# Impact of the Cornea Preservation Time Study on Donor Cornea Preservation Time and Surgeon Attitudes

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**ABSTRACT**

**Purpose:** Assess the Cornea Preservation Time Study (CPTS) impact on surgeon attitudes regarding preservation time (PT) and eye-bank-reported PT for donors intended for endothelial keratoplasty (EK).

**Methods:** Prior to CPTS recruitment (2012) and 6 months following primary results publication (2017), American Academy of Ophthalmology members with cornea interest were surveyed regarding their PT attitudes for EK donors. Eye banks provided PT data from 2010-2011, 2013-2014, and the first half of 2018 for all EK-intended donor corneas for domestic and international distribution. Differences over time were assessed with chi-square tests and logistic regression models for categorical responses, and t-tests and linear regression assessed comparisons of mean PT as reported by eye banks.

**Results:** 364 of 1,609 (22.6%) surgeons responded in 2012 and 297 of 1,872 (15.9%) in 2018. 98 surgeons (32%) in 2012 would accept donor corneas with PT >7 days compared to 122 (46%) in 2018 ($p<0.001$). Surgeons with >10 years' experience were likely to extend their PT limits to >7 days in 2018 vs 2012 (47% vs 28%, respectively, $p<0.001$). Eye-bank reported PT increased from 4.6 days in 2010 (N=9317 donors) to 5.1 days (N=7020 donors) in 2018, and donation year was significantly associated with mean PT in a multivariable analysis ($p<0.001$). Eye-bank reported PT >7 days increased from 3% in 2010 to 9% in 2018.

**Conclusions:** The CPTS may influence surgeon-expressed attitudes and eye bank reported PT, regarding acceptance of donor tissue preserved > 7 days, supporting tissue safety and effectiveness preserved up to 11 days for EK.

**Keywords:** corneal endothelium, eye banking, preservation time

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**Presentation:** The comprehensive list of participating CPTS clinical sites, investigators and coordinators; eye bank investigators; members of the Operations, Executive, Eye Bank Advisory, Data and Safety Monitoring Committee; Coordinating Center, Cornea Image Analysis Reading Center (CIARC), and Data Management and Analysis Center Staff; and the National Eye Institute staff have been previously published (Cornea 2015;34:601-608; *JAMA Ophthalmology* 2017;135:1401-09)

**Conflicts of interest:** Conflict of interest statement: Ms. Drury, Mr. Meinecke, and Mr. Ross are employees of their respective eye banks. Dr. Lass is a voluntary member of the Eversight and Cleveland Eye Bank Foundation Boards. None of these positions have a conflict of interest with this publication. The following authors have financial disclosures with companies that manufacture corneal storage solutions (considered relevant to this work): Dr. Mark Terry (Bausch & Lomb), and Dr. W. Barry Lee (Bausch & Lomb).

**Financial support:** Supported by cooperative agreements with the National Eye Institute, National Institutes of Health, Department of Health and Human Services EY20797 and EY20798. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Eye Institute or the National Institutes of Health. Additional support provided by: Eye Bank Association of America, The Cornea Society, Vision Share, Inc., Alabama Eye Bank, Cleveland Eye Bank Foundation, Eversight, Eye Bank for Sight Restoration, Iowa Lions Eye Bank, Lions Eye Bank of Albany, San Diego Eye Bank, and SightLife.

 

The Cornea Preservation Time Study (CPTS) was a randomized clinical trial of the effects of preservation time (PT) on graft success and endothelial cell loss after Descemet stripping automated endothelial keratoplasty (DSAEK) involving 1330 donor corneas from 23 eye banks.[1-3] The primary outcome papers reported that PT up to 11 days had little influence on graft success,[3] and that endothelial cell loss up to 13 days of PT was not influenced by PT.[2]

Prior to initiation of the trial in 2012, there was a general consensus among corneal surgeons and eye banks in the United States (US), centered largely around habit and unsubstantiated beliefs, that donor corneal tissue preserved for more than 7 days was inferior to tissue preserved for shorter times for penetrating keratoplasty (PKP) and/or endothelial keratoplasty (EK). This practice was prevalent despite US Food and Drug Administration (FDA) approval of 4-8˚C storage solutions for up to 14 days since the 1990s when Optisol GS (Bausch & Lomb, Inc.) was first approved.[4,5]

The rationale for performing the CPTS was to expand the corneal donor pool, which is impacted by a number of threats currently with more expected in the future. The demand for corneas has substantially increased with the advent of endothelial keratoplasty.[6] The Eye Bank Association of America (EBAA) Annual Statistical Report shows domestic EK surgical volume has increased from 1,398 grafts in 2005 to 28,993 in 2017.[6] It is expected to increase further because of the aging population with a spike over next 20 years in recipients 65 years of age and older in the US, and Fuchs endothelial corneal dystrophy (FECD) keratoplasties being performed at earlier stages of the disease.[6-8] Additional areas of concern which may restrict the future donor supply include increasing regulations and more extensive requirements to test for emerging infections[6] the exclusion of donors with a compromised medical-social history,[9] and increased EK donor tissue preparation complications in diabetic donors.[10-12] The Cornea Donor Study[13-16] (CDS) which preceded the CPTS, also attempted to expand the donor pool by establishing the success of older aged donors greater than 65 to 75 years of age for successful PKP. A survey of eye bank data from the time period during and after the published CDS results demonstrated a modest increase in donor age of corneas transplanted in the US from 1998-2009 and the authors speculated that the CDS may have played a role in this change.[17] A surgeon survey of attitudes regarding donor age prior to the CDS and following the release of its findings in 2008 and 2013,[13-16] however, was not conducted. The CDS studies, which focused on full thickness donor tissue for PKP, did provide some reassurance as to the use of older donor tissue that could apply to EK surgery.[7]

With the desire to measure the impact of the CPTS on surgeon attitudes toward PT and how this may have been reflected in an increase in the eye-bank-reported average PTs, we conducted surgeon and eye bank surveys in 2012 prior to CPTS and again after publication of the study results to specifically document changes in practice patterns. The current report summarizes the post-publication findings and implications for eye banking in the future.

