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Corneal Remodeling

Clinical Policy Bulletins | Medical Clinical Policy Bulletins

Number: 0023

Policy

I. **Post-Cataract Post-Transplant Corneal Surgery**

Aetna considers correction of surgically induced astigmatism with a corneal relaxing incision (including limbal relaxing incisions) or corneal wedge resection medically necessary if the member had previous penetrating keratoplasty (corneal transplant) within the past 60 months or cataract surgery within the last 36 months and both of the following criteria are met:

A. The degree of astigmatism must be 3.00 diopters or greater; *and*
B. The member must be intolerant of glasses or contact lenses.

Note: Correction of surgically induced astigmatism with a corneal relaxing incision (including limbal relaxing incisions) or corneal wedge resection is covered when medical necessity criteria are met, even if the member's plan excludes refractive surgery.

II. **Phototherapeutic Keratectomy**

Aetna considers phototherapeutic keratectomy (PTK) medically necessary for members with *any* of the following corneal conditions:

Policy History

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03/11/2022
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Review History

Definitions

Additional Information

Clinical Policy Bulletin Notes

A. Corneal scars and opacities (including post-traumatic, post-infectious, post-surgical, and secondary to pathology); *or*
B. Epithelial membrane dystrophy; *or*
C. Irregular corneal surfaces due to Salzmann's nodular degeneration or keratoconus nodules; *or*
D. Recurrent corneal erosions when more conservative measures (e.g., lubricants, hypertonic saline, patching, bandage contact lenses, gentle debridement of severely aberrant epithelium) have failed to halt the erosions; *or*
E. Superficial corneal dystrophy (including granular, lattice, and Reis-Bückler's dystrophy).

Aetna considers PTK experimental and investigational for the treatment of infectious keratitis and all other indications because it has not been shown to be safe and effective for these indications.

Note: Phototherapeutic keratectomy (PTK) should not be confused with photorefractive keratectomy (PRK). Although technically the same procedure, PTK is used for the correction of particular corneal diseases, whereas PRK involves use of the excimer laser for correction of refractive errors (e.g., myopia, hyperopia, astigmatism, and presbyopia) in persons with otherwise non-diseased corneas.

III. **Refractive Surgery**

Note: Aetna's standard HMO benefit plan excludes coverage of "radial keratotomy, including related procedures designed to surgically correct refractive errors". Traditional benefit plans generally exclude coverage for services "for or related to any eye surgery mainly to correct refractive errors". These exclusions apply to radial keratotomy (RK), astigmatic keratotomy, PRK, photoastigmatic keratectomy (PARK), laser-in-situ keratomileusis (LASIK), keratomileusis, epikeratophakia, implantation of intrastromal corneal ring segments, and other refractive surgical procedures.

For plans that do not have a specific contractual exclusion of refractive surgery, refractive surgery is considered experimental and investigational or not medically necessary, as is outlined below.

For the U.S. Food and Drug Administration (FDA)-approved indications and indications accepted by the American Academy of Ophthalmology (AAO), refractive surgical procedures are considered not medically necessary, because spectacles or contact lenses have been shown to provide more accurate corrections of refractive errors than refractive surgery.

A. *Radial keratotomy (RK)* is not considered medically necessary for the treatment of myopia ranging from -2.00 to -8.00 diopters because this refractive error can be corrected satisfactorily with eyeglasses or contact lenses. Radial keratotomy is considered investigational for treatment of myopia greater than -8.00 diopters and all other refractive errors because its effectiveness for these indications has not been established.

B. *Minimally invasive radial keratotomy (Mini-RK)* is considered experimental and investigational for the treatment of myopia and other indications.

C. *Astigmatic keratotomy (AK)* (arcuate incision, corneal wedge resection) is considered medically necessary when performed for the correction of surgically induced astigmatism following medically indicated cataract removal or corneal transplant surgery. Astigmatic keratotomy is considered investigational for treatment of all other refractive errors because its effectiveness for these indications has not been established.

D. *Hexagonal Keratotomy (HK)* is considered experimental and investigational for the treatment of hyperopia, or presbyopia following radial keratotomy because its effectiveness for these indications has not been established.

E. *Laser-in-situ keratomileusis (LASIK)* is considered not medically necessary for treatment of myopia between -1.0 and -15.0 diopters, with or without astigmatism up to 5.0 diopters, because this can be corrected satisfactorily with eyeglasses or contact lenses. Laser-in-situ keratomileusis is also considered not medically necessary for treatment of hyperopia up to + 6.0 diopters with or without astigmatism up to 5 diopters. Laser-in-situ keratomileusis is considered investigational for treatment of myopia greater than -15.0 diopters or hyperopia greater than + 6.0 diopters, for treatment of persons with astigmatism greater than 5.0 diopters, and for all other refractive errors. This clinical policy is based on the FDA-approved indications for LASIK.

F. *Standard keratomileusis (ALK)* is considered experimental and investigational for the treatment of all refractive errors because its effectiveness for trestment of refractive errors has not been proven.

G. *Epikeratoplasty (or epikeratophakia)* is considered medically necessary for the following indications: (i) for the treatment of childhood aphakia since contact lenses are difficult for children to use and intraocular lens implants may result in long-term complications in children; (ii) for the treatment of scarred corneas and corneas affected with endothelial dystrophy; (iii) for the treatment of adult aphakia in circumstances where secondary implantation of an intra-ocular lens is not feasible because reentering the eye could affect outcome (e.g., vitreous in the anterior chamber, history of uveitis, disorganized anterior chamber that cannot support an intraocular lens, significant corneal endothelial disease, or gross corneal irregularity after trauma).This procedure is considered investigational for correction of refractive errors and for all other cases of adult aphakia.

H. *Keratophakia* is considered investigational for correction of refractive errors because its effectiveness for the treatment of refractive errors has not been proven.

I. *Lamellar keratoplasty (non-penetrating keratoplasty)* is considered medically necessary for treatment of anterior necrotizing scleritis without inflammation (scleromalacia perforans), and corneal diseases, including scarring, edema, thinning, distortion, dystrophies, degenerations, and keratoconus. It is considered investigational for pterygium and when performed solely to correct astigmatism and other refractive errors because its effectiveness for these indications has not been established.

J. *Penetrating keratoplasty (PK) (corneal transplantation, perforating keratoplasty)* is considered medically necessary for treatment of corneal diseases, including: (i) to improve poor visual acuity caused by an opaque cornea; (ii) to remove active corneal disease, such as persistent severe bacterial, fungal, or amebic inflammation of the cornea (keratitis) after appropriate antibiotic therapy; (iii) to restore altered corneal structure or to prevent loss of the globe that has been punctured; and (iv) to treat corneal diseases, including bullous keratopathy, keratoconus, corneal scar with opacity, keratitis, corneal transplant rejection, Fuch's dystrophy, corneal degeneration, other corneal dystrophies, corneal edema, and herpes simplex keratitis. Penetrating keratoplasty is considered investigational when performed solely to correct astigmatism or other refractive errors because its effectiveness for these indications has not been established. Tissue procurement, preservation, storage and transportation associated with medically necessary corneal transplantation are also considered medically necessary. **Note**: Intralase-

Enabled Keratoplasty (IEK) is an accepted method of penetrating keratoplasty; there is no difference in laser versus cold knife outcomes.

K. *Photorefractive keratectomy (PRK) and Photoastigmatic keratectomy (PARK or PRK-A)* are considered not medically necessary for individuals with hyperopia of up to 6.0 diopters and myopia of up to -10.0 diopters, with or without astigmatism up to 4.0 diopters, because the refractive corrections achieved with PRK and PARK are less precise than that achieved by eyeglasses or contact lenses. Photorefractive keratectomy and PARK are considered investigational for individuals with hyperopia greater than 6.0 diopters, myopia greater than -10.0 diopters, astigmatism greater than 4.0 diopters, and for all other refractive errors. This policy is based on the FDA approved indications for PRK and PARK.

L. *Intrastromal corneal ring segments (INTACS)* (Addition Technology, Sunnyvale, CA) are considered not medically necessary for adults with mild myopia (from -1.0 to -3.0 diopters) that have less than 1 diopter of astigmatism. Aetna considers intrastromal corneal ring segments experimental and investigational for children, for persons with moderate-to- severe myopia (greater than -3.0 diopters), for persons with more than 1 diopter of astigmatism, and for hyperopia because their effectiveness for these indications has not been established. Intrastromal corneal ring segments are considered medically necessary for reduction or elimination of myopia or astigmatism in persons with keratoconus or pellucid marginal degeneration who are no longer able to achieve adequate vision using contact lenses or spectacles and for whom corneal transplant is the only remaining option, in persons with a clear central cornea and corneal thickness of 450 microns or greater at the proposed incision site. Intrastromal corneal ring segments are considered experimental and investigational for other indications because their effectiveness for indications other than the ones listed above has not been established. **Note**: Where indicated for keratoconus or pellucid marginal degeneration, INTACS are not excluded from coverage under plans that exclude coverage of refractive surgery. Please check benefit plan descriptions.

M. *Conductive Keratoplasty* is considered not medically necessary for the treatment of individuals who are at least 40 years of age, who have mild-to- moderate hyperopia (0.75 D to 3.25 D), who have 0.75 D or less astigmatism, and whose eyesight has changed very little over the previous 12 months (as demonstrated by a change of less than 0.50 D in refraction). Conductive keratoplasty is considered experimental and

investigational for keratoconus and all other indications because its effectiveness for these indications has not been established.

N. *Methods of thermokeratoplasty* other than conductive keratoplasty (see above), such as the superficial treatment of Gassett and Kaufman for keratoconus, holmium:YAG laser thermokeratoplasty (laser thermokeratoplasty or LTK), or the hot needle of Fyodorov, are considered experimental and investigational for treatment of refractive errors, keratoconus, and all other indications because their effectiveness for these indications has not been established.

O. *Orthokeratology* is considered investigational for correction of refractive errors and all other indications because its effectiveness for these indications has not been established.

P. *Scleral Expansion Surgery* is considered experimental and investigational for presbyopia and all other indications because its effectiveness for these indications has not been established.

Q. *Intraocular lens implants (clear lens extraction)* (aphakic intra-ocular lenses (IOLs)) are considered not medically necessary for correction of presbyopia, hyperopia, and myopia because these refractive errors can be corrected satisfactorily with eyeglasses or contact lenses. Intra-ocular lens implants are considered medically necessary for persons with aphakia (see CPB 0508 - Cataract Removal Surgery (../500_599/0508.html)).

R. *Implantable contact lenses (without lens extraction)* (phakic IOLs) (e.g., the Artisan [model 204 and 206] phakic IOL, also known as the Verisye [e.g., VRSM5US and VRSM6US] phakic IOL, and the Collamer lens [e.g., Visian ICL]) is considered not medically necessary for severe myopia because these refractive errors can be corrected satisfactorily with eyeglasses or contact lenses. The Artisan (model 204 and 206) phakic IOL is considered not medically necessary for: (i) the reduction or elimination of myopia in adults with myopia ranging from -5 to -20 diopters with less than or equal to 2.5 diopters of astigmatism at the spectacle plane and whose eyes have an anterior chamber depth (acd) greater than or equal to 3.2 millimeters; and, (ii) individuals with documented stability of refraction for the prior 6 months, as demonstrated by spherical equivalent change of less than or equal to 0.50 diopters. The Visian ICL is considered not medically necessary for adults 21 to 45 years of age to (i) correct myopia ranging from -3.0 diopters to less than or equal to -15.0 diopters with less than or equal to 2.5 diopters of astigmatism at the spectacle plane; (ii) to reduce myopia ranging from

greater than -15.0 diopters to -20.0 diopters with less than or equal to 2.5 diopters of astigmatism at the spectacle plane; and (iii) with an anterior chamber depth (acd) 3.00 mm or greater, and a stable refractive history within 0.5 diopter for 1 year prior to implantation. Phakic IOLs are considered experimental and investigational for all other indications because their effectiveness for indications other than the ones listed above has not been established.

IV. **Coverage of Corneal Remodeling Surgery to Correct Refractive Errors in Plans that Explicitly Cover Refractive Surgical Procedures**

Note: For members whose policies specifically include coverage for refractive surgery, refractive surgical procedures are covered for their FDA-approved indications and indications accepted by the AAO, without regard to medical necessity. (The FDA-approved indications for refractive surgical procedures are listed in section III above). Also, RK (which does not require FDA approval) is covered for indications recognized by the AAO as established -- mild to moderate myopia of -8.00 diopters or less. (See discussion of established indications for RK in section III above). Aetna's payment for these services does not constitute any determination by Aetna that those services are medically necessary.

V. **Keratoprosthesis (Artificial Cornea)**

The Boston Keratoprosthesis (Boston KPro) may be considered medically necessary for corneal blindness in members who meet the following medical necessity criteria:

A. The cornea is severely opaque and vascularized, with vision less than 20/400 in the affected eye and lower than optimal vision in the opposite eye; *and*
B. The member has had 2 or more prior failed penetrating keratoplasties (corneal transplants), with poor prognosis for further grafting; *and*
C. The member does not have end-stage glaucoma or retinal detachment.

Aetna considers the Boston KPro keratoprosthesis experimental and investigational for all other indications (e.g., treatment of primary congenital glaucoma; not an all-inclusive list) because their effectiveness for indiactions other than the one listed above has not been established.

Aetna considers the AlphaCor keratoprosthesis experimental and investigational because of insufficient evidence of its effectiveness.

