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Corneal Crosslinking with Novel UV Wavelengths

J. James Rowsey, MD, St. Michaels Eye and Laser Institute

Co-Authors: Asma Sharfeddin, PhD; Nathan D. Gallant, PhD; Capritta Roberts, DO; John Michaelos, MD; Brad Fouraker, MD; Craig Berger, MD; Ed S. Neister; John Neister; and Steve Hudson

Purpose: To evaluate the corneal crosslinking potential of novel UV wavelengths, including 222 nm, 282 nm, 308 nm, and 365 nm, compared to the current 365 nm with riboflavin. Can unique UV wavelengths provide more efficacious corneal cross-linking without the use of riboflavin?

Method: Donor eye bank corneas were mounted on an artificial anterior chamber with a prescribed pressure of 20 mm Hg and corneal thickness of 550-650 microns. After gentle epithelial removal the corneas were treated with 3mW/cm² calibrated wavelengths from FAR UV (222 nm) through UVC (282 nm), UVB (308 nm) and UVA (365 nm), and UVA (365 nm with 30 minutes of stromal loading with 0.1% riboflavin) for 10, 20, and 30 minutes, respectively. Riboflavin was added during treatment as per current patient protocols. At the end of each treatment period Young’s modulus of cornea stiffening perpendicular to the corneal surface was determined by a new nanoindentation technology. After 30 minutes of treatment the corneas were sectioned at 4 mm x 12 mm and placed in a tensiometer for repeat Young’s modulus testing of corneal stiffening by standard elongation of the collagen lamellae.

Results: Young’s modulus of the cornea (corneal stiffening) increased with all the UV wavelengths, with each providing a variable magnitude of stiffening depending on the time of exposure. 222 nm UV increased perpendicular nanoindentation (NI) stiffening by as much as 85% (144/78 ± 13% kilopascals = kPa) and longitudinal tensiometer stiffening by 37% (149/109 ± 8 megapascals = MPa) after 30 minutes of treatment. The larger magnitude of tensiometer tensile strength relates to the normal collagen orientation across the cornea. Importantly, 282 nm UVC increased corneal stiffening by 133% (35/15 ± 3.9 kPa) with only 10 minutes of treatment and 160% (39/15 ± 1.8 kPa) with 20 minutes of treatment and tensiometer tensile stiffening by 33% (65/49 ± 8 MPa). 308 nm UV light produced increased stiffening by 37% (10 min), 81% (20 min), and 213% (30 min), all of which exceeded the current standard Avedro 365 nm treatment with riboflavin 0% (10 min), 53% (20 min), and 159% (30 min).

Conclusion: Novel 282 nm UVC ultraviolet light treatment of donor corneas for 20 minutes without the use of riboflavin provides equal corneal stiffening to the current method of corneal cross-linking with 365 nm with riboflavin in 30 minutes. 308 nm UVB ultraviolet light without riboflavin increases Young’s modulus of corneal stiffening at 10, 20, and 30 minutes of treatment more than 365 nm UVA with the use of riboflavin loading for the same time periods. 308 nm UVB ultraviolet light without riboflavin may provide an alternative to the extant 365 nm wavelength treatment of corneal ectasias in a shorter treatment time.
Bowman Layer Transplantation for Advanced Keratoconus: Five-Year Results

Lamis Baydoun, MD, Netherlands Institute for Innovative Ocular Surgery

Co-Authors: Korine van Dijk, BSc; Esther Groeneveld-van Beek, MSc; Jack Parker, MD, PhD; Isabel Dapena, MD, PhD; and Gerrit Melles, MD, PhD

Purpose: To evaluate the mid-term clinical outcomes of Bowman layer (BL) transplantation for the treatment of advanced keratoconus.

Method: In this prospective, single-center, case series at a tertiary referral center, 20 eyes of 17 patients with advanced keratoconus underwent BL transplantation. BL-grafts were prepared from donor globes not eligible for penetrating or endothelial keratoplasty (PK/EK), and from previously excised corneoscleral buttons that were ineligible for PK, or had been denuded of Descemet’s membrane (DM) for DMEK-graft preparation. After preparation, grafts were stored in organ culture until the time of surgery. BL transplantation was performed by manually dissecting a mid-stromal pocket and inserting of isolated BL-graft into the pocket. Before and up to 5 years postoperatively, Scheimpflug-based corneal tomography measurements, best corrected spectacle and contact lens visual acuity (BSCVA and BCLVA), endothelial cell density, and complications were evaluated.

Results: Measured simulated and maximum keratometry (Kmean and Kmax) values were stable up to 5 years after surgery \( (p>0.105 \text{ and } p>0.261, \text{ respectively}) \), following an initial decrease from pre- to 1 month postoperatively \( (p<0.001) \). Mean logMAR BSCVA remained stable \( (p>0.985) \), after an initial improvement from pre- to 12 month postoperatively \( (p=0.026) \). Mean BCLVA did not change \( (p>0.317) \). A corneal hydrops occurred in one eye at 4½ years postoperatively; no other postoperative complications were observed. Endothelial cell density remained stable during the entire follow-up period \( (p>0.174) \).

Conclusion: Isolated BL-grafts can successfully be prepared from both whole donor globes and corneoscleral rims with equivalent success. Furthermore, after early postoperative corneal flattening, topographies were stable up to 5 years after BL transplantation, preserving BCLVA and contact lens tolerance, potentially allowing long-term postponement of penetrating or deep anterior lamellar keratoplasty.
Clinical Outcomes of Conjunctival Limbal Autograft in Patients with Unilateral Total Limbal Stem Cell Deficiency

Medi Eslani, MD,**  *Cincinnati Eye Institute, University of Cincinnati*

**Co-Authors:** Albert Cheung, MD; Khaliq Kurji, MD, MSc, FRCSC; Enrica Sarnicola, MD; Amit Govil, MD; and Edward J. Holland, MD

**Purpose:** To investigate the long-term outcomes of conjunctival limbal autograft (CLAU) in patients with unilateral limbal stem cell deficiency (LSCD).

**Method:** In this retrospective observational case series, the medical charts of patients with unilateral LSCD were reviewed. Patients who underwent CLAU and no other allograft ocular stem cell transplantation with a minimum follow-up of 1 year were included. Main outcome measures were ocular surface stability, best-corrected visual acuity (BCVA), and CLAU-related postoperative complications.

**Results:** Twenty-seven eyes fulfilled the inclusion criteria with a mean follow-up period of 4.15 ± 3.05 years (range 1 to 15.56 years). Ocular surface stability was achieved in 77.8% (n=21) of eyes at last follow-up, while 22.2% (n=6) developed only partial surface failure. Optical penetrating or deep lamellar anterior keratoplasty was performed in 44.45% (n=12). BCVA improved from 1.42 ± 0.95 mean logMAR (equivalent to 20/400) preoperatively to 0.53 ± 0.47 mean logMAR (equivalent to 20/70) at last follow-up (P<0.0001). BCVA ≥ 20/40 was achieved in 44.45% (n=12) at last follow-up. Microbial keratitis occurred in 14.81% (n=4). There were no other complications related to the CLAU procedure in the donor or recipient eyes.

