REVIEW ARTICLE

A new era in corneal transplantation: paradigm shift and evolution of techniques

Alvin L Young 楊樂昅
KW Kam 甘嘉維
Vishal Jhanji
Lulu L Cheng 鄭 路
Srinivas K Rao

Penetrating keratoplasty is the replacement of a diseased cornea with a full-thickness donor graft. In the last century, this 'gold standard' procedure was long established as the treatment of choice for various corneal diseases. The classical indications for a penetrating keratoplasty entailed optical, tectonic, therapeutic, and cosmetic issues. Over the past decade however, surgical advances have now enabled operations involving the cornea to be performed with a major shift in emphasis, such that penetrating keratoplasty has given way to lamellar (layered) keratoplasty. This review provides the latest updates on developments in the field of corneal transplantation and the nomenclature of different types of component surgery, particularly from the perspective of Hong Kong.

Introduction

The human cornea is a five-layered transparent structure which plays a pivotal role in optical refraction. From anterior to posterior, it consists of the epithelium, Bowman's layer, stroma, Descemet's membrane (DM), and endothelium. The main surgical layers are the epithelium, the stroma, and the endothelium (Fig 1). The corneal endothelium is composed of a single layer of hexagonal cells that act as a pump to constantly remove fluid from the stroma in order to maintain corneal clarity. Any malfunction to this critical layer—whether from various diseases, dystrophy, degeneration or rejection—results in loss of vision secondary to corneal oedema. On the other hand, diseases of the more anterior layers of the cornea may give rise to corneal opacities or scars, leading to a diminished visual acuity.

Over the past century, penetrating keratoplasty has been the mainstay of treatment of all types of corneal diseases causing visual impairment (Fig 2). The classical indications

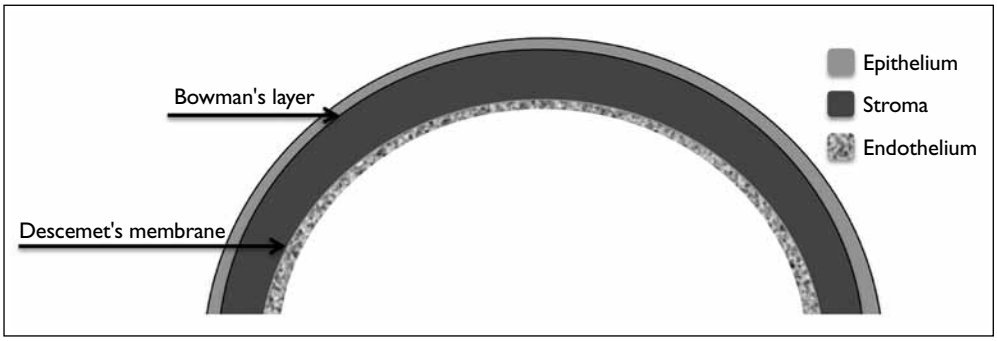

FIG 1. Schematic diagram of the normal cornea

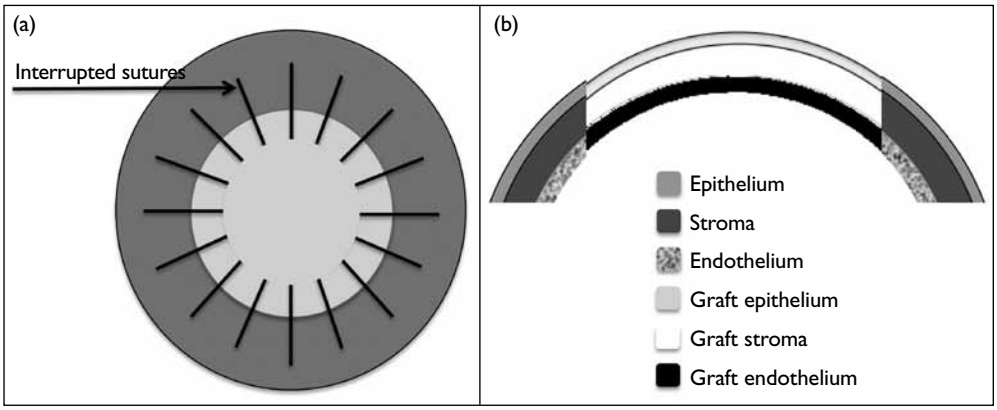

FIG 2. Schematic diagrams of (a) a full-thickness corneal graft (bird's eye view), and (b) a traditional penetrating keratoplasty (sagittal)

Key words
Corneal transplantation; Descemet stripping endothelial keratoplasty; Graft survival; Keratoplasty, penetrating

Hong Kong Med J 2012;18:509-16

Department of Ophthalmology and Visual Sciences, The Chinese University of Hong Kong, Prince of Wales Hospital, Shatin, Hong Kong
AL Young, MMedSc (Hons), FRCS (Irel)
KW Kam, MB, BS
V Jhanji, MD
LL Cheng, FCOphth HK
Darshan Eye Clinic, Chennai, India
SK Rao, FRCSEd

