ≤−0.50 D; this is the treatment range that has been approved by the FDA in the USA [55]. Outside the USA, myopia of up to −10.00 D combined with astigmatism of up to −5.00 D has been treated [56]. The problem associated with managing thin lenticules in low myopia correction has been attempted to be resolved experimenting with a wider optical zone. The FDA reported good visual outcomes with a minimum peripheral lenticule thickness of 15 μm [57–58], and with increasing surgeon experience, a 10 μm thick lenticule is recommended to avoid excess removal of stromal tissue. The SMILE procedure is still under investigation regarding hyperopic correction. However, encouraging preliminary results have been reported from using a lenticule profile of 7-mm optical zone with a 2-mm transition zone [59].

Surgical Techniques

LASIK

LASIK involves refractive correction by combining lamellar corneal surgery with the accuracy of the femtosecond laser. The surgical procedure involves two steps: (1) flap creation in the cornea and (2) ablation of the stromal tissue depending upon the desired refractive correction (Fig. 14.6). The flap creation process takes only a few seconds, with the use of either a mechanical microkeratome or a femtosecond laser. Femtosecond laser offers more precision and safety than the microkeratome. The flap is gently lifted to expose the stromal tissue, which is to be ablated. The ablation step involves ordinary, wavefront- or topography-guided excimer laser to permanently remove the desired amount of stromal tissue. In myopic ablation, the central cornea is flattened relative to the periphery, while in hyperopic ablation, the central cornea is made steeper relative to the periphery. Larger ablation diameters are needed for effective treatment of hyperopia compared to myopia. For hyperopic astigmatism, the flat meridian is steepened by ablating tissue along the paracentral area. Mixed astigmatism is corrected employing the crosscylinder and bitoric techniques [60]. In the crosscylinder technique, the cylinder power is divided into two symmetrical parts, and one-half is treated on the positive meridian while the other-half is treated on the negative meridian [60]. In the bitoric technique, a combination of paracentral and cylindrical ablation is employed to flatten the flat meridian, so that the axis is steepened [60–64].

The patient's refractive needs are considered when choosing wavefront- or topography-guided excimer laser profile. Wavefront technology can measure both the higher and lower order aberrations, as well as provide higher precision in increments of 0.10 D or smaller for the standard 0.25 D adjustment ceiling. Topography-guided LASIK takes into consideration the spherocylindrical correction as well as the corneal shape to calculate the ablation profile.

SMILE

The curved contact glass surface of the femtosecond laser is docked onto the patient's cornea. As the contact is made between the cornea and the contact glass, a tear film meniscus appears, and the patient is able to see the fixation target (a flashing green beam of light) clearly (Fig. 14.7a).