**Conclusion:** CLAU can provide long-term ocular surface stability and successful visual outcomes in patients with unilateral LSCD.
Assessing the Effects of Ripasudil, a Novel Rho Kinase Inhibitor, on Human Corneal Endothelial Cell Health

Andrew S. Goldstein, BS, University of Iowa Carver College of Medicine

Co-Authors: Benjamin T. Aldrich, PhD; Jessica M. Skeie, PhD; Gregory A. Schmidt, BS, CEBT; Cynthia R. Reed, RN, PhD; and Mark A. Greiner, MD

Purpose: To determine if a rho kinase inhibitor, ripasudil, can improve endothelial cell health in donor corneas.

Method: Peeled endothelial cell-Descemet’s membrane (EDM) tissues treated with 10 μm ripasudil and untreated controls were assayed for mitochondrial activity using extracellular flux analysis of oxygen. Additional EDM tissues treated with 1μm staurosporine and untreated controls were analyzed for cell viability using apoptosis and necrosis assays.

Results: Mitochondrial respiration metrics did not differ between ripasudil-treated and untreated tissues after exposure for one hour (P>0.25) or 24 hours (P>0.19). Following exposure to staurosporine, the percentage of necrotic corneal endothelial cells (CECs) did not differ (P=0.18) between ripasudil-treated (4.3%, SEM 0.7%) and untreated (6.8%, SEM 1.8%) tissues. In contrast, the percentage of apoptotic cells was lower (P=0.02) in ripasudil-treated tissues (2.8%, SEM 0.7%) compared to untreated controls (3.8%, SEM 0.9%) following exposure to staurosporine.

Conclusion: Mitochondrial respiration in CECs is not altered following acute exposures to ripasudil. However, CECs appear to gain some anti-apoptotic protective effect from a 24-hour treatment with ripasudil. These data suggest that ripasudil does not appear to pose any toxic effects on CECs and may help improve the integrity of the corneal endothelium.
The Results of Primary Descemet’s Stripping for the Treatment of Fuchs’ Dystrophy With and Without Postoperative Rho Kinase Inhibitor Drops: A Pilot Study

Marian S. Macsai, MD, NorthShore University HealthSystem

Co-Author: Mira Shiloach, MS, CRA

Purpose: To evaluate the effect of topical rho kinase inhibitors (RKI) in the postoperative period after primary Descemet’s stripping (PDS) for the treatment of Fuchs’ dystrophy (FD) in a prospective randomized non-masked pilot study.

Method: Patients with FD with gutatta limited to the central 5 mm of the cornea and a vision of less than 20/50 underwent PDS and were randomly treated with or without topical RKI during the postoperative period. Patients were evaluated for postoperative vision, pachymetry and endothelial cell counts.

Results: Twelve eyes of 12 patients (6 in each group) were observed for the first 3-month postoperative period. In the RKI group, patients reached V>20/40 in 5 weeks vs. 10 weeks in the no RKI group. The average endothelial cell count was 1020 in the RKI group vs. 703 in the no RKI group. The average pachymetry was 710 in the RKI group vs. 720 in the no RKI group.

Conclusion: The addition of topical RKI drops after PDS in FD may result in faster visual recovery and a higher endothelial cell count with no effect on the pachymetry at 3 months postop. Further studies are underway.
Pressure Sensitive Device for Intracorneal Dissection Depth Assessment

Alfonso Iovieno, MD, PhD, FRCSC, University of British Columbia; Arcispedale Santa Maria Nuova-IRCCS

Co-Authors: Luigi Fontana, MD, PhD; Caterina Salito, Eng; and Dario Bovio, Eng

Purpose: The aim of this study was to develop and test an innovative and inexpensive device for semi-quantitative determination of intracorneal dissection depth during deep anterior lamellar keratoplasty (DALK).

Method: A prototype device (Eye-CoDe) was designed to determine depth of intrastromal placement of a cannula based on the rebound pressure of an air stream emitted by a software controlled generator.

Ex vivo testing of the device was conducted in two experiments:

- In the first experiment, 12 human eye bank corneas were mounted on an artificial anterior chamber for deep anterior lamellar dissection using the “big bubble” technique. After partial thickness trephination (8.5 mm diameter, 400 microns) a cannula/syringe connected to the Eye-CoDe was introduced intrastromally and air injection was performed while recording the signal generated by the Eye-CoDe.

- In the second experiment, the cannula/syringe connected to Eye-CoDe was purposely introduced at different depths on 12 human eye bank corneas on an artificial anterior chamber (4 superficial, 4 deep, 4 transcorneal) while recording the signal generated by the Eye-CoDe. The depth of intrastromal placement of the cannula was measured using an anterior segment optical coherence tomographer (Spectralis, Heidelberg Engineering, Germany).

Results: In the first experiment, “big bubble” dissection was successful in 8 out of 12 cases. In all successful cases, Eye-CoDe was capable of detecting a measurable and repeatable decrease in tissue rebound pressure, which was not recorded in unsuccessful cases. In the second experiment, placement of the cannula at different stromal depths as measured by anterior segment OCT allowed detection of decrease in tissue rebound pressure only when the cannula was positioned within 100 microns from the endothelial plane.

Conclusion: The Eye-CoDe was shown ex vivo to produce a signal corresponding to deep placement of a DALK cannula and consequently effective pneumatic dissection via the “big bubble” technique. The use of such device could greatly aid in obtaining repeatable results in DALK.
Utility of HSV Serology in the Management of Corneal Pathology

John Wang, BS, + Case Western Reserve University

Co-Authors: Daniel Cherfan, MD, and Jeffrey Goshe, MD

Purpose: Herpes simplex viral (HSV) keratitis is frequently on the differential diagnosis for chronic or atypical corneal pathology. HSV serology is a rapid, widely available, relatively inexpensive blood test that when negative, may be useful to exclude HSV keratitis, obviating empiric antiviral therapy and minimizing medication adverse effects. Though previous population studies suggest the prevalence of HSV-1 and HSV-2 antibodies in adults is frequently greater than 50% and 15%, respectively, little literature addresses prevalence in patients presenting specifically with corneal pathology in which HSV is a possible diagnosis. The primary aim of this study is to determine the utility of obtaining HSV serology where herpes simplex is suspected by measuring how often serology impacted decision-making in diagnostically difficult cases.

Method: A retrospective analysis was performed based on data acquired from the Cole Eye Institute’s EMR system. A chart review was performed for all patients who presented to the Cole Eye Institute from 08/2011 to 12/2016 with a corneal condition for which HSV serology was performed. Patients with a known history of ocular herpes were excluded from the study. Patient demographics, presenting diagnosis, form and duration of any antiviral treatment, and follow-up duration were recorded.