## METHODS

Details of the CPTS protocol have been previously reported.[1] The protocol was approved by institutional review boards governing each investigational site, and individual participants gave written informed consent to participate in the study. The research adhered to the tenets of the Declaration of Helsinki. The protocol was registered and is publicly available at https://clinicaltrials.gov/ct2/show/NCT01537393. Participants were enrolled at 40 clinical sites and donor corneas were provided by 23 eye banks across the US.[1] Eyes undergoing DSAEK were randomly assigned to receive a donor cornea with PT of 0-7 days or 8-14 days; for participants with both eyes eligible, the first eye was assigned randomly to a PT group and the second eye was assigned to the alternate PT group.

The primary results on the relation of graft success[3] and endothelial cell loss[2] to PT were released electronically in October 2017 and in print in December 2017. Simultaneous to the electronic release of both papers, the results were presented at the Cornea and Eye Banking Forum in October 2017, held just prior to the annual American Academy of Ophthalmology (AAO) meeting. A master slide set of the primary results was subsequently distributed to all CPTS investigators to facilitate local and regional presentations and was also available on the public CPTS website. The main results were also presented (J.H.L.) at the Association for Cataract and Refractive Surgery (ASCRS) meeting in April 2018. Finally, the importance of promoting the findings of the CPTS to the corneal surgeon community by each eye bank director was presented at the EBAA annual meeting in June 2018 (D. Drury, personal communication).

### Surgeon Survey

As previously reported,[1] all 1,609 AAO member ophthalmologists who reported their subspecialty as cornea & external diseases in 2012 were mailed a survey inquiring about their preferences and patterns surrounding tissue selection for EK. When the 2012 survey was conducted, few corneal surgeons in the US were performing Descemet membrane endothelial keratoplasty (DMEK), with under 1500 cases performed nationwide that year.[6] Therefore,

 

questions were developed around EK in general and not specifically DSAEK or DMEK. The questions in the survey are found in **eFigure 1**. *(see page 9-11)* The identical survey was sent to an updated list of the 1,872 AAO member cornea & external disease subspecialists in June 2018, 7 months after the primary CPTS results were released,[2,3] with the addition of questions pertaining to the respondent's knowledge of the CPTS results. Again there was no attempt to separate preferences in regards to DSAEK vs. DMEK. Two requests were sent in each survey year, responses were anonymous, and were accepted on paper or online.

### Eye Bank Survey

To assess the impact of the CPTS on PT, eye banks were surveyed through an EBAA mass mailing to contribute demographic and donor cornea preparation data (PT, tissue preparation by eye bank or surgeon, donor age, and cause of death) on all donor corneas distributed domestically and internationally for DSAEK and DMEK in 2010, 2011, 2013, 2014, and the first six months of 2018. Donor mates were also calculated based on assumed match on year, eye bank, donor age, cause of death, death date, and preservation date. The number of eye banks providing data in 2010-2011, 2013-2014, and 2018 was 19, 18, and 23, respectively **e-Table-1** *(see page 12)*. Unlike the surgeon survey, eye bank data on both DSAEK and DMEK beginning in 2010 were collected, enabling us to investigate any differences in regards to PT for these two EK procedures.

### Statistical Methods

*Surgeon survey.* For each categorical factor, chi-square tests were used to compare the frequency distributions of surgeon survey responses between 2012 and 2018. Chi-square tests also were used to compare PT limitations between the two years separately among surgeons with more than 10 years of experience and those with up to 10 years of experience. Additionally, Wilcoxon tests were used to compare age and years of surgical experience between surgeon cohorts in 2012 and 2018.

From data in the 2018 survey, Chi-square tests also were used to compare longest acceptable PT between surgeons aware and unaware of the CPTS findings that were released in the fall of 2017.[2,3] Among surgeons who reported being aware of the CPTS findings in 2018, chi-square tests were used to compare the distribution of longest acceptable PT between surgeons who stated that the CPTS findings would change their pattern of behavior regarding PT and those who said it would not.

*Eye bank survey.* Two sample t-tests assuming equal variances in each group were used to compare mean PT between time periods, type of EK (DSAEK, DMEK), and domestic and international distribution of donor tissue. A backwards multivariable model selection procedure was used to determine factors associated with mean PT. Each factor was evaluated in a univariate mixed effects linear model with the correlation between donor eyes accounted for by a random effect. Factors with univariate $p < 0.10$ were chosen as candidate factors for the final model, with only those factors with $p < 0.01$ retained. In all models, eye bank was treated as a fixed effect,

All statistical analyses were conducted using SAS, version 9.4 (SAS Inc). All reported p-values were two-sided.