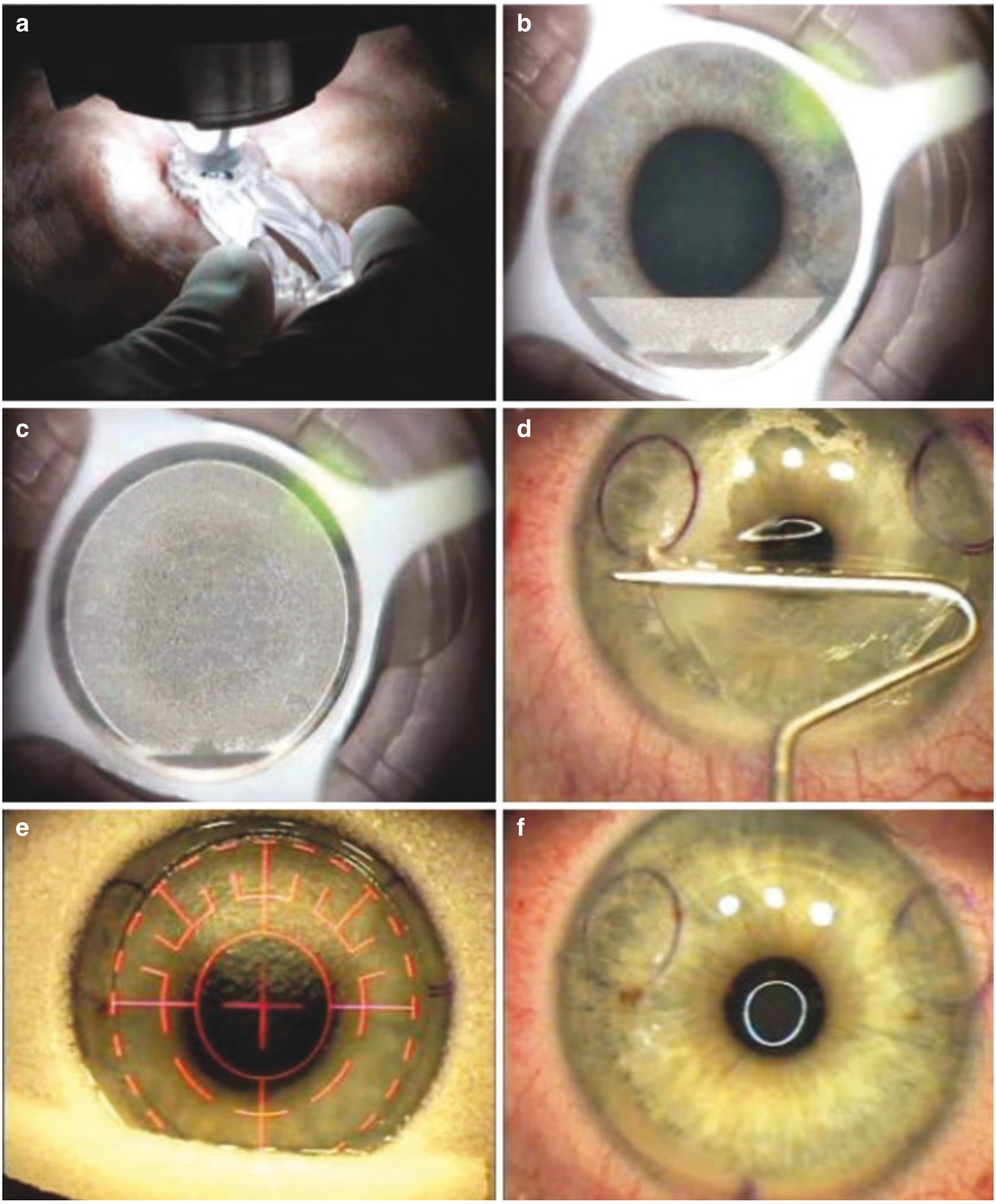

Fig. 14.6 Intralase™ femtosecond laser flap construction. (**a**) Placement of low pressure suction ring to align and stabilize the globe. A flat contact lens attached to the laser system is used to applanate the cornea. (**b**) Pocket is first constructed to collect the gases, then laser pulses are delivered in previously programmed raster pattern. (**c**) Construction of side cuts. (**d**) Lifting of flap from stromal bed after disappearance of cavitation bubbles. (**e**) Laser ablation of stromal bed. (**f**) Reposition of flap. (Reprinted with permission from: Hallak et al. [176])

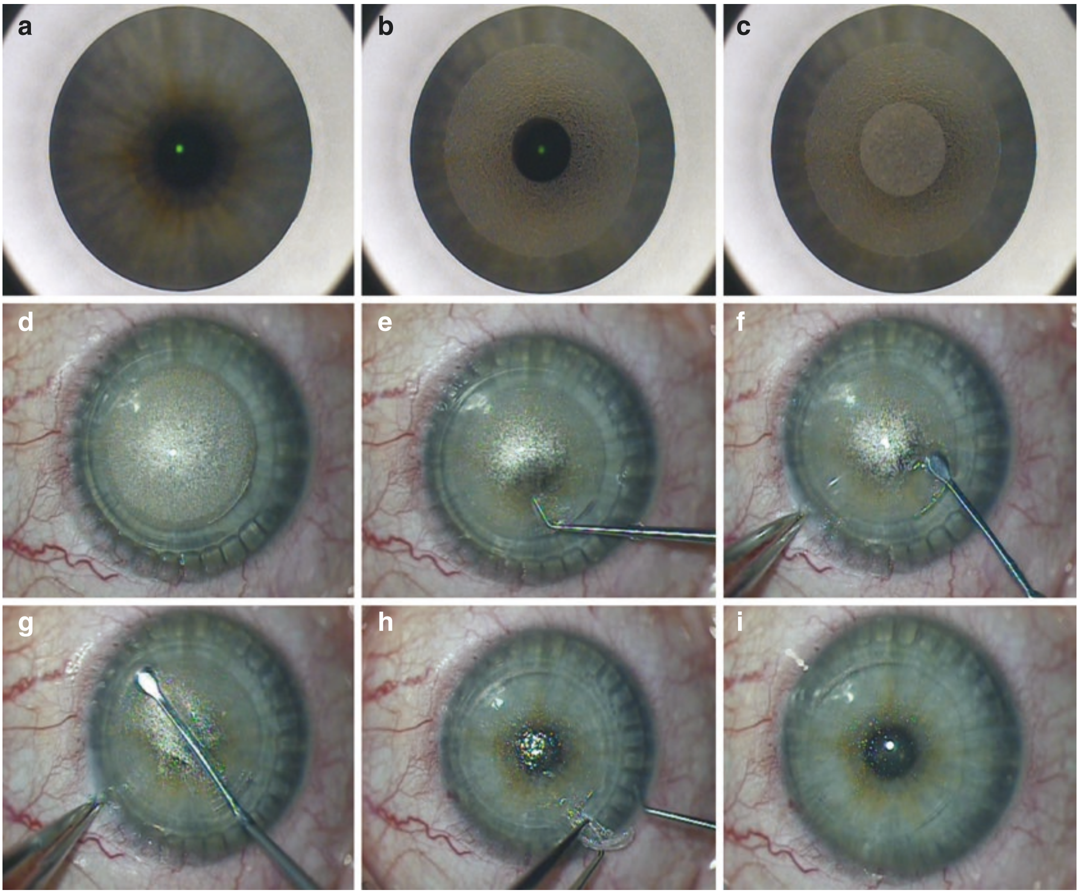

Fig. 14.7 SMILE surgery on a right eye. (**a**) Patient is asked to fixate green light. Note, this may not coincide with the center of the entrance pupil. Patient interface is aligned and suction started. (**b**) Refractive posterior surface of lenticule is created by spiraling-in application of femtolaser spots. (**c**) Anterior surface of lenticule is created parallel to anterior surface of the cornea (spiraling-out). (**d**) Complete laser application with superotemporal incision. (**e**) Sidecut is opened with a semisharp tip. First, the upper lenticular surface is entered. (**f**) Upper interface is separated using a blunt spoon-shaped SMILE spatula (custom-made). (**g**) Lower interface is separated. (**h**) Lenticule is extracted with microforceps. (**i**) Finished SMILE procedure. (Reprinted with permission from: Giri et al. [177])

The vergence of the fixation beam is focused according to the patient's refraction to allow for this clear sight of the fixation target. When the patient focuses directly on the fixation light, the corneal suction port is activated to fix the eye in position and to align the visual axis. Besides this patient-controlled centration approach, the surgeon can also use infrared light to confirm the centration and then activate the laser. After the initial stage of adequate suction, the patient is usually able to maintain fixation as the intraocular pressure (IOP) rise is relatively small.

