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Cornea Transplantation: The New Era of Endothelial Keratoplasty

INSIDE THIS ISSUE

Corneal transplantation has evolved rapidly over the past decade, as surgeons strive to refine selective tissue transplantation to treat diseases that affect specific layers of the cornea.

The first successful penetrating corneal transplantation was performed by Eduard Zirm in 1905. In 1931, Ramon Castroviejo, MD, while a fellow at Mayo Clinic, refined the techniques for penetrating keratoplasty (PK) familiar to cornea surgeons today. Although PK has been more popular than lamellar keratoplasty traditionally, the techniques for lamellar keratoplasty have advanced dramatically. At present, posterior lamellar (endothelial) keratoplasty is the treatment of choice for corneal endothelial disease, and deep anterior lamellar keratoplasty is strongly advocated for corneal stromal disease.

The majority of corneal transplantations at Mayo Clinic are performed for patients with Fuchs endothelial dystrophy. "Our experience with Descemet stripping endothelial keratoplasty, or DSEK, for these patients has developed favorably over the past 6 years," notes Sanjay V. Patel, MD, of the Department of Ophthalmology at Mayo Clinic in Rochester, Minnesota. "We have been fortunate to examine many of the patients receiving DSEK in our prospective evaluation of DSEK outcomes study, with 3 years of follow-up for many of the participants."

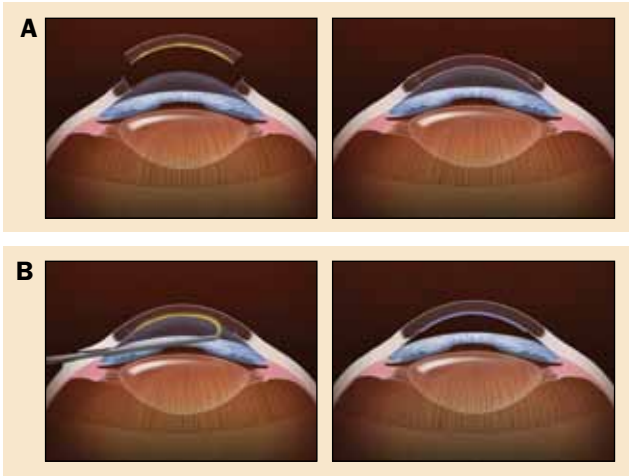

Figure. *A, In penetrating keratoplasty (PK) (left panel), the full-thickness host cornea is removed and replaced with a donor transplant that is secured to the host with sutures ((right panel). B, In Descemet stripping endothelium keratoplasty (DSEK) (left panel), the Descemet membrane and endothelium are stripped from the recipient and replaced with a thin posterior donor lenticule transplant through a small limbal incision (right panel).*

Visual Outcomes Gain Importance

Graft survival has been the traditional measure of success in corneal transplantation. The long-term survival of DSEK grafts, however, will be determined only with long-term follow-up. The risk of early endothelial failure (either primary or iatrogenic) is higher with DSEK than with PK. This outcome is explained by the high rate of endothelial cell loss caused by the surgical manipulation of the donor tissue (23% cell loss from preoperative at 1 month postoperative).

Despite the high initial rate of endothelial cell loss, the rate of subsequent cell loss rapidly diminishes, with 26% loss from preoperative at 6 months and 39% loss at 2 years. This rate is in contrast to the higher rate of cell loss after PK and it confirms the results of other published series. The reason for the low rate of central endothelial cell loss after 1 month is unknown, but it may relate to anatomical differences between DSEK and PK (Figure).

Because of promising intermediate-term endothelial cell loss rates and graft survival, visual characteristics are likely to become a more important measure of success in the future. Traditionally, visual outcomes have been difficult to interpret because of confounding factors and the variable ability to provide the best refraction for eyes with high refractive errors and irregular astigmatism after PK. Endothelial keratoplasty results in good uncorrected visual acuity with predictable postoperative refractive errors and low astigmatism.


Sanjay V. Patel, MD

As a result, measurement of visual outcomes will become easier and more standardized.