## RESULTS

### Surgeon Survey

In the 2012 surgeon survey, 364 (22.6%) of 1,609 surgeons responded, and of those who responded, 68% set < 8 days as their limit for PT.[1] In 2018, 297 (15.9%) of 1,872 surgeons responded to the survey. There were no differences between the two cohorts of surgeons based on age, years in practice or number of EK surgeries performed in the prior year. In 2012, the distribution of age and years in practice were 51 ± 12 and 19 ± 12 (mean ± SD), respectively (**Table 1**). In 2018, the respective distributions were 50 ± 12 and 18 ± 12. The surgeons surveyed in each year had similar standards regarding proceeding with surgery (or not) if tissue parameters were not met, and use of tissue based on cause of death and endothelial cell density (ECD) (**Table 2**).

***Table 1.*** *Comparison of Surgeon Cohorts from surveys between 2012 and 2018*

| | 2012 (N=364) | 2018 (N=297) | P-Value [a] |
|---|---|---|---|
| Age (years, *mean ± SD*) [b] | 51 ± 12 | 50 ± 12 | 0.20 |
| Years in practice (*mean ± SD*) [c] | 19 ± 12 | 18 ± 12 | 0.44 |
| Number of EKs performed in past 12 months *n (%)* [d] | | | 0.15 |
| 1 to 10 | 93 (30%) | 66 (24%) | |
| >10 to 25 | 102 (33%) | 82 (30%) | |
| >25 to 50 | 43 (14%) | 58 (21%) | |
| >50 to 75 | 35 (11%) | 25 (9%) | |
| >75 to 100 | 17 (6%) | 18 (7%) | |
| >100 | 19 (6%) | 21 (8%) | |

*[a]Based on a Wilcoxon test for continuous outcomes and a chi-squared test for discrete outcomes. [b]Excludes three surgeons with missing values in 2012 and one surgeon with a missing value in 2018. [c]Excludes four surgeons with missing values in 2012 and three surgeons with missing values in 2018. [d]Excludes 55 surgeons with missing values in 2012 and 27 surgeons with missing values in 2018.*

*SD = standard deviation; EK = endothelial keratoplasty*

***Table 2.*** *Comparison of surgeon survey responses between 2012 and 2018*

| | 2012 (N=364) | 2018 (N=297) | P-value [a] |
|---|---|---|---|
| **Cancel case if standards not met [b]** | | | 0.15 |
| Generally No | 124 (40%) | 130 (48%) | |
| Generally Yes | 179 (58%) | 135 (50%) | |
| No opinion | 6 (2%) | 5 (2%) | |
| **Cause of death influence use of donor tissue [c]** | | | 0.22 |
| No | 215 (70%) | 199 (73%) | |
| Yes | 76 (25%) | 66 (24%) | |
| No Opinion | 15 (5%) | 6 (2%) | |
| **Minimum acceptable endothelial cell density (cells/mm$^2$) [d]** | | | 0.19 |
| 2000-<2300 | 73 (24%) | 51 (19%) | |
| ≥2300 | 61 (20%) | 44 (17%) | |
| ≥2400 | 49 (16%) | 35 (13%) | |
| ≥2500 | 74 (25%) | 84 (32%) | |
| ≥2600 | 11 (4%) | 18 (7%) | |
| ≥2700 | 16 (5%) | 16 (6%) | |
| ≥2800 | 13 (4%) | 16 (6%) | |
| ≥3000 | 1 (1%) | 2 (1%) | |
| **Oldest acceptable donor age (years) [e]** | | | 0.04 |
| ≤55 | 2 (1%) | 1 (<1%) | |
| ≤60 | 10 (3%) | 6 (2%) | |
| ≤65 | 45 (15%) | 27 (10%) | |
| ≤70 | 103 (34%) | 73 (27%) | |
| No upper age limit | 143 (47%) | 161 (60%) | |
| **Longest acceptable PT (days) [f]** | | | <0.001 |
| 2-7 | 207 (68%) | 145 (54%) | |
| 8-14 | 98 (32%) | 122 (46%) | |
| **Slit lamp examination parameters influence decision of PT [g]** | | | 0.001 |
| No | 137 (45%) | 155 (57%) | |
| Yes | 154 (51%) | 98 (36%) | |
| No Opinion | 11 (4%) | 17 (6%) | |
| **ECD influence decision of PT [h]** | | | 0.52 |
| No | 73 (24%) | 77 (29%) | |
| Yes | 217 (72%) | 184 (68%) | |
| No Opinion | 10 (3%) | 9 (3%) | |
| **PT influence decision on donor age [i]** | | | 0.03 |
| No | 142 (47%) | 140 (52%) | |
| Yes | 104 (35%) | 66 (25%) | |
| No Opinion | 55 (18%) | 63 (23%) | |

*[a]Based on a chi-squared test. [b]Excludes 55 surgeons with missing values in 2012 and 27 surgeons with missing values in 2018. [c]Excludes 58 surgeons with missing values in 2012 and 26 surgeons with missing values in 2018. [d]Excludes 65 surgeons with missing values in 2012 and 31 surgeons with missing values in 2018. [e]Excludes 61 surgeons with missing values in 2012 and 29 surgeons with missing values in 2018. [f]Excludes 59 surgeons with missing values in 2012 and 30 surgeons with missing values in 2018. [g]Excludes 62 surgeons with missing values in 2012 and 27 surgeons with missing values in 2018. [h]Excludes 64 surgeons with missing values in 2012 and 27 surgeons with missing values in 2018. [i]Excludes 63 surgeons with missing values in 2012 and 28 surgeons with missing values in 2018.*

