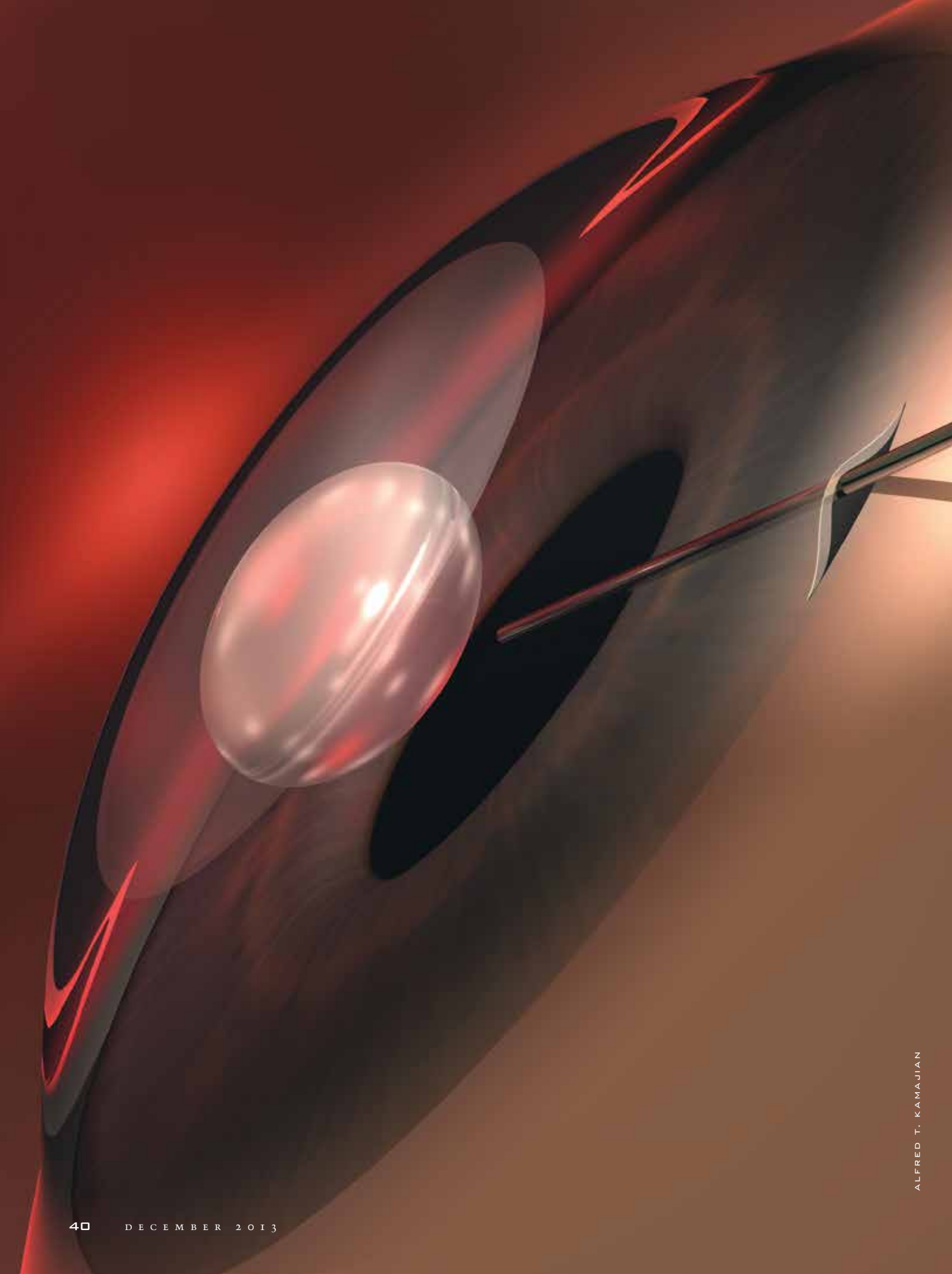


ALFRED T. KAMAJIAN

IS DMEK ON THE RISE?

How This Evolving Surgery Compares With DSAEK

BY ANNIE STUART, CONTRIBUTING WRITER

Five experts look at DMEK and DSAEK—their learning curves, visual results, rejection rates, and attachment challenges—and illuminate the strengths and weaknesses of the newer procedure relative to DSAEK.