To make the lenticule cut, the lower interface of the intrastromal lenticule is created in a spiral in pattern first (Fig. 14.7b), followed by a 360° sidecut, which is followed by a spiral out pattern creation of upper lenticule interface (Fig. 14.7c), and then finally by a 2–4 mm superior or superotemporal incision for access (Fig. 14.7d). The access incision connects the upper lenticule interface (also known as cap) to the corneal surface. Total suction time is independent of the refractive error treated and ranges from 25 to 35 s depending upon the mode used.

When it is time to remove the lenticule, the tissue planes are defined by opening up the small incision and by identifying the anterior and posterior interfaces of the lenticule (Fig. 14.7e). A blunt, circular tip dissector is used in a windshield wiper–like fashion with the fulcrum centered at the incision to separate the upper interface (Fig. 14.7f). The lower layer is dissected very similarly (Fig. 14.7g). A pair of microforceps is used to grasp the lenticule and extract the lenticule after the interface separation (Fig. 14.7h). The lenticule can also be directly scooped out from within the pocket using the latest lenticule separation dissector. Minimal washing of the interface with a balanced salt solution at the end of the procedure helps clear the Bowman's membrane folds and better visual outcomes on postoperative day 1 [65] in terms of uncorrected distance visual acuity (UDVA) and contrast sensitivity.

A variation of the lenticule extraction technique, called "lenticuloschisis," involving the gentle peeling of the lenticule off the stroma in a rhexis-like pattern instead of the actual dissection of the planes has also been reported [66]. The authors reported less surface roughness and irregularity on postoperative day 1 compared to the typical dissection technique. Prerequisites such as ideal bubble pattern, optimized energy levels, myopia of >3 D and good experience in conventional lenticule dissection technique were emphasized, however, before attempting the "lenticuloschisis technique."

Long-Term Visual Outcomes After SMILE

From 5-year comparison studies of SMILE and FS-LASIK for myopia, no statistically different refractive stability was found between the two groups, although myopic regression was observed in terms of total corneal refractive power (TCRP) [67]. Another 5-year study of the visual outcomes in 616 astigmatic myopic eyes showed that uncorrected visual acuity (UVAC) was better in the fifth year compared to the immediate aftermath of the procedure, with 88% eyes having UVAC of logMAR 0.1. The safety index was reported to be better on the fifth year than right after the invention with 92% eyes achieving refraction of 0.5 D within the SE target and 77% eyes losing no visual line. During the 5-year period, the SMILE-treated eyes showed regression of 0.24 D [68]. A third 5-year study of 56 myopic and myopic astigmatic eyes reported stable refractive outcomes with no significant changes in comparison to the 6-month follow-up results [69]. In this study, the spherical equivalent was reported to be −0.375 D with 32 of the 56 eyes gaining 1–2 Snellen lines, and no eyes losing 2 or more lines, and a long-term regression of 0.48 D. A 3-year follow-up study of the post-SMILE irregular astigmatism and curvature changes in 50 myopic astigmatic eyes showed a reduction of posterior astigmatism in high refractive corrections [70]. However, despite the compensatory effect of the posterior corneal surface, increase in irregularities was seen [70]. In contrast to the excimer laser–assisted techniques, the almost intact anterior lamellae and Bowman layer after SMILE could cause different kind of remodeling of anterior and posterior corneal surfaces after surgery. Han et al. reported 4-year refractive, wavefront aberrations and quality of life outcomes after SMILE for 47 moderate-to-high myopic eyes, concluding that the SMILE-corrected eyes showed predictable and stable refractive correction [71]. The reported efficacy index was 1.07 ± 0.16 with 89% eyes achieving the correction of ±0.5 D of the intended refractive correction.

Complications of SMILE and LASIK

Intraoperative complications during SMILE include suction loss, opaque bubble layer, incision bleeding, incision abrasion, incision tear, epithelial defect, subconjunctival hemorrhage, difficult lenticule extraction, tear, unintended posterior plane dissection, inaccurate laser placement, and cap perforation [72–81]. The postoperative SMILE complications include dry eye, ectasia, diffuse lamellar keratitis (DLK), and interface lamellar fluid [82–88].

Intraoperative complications of LASIK include inadequate exposure, suction loss, corneal epithelial defect, irregular or incomplete cut, decentered flap, free cap, buttonhole, pizza slicing, and limbal hemorrhage [89–101]. Femtosecond-specific intraoperative complications include vertical gas breakthrough, anterior chamber bubble, and opaque bubble layer [89, 102–106]. The photoablation-related intraoperative complications include decentration, central islands, uneven ablation, overcorrection, and undercorrection [89]. Other intraoperative complications include flap destruction, interface debris, and wrinkle. Early postoperative complications of LASIK include interface debris, flap displacement and flap folds, flap striae and flap folds, sliding or dislodged flap, flap/cap loss, DLK/shifting sands of Sahara, pressure induced stromal keratopathy (PISK), central toxic keratopathy, epithelial ingrowth, flap melt, and infectious keratitis [89, 107–110]. The late postoperative complications include regression, induced or iatrogenic keratectasia, night vision problems and glare, transient light sensitivity syndrome, rainbow glare, dry eye, and neurotrophic epitheliopathy [89, 111–118].

The most-noted advantage of the SMILE procedure over LASIK is less occurrence of dry eye, owing largely to the preservation of corneal nerves in SMILE from the absence of the flap cut. Overall, analyzing the various indicators for the dry eye such as TBUT, Schirmer's test, OSDI score, and tear film osmolarity indicates that the SMILE procedure does not appear to exacerbate dry eye symptoms, whereas FS-LSIK appears to do so to some extent, at least up to 6 months. The major meta-analyses of SMILE vs. FS-LASIK outcomes have reported significantly higher corneal sensitivity in SMILE than FS-LASIK, especially until postoperative 3 months [119–122]. Although no significant differences in the Schirmer's test have been reported between the two procedures by the major meta-analyses, TBUT scores have been reported to be significantly better for SMILE than for FS-LASIK [119–123]. The comparison of the subjective OSDI score have also been reported to be significantly worse in FS-LASIK by the five major meta-analyses studies [119–123].