Results: HSV serology was obtained in a total of 61 patients. Patients presented with chronic corneal ulcer (36.1%), chronic superficial keratitis (37.7%), chronic stromal keratitis (21.3%), and corneal transplant rejection (4.9%). We found the seroprevalence of HSV-1 and HSV-2 to be 37.9% and 16.7%, respectively. This is consistent with population-based studies with a lower than expected HSV-1 prevalence and a similar HSV-2 prevalence. Negative serologies impacted the decision-making in 29.0% of patients (defined as discontinuing antiviral medication, decreasing antiviral medication, electing not to start antiviral medication, or excluding HSV as a diagnostic consideration). Of note, no patients with negative serologies were ultimately diagnosed with HSV as the etiology of their corneal condition.

Conclusion: Although only useful when negative, our study indicates that obtaining HSV serology may play an important role in the decision-making for patients presenting with chronic or atypical corneal pathology in which HSV is a diagnostic consideration.
Incidence and Clinical Outcomes of Positive Donor Corneoscleral Rim Cultures

Carter Kirk, MD, Eye Consultants of Atlanta/Kirk Eye Center

Co-Authors: W. Barry Lee, MD, FACS, and Stephen Hamilton, MD

Purpose: To investigate the incidence and outcome of positive corneoscleral donor rim tissues transplanted at a private practice cornea group from 2015 to 2016.

Method: Retrospective cohort study. All corneal transplants performed at Eye Consultants of Atlanta/Piedmont Eye Surgery Center from 2015 to 2016 were reviewed. Corneoscleral rims of all transplanted tissues were sent for bacterial and fungal culture at Piedmont Atlanta Hospital or Emory Montgomery Laboratory.

Results: A total of 631 corneal transplants were performed at Piedmont Eye Outpatient Surgery Center from January 2015 to December 2016. There were 18 cases (2.9%) of positive fungal rim cultures, resulting in 3 clinical infections (16.7%). Fungal keratitis developed in all 3 cases, 2 of which progressed to endophthalmitis. All cases required surgical intervention for cure. There were 41 cases (6.5%) of positive bacterial rim cultures with no resultant clinical infections. Descemet’s stripping automated endothelial keratoplasty (DSAEK) and summer months were associated with a statistically significantly higher rate of positive fungal corneoscleral rim cultures, while death to preservation time and death to surgery time were not found to be risk factors.

Conclusion: Positive fungal rim cultures are an uncommon, but increasingly recognized, phenomenon. Given the high morbidity associated with clinical infection, we recommend routine culturing of corneoscleral rims for fungus and prompt prophylactic treatment of positive rims. The growing body of literature on fungal keratitis after transplantation suggests renewed consideration of adding antifungal treatment to donor culture media.
Outcomes of Allograft Ocular Surface Stem Cell Transplantation with Systemic Immunosuppression in Pediatric Patients

Albert Y. Cheung, MD, Virginia Eye Consultants

Co-Authors: Enrica Sarnicola, MD; Medi Eslani, MD; Khaliq Kurji, MD; Elizabeth Wright, LPN; Jens Goebel, MD; David K. Hooper, MD; Amit Govil, MD; and Edward J. Holland, MD

Purpose: To describe outcomes of allograft ocular surface stem cell transplantation (OSST) and the complication profile of systemic immunosuppression (SI) in pediatric patients with limbal stem cell deficiency (LSCD).

Method: We performed a retrospective chart review of 419 eyes that underwent OSST between May 2000 and April 2017. Patients aged ≤ 18 years at the time of first allograft OSST surgery who received SI were included. Ocular surface stability and SI adverse events were the primary outcome measures.

Results: A total of 19 eyes from 13 patients with mean age of 15.4 ± 2.9 years (range 9 to 18 years) were included. Mean follow-up was 5.4 ± 5.1 years after OSST. Etiology of LSCD included aniridia (n=13), chemical/thermal (n=2), Stevens-Johnson syndrome (n=2), and autoimmune polyendocrinopathy (n=2). At last follow-up, 14 eyes (74%) had a stable ocular surface, 1 eye (5%) developed partial failure, and 4 eyes (21%) developed total surface failure. Furthermore, 11 patients remained on SI for a mean total time of 4.9 ± 4.5 years (range 13 to 166 months) on SI. Initial SI consisted of oral tacrolimus and mycophenolate mofetil and was tolerated well by all patients with minimal adverse events.

Conclusion: This is the first study evaluating the use of SI in a pediatric population following OSST. OSST provided a stable ocular surface in the majority of pediatric patients with LSCD. Systemic immunosuppression is well-tolerated with an acceptable complication profile, but appropriate adherence and monitoring are essential for success in this population.
Incidence and Outcomes of Infectious Keratitis after Ocular Surface Stem Cell Transplantation

Enrica Sarnicola, MD,* Cincinnati Eye Institute

Co-Authors: Albert Y. Cheung, MD; Medi Eslani, MD; Khaliq Kurji, MD; Amit Govil, MD; and Edward J. Holland, MD

Purpose: To describe the incidence, clinical/microbiological characteristics, and outcomes of infectious keratitis in eyes with limbal stem cell deficiency (LSCD) that have undergone ocular surface stem cell transplantation (OSST).

Method: Retrospective chart review of 278 eyes that underwent OSST between January 2006 and December 2016. Eyes treated for a prior infectious keratitis (bacterial, fungal, or viral) were included. Demographics, risk factors, course, microbiological characteristics, and outcomes were assessed.

Results: A total of 52 eyes (18.7%) from 48 patients (28 men, 20 women) developed 75 episodes (culture-proven or presumed) of infectious keratitis (range 1–4 episodes) with mean follow-up of 5.3 ± 3.6 years after OSST. The most common LSCD etiologies included chemical/thermal (n=18, 27 episodes), aniridia (n=8, 8 episodes), Stevens-Johnson syndrome (n=11, 19 episodes), and mucous membrane pemphigoid (n=4, 8 episodes). There were 44 (58.7%) episodes of bacterial keratitis, 24 (32%) episodes of fungal keratitis, and 7 (9.3%) episodes of HSV keratitis. Of the culture-proven cases, Gram-positive bacteria (79%) and Candida species (73%) were the most common pathogens. Prior to infection, 33% had an epithelial defect, 91% were on systemic immunosuppression (SI), 65% were in a bandage contact lens, and 24% had a recent ocular surgery. While 75% resolved with antimicrobial treatment, 25% required a therapeutic keratoplasty (TPK), and 2 cases needed multiple TPKs.

Conclusion: Despite successful OSST surgery, infectious keratitis is relatively common, and aggressive medical and surgical therapy is warranted. Prophylactic topical antibiotics, SI treatment, and a cicatrizing conjunctivitis diagnosis may account for the high proportion of fungal keratitis in this population.