VI. Endothelial Keratoplasty

Aetna considers endothelial keratoplasty (Descemet's stripping endothelial keratoplasty (DSEK), Descemet's stripping automated endothelial keratoplasty (DSAEK), and Descemet's membrane endothelial keratoplasty (DMEK) medically necessary for the following indications in persons with endothelial failure and otherwise healthy corneas:

- Bullous keratopathy;
- Corneal edema (except corneal hydrops);
- Endothelial corneal dystrophy and other posterior corneal dystropies;
- Mechanical complications due to corneal graft or ocular lens prostheses;
- Rupture of Descemet's membrane.

Aetna considers endothelial keratoplasty procedures experimental and investigational for conditions with concurrent endothelial disease and anterior corneal disease, including anterior corneal dystrophies, anterior corneal scars from trauma or prior infection, ectatic conditions of the cornea such as keratoconus, pellucid marginal degeneration and ectasia after previous laser vision correction surgery, and for all other indications (e.g., corneal hydrops, iris atrophy, and toxic anterior segment syndrome) because their effectiveness for these indications has not been established.

VII. Collagen Cross-Linking for Keratoconus

Aetna considers epithelium-off photochemical collagen cross-linkage using riboflavin (Photrexa) and ultraviolet A medically necessary for keratoconus and keratectasia.

Aetna considers photochemical collagen cross-linkage experimental and investigational for all other indications because its effectiveness for other indications has not been established.

Aetna considers epithelium-on (transepithelial) collagen cross-linkage experimental and investigational for keratoconus, keratectasia, and all other indications.

Aetna considers performance of photochemical collagen cross-llinkage in combination with other procedures (CXL-plus) (e.g., intrastromal corneal ring segments, PRK or phakic intra-ocular lens implantation) experimental and investigational.

VIII. **Excimer Laser Crescent Keratectomy for Keratoconus**

Aetna considers crescent keratectomy performed with an excimer laser experimental and investigational for the management of keratoconus because the effectiveness of his approach has not been established.

Background

Refractive surgical procedures are considered by Aetna to be not medically necessary, because spectacles or contact lenses have been shown to provide more accurate corrections of refractive errors than refractive surgery. Although the efficacy of refractive surgery is improving, the accuracy and precision of the refractive corrections achieved is substantially less than that which can be achieved with spectacle correction. In a randomized prospective study of laser in situ keratomileusis (LASIK) and photorefractive keratectomy (PRK) for myopia, Hersh et al (1998) reported that 29.4 % of PRK patients and 27.1 % of LASIK patients had refractive corrections within 0.5 diopters of attempted correction at six months after surgery. In comparison, over 99 % of patients who are corrected with glasses or contact lenses achieve refractive corrections within 0.5 diopters of normal vision (Waring, 1990).

Although the safety of refractive surgical procedures is improving, these procedures are associated with significant risks of degradation of best corrected visual acuity, as well as glare, induced regular or irregular astigmatism, regression of effect, visual aberrations (including transient or permanent glare or starburst/halo effect), and decreased contrast sensitivity. These optical complications and their incidence are discussed

in a 1997 American Academy of Ophthalmology (AAO) Preferred Practice Pattern on Refractive Errors and a 1999 AAO Ophthalmic Procedures Assessment on PRK. According to the AAO Preferred Practice Pattern on Refractive Errors, "spectacles are the simplest and safest means of correcting a refractive error".

Radial Keratotomy (RK) involves the use of radial incisions in the cornea to correct mild to moderate myopia. According to guidelines from the AAO, radial keratotomy has been shown to be effective for treatment of myopia ranging from -2.00 to -8.00 diopters. Radial keratotomy has not been proven to be effective for treatment of myopia greater than -8.00 diopters or for other refractive errors. The established indications for radial keratotomy were based on the 1992 AAO Ophthalmic Procedures Assessment of Radial Keratotomy for Myopia. The AAO's position on RK was reaffirmed in the 1997 AAO Preferred Practice Pattern on Refractive Errors, which restated that RK is indicated for "[l]ow to moderate myopia".

Lindstrom (1995) stated that radial keratotomy (RK) is a common surgical technique for correcting myopia. The RK incisions, like any corneal incisions, permanently weaken the cornea and this structural weakening can cause several complications and side effects, including diurnal fluctuation, progressive hyperopic shift, and the potential for traumatic rupture of the keratotomy scars. This researcher described a new technique -- minimally invasive RK (mini-RK) -- that reduces the millimeters of cornea incised and presented preliminary laboratory and clinical results. In a cadaver eye study, 8 short, deep incisions extending from the 3.0 mm optical zone to the 7.0 mm optical zone produced 92 % of the efficacy of full-length incisions to the 11.0 mm optical zone. This finding was confirmed by intra-operative surgical keratometry in 6 patients in whom a 1 % increase in central corneal flattening was achieved when incisions were extended from the mini-RK configurations to full length. In a retrospective evaluation of 100 patients with -1.0 to -6.0 diopters (D) of myopia, 92 % of eyes were within 1.0 D of emmetropia and 94 % had 20/40 or best corrected visual acuity (BCVA). No significant complications were encountered. The author concluded that mini-RK may be a useful alternative to reduce the invasiveness of RK but retain its efficacy in eyes with low to moderate myopia.

Shoji et al (2003) reported a case of central corneal haze induced by mini-RK after PRK and subsequent deep lamellar keratoplasty. These investigators reported a case (1 eye of 1 patient) of central corneal haze that worsened after mini-RK was performed 2 years following PRK. Four years later, a second PRK was done, myopic regression was subsequently observed, and corneal haze persisted. Deep lamellar keratoplasty was performed and a corneal graft was taken, which was examined by light and electron microscopy. In the ablated area, irregularity of the basal membrane and hypertrophy of the corneal epithelium were observed. In the stromal layer, collagen fibers showed disorder in their disposition. Aggregated activated keratocytes were observed. An epithelial plug filling the gap of the RK incision persisted for 6 years after the mini-RK. The RK incision was easily divided when deep lamellar keratoplasty was performed and the patient obtained a stable visual outcome. The authors concluded that It is possible that mini-RK enhancement after PRK induced central corneal haze and reduces corneal integrity. Deep lamellar keratoplasty for refractory corneal haze after refractive surgery was useful in this eye.

Astigmatic Keratotomy (AK) (arcuate incision, corneal wedge resection) is a refractive surgical procedure similar to RK that is used to reduce astigmatism. Instead of radial incisions, a curvilinear pattern is used to smooth the areas of the cornea that are too steeply curved. In some instances, surgeons have combined RK with AK in patients with myopia with astigmatism. Variations of astigmatic keratotomy include the Ruiz Procedure and the Troutman Wedge Resection. Astigmatic keratotomy may be indicated for the correction of surgically induced astigmatism following medically indicated cataract removal or corneal transplant surgery. Astigmatic keratotomy has not been proven for treatment of other refractive errors. The 1997 AAO Preferred Practice Pattern on Refractive Errors states: "[T]here are few well-controlled, prospective clinical studies available on the procedure to date, performed either individually or in connection with other keratorefractive procedures".

Laser-In-Situ Keratomileusis (LASIK) is a type of laser surgery of the cornea to correct refractive errors, in which a slice of the patient's cornea is removed, shaped to the desired curvature with an excimer laser, and then sutured back to the remaining cornea. Laser-in-situ keratomileusis is approved by the Food and Drug Administration (FDA) for treatment of

myopia between -1.0 and -15.0 diopters, with or without astigmatism up to 5.0 diopters. Laser-in-situ keratomileusis has also been approved by the FDA for treatment of hyperopia up to + 6.0 diopters with or without astigmatism up to 5 diopters. Laser-in-situ keratomileusis has not been proven to be effective for treatment of myopia greater than -15.0 diopters or hyperopia greater than + 6.0 diopters, for treatment of persons with astigmatism greater than 5.0 diopters, and for other refractive errors.

Standard Keratomileusis (ALK) where the cornea is shaped with a microkeratome rather than with a laser, has not been proven to be an effective treatment for refractive errors. The 1997 AAO Preferred Practice Pattern on Refractive Errors states "In its 1995 assessment on ALK, the American Academy of Ophthalmology identified a lack of peer-reviewed literature, although there are a number of studies ongoing. In current clinical practice, ALK is being replaced by laser in situ keratomileusis".

Epikeratoplasty (or Epikeratophakia) is a refractive surgical procedure that involves placement of a pre-carved donor corneal lens on the surface of a patient's eye. Epikeratophakia may be indicated for the treatment of childhood aphakia since contact lenses are difficult for children to use and intraocular lens implants may result in long-term complications in children. This procedure may also be used on scarred corneas and corneas affected with endothelial dystrophy. In addition, although secondary implantation of an intraocular lens is the favored treatment of adult aphakia, there are circumstances where reentering the eye could affect outcome (e.g., vitreous in the anterior chamber, history of uveitis, disorganized anterior chamber that cannot support an intraocular lens, significant corneal endothelial disease, or gross corneal irregularity after trauma); in these cases of adult aphakia, epikeratophakia may be considered acceptable. This procedure is has not been proven to be effective for the correction of refractive errors and for all other cases of adult aphakia. The 1997 AAO Preferred Practice Pattern on Refractive Errors states that "[t]he results have been widely variable, and there have been significant complications. This procedure is not recommended for correction of myopic refractive errors, except in very unusual circumstances". This re-affirmed the 1995 AAO Ophthalmic Procedure Assessment of epikeratophakia.

Keratophakia involves implantation of a donor cornea within the corneal stroma to modify its refractive power. Keratophakia has not been proven to be effective for correction of refractive errors. Keratophakia was not addressed in the 1997 AAO Preferred Practice Pattern on Refractive Errors. However, an August 1992 AAO Ophthalmic Procedure Assessment of keratophakia concluded that they found only a "handful of reports" in peer-reviewed medical journals regarding keratophakia for correction of refractive errors, and few "well controlled studies". The AAO assessment raised questions about the safety and effectiveness of keratophakia. Since publication of the AAO's assessment, no additional clinical studies of keratophakia for refractive errors have been published, so the questions raised by that assessment remain unanswered.

Lamellar Keratoplasty (non-penetrating keratoplasty) is a corneal transplant procedure in which a partial thickness of the cornea is removed and the diseased tissue is replaced with a partial-thickness donor cornea. The donor eye is prepared by making a partial thickness trephine incision in the cornea and dissecting free the lamellar button. This procedure may be indicated for a number of corneal diseases, including scarring, edema, thinning, distortion, dystrophies, degenerations, and keratoconus. It is has not been proven to be effective for correction of astigmatism and other refractive errors.

Scleromalacia is defined as bilateral and painless degenerative thinning of the sclera occurring in individuals with rheumatoid arthritis (RA). In this condition rheumatoid nodules may develop in the sclera and cause perforation (scleromalacia perforans). Synonyms are necrotizing scleritis without inflammation; scleritis necroticans.

Mauriello and Pokorny (1993) reported the successful use of split-thickness dermal grafts for repair of corneal and scleral defects in 10 patients (11 eyes) who had non-infectious, impending, or overt ocular perforation. In all patients, traditional methods of reconstruction were deemed inappropriate or had already failed. Corneoscleral defects occurred after various operations: pterygium excision, retinal detachment repair, insertion of a kerato-prosthesis (Cardona implant) into an opaque, vascularized cornea, and penetrating keratoplasty. Other causes of corneoscleral defects were scleromalacia perforans, idiopathic systemic vasculitis, alkali burn, ocular cicatricial pemphigoid, and band keratopathy

with recurrent erosion following intra-ocular metallic foreign body. These investigators proposed the use of split-thickness grafts for the following: When adjacent conjunctiva is inadequate to cover a corneoscleral defect owing to its large size or great depth or to conjunctival scarring from previous operations, injury, or ocular cicatricial pemphigoid; or as an alternative to autogenous grafts such as conjunctiva, cartilage, fascia lata, tibial periosteum, or mucous membrane as well as to homologous scleral and lamellar grafts. Dermal grafts are advantageous in that they are autogenous, non-antigenic, survive on avascular surfaces, and self-epithelialize; therefore, need not be covered by conjunctiva. Furthermore, they are pliable, have excellent tensile strength, provide ample tactile support, and are abundantly available. Dermal grafts are harvested from the dermal bed of the thigh after an epidermal flap is hinged at one end.

Ayyala and Armstrong (1998) noted that post-operative endophthalmitis may present in an atypical fashion (absent or minimal anterior chamber reaction) in the presence of underlying immunosuppressive disorder. These researchers described an apparently healthy 58-year-old man who displayed endophthalmitis with minimal anterior chamber reaction following penetrating keratoplasty for granular corneal dystrophy with underlying acute myeloid leukemia. Scleromalacia perforans in association with pyoderma gangrenosum subsequently developed, leading to ciliary staphyloma and corneal melting. Pyoderma gangrenosum is an uncommon, idiopathic skin disease that may also have ocular manifestations.

Gu and colleagues (2013) reported 2 cases of peripheral ulcerative keratitis that were treated with lamellar keratoplasty.

Furthermore, an UpToDate review on “Treatment of scleritis” (Dana, 2021) states that “Treatment of scleritis always requires systemic therapy with non-steroidal anti-inflammatory drugs (NSAIDs), glucocorticoids, or other immunosuppressive drugs. In one study, 67 % of patients required either high-dose glucocorticoids or the combination of high-dose glucocorticoids and another immunosuppressive agent to control the disease]. In some patients, particularly those with peripheral ulcerative keratitis or scleromalacia perforans, surgical intervention is required to preserve vision or prevent globe rupture”.