*PT = preservation time; ECD = endothelial cell density*

There were significant differences in the responses between 2018 and 2012 indicating more surgeons were willing to accept corneas from older donors (60% vs. 47%, respectively, with no upper age limit; p=0.04) and with longer PT (46% vs. 32%, respectively, for donor corneas with PT 8 to 14 days; p<0.001). Additionally, responses in 2018 indicated that fewer surgeons were influenced by slit lamp examination parameters when deciding on acceptable PT (36% vs. 51%; p=0.001), and PT when deciding on an acceptable upper limit on donor age (25% vs. 35%; p=0.03) (**Table 2**). However, the impact of ECD on their decision regarding acceptable PT was not different between the two years (p=0.52). The distribution of PT acceptance limitations in each year is shown in **Figure 1**.

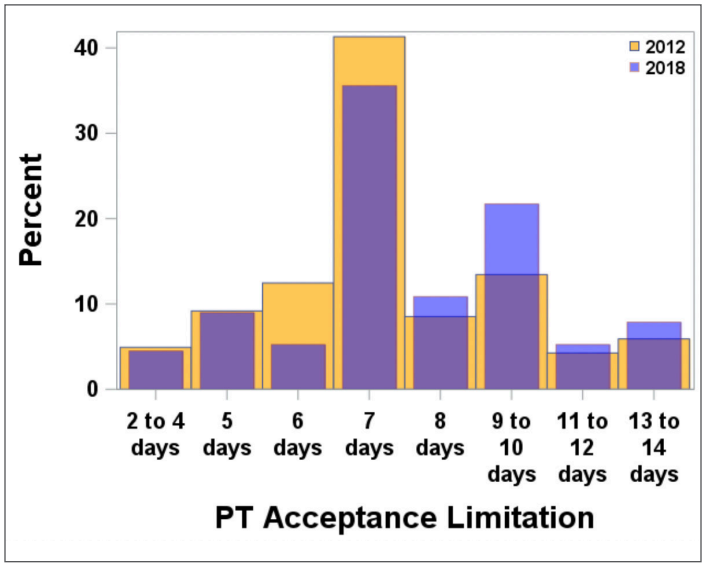


***Figure 1.*** *Distribution of preservation time (PT) acceptance limitations in the surgeon surveys*

Among surgeons who responded in 2018, the longest acceptable PT was greater for surgeons who were aware of CPTS (51% stated 8 to 14 days) compared to those who were not (33%; p=0.008) (**Table 3**). Additionally, 63% of

***Table 3.*** *Comparison of PT limits based on CPTS awareness in 2018*

| | Aware of the CPTS (N=186) | Unaware of the CPTS (N=81) | P-value [b] |
|---|---|---|---|
| **Longest Acceptable PT** | | | 0.008 |
| 2 to 7 days | 91 (49%) | 54 (67%) | |
| 8 to 14 days | 95 (51%) | 27 (33%) | |

*[a]Awareness was defined as having been aware of either or both CPTS primary results on PT impact on graft success and endothelial cell loss2,3*
*[b]Based on a chi-squared test*

*PT = preservation time; CPTS = Cornea Preservation Time Study*

surgeons who were aware of the CPTS stated that it would influence their limits on PT. However, the upper limit of PT was not significantly different between surgeons who stated that the CPTS would influence their future behavior (52% stated 8 to 14 days) compared to those who said it would not (49%; p=0.71).

In 2018, 47% of surgeons with more than 10 years of experience stated that their PT limit was >7 days compared to 28% who said the same in 2012 (p<0.001). However, among surgeons with at most 10 years of experience, 42% set their PT limitation above 7 days in 2018 which was similar to the 2012 response for this group (40%, p=0.73).

## Eye Bank Survey

*DSAEK.* Domestic data were collected from 18 - 23 eye banks in each of the three survey time points conducted (**e-Table 1**). In each year, the number of donor corneas for which data was provided ranged from 7,020 to 13,327, and the number of donors ranged from 5,138 to 9,378. In 2010, 2011, 2013, 2014, and 2018, the respective mean (±SD) PTs were 4.6 (±1.6), 4.7 (±1.7), 4.9 (±2.0), 5.0 (±1.9), and 5.1 (±1.7) days (**Table 4**). Thus, the mean PT steadily increased over time (**Figure 2**). In 2010, only 3% of tissues had a PT >7 days, compared to 5% in 2011 and 9% in each of the following three years. Mean PT was significantly higher in 2018 (5.1 ± 1.7) compared to 2010 (4.6 ± 1.6 days) (p<0.001).