*Resident
Prosthetic Replacement of the Ocular Surface Ecosystem Devices for Ocular Surface Disease in Pediatric Patients with Stevens-Johnson Syndrome

Yvonne Wang, MD,* Massachusetts Eye and Ear Infirmary

Co-Authors: Hajirah N. Saeed, MD; Rohini Rao, MD; James Chodosh, MD, MPH; and Deborah S. Jacobs, MD

Purpose: Prosthetic replacement of the ocular surface ecosystem (PROSE) treatment uses customized scleral lens prosthetic devices to support ocular surface function in ocular surface disease (OSD). We present an outcomes study of PROSE treatment in the pediatric patients affected by Stevens-Johnson syndrome and toxic epidermal necrolysis (SJS/TEN).

Method: This is a retrospective cohort study. We reviewed records from 1997 to 2011 from the Boston Foundation for Sight of patients age 18 or younger with SJS/TEN, who were seen in consultation for PROSE treatment. Age at consultation, age at the time of PROSE fitting, initial visual acuity (VA), initial and final VA with PROSE treatment, daily wear time, and device diameter were recorded among other data points.

Results: Thirty pediatric patients were seen in consultation. 55 eyes were fitted for PROSE and successful wear was documented in 42 eyes. The average age at presentation was 6.17 years. The median VA at the time of consult was 20/80. The average age at the time of first successful PROSE wear and dispense was 9 years (range 4-19). The median initial VA after PROSE fitting was 20/30 and was maintained at 20/30 at last follow-up visit. The average diameter of the final PROSE device was 17.23 mm with an average final wear time of 13 hours.

Conclusion: PROSE treatment is feasible in pediatric patients as young as age 4 with OSD caused by SJS/TEN, with improvement and stabilization of vision similar to what has been reported for adults.

*Resident
Boston Type I Keratoprosthesis as the Primary Penetrating Corneal Procedure

Todd Driver, MD,* Stein Eye Institute, UCLA

Co-Authors: Carolina Aravena, MD; Huong Duong, MD; Joseph G. Christenbury, MD; Fei Yu, PhD; Samar K. Basak, MD; and Anthony J. Aldave, MD

Purpose: Report the long-term outcomes of the Boston type I keratoprosthesis (KPro) as the primary penetrating corneal procedure in patients with a high risk of penetrating keratoplasty (PK) failure.

Method: Retrospective review of all KPro procedures performed by two surgeons between 5/1/04 and 12/31/15. Postoperative outcomes were compared between KPros performed as the primary penetrating corneal procedure (no prior PK) versus following PK failure (prior PK).

Results: A total of 262 KPros were implanted in 231 eyes (221 patients); 79 procedures were performed in 67 eyes (63 patients) with no prior PK. The most common indications in eyes with no prior PK were corneal scarring/vascularization (43%), SJS (22%), and chemical/thermal injury (22%). Preoperative glaucoma was significantly less common in the no prior PK group (39% vs. 75%, \( p < 0.0001 \)). While there was no significant difference in the percentage of eyes with preop CDVA \( \geq 20/200 \) (\( p = 0.36 \)), the percentage was significantly higher in the no prior PK group each of the first 4 years after surgery (all \( p \leq 0.023 \)). The most common postoperative complications were RPM (48%), PED (28%) and elevated IOP (22%), which was the only complication that was significantly more common in one group (31% in no prior PK group vs. 18%, \( p = 0.034 \)). No difference in KPro retention was observed over a mean follow-up period of approximately 3 years (\( p = 0.63 \)).

Conclusion: In eyes in which PK is associated with poor outcomes and in which KPros have been associated with an increased incidence of postop complications, KPro as the primary penetrating corneal procedure is associated with significantly greater percentage of eyes with CDVA \( \geq 20/200 \) in the first 4 years, likely due to a significantly lower prevalence of preop glaucoma. However, given a significantly higher incidence of postop IOP elevation in these eyes, longer follow-up is needed to determine if the difference in CDVA is maintained.

*Resident
Intraocular Light Scatter in Eyes with Implanted Boston Keratoprosthesis Type I

Faris Karas, MD,∗∗ University of Illinois, Eye and Ear Infirmary

Co-Authors: Andrea C. Arteaga, MD; Pablo Barrionuevo, PhD; Jason McAnany, PhD; and Maria S. Cortina, MD

Purpose: Boston Keratoprosthesis (KPro) has been proven to be a viable option for visual rehabilitation in patients with poor prognosis for penetrating keratoplasty, and its use has consistently increased during the past decade. After multiple modifications in KPro design and postoperative management, long-term retention, fewer complications and overall improved outcomes are now possible. Despite the good objective visual acuity (VA) achieved by some patients, many complain of significant glare resulting in visual dysfunction. This clinical finding motivated us to objectively measure light scattering in eyes with KPro.

Method: Light scatter was prospectively measured in 16 eyes of 16 patients with implanted KPro type 1 and VA of 20/150 or better and compared to 10 eyes of healthy control subjects using OCULUS C-Quant device. The measurements were done at repeated visits, with and without contact lenses.

Results: The mean age for the KPro group was 56.85 years (range 35–72) and for the control group was 58.74 years (range 32–74). Mean VA was 0.47 logMAR (SD± 0.23) and 0.01 logMAR (SD± 0.04) for the KPro group and control group, respectively. Intraocular light scatter was found to be significantly higher in patients with KPro when compared to healthy control subjects (logS values of 1.47 and 2.17, respectively, p<0.01). Measured light scatter in patients with titanium backplate KPro only approximated that of the control group (p=0.08) and was significantly higher than PMMA backplate KPro (logS 1.79). There was a trend toward reduced light scatter in patients with repeated measurements 1 year apart.

Conclusion: Glare seems to be a true visual phenomenon frequently experienced by many patients with KPro. In fact, light scatter measured in this study showed significantly higher values in eyes with KPro compared with healthy control eyes. Possibly due to its opaque nature, titanium backplate model appears to produce less light scatter than PMMA backplate model. Finally, it is possible that the need for glare treatment decreases over time.

∗∗Corneal Fellow
One Step Closer To A More Practical Artificial Cornea

Miguel Gonzalez-Andrades, MD, PhD,** Massachusetts Eye and Ear and Schepens Eye Research Institute

Co-Authors: Mirazul Mohammad Islam, PhD; Thibaut Divoux, PhD; Michael Haist, PhD; Roholah Sharifi, PhD; Eleftherios Paschalis, PhD; Andrea Cruzat, MD; Larisa Gelfand, MD; Franz Joseph Ulm, PhD; Francois Delori, PhD; James Chodosh, MD; and Claes H. Dohlman, MD, PhD

Purpose: The present process of assembly and implantation of the Boston Keratoprosthesis (B-KPro) has led to occasional errors, and the logistics are cumbersome and expensive. A simplified method is proposed. The B-KPro can be preassembled into a corneal graft and then transferred to a vial to be sterilized with $\gamma$-radiation (approved method for corneal grafts). The resulting combination can then be stored and transported. For such a procedure to be acceptable, it has to be shown that $\gamma$-radiation will not damage the B-KPro.

