APPRAISALS TO KERATOPLASTY
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Penetrating Keratoplasty

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Evolution of endothelial keratoplasty (EK): deep lamellar endothelial keratoplasty (DLEK) replaced by Descemet stripping endothelial keratoplasty (DSEK); Descemet stripping automated endothelial keratoplasty (DSAEK) currently performed most often; Descemet membrane (DM) endothelial keratoplasty (DMEK); outcomes — comparisons of penetrating keratoplasty (PKP) in one eye and DSAEK in fellow eye suggested better vision achieved with PKP, but patients prefer DSAEK because eye less dry

Factors influencing success of PKP: clear cornea necessary but not sufficient; refractive status depends on minimization of astigmatism induced by surgery and suturing, myopic shift caused by removal of sutures, anisometropia, and analysis of wavefront aberrations

Study I (Forster, 1997): evaluated selective interrupted suture techniques for control of astigmatism after PKP; used 12 interrupted 10-0 nylon sutures at each hour of clock, with 12-bite running suture; compared removal of selective sutures vs simultaneous removal of 6 alternative sutures at 6 to 8 wk after surgery; criteria for removal of sutures — removed first suture if >2 diopters (D) of astigmatism present; subsequently if astigmatism >3 D, removed selective sutures; results — group with totally selective suture removal had overall 2.1 D of refractive astigmatism at 1 yr (2.3 D by corneal topography); keratometry and corneal topography showed curvature of ≈46 D; average of 4.7 sutures removed (vs 9 removed in other group); myopia increased with increasing number of sutures removed

Study II (Dursun et al, 2003): to reduce myopia, used tighter continuous suture and average keratometry value (K) of 46 D instead of 45 D if intraocular lens (IOL) placed (eg, combined triple procedure, IOL exchange, or addition of secondary IOL); left more of interrupted sutures in place to minimize astigmatism; results — induced myopia reduced, but not statistically significantly; only 29% of patients had ≤1 D anisometropia; benefit seen only in patients receiving IOL; induced astigmatism increased

Study III (Munir et al, 2009): performed wavefront analysis of patients from study II and showed degree of induced irregular astigmatism, surface asymmetry index (SAI), and surface regularity index (SRI) correlated with higher order aberrations (HOA); found inconsistent or no correlation of HOA to best corrected visual acuity (VA) and no relationship with regular astigmatism; HOA differed significantly between 6-wk point and final visit (probably related to decrease in ocular surface disease over time); speaker’s interpretation — analysis of wavefront aberrations necessary for DSEK and deep anterior lamellar keratoplasty (DALK); important to study role of irregular astigmatism in anterior regions of cornea and role of thickened deep cornea in HOA; roles of anterior surface subepithelial and deep pathology unclear; recent paper (Patel, 2012) showed subepithelial changes in Fuchs dystrophy (FED) may contribute more to HOA after DSEK than thickened deep corneal membrane; also important to analyze HOA in DMEK

Study IV: to reduce anisometropia, evaluated use of oversized 0.25-mm donor tissue when correction of ≥1 D (myopic) intended, based on refraction of fellow eye; used same-sized graft when <1 D needed or with hyperopic or emmetropic fellow eye; technique — donor prepared with Barron-Hessburg trephine to depth of ≈0.3 mm; used K of 46 D for IOL combinations; selective suture removal identical to procedure in previous studies; spherical equivalent — 29% of eyes received oversized grafts; 71% received same-sized grafts; eyes with oversized grafts had spherical equivalent of ≈0.65 D vs 0.08 D with same-sized grafts at 12 mo; excluding eyes <20/50, oversized grafts had 1.35 D and same-sized had 0.14 D (close to statistically significant); most grafts had favorable outcomes; anisometropia — among patients with oversized grafts, 58% had ≤0.5 D, 64% had ≤1 D, and 75% had ≤1.5 D of anisometropia; among those with same-sized grafts, 44% had ≤0.5 D, 59% had <1 D, and 78% had <1.5 D (not significantly different); other outcomes — mean astigmatism <3 D; SRI and SAI similar to those in original studies (ie, 1 to 2); 44% of eyes achieved ≥20/30 VA at 12 mo and 48% at last visit; 66% achieved ≥20/50; among patients with VA <20/50, 6 of 75 had graft failure with recurrent corneal edema, and most others had macular disease; first pair of glasses needed at 6.4 mo; second correction usually needed within 1 yr