Correspondence to: Dr AL Young
Email: youngla@ha.org.hk

眼角膜移植新時代：技術發展新趨勢

「全層眼角膜移植手術」乃二十世紀用作治療大部份角膜病變最普及而標準的方法。手術的目的主要是移除患者本身受病變影響的眼角膜，然後置換由捐贈者提供的全部共五層的眼角膜。一般須接受「全層眼角膜移植手術」的病人大概分為四類：改善視力、鞏固眼球、治療以及改善外觀用途。過去十年，外科技術的進步大大提升眼角膜手術的種類和選擇。某部份眼角膜病患者可能因為其病變或疤痕只影響其角膜表層或底層，病人毋須更換全層角膜，於是「板層眼角膜移植手術」作為一種只更換部份角膜層的手術，將會更適合這類型病人。我們希望藉此探討眼角膜移植手術的最新發展，以及介紹在香港現有不同種類的「板層眼角膜移植手術」。

for penetrating keratoplasty were optical, tectonic (eg corneal melting or perforation), therapeutic (eg to deal with relentless infective keratitis despite maximal medical treatment), and cosmetic (rare in localities with graft scarcity such as Hong Kong).[1] Ever since the first successful human corneal transplant performed more than 100 years ago by Dr Eduard Zirm,[2] scientists have learned more about transplant immunology and the effective use of topical steroids in preventing and treating graft rejection. Consequently, the number of penetrating keratoplasties performed worldwide rose dramatically; half a million transplants have been performed to date. Recent advancements in microsurgical equipment and refinements in grafting techniques have led to the development of novel forms of lamellar keratoplasty, which entails replacing only the diseased tissue instead of the entire thickness of the cornea (Fig 3). In order to enhance the accuracy and precision during tissue dissection and preparation, some of these newer procedures combine the use of automated microkeratomes and/or laser machines. After dissection, tailored corneal components can then be transplanted into the recipient's eye replacing only the diseased tissue and leaving the unaffected corneal layers undisturbed. The advantages of lamellar surgery over penetrating keratoplasty are discussed in the following sections.

Evolution of corneal transplant

Anterior lamellar keratoplasty (ALK) was the first and most commonly performed operation in the 19th century, when little was known about transplant immunology and the significance of the corneal endothelium in allograft rejection, which was the prime reason for penetrating keratoplasty failure. It replaced only the anterior components of the cornea without disturbing (or treating) the corneal endothelium, thus circumventing the risk of immunological endothelial graft rejection. The idea of removing only the anterior layers of the cornea to treat conditions such as keratoconus, corneal dystrophies, and stromal scars had been around since the 1950s. However, visual outcomes were suboptimal after manual dissection mainly due to the irregular interface and residual stromal opacities. Consequently, ALKs fell out of favour over the next few decades and penetrating keratoplasty

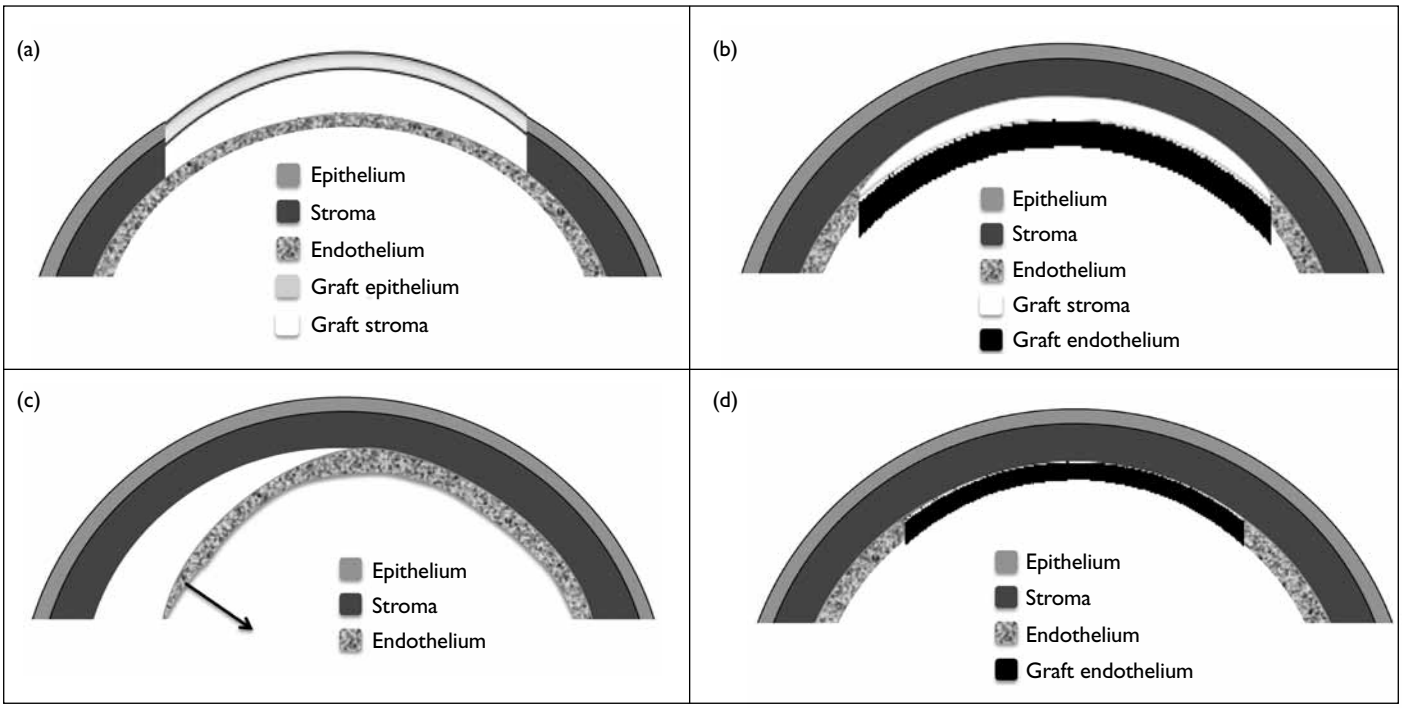

FIG 3. Schematic diagrams of (a) a deep anterior lamellar keratoplasty, (b) an endothelial keratoplasty, (c) the surgical stripping of Descemet's membrane in endothelial keratoplasty, and (d) Descemet's membrane endothelial keratoplasty