Method: We have evaluated the effect of $\gamma$-radiation on the medical PMMA that is used in the manufacturing of the B-KPro. 15-mm diameter discs of PMMA were submitted to either ethylene oxide sterilization (the presently used process for the B-KPro), or different doses of $\gamma$-radiation (10, 25 and 50 kGy), independently. Cell biocompatibility, mechanical strength, and optical quality of the material were evaluated. Moreover, the feasibility of assembling the B-KPro to an allograft and $\gamma$-irradiate afterward was also evaluated.

Results: There were no differences in cell biocompatibility among the samples, after culturing corneal epithelial cells and fibroblasts in contact with them ($p>0.05$). The mechanical evaluation by statistical nanoindentation showed no alterations of the PMMA after irradiation. The optical evaluation showed high levels of transparency for the ethylene oxide, 10 and 25 kGy groups. The absorbance of ultraviolet was higher for the 25 and 50 kGy groups. Technically, preassembly and irradiation of the B-KPro revealed no problems.

Conclusion: Sterilization of the B-KPro using $\gamma$-radiation has no detectable influence on the biocompatibility, mechanical or optical properties of the device. The preassembly of the B-KPro to a donor cornea, followed by sterilization with $\gamma$-radiation, allowing long-term storage and easy shipment, emerges as an efficient and safe procedure.

**Corneal Fellow
Incidence and Outcomes of Infections in the Cornea Preservation Time Study

Shahzad Mian, MD, University of Michigan

Co-Authors: Anthony J. Aldave, MD; Elmer Y. Tu, MD; Loretta B. Szczotka-Flynn, OD, PhD; Allison R. Ayala, MS; Wendi Liang, MSPH; Roy Beck, MD, PhD; Jonathan H. Lass, MD; and Cornea Preservation Time Study Group

Purpose: To assess incidence and outcomes of infectious keratitis and endophthalmitis after DSAEK in the Cornea Preservation Time Study (CPTS).

Method: A total of 1,330 eyes undergoing DSAEK enrolled in the CPTS were randomized to receive donor corneas with preservation time (PT) of 0-7 days (675 eyes) or 8-14 day PT (655 eyes) across 40 sites. Donor rim cultures, not required by the CPTS protocol, were available in 401 (59%) eyes in the 0-7 day PT group and 393 (60%) eyes in the 8-14 day PT group. Cases of ocular infections were identified and data were collected regarding donor corneal tissue characteristics including PT, donor and recipient and mate tissue cultures, and recipient outcomes.

Results: Positive fungal cultures were found in 2.5% (10/401) in the 0-7 day PT group and 1.3% (5/393) in the 8-14 day PT group. Postkeratoplasty infection developed in three eyes (0.2%): two eyes developed infectious keratitis (Candida albicans and Candida glabrata), both in the 8-14 day PT group (0.3%; 2/655); and one eye developed endophthalmitis (E. coli) in the 0-7 day PT group (0.1%; 1/675). All three patients recovered CDVA > 20/30.

Conclusion: Results from routine culturing techniques in the multi-center CPTS did not suggest any association between PT and incidence of positive fungal cultures. The overall incidence of infectious keratitis and endophthalmitis is low after DSAEK with ultimately good visual outcomes.
A Comparison of Topical 5-Fluorouracil 1% and Topical Interferon Alfa-2b as Primary Treatment Modalities for Ocular Surface Squamous Neoplasia

Nandini Venkateswaran, MD,* Bascom Palmer Eye Institute

Co-Authors: Anat Galor, MD, MSPH, and Carol L. Karp, MD

Purpose: To compare the efficacy of topical 5-fluorouracil (5FU) and interferon alfa-2b (IFN) as primary treatment modalities for ocular surface squamous neoplasia (OSSN).

Method: A pharmacy database was used to identify all patients with OSSN who were treated with either 5FU or IFN as primary treatment modalities for OSSN at our institution between January 2013 and July 2016. Patients were excluded if either agent was used as adjuvant surgical therapy, if treatment was not completed, or if patients were lost to follow-up, still in active treatment, or not primarily managed at our institution. Fifty-four patients who received 5FU as primary treatment modality and 48 patients who received IFN as primary treatment modality for OSSN were identified. Retrospective chart reviews were conducted. Primary outcome measures were the frequency of clinical resolution and time to OSSN recurrence by treatment modality. A secondary outcome was the frequency of complications associated with each therapy.

Results: The mean age of the population was 68 with a standard deviation (SD) of 13.4. Demographics between groups were comparable except for a higher number of Hispanics treated in the 5FU group. The frequency of OSSN resolution was higher with 5FU (96.3%, n=52) than with IFN (81.3%, n=39), p=0.014. However, in those with resolved OSSN, time to resolution was similar between both agents (5FU with mean of 196 days and SD 135.2 versus IFN with mean of 166 days and SD 86.0, p=0.173). 11.5% of lesions (n=6) treated with 5FU recurred while 5.1% of lesions (n=2) treated with IFN recurred, p=0.459. Kaplan Meier survival curves of OSSN recurrence were similar between the groups, p=0.16. Regarding complications, 5FU most frequently caused pain (24.1%, n=13), tearing (22.2%, n=12), and redness (20.4%, n=11), while IFN was overall well-tolerated.

Conclusion: This is the first head-to-head comparison study between 5FU and IFN as primary treatment modalities for OSSN. Tumors were more likely to resolve with 5FU as compared to IFN, but 5FU was associated with a higher, but not statistically significant, recurrence rate.

*Resident
Comparison of 5-Year Graft Survival and Rejection Episode Rates with DMEK vs. DSEK

David Price, BS,* Cornea Research Foundation of America

Co-Authors: Marianne O. Price, PhD; Meagan Kelley, BS; and Francis W. Price Jr., MD

Purpose: To compare the 5-year graft survival, endothelial cell loss, and rejection episode rates with DMEK and DSEK.

Method: This study reviewed outcomes of a consecutive series of 1312 DSEK and 688 DMEK cases performed by 9 surgeons to treat Fuchs’ dystrophy and included the surgeons’ first cases. Survival rates were calculated by Kaplan-Meier analysis.

Results: Using criteria from the Cornea Preservation Time Study, the 5-year cumulative graft rejection episode rates were 2% with DMEK and 8% with DSEK (p<0.0001). African Americans had a significantly higher risk of rejection than other races (p<0.0001). Experiencing a rejection episode was not a significant predictor of graft failure within 5 years of surgery, p=0.90. Overall, 111 grafts failed or were replaced within 5 years for any reason, and the cumulative 5-year survival rate was 93% with both DSEK and DMEK, p=0.86. The median 5-year endothelial cell loss was comparable with DMEK and DSEK (47% and 45%, respectively, p=0.69). Graft survival was not significantly impacted by donor sex (p=0.84) nor by donor/recipient sex matching (p=0.17 for male recipients and p=0.67 for female recipients).