Selection of patients for PKP: appropriate for patients with pseudophakic corneal edema and probable preexisting HOA or scarring anteriorly

Lamellar Keratoplasty

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Background: anterior lamellar keratoplasty (ALK) involves partial removal of anterior stroma and transplantation with anterior stroma from donor; interface haze represents key challenge;

Educational Objectives
The goal of this program is to improve the use and outcomes of keratoplasty. After hearing and assimilating this program, the clinician will be better able to:

1. Perform penetrating keratoplasty (PKP) with techniques that minimize induced astigmatism, myopic shift, and anisometropia.
2. Assess the relationship between higher order aberrations and degree of induced irregular astigmatism after PKP.
3. Select appropriate patients and optimize techniques used for lamellar keratoplasty.
4. Prepare donor tissue for use in endothelial keratoplasty.
5. Summarize the roles of rho-associated kinase inhibitor and Nrf2 in proposed novel treatment strategies for endothelial dysfunction.

Faculty Disclosure
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DALK attempts to push interface down to level of DM (nearly full-thickness transplantation); DSEK adds small amount of stroma along with endothelium and DM; DMEK replaces only endothelium and DM

Advantages of lamellar surgery: PKP — produces full-thickness wound covering 360°; increases risk for corneal hemorrhage, possibly endophthalmitis, and synechiae; DALK — uses smaller incisions that reduce risks; because endothelium not transplanted, frequency of most common type of rejection reduced; epithelial rejection possible; Stromal rejection rare; visual recovery rapid with earlier removal of sutures (as in DSEK); expands pool of potential cornea donors

Disadvantages of lamellar surgery: technically complex; DALK not appropriate if patient has endothelial dysfunction or interface haze; DSEK inappropriate for patients with stromal scarring; DALK originally produced irregular stroma-to-stroma interface causing haze; currently “big bubble technique” used

Indications: keratoconus, corneal scarring, ectatic disease, eg, after laser in situ keratomileusis (LASIK), and stromal dystrophies that do not involve endothelium or DM; intact healthy endothelium required

Techniques: start with partial trephination of anterior 66% of cornea; layer-by-layer dissection — gentlest approach but time consuming; helpful if patient has adhesions or previous rupture of DM; air-assisted techniques — fills anterior chamber (AC) with air to enable dissection closer to DM; hydrodecellimation — deep stroma hydrated to increase visualization and ease of handling

Modified big bubble technique: use 27-gauge needle on 5-mL syringe inserted deep into stroma; inject air forcefully into area of least resistance at pre-D (creating white area); perform paracentesis to relieve spike in intraocular pressure (IOP); inject air bubble to cause DM to fold out into AC and air bubble to go peripherally; perform viscodiscission, placing viscoelastic into area in front of DM; enter area (good bubble required to prevent entry into AC) and develop anterior 66% of cornea with crosshairs blunt scissors creating scleral criss-cross across cornea; perform lamellar dissection of remaining stroma if needed; remove endothelium and DM from donor (speaker uses 0.25-mm oversized graft) and secures with interrupted sutures (as with PKP)

Outcomes: similar to those with PKP; astigmatism still problematic because of many sutures; some interface haze remains that can limit VA; visual recovery faster because sutures removed earlier; reduces long-term use of steroids (tapered off after ≥1 yr); loss of endothelial cells — immediate loss caused by surgery; no loss seen from rejection (advantage over PKP); histopathologic outcomes — small amount of posterior stroma remains (probably contributes to interface haze)