became the predominant corneal transplantation surgery. However, the long-term survival of full-thickness grafts was not as high as for other solid organ transplants. In the Australian Corneal Graft Registry, graft survival dropped from 90% at 1 year post-transplant to only 59% at 10 years.[3] In a similarly designed study from India, graft survival dropped from 79% at 1 year to 46% in only 5 years.[4] Bourne et al[5] were among the earliest to describe continuous endothelial cell attrition conforming to bi-exponential decay. This observation was echoed by other groups reporting a 70% endothelial cell loss 5 years post-transplantation.[6]

Component surgery of the cornea and resurgence of lamellar keratoplasty

In view of the unavoidable long-term attrition of the corneal endothelium and thus graft failure after penetrating keratoplasty, and the fact that corneal disease may only affect specific layers of the cornea, alternatives to penetrating keratoplasty were sought. Lamellar keratoplasty or partial-thickness corneal transplantation techniques were revisited by corneal surgeons. Unlike penetrating keratoplasty, lamellar keratoplasty removes only the diseased layers of the cornea without unnecessary replacement of the unaffected healthy corneal tissue layers.

Advances in techniques and tools in the past decade have enabled surgeons to improve the results of lamellar corneal keratoplasties. The development of better microscopes, tailored instruments, microkeratomes and lasers for precise dissection, have renewed interest in lamellar corneal transplantation techniques. Anterior lamellar keratoplasty has become the procedure of choice for replacement of the anterior corneal layers with preservation of the vital host endothelial layer. Endothelial keratoplasty (EK) is now the procedure of choice for the replacement of the diseased endothelium, while avoiding unnecessary surgery on a healthy anterior surface and stroma.

Anterior lamellar keratoplasty

Endothelial graft rejection is one of the major reasons for graft failure after penetrating keratoplasty. Studies have shown that more than half of all penetrating keratoplasty graft failures may be related to an acute episode of endothelial graft rejection or to late endothelial decompensation as a result of gradual endothelial cell loss. In a multivariate analysis of risk factors for developing graft failure, preoperative vascularisation or inflammation and low donor endothelial cell counts were significant predictors of graft failure.[1,6] Theoretically therefore, avoiding unnecessary endothelial replacement and preserving the recipient's healthy endothelium, ALK confers significant improvement in terms of graft survival. It is suitable for corneal stromal diseases that spare the corneal endothelium, stromal scarring, corneal stromal dystrophies and ectatic disorders such as keratoconus or post-LASIK (laser-assisted stromal in-situ keratomileusis) ectasia.

In ALK, the superficial layers of the host's cornea are removed, leaving the anterior chamber of the eye, the deeper layers of the recipient cornea, and the recipient's endothelium, intact. For conditions affecting the deeper layers of the cornea, deep anterior lamellar keratoplasty (DALK) is carried out, which replaces both the host's epithelium and deep stroma with healthy donor tissue (Fig 3a). The most obvious advantage of anterior lamellar transplantation is the absence of endothelial graft rejection.

Deep anterior lamellar keratoplasty

Deep anterior lamellar keratoplasty is usually classified into pre-descemetic DALK (pdDALK) and maximum depth / descemetic DALK (MD-DALK / dDALK) where the DM is completely bared. For pdDALK, it is usually performed manually by dissecting the corneal stroma down to the posterior 10% without fully reaching DM. In MD-DALK / dDALK, the entire corneal stroma is removed all the way down to the level of the DM.[7] This could be achieved by a variety of techniques, involving injection of air or viscoelastic and aiming to completely separate the posterior stroma from the DM.[8,9] The 'gold standard' technique for baring of the DM was described by Anwar and Teichmann[10] ("Big Bubble Technique") in which a forceful jet of intrastromal air is used to split the DM from the posterior stroma. Other alternatives, such as injection of viscoelastic or balanced salt solution, have also been tried with variable success.[11-15]

The visual results tend to improve with deeper and smoother dissection during ALK. In pdDALK, the residual stroma may result in an irregular ocular interface, leading to suboptimal best-corrected visual acuity (BCVA). On the other hand, MD-DALK / dDALK produce a consistently smooth stromal bed and visual outcomes tend to be better with less interface haze or residual scarring. A recently published series and a technology assessment report by the American Academy of Ophthalmology reviewed the published literature on DALK and compared DALK with penetrating keratoplasty. Eleven comparative studies with level II and level III evidence were identified that compared the results of DALK and penetrating keratoplasty procedures directly. Overall, DALK was found to be equivalent to penetrating keratoplasty for the outcome measure of BCVA and for preservation of endothelial cell density.[16-22]

One major disadvantage of MD-DALK / dDALK was the steep surgical learning curve. In practice,

even in the hands of subspecialty surgeons, it is not always easy to achieve total baring of the DM and there is a significant risk of inadvertent rupture of DM. In cases with macroperforation of the DM, the procedure is aborted and conversion to penetrating keratoplasty becomes mandatory.

