Successful Implementation of a Program for Increasing Donor Eyes for Research: The Duke-Miracles In Sight Program

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Abstract

Purpose: Although essential for development of ocular therapeutics, the quality and quantity of human donor eyes for research have been on the decline. To streamline procurement protocols, provide better medical documentation of tissue, and improve freshness and number of eyes, a pilot cooperative program was undertaken between the Duke University Eye Center and Miracles In Sight Eye Bank.

Methods: For research eye donors who expire at Duke University Hospital, age restrictions to procurement were lifted, access to donors' electronic medical records was granted to researchers, and eye tissue was delivered directly to scientists. The number of eye pairs received per month and the time from death to arrival in the laboratory were documented, and independent-samples *t*-tests were used to compare the number of paired eyes and the death-to-laboratory time before and after implementation of the program. A cost analysis of the program was also conducted.

Results: Implementation of the program decreased the time from death to arrival in the laboratory from an average of 22.1 ± 1.5 h ($n = 22$) to 11.6 ± 0.8 h ($n = 75$) for a pair of eyes ($P < 0.0001$). Moreover, the number of whole eye pairs increased from 1.57 ± 0.32 to 3.26 ± 0.27 donors per month ($P = 0.0019$). Cost analysis indicates that our program is financially viable and sustainable for the eye bank.

Conclusions: The Duke-Miracles In Sight Program implemented a number of operational changes that resulted in improved quantity and quality of ocular tissue to researchers. Such a model appears feasible for adoption between other eye centers and eye banks.

Introduction

SCIENTISTS FACE A shortage of donated human eye tissue for sight-saving research. Critically, research on human eye tissue is essential for understanding eye diseases, especially uniquely human disorders like primary open-angle glaucoma and age-related macular degeneration (AMD). Availability of human eye tissue is particularly important for effective development of ocular therapeutics for these and other uniquely human diseases. While numerous animal models are in use for ophthalmic drug discovery,^{1,2} unique features of human eyes, such as melanin distribution, significantly affect pharmacokinetics, including drug binding, delivery, and toxicity.³ Moreover, successful culturing of

human ocular cells depends upon fresh human eye tissue. Therefore, increased availability of donated human ocular tissue is therefore critical for research in ophthalmic therapeutics.

A recent survey revealed that many patients with ophthalmic diseases would consider donating their eyes for research,⁴ which is consistent with prior research on patient and family experiences in consenting to eye donation.^{5–7} However, numerous barriers prevent successful donation of postmortem eyes from interested donors to the laboratories of scientists who conduct research on ocular tissue. These barriers include cost of tissue acquisition versus reimbursement from researchers, lack of tissue meeting researcher criteria (such as a particular window of death-to-preservation time),

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and insufficient clinical documentation of the tissue.⁸ Close collaboration between eye banks and researchers could help to mitigate these barriers.

In this report, we describe the implementation of a pilot collaborative program between Duke University Eye Center and Miracles In Sight Eye Bank to improve procurement of eye tissue from donors who expire at our affiliated medical center. The Duke-Miracles In Sight Program aims to improve the volume, quality, and documentation of ocular tissue for research by streamlining procurement protocols for research tissue and by providing electronic medical record (EMR) access to scientists. The coprimarily outcomes of this study were the number of donated eyes received by the eye center and the time interval from death to arrival in the laboratory after implementation of the program. In addition, a cost analysis was conducted to determine the long-term financial viability of the program for the nonprofit organization, Miracles In Sight Eye Bank.

Methods

To initiate the program, eye bank administrators and scientists met and identified relevant issues that prevent successful procurement of eye tissue for research. A consensus was reached between the 2 groups on acceptable and achievable changes to improve procurement of research tissue donations. These actionable issues included the elimination of (1) current protocol limits of automatic exclusion of eyes from donors over 70 and under 4 years of age at death, (2) transport time to and from the Miracles In Sight main office in Winston-Salem (for triage and evaluation), and (3) inadequate medical documentation associated with eye tissue. Accordingly, our new protocol created referral age windows for research donors to include newborn to 4 years old and 70–90 years old. The protocol specified a convenient time window for the eye bank technician to call a single contact number and to arrange delivery of tissue directly from Duke University Hospital to the Duke University Eye Center, without first routing it through the eye bank's main office. The Duke University Institutional Review Board reviewed the Miracles In Sight consent form and determined that signed consent given by next of kin for the eye bank to access a donor's EMR also permits access by researchers who are using the tissue.

