Published in final edited form as:

Ophthalmology. 2008 April ; 115(4): 627–632.e8. doi:10.1016/j.ophtha.2008.01.004.

Donor Age and Corneal Endothelial Cell Loss 5 Years after Successful Corneal Transplantation: Specular Microscopy Ancillary Study Results

Cornea Donor Study Investigator Group *

Abstract

Objective—To determine whether endothelial cell loss 5 years after successful corneal transplantation is related to the age of the donor.

Design—Multicenter, prospective, double-masked clinical trial.

Participants—Three hundred forty-seven subjects participating in the Cornea Donor Study who had not experienced graft failure 5 years after corneal transplantation for a moderate-risk condition (principally Fuchs' dystrophy or pseudophakic corneal edema).

Testing—Specular microscopic images of donor corneas obtained before surgery and postoperatively at 6 months, 12 months, and then annually through 5 years were submitted to a central reading center to measure endothelial cell density (ECD).

Main Outcome Measure—Endothelial cell density at 5 years.

Results—At 5 years, there was a substantial decrease in ECD from baseline for all donor ages. Subjects who received a cornea from a donor 12 to 65 years old experienced a median cell loss of 69% in the study eye, resulting in a 5-year median ECD of 824 cells/mm² (interquartile range, 613–1342), whereas subjects who received a cornea from a donor 66 to 75 years old experienced a cell loss of 75%, resulting in a median 5-year ECD of 654 cells/mm² (interquartile range, 538–986) (*P* [adjusted for baseline ECD] = 0.04). Statistically, there was a weak negative association between ECD and donor age analyzed as a continuous variable (*r* [adjusted for baseline ECD] = −0.19; 95% confidence interval, −0.29 to −0.08).

Conclusions—Endothelial cell loss is substantial in the 5 years after corneal transplantation. There is a slight association between cell loss and donor age. This finding emphasizes the importance of longer-term follow-up of this cohort to determine if this relationship affects graft survival.

Corneal clarity after penetrating keratoplasty can be affected by endothelial cell loss over time. The exact cause of postoperative cell loss is unknown but may be a result of donor or preservation factors, surgical stress, cellular interactions between the donor and recipient, immune reaction, normal or accelerated cellular aging, or glaucoma. The Eye Bank Association of America requires endothelial cell density (ECD) determination via specular microscopy as a standard corneal tissue evaluation method but does not require a minimum cell density for transplant suitability.¹ Clinicians typically prefer donor corneas with a high pre-operative ECD in order to offset posttransplant cell loss under the belief that this will improve the probability of graft survival.

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*See "Appendix 2" (available at <http://aaojournal.org>) for a list of Group members.

Past studies evaluating endothelial cell loss after corneal transplantation have produced conflicting results with regard to the effect of donor age. Some studies suggest that there is no difference in endothelial cell loss comparing older and younger donor tissue,^{2–5} whereas other studies suggest that there is a relationship between endothelial cell loss and donor age.^{6–8}

The Cornea Donor Study (CDS) has evaluated the effect of donor age on 5-year graft survival in eyes undergoing cornea transplantation for a corneal condition associated with moderate risk of graft failure, principally Fuchs' dystrophy and pseudophakic corneal edema. As measurement of corneal ECD by specular microscopy can serve as an indicator of the health of the cornea, the Specular Microscopy Ancillary Study (SMAS) was developed to evaluate the effect of donor factors, specifically donor age, on endothelial cell loss during the 5 years after penetrating keratoplasty. In a separate article,⁹ we report that 5-year graft survivals were similar in transplants using corneas from donors 66 to 75 years old and those using corneas from donors 12 to 65 years old (86% vs. 86%). In this article, we report on the relationship between donor age and ECD in successful grafts 5 years after penetrating keratoplasty.

Materials and Methods

Details of the CDS protocol have been reported,^{10,11} and pertinent aspects are briefly described here. The protocol was approved by institutional review boards at each investigational site, and each subject gave written informed consent to participate in the study. Eligible subjects were between 40 and 80 years old and had a corneal disease associated with endothelial dysfunction and moderate risk of failure (principally Fuchs' dystrophy and pseudophakic corneal edema). Eligible corneas were from donors 10 to 75 years old (though the youngest donor was 12) with an eye bank-measured ECD from 2300 to 3300 cells/mm². On the day of tissue assignment for each study subject, a Web-based computer program was used to select a cornea from those available at the eye bank that met the study eligibility criteria. The assignment was made without regard to age or any other subject characteristics. If an eligible cornea was not available, one was imported from another eye bank. Clinical investigators and subjects were masked to all characteristics of the donor cornea including age and ECD. Pre-operative management, surgical technique, and postoperative care, including prescription of medications, were provided according to each investigator's customary routine.