Recent advances aim to improve precision in dissection either by using an automated microkeratome (automated lamellar therapeutic keratoplasty) or a femtosecond laser machine (Femto-DALK / FS-DALK). The microkeratome-assisted ALK system employs the use of microkeratomes as in LASIK, to perform automated lamellar dissection of both the donor and recipient cornea. Variable depths of lamellar dissection can be selected according to different head sizes. Automated lamellar therapeutic keratoplasty achieves a smoother and enhanced dissection quality compared to manual dissection, with greater ease and reproducibility with better visual and refractive outcomes compared to manual dissection. In particular, automated lamellar therapeutic keratoplasty is useful in complicated cases following LASIK and other forms of corneal refractive surgery such as for post-LASIK infectious keratitis.

Recent advances in femtosecond laser technology have enabled corneal surgeons to dissect the corneal stroma as close as 100 microns from the anterior chamber. This is an excellent option for cases deemed not to require complete baring of DM. However, these techniques may not yield optically pure deep stromal dissections comparable to those of MD-DALK / dDALK.

Femtosecond lasers are being introduced to perform all forms of keratoplasties—from penetrating to anterior and posterior lamellar procedures. Clinical trials to assess femtosecond lasers entailing deeper lamellar ablations are now ongoing. These lasers may ultimately provide more accurate depths and precision for lamellar dissection than that of microkeratome devices, with a less steep learning curve than for conventional deep lamellar keratoplasty.

Overall, DALK surgery has many advantages over the traditional full-thickness corneal transplantation surgery. Being an extra-ocular procedure, DALK does not require an open-sky surgery, thus obviating the associated risks of acute deflation of the globe. It also precludes the risk of endothelial graft rejection in the postoperative period, which is the major cause of graft failure after penetrating keratoplasty. Visual outcomes are at least as good as those after penetrating keratoplasty. A repeat surgery, if deemed necessary, does not confer a high risk of graft failure. Advances in femtosecond laser systems aim to make anterior lamellar surgical procedures more accurate and safer.

Posterior lamellar keratoplasty

The wound from a penetrating keratoplasty never heals to become as strong as the original cornea. Accordingly, patients who undergo penetrating keratoplasty are at an increased risk of traumatic injury for the remainder of their lives. Endothelial keratoplasty makes it possible to transplant corneal endothelium through a small incision, similar to that used in cataract surgery, leaving the eye much stronger. Its advantages compared to a standard penetrating keratoplasty include better structural integrity of the cornea, absence of sutures on the corneal surface, faster visual recovery, and the chances of endothelial graft rejection are possibly reduced.

Posterior lamellar keratoplasty, now better known as EK, is a lamellar grafting procedure that involves selective replacement of the corneal endothelium without disturbing the epithelium with preservation of various amount of stroma (Fig 3b). Selective replacement of corneal endothelium can be performed in these cases, which leaves the anterior part of the host cornea intact. For indications such as Fuchs' endothelial dystrophy, which primarily affects the endothelium, owing to its unique characteristics, EK has gained wide acceptance and is rapidly replacing conventional penetrating keratoplasty in the United States. United States corneal transplant statistics show that the EK rate rose from only 18% for all grafts in 2006, to 37% in 2007 of all corneal transplants performed in the country. A similar rising trend in terms of popularity of EK was observed in countries outside the United States.[23]

There are two approaches that have been described for endothelial replacement. The anterior approach (corneal flap technique) was explored as early as in the 1960s.[24,25] This technique involves the creation of an anterior corneal flap, either manually or with a microkeratome, followed by trephination of the posterior corneal stroma. A posterior lamellar button from the donor graft is then placed and repositioned in the recipient bed followed by closure of the flap with sutures. The same technique was later on coined into various terms, including endothelial lamellar keratoplasty by Jones and Culbertson,[26] endokeratoplasty by Busin et al,[27] and microkeratome-assisted posterior keratoplasty by Azar et al.[28] Because the anterior approach is an open-sky procedure that fashions as a conventional penetrating keratoplasty, it is technically more difficult to perform and sutures are still required after disturbance to the anterior ocular surface.

In 1956, Tillett[29] performed the first EK on a human by suturing the posterior donor endothelium tissue onto the recipient stromal bed. Meanwhile, ophthalmologists explored the possibility of creating a scleral-limbal tunnel behind the cornea for the removal of diseased endothelium and reinsertion of

donor lamella without disturbing the corneal surface. Ko et al[30] published their successful technique on a rabbit eye model in 1993. In 1998, Melles et al[31] adopted the scleral-limbal technique in their posterior approach to endothelial replacement and coined the term 'posterior lamellar keratoplasty'. In 2000-2001, Terry and Ousley[32,33] modified the procedure and performed sutureless endothelial transplantation surgery on their first series of patients in the United States. They then renamed the procedure 'deep lamellar endothelial keratoplasty'. Several other authors reported good visual outcomes with this procedure compared to conventional penetrating keratoplasty.