In case a retreatment is desired after the SMILE procedure, surface ablation has been reported to be a safe method of secondary enhancement by Siedlecki et al. who enhanced 43 of 1963 SMILE-treated eyes (2.2%) with intraoperative mitomycin C and surface ablation [124]. A second SMILE procedure below the existing interface also has been reported to be feasible by Donate and Thaeron [125]. When the lenticule cap is thin between 100 and 110 μm, FS-LASIK can be performed by converting the cap into the flap although the usable optical zone is limited with this method. A special software called "Circle software" is offered by VisuMax for cap-to-flap conversion where the flap is larger in diameter than the original cap [126].

Presbyopic Corneal Implants and ICRS for KC

The concept of refractive corneal implants was first introduced by Dr. Jose Barraquer in 1949 [127–128]. Refractive corneal implants in use today can be divided into two broad categories: those that seek to address presbyopia and those that seek to primarily address irregular corneal astigmatism, such as in the setting of keratoconus. Presbyopic corneal implants are generally placed within the anterior stroma of the nondominant eye. These can be further divided into three categories: (1) those that have a small aperture and work by creating a pinhole effect (2) those that work by reshaping the central anterior corneal curvature and (3) those that have concentric rings with add power within the outer ring, similar to a multifocal contact lens or intraocular lens.

Presbyopic Implants

An example of the first category of presbyopic corneal implants is the KAMRA inlay (AccuFocus, Inc.). This implant was approved by the FDA in 2015. KAMRA is approximately 6 microns in thickness and 3.8 mm in diameter, with a 1.6 mm central opening. The small central opening creates a pinhole effect, allowing for

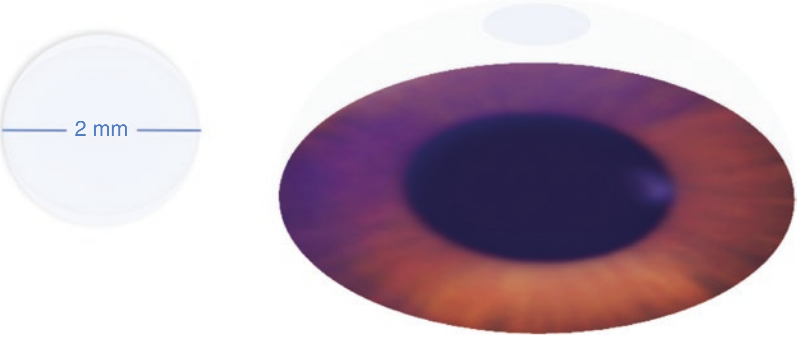

Fig. 14.8 Raindrop Near Vision Inlay

sharp near vision while preserving distance acuity. Three-year results from the FDA clinical trial cohort revealed that 87.1 percent of nondominant emmetropic presbyopic eyes with a KAMRA inlay saw 20/40 or better at near without correction [129].

The Raindrop Near Vision inlay (ReVision Optics, Inc.) is an example of the second category of presbyopic corneal implants and was approved by the FDA in 2016. This implant was a 2.0 mm diameter clear hydrogel inlay and worked by increasing the central corneal curvature, thereby creating a hyperprolate anterior corneal surface; near objects could be viewed using central rays while distance objects could be viewed using paracentral rays (Fig. 14.8). Whitman et al. reported the results of a 1-year safety and efficacy study in which 373 nondominant emmetropic presbyopic eyes received the Raindrop inlay [130]. This study showed that 93 percent achieved an uncorrected near visual acuity of 20/25 or better. Eighteen inlays required replacement, usually due to decentration soon after placement; however, these eyes tended to have excellent visual outcomes. Revision Optics removed the Raindrop from the market in early 2018, presumably due to poor adoption among refractive surgeons.

Finally, an example of the third category of presbyopic corneal implants is the Presbia Flexivue Microlens (Presbia PLC). This implant is a 3.0 mm diameter clear hydrogel inlay, with a plano central zone, and a surrounding ring with an add power ranging between +1.50 diopters and +3.50 diopters (Fig. 14.9). It is currently undergoing FDA trials in the USA. In a study by Malandrini et al. from Italy, 26 presbyopic emmetropic eyes received the implant, and the mean uncorrected near visual acuity was 20/25 at 36 months postoperatively [131].

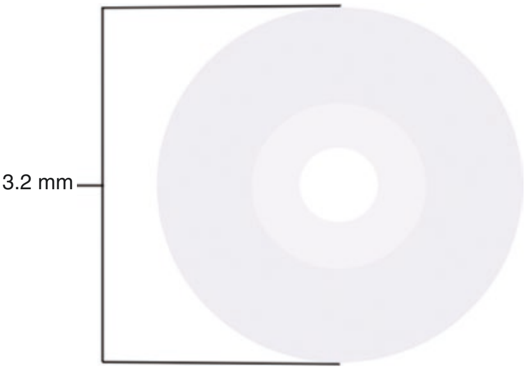

Fig. 14.9 Presbia Flexivue Microlens

Intracorneal Ring Segments

The second broad category of refractive corneal implants, which primarily seek to address irregular corneal astigmatism, is comprised of intrastromal corneal ring segments (ICRS) (Fig. 14.10). These were first proposed by Fleming et al. in 1989 [132]. The authors constructed a mathematical model to determine the change in corneal curvature that may occur with the placement of an intrastromal corneal ring. Subsequently, Intacs corneal implants (Addition Technology, Inc.) were approved by the FDA in 1999 for use in the correction of mild to moderate

