Corneal transplantation surgery has evolved since 1905, when Eduard Zirm, MD, completed the first successful penetrating keratoplasty (PKP) procedure on a 45-year-old farm laborer in what is now the Czech Republic. In the first half of the 20th century, anterior lamellar keratoplasty, a partial-thickness technique that selectively replaces the front part of the diseased cornea, was the dominant procedure. But in the 1950s, with the discovery of the important role of the endothelium in maintaining corneal clarity and with advances in the understanding of corneal graft rejection, PKP gradually took center stage.

After more than 50 years of PKP as the leading corneal grafting technique, surgeons began circling back to the philosophy “less is more” about 10 years ago. Although traditional PKP remains the gold standard, several new transplant techniques have been developed that aim to spare the healthy corneal layers, replacing with donor tissue only those that are diseased.

**PKP Overview**

PKP continues to be the gold standard in keratoplasty for several reasons. First, until approximately 5 years ago, PKP was the only corneal transplantation technique that we knew was effective and straightforward to perform and, therefore, that surgeons learned during their corneal fellowships. Second, PKP suits the majority of indications for corneal transplantation, be it stromal disease or endothelial dysfunction. Third, cases that initially present with disease in one layer eventually progress to having all the layers of the cornea affected. These late-stage presentations will require full-thickness corneal replacement. For example, only the endothelial layer requires replacement in a patient with early Fuchs endothelial dystrophy; however, when Fuchs is left untreated, chronic edema of the overlying stroma and bullous keratopathy with repeated epithelial breakdown result in permanent stromal scarring. In such cases, there is usually no recourse, and we must exchange the whole cornea. Last, PKP is a relatively straightforward procedure that really requires only the use of circular trephines of varying diameters to effect full-thickness replacement of the central cornea.

Many surgeons have recently evolved their PKP techniques with the use of a femtosecond laser instead of a mechanical trephine to cut the recipient and donor corneas. The advantage of a femtosecond laser is that it can produce various sophisticated trephination edge margins with precision. When we mechanically trephine the cornea, only a straight vertical cut is possible; with a laser, however, the cut profile can be made in a variety of shapes including beveled or stepped edges, such as zig-zag and top-hat configurations. These more complex wounds, with a step or a slope in the cut margins, create a secure graft that is more resistant to trauma than the straight trephine cut.

As yet, laser-enabled PKP is not fully in the mainstream for several reasons: (1) studies generally show that the added precision with femtosecond lasers, although more time-consuming, does not seem to reduce the degree of post-PKP corneal astigmatism, (2) the lasers usually cannot penetrate or cut through scar tissue or densely opaque corneas, and (3) additional cost and laser time is involved.

Conceptually, PKP can be performed in any eye with cloudy vision as a result of a diseased cornea. Surgeons have...
enjoyed much success with this technique; however, it is not free from disadvantages. For starters, quality of vision can be distorted after surgery due to the large number of sutures in the cornea, and post-PKP corneal astigmatism continues to be a major cause of poor visual quality. Additionally, full-thickness corneal replacement leaves the eye relatively weak, and the wound can break down in the event of trauma, even many years after surgery. The major cause of graft failure is still allograft rejection, mainly affecting the endothelial cell layer. In fact, long-term graft survival may be compromised, as many indications for corneal transplantation such as pseudophakic corneal edema, one of the most common indications, may eventually result in endothelial failure either due to endothelial rejection or to gradual loss of endothelial cells with time.

LAMELLAR KERATOPLASTY OVERVIEW

In the past few years, surgeons have begun to move away from PKP and toward lamellar transplantation techniques, which many surgeons refer to as selective lamellar keratoplasty because only the diseased layers of the cornea are exchanged for donor tissue. In a nutshell, either the stroma is removed using an anterior lamellar keratoplasty (ALK) technique, leaving the healthy endothelial layers intact, or the endothelium is removed and the overlying stroma is left intact using an endothelial keratoplasty (EK) technique. Because many corneal diseases initially affect only selected layers of the cornea, it makes sense to preserve as much of the patient’s own healthy cornea as possible.

ALK. Compared with PKP, the ALK procedure has two major advantages. First, it significantly reduces the risk for postoperative complications and graft rejection because it leaves the healthy Descemet membrane and endothelium intact. This obviates the risk of endothelial rejection, which is the most common form of allograft rejection and is more likely to result in overall graft failure compared with stromal or epithelial rejection, which can more often be fully reversed with topical steroids. Second, because rejection becomes less of a problem, topical steroid regimens can be reversed with topical steroids. Second, because rejection becomes less of a problem, topical steroid regimens can be reversed with topical steroids.

Take-Home Message

- Conceptually, PKP can be performed in any eye with cloudy vision as a result of a diseased cornea.
- Selective lamellar keratoplasty techniques exchange only the diseased layers of the cornea for donor tissue.
- Minimal refractive change or refractive surprises occur after DSAEK, apart from a mild degree of hyperopic shift due to the presence of the donor lenticule.
- DMEK has some advantages compared with DSAEK, including the promise of better visual outcomes; however, the surgical technique is extremely challenging.
recovery—often within a few weeks—as compared with PKP, in which it may take 6 months or more for visual stability. More important, because we are not transplanting a lot of tissue in DSAEK, some studies have shown a low risk of graft rejection (4% to 8%).8-10 Compared with about 10% to 18% after full-thickness PKP.11