To minimise the risk from recipient stromal dissection and improve the quality of the graft-host interface, Melles et al[34,35] revolutionised the field of posterior lamellar keratoplasty by introducing the technique that strips away the unhealthy DM of the recipient cornea, a procedure known as descemetorhexis. This procedure is less traumatic to the cornea and anterior segment, and creates a better posterior surface for positioning the donor tissue. Price and Price[36] then applied the technique of descemetorhexis to their patients and published the earliest results from this new surgical technique. They renamed the procedure as Descemet's stripping endothelial keratoplasty (DSEK). In 2006, Gorovoy[37] introduced the addition of an artificial anterior chamber (Fig 4) and an automated microkeratome for harvesting the donor posterior lamella and endothelium, and coined the term Descemet's stripping automated endothelial keratoplasty (DSAEK).

Descemet's stripping endothelial keratoplasty

Principally, DSEK removes the diseased DM and endothelium of the recipient's cornea (Fig 3c), which is replaced with a posterior lamellar lenticule consisting of posterior stroma, DM and endothelium from a healthy donor (Fig 3b). The donor tissue is inserted into the recipient eye through a peripheral incision and is attached to the posterior corneal surface by a tamponade effect (air bubble placed in the anterior chamber; Fig 5). A mechanical microkeratome can also be used to simplify the donor tissue dissection as is done for DSAEK. An automated microkeratome is useful for obtaining a smooth posterior donor lamella with a reduced risk of donor perforation.

Endothelial keratoplasty candidates include patients with Fuchs' dystrophy, pseudophakic or aphakic bullous keratopathy, posterior polymorphous dystrophy, iridocorneal endothelial syndrome and endothelial decompensation from trauma, previous surgery or laser peripheral iridotomy. In patients with keratoconus or corneal stromal scarring that would otherwise limit visual potential, EK would not be an option.

Despite the advantages of EK over conventional penetrating surgery, as with any other new interventional procedures, new complications have emerged with this form of surgery.[38,39] Commonly encountered complications include donor lamella dislocation and donor endothelial cell loss or damage during graft insertion. One of the major

FIG 4. Artificial anterior chamber used for preparation of donor lenticule before endothelial keratoplasty

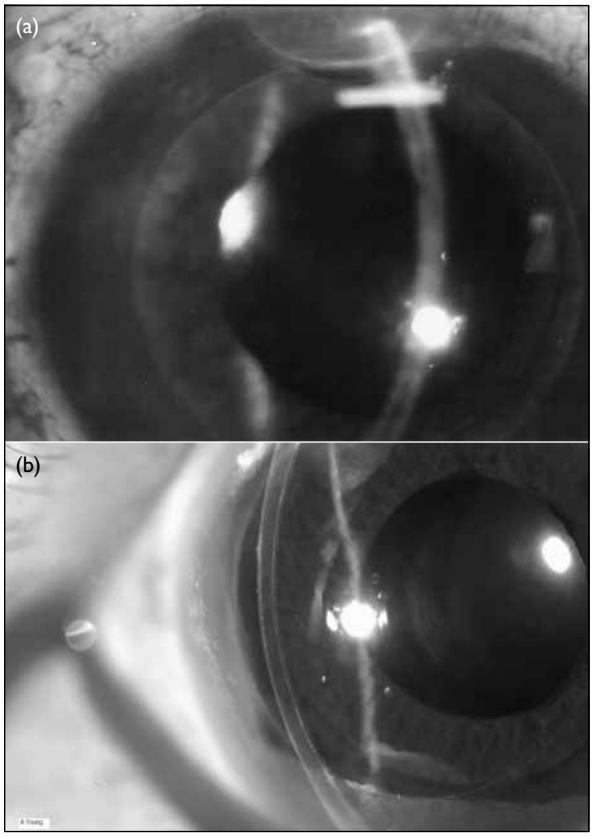

FIG 5. Slit lamp photographs showing (a) the early postoperative appearance of a case after endothelial keratoplasty, and (b) the well-apposed graft after endothelial keratoplasty

challenges in EK is to reduce endothelial cell damage or loss during the surgery. Traditionally, the donor lenticule insertion was folded in the form of a 60:40 'taco' and inserted with the help of special forceps through a peripheral corneal incision.[40] The folding of the donor lenticule as well as handling with the forceps could potentially cause trauma and loss of the endothelial cells, even with a smooth operation. This explains the higher rate of iatrogenic graft failure of 1 to 45% compared to penetrating surgery.[41-43] The damage is expected to be higher in Asian eyes with more shallow anterior chambers than Caucasians.[44]

To help secure the graft and maintain correct orientation, alternatives to forceps insertion have been developed. For example, a suture pull-through technique in which a 10-0 prolene suture is passed through a 5-mm superior lamellar incision and across the anterior chamber to exit through the cornea 1 mm beyond the edge of stripped DM has been used.[45] More recently, various insertion devices such as Busin's glide and EndoGlide have been replacing other manual techniques of donor insertion.[46,47] These devices depend on the insertion of intra-ocular implants through a small incision thereby leaving the eye without any sutures. Studies examining the long-term safety and outcomes of these various devices will reveal whether they are indeed superior.

Donor lamellar graft dislocation is another complication after EK.[38] Partial air fill at the end of the surgery may reduce the frequency of graft dislocation while increasing the risk of pupillary block in eyes with shallow anterior chambers. Use of full-thickness slit wounds to drain the fluid from the graft-host interface are also being used to improve adherence between the donor's and host's tissues. If the graft is dislocated, it is imperative to diagnose and manage the problem promptly to avoid permanent damage to the donor endothelium. Typically, gas is injected into the anterior chamber to reattach the dislocated donor lenticule. However, repeated attempts to reattach the donor lamellar graft with gas injection may exacerbate endothelial cell loss. Although the results of EK have been encouraging, the surgery has a steep learning curve and warrants appropriate selection of patients and surgical technique in order to ensure good surgical and visual outcomes for the patient.[44] Similar to DALK, recent advances in femtosecond laser technology have also enabled corneal surgeons to apply femtosecond laser for EK.