Penetrating Keratoplasty (PK) (corneal transplantation, perforating keratoplasty) is a corneal transplant procedure involving replacement of the full thickness of the cornea with donor cornea, but retaining the peripheral cornea. As with lamellar keratoplasty, this procedure may be indicated for a number of corneal diseases. Most PKs are performed to improve poor visual acuity caused by an opaque cornea. Penetrating keratoplasty has also been used to remove active corneal disease, such as persistent severe bacterial, fungal, or amebic inflammation of the cornea (keratitis) after appropriate antibiotic therapy. Penetrating keratoplasty has also been performed to restore altered corneal structure or to prevent loss of the globe that has been punctured. The most common indications for PK are bullous keratopathy, keratoconus, corneal scar with opacity, keratitis, corneal transplant rejection, Fuch's dystrophy, corneal degeneration, other corneal dystrophies, corneal edema, and herpes simplex keratitis. Penetrating keratoplasty has not been proven to be effective for correcting astigmatism or other refractive errors.

Bahar and colleagues (2009) compared the outcomes of IntraLase-enabled top hat penetrating keratoplasty (IEK) versus retrospective results of manual top hat penetrating keratoplasty (TH-PKP) and conventional PKP. This non-randomized prospective study included 94 eyes: 23 eyes underwent IEK, 36 TH-PKP and 35 conventional PKP. Pre-operative and post-operative manifest refraction, uncorrected and BSCVA, high-order ocular aberrations (HOA), endothelial cell counts and complications were analyzed. At 12 months of follow-up, the mean log MAR BSCVA was 0.32 (SD 0.31) in the IEK group, 0.53 (0.36) in the TH PKP group ($p = 0.03$) and 0.39 (0.30) in the conventional PKP group ($p = 0.4$). The mean spherical equivalent was similar between the groups and was less than -2.2 diopters. The mean cylinder was similar in the IEK and conventional PKP group (3.6 (1.9) diopters and 4.1 (1.8) diopters, respectively), and was significantly lower than the TH-PKP group (5.1 (3.2) diopters, $p = 0.04$). The complications rate and high-order ocular aberrations were similar between the 3 groups studied. The mean endothelial cell loss was significantly lower at 12 months of follow-up in the IEK and the TH-PKP groups versus conventional PKP (32.4 % and 22.3 % versus 40.8 %, respectively) ($p = 0.05$). The mean time to suture removal was 4.1 (1.2) months in the IEK group and 3.9 (1.5) months in the TH-PKP group versus 9.7 (1.1) months in the conventional PKP group ($p < 0.0001$). The authors concluded that IEK is a safe and stable

procedure. It resulted in higher endothelial counts and faster suture removal in comparison with the conventional PKP, and has less astigmatism and better BSCVA in comparison with the manual TH-PKP.

In a retrospective, comparative, case-series study, Mashor et al (2011) compared the visual and refractive outcomes after deep anterior lamellar keratoplasty (DALK) and IEK for keratoconus; 18 eyes that underwent DALK and 18 that had IEK for keratoconus were included in this analysis. Main outcome measures included pre-operative and post-operative BSCVA, refraction, HOA, and complication rate were compared between the 2 groups after all suture removals. Mean time to all suture removal was 11.91 months for the DALK and 6.7 months for the IEK. The mean logMAR BSCVA of patients in the DALK group was 0.28 (20/38) and 0.37 (20/46) in the IEK group ($p < 0.211$). The final sphere was -5.62 and -0.53 in the DALK and IEK groups, respectively ($p < 0.973$). There was statistically significant difference in the astigmatism between the 2 groups with mean manifest cylinder of 3.13 in the DALK group and 5.78 in the IEK group ($p < 0.011$). Total HOA (DALK 6.11 versus IEK 9.32, $p < 0.036$) and total spherical aberrations (DALK 0.44 versus IEK 0.71, $p < 0.041$) were both significantly higher in the IEK group. A total of 44.4 % of eyes underwent astigmatic keratotomy after IEK compared to 5.6 % of eyes in the DALK group ($p < 0.018$; odds ratio [OR] = 13.6 [1.48, 125.31]). Overall complication rates were similar for DALK and IEK groups. The authors concluded that BSCVA and complication rates were similar after DALK and IEK, but each technique has its advantage; IEK offered shorter time to suture removal whereas DALK offered lower post-operative astigmatism and HOA rates.

Shehadeh Mashor et al (2014) compared the outcomes with IEK using Top Hat (TH) versus Zig Zag (ZZ) configuration. This was a retrospective comparative study of 24 eyes that underwent TH and 10 eyes that underwent ZZ IEK. There were no significant differences in LogMar BSCVA (TH- IEK = 0.3; ZZ-IEK = 0.18, $p = 0.18$), spherical equivalent (TH-IEK = -3.55±3.7 diopters (D); ZZ-IEK = -2.69 ± 4.85 D, $p = 0.60$), manifest cylinder (TH-IEK = 3.79 ± 2.43 D; ZZ-IEK = 4.61 ± 3.29 D, $p = 0.45$), topographic astigmatism (TH-IEK = 3.67 ± 2.34 D; ZZ-IEK = 4.26 ± 1.1 D, $p = 0.63$), total HOA (TH-IEK = 8.26 ± 3.53; ZZ-IEK = 8.1 ± 4.71, $p = 0.92$), endothelial cell density change from baseline (TH-IEK = -41.55 % ± 15.86; ZZ-IEK = -25.45 % ± 30.66, $p = 0.22$) or time to suture removal

in months (TH-IEK = 7.48 ± 4.07; ZZ-IEK = 6.93 ± 2.71, p = 0.75). There was no difference in requirements for astigmatic keratectomy (TH-IEK = 54.2 % ± 13; ZZ-IEK = 50 % ± 5, OR = 1.18) or complications (TH-IEK = 25 % ± 6; ZZ-IEK = 30 % ± 3, OR = 0.78). The authors concluded that TH-IEK and ZZ-IEK had comparable visual and refractive outcomes, wound healing and endothelial cell counts at 1-year.

Photorefractive Keratectomy (PRK) is a refractive surgical procedure involving the reshaping of the surface of the cornea with an excimer laser to correct mild-to-moderate myopia. *Photoastigmatic keratectomy (PARK or PRK-A)* is a refractive surgical procedure to correct myopia with astigmatism. These procedures have been approved by the FDA for treatment of hyperopia of up to 6.0 diopters and myopia of up to -10.0 diopters, with or without astigmatism up to 4.0 diopters. Photorefractive keratectomy and PARK have not been proven effective for correction of hyperopia greater than 6.0 diopters, myopia greater than -10.0 diopters, astigmatism greater than 4.0 diopters, and other refractive errors. A 1999 AAO Ophthalmic Procedures Assessment on PRK and PARK concluded that it "appears to be safe and effective procedure for the treatment of low to moderate degrees of myopia and astigmatism. Results for high degrees of myopia are associated with poorer outcomes, that is, longer stabilization periods, greater need for retreatment, and increased loss of lines of BSCVA [best spectacle corrected visual acuity]".

Phototherapeutic Keratectomy (PTK) is the same surgical procedure as PRK, but is used for the treatment of corneal diseases. PTK has been approved by the FDA to treat the following corneal conditions: (i) superficial corneal dystrophy (including granular, lattice, and Reis-Bückler's dystrophy); (ii) epithelial membrane dystrophy; (iii) irregular corneal surfaces due to Salzmann's nodular degeneration or keratoconus nodules; (iv) corneal scars and opacities (including post-traumatic, post-infectious, post-surgical, and secondary to pathology); (v) recurrent corneal erosions when more conservative measures (e.g., lubricants, hypertonic saline, patching, bandage contact lenses, gentle debridement of severely aberrant epithelium) have failed to halt the erosions. PTK has not been proven to be effective for treatment of infectious keratitis or other diseases. If used unilaterally PTK will induce a certain degree of anisometropia since it induces a shift in refraction to the hyperopic (farsighted) side. This hyperopic shift might be welcomed in myopes but may be problematic for emmetropes or low myopes.

Intrastromal Corneal Ring Segments (INTACS) (Addition Technology, Sunnyvale, CA) have been approved by the FDA for adults with mild myopia (from -1.0 to -3.0 diopters) that have less than 1 diopter of astigmatism. Intrastromal corneal ring segments have not been proven to be effective in children, and for correction of moderate to severe myopia (greater than -3.0 diopters), for correction of refractive errors in persons with more than 1 diopter of astigmatism, and for correction of hyperopia. Intrastromal corneal ring segments have been approved by the FDA for reduction or elimination of myopia or astigmatism in persons with keratoconus who are no longer able to achieve adequate vision using contact lenses or spectacles and for whom corneal transplant is the only remaining option. INTACS involves inserting a flexible ring beneath the surface of the cornea to elevate the edge of the cornea. This effectively flattens the front of the eye, decreasing nearsightedness. Different size rings are used to correct different amounts of nearsightedness. Boxer Wachler et al (2003) reported on a retrospective study of 74 eyes of 50 persons who received INTACS implantation. The investigators found that the mean improvement in uncorrected visual acuity in persons with keratoconus who received INTACS was four lines of uncorrected visual acuity and two lines of best corrected visual acuity. The investigators also reported decreases in irregular astigmatism. In a prospective study involving 10 patients with keratoconus, Colin et al (2000) reported a 70 % improvement in uncorrected visual acuity and a 50 % improvement in best corrected visual acuity. INTACS was approved by FDA for use in keratoconus under a Humanitarian Device Exemption (HDE), as the FDA has determined that INTACS are a medical device intended to treat a condition that affects fewer than 4,000 individuals per year in the United States (FDA, 2004). INTACS are approved for the reduction or elimination of myopia or astigmatism in persons with keratoconus, who are no longer able to achieve adequate vision with their contact lenses or spectacles, so that their functional vision may be restored and the need for corneal transplant procedure may potentially be postponed. According to the FDA, the specific subset of keratoconic patients proposed to be treated with INTACS prescription inserts are those who:

(i) have experienced a progressive deterioration in their vision, such that they can no longer achieve adequate functional vision on a daily basis with their contact lenses or spectacles; (ii) who are 21 years of age or older; (iii) who have clear central corneas; (iv) who have a corneal thickness of 450 microns or greater at

the proposed incision site; and (v) who have corneal transplantation as the only remaining option to improve their functional vision (FDA, 2004).

According to guidance from the National Institute for Health and Clinical Excellence (2007), INTACS can also be used for pellucid marginal degeneration, a non-inflammatory, peripheral corneal thinning disorder characterized by the erosion of the peripheral band of the inferior cornea.

There is limited evidence for the use of INTACS for corneal ectasia not secondary to keratoconus. A technology assessment concluded that the evidence for the use of INTACS for corneal ectasias other than primary keratoconus consists of case reports and small case series (MAS, 2009).

Conductive Keratoplasty involves the application of radiofrequency thermal energy to increase the curvature of the cornea and thereby reduce hyperopia. Conductive keratoplasty using the ViewPoint CK System (Refractec Inc., Irvine, CA) has been approved by the FDA for treatment of patients who are at least 40 years of age, who have mild to moderate hyperopia (0.75 D to 3.25 D), who have 0.75 D or less astigmatism, and whose eyesight has changed very little over the previous 12 months (as demonstrated by a change of less than 0.50 D in refraction). Conductive keratoplasty has not been proven to be effective for correction of other refractive errors. According to the FDA, conductive keratoplasty temporarily improves distance vision in far-sighted people. Although some patients may retain some or all of the correction achieved during surgery, for most people the amount of farsightedness correction is temporary and will decrease over time. Vision without glasses is improved after conductive keratoplasty, but some people still need glasses or contact lenses. Since it corrects only farsightedness, CKSM does not eliminate the need for reading glasses. Conductive keratoplasty has not been proven to be effective as a treatment of keratoconus.

Methods of thermokeratoplasty other than conductive keratoplasty, such as the superficial treatment of Gassett and Kaufman for keratoconus, holmium:YAG laser thermokeratoplasty (laser thermokeratoplasty or LTK), or the hot needle of Fyodorov, have not been proven to be effective for the treatment of refractive errors or keratoconus. These methods of

thermokeratoplasty have been abandoned because the corneal wound healing response produced postoperative scarring and instability (Waring, 1995).

Orthokeratology involves the application of sequentially flatter hard contact lenses to flatten the cornea and thereby reduce myopic refractive error. Orthokeratology has not been proven to be effective for the treatment of refractive errors. The AAO Preferred Practice Pattern on Refractive Errors states that "[a]ttempts to predict which patients will respond to orthokeratology based on ocular biomechanical or biometric parameters have not been successful. The effects of orthokeratology have been unpredictable and poorly controlled. … This approach is not recommended".