Conclusion: Five-year graft survival was comparable with DMEK and DSEK. Although DMEK had a significantly lower risk of immunologic rejection, few rejection episodes resulted in graft failure within 5 years with either procedure.
Descemet's Membrane Endothelial Keratoplasty (DMEK) Versus Descemet's Stripping Endothelial Keratoplasty (DSEK) in Patients with Prior Glaucoma Surgery: A Comparison of Matched Pairs

Shawn Lin, MD, MBA,* Stein Eye Institute, UCLA

Co-Authors: Pitchaya Prapaipanich MD; Fei Yu, PhD; Joseph Caprioli, MD; Simon Law, MD; Sophie Deng, MD; and Anthony J. Aldave, MD

Purpose: To evaluate the outcomes of Descemet's membrane endothelial keratoplasty (DMEK) and Descemet's stripping endothelial keratoplasty (DSEK) in eyes with prior trabeculectomy and/or tube shunt implantation.

Method: This is a retrospective study of 162 consecutive DMEK and 597 consecutive DSEK procedures performed between August 2006 and December 2016. Among these patients, 59 DMEK (36%) and 154 DSEK (26%) procedures were performed in eyes with prior trabeculectomy and/or tube shunt implantation. For this study, we used SAS v9.4 to select a population of DMEK (n=47) and DSEK (n=47) procedures matched by preop visual acuity, lens status, and surgical indication.

Results: The length of follow-up was 10.0 months in the DMEK group and 10.3 months in the DSEK group (p=0.72). Best-corrected visual acuity (BCVA) improved by -0.87 logMAR units in the DMEK group and -0.47 logMAR units in the DSEK group (p=0.03). Visual acuity was significantly better in the DMEK group at 1, 3, and 12 months, with a trend toward significance at month 6 (p=0.055). Secondary graft failure at 1 year was significantly lower in the DMEK group (2%) versus the DSEK group (17%, p=0.016). There was not a significant difference between primary graft failure in the DMEK group (2%) vs. the DSEK group (4%, p=1.00). Air injection rate was higher in the DMEK group (23%) versus the DSEK group (11%), but this was not a significant difference (p=0.17). There was no significant difference in donor endothelial cell count (ECC) (p=0.5871). A subset of procedures had endothelial cell loss data (DSEK n=27, DMEK n=29). Among this subset, endothelial cell loss percentage was higher in the DMEK group (- 54%) versus the DSEK group (- 47%) but was not statistically significant (p=0.35).

Conclusion: This study is the largest matched comparison of DMEK and DSEK patients with prior glaucoma surgery, and demonstrates the advantages of the DMEK procedure in this population group. Visual acuity improves faster in the DMEK group, and overall visual acuity at 12 months is significantly better. In addition, the risk of graft failure is lower in the DMEK study population. Given these benefits, we would advocate for the use of DMEK corneal transplant in eyes with prior glaucoma surgery.

*Resident
Outcomes of Eye Bank Prepared Pre-stripped, Pre-stained, and Pre-loaded Descemet’s Membrane Endothelial Keratoplasty (p³DMEK)

Nathan Liles, MD, MPH,* University of Michigan

Co-Authors: Shahzad Mian, MD; Purak Parikh, MD; Nicholas Hicks; and Munira Hussain, MS

Purpose: To assess feasibility and early outcomes of eye bank prepared p³DMEK.

Method: A prospective cohort of patients undergoing DMEK with eye bank prepared p³DMEK tissue was studied. Primary outcomes included primary graft failure, graft detachment, and need for rebubbling. Secondary outcomes included baseline and post-operative visual acuity at 1 week, 1 month, and 3 months. Baseline and 3-month postoperative pachymetry, refraction, and specular microscopy endothelial counts were also analyzed.

Results: 17 eyes of 16 patients were enrolled with a mean follow-up of 66 days (range 8 – 118 days). 8 patients completed 3 months of follow-up with a mean corrected distance visual acuity of 20/22 (95% CI 20/20–20/25). At postoperative month 3, the mean change in donor endothelial cell counts and recipient pachymetry were – 312 cells/mm² (95% CI -210 – −414) and –84.9 μm (95% CI -51.0 – −118) respectively. Mean case time was 37 minutes (95% CI 27–47) for p³DMEK with phacoemulsification and 26 minutes (95% CI 21–31) for p³DMEK alone. For comparison, mean case time by the same surgeon for 21 patients undergoing standard DMEK with phacoemulsification or DMEK alone was 46 minutes (95% CI 43–49) and 36 minutes (95% CI 29–43). Two grafts underwent rebubbling at post-operative days 15 and 16 and 1 patient had pupillary block requiring partial removal of SF6.

Conclusion: Eye bank prepared p³DMEK tissue is safe and can provide good early clinical outcomes.

*Resident
Fungal Interface Keratitis After Descemet’s Membrane Endothelial Keratoplasty

Friedrich Kruse, MD, *University of Erlangen-Nuremberg*

**Co-Authors:** Victor A. Augustin, MD; and Theofilos Tourtas, MD

**Purpose:** To evaluate the incidence, clinical course and management options of fungal interface keratitis after Descemet’s membrane endothelial keratoplasty (DMEK).

**Method:** Single-center retrospective observational case series of 3600 eyes undergoing DMEK at the Department of Ophthalmology, University of Erlangen-Nuremberg. Five patients with fungal interface keratitis were detected and analyzed. Analysis included preoperative characteristics of corneal grafts, patient’s clinical courses, and therapeutic approaches.

**Results:** Fungal interface keratitis after DMEK occurred in 5 out of 3600 cases (0.0014%). Short term cultured grafts from the United States (n=3) and organ cultured grafts from Europe (n=2) were used. Microbiological culture medium analysis showed the growth of *Candida* in all cases (2x *C. tropicalis*, 2x *C. albicans*, 1x *C. orthopsilosis*). After appearance of clinical signs of interface keratitis and microbiological confirmation of *Candida*, all patients received antifungal topical and systemic treatment as well as intracameral application of antifungal medication. The best results were achieved by immediate graft exchange, intracameral application of voriconazole and amphotericin B for 20 minutes combined with topical voriconazole 1%/amphotericin B 0.5% and systemic voriconazole 8 mg/kg.

**Conclusion:** Fungal interface keratitis is a rare clinical entity during the early postoperative period after DMEK. Based on our experience, treatment of choice after suspicion and diagnosis of fungal interface keratitis should be immediate graft exchange and application of voriconazole and amphotericin B in the anterior chamber. Based on our findings addition of a broad spectrum antifungal agent to the culture medium should be considered.
Some Like it Hot: Real World Results of Tissue Evaluation After Implementation of a Rapid Warming Protocol

Jameson Clover, CEBT, Lions VisionGift

Co-Authors: Amy Ansin, BS; Christopher G. Stoeger, MBA, CEBT; Mark Terry, MD; and Khoa D. Tran, PhD

Purpose: To compare tissue evaluation times and specular image quality of donor corneas before and after implementation of rapid tissue warming at a single eye bank.