Participation in the SMAS was optional for eye banks, clinical sites, and subjects. Participating eye banks and sites were required to have a specular microscope that could capture an external calibration lens image and to have the ability to transmit images in an acceptable format (electronic.bmp file by e-mail, disk, 0.5-inch VHS videotape, or 35-mm negative film). Of the 1090 eligible subjects participating in the CDS, the SMAS included 596 subjects who participated at 45 CDS clinical sites. Donor corneas were assigned to the SMAS subjects by 31 of 43 participating CDS eye banks; but not all of them provided donor images for SMAS analyses. The cohort for this article included the 347 subjects who had a successful transplant at 5 years for whom specular microscopy was performed between 54 and 66 months after surgery. Of the 249 subjects not included, 55 had experienced a graft failure, 51 had died, 26 had been lost to follow-up or had withdrawn, and 117 had a successful transplant but did not have gradable specular microscopic images within this time window.

Baseline Donor Endothelial Cell Density

Cornea Donor Study eye banks followed their standard procedures for donor cornea preparation, capture of specular microscopic endothelial images, and determination of ECD. The eye banks participating in the SMAS utilized specular microscopes from 1 of 5 different companies: BioOptics Inc. (Portland, OR); CooperVision (no longer manufactured); HAI Laboratories, Inc. (Lexington, MA); Konan Medical Corp. (Torrance, CA); or Tomey Corp. USA (Phoenix, AZ). The baseline ECD was determined by the Specular Microscopy Reading

Center (SMRC) for 229 (66%) corneas and was provided by the eye bank for 118 (34%) corneas assigned by eye banks not participating in the SMAS. A single image of the central endothelium of each study donor cornea was sent by the eye banks participating in the SMAS to the SMRC for ECD determination. The time from death to image capture was not recorded.

Postoperative Donor Endothelial Cell Density

For subjects participating in the SMAS, specular microscopic images of the central endothelium were obtained at CDS follow-up visits 6 and 12 months after transplant and then annually through 5 years, provided that a regraft had not been performed. Three specular images were obtained at each visit utilizing contact or noncontact specular microscopes from 1 of 5 different companies: BioOptics, CooperVision (no longer manufactured), Konan Medical Corp., Tomey Corp. USA, and Nidek Inc. (Fremont, CA). This article primarily reports on ECD at 5 years in successful transplants. A separate article will describe longitudinal changes in ECD and evaluate the predictive value of ECD measurements for graft failure.

Specular Microscopy Reading Center Procedures and Quality Control

The SMRC at Case Western Reserve University and University Hospitals Case Medical Center in Cleveland was responsible for determining the ECD for both baseline donor image and postoperative subject images. Assessments of image quality and ECD were made by the SMRC using standardized procedures. Details of SMRC procedures have been described for donor images, including reader training and certification, image quality grading, image calibration, variable frame analysis for ECD determination, and adjudication procedures for image quality and ECD determination.^{12,13} Procedures for assessment of postoperative images were similar, although quality criteria were modified to accommodate good images that would otherwise be excluded because of high magnification or low ECD. Pertinent information is summarized here. The ECD of all analyzable images was independently determined by 2 readers using the variable frame analysis method. If the ECDs determined by the 2 readers differed by $\geq 5.0\%$, a third independent determination of ECD was made by an adjudicator. Final ECD was the average of all ECDs that were within 5.0% of each other. Readers were masked to all information about the donor corneas and study subjects. Throughout the study, the CDS Coordinating Center selected clinical images for repeat masked image quality grading and ECD determination to assess both intraobserver and interobserver variability. Quality control results were similar to published findings of quality control analyses for donor images¹²; there was excellent intraobserver and interobserver agreement for image quality assessment and ECD measurement.

Statistical Methods

Only subjects with 5-year specular images captured 54 to 66 months from the date of surgery whose transplant was classified as a success at 5 years were included in the analysis. The relative difference (referred to as percent change or loss) between baseline and 5-year cell ECDs was calculated by subtracting the baseline ECD from the 5-year cell ECD and then dividing by the baseline ECD. This difference is expressed as a percent relative to the baseline ECD, with negative numbers corresponding to loss of cells. For cases in which the baseline donor specular image was not analyzed by the SMRC, the ECD determined by the eye bank was used.

A comparison of baseline ECD between donor age groups was performed using the Wilcoxon rank-sum test. The 5-year ECD values were not normally distributed; therefore, the 5-year ECD and 5-year percent cell loss were compared by donor age groups based on ranks. For each variable, the rank scores were transformed to have a normal distribution (van der Waerden scores). The resulting values were used as the dependent variable in analysis of covariance models adjusting for baseline ECD. The relationship between the 5-year percent cell loss and

donor age as a continuous variable was assessed by Spearman correlation coefficient; a partial correlation coefficient was used to adjust for the baseline value.