In an ophthalmic technology assessment performed for the AAO, Van Meter et al (2008) reviewed the published literature to evaluate the safety of overnight orthokeratology (OOK) for the treatment of myopia. Repeated searches of peer-reviewed literature were conducted in PubMed and the Cochrane Central Register of Controlled Trials for 2005, 2006, and 2007. The searches yielded 495 citations. The panel reviewed the abstracts of these articles and selected 79 articles of possible clinical relevance for review. Of these 79 full-text articles, 75 were determined to be relevant to the assessment objective. No study was rated as having level I evidence. Two pre-market applications to the FDA were rated as having level II evidence. There were 2 studies rated as having level II evidence. The main source of reports of adverse events associated with OOK was 38 case reports or non-comparative case series (level III evidence). The authors concluded that the prevalence and incidence of complications associated with OOK have not been determined. Complications, including more than 100 cases of infectious keratitis resulting from gram-positive and gram-negative bacteria and Acanthamoeba, have been described in case reports and case series representing observations in undefined populations of OOK users. Data collection was non-standard. Risk factors for various complications can not be determined. Because OOK puts patients at risk for vision-threatening complications they may not encounter otherwise, sufficiently large well-designed cohort or randomized controlled studies are needed to provide a more reliable measure of the risks of treatment and to identify risk factors for complications. These investigators also stated that OOK

for slowing the progression of myopia in children also needs well-designed and properly conducted controlled trials to examine its effectiveness. Because of variations in orthokeratology practice, a wide margin of safety should be built into OOK regimens.

Scleral Expansion Surgery has not been proven to be effective for treatment of presbyopia. Scleral expansion surgery involves making small incisions in the eye and inserting bands to stretch the part of the sclera that lies beneath the ciliary muscles that control accommodation (NICE, 2004). This procedure is claimed to improve accommodation. An assessment of scleral expansion surgery by the National Institute for Clinical Excellence (2004) recommended that "this procedure should not be used". Based on an assessment of available published evidence, the assessment concluded that "[c]urrent evidence on the safety and efficacy of scleral expansion surgery for presbyopia is very limited" and that "[a]ll studies identified were of poor quality". The assessment explained that "[t]here is no evidence of efficacy in the majority of patients" and that "[t]here are also concerns about the potential risks of the procedure".

Glasser (2008) noted that a variety of surgical procedures has been considered for restoring accommodation to the presbyopic eye, including surgical expansion of the sclera, using femtosecond lasers to treat the lens or with so-called accommodative IOLs. The author stated that evidence suggests that scleral expansion can not and does not restore accommodation.

Intraocular Lens Implants (Clear Lens Extraction) (Aphakic Intraocular Lenses (IOLs)) have been approved by the FDA for correction of presbyopia, hyperopia, and myopia. Clear lens extraction is similar to cataract removal surgery in that the natural lens is removed and replaced with an intra-ocular lens.

Implantable Contact Lenses (Without Lens Extraction) (Phakic IOLs) (e.g., the Artisan [model 204 and 206] phakic IOL, also known as the Verisye [e.g., VRSM5US and VRSM6US] phakic IOL, and the Collamer lens [e.g., Visian ICL]). Phakic IOLs are new devices used to correct near-sightedness. These thin lenses are implanted permanently into the eye to help reduce the need for glasses or contact lenses. Phakic refers to the fact that the lens is implanted into the eye without removing the

eye's natural lens. During phakic lens implantation surgery, a small incision is made in the front of the eye. The phakic lens is inserted through the incision and placed just in front of or just behind the iris. The Artisan (model 204 and 206) phakic IOl is indicated for: (i) the reduction or elimination of myopia in adults with myopia ranging from -5 to -20 diopters with less than or equal to 2.5 diopters of astigmatism at the spectacle plane and whose eyes have an anterior chamber depth (acd) greater than or equal to 3.2 millimeters; and, (ii) individuals with documented stability of refraction for the prior 6 months, as demonstrated by spherical equivalent change of less than or equal to 0.50 diopters. The Visian ICL is indicated for adults 21 to 45 years of age to (i) correct myopia ranging from -3.0 diopters to less than or equal to -15.0 diopters with less than or equal to 2.5 diopters of astigmatism at the spectacle plane; (ii) to reduce myopia ranging from greater than -15.0 diopters to -20.0 diopters with less than or equal to 2.5 diopters of astigmatism at the spectacle plane; and (iii) with an anterior chamber depth (acd) 3.00 mm or greater, and a stable refractive history within 0.5 diopter for 1 year prior to implantation. Implantable contact lenses have not been proven to be effective for other indications.

Keratoprostheses have not been proven to be as effective as penetrating keratoplasty using corneal graft tissue. Some patients cannot undergo the standard penetrating keratoplasty using donor tissue for several reasons (e.g., disease severity, severe involvement of the conjunctiva, objection to the use of donor tissue, failed past donor tissue transplants, or when measures required to prevent graft rejection are medically contraindicated). For these individuals, penetrating keratoplasty using a keratoprosthesis has been employed as an alternative. The Alberta Heritage Foundation for Medical Research (AHFMR, 2001) noted that there is inadequate evidence to prove the safety and effectiveness of any keratoprosthesis model, and as keratoprosthesis models keep evolving, these new versions have not yet been proven in human trials with sufficient follow-up and patient numbers. The AHFMR further stated that "currently there is no consensus in the literature on optimal device and implantation techniques, and no accepted standard for this procedure. In general, keratoprosthesis surgery is complicated, has a narrow safety margin, and requires intensive follow-up, thus a conservative approach is currently recommended by the eye specialists in this area". Alio and colleagues (2004) reported that corneal keratoprosthesis (BIOKOP I, II) did not provide a stable anatomical relation with the surrounding ocular

structures. Its ability to restore vision is limited to a short post-operative period in eyes implanted with severe ocular surface disease. The National Institute of Clinical Excellence (NICE, 2004) stated that current evidence on the safety and efficacy of insertion of hydrogel keratoprosthesis does not appear adequate for this procedure to be used without special arrangements for consent and for audit or research.

There is evidence of the effectiveness of the Boston Keratoprosthesis (K-Pro), also known as the Dohlman Doane Boston KPro, for patients with prior failed grafts or as a primary procedure for patients with ocular surface diseases or other conditions that put them at high risk for failed penetrating keratoplasty. The success rate for K-Pro is lower than it is for a low-risk first penetrating keratoplasty in patients with low-risk diagnoses. But, compared to historical controls, the K-Pro success rate may be higher than for repeat penetrating keratoplasty in patients with prior graft failure and other high-risk diagnoses.

Tan et al (2008) established a multi-disciplinary surgical program for osteo-odonto-keratoprosthesis (OOKP) surgery in Asia and evaluated the safety and effectiveness of this keratoprosthesis in end-stage corneal and ocular surface disease. A total of 16 adults of Asian ethnic origin, bilaterally blind with end-stage corneal blindness from Stevens-Johnson syndrome, or severe chemical or thermal burns were included in this study. Osteo-odonto-keratoprosthesis surgery involves 2 procedures-in stage 1, an autologous canine tooth is removed, modified to receive an optical polymethyl methacrylate cylinder, and implanted into the cheek. The ocular surface is denuded and replaced with full-thickness buccal mucosa. Stage 2 surgery, performed 2 to 4 months later, involved retrieval of the tooth-cylinder complex and implanting it into the cornea, after reflection of the buccal mucosal flap, corneal trephination, iris and lens removal, as well as anterior vitrectomy. Concurrent glaucoma and vitreoretinal procedures were also performed at either stage, as required. Main outcome measures included visual acuity (VA), field of vision, anatomical integrity and stability, as well as ocular and oral complications related or unrelated to the OOKP device. Osteo-odonto-keratoprosthesis surgery was performed on 15 patients, with a mean follow-up of 19.1 months (range of 5 to 31). Intra-operative complications included expulsive hemorrhage (keratoprosthesis device not implanted), tooth fracture (n = 1), oronasal fistula (n = 1), and mild inferior optic tilt (n = 1).

Anatomical stability and keratoprosthesis retention has been maintained in all eyes, with no dislocation, extrusion, retro-prosthetic membrane formation, or keratoprosthesis-related infection. Other complications not directly related to device insertion included retinal detachment (RD) related to silicone oil removal (n = 1) and endophthalmitis related to endoscopic cyclophotocoagulation performed 1 year after OOKP surgery (n = 1). Eleven patients (73.3 %) attained a stable best spectacle-corrected VA of at least 20/40 or better, whereas 9 (60 %) attained stable 20/20 vision. Four patients achieved their best visual potential, ranging from 20/100 to counting fingers vision, related to pre-existing glaucomatous optic neuropathy or previous RD. The authors concluded that establishment of their OOKP program suggested that OOKP surgery has the potential to restore good vision to the most severe cases of corneal blindness in an Asian setting, with minimal device-related complications. They stated that longer follow-up (5 years) of these cases is currently underway.

In a review on "Corneal transplantation", Tran and colleagues (2012) noted that in cases of multiple failed corneal transplants or ocular surface diesease for which corneal transplants are likely to fail, artificial corneas (keratoprostheses) have an important role. Several keratoprostheses have been described such as the OOKP, the AlphaCor, and the Boston keratoprosthesis. The AlphaCor is now rarely used because of complications. The Boston type 1 keratoprosthesis (both aphakic and pseudophakic versions) is the most widely used and viable alternative to conventional corneal transplantation.

Chen and colleagues (2020) noted that individuals who have failed 1 or more full thickness penetrating keratoplasties may be offered repeat corneal surgery using an artificial or donor cornea. An artificial or prosthetic cornea is known as a keratoprosthesis. Both donor and artificial corneal transplantations involve removal of the diseased and opaque recipient cornea (or the previously failed cornea) and replacement with another donor or prosthetic cornea. In a Cochrane review, these researchers examined the effectiveness of artificial versus donor corneas in individuals who have had 1 or more failed donor corneal transplantations. They searched the Cochrane Central Register of Controlled Trials (CENTRAL) (which contains the Cochrane Eyes and Vision Trials Register) (2019, Issue 11); Ovid Medline; Ovid Embase;

LILACS (Latin American and Caribbean Health Sciences Literature database); ClinicalTrials.gov; and the World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP). These investigators did not use any date or language restrictions in the electronic search for trials; and they last searched the electronic databases on November 4, 2019. Two review authors independently evaluated reports from the electronic searches to identify randomized controlled trials (RCTs) or controlled clinical trials; any discrepancies were resolved by discussion or consultation. They used standard methodological procedures expected by Cochrane. For discussion purposes, these investigators summarized findings from relevant comparative case series; they performed no data synthesis. These researchers did not identify any RCTs or controlled clinical trials comparing artificial corneas with donor corneas for repeat corneal transplantations. The authors concluded that the optimal management for individuals who have failed a conventional corneal transplantation is unknown. To-date, in some centers, artificial corneal devices are routinely recommended after just 1 graft failure, while in other centers, they are not recommended until after multiple graft failures, or not at all. There have been no controlled trials comparing the visual outcomes and complications of artificial corneal devices (especially the Boston type 1 keratoprosthesis, which is the most commonly implanted artificial corneal device) with repeat donor corneal transplantation, in order to guide surgeons and their patients. These investigators stated that such a trial is needed and would offer significant benefit to an ever-increasing pool of individuals with visual disability due to corneal opacification, most of whom are still in productive stages of their lives.

The Boston KPro Keratoprostheses for the Treatment of Irido-Corneal Endothelial Syndromes

Phillips and associates (2015) assessed the outcome of the KPro-1 in eyes with irido-corneal endothelial syndromes and failed keratoplasties. These investigators performed a retrospective review of every eye with a history of irido-corneal endothelial syndrome and a failed corneal transplant that was treated with a KPro-1 at a tertiary eye care center between January 1, 2008 and July 1, 2014. The main outcome measures were visual outcome, prosthesis retention, and post-operative complications. A total of 4 eyes met the inclusion criteria; 2 eyes had

essential iris atrophy and 2 eyes had Chandler syndrome. All 4 eyes had failed corneal transplants and successful glaucoma drainage devices. The mean patient age at the time of KPro-1 surgery was 68.3 years (range of 60 to 80 years). The mean post-operative follow-up duration was 47 months (range of 27 to 69 months). Pre-operatively, the BCVA was worse than 20/200 in all 4 eyes, including 2 eyes that had hand motions vision. After KPro-1, all 4 eyes initially obtained a BCVA of greater than or equal to 20/70. At the most recent examination, the BCVA was still greater than or equal to20/100 in 3 eyes. The KPro-1 device was retained in all 4 eyes. Post-operative complications included glaucoma progression (1 eye), a retro-prosthetic membrane (1 eye), and sterile vitritis (1 eye). The authors concluded that the Boston KPro-1 may offer a better prognosis than repeat traditional keratoplasty in re-establishing corneal clarity in eyes with irido-corneal endothelial syndromes. Moreover, they noted that despite anatomic success, visual rehabilitation may be compromised by pre-existing glaucomatous optic neuropathy and its post-operative progression. These preliminary findings need to be validated in well-designed studies.

The Boston KPro Keratoprostheses for the Treatment of Primary Congenital Glaucoma

Haugsdal and colleagues (2016) evaluated the KPro-1 in treatment of eyes with primary congenital glaucoma. These researchers performed a retrospective review of every eye with congenital glaucoma that was treated with a KPro-1 at a tertiary eye care center between January 1, 2008 and July 1, 2014. The main outcome measures were visual outcome, prosthesis retention and post-operative complications. A total of 6 eyes of 6 patients met the inclusion criteria. This included 2 pediatric patients, aged 6 months and 6 years, and 4 adults who were 27 to 33 years of age. Pre-operatively, the BCVA was worse than 20/400 in every eye. Three eyes had hand motions and 1 eye had light perception vision. After a mean follow-up period of 31 months (range of 16 to 51 months), 3 eyes (50.0 %) had a BCVA that was greater than or equal to 20/400. Overall, the BCVA improved in 4 eyes (66.7 %), and remained the same in 2 eyes (33.3 %). The device was retained in 6 eyes; 1 or more complications occurred in 5 eyes (83.3 %) and included sterile corneal ulceration (3 eyes), retro-prosthetic membrane formation (3 eyes), progressive glaucomatous optic neuropathy (2 eyes), device

extrusion (1 eye) and an epi-retinal membrane (1 eye). The authors concluded that the Boston KPro-1 had an excellent prognosis for retention in eyes with congenital glaucoma. However, the visual prognosis remains guarded due to the high prevalence of pre-existing ocular co-morbidity and the common occurrence of sight-threatening post-operative complications.