Method: This retrospective study compares the evaluation of 494 donor corneas. All corneas were stored in Optisol-GS. Group 1 contains 247 corneas evaluated immediately before implementation of a tissue incubator. Group 2 contains 247 corneas evaluated immediately after implementation. Total evaluation times (including specular microscopy and 2 slit-lamp exams) were calculated and compared. Representative specular images of donor corneas were rated and compared using a previously described scale by two masked readers.

Results: Donor tissue characteristics were not significantly different between the two groups (age, \( P=0.99 \); gender, \( P=0.93 \); lens status, \( P=0.08 \); and endothelial cell densities, \( P=0.31 \)). Averaged total evaluation time for Group 2 corneas was \(~3\) hours, with \(88\%\) of evaluations completed in one day (i.e., 1 warming cycle). In contrast, only \(60\%\) of corneas from Group 1 were completely evaluated in one day, and the averaged evaluation times for those corneas was \(~4.25\) hours \((P<0.01)\). Time out of refrigeration until specular image acquisition for Group 2 was 1.75 hours compared to 3.1 hours for Group 1 \((P<0.01)\). Further, 71\% of specular images from Group 2 were categorized as “good” or “excellent” quality, while only 30\% of corneas from Group 1 received those ratings.

Conclusion: Rapid tissue warming cuts down on tissue evaluation time, decreases time donor corneas are out of cold storage, and dramatically reduces tissue exposure to multiple warming cycles during tissue evaluation.
Development of a New Corneal Storage Medium with Antimycotic Tablet

Jana D’Amato Tóthová, PhD, Alchilife S.r.l.

Co-Authors: Francesca Pateri, MSc; Laura Giurgola, MSc; Anna Limongelli, MSc; Daniela Tomasiello; Elisabetta Frigerio; and Raffaela Mistó, PhD

Purpose: Cold corneal storage media available on the market do not contain antimycotics. A new corneal storage medium with an antimycotic tablet (Kerasave, AL.CHI.MI.A. S.r.l.) was developed to prevent fungal contamination of donor corneas intended for transplantation. The aim of this study was to assess the antimycotic activity of the new cold storage medium, Kerasave, and to evaluate the quality of donor corneas preserved in the medium at 4°C for 14 days in comparison with Optisol GS.

Method: Kerasave antimycotic activity was determined by in vitro time-kill studies using sterile porcine corneal tissues, contaminated with 10^5 cfu/ml of C. albicans (ATCC 10231 and clinical isolate). The killing rate of the microorganisms was monitored at 4°C after 5 and 10 days of incubation in Kerasave. Kerasave performance was assessed on 16 pairs of human corneas not suitable for transplantation, procured and evaluated according to standard procedures of Monza Eye Bank, Italy. One cornea was transferred in Kerasave and the contralateral in Optisol GS. Endothelial cell density (ECD), measured by specular microscopy (Keratoanalyzer, Konan), was evaluated pre-processing, and after 7 and 14 days of storage at 4°C. Endothelial cell morphology and mortality were determined according to Stocker method, and epithelial integrity and corneal transparency were evaluated using a slit lamp.

Results: In vitro kill-time studies showed 3.6 log_{10} reduction for both Candida strains after 5 days of incubation at 4°C and 4 log_{10} reduction was observed for both strains after 10 days of incubation. Kerasave- and Optisol-GS-treated tissues showed similar ECD, mortality and endothelial morphology after 7 and 14 days of cold storage. Slit lamp analysis showed comparable corneal transparency and epithelial integrity in both groups.

Conclusion: The new cold storage medium with antimycotic tablet Kerasave exhibited an excellent antimycotic activity and biocompatibility with donor corneas after corneal storage at 4°C for up to 14 days.
Outcomes of Secondary Penetrating Keratoplasty Graft Failure Managed by Descemet’s Membrane Endothelial Keratoplasty

Nicolas Cesário Pereira, MD, Sorocaba Eye Bank and UNIFESP

Co-Authors: Nicolas Cesário Pereira, MD; Adriana dos Santos Forseto, PhD; Michele Wong, MD; and Henrique Delloiagono, MD

Purpose: To describe the clinical outcomes of Descemet’s membrane endothelial keratoplasty (DMEK) performed for secondary graft failure after penetrating keratoplasty (PK).

Method: Retrospective study, including 47 eyes of 42 patients undergoing DMEK after a secondary PK graft failure by a single surgeon (N.C.P.) from July 2014 to July 2017 at Sorocaba Eye Bank/Sorocaba Ophthalmology Hospital. Best spectacle corrected visual acuity (BSCVA), biomicroscopy, previous eyes diseases and complications were evaluated.

Results: There were no intraoperative complications. Graft detachment occurred in two eyes (4.2%) with preexisting tube from glaucoma-draining device implanted, and were successfully managed with rebubbling. One eye had a secondary graft failure due to a stromal scar after infectious keratitis. Two eyes with preexisting tube from glaucoma-draining device implanted had late secondary graft failure (at 1 and 3 years after DMEK). One patient with 3 previous PK and a vascularized cornea developed graft rejection at 4 months postoperatively and evolved to secondary graft failure. At the last follow-up visit (from 1 month to 3 years), excluding the eyes with low visual potential, 88.5% achieved BSCVA of 20/40 or better, 73% 20/30 or better, 38.4% 20/25 or better, and 19.2% 20/20 or better. From the eyes with good visual potential, there were 3 eyes (11.5%) that needed rigid contact lenses for visual rehabilitation. There were 16 eyes with associated ocular conditions as tubes, fixated intraocular lenses or were vitrectomized. A combined procedure was performed in 8 patients with associated cataract.

Conclusion: DMEK is a great option to manage secondary graft failure after PK in selected cases, with fast visual rehabilitation and reduced risk of intraoperative complications. Visual rehabilitation can be limited due to associated retinal conditions and irregular corneas. Rebubbling rate was low and associated to preexisting tubes from glaucoma-draining devices.
Microneuromas May Allow Differentiation of Patients with Neuropathic Corneal Pain From Dry Eye Disease

Hamid-Reza Moein, MD, Tufts Medical Center

Co-Authors: Gabriela Dieckmann, MD; Alessandro Abbouda, MD; Nicholas Pondelis, BS; Arsia Jamali, MD, MPH; Zeina Salem, MD; and Pedram Hamrah, MD

Purpose: The diagnosis of neuropathic corneal pain (NCP) is challenging and most often difficult to differentiate from dry eye disease (DED). In addition to pain, NCP can present with similar signs and symptoms of DED. Thus, objective diagnostic tools to identify patients with NCP are needed. The purpose of this study is to compare subbasal corneal nerve and immune dendritiform cell alterations between patients with DED and NCP.