Descemet's membrane endothelial keratoplasty

Ophthalmic surgeons have constantly endeavoured to reduce the thickness of the DSAEK donor lenticule, aiming to improve visual outcomes and reduce the magnitude for potential hyperopic shift after the surgery. The concept of eliminating corneal stromal support from the donor lenticule was realised in another surgical technique termed Descemet's membrane endothelial keratoplasty (DMEK), whereby only the DM together with its endothelial cells are transplanted into the host eye (Fig 3d).[48] This was to ensure faster visual recovery and a higher chance of achieving 20/20 visual acuity postoperatively. However, the major challenges associated with DMEK are the preparation as well as insertion of the donor lenticule inside the anterior chamber of the recipient eye. The main problem is the potential high wastage rate of grafts secondary to a higher repositioning rate.[49] Due to the above, this technique has been less popular with the corneal surgeons compared to DSEK/DSAEK.

A newer concept 'ultra-thin' DSAEK has been developed in which the donor lenticule is prepared with a 'double pass' technique using a microkeratome. The thinner donor lenticule is less than 100 microns in thickness and still retains the corneal stromal support which enables its easier handling (comparing to DMEK) during preparation as well as insertion into the host anterior chamber.

Overall, EK has the advantages of more rapid visual recovery. Visual outcomes and survival are comparable to penetrating keratoplasty. Unlike conventional penetrating surgery, EK is performed as a closed eye procedure, and hence minimises the risk of rare but severe complications such as suprachoroidal haemorrhages. Furthermore, since EK surgery is performed through a small incision, it leaves a tectonically much stronger eyeball. Absence of corneal surface sutures avoids any astigmatic shift and enables much faster visual rehabilitation postoperatively. It has been suggested that EK is associated with a lower likelihood of graft rejection because of the smaller volume of tissue being transplanted.

Lamellar keratoplasty: local perspective

As with solid organs, Asians have significantly lower corneal graft donor rates than developed cultures such as the United States or Europe. According to the Hospital Authority Lions Eye Bank figures, the annual number of corneas collected averaged just over 200 per annum over the past 5 years or so. Of the 208 corneal transplantation surgeries performed in Hong Kong in 2007, 170 (82%) were full-thickness, 27 (13%) were lamellar and an additional 11 (5%) were endothelial. In the year 2011, a total of 207 corneas were transplanted. Of these, 123 (59%) entailed penetrating keratoplasty, 73 (34%) lamellar keratoplasty of which 41 (19%) were for EK thereby reflecting the global trend towards an increasing proportion of anterior or posterior lamellar keratoplasties. The waiting time for a suitable donor is usually protracted and by the time a patient is due for transplantation, the premorbid would often

have deteriorated and progressed. Patients initially indicated for lamellar keratoplasty may by the time of the actual operation no longer be suitable, often due to surface scarring. As a result, a relatively higher portion of our patients (in comparison to western societies) still undergo full-thickness grafts.

Given the context of donor shortages in Hong Kong, even before the paradigm shift towards doing more lamellar keratoplasty, none of the valuable donated corneal buttons went to waste. In the past, the main donor button would have been used for a full-thickness transplant. The residual donor rim could be divided into four pieces; these smaller pieces of donor rim may be used in complex glaucoma surgery or for any other ocular operations for which addition of corneoscleral tissue is necessary (eg patching or repairs). Typically, one donor button would have benefited five recipients. With the increasing rate of lamellar keratoplasties nowadays, the main donor button may be split into two layers, transplanted as an ALK and an EK, and the rim similarly may be used as above, thus six recipients may benefit.[50] Furthermore, with selective layer transplantation, donors who have an unhealthy anterior part of the eye may still donate the posterior layer to be used for EK,[51] and those with unhealthy endothelium yet a relatively healthy anterior layer may still be useful for ALK. This could expand the cornea donor pool potential and hopefully reduce the waiting lists.

At our centre in Hong Kong, EK was first performed in January 2005.[40] In our long-term outcome review of 22 cases performed between 2005 and 2009,[52] there was a graft dislocation rate of only 4.5%. At the last follow-up (mean, 47; standard deviation, 14 months), BCVA was better than 20/70 in 41% of cases. Causes of poor BCVA included primary graft failure (n=4), graft decompensation (n=4), advanced glaucoma (n=2), and irreversible graft rejection (n=2). Grafts remained clear in 12 (55%) of cases at the last follow-up with an average graft survival of 20 (standard deviation, 18; median, 18) months. Our local results are promising and compared favourably to published figures.[53,54] Factors of each individual patient need to be thoroughly balanced before considering EK to allow for optimised long-term success.

Given appropriate training and acquisition of expertise, good outcomes are achievable even for technically more difficult small oriental eyes.

Conclusion

There has been a major paradigm shift towards lamellar corneal transplantation. Now, not only can we replace specific diseased corneal layers while maintaining visual outcomes and graft survival, lamellar surgery enables more efficient use of limited cornea donations to benefit more recipients. Newer developments in techniques and technology on the horizon will require longer-term studies to ascertain their efficacy, long-term outcomes, and safety.