Postoperative Visual Acuity Outcomes

The main visual advantage of DSEK over PK is the ability to provide a predictable postoperative spherical equivalent with little, if any, induced cylinder. For many patients, this outcome results in good uncorrected visual acuity (20/50, Snellen equivalent, in our study at 2 years).

Because visual acuity varies less after endothelial keratoplasty than after PK, it is likely to become a more important determinant of success in endothelial keratoplasty. "We assessed multiple aspects of vision after DSEK in our prospective study, in which patients with other causes of decreased vision have been excluded," says Dr Patel. Outcomes include the following:

- At 2 years, one-third of the participants have 20/20 visual acuity or better. Mean best corrected visual acuity is 20/28. Better postoperative visual acuity is associated with better preoperative acuity and younger age.
- Many patients do not achieve 20/20 acuity after DSEK. However, they do note subjective improvement in their quality of vision. Graft thickness does not affect visual acuity. Other factors have yet to be determined.
- In pseudophakic eyes after DSEK, the center and the peripheral domains of the retinal image point-spread function are degraded compared with otherwise healthy pseudophakic eyes of similar age. This outcome implies that eyes after DSEK have considerably more high-order aberrations and intraocular forward scatter (disability glare) than healthy, pseudophakic eyes.
- Results also indicate that scattered light originates and persists from the subepithelial region of the host cornea, whereas interface scatter diminishes over the first 2 years after surgery.

The exact contributions of all of these variables to postoperative vision have not been fully elucidated. Nevertheless, it is becoming apparent that chronic changes in the retained host cornea affect the optical properties of eyes after DSEK.

The field of endothelial keratoplasty continues to evolve. "Descemet membrane endothelial keratoplasty (DMEK) is on the horizon," says Dr Patel. "The success and adoption of DMEK will depend on whether it can provide better graft survival or vision than DSEK. Although initial reports suggest improved visual outcomes with DMEK, this result will be confirmed only through standardized vision assessment in a randomized controlled trial. Our observational study after DSEK continues in a follow-up phase, and we expect it will provide longer-term outcomes of the procedure."

New Scleral Contact Lens Offers Hope for Patients With Severe Corneal Disease


Muriel M. Schornack, OD

Scleral contact lenses allow cornea subspecialists to deal more effectively with many patients whose corneal disease has frustrated ophthalmologists' best efforts. These patients share a common longing for a remedy to the problems of tear film, ocular surface, and optical dysfunctions that prevent the pain-free, aberration-free corneal performance that most people take for granted. The patients' problems are the result of various conditions:

- Dry eye and pain despite diligent adherence to standard remedies
- Keratoconus or corneal trauma with irregular astigmatism too severe to allow a comfortable fit with standard rigid contact lenses
- Exposure keratopathy from incomplete eyelid excursion
- Filamentary keratitis or other causes of corneal epithelial irregularity that cannot be treated with standard soft bandage contact lenses

Almost universally, these patients balk at the suggestion that a contact lens will solve their problems. "The patient with severe keratoconus imagines another unstable, uncomfortable lens fit," says Muriel M. Schornack, OD, with the Department of Ophthalmology at Mayo Clinic in Rochester, Minnesota. "The patient with dry eye worries about a lens abrading the compromised epithelial layer and worsening the pain from the exquisitely sensitive plexus of corneal nerves. The patient with ocular exposure does not understand how this lens will protect the eye any better than previous methods of therapy. Then we show the patient a scleral lens that has a design radically different from a soft or rigid lens."

Scleral lenses are generally 18 mm or more in diameter. They are supported entirely by a wide flange or haptic that rests on the sclera while completely vaulting the cornea and limbus. A fluid reservoir is maintained between the posterior surface of the lens and the anterior corneal surface. In cross section, the design is similar to a dome on a church (Figure).

Scleral support is the key to improved comfort compared with corneal lenses because of the lower density of pain fibers in the sclera than in the cornea. The cornea of a patient with severe dry eye or

exposure keratopathy is bathed with fluid continuously. The lack of contact between the posterior lens surface and the cornea keeps the patient with irregular astigmatism comfortable while the spherical anterior surface of the lens neutralizes visual aberration caused by corneal irregularity.