Furthermore, an UpToDate review on “Primary infantile glaucoma” (Olitsky and Reynolds, 2016) does not mention the use of keratoprosthesis/artificial cornea as a therapeutic option.

It should also be noted that the use of keratoprosthesis is often associated with glaucoma development or progression of pre-existing glaucoma. Banitt (2011) reviewed the causes and treatment of glaucoma in Boston K-Pro recipients. Glaucoma exists in up to 75 % of patients who undergo K-Pro surgery. After K-Pro placement, intra-ocular pressure (IOP) is measured by digital palpation, which has been found to be reliable in trained observers. The onset or progression of glaucoma in K-Pro patients should be monitored through visual field testing, direct visualization and structural imaging of the optic nerve. Although medical therapy is an option, 50 to 75 % of K-Pro recipients are surgically managed with a glaucoma drainage device (GDD) or, less commonly, cyclophotocoagulation. The author concluded that glaucoma is a common and permanent blinding sequelae of K-Pro surgery; in K-Pro patients, elevated IOP and changes in the optic nerve head should result in a high index of suspicion for glaucoma. Management is frequently surgical and typically entails placement of a GDD.

Kamyar and co-workers (2012) stated that while the Boston type I KPro is an effective option for management of eyes with poor prognosis for primary or repeat PK, visual potential is limited by pre-operative co-morbidities; glaucoma development or progression of pre-existing glaucoma is a significant cause of post-operative visual loss. They stated that rigorous peri-operative management of elevated IOP is essential for long-term success of KPro surgery.

Furthermore, Nguyen and Chopra (2014) noted that in keratoprosthesis recipients, glaucoma often leads to permanent loss of sight. It is imperative that these patients be monitored with vigilance by a multi-

disciplinary team to prevent progression. Pooled data from multiple centers and technologic innovations will assist the surgeon to design a surgical approach and post-operative management regimen for the individual recipient.

Descemet's Stripping Automated Endothelial Keratoplasty (DSAEK) is being investigated as a treatment for corneal endothelial dysfunction. The procedure employs a mechanical microkeratome to harvest the donor corneal lenticule and mechanical stripping of the diseased host endothelium and Descemet's membrane. It has been used to treat corneal dysfunction associated with Fuchs' endothelial dystrophy, bullous keratopathy, irido-corneal endothelial syndrome or a failed penetrating graft. Koenig and Covert (2007) reported their early results of DSAEK (n = 26). They found that despite a smooth graft-host interface, only 2 subjects achieved greater than or equal to 20/25 vision. The average visual results were comparable to vision after deep lamellar endothelial keratoplasty. Although patients experienced excellent post-operative acuity with minimally induced surgical astigmatism, nearly 1/3 of the donor lenticules needed to be either re-positioned or replaced.

In a prospective study (n = 9), Mearza and colleagues (2007) reported their clinical experience and 12-month findings of DSAEK. They concluded that DSAEK provided excellent refractive and reasonable visual outcomes in this limited series, but there were frequent problems with dislocation of the donor tissue, and the graft failure rate was high. The graft failures may be linked to excessive endothelial damage, and the high dislocation rate may be linked to not filling the anterior chamber totally with air after insertion of the donor. They stated that further development of the procedure is needed. Additionally, Price and Price (2007) noted that continued evolution of this relatively new technique will aid to reduce complications and further improve outcomes.

In a retrospective observational case series, Oster et al (2009) characterized the clinical and histological features of primary graft failure after DSAEK. A total of 16 cases of DSAEK graft failure from 15 patients, all with detailed histological examination of failed graft tissue were included in this study. Hematoxylin-eosin, periodic acid-Schiff staining, and light microscopy were used to examine the failed DSAEK graft tissue from all patients. Main outcome measures included examination of

specimens for corneal endothelial cell viability and host-donor interface characteristics. Clinical history revealed that 88 % (14/16) of studied DSAEK grafts detached before failure, and pathological examination found that 75 % (12/16) of failed grafts had atrophic corneal endothelium. Examples of residual host Descemet's membrane in the graft site and improper donor trephination were also identified. The authors concluded that marked loss of the corneal endothelium is the prominent feature of primary DSAEK graft failure. Examples of surgical features, such as incomplete Descemet's stripping and residual full-thickness cornea with a DSAEK graft, were shown.

In a position paper, the American Academy of Ophthalmology (Lee et al, 2009) explains that endothelial keratoplasty procedures offer an alternative to penetrating keratoplasty to replace diseased endothelium with healthy donor tissue, without the need to remove the entire cornea. Introduced in 1988, deep lamellar endothelial keratoplasty (DLEK), which involves the creation of a deep lamellar pocket and replacement of posterior stroma with healthy donor tissue, allowed more rapid visual rehabilitation and a smaller incision than penetrating keratoplasty, but it was difficult to learn and time consuming. Descemet's stripping endothelial keratoplasty (DSEK) was introduced in 2005, and Descemet's stripping automated endothelial keratoplasty (DSAEK) was introduced in 2006; these procedures have supplanted DLEK. These methods for EK involve removal of Descemet's membrane and endothelium and replacement with donor tissue. When donor tissue is comprised of Descemet's membrane and endothelium alone, the technique is known as Descemet's membrane endothelial keratoplasty (DMEK). The AAO position paper states that endothelial keratoplasty procedures are associated with a smaller incision and faster visual rehabilitation than penetrating keratoplasty. The position paper states that there remain concerns about potential complications and long-term efficacy of endothelial keratoplasty, including concerns about graft dislocations, endothelial cell loss, and failed grafts. The AAO position paper cites the conclusions of an AAO Technology Assessment, which acknowledge the relatively short-term follow up and varying surgical techniques in the literature, but states "there is no evidence that DSAEK carriers unacceptable risks for surgical treatment of endothelial corneal disease. In comparison to PK, DSAEK appears at least equivalent in terms of safety, efficacy, surgical risks, and complications rates and superior to PK

in terms of refractive stability, postoperative refractive outcomes, wound and suture-related complications, and intraoperative choroidal hemorrhage risk".

An assessment of endothelial keratoplasty by the National Institute for Health and Clinical Excellence (NICE, 2008) found adequate evidence to support the use of this procedure. The NICE assessment cited comparative studies which found better visual acuity and a lower incidence of astigmatism with endothelial keratoplasty compared with penetrating keratoplasty. The specialist advisors to NICE listed adverse events of endothelial keratoplasty reported in the literature or anecdotally as graft dislocation, graft failure and rejection, interface opacification, and loss of best spectacle corrected visual acuity.

Collagen Crosslinking has been investigated as a treatment for Keratoconus. Animal studies have shown a significant increase in corneal biomechanical stiffness after collagen crosslinking by combined riboflavin (Photrexa)/ultraviolet-A (UVA) treatment. Riboflavin/UVA-induced collagen crosslinking has been studied, primarily in Europe, as a method for bringing the progression of keratoconus to a halt. However, most of the current literature is from small, uncontrolled studies with limited follow-up.

In epithelium-off collagen crosslinking (CXL), the epithelium is first abraded with a blunt spatula to allow penetration of riboflavin into the corneal tissue (NICE, 2013). Riboflavin eye drops are applied to the corneal surface before the procedure and intermittently during the procedure. The corneal surface is exposed to UVA radiation. Postoperatively, topical antibiotics and antiinflammatory drops are normally prescribed, with topical steroids if necessary. In some cases, a bandage contact lens may also be used for a few days. The procedure is done on one eye at a time and may also be repeated if needed.

In epithelium-on (transepithelial) CXL, the corneal epithelial surface is left intact (or may be partially disrupted) and a longer riboflavin loading time is needed (NICE, 2013). Sometimes the procedure is used in combination with other interventions such as intrastromal corneal ring segments,

photorefractive keratectomy (PRK) or phakic intraocular lens implantation to improve visual acuity. These combination procedures are referred to as 'CXL-plus'.

The mechanism of action of the CXL procedures is not fully understood: they may increase the number of 'anchors' that bond collagen fibers together and strengthen the cornea (NICE, 2013). This is expected to stop the progression of the disease but the duration of benefit is uncertain.

Interim results of a randomized controlled trial of collagen cross-linking with riboflavin and ultraviolet A (UVA) irradiaiton have been published (Wittig-Silva et al, 2008), reporting an apparent stabilization of refractive results. However, enrollment in the study is not complete and followup has been short. Subjects with documented progression of keratoconus were separately randomized into either treatment or control groups. Collagen crosslinking was performed using riboflavin and UVA. At the time of publication, 66 eyes of 49 patients had been enrolled and randomized. Interim analysis of treated eyes showed a flattening of the steepest simulated keratometry value (K-max) by an average of 0.74 diopters (D) ($p = 0.004$) at 3 months, 0.92 D ($p = 0.002$) at 6 months, and 1.45 D ($p = 0.002$) at 12 months. The investigators reported that a non-significant trend toward improvement in best spectacle-corrected visual acuity was also observed. In the control eyes, mean K-max steepened by 0.60 D ($p = 0.041$) after 3 months, by 0.60 D ($p = 0.013$) after 6 months, and by 1.28 D ($p < 0.0001$) after 12 months. The investigators reported that best spectacle-corrected visual acuity decreased by logMAR 0.003 ($p = 0.883$) over 3 months, 0.056 ($p = 0.092$) over 6 months, and 0.12 ($p = 0.036$) over 12 months. The investigators stated that no statistically significant changes were found for spherical equivalent or endothelial cell density.

Coskunseven et al (2009) evalauted the progression of keratoconus in patients treated with collagen cross-linking with riboflavin and ultraviolet A (UVA) irradiation. A total of 38 eyes of 19 patients with progressive keratoconus were enrolled in a prospective comparative study. Average follow-up was 9 +/- 2 months (range of 5 to 12 months). The worse eye was treated with collagen cross-linking, and the fellow eye served as the control. Corneal epithelium was mechanically removed. Riboflavin 0.1 %

solution in dextran T-500 20 % solution was applied every 2 to 3 minutes for 30 minutes throughout the irradiation. Ultraviolet A irradiation (370 nm) was performed using a commercially available UVA lamp for 30 minutes. The group treated with collagen crosslinking demonstrated a mean decrease (less myopic) in spherical equivalent refraction and cylinder of 1.03 +/- 2.22 diopters (D) (range of -5.25 to +3.75 D) and 1.04 +/- 1.44 D (range of -2.00 to +4.00 D), respectively ($p < 0.01$), and an increase in uncorrected visual acuity (UCVA) and best spectacle-corrected visual acuity (BSCVA) of 0.06 +/- 0.05 (range of 0.00 to 0.20) and 0.10 +/- 0.14 (range of -0.10 to 0.34), respectively ($p < 0.01$). The maximal curvature decreased by 1.57 +/- 1.14 D (range of 0.00 to 3.90 D), and intraocular pressure increased by 2 +/- 2 mmHg (range of -1 to 6 mmHg), which was statistically significant. No statistical difference was noted regarding central corneal thickness ($p = 0.06$) and endothelial cell count ($p = 0.07$). The untreated group showed no statistical difference for any of the clinical parameters, apart from UCVA and BSCVA, which decreased by 0.08 +/- 0.12 (range of -0.40 to 0.10) and 0.06 +/- 0.09 (range of -0.20 to 0.10), respectively ($p < 0.01$). The authors concluded that riboflavin/UVA collagen cross-linking appears to be efficacious in inhibiting the progression of keratoconus by reducing the corneal curvature, spherical equivalent refraction, and refractive cylinder in eyes with progressive keratoconus at average 9-month follow-up.

Grewal et al (2009) assessed changes in corneal curvature, corneal elevation, corneal thickness, lens density, and foveal thickness after corneal collagen crosslinking with riboflavin and UVA light in eyes with progressive keratoconus. Subjective refraction, best corrected visual acuity (BCVA), Scheimpflug imaging, and optical coherence tomography were performed preoperatively and 1 week, 1, 3, and 6 months, and 1 year after crosslinking. There were no significant differences ($p > 0.05$) in mean values between pre-operatively and 1 year post-operatively, respectively, in BCVA (0.22 +/- 0.10 and 0.20 +/- 0.10), spherical equivalent (-6.30 +/- 4.50 diopters (D) and -4.90 +/- 3.50 D), or cylinder vector (1.58 x 7(degrees) +/- 3.8 D and 1.41 x 24(degrees) +/- 3.5 D). There was no significant difference in mean measurements between pre-operatively and 1 year post-operatively, respectively, for central corneal thickness (458.9 +/- 40 microm and 455.2 +/- 48.6 microm), anterior corneal curvature (50.6 +/- 7.4 D and 51.5 +/- 3.6 D), posterior corneal curvature (-7.7 +/- 1.2 D and -7.4 +/- 1.1 D), apex anterior ($p = 0.9$),

posterior corneal elevation (p = 0.7), lens density (p = 0.33), or foveal thickness (175.7 +/- 35.6 microm and 146.4 +/- 8.5 microm; p = 0.1). The authors concluded that stable BCVA, spherical equivalent, anterior and posterior corneal curvatures, and corneal elevation 1 year after crosslinking indicate that keratoconus did not progress. Unchanged lens density and foveal thickness suggest that the lens and macula were not affected after UVA exposure during crosslinking.