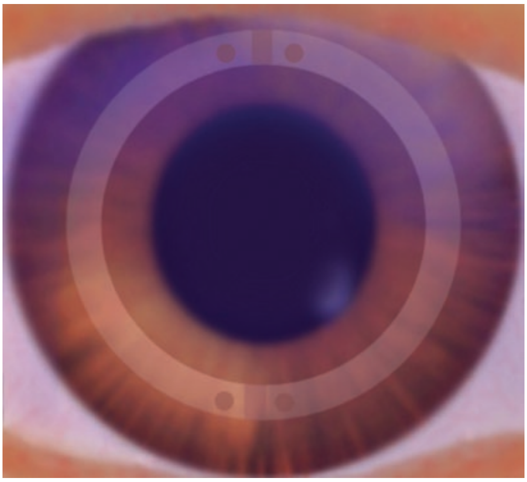

Fig. 14.10 Intracorneal ring segments

myopia, and in 2004 received a Humanitarian Device Exemption for use in the treatment of keratoconus. Unlike presbyopic corneal implants, which are typically placed in the anterior corneal stroma, ICRS are typically placed in the posterior corneal stroma, which facilitates their flattening effect.

In addition to Intacs, there are other ICRS types with varying specifications, including Ferrara (Mediphacos, Inc.), Myoring (Dioptex), and Bisantis (Opticon 2000 SpA and SolekoSpA). The position of ICRS can be determined with high precision using anterior segment optical coherence tomography [133]. Complications may include anterior or posterior extrusion of the ring segment as well as continued intolerance or inability to wear contact lenses for refractive correction.

It should be noted that the number of patients who require either ICRS or corneal transplantation in the setting of keratectasia may be decreasing due to the increased utilization of corneal collagen crosslinking (CXL), which was approved by the U.S. Food and Drug Administration in 2016. In addition to decreasing or halting the progression of keratectasia, CXL can lead to improvements in corneal astigmatism and visual acuity in some patients. As noted previously, its use has also been described in conjunction with PRK.

Indications and Contraindications

Presbyopic corneal implants may be considered for the nondominant eye in presbyopic patients, typically between 40 and 60 years of age, who have not yet developed a visually significant cataract. The primary indication is the correction of presbyopia. The central and paracentral cornea must be clear, and the corneal stroma must have adequate thickness. Although they may be placed in presbyopic emmetropic patients, they may also be considered in patients with refractive error as well as at the time of LASIK surgery. Similar to other refractive procedures, contraindications include corneal inflammation or infection (including herpes simplex virus or herpes zoster virus keratitis), neurotrophic keratopathy, and autoimmune disorders such as rheumatoid arthritis. Patients with a large angle kappa may be poor candidates for this procedure.

Patients with steep corneas that are not amenable to correction with a rigid contact lens (e.g., due to contact lens intolerance) but have adequate corneal thickness in the mid-periphery (at least 400 to 450 microns) may be candidates for ICRS. The central and paracentral cornea must be clear. The contraindications for ICRS are similar to other refractive procedures.

Surgical Techniques

A presbyopic corneal implant is placed into the patient's nondominant eye. It may be placed either within a stromal pocket or beneath a flap. After instillation of topical anesthetic, antisepsis (e.g., povidone-iodine), and placement of an eyelid speculum, the stromal pocket or flap may be created using a microkeratome or a femtosecond laser. A stromal pocket may be preferable due to less corneal nerve damage as well as a lower risk of decentration of the implant, and a femtosecond laser provides a more consistent depth and configuration (for either a stromal pocket or flap). The depth of insertion within the stroma depends on which implant is being placed.

The implant is typically inserted using instruments that are specifically designed for the device. Appropriate positioning of the implant is critical. The Purkinje light reflex (with the patient fixating on the light) should be used as a primary guide with positioning over the pupillary center as a secondary guide. As noted above, patients with a large angle kappa may be poor candidates for this procedure. A topical steroid and antibiotic are given postoperatively.

The initial steps for ICRS placement are similar to those for presbyopic corneal implants. After placement of an eyelid speculum, the area of the cornea overlying the pupillary center is marked with a Sinskey hook. Using a mechanical technique, a 1–2 mm radial incision is made at approximately 70–80% depth using a preset diamond knife (the depth is determined using preoperative pachymetry). A semiautomated suction ring is then placed around the limbus after which semicircular dissectors are inserted in each direction through the radial incision (clockwise and counterclockwise) to create stromal pockets. The suction ring is then removed, and the ICRS are inserted into the stromal pockets. A circular stromal pocket may also be created using a femtosecond laser at 70–80% stromal depth. A topical steroid and antibiotic are given postoperatively.

Conclusion

Presbyopic corneal implants may improve near visual function in the appropriately selected patient population. Further research and development may lead to broader acceptance and utilization of this technology. ICRS may be used to reduce corneal astigmatism in patients with keratectasia, including from keratoconus and postrefractive surgery ectasia. Similar to presbyopic corneal implants, appropriate patient selection is critical for success with this procedure.

Lenticular Refractive Surgery

Lenticular refractive surgery includes surgery involving the crystalline lens of the eye. The lens can be absent (aphakia) or present (phakia) and the surgeries can involve procedures to correct cataracts, astigmatism, and presbyopia. Cataracts most often cause aphakia, but aphakia can also occur due to certain injuries that damage the lens, or partially (subluxation)/completely detach the lens of the eye, or they can be congenital due to genetics. Surgeries for treating aphakia can include removing the damaged lens if necessary (pseudophakic), and then implanting artificial lens. The surgical outcomes are typically good; however, some complications such as aphakic glaucoma, and vitreous and retinal detachment are known to occur. Phakic lenticular surgery involves implanting a special type of intraocular lens to correct myopia or myopic astigmatism, leaving the natural lens of the eye untouched. The presbyopia-correcting lenticular surgery involves implanting multifocal, accommodating and extended depth of focus IOLs.