Patients included in this study expired at Duke University Hospital. Donors were excluded from this program if they were eligible to donate their eyes for corneal transplantation or if their next of kin disapproved of the procurement of their eyes for research.

For each donor death reported at Duke University Hospital, a donor center coordinator at the Miracles In Sight Eye Bank called the donor's next of kin to administer a screening questionnaire and dispatched a surgical recovery specialist, per standard procedure. From here, the procurement process adhered to a new protocol for potential research donors. The donor coordinator administered informed consent with the next of kin, gathered relevant information from hospital staff, and held a discussion with the donor's family to document a research-specific medical–social history.

Once consent for research was obtained by the donor center coordinator (Supplementary Fig. S1; Supplementary Data are available online at www.liebertpub.com/jop); the surgical recovery specialist enucleated and immediately

delivered the eyes to the Duke University Eye Center, where designated research personnel obtained and processed the tissue for experiments. Paperwork, including a copy of the donor's chart and documentation of tissue recovery, was then delivered to the Miracles In Sight Eye Bank along with a blood sample from the donor. The blood sample was tested using a custom serological panel created for the specific needs of Duke researchers, and results of the serological panel were sent to the laboratory by e-mail within 24–48 h of receipt by the eye bank. For this process, a 1-time expense was incurred on the eye bank to amend their database to accommodate tracking of weekly progress and direct delivery of tissue to Duke University Eye Center laboratories. See Fig. 1 for a process diagram that illustrates the Duke-Miracles In Sight Program protocol.

To measure the influence of the Duke-Miracles In Sight Program, the number of donated whole eye pairs and their time from death to arrival in the laboratory were recorded. A pre-postanalysis was conducted by comparing the mean number of eye pairs and mean death-to-laboratory time from the 52 weeks proceeding implementation of the program to the mean number and mean time interval during the first 98 weeks after program implementation. For pre-post comparisons, we only included eyes obtained from the Miracles In Sight Eye Bank and used the same inclusion/exclusion criteria pre- versus postprogram implementation. Data are reported as mean $\pm$ standard error, and independent-samples *t*-test was used for pre- and postimplementation comparisons.

Results

Implementation of the Duke-Miracles In Sight Program reduced the death-to-laboratory time in half, from an average of 22.1 ± 1.5 h ($n = 22$) during the 52 weeks before the

FIG. 1. Process diagram of the Duke-Miracles In Sight Program. EMR: electronic medical records; MIS, Miracles In Sight Eye Bank; Re, regarding.

FIG. 2. Measures of quality and quantity of donor eyes received as a result of the Duke-Miracles In Sight Program. Shown are bar graphs of the time interval from death to arrival in the laboratory for whole eye pairs before and after implementation of the Duke-Miracles In Sight Program. (A) Shows a comparison of the death-to-arrival time for eyes received pre- versus postimplementation of the program, expressed as binned data in 4 time intervals. (B) Displays average time to arrival for all whole eye pairs received, pre- versus postimplementation (* $P < 0.05$). (C) Shows the number of eye pairs received over time since the program's induction. Months are represented numerically.

program to 11.6 ± 0.8 h ($n = 75$) during the 98 weeks after implementation for each eye pair ($P < 0.0001$) (Fig. 2A, B). In addition to improved tissue quality, the program also resulted in an increased quantity of eye pairs successfully procured to the laboratory from 1.57 ± 0.32 to 3.26 ± 0.27 donors per month ($P = 0.0019$). Figure 2C depicts the number of eyes per month that was received since the inception of the new program. Data show that we have gradually increased the number of eyes per month, starting with 1 pair per month in August 2013 to as many as 7 pairs per month by mid-2015. Importantly, we have improved the number of eyes that we received in 6 h or less postmortem (16 pairs postcollaboration vs. 0 precollaboration), which is critical for time-sensitive analyses like proteomics,^{9,10} metabolomics,¹¹ and expression studies.^{12,13}