Acknowledgements

We would like to thank Ms Janice Wong, Mr Galen Chow, Mr Daniel To, Dr Victoria Wong, and Dr Stanley Chi of Hospital Authority Lions Eye Bank for their kind assistance with provision of local data.

References

1. Tan DT, Janardhanan P, Zhou H, et al. Penetrating keratoplasty in Asian eyes: the Singapore Corneal Transplant Study. Ophthalmology 2008;115:975-82.e1.
2. Zirm E. Eine erfolgreiche totale Keratoplastik [in German]. Arch Ophthamologie 1906;64:580-93.
3. Williams KA, Roder D, Esterman A, Muehlberg SM, Coster DJ. Factors predictive of corneal graft survival. Report from the Australian Corneal Graft Registry. Ophthalmology 1992;99:403-14.
4. Dandona L, Naduvilath TJ, Janarthanan M, Ragu K, Rao GN. Survival analysis and visual outcomes in a large series of corneal transplants in India. Br J Ophthalmol 1997;81:726-31.
5. Bourne WM, Hodge DO, Nelson LR. Corneal endothelium five years after transplantation. Am J Ophthlmol 1994;118:185-96.
6. Inoue K, Amano S, Oshika T, Tsuru T. Risk factors for corneal graft failure and rejection in penetrating keratoplasty. Acta Ophthalmol Scand 2001;79:251-5.
7. Luengo-Gimeno F, Tan DT, Mehta JS. Evolution of deep anterior lamellar keratoplasty (DALK). Ocul Surf 2011;9:98-110.
8. Chau GK, Dilly SA, Sheard CE, Rostron CK. Deep anterior lamellar on air with lyophilised tissue. Br J Ophthalmol 1992;76:646-50.
9. Caporossi A, Simi C, Licignano R, Traversi C, Balestrazzi A. Air-guided deep manual lamellar keratoplasty. Eur J Ophthalmol 2004;14:55-8.
10. Anwar M, Teichmann KD. Deep lamellar keratoplasty: surgical techniques for anterior lamellar keratoplasty with and without baring of Descemet's membrane. Cornea 2001;24:274-83.
11. Amayem AF, Anwar M. Fluid lamellar keratoplasty in keratoconus. Ophthalmology 2000;107:76-9; discussion 80.
12. Sugita J, Kondo J. Deep lamellar keratoplasty with complete removal of pathological stroma for visual improvement. Br J Ophthalmol 1997;81:184-8.
13. Melles GR, Remeijer L, Geerards AJ, Beekhuis WH. A quick surgical technique for deep, anterior lamellar keratoplasty using visco-dissection. Cornea 2000;19:427-32.
14. Shimmura S, Shimazaki J, Omoto M, Teruya A, Ishioka M, Tsubota K. Deep lamellar keratoplasty (DLKP) in keratoconus patients using viscoadaptive viscoelastics. Cornea 2005;24:178-81.