Less than a decade ago, corneal transplantation took a big leap forward with the introduction of Descemet's stripping endothelial keratoplasty (DSEK), which removes only Descemet's membrane and the diseased endothelium and replaces them with a thin, tripartite donor graft of posterior corneal stroma, Descemet's membrane, and healthy endothelium. Then came DSAEK, in which the donor graft is prepared with an automated microkeratome, allowing for easier donor preparation and reproducible results by surgeons and eye bank technicians.[1]

DSAEK has proved to have many advantages over penetrating keratoplasty (PK) and its endothelial predecessors (see "A Brief History of Endothelial Keratoplasty"). Now DSAEK is being compared with a newer technique, Descemet's membrane endothelial keratoplasty (DMEK), which has emerged as a promising alternative—grafting only Descemet's membrane and endothelium, allowing for a pure anatomical replacement of only what was removed and the possibility of even better vision with quicker healing.[1]

Although indications for these procedures are similar, each has unique benefits and drawbacks. Five cornea surgeons offer their perspectives on the procedures and their thoughts on whether it may be time to move to the newer surgery.

Indications for DSAEK and DMEK

Whether the endothelium is diseased or damaged, a similar general pool of patients can benefit from either DSAEK or DMEK, said Allan R. Slomovic, MD, at the Toronto Eye Surgery Centre in Canada. "These are mainly patients with a failed corneal transplant, Fuchs endothelial dystrophy, pseudophakic corneal edema, or iridocorneal endothelial (ICE) syndrome," he said.

However, it's more challenging to perform DMEK, as the graft is quite fragile and difficult to handle, said Neda Shamie, MD, at the Keck School of Medicine in Los Angeles; and for this reason, some cases may be better suited for DSAEK, such as eyes with large iris defects or tube shunts.

Still, even for most of these challenging cases, some surgeons, including Arthur W. Giebel, MD, in Walla Walla, Wash., and Jeffrey J. Ing, MD, in Stockton, Calif., have come to favor DMEK over DSAEK because of DMEK's quick healing and excellent visual

results. "Our goal is not to just do a surgery but to help the patient get the best vision they can in the quickest amount of time and to avoid or minimize the risks of rejection, which they will have for the rest of their lives," said Dr. Giebel. Adding his vote of confidence, Dr. Ing said, "DMEK is definitely my procedure of choice for endothelial replacement."

DSAEK: Easier Learning Curve

From preparation to insertion to unfolding techniques, DSAEK has a more manageable learning curve than DMEK.

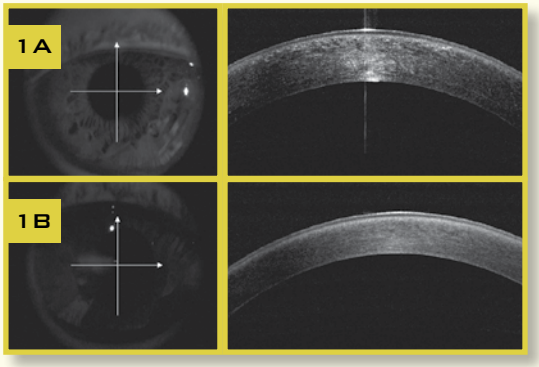
DSAEK: Tested and true. With nearly 10 years of testing, DSAEK is a more predictable procedure, said Dr. Shamie. Online videos and multiple courses have made it easier to teach, learn, and apply. Advanced tools, such as the EndoSerter, Tan EndoGlide, and Busin Glide have simplified insertion and opening of the graft, further minimizing risks.

Optimization of DSAEK, in fact, has made it more difficult for surgeons to consider the switch to DMEK, said Leejee H. Suh, MD, a DSAEK surgeon at Columbia University, who is nonetheless on the cusp of making the jump herself.

DMEK: Still evolving. The DMEK technique, on the other hand, is evolving, said Dr. Shamie, who continues to modify her surgical approach, choosing from a range of techniques based on the track records of more experienced surgeons. "It hasn't yet reached its optimal point of perfection—of minimal damage to the endothelium or ease of graft transfer and reproducibility in teaching others," she said.

Numerous aspects of the DMEK procedure present surgical challenges, including the following.