***Table 4.*** *Distribution of mean PT over time in the domestic DSAEK data*

| | | | |
|---|---|---|---|
| 2010 | 9,317 | 4.6 ± 1.6 | 3% / 97% |
| 2011 | 11,533 | 4.7 ± 1.7 | 5% / 95% |
| 2013 | 13,327 | 4.9 ± 2.0 | 9% / 91% |
| 2014 | 12,815 | 5.0 ± 1.9 | 9% / 91% |
| 2018 | 7,020 | 5.1 ± 1.7 | 9% / 91% |

*PT = preservation time; DSAEK = Descemet stripping automated endothelial keratoplasty*

Mean PT varied considerably by eye bank. In total, mean PT for domestic DSAEKs performed between 2010 and 2018 increased in 10 eye banks (p<0.05 for all 10 eye banks). Among these 10 eye banks, the increase in mean PT from 2010 to 2018 ranged from 0.4 days to 1.7 days. The number of donor corneas among these 10 eye banks ranged from 15 to 1,132 in 2010 and from 52 to 2,171 in 2018. Mean PT decreased from 5.4 days to 4.9 days in only one eye bank between 2010 and 2018 (p<0.001). For the remaining 6 eye banks with data in 2010 and 2018, mean PT was not significantly different between the two years (p>0.05 for all 6 eye banks).

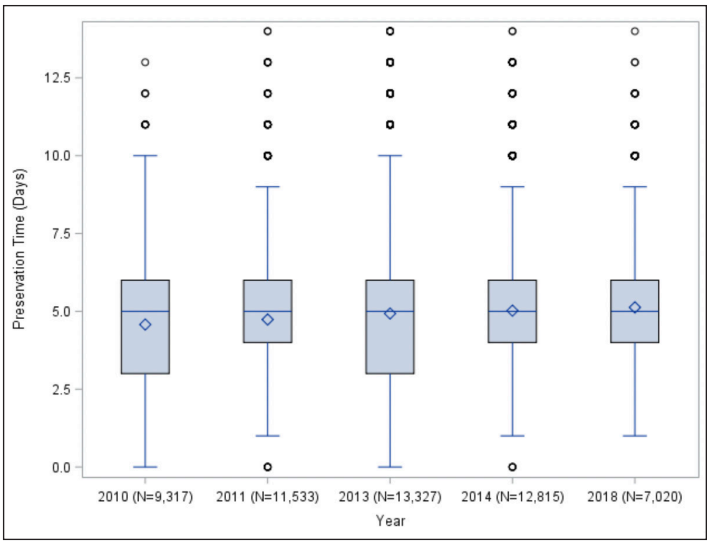


***Figure 2.*** *Distribution of mean preservation time among domestic Descemet stripping automated endothelial keratoplasties from eye banks*

In the multivariable analyses including all eye banks providing domestic DSAEK data, year, eye bank, cause of death, and lamellar dissection source (eye bank vs. surgeon prepared) were found to be associated with mean PT (p<0.001 for all factors). Based on the multivariable model, mean PT was significantly higher in each year compared to 2010 Mean PT for surgeon-lamellar-dissected-corneas was 0.19 days less than mean PT for eye-bank-prepared corneas (95% CI 0.14 to 0.23 days less).

Regarding internationally distributed tissue for DSAEKs, mean (±SD) PT was 7.0 (±2.2) days among 897 corneas, 6.9 (±2.1) among 1,246 corneas, 6.9 (±2.2) among 1,815 corneas, 7.2 (±2.2) among 2,061 corneas, and 7.2 (±2.1) among 1,039 corneas in 2010, 2011, 2013, 2014, and 2018, respectively (**eTable 2**) *(see page 12)*. In all five of these years, mean PT was approximately two days longer for international DSAEKs than for domestic DSAEKs (p<0.001 for all years).

*DMEK.* For the domestically distributed tissue for DMEKs, the respective mean PT (±SD) in each year was 3.9 (±1.2) days among 12 corneas, 5.8 (±3.1) among 42 corneas, 4.9 (±2.0) among 651 corneas, 5.5 (±2.1) among 1,713 corneas, and 5.0 (±1.7) among 4,000 corneas (**eTable 2**). Mean PT for domestic DMEKs was significantly different from that of domestic DSAEKs in 2011 (5.8 vs. 4.7 days; p<0.001), 2014 (5.5 vs. 5.0 days; p<0.001), and 2018 (5.0 vs. 5.1 days; p<0.001), but not in 2010 (3.9 vs. 4.6 days; p=0.15) or 2013 (4.9 vs. 4.9 days; p=0.76). The number of donor tissues distributed internationally for DMEKs was too low in 2010 to report over this period of time and is not provided.

## DISCUSSION

After conducting a masked multi-center clinical trial that demonstrated that PT was unrelated to graft success and endothelial cell loss three years after DSAEK up to 11 days of donor corneal storage, communicated by means of high impact publications[2,3] and national presentations, we assessed the impact on surgeon attitudes eye bank practices. This analysis and report is the first step in measuring the influence of the CPTS results on surgeon attitudes regarding PT for hypothermically stored donor corneas utilizing a representative group of corneal surgeons in the US. We have also performed a preliminary assessment of the translation of those attitudes into actual PTs utilized as reported by similarly representative eye banks.[2,3]

Our surgeon survey demonstrated that nearly 50% of surgeons in 2018 would accept donor corneas with a PT greater than 7 days, an increase of 14% from six years previously. The acceptability of donor corneas with PT > 7 days was greater in surgeons who were aware of the CPTS findings and in those with more surgical experience. However, this leaves over 50% of surgeons who, in 2018, still do not accept donor corneas past 7 days PT, providing an opportunity for further educational efforts to inform surgeons and change practice patterns based on the CPTS findings. The effort of changing practice patterns is a gradual process. For example, using our CPTS surgeon survey data to examine changes in practice patterns related to donor age, 47% of surgeons in 2012 had no donor age limit compared to 60% of surgeons in 2018; this increase in acceptance of older donor age appears to continue to change 10 years after the release of the CDS findings.[13,15]