15. Manche EE, Holland GN, Maloney RK. Deep lamellar keratoplasty using viscoelastic dissection. Arch Ophthalmol 1999;117:1561-5.
16. Coombes AG, Kirwan JF, Rostron CK. Deep lamellar keratoplasty with lyophilised tissue in the management of keratoconus. Br J Ophthalmol 2001;85:788-91.
17. Shimazaki J, Shimmura S, Ishioka M, Tsubota K. Randomized clinical trial of deep lamellar keratoplasty vs penetrating keratoplasty. Am J Ophthalmol 2002;134:159-65.
18. Watson SL, Ramsay A, Dart JK, Bunce C, Craig E. Comparison of deep lamellar keratoplasty and penetrating keratoplasty in patients with keratoconus. Ophthalmology 2004;111:1676-82.
19. Muraine MC, Collet A, Brasseur G. Deep lamellar keratoplasty combined with cataract surgery. Arch Ophthalmol 2002;120:812-5.
20. Borderie VM, Werthel AL, Touzeau O, Alouch C, Boutboul S, Laroche L. Comparison of techniques used for removing the recipient stroma in anterior lamellar keratoplasty. Arch Ophthalmol 2008;126:31-7.
21. van Dooren BT, Mulder PG, Nieuwendall CP, Beekhuis WH, Melles GR. Endothelial cell density after deep anterior lamellar keratoplasty (Melles technique). Am J Ophthalmol 2004;137:397-400.
22. Reinhart WJ, Musch DC, Jacobs DS, Lee WB, Kaufman SC, Shtein RM. Deep anterior lamellar keratoplasty as an alternative to penetrating keratoplasty: a report by the American Academy of Ophthalmology. Ophthalmology 2011;118:209-18.
23. Tan DT, Anshu A, Mehta JS. Paradigm shifts in corneal transplantation. Ann Acad Med Singapore 2009;38:332-8.
24. Culbertson WW. Endothelial replacement: flap approach. Ophthalmol Clin North Am 2003;16:113-8,vii.
25. Polack FM. Queratoplastia lamellar posterior. Revista Peruana Oftalmologia 1965;2:62-4.
26. Jones DT, Culbertson WW. Endothelial lamellar keratoplasty (ELK) [abstract]. Invest Ophthalmol Vis Sci 1998;39(Suppl):76S.
27. Busin M, Arffa RC, Sebastiani A. Endokeratoplasty as an alternative to penetrating keratoplasty for the surgical treatment of diseased endothelium: initial results. Ophthalmology 2000;107:2077-82.
28. Azar DT, Jain S, Sambursky R, Strauss L. Microkeratome-assisted posterior keratoplasty. J Cataract Refract Surg 2001;27:353-6.
29. Tillett CW. Posterior lamellar keratoplasty. Am J Ophthalmol 1956;41:530-3.
30. Ko W, Freuh B, Shield C, Costello M, Feldman S. Experimental posterior lamellar transplantation at the rabbit cornea [abstract]. Invest Ophthalmol Vis Sci 1993;34(Suppl):1102S.
31. Melles GR, Eggink FA, Lander F, et al. A surgical technique for posterior lamellar keratoplasty. Cornea 1998;17:618-26.
32. Terry MA, Ousley PJ. Deep lamellar endothelial keratoplasty in the first United States patients: early clinical results. Cornea 2001;20:239-43.
33. Terry MA, Ousley PJ. Replacing the endothelium without corneal surface incisions or sutures: the first United States clinical series using the deep lamellar endothelial keratoplasty procedure. Ophthalmology 2003;110:755-64; discussion 764.
34. Melles GR, Lander F, Rietveld FJ. Transplantation of Descemet's membrane carrying viable endothelium through a small scleral incision. Cornea 2002;21:415-8.
35. Melles GR, Wijdh RH, Nieuwendaal CP. A technique to excise the descemet membrane from a recipient cornea (descemetorhexis). Cornea 2004;23:286-8.
36. Price FW Jr, Price MO. Descemet's stripping with endothelial keratoplasty in 50 eyes: a refractive neutral corneal transplant. J Refract Surg 2005;21:339-45.
37. Gorovoy MS. Descemet-stripping automated endothelial keratoplasty. Cornea 2006;25:886-9.
38. Price FW Jr, Price MO. Descemet's stripping with endothelial keratoplasty in 200 eyes: early challenges and techniques to enhance donor adherence. J Cataract Refract Surg 2006;32:411-8.
39. Young AL, Tam PM, Lau TT, Cheng LL, Rao SK, Lam PT. Case of post Descemet stripping endothelial keratoplasty retrocorneal fibrous membrane. Clin Experiment Ophthalmol 2009;37:418-9.
40. Young AL, Rao SK, Cheng LL, Lam PT. Endothelial keratoplasty. Hong Kong J Ophthalmol 2008;12:18-25.
41. Mearza AA, Qureshi MA, Rostron CK. Experience and 12-month results of descemet-stripping endothelial keratoplasty (DSEK) with small-incision technique. Cornea 2007;26:279-83.
42. Koenig SB, Covert DJ. Early results of small-incision Descemet's stripping and automated endothelial keratoplasty. Ophthalmology 2007;114:221-6.
43. Rao SK, Leung AT, Young AL, Fan DS, Lam DS. Is there a minimum endothelial cell count for a clear cornea after penetrating keratoplasty? Indian J Ophthalmol 2000;48:71-2.
44. Young AL, Rao SK, Lam DS. Endothelial keratoplasty: where are we? Clin Experiment Ophthalmol 2008;36:707-8.
45. Macsai MS, Kara-Jose AC. Suture technique for Descemet stripping and endothelial keratoplasty. Cornea 2007;26:1123-6.
46. Terry MA, Saad HA, Shamie N, et al. Endothelial keratoplasty: the influence of insertion techniques and incision size on donor endothelial survival. Cornea 2009;28:24-31.
47. Mehta JS, Por YM, Beuerman RW, Tan DT. Glide insertion technique for donor cornea lenticule during Descemet's stripping automated endothelial keratoplasty. J Cataract Refract Surg 2007;33:1846-50.
48. Melles GR, Ong TS, Ververs B, van der Wees J. Descemet membrane endothelial keratoplasty (DMEK). Cornea 2006;25:987-90.
49. Guerra FP, Anshu A, Price MO, Giebel AW, Price FW. Descemet's membrane endothelial keratoplasty: prospective study of 1-year visual outcomes, graft survival, and endothelial cell loss. Ophthalmology 2011;118:2368-73.
50. Vajpayee RB, Sharma N, Jhanji V, Titiyal JS, Tandon R. One donor cornea for 3 recipients: a new concept for corneal transplantation surgery. Arch Ophthalmol 2007;125:552-4.
51. Phillips PM, Terry MA, Shamie N, et al. Descemet's stripping automated endothelial keratoplasty (DSAEK) using corneal donor tissue not acceptable for use in penetrating keratoplasty as a result of anterior stromal scars, pterygia, and previous corneal refractive surgical procedures. Cornea 2009;28:871-6.
52. Young AL, Kwok RP, Fan AH, Rao SK, Lam DS. Five year endothelial keratoplasty graft survival and outcome in a tertiary teaching hospital in Hong Kong. Proceedings of the XXIX Congress of the European Society of Cataract & Refractive Surgeons; 2011 Sep 17-21; Vienna, Austria.
53. Lee WB, Jacobs DS, Musch DC, Kaufman SC, Reinhart WJ, Shtein RM. Descemet's stripping endothelial keratoplasty: safety and outcomes: a report by the American Academy of Ophthalmology. Ophthalmology 2009;116:1818-30.
54. Price MO, Fairchild KM, Price DA, Price FW Jr. Descemet's stripping endothelial keratoplasty five-year graft survival and endothelial cell loss. Ophthalmology 2011;118:725-9.