Phakic IOLs

Phakic IOLs are becoming increasingly popular due to the comparable visual and refractive outcomes as LASIK. In contrast to LASIK, the phakic IOLs do not require tissue ablation, instead they work by combining the power of the implanted lens with that of the natural lens to achieve 20/20 or better vision. A major advantage of the phakic IOL over LASIK is the capability of refractive correction of very high myopia levels of up to 23D, high hyperopia levels of up to 21D, and astigmatism of up to 7D [134]. Numerous studies have reported better visual outcomes after pIOL implantation in highly myopic patients than after LASIK [135–140]. Other advantages common for all pIOL models include excellent refractive stability, improved visual acuity, retention of accommodation, rapid visual recovery, and reversibility [136, 138, 141–142]. Complications include increased intraocular pressure from blockage of aqueous outflow, and intraocular tissue injuries although these are rare overall [143–144]. The IOLs are made of biomaterials carefully chosen to ensure great long-term uveal and capsular biocompatibility [145], material adhesiveness (expectation is that the IOL gets fused with the anterior and posterior capsule to prevent decentration and rotation) [146], and nutritional health of the cornea. Overall, phakic IOLs are the best option for the surgical correction of high refractive errors. The two broad varieties of phakic IOLS available for clinical use include anterior chamber phakic IOLs (AC PIOLs) and posterior chamber phakic IOLs (PIOLs).

Anterior Chamber Phakic IOLs (AC PIOLs)

The anterior chamber models are of two subtypes: [1] angle supported and [2] iris claw. The anterior chamber angle-supported phakic IOLs include AcrySof Cachet (Alcon, Fig. 14.11a), Visian ICL (Staar Surgical, Fig. 14.11b), and Veriflex IOL (Fig. 14.11c). AcrySof IOL is only available for myopia correction (−6.00 to −16.50D) and comes in four sizes (12.5 mm, 13.0 mm, 13.5 mm, and 14.0 mm). The Visian ICL is available for myopia correction (−0.25 to −18.00D, hyperopia correction (0.50 to 10.00D) and astigmatism correction (−6.00 to 6.00D, the brand name is Toric ICL). It is designed to fit in the ciliary sulcus and comes in four sizes for myopia/myopic astigmatism (12.1, 12.6, 13.2, and 13.7 mm) and in four sizes for hyperopia (11.6, 12.1, 12.6, and 13.2 mm) [147]. The Veriflex IOL is available for myopia correction (−2.00 to −14.50 D) and astigmatism correction (up to −5.00, provided that the sphere plus cylinder does not exceed −14.50 D) [148]. It was developed based on the Verisyse platform and can achieve precise centration over the pupil and high rotational stability but requires some surgical skills for enclavation [149].

Posterior Chamber Phakic IOLs (PIOLs)

Three phakic posterior chamber IOLs are currently available: the Implantable Contact Lens

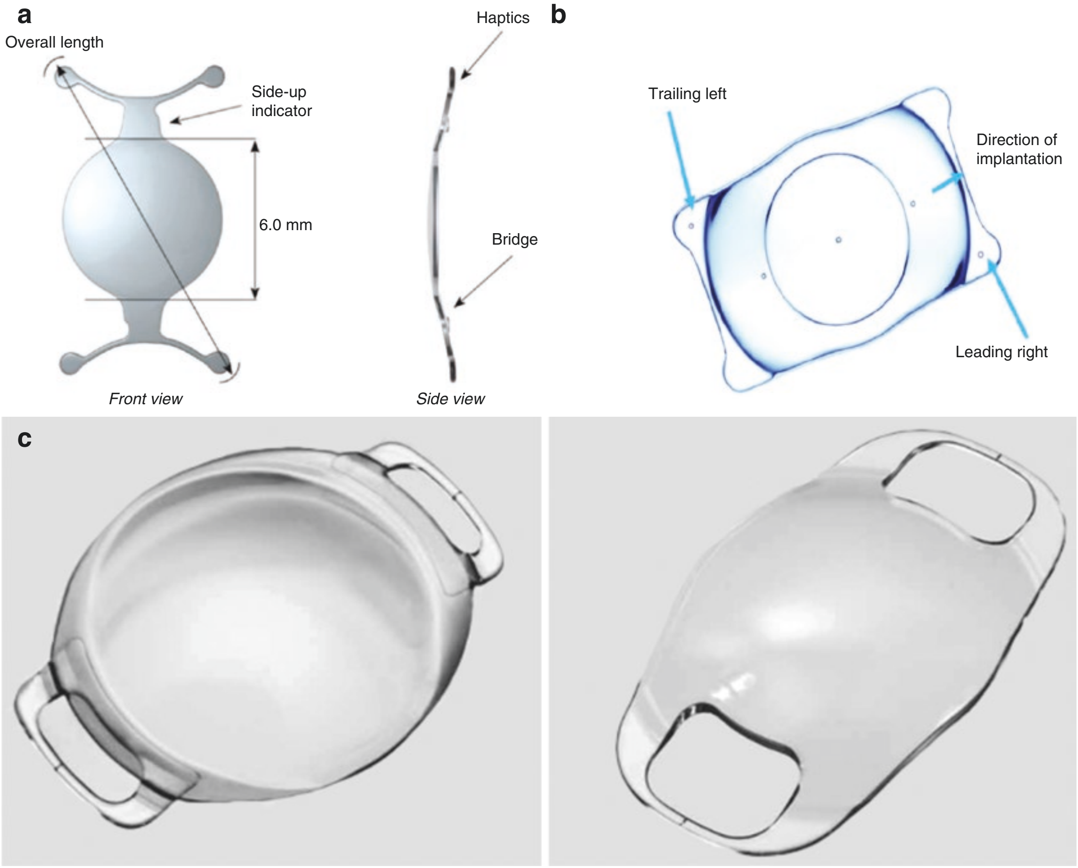

Fig. 14.11 Anterior chamber phakic IOLs (AC IOLs). (**a**) AcrySof Cachet (Alcon) IOL. (**b**) Visian ICL. (**c**) Veriflex IOL