It is not obvious why, among some surgeons, there continues to be a negative attitude regarding PT for donor corneas stored hypothermically over 7 days. In the U.S., the FDA approval of 4˚C corneal storage solutions for up to 14 days in the early 1990s was based upon *ex vivo* endothelial survival in culture, as clinical trials were not required or conducted by the manufacturer or investigators.[18,19] Prior to the CPTS and subsequent to FDA approval, there were limited reports on the relationship of extended PT beyond 7 days to graft success following PKP[20-23] and EK[24-27] and none of them was sufficiently compelling to alter practice patterns in the US. Since the CPTS was initiated in 2011 there have been only a few studies addressing PT in hypothermically stored donor corneas and these have demonstrated no detrimental effects of longer PT. Laaser et al found no difference in ECD at 6 month for Optisol GS-stored corneas ranging from 24 to 336 hours (median, 226 hours) compared to organ-culture-stored corneas ranging from 70 to 868 hours (median, 487 hours) in 82 patients.[28] Feng et al found no difference in % endothelial cell loss at 3 months with death-to-use time ranging from 2 to 10 days in Optisol GS.[29] Now with the CPTS data available, a more compelling argument can be made to corneal surgeons and those in training to substantiate changes in established practice habits surrounding PT and keratoplasty.

Our eye bank survey was intended to measure whether a shift in surgeon attitudes, as evidenced by a change in average PT of the donor tissue accepted over the period of the CPTS and after release of its findings in the fall of 2017, occurred. We found that, although a steady increase in the mean donor tissue PT occurred yearly during the study and the percentage of donor tissues used domestically beyond 7 days increased from 3% in 2010 to 9% by 2014, the percentage remained unchanged through June 2018. The eye bank data collection was representative of the greater domestic DSAEK placement, as our 2014 data on corneas intended for DSAEK from 18 participating eye banks, for example, represented 55% (12,815 of 23,100) of the total DSAEKs reported by the EBAA in 2015 for the 2014 annual year.[30] However, there was a considerable spread in PT between eye banks, suggesting surgeon preferences on donor, donor PT, donor preparation, and how eye banks managed these preferences widely varied. This wider variation may be in part due to greater demands by some surgeons for more restrictive specific donor characteristics that are not evidence-based.[31,32]

Other confounding factors that may have impacted PT values between 2010/11 and 2018 include DMEK growth,[6] and increasing pre-loading of DSAEK and now DMEK grafts with generally one day between loading and surgery. The increase in advance commitments for international distribution of donor tissue early in the preservation time period, may also have affected the PT data, possibly accounting for why the percentage of donor corneas for internationally distributed donor tissue for DSAEK with a PT beyond 7 days actually declined between 2014 and 2018 (35% to 31%). Another possible explanation for the lack of increase PT in the 2018 eye bank data is that data collected in the immediate 6 months following release of the CPTS primary papers[2,3] may not have allowed enough time for shifting practice patterns to have occurred. The PT of donor tissue distributed domestically and internationally for all PKPs and EKs should be monitored over many years to better detect the translation of changing attitudes into changing practice patterns with time. The authors have recommended to the EBAA that this information be collected as part of the annual statistical report for 2019 and thereafter (S.B.H., presented at the EBAA Medical Advisory Board Meeting, Chicago, IL, October 2018).

The greatest strength of our impact study was that it was pre-planned with both surgeon and eye bank data evaluated, and an excellent sampling of the domestic pool of donors intended for DSAEK and DMEK during and after the study period. In addition, participating surgeons and eye banks represented an excellent cross section of domestic academic and private surgical practices utilizing both large and smaller eye banks. The main weakness of our study was the relatively low survey response rate from AAO members who reported their subspecialty as cornea & external diseases, 23% in 2012 and 16% in 2018. Also, as with all polling, the accuracy of the results is completely dependent on the veracity of the responses. Nevertheless, those responding were motivated enough to provide this information as a basis for future examination of the attitude towards PT as keratoplasty surgery continues to evolve. Unfortunately there is no single registry of US surgeons in organizations such as the AAO, Cornea Society, or EBAA, making it difficult to know exactly who is performing keratoplasties in the US. This is in contrast to successful graft registries found in Australia[33] and the United Kingdom.[34] The establishment of an effective corneal graft registry in the US would very much facilitate future studies.

In summary, an early 6-month post publication survey of the impact of CPTS results has demonstrated an increased surgeon willingness to extend PT for hypothermically stored corneas compared with previous attitudes, particularly in those surgeons who are aware of the results.Greater awareness of the PT findings of the CPTS will be facilitated as other publications are released as to the other donor, recipient, operative, and postoperative factors that are associated with better DSAEK graft success and lower endothelial cell loss.[35-37] The acceptance of extended PT will continue to reap benefits for eye banks with more time to evaluate a challenged donor pool and more time to process and distribute donor tissue domestically and internationally.