- **Tissue prep.** Manually stripping the approximately 15-µm-thick Descemet's membrane and endothelium from a donor cornea with fine forceps is challenging—even for an experienced cornea surgeon, said Dr. Slomovic. Still, success rates hover around 95 percent,[1] and Dr. Ing and Dr. Giebel have improved upon this by developing special harvesting techniques.[2] Fortunately, more and more eye banks are now preparing the donor tissue, said Dr. Suh, which removes this variable from the surgical equation.
- **Graft transfer.** "The DMEK graft behaves like no other graft we've ever worked with," said Dr. Shamie. "After peeling, it scrolls like a cigar roll with the endothelium on the outside." This means the injector must provide a protective vehicle. On the upside, said Dr. Ing, DMEK's much thinner rolled tissue can be inserted through a smaller 2.4-mm incision, about half the size used in DSAEK.
- **Unfolding.** Still, a DMEK graft is very fragile tissue, which can tear or split if pulled too much. This is a core issue for DSAEK surgeons who are considering a move to DMEK, said Dr. Suh. "If you have a corneal transplant down to a shorter procedure, trying to unfold a thin membrane for much longer can really put a damper on things."
- **Hands off.** Handling DMEK tissue is quite different, agreed Dr. Giebel. "We weren't trained to position tissue without touching it. Therefore, we have to think about how the tissue behaves, not how we want it to behave. You can touch and manipulate a DSAEK graft to move it into position," said Dr. Giebel, "but with DMEK, you need to think about the movement of fluid, eddy currents, pressure differences, and surface tension to induce the movement you want."



One of Dr. Giebel's patients underwent a different endothelial procedure in each eye. (1A) DSAEK in the left eye. (1B) DMEK in the right eye.

DMEK: Better Visual Results

Vision is where DMEK really shines. Although many case series have highlighted the superior functional results of DSAEK over PK at early or intermediate stages of disease, DSAEK loses some ground when compared with DMEK.[1]

DMEK results. A higher percentage of patients attain 20/20 vision with DMEK, said Dr. Slomovic. "There may be better contrast acuity and fewer higher-order aberrations," he added. From 36 to 79 percent of DMEK patients achieve visual acuity of 0.8 or more, compared with 23 to 47 percent of DSAEK patients.[1]

Providing an extra level of clarity is a big impetus for transitioning to DMEK, said Dr. Suh. Patients who've had both procedures prefer DMEK, hands down, she said.

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DSAEK weaknesses. When it comes to DSAEK, several factors help explain why visual results may lag behind those of DMEK.

- **Poorer optical clarity.** In addition to Descemet's membrane and endothelial cells, the DSAEK donor graft contains around 100 µm of posterior corneal stroma, said Dr. Shamie, so it's not a pure anatomical replacement of what's been removed. "My personal feeling is that the stroma-to-stroma interface is not optically clear with DSAEK and, therefore, results in suboptimal vision initially," she said.

DMEK, on the other hand, replaces only the tissue that has been removed—Descemet's membrane and the diseased endothelium, said Dr. Shamie. "Unlike DSAEK's stroma, which has an index of refraction," said Dr. Giebel, "DMEK tissue is so thin, it's optically neutral."

- **Aberrations.** Dr. Giebel pointed out another potential problem related to the DSAEK donor graft. "When you have a curvature mismatch between donor and host, the donor is forced to conform to the host, and the stretching and squishing creates ripples that we've all seen in both DSAEK and DMEK [Fig. 2]." But the problem is worse with DSAEK. "In DSAEK, these bending ripples of stroma create irregular astigmatism and higher-order aberrations," he said.
- **Hyperopic shifts.** The microkeratome used for DSAEK cuts thinner centrally and thicker in the periphery, creating a graft that is not uniform across its diameter and thus causing more aberrations. "In addition to inducing a minus lens, DSAEK donors are on average flatter than the host corneas," said Dr. Giebel.

A curvature mismatch of this DMEK graft will mold to the host eventually. However, if this were a DSAEK graft, it would carry with it optical properties, possibly warping the vision and causing irregular astigmatism and aberrations in addition to inducing a minus lens.