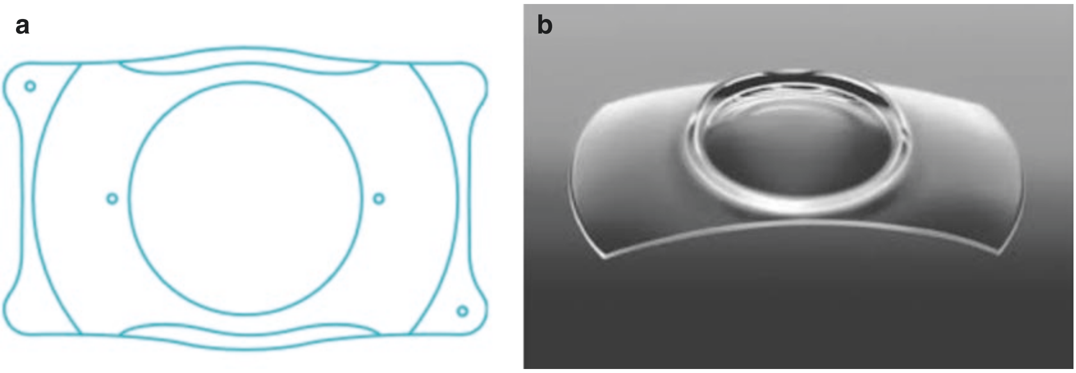

Fig. 14.12 (**a**) STAAR surgical ICL – made of collagen copolymer (acrylic and less than 0.1% porcine collagen) with a refractive index of 1.45 at 35 °C; optical zone diameter between 4.5 and 5.5 mm for myopia and 5.5 mm for hyperopia; available powers of −3 to −23 D for myopia and + 3 to 21.5 D for hyperopia. The new (2011) model, V4c Visian ICL with KS Aquaport, VICMO incorporates a central 0.36 mm diameter port that precludes the need for preoperative iriditomies (**b**) CIBA PRL – made of ultrathin silicon polymer, with refractive index of 1.46; length of 10.8 or 11.3 mm (myopia) and 10.6 mm (hyperopia); and width of 6.0 mm; available powers of −3 to −20 for myopia and + 3 to +15 for hyperopia

(ICL; STAAR Surgical), the Phakic Refractive Lens (PRL; CIBA Vision, Embrach, Switzerland), and the Sticklens, (IOLTech, France), which is currently under evaluation (Figs. 14.12a, b). Reported complications include endothelial cell loss and lens opacification. A 8-year follow-up study reported the opacification rate of 5% at 8 years, with phacoemulsification rate of 5% (41 eyes total) [150] while a 10-year follow-up study reported 28% at 10 years, with phacoemulsification rate of 17% at 10 years (111 eyes total), respectively [151]. Another 10-year follow-up study reported 55% lens opacification (CI 45–63%) with 18% phacoemulsification rate (CI 10–26%) out of 133 eyes [152]. With the zonular-supported PRLs, although quite infrequent, cataract formation and a rare, specific complication of PIOL, posterior luxation, are reported. Preservation of corneal anatomy and asphericity, image magnification, potential gain in vision lines, and less reduction of contrast sensitivity are some of the advantages of PIOLs over refractive surgery. Compared to AC PIOLs, the advantages of PIOLs are fewer incidences of halos and glare and less endothelial cell destruction. However, some complications that may occur include cataract formation, endothelial cell damage, pupillary block glaucoma, pigment dispersion, inflammation, and infection. Cataract formation incidence is also higher for PC PIOLs compared to AC PIOLs because of the normal nutrition impairment of the natural lens due to proximity between it and the IOL [153].

Toric IOLs

Toric IOLs are suitable for treating both cataract and astigmatism simultaneously. The first toric IOL was designed by Shimizu et al. in 1992 to correct corneal astigmatism during cataract surgery [154]. This lens was a three-piece polymethyl methacrylate (PMMA) nonfoldable IOL that required a large 5.7 mm corneal incision. Two kinds of toric phakic IOLs are available that are suitable for postkeratoplasty surgery: [1] the iris-fixated toric Artisan/Verisyze and [2] the posterior chamber Visian T-ICL (toric implantable Collamer lens). The IOLs can be placed opposite a clear corneal incision, on the corneal incision on the step meridian, on the peripheral corneal relaxing incision (up to 9D) to treat astigmatism [155]. It is important to measure preoperative corneal astigmatism accurately, and these can be achieved by methods of corneal topography, manual and automated keratometry, and Scheimpflug imaging. The IOL power calculations can be done by calculation programs available; standard astigmatism vector analysis based individually calculated personalized IOL calculation is more accurate than standard calculation method.

Typically, good visual outcomes are reported toric IOL implantation with a very small amount of residual astigmatism [156–158]. Multifocal toric IOL implantation can offer spectacle independence for near, distance, and intermediate vision independent of corneal astigmatism [159–160]. However, there are chances for more complications after multifocal toric IOL implantations such as accurate estimation of corneal astigmatism and rotational stability [159]. Overall, toric IOLs are reported to provide satisfactory astigmatism correction, often providing better results than monofocal IOLs or limbal relaxing incisions (LRIs) [156]. Bilateral toric IOLs are even reported to improve subjective vision quality [157].

APHAKIC IOLs

Charles Kelman started the modern era of cataract surgery with the introduction of phacoemulsification surgery in 1967 [161]. Cataract surgeries can be performed with multifocal, accommodating or toric IOLs.