All reported *P* values are 2 sided. All statistical analyses were conducted using SAS software (version 9.1, SAS Inc., Cary, NC).

Results

Mean age at the time of transplantation of the 347 subjects included in the analysis was 69 years; 224 (65%) of the subjects were female, and 333 (96%) were Caucasian, 9 (3%) African American, 2 (<1%) Hispanic, and 3 (<1%) other race. Indications for corneal transplantation included Fuchs' dystrophy in 264 (76%), pseudophakic/aphakic corneal edema in 72 (21%), and a variety of other causes in 11 (3%). One hundred twenty-six eyes (36%) were pseudophakic and 16 (5%) aphakic at the time of transplant. After transplant, 69 (20%) eyes were phakic, 270 (78%) pseudophakic, and 8 (2%) aphakic. A cornea from a donor 12.0 to <66.0 years old was assigned to 239 (69%) of the subjects, and a cornea from a donor 66.0 to <76.0 to 108 (31%). The full donor age distribution is shown in Figure 1 (available at <http://aaojournal.org>). Subject characteristics were similar in the older and younger donor age groups (Table 1 [available at <http://aaojournal.org>]). Baseline donor ECDs were similar in the study eyes included in the analysis, eyes that were part of the SMAS but did not have a gradable 5-year ECD, eyes in the SMAS that had a graft failure before 5 years, and eyes of CDS subjects who did not participate in the SMAS. Clinical characteristics of these different groups were similar, except that those who had a graft failure were more likely to have pseudophakic corneal edema as the indication for transplantation, whereas those without graft failure who participated in the SMAS were more likely to have Fuchs' dystrophy as the indication (Table 2 [available at <http://aaojournal.org>]).

At baseline, the median donor corneal ECD was 2698 cells/mm² (interquartile range, 2481–2895) in the 347 SMAS subjects. Corneas from 12- to 65-year-old donors had a median baseline cell density (2731 cells/mm² [interquartile range, 2503–2924]) higher than that of corneas from donors 66 to 75 (2585 cells/mm² [inter-quartile range, 2445–2792]) (*P* = 0.002).

At 5 years, the ECD had decreased from baseline by a median of 70%. Results were similar when the cohort was restricted to the 229 cases with an SMRC-determined baseline cell count (median = 70%; Table 3 [available at <http://aaojournal.org>]). Percent loss of endothelial cells from baseline to 5 years was not related to the baseline ECD (*r* = 0.07; 95% confidence interval [CI], –0.03 to 0.18), but there was a mild correlation between baseline ECD and 5-year ECD (*r* = 0.27; 95% CI, 0.17–0.36) (Fig 2 [available at <http://aaojournal.org>]).

Cell loss was substantial in both older and younger donor groups (Fig 3). At 5 years, there was a slight negative association between ECD and donor age (*r* [adjusted for baseline ECD] = –0.19; 95% CI, –0.29 to –0.08; Fig 4 [available at <http://aaojournal.org>]) as well as between percent cell loss from baseline to 5 years and donor age (*r* [adjusted for baseline ECD] = –0.19; 95% CI, –0.29 to –0.08; Fig 5). Subjects who received a cornea from a 12- to 65-year-old donor experienced a median cell loss of 69% in the study eye resulting in a 5-year median ECD of 824 cells/mm² (interquartile range, 613–1342), whereas subjects who received a cornea from a 66- to 75-year-old donor experienced a cell loss of 75% resulting in a median 5-year ECD of 654 cells/mm² (interquartile range, 538–986) (for percent loss, unadjusted *P* = 0.03, *P* adjusted for baseline ECD = 0.04; for 5-year ECD, unadjusted *P* = 0.005, *P* adjusted for baseline ECD = 0.04). For each donor age, Figure 1 shows the proportion of cases with a 5-year cell count <1000 cells/mm². In an exploratory analysis, there was slightly less cell loss in corneas from donors at the younger end of the range of donor ages (Table 4, Fig 6 [the latter available at <http://aaojournal.org>]). For instance, the 48 subjects who received a cornea from

a 12- to 40-year-old donor had a median 5-year cell loss of 63%, compared with 72% in the 299 subjects who received a cornea from an older donor (unadjusted $P = 0.003$, P adjusted for baseline ECD = 0.005).

Discussion

The SMAS was developed to measure corneal ECD changes over time in the CDS population. The ECD declines with age in the normal cornea. This process of cell loss is greatly accelerated after penetrating keratoplasty and persists for years after transplantation.⁷ Thus, chronic endothelial cell loss after penetrating keratoplasty is a recognized phenomenon that can impact graft survival.