With DSAEK, you have to be concerned about a significant hyperopic shift—maybe 1, 2, or even 3 D, said Dr. Ing. "There may be a tiny shift with DMEK, but only because the swollen cornea had an index of refraction that was higher than normal."[3]

- **Slower results.** "With a DSAEK patient who has 20/30 to 20/50, you hope to get a line of improvement year by year," said Dr. Shamie. Remodeling occurs in the stroma-to-stroma interface, allowing vision to improve over time, she said. "A healthy eye has a reasonably good chance of reaching 20/20 or 20/25 at two or three years. But by comparison, it is not unusual for our DMEK patients to see 20/20 just

COST-EFFECTIVENESS

Which endothelial procedure is the more cost-effective? Some say the answer is DMEK.

Learning to share. Currently, eye banks follow the dictum of "one tissue, one patient," said Dr. Ing. "But rather than discarding tissue unused for DMEK, there's the potential to expand its use." With a change in this policy, he said, it might be possible to use the Descemet's membrane and endothelium for DMEK, the stromal tissue for an anterior lamellar kerotoplasty, and the donor rim for a limbal stem cell transplant. "In an era when we're trying to cut costs, this makes sense," he said.

Age has its benefits. Dr. Ing also cites the advantage of harvesting tissue "that nobody else wants" for DMEK. Tissue from older donors unfolds more easily in the anterior chamber with less peripheral scrolling. And donor cornea studies show that it performs just as well as younger tissue.[1]

Fewer bells and whistles. DMEK also doesn't require a microkeratome, said Dr. Ing, which can cost as much as an additional $800 to procure precut corneal tissue. As a surgeon who volunteers overseas, Dr. Ing added, "With DMEK, you also don't need any other special instruments, which makes it an easier procedure to take to the developing world."

1 Cornea Donor Study Investigator Group et al. *Ophthalmology.* 2008;115(4):620-626.e6.

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weeks after surgery. This rapid and early vision recovery is what offers the 'wow' factor for these patients."

Dr. Giebel agreed, saying, "I plan for everyone to be seeing 20/25 or better, with a lot of 20/15s at six months."

DMEK: Lower Rejection Rates

Many surgeons ultimately get good visual results with DSAEK, said Dr. Ing, so why take the time to learn DMEK? The rejection data are undeniable, he said. "Less antigenic material in the eye causes lower rejection rates," said Dr. Slomovic, which is critical because rejection is an important cause of graft failure.

Rejected. Compared with rejection rates of 0 to 14 percent within two years of DSAEK, DMEK transplant rejection is seen in just 1 to 3 percent of cases in the same period.[1] Francis W. Price, MD, has even reported a 0.5 to 1 percent rejection rate, said Dr. Slomovic.

Steroid levels. Given the very low rate of rejection, there has been some discussion about whether long-term steroids are required following a DMEK, said Dr. Slomovic. "However, long-term studies are needed."

Dr. Ing keeps his DMEK patients on a steroid indefinitely, using loteprednol (Lotemax), which has a low risk of cataract and glaucoma side effects. "The only rejections I've seen have been in people who've stopped their steroids due to a misunderstanding," he said. Dr. Shamie also continues the use of steroids after DMEK. "But if a patient experienced increased IOP, I'd be less nervous about tapering the steroids more quickly than I would be with my DSAEK patients," she said.

DMEK: Attachment May Be More Worrisome

The postsurgery periods for DSAEK and DMEK are relatively similar. For instance, endothelial cell loss is comparable for both procedures, and rates are higher earlier than with PK, due to manipulation of the graft.[1] With no need for sutures, both DSAEK and DMEK grafts adhere to the posterior surface of the host cornea with the help of an air bubble, which keeps the tissue in apposition until it can adhere by itself, said Dr. Giebel. Dr. Ing has his DMEK—and DSAEK—patients lie on their backs for a day and a half, with other follow-up protocols mainly the same.

DMEK: Rebubbling concerns. For both procedures, dislocation of the graft is a chief concern, but whether and when to rebubble may be more front-of-mind for DMEK surgeons.

- **Trickier tissue.** Managing dislocations with a thin membrane is trickier than with bulkier tissue, said Dr. Suh. "So a lot of DMEK surgeons leave a large, full air bubble and provide a peripheral iridotomy to prevent problems such as a pupillary block."
- **Complete dislocations.** Dr. Shamie noted that concern about progression to a full dislocation is one reason for the higher rebubble rate in DMEK and for the lower threshold for rebubbling a DMEK graft. "A fully dislocated DMEK graft is far more difficult—and in some cases impossible—to reattach given poor visualization.