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*eFigure 1:*

# Cornea Preservation Time Survey

**Section 1: These first few questions ask a little bit about you and the patients you see.**

**Q1** **What is your current age?**

_____

**How long have you been in practice since completing your training?**

_____

**Q3** **Have you ever performed endothelial keratoplasty (EK) including Descemet Stripping Endothelial Keratoplasty (DSEK) or Descemet Stripping Automated Endothelial Keratoplasty (DSAEK)?**

- YES ❑
- NO [End Survey Now] ❑

**Q4** **How many years have you been performing EK?**

_____

**Q5** **Approximately how many EKs have you performed in the past 12 months?**

- a.1 to 10 ❑
- b.>10 to 25 ❑
- c.>25 to 50 ❑
- d.>50 to 75 ❑
- e.>75 to 100 ❑
- f.>100 ❑

**Q6** **What percent of your patients with Fuchs' dystrophy or bullous corneal disease with no evidence of central stromal scarring or tube shunts would you consider for EK?**

- a.None ❑
- b.~5% ❑
- c.~25% ❑
- d.~50% ❑
- e.~75% ❑
- f.100% ❑

**Section 2: The next set of questions asks you to think about how you make decisions to accept or reject donor tissue for EK.**

**Q7** **Would you cancel a scheduled EK case if the donor tissue did not fit your normal range of acceptable parameters [i.e. donor age, death to preservation time (time from death to storage in preservation medium), cause of death, preservation time (time from storage in preservation medium to surgery), cell count], if otherwise meets local eye bank medical director acceptable standards?**

- a.Generally yes ❑
- b.Generally no ❑
- c.No opinion ❑

**Q8** **Does the time from death to preservation, if the tissue is refrigerated within 10 hours of death, influence your decision on acceptable preservation time, understanding that guidelines are within Eye Bank Association of America (EBAA) standards?**

- a.Yes ❑
- b.No ❑
- c.No opinion ❑

**Q8a** **If yes, what is your limit on death to preservation time, if tissue is refrigerated?**

- a.<13 hours ❑
- b.13 to 15 hours ❑
- c.16 to 18 hours ❑
- d.19 to 20 hours ❑
- e.>20 hours ❑
- f.Don't know ❑

**Q9** **If the tissue is not refrigerated within 10 hours of death, does the time from death to preservation influence your decision on acceptable preservation time, understanding that guidelines are within EBAA standards**

- a.Yes ❑
- b.No ❑
- c.No opinion ❑

**Q9a** **If yes, what is your limit on death to preservation time, if tissue is not refrigerated?**

- a.<6 hours ❑
- b.6 to 7 hours ❑
- c.8 to 9 hours ❑
- d.10 or greater hours ❑
- e.Don't know ❑

**Q10** **What is your current limit for accepting donor tissue from the time the cornea is processed and preserved in medium to surgery (preservation to surgery time) for EK?**

- a.2 to 4 days ❑
- b.5 days ❑
- c.6 days ❑
- d.7 days ❑
- e.8 days ❑
- f.9 to 10 days ❑
- g.11 to 12 days ❑
- h.13 to 14 days ❑

**Q11** **Does cause of death influence your decision on the acceptable preservation time?**

- Yes ❑
- No ❑
- No Opinion ❑

**Q12** **If cause of death does influence your decision, what cause(s) of death? (check all that apply)**

- Cardiovascular disease ❑
- Diabetes ❑
- Non-metastatic cancer ❑
- Metastatic cancer ❑
- Respiratory disease ❑
- Suspected pneumonia but no evidence for sepsis ❑
- Cerebrovascular accident ❑
- Trauma ❑
- High white count ❑
- Other cause of death Please describe _____ ❑

**Q13** **Do the slit lamp examination parameters of the donor's Descemet's membrane influence your decision on the acceptable preservation to surgery time, understanding that guidelines are within EBAA standards?**

- Yes ❑
- No ❑
- No Opinion ❑

**Q13a** **If yes, what parameter (s)?**

- Folds? ❑
- Location of folds? Peripheral Central Both ❑
- Peripheral tears or peels? ❑

**Q14** **Do the slit lamp and specular microscopic parameters of the donor endothelium influence your decision on preservation to surgery time, understanding that guidelines are within EBAA standards?**

- Yes ❑
- No ❑
- No Opinion ❑

**Q14a** **If yes, what parameter (s)?**

- Stress lines? ❑
- Pseudoguttae? ❑
- Polymegathism? ❑
- Pleomorphism? ❑

**Q15** **Would the initial endothelial cell count influence your decision on accepting donor tissue preserved longer than your usual limit on preservation time for EK as long as within the minimum cell count for your eye bank?**

- Yes ❑
- No ❑
- No Opinion ❑

**Q16** **1.What is your current minimum cell count on accepting tissue for EK?**

- a.Between 2000 cells/mm$^2$ and less than 2300 cells/mm$^2$ ❑
- b.2300 cells/mm$^2$ ❑

c.2400 cells/mm² ❑
d.2500 cells/mm² ❑
e.2600 cells/mm² ❑
f.2700 cells/mm² ❑
g.2800 cells/mm² ❑
h.3000 cells/mm² or greater ❑

**Q17 1.What minimum cell count would be acceptable to go longer than your usual limit on preservation time?**

a.2300 cells/mm² ❑
b.2500 cells/mm² ❑
c.2600 cells/mm² ❑
d.2700 cells/mm² ❑
e.2800 cells/mm² ❑
f.3000 cells/mm² or greater ❑