TABLE 1. COST ANALYSIS OF THE DUKE-MIRACLES IN SIGHT PROGRAM PER DONOR

Item	Cost
Direct costs	
Supplies	\$37.99
Staffing (SRS and Donor Center)	\$139.00
Serology testing	\$165.50
Transportation	\$7.80
Processing (laboratory staff and supplies)	\$50.00
Total direct costs per donor	\$400.29
Indirect costs ^a	
Call center	Varies
Capital expenditure for research database	\$10,000 amortized over 5 years
Fleet depreciation	5 year straight line, weighted based on donor frequency
Facilities and IT infrastructure	Varies
Administrative and support staff	Varies
Total indirect costs	Varies

^aAll costs, especially indirect costs, will vary between eye banks and are dependent on square footage, donor volume, accounting methods, and so on.

IT, information technology; SRS, surgical recovery specialist.

To assess the financial viability of the Duke-Miracles In Sight Program for the eye bank, a cost analysis was conducted to estimate program expenses (Table). For each donor referral, the process of screening, recovery, testing, and delivery incurred a total of approximately \$400.00 in direct costs. Direct costs included supplies, serology testing, transportation, paperwork processing, and wages related to full-time and per diem employees. The current eye bank organizational and workflow structures include excess capacity and enable Miracles In Sight to implement this process without needing to significantly increase the indirect costs, which consist of expenses relating to call center infrastructure, vehicle depreciation, information technology infrastructure, and facilities. However, there was a 1-time capital expenditure for designing and implementing a research database that was amortized over 5 years. These costs will vary between eye banks and are dependent on facility square footage, donor volume, accounting methods, and the viability of the associated transplant program. In total, the sum of direct costs per donor was estimated at \$400.00.

For reimbursement of these costs, the Duke University Eye Center contributes \$400 per globe, or \$800 per bilateral donor. Therefore, the difference of reimbursement and total costs of participating in the Duke-Miracles In Sight Program results in a contribution margin of \$400.00 less the indirect costs per bilateral donor for the eye bank. This demonstrates not only the financial viability of the program but also the potential for future efficiencies and expansion due to a positive contribution margin for the participating eye bank with excess operational capacity.

Discussion

With a shortage of human eye tissue, particularly whole globes, available for research, scientists and eye banks must identify novel methods of obtaining and processing tissue to fill research needs. In the present report, we describe the pilot Duke-Miracles In Sight Program, in which eye bank surgical recovery specialists deliver eye tissue for research from donors who expire at Duke University Hospital directly to the adjoining Duke University Eye Center. In addition, we have found that the consent form administered to the donor's family allows the research team to access medical information from the donor's EMR after expiration to ensure adequate documentation of the donated tissue.

This novel collaboration has doubled the number of donated eyes received by the eye center and has reduced the time from death to arrival in the laboratory by half. A cost analysis by Miracles In Sight has found the program financially viable, with reimbursement for eye tissue far exceeding the cost of procurement and delivery for bilateral donors. Thus, we are confident that this program is beneficial both for scientists, who receive more donor eyes with reduced death-to-laboratory time and better medical documentation, and for the eye bank, which receives adequate reimbursement for procurement of research tissue. Most importantly, this collaboration allows eye donors and their families to fulfill their wish to make a valuable anatomic gift to research.

Eye banks and ophthalmic researchers have long had a collaborative relationship. Although the primary mission of eye banks is restoration of sight through tissue transplantation, research has been a core component of the eye bank agenda since their inception and remains part of the mission of the Eye Bank Association of America (EBAA).^{14,15} In fact, 17,384 donated tissues were distributed for research by EBAA-affiliated eye banks in the United States in 2013 out of 123,079 total donated tissues.¹⁶ Notably, this represents a 10% decrease in distribution of tissue for research compared to 2012, despite a 5% increase in the total number of tissues acquired.¹⁶ Although the financial cost of providing research tissue is of understandable concern to eye banks,¹⁷ cost analysis of this pilot program indicates that provision of research tissue can be sustainable, given the expenses of procurement and related activities at our eye bank and the reimbursement provided by our academic eye center.