Complications: perforation of DM — possible to salvage small late tears; early tears may require excision and conversion to PKP; wrinkles in interface — excess DM possible when patients with conic corneas receive transplant of flat cornea; vascularization or keratitis in interface; Stromal rejection possible; pseudoanterior chamber may resolve spontaneously or may require insertion of another bubble

Endothelial Keratoplasty

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Indications: FD, posterior polymorphous dystrophy, pseudophakic bullous keratopathy (PKB), trauma, iridocorneal-endothelial (ICE) syndrome, or failed PKP or graft rejection; special considerations — glaucoma shunts, synechiae, aniridia, aphakia, AC IOL, inability of patient to lie flat, and failed PKP

Advantages: decreased risk for catastrophic intraoperative complications (eg, suprachoroidal hemorrhage) or postoperative traumatic injury (eg, open globe caused by wound dehiscence); preservation of host corneal epithelium and minimal suturing reduces risk for infection and ocular surface disease; decreases surgically induced neurotrophic cornea; causes less astigmatism, but ≈1-D hyperopic shift typical with DSEK; may cause less glaucoma and less rejection; faster return to normal activities

Donor preparation: DSEK — either microkeratome or femtosecond laser-guided; results similar for surgeon-dissected and eye bank tissue; attempts to precut tissue with IntraLase less successful because of creation of rougher surface and potential damage to endothelium by photodisruption; donor usually cut to size of 8 to 9 mm to provide more endothelial cells

Stripping of DM (descemetorhexis): performed under air, fluid, or viscoelastic; removes thick, scarred, guttall DM; in FD, irregularities of guttall in DM cause scatter of light; stripping possibly not necessary in PBK where DM less diseased or in cases of graft failure

Graft attachment: may be enhanced by venting or by suturing to cornea; secure graft with 3 to 4 sutures for 2 wk in cases of aphakia and/or aniridia; roughening of donor stroma can enhance attachment; with other anterior segment pathology (eg, no lens, limited iris), suture lens to iris or do scleral sutured lens

Insertion of folded tissue: minimizes loss of endothelial cells; important because corneal endothelium does not proliferate in vivo; forceps commonly used with 60/40 fold of tissue; pull-through techniques — may use glides (modified Sheets glide used for AC IOL or Tan EndoGlide with closed chamber system) or suture pull-through technique; advances made in injectors that use 4- to 5-mm incisions

Complications: induction of astigmatism by incision; hyperopic shift caused by addition of DSEK tissue; tissue folds; interface haze; final VA <20/20; methods to decrease stromal thickness under investigation

DMEK: dissection of DM for DMEK more difficult in young corneas; unrolling scroll of DM with endothelial cell layer technically difficult compared to DSEK; complications include difficulty of preparation of donor tissue, unsuccessful attachment, poor function of donor tissue, and iatrogenic graft failure

DM automated endothelial keratoplasty (DMAEK): thickness of rim facilitates insertions of tissue; donor preparation — donor tissue dissected with microkeratome, central big bubble formed, stroma excised over bubble, and tissue punched with trephine

Ultra thin DSAEK: stroma hydrated with hypo-osmotic agent; first corneal debulking performed with microkeratome (300-μm head) that removes 66% of stroma and leaves 150- to 200-μm lamella; second cut performed with dedicated smaller (50- or 90-μm) head; ultra thin grafts available from tissue banks; studies show promising results with newer femtosecond lasers with lower pulse energy and high frequency

Ultra thin tissue: potential advantages include faster visual recovery, better final VA, and compatibility with injector systems; disadvantages of DMEK and DMAEK include difficult donor preparation, extensive postoperative management, high (50%) rate of rebubbling, and graft failure

Tissue usage: study showed 2-fold increase in need for replacement of corneal tissue in EK vs PKP; DSAEK — rates of graft failure ≈3%/yr and graft dislocation 16% (variable); rates of graft rejection, high IOP, and late graft failure (years 2-5) lower than for PKP; DSAEK associated with slightly lower cost than PKP (Prabhu, 2012); for DMEK, improved VA expected to increase to quality of life but rate of dislocations increased also