**Q18 1.What is the oldest donor age acceptable for you for EK?**

a.No older than 50 ❑
b.No older than 55 ❑
c.No older than 60 ❑
d.No older than 65 ❑
e.No older than 70 ❑
f.No upper age limit ❑

**Q19 Would you change your upper limit on donor age if the preservation time was longer than your usual limit?**

Yes ❑
No ❑
No Opinion ❑

**Q19a If yes, how would your upper limit change?**

a.No older than 50 ❑
b.No older than 55 ❑
c.No older than 60 ❑
d.No older than 65 ❑
e.No older than 70 ❑
f.No upper age limit ❑

**Q20 1.What is the minimum donor age acceptable for you for EK?**

a.No younger than 50 ❑
b.No younger than 40 ❑
c.No younger than 30 ❑
d.No younger than 20 ❑
e.No minimum age limit ❑

**Q21 Would you change your lower limit on donor age if the preservation time was longer than your usual limit?**

Yes ❑
No ❑
No Opinion ❑

**Q21a If yes, how would your lower limit be?**

a.No younger than 50 ❑
b.No younger than 40 ❑
c.No younger than 30 ❑
d.No younger than 20 ❑
e.No younger than 10 ❑

**Q22. Are you aware of the results from the following publications and/or presentations (check all those you are aware about):**

a. Rosenwasser GO, Szczotka-Flynn LB, Ayala AR, Liang W, Aldave AJ, et al. **Effect of cornea preservation time on Descemet's Stripping Automated Endothelial Keratoplasty success: Results of a randomized non-inferiority trial.** JAMA Ophthalmology. 2017;135(12):1401-1409. ❑

b. Lass JH, Benetz BA, Verdier DD, Szczotka-Flynn LB, et al. **Corneal endothelial cell loss 3 years after successful Descemet's Stripping Automated Endothelial Keratoplasty in the Cornea Preservation Time Study.** JAMA Ophthalmology. 2017;135(12):1394-1400 ❑

c. Cornea and Eyebanking Forum Nov. 2017. **Results of the Cornea Preservation Time Study**. ❑

d. Other presentation of the results of the Cornea Preservation Time Study ❑
list meeting you heard the results_____

**Thank you for completing this survey regarding cornea preservation time.**

***e-Table 1.*** *Eye Banks Contributing Data on Preservation Time between 2010 and 2018*

**A. Eye Banks participating in the Cornea Preservation Time Study (CPTS)**

1. Cincinnati Eye Bank
2. CorneaGen (formerly SightLife)
3. Eversight (formerly Midwest Eye-Banks and Cleveland Eye Bank)
4. Florida Lions Eye Bank
5. Georgia Eye Bank, Inc.
6. Gift of Life Donor Program
7. Iowa Lions Eye Bank
8. Kentucky Lions Eye Bank
9. Keralink International (formerly Tissue Banks International)
10. Lions Eye Bank Albany
11. Lions Eye Bank of Wisconsin
12. Lions Gift of Sight, University of Minnesota (formerly Minnesota Lions Eye Bank)
13. Lions VisionGift
14. Miracles in Sight (formerly The North Carolina Eye Bank)
15. OneLegacy
16. San Diego Eye Bank
17. Saving Sight (formerly Heartland Lions Eye Banks)
18. The Eye-Bank for Sight Restoration, Inc.
19. The University of Texas Southwestern Medical Center
20. Utah Lions Eye Bank
21. VisionFirst (formerly Indiana Lions Eye Bank)

**B. Eye Banks contributing data but not participating in the CPTS**

1. Alabama Eye Bank
2. Lions Medical Eye Bank of Eastern Virginia
3. Mid-America Transplant Services
4. Upstate New York Transplant Services, Syracuse University

***eTable 2.*** *Distribution of mean PT for DMEK data and international DSAEK data*

| | International DSAEK | | | Domestic DMEK | | | International DMEK | | |
|---|---|---|---|---|---|---|---|---|---|
| **Year** | **N** | **Mean ± SD of PT (Days)** | **Distribution of 8-14 Days / 0-7 Days** | **N** | **Mean ± SD of PT (Days)** | **Distribution of 8-14 Days / 0-7 Days** | **N** | **Mean ± SD of PT (Days)** | **Distribution of 8-14 Days / 0-7 Days** |
| 2010 | 897 | 7.0 ± 2.2 | 26% / 74% | 12 | 3.9 ± 1.2 | 0% / 100% | 0 | NA | NA |
| 2011 | 1,246 | 6.9 ± 2.1 | 27% / 73% | 42 | 5.8 ± 3.1 | 17% / 83% | 0 | NA | NA |
| 2013 | 1,815 | 6.9 ± 2.2 | 31% / 69% | 651 | 4.9 ± 2.0 | 9% / 91% | 23 | 7.1 ± 2.3 | 43% / 57% |
| 2014 | 2,061 | 7.2 ± 2.2 | 35% / 65% | 1,713 | 5.5 ± 2.1 | 14% / 86% | 61 | 7.2 ± 3.3 | 49% / 51% |
| 2018 | 1,039 | 7.2 ± 2.1 | 31% / 69% | 4,000 | 5.0 ± 1.7 | 6% / 94% | 592 | 8.1 ± 2.5 | 52% / 48% |

*DSAEK = Descemet stripping automated endothelial keratoplasty*
*DMEK = Descemet membrane endothelial keratoplasty*
*PT = preservation time*
*SD = standard deviation*