In this study, we found that endothelial cell loss among successful transplants was substantial during the first 5 years after PK. Half of the transplanted corneas experienced a cell loss of $\geq 70\%$. At 5 years, half of the corneas were found to have an ECD < 778 cells/mm². Although the median cell loss among corneas from donors over 65 was slightly higher than that among corneas from donors 65 and under, the median cell loss among the corneas from younger donors was still 69%, and half of the corneas from this young donor group had a 5-year ECD of < 824 cells/mm². In contrast to previous studies, the strengths of the SMAS study include its large sample, masking of surgeons to donor age, standardization of specular microscopy imaging techniques at eye banks and clinical sites, and use of a central reading center with standardized quality-control procedures for ECD measurements. The comparison of endothelial cell loss between the older and younger donor groups, which is limited to cases with a successful graft at 5 years, has validity because graft success rates were similar in the two groups.⁹

Substantial posttransplant cell loss, as that found among this cohort, has been observed in previous studies. After 3 years, Bertelmann et al reported a cell loss of 54% among 193 grafts for a variety of low- to high-risk indications.⁵ Bourne et al¹⁴ reported a mean cell loss at 5 years of 59% among successful grafts. These cell loss rates highlight the importance of continued research into ways to improve overall corneal health through advances in corneal preservation and postoperative management. This may become increasingly relevant with the advent of endothelial keratoplasty, which is potentially even more traumatic to the endothelium at the time of surgery than standard penetrating keratoplasty.¹⁵

With regard to the effect of donor age, prior studies evaluating endothelial cell loss after penetrating keratoplasty have produced conflicting results. Some studies have suggested that changes in endothelial cell loss are unrelated to the age of the donor. Abbott et al² evaluated the effect of donor age on ECD in 55 clear grafts followed for an average of 17 years (minimum, 10) and found similar central and peripheral cell densities when comparing grafts of donor age < 50 , 50 to 64, and > 64 . Similar findings were reported after 4 to 6 years of additional follow-up of this same cohort.⁴ Although the Bourne et al early data showed an association between donor age and endothelial cell loss (after 1 year, mean endothelial cell loss was 29% for tissue from donors < 25 years old, 34% for 25- to 49-year-olds, and 38% for ≥ 50 -year-olds), a significant association was not present at 3 years.¹⁴ After 10 years of follow-up of 119 subjects from this same cohort, Ing et al¹⁶ reported that younger donor age was associated with greater cell loss than older donor age, a finding that was still present after 15 years of follow-up.⁸ This finding may have been due to the high graft failure rate among older donors, which might have biased the cell density results due to the loss of data from eyes with low ECD. There are also past studies suggesting that endothelial cell loss is higher after corneal transplantation with older donor tissue than after transplantation with younger donor tissue. Ruusuvaara⁷ assessed ECDs 1 month to 11 years after grafting, finding that ECD was higher in the 38 transplants from donors ≤ 45 years than in the 58 from donors > 45 . However, there was no difference comparing ECDs of donors ages 46 to 60, 61 to 70, and > 70 . Musch et al⁶ found that among

265 grafts that had not experienced an endothelial rejection reaction when assessed at 12 months, the mean endothelial cell loss was significantly less in tissue from donors <25 but was similar when comparing tissue from donors 25 to 49 and ≥ 50 .

In conclusion, 5 years after a successful cornea transplant for a moderate-risk corneal condition, there is a slight association between donor age and endothelial cell loss. The clinical importance of this slight association is not known, and only with further follow-up will we be able to determine if it impacts on the relationship between donor age and graft survival. Of greater importance, however, is the finding that, irrespective of donor age, endothelial cell loss is substantial over the first 5 years after transplant even when the graft has been successful. Because ECD is an indicator of the health of the cornea, we plan to observe this cohort for an additional 5 years to determine how the substantial decrease in ECD at 5 years impacts the transplant success rate over a longer period.

Acknowledgments

Supported by the National Eye Institute, Bethesda, Maryland (cooperative agreement nos. EY12728, EY12358). Additional support provided by Eye Bank Association of America, Washington, DC; Bausch & Lomb, Inc., Rochester, New York; Tissue Banks International, Baltimore, Maryland; Vision Share, Inc., Apex, North Carolina; San Diego Eye Bank, San Diego, California; Cornea Society, Fairfax, Virginia; Katena Products, Inc., Denville, New Jersey; ViroMed Laboratories, Inc., Minnetonka, Minnesota; Midwest Eye-Banks (Michigan Eye-Bank, Illinois Eye-Bank), Ann Arbor, Michigan; Konan Medical Corp., Torrance, California; Eye Bank for Sight Restoration, New York, New York; SightLife, Seattle, Washington; Sight Society of Northeastern New York (Lions Eye Bank of Albany), Albany, New York; and Lions Eye Bank of Oregon, Portland, Oregon.