Patients quickly understand the logic and elegance of the design and recognize that this is not a typical contact lens.

Before 2006, Mayo Clinic ophthalmologists referred patients potentially needing a scleral lens to Boston for fitting with the Boston Ocular Surface Prosthesis Device (Boston Foundation for Sight, Needham, Massachusetts), designed by Perry Rosenthal, MD. This lens, custom fit to the scleral and corneal parameters of each eye, provided excellent results for most patients. However, the relatively high cost and limited access to the devices initially hindered widespread application. "We searched for a commercially available lens that could provide similar success for less expense," says Dr Schornack.

At Mayo, Dr Schornack began fitting scleral lenses using the Jupiter design scleral lens, available from Visionary Optics (New York, New York) and Essilor Contact Lenses (Dallas, Texas). Since 2006, Mayo has treated 275 eyes of 180 patients. Lens fitting is based on a series of premade diagnostic scleral lenses that differ in diameter and base curve. Lenses can be customized to provide excellent vision and comfort for each patient. These lenses cost up to 75% less than proprietary designs, and so offer the patient a more affordable alternative for treatment.

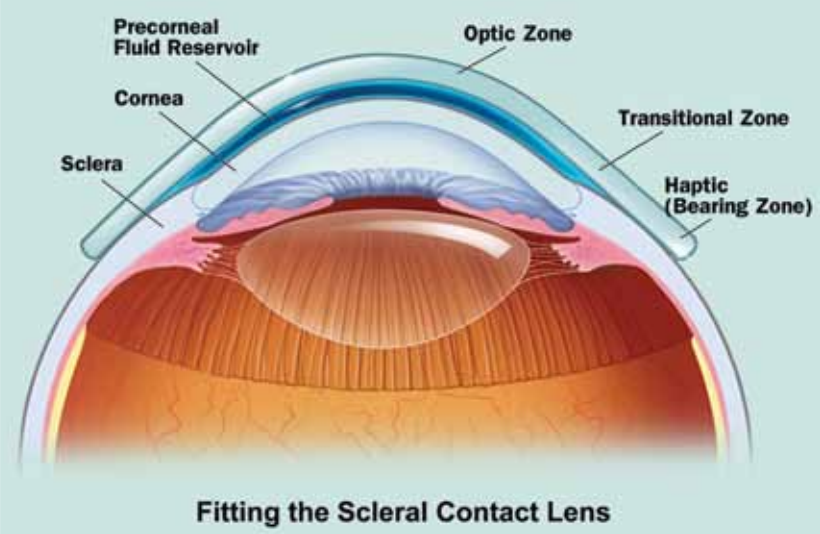

Figure. *The scleral lens is supported by the sclera and vaults the surface of the cornea. It provides the excellent optics of a rigid contact lens without lens-cornea interaction and with a stable fluid reservoir between the lens and corneal surface.*

Amblyopia Studies Compare Treatment Effectiveness

The Pediatric Eye Disease Investigator Group (PEDIG), led by Jonathan M. Holmes, MD, of the Department of Ophthalmology at Mayo Clinic in Rochester, Minnesota, addresses the need for evidence-based medicine in pediatric ophthalmology. This network of pediatric eye care providers in both academic and private practice settings conducts randomized clinical trial and large-scale observational studies, funded by the National Institutes of Health.

PEDIG member sites have completed 14 studies to determine which treatments are most effective for patients with amblyopia. Twelve of the studies, which address anisometropic, strabismic, combined, and bilateral refractive amblyopia (but not unilateral deprivation amblyopia), were conducted at Mayo Clinic.

Amblyopia Responds to Low-Intensity Treatment

Amblyopia is the most common cause of unilateral vision loss in children and young adults. It is characterized by the brain's suppression of 1 eye, associated with anisometropia, strabismus, or deprivation. Bilateral amblyopia is most often associated with high refractive error in each eye.

"We have discovered that most cases of amblyopia can be treated successfully with low-intensity treatment," says Dr Holmes. "Treating first with spectacles alone substantially improves visual acuity in many children with anisometropic amblyopia, bilateral refractive amblyopia, and even strabismic amblyopia."