The downside to DSAEK is that it is a completely new surgical procedure to master, and surgical techniques are still in evolution. Whereas the original standard thickness of the donor lenticule was 150 µm (range, 100–200 µm), the trend now is ultrathin DSAEK using donor lenticules that are often less than 100 µm in thickness. Although yet to be resolved, several studies now suggest that thinner donors result in better BCVAs and that a higher percentage of patients with ultrathin DSAEK attain 20/20 vision.12 However, surgical handling of very thin donor tissue is more challenging and prone to the possibility of greater endothelial cell damage as a consequence.13

The technical challenge with DSAEK is handling the delicate donor tissue; the monolayer of endothelial cells must not be touched. Early studies of DSAEK showed significant endothelial cell loss, about 35% to 40%,14 largely related to damage to endothelial cells caused by folding the donor tissue with forceps, inserting it through a small incision, and unfolding the tissue in the correct orientation into the anterior chamber. This is known as the taco folding technique. Although this technique is still often used today, over the past few years surgeons have devised surgical techniques or donor inserter devices such as the Busin Glide (Moria), EndoGlide (Network Medical Products, UK), and EndoSerter (Ocular Systems Inc.) in an attempt to reduce intraoperative endothelial cell loss during this crucial step in the surgery. For instance, with our device, the EndoGlide, which was the first US Food and Drug Administration (FDA)-approved disposable inserter for this purpose, the donor is coiled with minimal endothelial surface contact into a chamber. This chamber is then inserted through a corneal or scleral wound and pulled into the eye using coaxial microforceps inserted through a nasal paracentesis. Our technique produces more surgical control of the donor and has now been shown by at least three studies to reduce endothelial cell loss rates to around 15% to 20% at 6 months.15-17 This is about 50% lower than the cell loss occurring with the taco fold technique, in which forceps are used to guide insertion. In one study comparing the EndoGlide to the Busin glide, significantly less endothelial cell loss was shown with the former.16 Two other studies with the EndoGlide are currently in press. One describes a prospective 100-patient study in standard Fuchs dystrophy and pseudophakic bullous keratopathy cases, in which 6- and 12-month endothelial cell loss rates of 13.5% and 14.9%, respectively, were achieved. The other is a retrospective study of 45 complex cases including eyes with prior vitrectomy, glaucoma surgery, and failed PKPs, in which the 6- and 12-month endothelial cell losses were 17.9% and 27.0%, respectively.

DMEK. During Descemet membrane endothelial keratoplasty (DMEK), only Descemet membrane with healthy endothelium is transplanted; this provides the most anatomically correct EK procedure and, unlike DSAEK, avoids a stroma-to-stroma interface. The first step in DMEK is to carefully and completely peel the Descemet membrane from the donor tissue without inducing endothelial cell damage or tearing. Detached donor Descemet membrane automatically scrolls up on itself and, thus, may be inserted or injected in a scrolled manner into the eye. The surgeon then attempts to unscroll the donor in the right orientation and appose it, without folds or wrinkles, onto the recipient stromal surface using air tamponade.

There are several advantages of DMEK. Without a stroma-to-stroma interface or unnecessary additional stroma, which in DSAEK increases overall corneal thickness, DMEK has been shown to provide superior visual outcomes compared with DSAEK, and more eyes achieve acuities of 20/20 and even 20/15.18-20 There is potentially less cost involved in DMEK surgery, as microkeratome precutting of donor tissue is not required, but a major advantage emerging is the fact that DMEK appears to have even less risk of allograft rejection than DSAEK, with studies suggesting the risk to be 1% or less.18-20

This surgery comes with a penalty, however, as the procedure is surgically very challenging. Donor preparation carries a risk of tearing Descemet membrane and losing donor tissue. Additionally, handling the scrolled donor in the anterior chamber presents major challenges. First, the donor always scrolls up with the endothelial cell layer outermost, so that direct handling of the donor results in cell loss. Second, surgeons must unscroll and position the donor in the right orientation, adjacent to the recipient stroma, by means of small jets of balanced saline solution and air bubbles—of course without the use of an ophthalmic viscosurgical device. Third, the donor has a tendency to wrinkle and partially detach after surgery, and rebubbling rates after DMEK remain higher than after DSAEK, as do primary graft failure rates especially during the steep learning curve of this form of surgery. Finally, reported endothelial cell loss rates remain generally high, around 35% to 40%.

Because of these surgical challenges and the fact that DMEK surgery is still at a relatively early stage of evolution, DMEK is currently performed by only a few pioneering surgeons and centers worldwide and accounts for less than 5% of all EK procedures; however, it could be a future standard of care if we can solve the surgical problems of handling this extremely delicate tissue.
ConClUsion

PKP remains a one-size-fits-all technique for corneal transplantation; however, newer procedures allow surgeons to replace only the portion of cornea that is diseased. Targeting transplantation of either the anterior or posterior layers of the cornea can lead to better visual quality and faster visual rehabilitation and reduce the risk for graft rejection. Although PKP remains the gold standard for many reasons, selective lamellar keratoplasty techniques including DALK, DSAEK, and DMEK hold great promise for the future. Additionally, in the future, it may be possible to culture donor corneal endothelial cells that could be injected into the recipient eye in place of formal transplantation surgery. Several groups in Asia, the United States, and Europe are now actively working on human endothelial cell culturing.

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1. Zirm E. Eine erfolgreiche totale Keratoplastik [translated from German by Chris Sandison, Technical Translations from German, Bath]. Graefe’s Arch Ophthalmol. 1906;64580–593.593.