Caporossi et al (2010) reported the long-term results of 44 keratoconic eyes treated by combined riboflavin ultraviolet A collagen cross-linking in the first Italian open, non-randomized phase II clinical trial, the Siena Eye Cross Study. After Siena University Institutional Review Board approval, from September 2004 through September 2008, 363 eyes with progressive keratoconus were treated with riboflavin ultraviolet A collagen cross-linking. Forty-four eyes with a minimum follow-up of 48 months (mean of 52.4 months; range of 48 to 60 months) were evaluated before and after surgery. Examinations comprised uncorrected visual acuity, best spectacle-corrected visual acuity, spherical spectacle-corrected visual acuity, endothelial cells count (I Konan, Non Con Robo; Konan Medical, Inc., Hyogo, Japan), optical (Visante OCT; Zeiss, Jena, Germany) and ultrasound (DGH; Pachette, Exton, Pennsylvania, USA) pachymetry, corneal topography and surface aberrometry (CSO EyeTop, Florence, Italy), tomography (Orbscan IIz; Bausch & Lomb Inc., Rochester, New York, USA), posterior segment optical coherence tomography (Stratus OCT; Zeiss, Jena, Germany), and in vivo confocal microscopy (HRT II; Heidelberg Engineering, Rostock, Germany). Keratoconus stability was detected in 44 eyes after 48 months of minimum follow-up; fellow eyes showed a mean progression of 1.5 diopters in more than 65 % after 24 months, then were treated. The mean K value was reduced by a mean of 2 diopters, and coma aberration reduction with corneal symmetry improvement was observed in more than 85 %. The mean best spectacle-corrected visual acuity improved by 1.9 Snellen lines, and the uncorrected visual acuity improved by 2.7 Snellen lines. The authors concluded that the results of the Siena Eye Cross Study showed a long-term stability of keratoconus after cross-linking without relevant side effects. The uncorrected visual acuity and best spectacle-corrected visual acuity improvements were supported by clinical, topographic, and wavefront modifications induced by the treatment.

In a prospective, randomized-controlled clinical trial, Greenstein et al (2011) evaluated changes in corneal topography indices after corneal collagen crosslinking (CXL) in patients with keratoconus and corneal ectasia and analyze associations of these changes with visual acuity. Corneal collagen crosslinking was performed in eyes with keratoconus or ectasia. Quantitative descriptors of corneal topography were measured with the Pentacam topographer and included 7 indices:

(i) index of surface variance, (ii) index of vertical asymmetry, (iii) keratoconus index, (iv) central keratoconus index, (v) minimum radius of curvature, (vi) index of height asymmetry, and (vii) index of height decentration. Follow-up was 1 year. The study comprised 71 eyes, 49 with keratoconus and 22 with post-LASIK ectasia. In the entire patient cohort, there were significant improvements in the index of surface variance, index of vertical asymmetry, keratoconus index, and minimum radius of curvature at 1 year compared with baseline (all $p < 0.001$). There were no significant differences between the keratoconus and ectasia subgroups. Improvements in post-operative indices were not correlated with changes in corrected or uncorrected distance visual acuity. The authors concluded that there were improvements in 4 of 7 topography indices 1 year after CXL, suggesting an overall improvement in corneal shape. However, no significant correlation was found between the changes in individual topography indices and changes in visual acuity after CXL.

In a randomized, prospective, and comparative study, Henriquez et al (2011) evaluated the safety and effectiveness of CXL by riboflavin/UV light for the treatment of keratoconus. This study involved 10 eyes with keratoconus diagnosed between September 2006 and January 2008. Each patient underwent CXL in the keratoconus eye. Pre-operative and post-operative (at 1, 3, 6, and 12 months) biomicroscopy examinations, distance uncorrected and best-corrected visual acuities, refractive error, endothelial cell counts, keratometry readings, ultrasound pachymetry, macular thickness, and Scheimpflug analyses were performed and compared. Mean uncorrected visual acuity was 1.18 logarithm of the minimum angle of resolution pre-operatively and 0.46 logarithm of the minimum angle of resolution at 12 months post-operatively ($p < 0.001$). Statistically significant reductions in the mean maximum [2.66 D, $p = 0.04$] and minimum (1.61 D, $p = 0.03$) keratometry values were present at 12 months post-operatively, in addition there was a 2.25 D reduction in

the mean spherical equivalent (p = 0.01). At the end of follow-up, 8 (80 %) and 6 (60 %) of the 10 eyes showed a decrease in the anterior and posterior elevation values, respectively, and the thinnest point of the cornea was statistically thinner by a mean of 13.4 µm (p = 0.03). No statistically significant differences were found between pre-operative and post-operative endothelial cell counts and macular thicknesses. The improvements in visual acuity, keratometry readings, and spherical equivalent values occurred progressively during follow-up. The authors concluded that CXL procedure is a safe treatment for keratoconus, yields good visual results, and reduces the progression of the disease, but long follow-up is necessary.

Letko et al (2011) noted that "[d]espite the lack of large multicenter prospective randomized trials, CXL has gradually become a favorite treatment tool and first line treatment for keratoconus and related corneal conditions. Although available data suggest that CXL administered with the currently widely adopted treatment parameters is safe, effective, and well tolerated, further improvements are likely to come in the future. One of the improvements is development of protocols that do not require epithelial removal, which will likely lead to reduction of risk for infectious keratitis and stromal scarring, and increase in patient comfort. Delivery of riboflavin into the cornea through intact epithelium, or through a femtosecond laser-created pocket could become an alternative to currently widely accepted administration of riboflavin that requires removal of the corneal epithelium .... Ultimately, development of topical medications capable of inducing CXL that could be self-administered would further revolutionize treatment of keratoconus and related conditions. Several drugs including genipin, glutaraldehyde, glyceraldehydes, and aliphatic b-nitro alcohols were identified, but further investigations are needed before any of these compounds could be introduced to clinical practice".

Guidance from the National Institute for Health and Clinical Excellence (NICE, 2013) concluded that there is adequate evidence on the safety and efficacy of epithelium-off CXL using riboflavin and ultraviolet A for keratoconus and keratectasia. NICE found inadequate evidence of the safety and efficacy of epithelium-on (transepithelial) CXL. NICe found that most of the published evidence on photochemical corneal collagen cross-linkage (CXL) using riboflavin and ultraviolet A (UVA) for

keratoconus and keratectasia relates to the technique known as 'epithelium-off' CXL'. The NICE guidance explained that "epithelium-on (transepithelial) CXL" is a more recent technique and less evidence is available on its safety and efficacy. The guidance noted that either procedure (epithelium-off or epithelium-on CXL) can be combined with other interventions, and the evidence base for these combination procedures (known as 'CXL-plus') is also limited.

An assessment by the Candian Agency for Drugs and Technologies in Health (CADTH, 2012) found one technology assessment (citing Stenevi et al, 2011) that concluded that there was low to moderate quality evidence to support the efficacy oof DXL for the treatment of keratoconus. The authors of the technology assessment also concluded that the use of CXL for the treatment of keratoconus represented a lower direct cost to the health care system than corneal transplantation. The assessment reported that the authors of 12 of the 14 randomized and nonrandomized studies included in the asssessment concluded that there was improvement or stability of keratoconus following treatment with CXL.

Konstantopoulos and Mehta (2015) noted that CXL is a procedure that primarily aims to increase corneal stiffness. Although used for a variety of conditions, it is most commonly applied to the treatment of keratoconus. Collagen cross-linking involves irradiation of the cornea with UVA irradiation after it has been soaked with riboflavin (vitamin B), a photosensitizer. In conventional treatment, based on the Dresden protocol, a minimum corneal thickness threshold of 400 μm is recommended and UVA (370 nm) irradiation of 3 mW/cm irradiance is applied for 30 mins, resulting in a cumulative dose of 5.4 J/cm. Evidence presented in this review showed that conventional CXL stabilizes the vision and corneal topographic parameters in the majority of treated patients, with only a small failure rate. It has a good safety profile with no endothelial cell loss and a small risk of corneal infiltration and infection. To reduce the treatment duration, accelerated protocols of similar efficacy have been sought. In accelerated protocols, UVA irradiation of higher irradiance, typically 9 mW/cm, is applied for a shorter time, typically 10 mins. The evidence, limited to small studies with short follow-up, showed that they may also stabilize the vision and the ectasia, with no additional

safety concerns highlighted. The authors concluded that randomized controlled studies are needed to confirm the encouraging results and non-inferiority to conventional treatment.

Lamellar Keratectomy is a surgical procedure used to correct high degrees of myopia, and low-to-moderate amounts of hyperopia. There is a lack of evidence regarding the effectiveness of lamellar keratectomy for the treatment of epithelial ingrowth following LASIK.

In a retrospective study, Rojas et al (2004) evaluated the safety and effectiveness of mechanical debridement and suturing of the LASIK flap in the treatment of clinically significant epithelial ingrowth after LASIK. A total of 20 eyes (n = 19 patients) in which clinically significant epithelial ingrowth developed after LASIK were treated with lifting of the flap, scraping of the epithelial ingrowth, and flap suturing. Primary outcome measurements including recurrence of ingrowth, uncorrected VA, manifest refraction, best spectacle-corrected VA, and complications were evaluated at the last post-operative examination. At the last post-operative examination (mean +/- SD, 10.5 +/- 14.3 months; range of 1.5 to 64 months), 100 % of eyes had no recurrence of clinically significant epithelial ingrowth. The uncorrected VA changed from 20/20 or better in 7 eyes (35 %) and 20/40 or better in 15 eyes (75 %) pre-operatively to 20/20 or better in 9 eyes (45 %) and 20/40 or better in 16 eyes (80 %) at the last follow-up examination. There was no significant change in the mean logarithm of the minimum angle of resolution (logMAR) uncorrected VA before (mean +/- SD, 0.3 +/- 0.5; range of -0.1 to 1.7) and after surgery (mean +/- SD, 0.2 +/- 0.4; range of -0.1 to 1.7) (p = 0.40). Mean +/- SD spherical equivalent changed from -0.21 +/- 0.82 diopters (D) (range of -1.25 to 1.00 D) pre-operatively to -0.53 +/- 0.89 D (range of -2.50 to 0.38 D) at last follow-up (p = 0.30). No eyes lost 2 or more lines of best spectacle-corrected VA, and there were no complications associated with the treatment. The authors concluded that suturing the LASIK flap in addition to mechanical debridement of epithelial ingrowth is a safe and effective treatment for clinically significant epithelial ingrowth after LASIK.

Kymionis et al (2009) reported a patient with severe post-LASIK epithelial ingrowth and keratolysis treated with flap amputation and photo-therapeutic keratectomy (PTK) with adjuvant intra-operative mitomycin C

(MMC). A 55-year-old woman was referred to the authors' department due to severe post-LASIK epithelial ingrowth with corneal melting 2 years after primary LASIK. The patient had had 2 previous attempts for epithelial ingrowth treatment (flap lift and epithelial ingrowth manual removal) that were unsuccessful. Slit lamp biomicroscopy and anterior segment optical coherence tomography showed extensive epithelial ingrowth and keratolysis (thinning of the LASIK flap) while the patient had photophobia and could not tolerate contact lenses. Flap amputation with subsequent PTK (in order to smooth out the corneal irregularities caused by the keratolysis and/or variations in flap thickness) and adjuvant intra-operative MMC application for 2 minutes was performed. There were no intra- or post-operative adverse events seen during the follow-up period. Six months after the procedure, uncorrected VA improved to 20/40 compared with 20/50 pre-operatively, while best spectacle-corrected VA improved from 20/40 to 20/32. The topographical astigmatism was decreased from 3.24 diopters (D) to 1.00 D. The authors concluded that flap amputation with PTK and adjuvant intra-operative MMC is an option for the management of severe post-LASIK epithelial ingrowth with keratolysis.

Rapuano (2010) reviewed the management of epithelial ingrowth after LASIK. Data of all patients referred to the Wills Eye Cornea Service after having undergone LASIK were reviewed. Charts of all patients with the diagnosis of epithelial ingrowth were analyzed. Data included patient demographics, previous ocular history, visual acuity, size and location of the ingrowth, and management. Additional data on eyes that underwent removal of the ingrowth at Wills were obtained. A total of 305 patients (153 females and 152 males, mean age of 44.7 years) were referred for eye problems after LASIK during the study period. Epithelial ingrowth was confirmed in 46 patients (15 %) (19 females and 27 males, mean age of 47.4 years) involving 55 eyes (27 right and 28 left). Patients with epithelial ingrowth were seen at a mean of 26 months after LASIK (range of 0.5 to 108 months). Twenty-four eyes had undergone previous enhancements, 2 twice. Fourteen eyes had undergone previous removal of epithelial ingrowth, 8 more than once (range of 2 to 8). In 35 eyes, simple observation was recommended. In 7 eyes, epithelial removal was recommended to the referring physician. Thirteen eyes underwent flap lift and epithelial removal at Wills Eye; 9 included flap suturing. One eye required repeat treatment with flap suturing and fibrin glue, after which no

recurrence was found. In the other 12 eyes, there was no recurrence in 9, small recurrences in 2, and a large recurrence in 1 eye (mean follow-up of 16 months). The authors concluded that epithelial ingrowth after LASIK is not rare in the authors' referral practice. Mild ingrowth can be observed, whereas significant ingrowth can respond well to removal with a low chance of significant recurrence.