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Appendix 1: Writing Committee

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Appendix 2: Cornea Donor Study Investigator Group

Clinical Sites

Listed in order of number of patients enrolled in the CDS are the Specular Microscopy Ancillary Study clinical sites with city and state, site name, and names of the investigators (ordered alphabetically) who participated in the study as part of the CDS Investigator Group.

Southfield, Michigan, Michigan Cornea Consultants, PC. Christopher Y. Chow, MD, Steven P. Dunn, MD, David G. Heidemann, MD.

Albany, New York, Cornea Consultants of Albany. Michael W. Belin, MD, Robert L. Schultze, MD.

Grand Rapids, Michigan, Verdier Eye Center, P.C. David D. Verdier, MD.

Cleveland, Ohio, Case Western Reserve University and University Hospitals Case Medical Center. Jonathan H. Lass, MD, William J. Reinhart, MD, Joseph M. Thomas, MD.

Chicago, Illinois, University of Illinois at Chicago. Joel Sugar, MD, Elmer Tu, MD.

Cincinnati, Ohio, Cincinnati Eye Institute. Edward J. Holland, MD.

Charlotte, North Carolina, Horizon Eye Care. Paul G. Galentine, MD, David N. Ugland, MD.

Chicago, Illinois, Northwestern University. Robert S. Feder, MD.

Madison, Wisconsin, Davis Duehr Dean Clinic. Christopher R. Croasdale, MD.

Lancaster, Pennsylvania, Eye Physicians of Lancaster. Francis J. Manning, MD.

Dallas, Texas, University of Texas Southwestern Medical Center at Dallas. R. Wayne Bowman, MD, H. Dwight Cavanagh, MD, PhD, Mohamed-Sameh H. El-Agha, MD, James P. McCulley, MD.

San Diego, California, Eye Care of San Diego. John E. Bokosky, MD.

Atlanta, Georgia, Eye Consultants of Atlanta, P.C. Stephen M. Hamilton, MD, Gina C. Jayawant, MD, W. Barry Lee, MD.

Seattle, Washington. Matthew S. Oliva, MD, Walter M. Rotkis, MD.

Atlanta, Georgia, Emory University. R. Doyle Stulting, MD, PhD.

Fort Myers, Florida, Eye Associates of Fort Myers. Mark S. Gorovoy, MD.

Burlington, Massachusetts, Lahey Clinic. Sarkis H. Soukiasian, MD.

Tulsa, Oklahoma, Eye Institute. Marc A. Goldberg, MD.

Charleston, West Virginia, Charleston Eye Care, PLLC. James W. Caudill, MD.

Delray Beach, Florida, Delray Eye Associates, P.A. Steven I. Rosenfeld, MD.

Louisville, Kentucky. Richard A. Eiferman, MD.

Minneapolis, Minnesota, Minnesota Eye Consultants, P.A. Elizabeth A. Davis, MD, David R. Hardten, MD, Richard L. Lindstrom, MD.

Scranton, Pennsylvania, Northeastern Eye Institute. Thomas S. Boland, MD, Stephen E. Pascucci, MD.

Tallahassee, Florida, Eye Associates of Tallahassee. Jerry G. Ford, MD.

Langhorne, Pennsylvania. Sadeer B. Hannush, MD.

Seattle, Washington, Virginia Mason Medical Center. Thomas D. Lindquist, MD, PhD.

Portland, Oregon, Northwest Corneal Services. Terry E. Burris, MD.

Iowa City, Iowa, University of Iowa. John E. Sutphin, MD, Ayad A. Farjo, MD, Kenneth M. Goins, MD.

Pittsburgh, Pennsylvania. Peter J. Berkowitz, MD.

Ann Arbor, Michigan, W. K. Kellogg Eye Center, University of Michigan. Qais A. Farjo, MD, Roger F. Meyer, MD, H. Kaz Soong, MD, Alan Sugar, MD.

Rochester, Minnesota, Mayo Clinic College of Medicine. Keith H. Baratz, MD.

Lancaster, Pennsylvania, Eye Doctors of Lancaster. Barton L. Halpern, MD, Mark A. Pavilack, MD (now at Tidewater Eye Center, Virginia Beach, VA).

Indianapolis, Indiana, Price Vision Group. Kendall Dobbins, MD, Francis W. Price, Jr, MD, William G. Zeh, MD.

Columbia, Missouri, University of Missouri. John W. Cowden, MD.

Cleveland, Ohio, Cleveland Clinic Foundation. David M. Meisler, MD.

Philadelphia, Pennsylvania, Corneal Associates, P.C. Elisabeth J. Cohen, MD, Peter R. Laibson, MD, Christopher J. Rapuano, MD.

Charleston, South Carolina, Medical University of South Carolina. Kerry D. Solomon, MD.