Method: This cross-sectional study included patients with DED (n=19), NCP (n=20), and age and sex-matched normal controls (n=16), who underwent central corneal laser in vivo confocal microscopy (IVCM, HRT3/RCM). Subbasal corneal nerve density and morphology (nerve beading, bead-like formation along the nerves), presence of microneuromas (enlarged nerve terminal sprouts), and dendritiform cell density (DCD) were assessed and compared between the groups by 2 masked observers.

Results: Total nerve density was decreased in both NCP patients (10.6±2.0 mm/mm²) and DED (13.0±1.1 mm/mm²) as compared to normal controls (23.9±0.9 mm/mm²; p<0.001). While total nerve density was lower in patients with NCP as compared with DED, it was not statistically significant (p=0.42). Nerve beading was present in all DED and NCP patients and in 14/16 of control group (P=0.15). Interestingly, microneuromas were observed in all patients with NCP, while they were not detected in any of the patients with DED (sensitivity and specificity of 100%). DCD was increased in both NCP (70.2±28.9 cells/mm²) and DED (81.1±19.2 cells/mm²) as compared to normal controls (24.8±4.4 cells/mm²; p=0.10). However, there was no significant difference in DCD between DED and NCP patients (p=0.79).

Conclusion: IVCM may be used as an adjunct diagnostic tool to differentiate NCP from DED. Micro-neuromas might serve as a sensitive and specific criterion in differentiating patients with NCP from DED.
Comparison of Descemet’s Membrane Endothelial Keratoplasty Pressurized with Different Intraocular Pressure Levels

José Álvaro Pereira Gomes, PhD, Sorocaba Eye Bank and UNIFESP

Co-Authors: Nicolas Cesário Pereira, MD; Adriana dos Santos Forseto, PhD; Heanes Troglio Pfluk, MD; André Jerez Rezala, MD

Purpose: To compare the results and rebubbling rates of Descemet’s membrane endothelial keratoplasty (DMEK) using an air bubble to fixate the graft, pressurized with different intraocular pressure levels.

Method: Randomized prospective study, including Fuchs’ dystrophy patients. Group 1 included patients who underwent DMEK using an air bubble to fixate the graft, with an intraocular pressure (IOP) of 40 mm Hg (38 to 42 mm Hg) for 20 minutes, then the pressure was reduced to 20 mm Hg (18 to 22 mm Hg) at the end of the procedure. Group two underwent DMEK with the same surgical technique but using an air bubble to fixate the graft with an IOP of 20mmHg (18 to 22 mm Hg) at the end of the procedure. All surgeries were performed by the same surgeon (N.C.P.). All donor corneas were stored with cold storage medium, and all grafts were prepared intraoperatively. IOP was measured with Perkins handheld tonometer. Clinical results, rebubbling rates, and complications were described.

Results: 136 patients were included, 68 patients in group 1 and 68 in group 2. Rebubbling was required for 2 patients in group 1 (2.9%) and 6 patients in group 2 (8.8%). No primary graft failure or pupillary block were observed. One patient presented with high intraocular pressure in the first postoperative day, and the air bubble was partially released to lower the pressure.

Conclusion: Pressurizing the anterior chamber with an air bubble with a higher intraocular pressure at the end of DMEK reduces the rebubbling rates.
The Utility of the Hybrid-DMEK Pull-Through Technique for Complex DMEK Surgery

Donald Tan, FRCS, Singapore National Eye Centre

Purpose: The hybrid-DMEK (HDMEK) procedure uses a controlled pull-through technique to deliver the DMEK donor tissue using the EndoGlide DSAEK inserter and has been performed in 60 clinical cases. We report on the utility of this procedure in 26 of these cases involving complicated or complex eyes with multiple anatomical comorbidities, in which conventional DMEK would be relatively contraindicated, in an attempt to assess surgical feasibility of the HDMEK procedure in these more challenging surgical scenarios.

Method: The two main indications for performing DMEK in these complex eyes was for the low allograft rejection risk (as compared to DSAEK or PK) in cases of high risk rejection such as previous failed grafts, and for cases with complex, crowded anterior chambers with PAS etc, where there was less anterior chamber space to place a DSAEK graft without iris or angle contact. In all cases, HDMEK donor graft insertion was only performed after correction of the anatomical abnormalities, such as PAS synechiolysis, previous DSAEK lenticule removal, AC-IOL removal, vitrectomy, and secondary IOL fixation. Aniridic eyes were left aniridic in this series. All eyes with the exception of aniridic eyes had inferior peripheral iridectomies performed, and a full chamber of air was left at the end of surgery.

Results: All 26 complicated cases were cases of severe pseudophakic (n=22) or aphakic bullous keratopathy (n=4) with various combinations of anatomical AC comorbidities that included extensive peripheral anterior synechiae (PAS, n=8), failed PKs or DALKs (n=7), failed DSAEKs (n=5), presence of functioning glaucoma drainage tubes (n=6), presence of AC-IOLs requiring removal, vitrectomy and transscleral posterior chamber IOL fixation (n=5), aniridia (n=3), ICE syndrome (n=3), severe PBK or ABK with very poor view of the AC, and dislocated IOLs requiring vitrectomy and IOL refixation (n=2). 13 of the 26 eyes had preexisting glaucoma treated medically or surgically prior to DMEK surgery. Mean follow-up period was 3.9 months (range 1-8 months). HDMEK was successful in 25 of the 26 eyes, with one primary graft failure due to extensive fibrin formation and persistent graft detachment in an infant with ABK, which required subsequent DMEK graft exchange. Several eyes had limited areas of peripheral graft attachment, which resolved spontaneously, and only 2 eyes required rebubbling. No rejections have occurred to date. Postoperative complications (which did not lead to DMEK graft failure) included recurrence of PAS in 2 eyes, postoperative fibrin in 3 eyes, cytomegalovirus (CMV) endotheliitis in 2 eyes (successfully treated medically), and IOL optic capture (repositioned at the slit-lamp). Postoperative glaucoma management remained medically controlled in all the 13 eyes with pre-existing glaucoma. Best-corrected visual acuity in cases with at least 1 month of follow-up (n=17 eyes) was 20/20 in 6 eyes, 20/40 or better in 12 eyes, 20/60 or better in 16 eyes, and CF in 1 eye with end-stage glaucoma. Endothelial cell counts at 6 months were available in 9 eyes, with an average of 1625 cells/mm², representing a mean endothelial cell loss of 41%.

Conclusion: The HDMEK pull-through technique is a viable surgical procedure to perform DMEK in high risk, challenging and complex cases with multiple anterior segment comorbidities. The potential advantages of performing DMEK in complicated cases include the significant reduction of allograft rejection, and the avoidance of postoperative iris contact with the thin DMEK graft in compromised anterior chambers.
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