Elderkin et al (2011) reported the successful treatment of 2 patients who developed flap necrosis preceded by recurrent epithelial ingrowth and interface fluid syndrome after LASIK. Patient 1 was treated with epithelial debridement and flap suturing; while patient 2 was initially treated with epithelial debridement and flap suturing, but developed recurrent epithelial ingrowth in the right eye and 2 weeks later in the left eye. Patient 1 developed diffuse interface fluid accumulation in the left eye after epithelial debridement and flap suturing and was treated with timolol meleate 0.5 % solution and methazolamide. The interface fluid resolved and the cornea and flap became clear. Slit-lamp examination identified a small area of epithelial ingrowth recurrence, which has remained stable for 3 years. Patient 2 was successfully re-treated with epithelial debridement followed by fibrin tissue adhesive application. Five months after debridement and fibrin tissue adhesive, no recurrence of epithelial ingrowth or interface fluid accumulation was noted. The authors concluded that epithelial ingrowth and interface fluid syndrome may be associated with secondary flap necrosis following LASIK, which can be effectively treated with debridement and flap suturing or fibrin tissue adhesive application.

Hexagonal Keratotomy employs a computer-assisted microkeratome to reshape the cornea. It works similarly to a carpenter’s plane, making a hexagonal pattern of cuts versus the radial cuts seen in RK. Hexagonal keratotomy has been used for the treatment of hyperopia that occurs naturally, and also for the treatment of presbyopia following RK. Hexagonal keratotomy is associated with highly variable results and a number of complications have been reported following this procedure, including irregular astigmatism, wound healing abnormalities as well as corneal ectasia (Werblin, 1996; Mehta et al, 2012). Hexagonal keratotomy is now rarely used since newer techniques in refractive surgery have been developed.

Crescent Keratectomy performed with an Excimer Laser for the Management of Keratoconus

Carriazo and Cosentino (2017) described a novel technique to re-shape the ectatic cornea by means of crescent keratectomy performed with an excimer laser using a mask. A crescent-shaped perforation at the base of the mask allowed the laser ablation to be directed only to the intended region, shielding the remaining cornea. This technique was performed in 3 eyes of 3 patients with keratoconus grade 2 to 3. Arcs of 180° and 360° had been performed depending on the severity of the keratoconus. The edges of the crescent were closed by 10-0 nylon interrupted sutures. At 1 year post-operatively, all cases showed improvement in VA, keratometry, and corneal topography. The treatment also reduced optical aberrations and shortened the anterior chamber depth. The authors concluded that although the preliminary results were promising, there is a need to standardize a nomogram of this technique for treating keratoconus.

Endothelial Keratoplasty for the Treatment of Toxic Anterior Segment Syndrome

Necip and colleagues (2021) examined the outcomes of DMEK in patients with toxic anterior segment syndrome (TASS). A total of 13 eyes of 13 patients who underwent DMEK for endothelial decompensation secondary to TASS were retrospectively reviewed. A comprehensive ocular examination including best-corrected visual acuity (BCVA), slit-lamp biomicroscopy, IOP measurement, fundus evaluation, and measurement of central corneal thickness were carried out in all patients at pre-operatively and post-operatively. There were 8 men and 5 women, with an average age of 56 ± 19 years. The mean follow-up was 8.7 ± 3.5 months. The time interval between the onset of TASS and DMEK was 4.9 ± 6.6 months (range of 1.5 to 26 months); 12 of 13 grafts were clear at last visit. The mean pre-operative BCVA was 20/666 (range of hand motion to 20/200), and the mean BCVA was 20/36 (range of hand motion to 20/20) at the post-operative last visit ($p = 0.003$). The decrease in mean pachymetry from pre-operative (768 ± 69 μm) to post-operative last visit (523 ± 71 μm) was statistically significant ($p < 0.001$). The authors concluded that DMEK appeared to be a safe and effective therapeutic option in eyes with TASS-related endothelial decompensation. This was

a small (n = 13) study with relatively short-term follow-up (mean of 8.7 months). These preliminary findings need to be validated in well-designed studies.

Endothelial Keratoplasty for the Treatment of Corneal Hydrops

In a retrospective study, Bachmann and associates (2019) described a new surgical option for the treatment of acute corneal hydrops in keratoconus and presented the first results. This study included 3 patients who presented to the authors' clinic with a massive corneal hydrops in acute keratoconus and were treated by mini-Descemet membrane endothelial keratoplasty (DMEK). According to the size and the shape of the gap in the patient's Descemet membrane (DM), 1 DMEK graft was trephined with a round 5-mm punch. The other grafts were trimmed with a razor blade to a width of about 3 mm and a length adjusted to the length of the defect of the recipients' DM. The graft was inserted with a regular IOL shooter. Correct unfolding of the graft was controlled by using intra-operative optical coherence tomography (OCT). At the end of the surgery, the graft was attached to the posterior corneal surface by a small air bubble. Thereafter, the complete anterior chamber was filled with 20 % SF6 gas. All 3 patients (age of 32 ± 3 years on average) showed a rapid increase in uncorrected VA from the logarithm of the minimum angle of resolution (LogMAR) 1.66 (± 0.46) before mini-DMEK to the LogMAR 1.2 (± 0.3) within 6 to 8 weeks after mini-DMEK. The thickest corneal point within the edematous cornea decreased in all 3 patients (1,088 ± 280 µm before surgery versus 630 ± 38 µm 1 week after surgery). One mini-DMEK failed in a 1st attempt. In this patient, the recipient DM was under strong tension and showed a pronounced dehiscence; thus, a small part of the recipient's DM around the pre-existing gap in DM was removed before a 2nd mini-DMEK graft was placed successfully. The other 2 patients developed partial graft detachment within 1 to 2 weeks after surgery; however, the corneas of these patients were dehydrated to physiological levels after mini-DMEK, and despite partial detachment, there was no relapse of the hydrops. The authors concluded that mini-DMEK could be helpful in patients with larger defects and detachments of DM in very ectatic corneas in the acute phase of corneal hydrops in acute keratoconus. These patients may not be successfully treated by intra-cameral gas application alone or in

combination with pre-Descemetal sutures. Moreover, these researchers stated that further investigations are needed to identify factors helping to decide on the best surgical approach in hydrops in acute keratoconus.

Blitzer and colleagues (2021) described severe acute corneal hydrops in a patient with previously undiagnosed keratoconus, in which anterior segment optical coherence tomography (AS-OCT) revealed a protruding ridge of tissue on either side of DM break, treated successfully with ultrathin Descemet-stripping automated endothelial keratoplasty (UT-DSAEK). A 32-year old man presented with severe corneal hydrops in left eye. He was treated conservatively with hypertonic saline. Serial AS-OCT revealed persistent edema and haze overlying a break in DM, with a ridge of protruding tissue on either side. Based on these findings, UT-DSAEK was carried out. Intra-operatively, the ridge of tissue remained firmly adhered after DM removal and was felt to possibly represent posterior stroma. The patient's uncorrected VA improved to 20/80. Literature review revealed 1 case with similar AS-OCT findings who underwent penetrating keratoplasty; histopathology was reported to show Descemet scrolls on either side of the break, but the analysis of this and other reports suggested that an additional layer of tissue is contained within the scroll along with DM. The authors concluded that this case demonstrated severe corneal hydrops in the setting of keratoconus, in which AS-OCT revealed a ridge of protruding tissue on either side of a break in DM. UT-DSAEK led to resolution of corneal edema and improvement in stromal haze and VA. Moreover, these investigators stated that further research is needed to determine the precise role of endothelial keratoplasty and potential role of posterior stromal rupture in some cases of acute corneal hydrops.

CPT Codes / HCPCS Codes / ICD-10 Codes

Information in the [brackets] below has been added for clarification purposes. Codes requiring a 7th character are represented by "+":

Code	Code Description
***Post-Cataract Post-Transplant Corneal Surgery*:**	
CPT codes covered if selection criteria are met:	

Code	Code Description
65772	Corneal relaxing incision for correction of surgically induced astigmatism
65775	Corneal wedge resection for correction of surgically induced astigmatism
Other CPT codes related to the CPB:	
65750 - 65755	Keratoplasty (corneal transplant); penetrating (in aphakia or pseudoaphakia)
65770	Keratoprosthesis
Other HCPCS codes related to the CPB:	
V2100 - V2499	Spectacle lenses
V2500 - V2599	Contact lens
ICD-10 codes covered if selection criteria are met:	
H52.201 - H52.229	Astigmatism
T85.310+ - T85.328+ T85.390+ - T85.398+	Mechanical complication of other ocular prosthetic devices, implants and grafts [corneal graft]
Z94.7	Corneal transplant status
Z98.41 - Z98.49	Cataract extraction status
***Phototherapeutic Keratectomy*:**	
Other CPT codes related to the CPB:	
65760	Keratomileusis
HCPCS codes covered if selection criteria are met:	
S0812	Phototherapeutic keratectomy (PTK)
ICD-10 codes covered if selection criteria are met:	
B94.0	Sequelae of trachoma
E50.6	Vitamin A deficiency with xerophthalmic scars of cornea
H17.00 - H17.9	Corneal scars and opacities
H18.451 - H18.459	Nodular corneal degeneration
H18.501 - H18.59	Hereditary corneal dystrophies

Code	Code Description
H18.601 - H18.629	Keratoconus
H18.821 - H18.829	Corneal disorder due to contact lens
H18.831 - H18.839	Recurrent erosion of cornea
Q13.3	Congenital corneal opacity
Q13.4	Other congenital corneal malformations
S05.00x+ - S05.02x+	Injury of conjunctiva and corneal abrasion without foreign body
S05.10x+ - S05.12x+	Contusion of eyeball and orbital tissue
Z85.840	Personal history of malignant neoplasm of eye
ICD-10 codes not covered for indications listed in the CPB:	
A18.50 - A18.59	Tuberculosis of eye
A30.5	Lepromatous leprosy
A50.31	Late congenital syphilitic interstitial keratitis
A54.33	Gonococcal keratitis
A71.0 - A71.9	Trachoma
B00.52	Herpesviral keratitis
B02.33	Zoster keratitis
B05.81	Measles keratitis and keratoconjunctivitis
H16.031 - H16.039	Corneal ulcer with hypopyon
H16.061. H16.039	Mycotic corneal ulcer
H16.251 - H16.259	Phlyctenular keratoconjunctivitis
H16.291 - H16.299	Other keratoconjunctivitis

Code	Code Description
H16.311 - H16.319	Corneal abscess
H44.20 - H44.23	Degenerative myopia
H44.2A1 - H44.2E9	Degenerative myopia with choroidal neovascularization, macular hole, retinal detachment, foveoschisis or other maculopathy
H52.00 - H52.4	Disorders of refraction
H52.6	Other disorders of refraction
H52.7	Unspecified disorder of refraction
***Refractive Surgery*:**	
***Radial keratotomy*:**	
CPT codes covered if selection criteria are met:	
65771	Radial keratotomy
Other HCPCS codes related to the CPB:	
V2100 - V2499	Spectacle lenses
V2500 - V2599	Contact lens
ICD-10 codes covered if selection criteria are met:	
H52.10 - H51.13	Myopia
ICD-10 codes not covered for indications listed in the CPB:	
H52.00 - H52.03 H52.201 - H52.4	Disorders of refraction (other than myopia)
H52.6	Other disorder of refraction
H52.7	Unspecified disorder of refraction
Minimally invasive radial keratotomy **no specific code:**	
ICD-10 codes not covered for indications listed in the CPB (not all-inclusive):	
H52.10 - H52.13	Myopia
***Astigmatic keratotomy (AK)*:**	
CPT codes covered if selection criteria are met:	

Code	Code Description
65772	Corneal relaxing incision for correction of surgically induced astigmatism
65775	Corneal wedge resection for correction of surgically induced astigmatism
Other CPT codes related to the CPB:	
65400 - 65600	Cornea excision, removal or destruction, or cryotherapy of lesion on cornea
ICD-10 codes covered if selection criteria are met:	
H52.201 - H52.229	Astigmatism
T85.310+ - T85.328+ T85.390+ - T85.398+	Mechanical complication of other ocular prosthetic devices, implants and grafts [corneal graft]
Z94.7	Corneal transplant status
Z98.41 - Z98.49	Cataract extraction status
ICD-10 codes not covered for indications listed in the CPB:	
H52.00 - H52.13 H52.31- H52.4	Disorders of refraction (other than astigmatism)
H52.6	Other disorders of refraction
H52.7	Unspecified disorder of refraction
***Hexagonal keratotomy*:**	
No specific code	
ICD-10 codes not covered for indications listed in the CPB :	
H52.00 - H52.03	Hypermetropia [hyperopia]
H52.4	Presbyopia
***Laser in-situ keratomileusis*:**	
CPT codes covered if selection criteria are met:	
65760	Keratomileusis
HCPCS codes covered if selection criteria are met:	
S0800	Laser in situ keratomileusis (LASIK)
Other HCPCS codes related to the CPB:	