Narberth, Pennsylvania, Ophthalmic Subspecialty Consultants. Parveen K. Nagra, MD, Irving M. Raber, MD.

Boston, Massachusetts, Boston University School of Medicine. Kenneth C. Chern, MD.

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Spokane, Washington, Spokane Eye Clinic. Lance E. Olson, MD, Erik D. Skoog, MD.

Eye Banks

Listed in order of number of patients enrolled in the CDS are the eye banks participating in the Specular Microscopy Ancillary Study, with city and state and names of the eye bank directors and coordinators who participated in the study during the enrollment phase (C = coordinator; D = director).

Midwest Eye-Banks (Ann Arbor, Michigan, Michigan Eye-Bank; Chicago, Illinois, Illinois Eye-Bank). Florence M. Johnston (D), Kyle L. Mavin (C), Kristen E. McCoy (C), Michael B. O'Keefe (C).

Tissue Banks International (Boston, Massachusetts, New England Eye & Tissue Transplant Bank; Bismarck, North Dakota, Lions Eye Bank of North Dakota, Inc.; Oakland, California, Northern California Transplant Bank). Gerald J. Cole, MBA (D), Diane F. Johnston (C), Mark A. Jones (C), Sameera M. Farazdaghi, MPH (C), Elizabeth N. Walunas (C).

Seattle, Washington, SightLife. Monty M. Montoya, MBA (D), Bernie Iliakis (C), Rick D. McDonald (C), Misty L. Ostermiller (C), Cathy E. Saltwick (C).

Allentown, Pennsylvania, Northeast Pennsylvania Lions Eye Bank, Inc. Mark H. Weaver (D), Michael J. Christ (C), Mark B. Gross (C).

Minneapolis, Minnesota, Minnesota Lions Eye Bank. Carol R. Engel (D), Raylene A. Dale (C), Stephanie K. Hackl (C), Elena J. Henriksen (C), Kathryn J. Kalmoe (C), Jennifer M. Larson (C), Jackie V. Malling (C), Brian J. Philippy (C).

Albany, New York, Sight Society of Northeastern New York. Maryann Sharpe-Cassese, RN, MSN (D), Sue M. Hayes (C).

Philadelphia, Pennsylvania, Lions Eye Bank of Delaware Valley. Robert E. Lytle (D), David A. Rechtshaffen (C).

Atlanta, Georgia, Georgia Eye Bank, Inc. Bruce Varnum (D), Erin B. Angel (C), Matt D. Durell (C), Teresa R. Williams (C).

Cleveland, Ohio, Cleveland Eye Bank. Susan V. Janssen (D), Brian E. Kraus (C), Marcy B. McLain (C), Jackie A. Rossi (C).

Phoenix, Arizona, Donor Network of Arizona. Gregory C. Davis (D), Tara L. Chavez (C), Lori D. Oswald (C), Noreen B. Ruiz (C).

San Diego, California, San Diego Eye Bank. Jeffrey G. Penta, MBA (D), Wayne E. Dietz (C), Jennifer L. Nary (C).

Charleston, West Virginia, Medical Eye Bank of West Virginia. Kenneth R. Sheriff (D), Nancy C. Driver (C).

Charlotte, North Carolina, Lifeshare of the Carolinas. William J. Faircloth (D), Paul E. Williams (C).

Winston-Salem, North Carolina, North Carolina Eye Bank, Inc. Kurt Weber, MA, MBA (D), Jerry W. Barker (C), Donna M. Bridges (C), Lee Chenier (C), Mark Soper (C).

Pittsburgh, Pennsylvania, Center for Organ Recovery and Education. Robert C. Arffa, MD, Michael A. Tramber (C).

Aurora, Colorado, Rocky Mountain Lions Eye Bank. Edmund Jacobs (D), Michael P. Filbin (C), James I. Mather (C), Christopher M. McGriff (C), Eric E. Meinecke (C).

Iowa City, Iowa, Iowa Lions Eye Bank. Patricia J. Mason (D), Garret D. Locke (C), Janice F. Reiter (C).

Norfolk, Virginia, Lions Medical Eye Bank of Eastern Virginia, Inc. David E. Korroch (D), Penelope M. Thomas (C).

Galveston, Texas, Southeast Texas Lions Eye Bank, Inc. Wayne A. Lange (D, C), Rosemary F. Moore (C).

Memphis, Tennessee, Mid-South Eye Bank for Sight Restoration. Lee J. Williams (D), Yvette D. Friedhoff (C).

Specular Microscopy Reading Center

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Figure 1. Number of subjects assigned a cornea by each year of donor age. ECD = endothelial cell density (cells/mm²).

Figure 2. Endothelial cell density at 5 years versus baseline for subjects with a successful graft at 5 years ($N = 347$). Spearman correlation coefficient (95% confidence interval) = 0.27 (0.17–0.36).