Cataract Surgery with Multifocal IOLs (MFIOLs)

Multifocal IOLs are usually the preferred option for achieving spectacle independence across a wide range of distances postcataract and postrefractive lens exchange surgery. Most important factors that influence the choice of MFIOLs include patient's age, needs, lifestyle, and psychological profile; patient's pupil reactivity and size in various light conditions; patient's ophthalmic condition and associated eye comorbidities (especially relating to contrast sensitivity function); evidence from peer-reviewed literature, especially the defocus curve of the lens; and surgeon's attitude, education, and experience [162]. Three designs of available MFIOLs are refractive, diffractive, and a combination of the former two designs. Refractive MFIOLs can be rotationally symmetric or asymmetric, and work by providing appropriate focus for both near and distant objects through the annular zones of various refractive powers. Pupil size dynamics and decentration, intolerance to kappa angle, rough areas between zones (contributing to potential halos and glare), and loss of contrast sensitivity affect the visual outcomes of refractive MFIOLs [162]. Diffractive MFIOLs contain diffractive microstructures in concentric zones and decreasing distance between the annular zones, called the Fresnel-zone plate to produce optic foci. Near multifocality is achieved by the combination of anterior and posterior surface powers along with 1st order diffraction, while distance multifocality is achieved by the combination of anterior and posterior surface powers along with 0th order diffraction [162]. Compared to the refractive MFIOLs, the diffractive MFIOLs are more tolerant to the decentration and kappa angle, and less pupil size dependent, but they have a higher potential for glare and halos due to the nontransition areas. Some commonly used MFIOLs include Restor bifocal IOL, AcrySof refractive-diffractive IOL, PanOptix (Alcon) trifocal/refractive IOL, At Lisa (Carl Zeiss Meditec) bifocal/trifocal diffractive IOL, and Mplus Lentis (Oculentis) bifocal refractive IOL [155].

A systematic review and meta-analysis [163] of multifocal vs monofocal IOL outcomes based on 21 randomized controlled trials (RCTs) with 22,951 subjects found that MFIOLs performed better on uncorrected intermediate VA (at 60 cm) and uncorrected near VA, as well as distance corrected intermediate VA (at 60 cm) and distance corrected near VA compared to the monofocal IOLs. No statistically significant differences were found between the two groups for uncorrected and corrected distance VA. In terms of contrast sensitivity and spectacle independence, the MFIOL group performed better than the monofocal group; however, the patients experienced greater amounts of glare and halos in the MFIOL group [163]. A few other studies also have reported more dysphotopsia, glare, and halo (3.5 times more) in MFIOLs in comparison to monofocal IOL implantations [164–165], although dysphotopsia tends to reduce over time due to neuroadaption. Other issues resulting from multifocal IOLs are night driving and low-contrast issues [166]. Another interventional case series study [167] of 26 emmetropic presbyopic patients who underwent trifocal diffractive IOL implantation following femtolaser-assisted cataract surgery (FLACS) and refractive lens exchange (RLE) found satisfactory near, intermediate, and distance visual outcomes at 6 months. No intraoperative or postoperative complications were observed, and 96% [24] patients said that they would recommend the procedure to their family and friends [167].

Cataract Surgery with Accommodating IOLs

Accommodating IOLs work by providing dynamic increase of dioptric power as per the focus needs at near, intermediate or distance vergence [168–169]. The IOL mechanisms can be truly accommodating or pseudoaccommodating. Pseudoaccommodative mechanisms include miosis, higher-order aberration induction and lens tilt [168]. Shape changing, single or dual optic position changing, lens filling, and refractive index modulating mechanisms are some of the design strategies that are employed in designing accommodating IOLs [168]. The Crystalens® (Crystalens Bausch and Lomb, Inc., Rochester, NY) was the first accommodating IOL to be approved by the FDA – the original version was approved in 2003, the "high-definition" version in 2008, and the toric version in 2010. Trulign® (also by Bausch and Lomb) is another accommodating IOL to be approved by the FDA, but it is currently only allowed to be described as offering "a broad range of vision" instead of accommodating [170]. The Crystalens is a biosil-based hinged plate-haptic IOL, which is thought to provide accommodation through changing the position and shape of the axis [168]. A 2010 meta-analysis [171] comparison of accommodating and monofocal IOLs restoring accommodation after cataract surgery looked at 12 RCTs with 727 eyes and found greater anterior displacement of accommodating IOLs (an average of 0.84 mm displacement has been reported from cyclopentolate cycloplegia to pilocarpine-stimulated accommodation [172]), although heterogeneity was reported among different studies using different testing methodologies.

Good visual outcomes are reported in the literature with the implantation of accommodating IOLs. In a study of patient satisfaction levels at a mean of 5.4 years after cataract surgery implantation with bilateral accommodating IOL, 90% of 68 patients reported being "very satisfied" [173]. The study compared the patient satisfaction rates between accommodating IOL and multifocal IOL implantations; patients in MFIOL group experienced more glares and halos compared to the accommodating IOL group [173]. A complication that can occur during the accommodative effort with Crystalens is capsular contraction syndrome, occurring from the changes in the tilt/shape of the IOL (called "accommodative arching"). The "accommodative arching" can temporarily induce myopic astigmatism and/or higher-order aberrations. These effects are varied depending on the variability of capsular bag size, fibrosis, and medications with anticholinergic side effects. In some cases, the "accommodative arching" can alter the intended position of the IOL optic, resulting in a z-syndrome with asymmetric capsular contraction leading to astigmatism along the IOL axis [168]. Some methods to mitigate the complication of z-syndromes include early treatment of capsular fibrosis and striate with Nd:YAG laser, insertion of capsular tension ring and IOL exchange depending on the severity of the condition [168, 174]. Measures to avoid the formation of z-syndrome includes creating a round, central capsulorhexis with anterior capsule covering plate haptics, polishing the underside of anterior capsular leaflets, meticulous cortical cleanup, rotation of IOL vaulted posteriorly along the posterior capsule, and construction of a water-tight wound [175].

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