Code	Code Description
V2100 - V2499	Spectacle lenses
V2500 - V2599	Contact lens
ICD-10 codes covered if selection criteria are met:	
H52.10 - H52.13	Myopia
H52.201 - H52.229	Astigmatism
ICD-10 codes not covered for indications listed in the CPB:	
H52.6	Other disorders of refraction
H52.7	Unspecified disorder of refraction
***Standard keratomileusis (ALK)*:**	
CPT codes not covered for indications listed in the CPB:	
65760	Keratomileusis
ICD-10 codes not covered for indications listed in the CPB:	
H52.00 - H52.4	Disorders of refraction
H52.6	Other disorders of refraction
H52.7	Unspecified disorder of refraction
***Epikeratoplasty (or epikeratophakia)*:**	
CPT codes covered if selection criteria are met:	
65767	Epikeratoplasty
Other HCPCS codes related to the CPB:	
V2500 - V2599	Contact lens
ICD-10 codes covered if selection criteria are met:	
E50.6	Vitamin A deficiency with xerophthalmic scars of cornea
H17.0 - H17.9	Corneal scars and opacity
H18.511 - H18.519	Endothelial corneal dystrophy
H27.00 - H27.03	Aphakia
Q12.3	Congenital aphakia

Code	Code Description
T85.310+ - T85.328+ T85.390+ - T85.398+	Mechanical complication of other ocular prosthetic devices, implants and grafts [corneal graft]
ICD-10 codes not covered for indications listed in the CPB:	
H52.00 - H52.4	Disorders of refraction
H52.6	Other disorders of refraction
H52.7	Unspecified disorder of refraction
***Keratophakia*:**	
CPT codes not covered for indications listed in the CPB:	
65765	Keratophakia
Other HCPCS codes related to the CPB:	
V2785	Processing, preserving, and transporting corneal tissue
ICD-10 codes not covered for indications listed in the CPB:	
H52.00 - H52.4	Disorders of refraction
H52.6	Other disorders of refraction
H52.7	Unspecified disorder of refraction
***Lamellar keratoplasty (non-penetrating keratoplasty)*:**	
CPT codes covered if selection criteria are met:	
65710	Keratoplasty (corneal transplant); anterior lamellar
Other HCPCS codes related to the CPB:	
V2785	Processing, preserving, and transporting corneal tissue
ICD-10 codes covered if selection criteria are met:	
E50.6	Vitamin A deficiency with xerophthalmic scars of cornea
H15.051 - H15.059	Scleromalacia perforans
H17.0 - H17.9	Corneal scars and opacity
H18.20 - H18.239	Corneal edema
H18.40 - H18.49	Corneal degenerations
H18.50 - H18.59	Hereditary corneal dystrophies

Code	Code Description
H18.601 - H18.629	Keratoconus
H18.70 - H18.799	Other corneal deformities
Q13.4	Other congenital corneal malformations
ICD-10 codes not covered for indications listed in the CPB:	
H11.001 - H11.069	Pterygium
H52.00 - H52.4	Disorders of refraction
H52.6	Other disorders of refraction
H52.7	Unspecified disorder of refraction
***Penetrating keratoplasty (PK) (corneal transplantation, perforating keratoplasty)*:**	
CPT codes covered if selection criteria are met:	
65730	Keratoplasty (corneal transplant); penetrating (except in aphakia or pseudoaphakia)
0289T	Corneal incisions in the donor cornea created using a laser, in preparation for penetrating or lamellar keratoplasty (List separately in addition to code for primary procedure)
0290T	Corneal incisions in the recipient cornea created using a laser, in preparation for penetrating or lamellar keratoplasty (List separately in addition to code for primary procedure)
HCPCS codes covered for indications listed in the CPB:	
V2785	Processing, preserving, and transporting corneal tissue
ICD-10 codes covered if selection criteria are met:	
B00.50	Herpesviral ocular disease, unspecified
B00.52	Herpesviral keratitis
B02.33	Zoster keratitis
B94.0	Sequelae of trachoma
E50.6	Vitamin A deficiency with xerophthalmic scars of cornea
H16.001 - H16.9	Keratitis
H17.0 - H17.9	Corneal scars and opacities

Code	Code Description
H18.20 - H18239	Corneal edema
H18.40 - H18.49	Corneal degenerations
H18.50 - H18.59	Hereditary corneal dystrophies
H18.601 - H18.629	Keratoconus
H18.711 - H18.719	Corneal ectasia
H20.811 - H20.819	Fuchs' heterochromic cyclitis
Q13.3	Congenital corneal opacities
Q13.4	Other congenital corneal malformations
S01.80xS - S01.85xS	Open wound of other parts of head, sequela
S05.20 - S05.92	Open wound of eyeball
T85.310+ - T85.328+ T85.390+ - T85.398+	Mechanical complication of other ocular prosthetic devices, implants and grafts [corneal graft]
T86.90 - T86.99	Complication of unspecified transplanted organ and tissue
T86.890 - T86.899	Complications of other transplanted
Z94.7	Corneal transplant status
ICD-10 codes not covered for indications listed in the CPB:	
H52.00 - H52.4	Disorders of refraction
H52.6	Other disorders of refraction
H52.7	Unspecified disorder of refraction
***Photorefractive keratectomy (PRK) and Photoastigmatic keratectomy (PARK or PRK-A)*:**	
CPT codes covered if selection criteria are met:	
65760	Keratomileusis
HCPCS codes covered if selection criteria are met:	

Code	Code Description
S0810	Photorefractive keratectomy (PRK)
HCPCS codes not covered for indications listed in the CPB:	
S0596	Phakic intraocular lens for correction of refractive error
Other HCPCS codes related to the CPB:	
V2100 - V2499	Spectacle lenses
V2500 - V2599	Contact lens
ICD-10 codes covered if selection criteria are met:	
H52.00 - H52.03	Hypermetropia
H52.10 - H52.13	Myopia
H52.201 - H52.229	Astigmatism
ICD-10 codes not covered for indications listed in the CPB:	
H52.00 - H52.03 H52.201 - H52.204	Disorders of refraction (other than myopia)
H52.6	Other disorders of refraction
H52.7	Unspecified disorder of refraction
***Intrastromal corneal ring (INTACS)*:**	
CPT codes covered if selection criteria are met:	
65785	Implantation of intrastromal corneal ring segments
ICD-10 codes covered if selection criteria are met:	
H18.461 - H18.469	Peripheral corneal degeneration
H18.601 - H18.629	Keratoconus
H52.00 - H52.03	Hypermetropia
H52.10 - H52.13	Myopia
H52.201 - H52.229	Astigmatism

Code	Code Description
Other HCPCS codes related to the CPB:	
V2100 - V2499	Spectacle lenses
V2500 - V2599	Contact lens
***Conductive Keratoplasty (no specific codes)*:**	
Other CPT codes related to the CPB:	
65771	Radial keratotomy
Other HCPCS codes related to the CPB:	
V2100 - V2499	Spectacle lenses
V2500 - V2599	Contact lens
ICD-10 codes not covered for indications listed in the CPB:	
H18.601 - H18.629	Keratoconus
H52.00 - H52.03	Hypermetropia
H52.10 - H52.13	Myopia
H52.201 - H52.229	Astigmatism
***Methods of thermokeratoplasty other than conductive keratoplasty (no specific codes)*:**	
ICD-10 codes not covered for indications listed in the CPB:	
H18.601 - H18.629	Keratoconus
H52.00 - H52.4	Disorders of refraction
H52.6	Other disorders of refraction
H52.7	Unspecified disorder of refraction
***Orthokeratology (no specific codes)*:**	
Other CPT codes related to the CPB:	
92070	Fitting of contact lens for treatment of disease, including supply of lens
92310 - 92326	Contact lens services
Other HCPCS codes related to the CPB:	
V2500 - V2599	Contact lens
ICD-10 codes not covered for indications listed in the CPB:	
H52.00 - H52.4	Disorders of refraction

Code	Code Description
H52.6	Other disorders of refraction
H52.7	Unspecified disorder of refraction
***Scleral Expansion Surgery (no specific codes)*:**	
ICD-10 codes not covered for indications listed in the CPB:	
H52.4	Presbyopia
***Intraocular lens implants (clear lens extraction) (aphakic intraocular lenses (IOLS))*:**	
CPT codes not covered for indications listed in the CPB:	
66840	Removal of lens material; aspiration technique, 1 or more stages
66940	extracapsular (other than 66840, 66850, 66852)
66985	Insertion of intraocular lens prosthesis (secondary implant), not associated with concurrent cataract removal
HCPCS codes not covered for indications listed in the CPB:	
C1780	Lens, intraocular (new technology)
Q1004	New technology intraocular lens category 4 as defined in Federal Register notice
Q1005	New technology intraocular lens category 5 as defined in Federal Register notice
V2630	Anterior chamber intraocular lens
V2631	Iris supported intraocular lens
V2632	Posterior chamber intraocular lens
V2788	Presbyopia correcting function of intraocular lens
ICD-10 codes not covered for indications listed in the CPB:	
H52.00 - H52.03	Hypermetropia
H52.10 - H52.13	Myopia
H52.4	Presbyopia
***Keratoprosthesis (artificial cornea)*:**	
CPT codes covered if selection criteria are met:	
65770	Keratoprosthesis [AlphaCor keratoprosthesis not covered]
HCPCS codes covered if selection criteria are met:	
C1818	Integrated keratoprosthesis

Code	Code Description
L8609	Artificial cornea
Other HCPCS codes related to the CPB:	
V2630	Anterior chamber intraocular lens
V2631	Iris supported intraocular lens
V2632	Posterior chamber intraocular lens
ICD-10 codes covered if criteria are met:	
B00.50	Herpesviral ocular disease, unspecified
B00.52	Herpesviral keratitis
B02.33	Zoster keratitis
B94.0	Sequelae of trachoma
E50.6	Vitamin A deficiency with xerophthalmic scars of cornea
H16.001 - H16.9	Keratitis
H17.00 - H17.9	Corneal scars and opacities
H18.20 - H18.239	Corneal edema
H18.40 - H18.49	Corneal degenerations
H18.50 - H18.59	Hereditary corneal dystrophies
H18.601 - H18.629	Keratoconus
H18.711 - H18.719	Corneal ectasia
H20.811 - H20.819	Fuch's heterochromic cyclitis
Q13.3	Congenital corneal opacities
Q13.4	Other congenital corneal malformations
S01.80xS - S01.85xS	Open wound of other part of head, sequela
S05.20 - S05.92	Open wound of eyeball

Code	Code Description
T85.310+ - T85.328+ T85.390+ - T85.398+	Mechanical complication of other ocular prosthetic devices, implants and grafts [corneal graft]
T86.890 - T86.899	Complications of other transplanted tissue
T86.90 - T86.99	Complications of unspecified transplanted organ and tissue
Z94.7	Cornea transplant status
ICD-10 codes not covered for indications listed in the CPB:	
H33.001 - H33.8	Retinal detachments and breaks
Q15.0	Congenital glaucoma
***Endothelial keratoplasty (DSEK, DSAEK, and DLEK)*:**	
CPT codes covered if selection criteria are met:	
65756	Keratoplasty (Corneal Transplant); endothelial
65757	Backbench preparation of corneal endothelial allograft prior to transplantation (List separately in addition to code for primary procedure)
ICD-10 codes covered if selection criteria are met:	
H18.10 - H18.13	Bullous keratopathy
H18.20	Unspecified corneal edema
H18.211 - H18.219	Corneal edema secondary to contact lenses
H18.221 - H18.229	Idiopathic corneal edema
H18.231 - H18.239	Secondary corneal edema
H18.331 - H18.339	Rupture in Descemet's membrane
H18.511 - H18.519	Endothelial corneal dystrophy
H18.59	Other hereditary corneal dystrophies

Code	Code Description
T85.21x+ - T85.29x+	Mechanical complication of intraocular lens
T85.310+ - T85.328+ T85.390+ - T85.398+	Mechanical complication of other ocular prosthetic devices, implants and grafts [corneal graft]
ICD-10 codes not covered for indications listed in the CPB:	
H17.00 - H17.9	Corneal scars and opacity
H18.461 - H18.469	Peripheral corneal degeneration
H18.59	Other hereditary corneal dystrophies
H18.601 - H18.629	Keratoconus [corneal hydrops]
H18.711 - H18.719	Corneal ectasia
H21.241 - H21.249	Degeneration of pupillary margin [atrophy of sphincter of iris]
H21.261 -H21.269	Iris atrophy (essential) (progressive)
H21.29	Other iris atrophy
H59.89	Other postprocedural complications and disorders of eye and adnexa, not elsewhere classified [toxic anterior segment syndrome]
Q13.89	Other congenital malformations of anterior segment of eye [toxic anterior segment syndrome]
Collagen crosslinking by combined riboflavin/ultraviolet-A (UVA) treatment Epithelium-off photochemical (CXL) :	
No specific code	
CPT codes covered if selection criteria are met:	
0402T	Collagen cross-linking of cornea (including removal of the corneal epithelium and intraoperative pachymetry when performed)
Other HCPCS codes related to the CPB:	
J2787	Riboflavin 5'-phosphate, ophthalmic solution, up to 3 mL

Code	Code Description
ICD-10 codes covered if selection criteria are met:	
H18.601 - H18.629	Keratoconus
H18.711 - H18.719	Corneal ectasia
Q12.0	Congenital cataract
Collagen crosslinking, Epithelium-on (transepithelial) collagen cross-linkage (CXL plus) :	
No specific code	
ICD-10 codes not covered for indications listed in the CPB (not all-inclusive):	
H18.601 - H18.609	Keratoconus
H18.711 - H18.719	Corneal ectasia
Q13.4	Other congenital corneal malformations
***Excimer laser crescent keratectomy* - no specific code:**	
ICD-10 codes not covered for indications listed in the CPB (not all-inclusive):	
H18.601 - H18.609	Keratoconus

The above policy is based on the following references:

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