If improvement with spectacles alone is incomplete, several treatment options are available. Each option gives the amblyopic eye an advantage by blurring or blocking the fellow, nonamblyopic eye. These options include the following:

- A patch placed over the fellow eye (as little as 2 hours each day)
- Atropine drops administered to the fellow eye (as little as 1 drop twice weekly)
- A blurring filter applied to the spectacle lens over the fellow eye


Jonathan M. Holmes, MD

Studies Compare Treatment Types and Intensities

PEDIG amblyopia treatment studies include head-to-head comparisons of treatments and evaluations of different treatment intensities. The studies showed that treating the fellow eye with a drop of atropine every day had a similar effect to

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patching the fellow eye for 6 or more hours each day. Using a specially developed questionnaire, researchers also found that parents and children tended to prefer the atropine drop to the eye patch.

After the initial study was completed, atropine drops became more widely used for the treatment of amblyopia. In a PEDIG subsequent study, a third option—a blurring filter over the spectacle lens in front of the nonamblyopic eye—was also found to be effective.

PEDIG researchers completed a series of studies to investigate the needed amount of patching and the needed frequency of atropine drops. These studies indicated that the intense regimes routinely prescribed were not necessary for most children. Patching 2 hours each day or using the atropine drop twice weekly was effective in many cases.

"The study that has changed my practice the most and profoundly improved quality of life for children with amblyopia and their parents, is the study that found 2 hours of daily patching effective for more than 60% of children," says Dr Holmes.

New Studies Recruiting Patients

Researchers at Mayo Clinic are conducting a study of levodopa, an oral medication that may prove to be an adjunct to patching for children aged 7 to 13 years. Earlier PEDIG studies found that many children with amblyopia in this age-group were responsive to patching, but that the response often was incomplete at these ages.

Two additional PEDIG studies underway at Mayo address residual amblyopia. These studies investigate how often children respond to increased intensity patching or augmented atropine treatment, when improvement is incomplete with 2 hours of daily patching or twice-weekly atropine. Mayo is actively recruiting patients aged 7 to 13 years with amblyopia for the levodopa study and patients aged 3 to 6 years for the residual amblyopia studies.

Dr Holmes is the Joseph E. and Rose Marie Green Professor of Visual Sciences at Mayo Clinic. He is the national network chair of PEDIG and leads Mayo's levodopa study and residual amblyopia studies.

"Antiviral Treatment Thwarts Recurring Eye Problems From Herpes Simplex" Is a Medscape Most-Read Article

An article about research conducted by Keith H. Baratz, MD, and colleagues at Mayo Clinic was the second most-read story of 2010 by Medscape subscribers registered as eye specialists. Fran Lowry's article "Antiviral Treatment Thwarts Recurring Eye Problems From Herpes Simplex" is based on a study published in the *Archives of Ophthalmology* in September 2010.

The paper, "Incidence, Recurrence, and Outcomes of Herpes Simplex Virus Eye Disease in Olmsted County, Minnesota, 1976-2007: The Effect of Oral Antiviral Prophylaxis," was based on a generation of cases in Olmsted County.

"Our objective was to provide an estimate of the incidence of herpes simplex virus (HSV) eye disease in a community-based cohort," notes Dr Baratz. "We also wanted to investigate the effect of prophylactic oral antiviral therapy on HSV recurrences and outcomes."

All Olmsted County residents who received a diagnosis of ocular HSV infection from 1976 through 2007 were retrospectively reviewed for the study. The frequency of recurrences and adverse outcomes were compared between a patient group with no treatment and a patient group treated prophylactically with oral antiviral medication.


Keith H. Baratz, MD

"The research indicated that for patients in the study, oral antiviral prophylaxis was associated with a decreased risk of recurrence of epithelial keratitis, stromal keratitis, conjunctivitis, and blepharitis due to HSV infection," says Dr Baratz.

The research was sponsored by Mayo Clinic and the Research to Prevent Blindness, New York, New York. Dr Baratz was the senior author. The other authors were Ryan C. Young, BA, medical statistician David O. Hodge, MS, and Thomas J. Liesegang, MD.

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