Figure 3. Endothelial cell density (cells/mm²) over time for subjects with a successful graft at 5 years. In the box plots, horizontal lines denote medians, and the bottom and top of the boxes represent the 25th and 75th percentiles.

Figure 4.

Five-year endothelial cell density (ECD) by donor age for subjects with a successful graft at 5 years ($N = 347$). Spearman correlation coefficient (95% confidence interval) = -0.23 (-0.33 to -0.13); partial Spearman correlation coefficient adjusted for baseline ECD = -0.19 (-0.29 to -0.08).

Figure 5.

Percent change in endothelial cell density (ECD) from baseline to 5 years by donor age for subjects with a successful graft at 5 years ($N = 347$). Spearman correlation coefficient (95% confidence interval) = -0.20 (-0.30 to -0.09); partial Spearman correlation coefficient adjusted for baseline ECD (95% CI) = -0.19 (-0.29 , -0.08).

Figure 6.

Percent change in endothelial cell density from baseline to 5 years in donor age groups for subjects with a successful graft at 5 years. In the box plots, black dots denote mean values, horizontal lines are medians, and the bottom and top of the boxes represent the 25th and 75th percentiles.

Table 1

Comparison of Specular Microscopy Ancillary Study Participants by Donor Age (N = 347)

Baseline Recipient Characteristic	Donor Age <66 (N = 239)	Donor Age ≥ 66 (N = 108)
Age		
Mean (standard deviation)	68 (9)	70 (8)
Median (interquartile range)	70 (64–75)	72 (66–76)
Gender (female)	149 (62)	75 (69)
Race		
Caucasian	231 (97)	102 (94)
African American	6 (3)	3 (3)
Hispanic	0	2 (2)
Asian	1 (<1)	0
Other	1 (<1)	1 (<1)
Current cigarette smoker	12 (5)	8 (7)
Use of glaucoma medications at baseline	17 (7)	5 (5)
Prior glaucoma surgery	9 (4)	5 (5)
Diagnosis		
Fuchs' dystrophy	182 (76)	82 (76)
Pseudophakic/aphakic corneal edema	49 (21)	23 (21)
Other	8 (3)	3 (3)
Preoperative lens status		
Phakic	149 (62)	56 (52)
Pseudophakic	81 (34)	45 (42)
Aphakic	9 (4)	7 (6)
Postoperative lens status		
Phakic	52 (22)	17 (16)
Pseudophakic	181 (76)	89 (82)
Aphakic	6 (3)	2 (2)
Recipient bed size (mm)* [mean (standard deviation)]	7.9 (0.3)	7.9 (0.3)
Baseline cell density [†] (cells/mm ²)		
Mean (standard deviation)	2724 (303)	2615 (264)
Median (interquartile range)	2731 (2503–2924)	2585 (2445–2792)
1708–2300	16 (7)	9 (8)
2300–2499	43 (18)	26 (24)
2500–2699	50 (21)	30 (28)
2700–2899	64 (27)	26 (24)
2900–3099	40 (17)	13 (12)
3100–3300	19 (8)	4 (4)
3300–3540	7 (3)	0

N (%) unless otherwise specified.

* One subject with missing size.

[†]Includes baseline cell density from eye bank for 118 eyes and from reading center for 229 eyes.

Table 2

Comparison of Specular Microscopy Ancillary Study (SMAS) Participants with Nonparticipants