New approaches: repopulation — study (Dirisamer, 2012) showed cornea may become clear, even if DMEK graft detached, by repopulation of recipient posterior stroma with endothelial cells by migration from either donor or recipient (unknown which); suggests DM endothelial transfer (DMET) possible from...
free-floating graft: ability of cells to regenerate appears better with FD than PKB; rho-associated kinase (ROCK) inhibitor eye drops — ROCK inhibitor stimulated proliferation and migration of cells after cryogenic injury of central endothelial cells in rats (Koizumi, 2012); in primates, injection of endothelial cells with Y-27832 (ROCK inhibitor) caused better clearing of cornea than in controls without ROCK inhibitor (Okumura, 2012); clearance of cornea in patients with FD achieved in Japan; patients with FD may have residual endothelium

Prevention of endothelial cell loss before transplantation: postmitotic arrest of endothelial cells and constant exposure to UV light causes oxidative damage to DNA, apoptosis, morphologic changes, and imbalance between oxidants and antioxidants; these cause loss of cells, deposition of extracellular matrix (ie, guttae), corneal edema, and scatter of light; Nrf2 molecule activated under oxidative stress and migrates into nucleus, causing activation of protective enzymes; in corneal epithelium of patients with FD, migration of Nrf2 and activation of enzymes deficient (Bitar, 2012); stimulation of Nrf2 with agonists (eg, sulforaphane) stimulates migration of Nrf2 into nucleus, activates antioxidant enzymes, and protects cells against apoptosis

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1. Refractive status after penetrating keratoplasty (PKP) depends on which of the following factors?
   (A) Degree of astigmatism induced by surgery and suturing
   (B) Minimization of myopic shift caused by removal of sutures
   (C) Minimization of anisometropia
   (D) A, B, and C

2. Which of the following has been shown to increase the myopic shift seen after PKP?
   (A) Number of sutures inserted
   (B) Use of interrupted sutures at each hour of clock
   (C) Number of sutures removed
   (D) Use of tight continuous sutures

3. Which of the following has been shown to correlate with higher order aberrations after PKP?
   (A) Best corrected visual acuity
   (B) Surface regularity index
   (C) Regular astigmatism

4. Which of the following has been shown to reduce anisometropia after PKP?
   (A) Use of 0.25-mm donor tissue when correction of 1 D (myopic) intended, based on refraction of fellow eye
   (B) Use of same-sized graft when correction of <1 D needed or with hyperopic or emmetropic fellow eye
   (C) Use of tight continuous sutures
   (D) None of the above

5. All the following are indications for deep anterior lamellar keratoplasty (DALK), except:
   (A) Keratoconus
   (B) Corneal scarring
   (C) Endothelial dysfunction
   (D) Ectatic disease, eg, after laser in situ keratomileusis (LASIK)

6. An advantage of DALK compared to PKP is that astigmatism is reduced because the sutures are removed earlier.
   (A) True
   (B) False

7. All the following are typical after endothelial keratoplasty (EK), except:
   (A) Decreased risk for suprachoroidal hemorrhage
   (B) Reduced risk for infection and ocular surface disease
   (C) 1-D myopic shift after Descemet stripping EK (DSEK)
   (D) Decreased surgically induced neurotrophic cornea

8. Dissection of Descemet membrane (DM) for DMEK is more difficult in young corneas.
   (A) True
   (B) False

9. A study has shown that the rate of _______ is(are) lower with Descemet stripping automated endothelial keratoplasty
   (DSAEK) than with PKP.
   (A) Graft rejection
   (B) Elevated intraocular pressure
   (C) Late graft failure
   (D) A, B, and C

10. Recent studies suggest rho-associated kinase (ROCK) inhibitor may stimulate which of the following effects?
    (A) Migration of Nrf2 into the nucleus
    (B) Protection of endothelial cells against apoptosis
    (C) Proliferation and migration of endothelial cells after cryogenic injury
    (D) Prevention of graft rejection after DSAEK

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