But, said Dr. Ing, although risk of dislocation is a concern, complete detachment with DMEK is rare. DMEK creates a much tighter vacuum, agreed Dr. Giebel, making it tougher to dislodge once adhered.

In fact, there's a greater potential to completely dislodge a DSAEK graft, Dr. Giebel added, given that it's not strongly attached until the endothelial cells cover the vertical edge of the cut (Fig. 3), sealing it off and creating good adhesion.

On the other hand, said Dr. Shamie, "a partially dislocated DSAEK graft could reattach spontaneously. Even if it progresses to a full detachment, rebubbling and repositioning the graft is not very difficult."

- **Scrolling.** Another potential problem arises from curvature mismatches between the donor and host, which can allow fluid to seep in, creating peripheral clefts with localized scrolling in DMEK, said Dr. Giebel. "DSAEK tissue may cleft, but not scroll, due to the rigidity of the added stroma." In DMEK, most peripheral clefts resolve on their own, he said, "but rebubbling might be done to speed visual recovery or save endothelial cells. One's personal choice or

A DSAEK graft adds thickness, making it important to seal the edges for a good vacuum.

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judgment influences the rebubble rate."

DMEK: Tips for better attachment. Early on, experienced DSAEK surgeons transitioning to DMEK had high rebubble rates and high failure rates, said Dr. Shamie. However, experienced DMEK surgeons such as Francis W. Price, MD, and Friedrich Kruse, MD, are improving upon these results by modifying techniques, she said.

- **Modified Jones tube.** Dr. Shamie said of her technique: "I currently use a modified Jones tube [developed by Michael D. Straiko, MD, at Devers Eye Institute in Oregon] for graft insertion and a no-touch technique of shallowing the chamber, tapping the corneal surface, and injecting fluid to cause a fluid wave that helps with the graft opening."
- **Little or no overlap.** Dr. Ing said, "With my first DMEK cases, I was rebubbling up to 70 percent of my patients." Now that number is closer to 10 to 15 percent, he said. "It gets better as we improve technique." One helpful enhancement, he said, is to closely match donor and recipient tissue diameters, with little or no overlap.
- **Bare stroma at edges.** Dr. Shamie prefers to remove a larger area of the host's Descemet's membrane. "In my experience, the donor DMEK graft adheres better to the bare recipient stroma," she said, adding that this has significantly lowered her dislocation rates. "On

A BRIEF HISTORY OF ENDOTHELIAL KERATOPLASTY

In 1905, Eduard Zirn, MD, performed the first successful corneal tissue transplant, replacing all five layers of the cornea: epithelium, Bowman's layer, stroma, Descemet's membrane, and endothelium.[1] "For a long time, all we had was PK—one answer for many different significant corneal problems," said Dr. Slomovic.

PLK. To avoid postoperative complications such as astigmatism and problems with wound healing, Charles W. Tillett III, MD, proposed in 1956 replacing only the back part of the cornea (posterior lamellar keratoplasty, PLK).[1,2]

Gerritt R. Melles, MD, PhD, was the initial mind behind the clinical application of endothelial keratoplasty, said Dr. Shamie, becoming the first to perform sutureless PLK in 1999.[2]

DLEK. Mark A. Terry, MD, then took this to the mainstream in the United States, she said, by starting laboratory-based experiments at an eye bank to modify and simplify the technique, creating new tools and describing deep lamellar endothelial keratoplasty (DLEK) in 2000.[2] From his very first patient, Dr. Terry started collecting data, said Dr. Shamie, and began creating one of the most complete, longest-running prospective databases on EK in the world.

DSEK. A big advance came with the introduction of descemetorhexis—described by Dr. Melles in 2004 and pioneered by Francis W. Price, MD, in the United States.[2] DSEK left the recipient corneal stroma in place, said Dr. Shamie, which greatly simplified the technique.

After its introduction, said Dr. Slomovic, DSEK quickly overtook PK for treatment of Fuchs dystrophy and pseudophakic corneal edema. A fast learning curve combined with significant advantages—faster visual rehabilitation, less refractive error, a smaller wound, a more intact eye, and the use of topical and intracameral anesthesia—led to its speedy adoption.