Baseline Recipient Characteristic	Cornea Donor Study Subjects in the SMAS without Graft Failure		Cornea Donor Study Subjects in the SMAS with Graft Failure (N = 55)	Cornea Donor Study Subjects Not in the SMAS (N = 494)
	5-Year Endothelial Cell Density (N = 347)	No 5-Year Endothelial Cell Density (N = 194)		
Age				
Mean (standard deviation)	69 (8)	71 (8)	73 (8)	70 (9)
Median (interquartile range)	71 (64–75)	73 (66–76)	75 (69–79)	72 (65–77)
Gender (female)	224 (65)	117 (60)	36 (65)	320 (65)
Race				
Caucasian	333 (96)	178 (92)	50 (91)	450 (91)
African American	9 (3)	11 (6)	5 (9)	25 (5)
Hispanic	2 (<1)	2 (1)	0	9 (2)
Asian	1 (<1)	1 (<1)	0	6 (1)
Other	2 (<1)	2 (1)	0	4 (<1)
Donor age				
Mean (standard deviation)	57 (15)	58 (15)	60 (11)	59 (13)
<66	239 (69)	115 (59)	39 (71)	314 (64)
≥66	108 (31)	79 (41)	16 (29)	180 (36)
Current cigarette smoker	20 (6)	19 (10)	3 (5)	60 (12)
Use of glaucoma medications at baseline	22 (6)	21 (11)	15 (27)	86 (17)
Prior glaucoma surgery	14 (4)	7 (4)	14 (25)	36 (7)
Diagnosis				
Fuchs' dystrophy	264 (76)	112 (58)	18 (33)	282 (57)
Pseudophakic/aphakic corneal edema	72 (21)	73 (38)	34 (62)	190 (38)
Other	11 (3)	9 (5)	3 (5)	22 (4)
Preoperative lens status				
Phakic	205 (59)	76 (39)	10 (18)	199 (40)
Pseudophakic	126 (36)	103 (53)	42 (76)	263 (53)
Aphakic	16 (5)	15 (8)	3 (5)	32 (6)
Postoperative lens status				
Phakic	69 (20)	26 (13)	4 (7)	63 (13)
Pseudophakic	270 (78)	164 (85)	48 (87)	413 (84)
Aphakic	8 (2)	4 (2)	3 (5)	18 (4)
Baseline cell density* (cells/mm ²)				
Mean (standard deviation)	2690 (296)	2667 (337)	2644 (257)	2662 (279)
Median (interquartile range)	2698 (2481–2895)	2665 (2435–2894)	2634 (2478–2840)	2651 (2464–2857)
<2300	25 (7)	21 (11)	4 (7)	37 (7)
2300–2499	69 (20)	43 (22)	11 (20)	108 (22)
2500–2699	80 (23)	39 (20)	17 (31)	134 (27)
2700–2899	90 (26)	46 (24)	12 (22)	118 (24)
2900–3099	53 (15)	24 (12)	11 (20)	69 (14)

Baseline Recipient Characteristic	Cornea Donor Study Subjects in the SMAS without Graft Failure		Cornea Donor Study Subjects in the SMAS with Graft Failure (N = 55)	Cornea Donor Study Subjects Not in the SMAS (N = 494)
	<i>5-Year Endothelial Cell Density (N = 347)</i>	<i>No 5-Year Endothelial Cell Density (N = 194)</i>		
3100–3300	23 (7)	16 (8)	0	21 (4)
>3300	7 (2)	5 (3)	0	7 (1)

N (%) unless otherwise specified.

* Includes density from eye bank for 432 eyes and from reading center for 658 eyes.

Table 3

Five-Year Endothelial Cell Density (ECD) in Eyes with a Successful Transplant Using Baseline Specular Microscopy Reading Center–Determined ECD (N = 229)

Donor Age	N	Baseline ECD [Median (Interquartile Range)] (cells/mm ²)	5-Year ECD [Median (Interquartile Range)] (cells/mm ²)	% Change from Baseline to 5 Years* [Median (Interquartile Range)]
Overall	229	2668 (2432–2892)	778 (566–1336)	–70% (–77% to –50%)
66.0–<76.0	67	2562 (2414–2798)	649 (522–1336)	–75% (–79% to –53%)
12.0–<66.0	162	2679 (2446–2905)	819 (587–1342)	–69% (–77% to –49%)
56.0–<66.0	75	2681 (2446–2938)	748 (563–1127)	–71% (–79% to –56%)
41.0–<56.0	60	2618 (2426–2824)	797 (582–1440)	–69% (–76% to –43%)
12.0–<41.0	27	2812 (2562–3062)	1074 (786–1624)	–64% (–70% to –47%)

* Endothelial cell density at 5 yrs minus ECD at baseline divided by ECD at baseline and multiplied by 100%. A negative number indicates loss of cells.

Table 4

Five-Year Endothelial Cell Density (ECD) in Eyes with a Successful Transplant (N = 347)

Donor Age	N	Baseline ECD* [Median (Interquartile Range)] (cells/mm ²)	5-Year ECD [Median (Interquartile Range)] (cells/mm ²)	% Change from Baseline to 5 Years [†] [Median (Interquartile Range)]
Overall	347	2698 (2481–2895)	778 (574–1267)	–70% (–77% to –55%)
66.0–<76.0	108	2585 (2445–2792)	654 (538–986)	–75% (–79% to –62%)
2.0–<66.0	239	2731 (2503–2924)	824 (613–1342)	–69% (–77% to –51%)
156.0–<66.0	109	2700 (2481–2904)	748 (587–1127)	–70% (–78% to –56%)
41.0–<56.0	82	2674 (2494–2850)	787 (584–1416)	–71% (–77% to –46%)
12.0–<41.0	48	2858 (2715–3090)	1048 (793–1432)	–63% (–72% to –51%)

* Includes baseline ECD from eye bank for 118 eyes and from reading center for 229 eyes.

[†] Endothelial cell density at 5 years minus ECD at baseline divided by ECD at baseline and multiplied by 100%. A negative number indicates loss of cells.