Currently, researchers obtain ocular tissue from eye banks using at least 3 previously described strategies. These include using a clearinghouse that identifies and delivers tissue according to protocols from researchers, systematic recovery of all available tissue to find those that meet research criteria, and utilizing a registry based on donor pledges.⁸ A large clearinghouse provider of ocular tissue is the National Disease Research Interchange (NDRI), which draws from multiple eye bank sources to pair donated tissue with researchers' protocols.¹⁸ The Duke-Miracles In Sight Program builds upon this clearinghouse method, but simplifies the process so that research tissue is brought directly to scientists at the medical center in which the tissue is procured. To our knowledge, the Duke-Miracles In Sight Program is the first of its kind to be reported, and we believe it can be successfully replicated at other academic centers and eye banks.

An alternative larger-scale strategy for obtaining eye tissue for research has been proposed as a pledge-based donor registry. This eye donation registry for research would utilize an advance directive as an addendum to the existing Donate Life donor registry, which maintains the list of registered organ and tissue donors. This addendum would allow donors to indicate their desire to make an anatomical gift for research and grant researchers access to their medical records after death.⁴ Surveys of ophthalmic patients and their family members have shown interest and support for establishment of the registry,⁴ and eye care providers have indicated that an eye donation registry for research would improve how they work with patients who wish to donate their eyes to science.¹⁹ There is precedent for pledge-based registries for research in the United States, including the

National Temporal Bone Registry^{20,21} and the Department of Veterans Affairs Biorepository Brain Bank.²² Similar to the Duke-Miracles In Sight Program, an eye donation registry for research would mitigate barriers for researchers, such as a lack of tissue (because donors unsuitable for corneal donation could have their eyes procured for research) and poor documentation (by allowing access to EMRs). In fact, the proliferation of EMRs will likely make it easier to "flag" registered donors upon their passing.

Because of the tremendous unmet need, implementation of a similar pledge-based registry is currently underway. Eversight Eye Banks is developing a disease-specific registry that would allow patients with diseases like AMD, diabetic retinopathy, and glaucoma to register their post-mortem eye tissue to a designated ocular tissue biobank for researchers. This biobank would allow researchers access to masked demographic information and medical records along with the research tissue.²³ Innovative collaborations between scientists and eye banks may help to ameliorate the shortage of tissue available for important research on blinding diseases.

Our study has several limitations. By utilizing a pre-postdesign, our results could be attributed to a number of confounding variables, including an influx of donor eyes not related to implementation of the Duke-Miracles In Sight Program, but our long-term follow-up of 98 weeks makes this unlikely. A stronger experimental design could involve a crossover experiment by which coprimary outcomes are re-examined after returning to preimplementation protocols, allowing a number of confounds to be evaluated. In addition, our study examines the effects of a pilot program between a particular eye bank and university eye center, and numerous regulatory factors could preclude the implementation of this program elsewhere. In particular, our ability to access EMRs from a single-source hospital greatly facilitated implementation of the program, and such readily accessible EMRs may not be available to researchers at other academic centers. In the same vein, our department's close association with our affiliated university hospital helped to streamline our protocol's procedures and costs in a way that may not be available for all laboratories. Nonetheless, we are confident that this program could warrant consideration by other institutions, which could initiate discussions with regional eye banks to identify acceptable and achievable procedure changes to modify procurement protocols, as we describe in the Methods section.

Due to diminishing availability, researchers resort to several strategies to obtain human eye tissue, particularly whole globes. Although limited to the experiences of 1 eye bank and 1 academic eye center, the pilot Duke-Miracles In Sight Program successfully mitigated major barriers for obtaining quality eye tissue for research. As a result, the number of donated human eyes delivered to our eye center has increased, and the death-to-laboratory time has been reduced. This collaboration is financially feasible and embodies the shared mission of both participating institutions: promoting research to cure blinding eye diseases, while carrying out the wishes of the recently deceased to donate their valuable eyes to research.

Author Disclosure Statement

No competing financial interests exist.

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