DSAEK. Still, with hand-cut lamellar dissections for DSEK, donor preparation posed a challenge. In 2006, Mark S. Gorovoy, MD, proposed using a microkeratome.[2] "Automation of both recipient and donor preparation meant that many more people started doing the surgery," said Dr. Shamie. "But what really brought DSAEK into the mainstream was the preparation of donor grafts by the eye bank."

DMEK. Dr. Melles published his first paper on DMEK in 2006,[2] said Dr. Shamie. But despite superb visual results, adoption of this approach still lags. Although the number of DMEK and DMAEK procedures more than doubled in the United States from 344 in 2011 to 748 procedures in 2012, this remains a small fraction of the 2012 total for DSEK, DSAEK, and DLEK combined: 22,301—exceeding PK at 21,422.[3]

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1 Maier P et al. *Dtsch Arztebl Int.* 2013;110(21):365-371.

2 Thomas J, ed. *Corneal Endothelial Transplant: DSAEK, DMEK & DLEK.* New Delhi, India: Jaypee Brothers Medical Publishers; 2010:146-147.

3 Eye Bank Association of America. 2012 Eye Banking Statistical Report. Washington, D.C.: Eye Bank Association of America; 2013:67. www.restoresight.org/wp-content/uploads/2013/04/2012_Statistical_Report_FINAL-reduced-size-4-10.pdf.

OCT imaging, I have noticed that areas of peripheral nonadherence coincide with the donor's Descemet's membrane overlapping the edge of the host Descemet's."

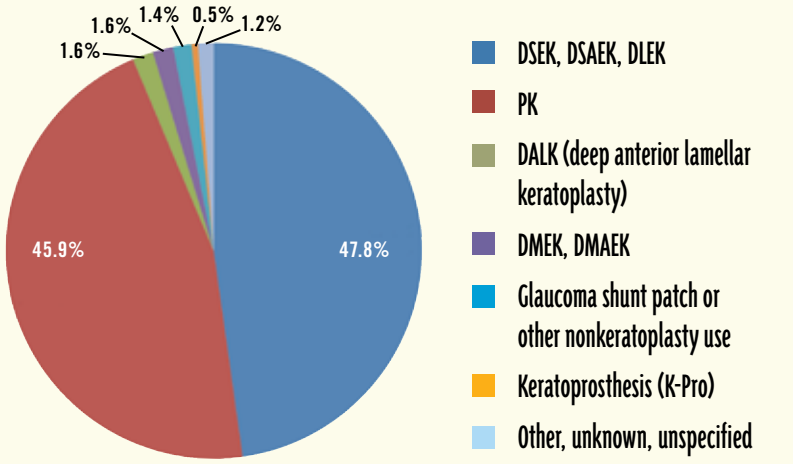
Jump In?

Learning curves have undoubtedly dampened enthusiasm for DMEK. But Dr. Ing challenges his colleagues to take another look from the perspective of their patients.

"If you were a patient and knew there was a procedure that produced a significantly higher chance of 20/20 vision and a rejection rate that was one-tenth of the next best procedure," he suggested, "wouldn't you want your surgeon to make the time and effort to learn the procedure, or at least discuss possible referral to a DMEK surgeon?"

The transition from DSAEK to DMEK has been much slower than from PK to DSAEK. But this might be about to change, suggested Dr. Suh. "There may be a bigger push in this direction if more and more surgeons are provided tissue that is easy to use and readily available, and if patients come to realize there is a procedure that provides better visual acuity. I think we all need to take the leap." ■

2012 Domestic Use of Corneas



PK, in red, and Descemet's stripping endothelial keratoplasty (DSEK), DSAEK, and deep lamellar endothelial keratoplasty (DLEK), in blue, still comprise the vast majority of lamellar procedures in the United States. DMEK is shown in purple.

SOURCE: Eye Bank Association of America. 2012 Eye Banking Statistical Report.

1 Maier P et al. *Dtsch Arztebl Int.* 2013;110(21):365-371.

2 Price FW, Price MO. *DSEK: What You Need to Know About Endothelial Keratoplasty.* Thorofare, NJ: Slack; 2009.

3 Ham L et al. *J Cataract Refract Surg.* 2011;37(8):1455-1464.

More in Coming Months

Watch Clinical Update for expert discussion of the steps and nuances of DSAEK (January) and DMEK (February).

MEET THE EXPERTS

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