23

Surgical Correction of Keratoconus: Different Modalities of Keratoplasty and Their Clinical Outcomes

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23.1 Introduction

Surgical treatment of keratoconus has received considerable attention and a formidable number and variety of surgical procedures, before keratoplasty was even considered the most suitable procedure [1]. Surgical options that have been proposed include intraocular operations such as paracentesis of the anterior chamber, lens extraction or needling, or deviation of the pupil by incarcerating the iris in a corneal incision to achieve a stenopeic slit-like pupil; cone excision procedures; or flattening techniques by scar formation, brought by cauterization of the conus with chemicals, electrocautery, high frequency current, or by splitting of Descemet membrane [1].

Before keratoplasty became an option, Alfred Appelbaum in 1936 [2] stated concerning the surgical treatment of keratoconus “surgical intervention aims to produce flattening of the cornea in order to improve eyesight. When no degree of useful vision is obtained with the use of contact glasses, operative intervention may be considered-but no sooner. Only in cases of advanced or nearly hopeless conditions should the patient undergo operation. Most ophthalmologists agree with this. Too much cannot be expected of surgical treatment. At best, it gives a result far from ideal and none too lasting. The unsightliness which inevitably follows must be anticipated, and the appearance of the eye is always marred to some extent.”

Castroviejo a Spanish ophthalmologist born in Logroño, Spain, performed the first penetrating keratoplasty (PKP) for keratoconus in 1936 [1] in the Columbia Presbyterian Medical Center in New York. Several years later in an article about keratoplasty for the treatment of keratoconus he concluded that keratoplasty was the only surgical procedure that fulfilled the two essential requirements for treating keratoconus: surgery had to be limited to the cornea, and the whole corneal protrusion had to be removed and replaced with normal tissue of normal curvature and thickness, leaving the pupillary area free of scarring. Based on his experience, when a suitable technique was used, the percentage of permanently, greatly improved vision was from 75 to 90 % [1].

Lamellar keratoplasty (LKP) was described earlier than penetrating keratoplasty. However, although Arthur von Hippel performed the first

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successful LKP in man in 1888 [3], decades earlier than the first successful human PKP by Edward Zinn, this technique was abandoned in 1914 for PKP, and was not reintroduced until the1940s [4]. However, the concept of deep lamellar keratoplasty extending down to Descemet membrane is relatively new. Gasset reported a series of keratoconus patients in the late 1970s who received full-thickness grafts stripped of Descemet's membrane transplanted into relatively deep lamellar beds and enjoyed good surgical results with 80 % of cases achieving 20/30 or better vision [5]. Dissection of host tissue 'close to' the Descemet's membrane and the term 'deep lamellar keratoplasty' (DLKP) in the conventional sense were first introduced by Archilla in 1984, who also showed the use of intrastromal air injection to opacify the corneas a method to facilitate removal of host tissue [6]. Sugita and Kondo reported the first extensive study on the results of DLKP compared with PKP in 1997 [7]. They showed that postoperative visual acuity was similar between DLKP and PKP, with no episodes of immunological rejection in over 100 eyes followed. Despite the clear benefits of DLKP, the classical technique of removing stroma layer by layer was at that stage time consuming and was greatly dependent on surgical experience. Only in the last two decades DLKP has gained momentum thanks to improvement in surgical techniques and the availability of new surgical instruments and devices. Probably the two most relevant papers on techniques were those from Melles and Anwar.

In 1999, Melles described a technique to visualize the corneal thickness and the dissection depth during surgery creating an optical interface at the posterior corneal surface by filling the anterior chamber with air completely [8]. In 2002, Anwar described his popular "big-bubble" technique in baring Descemet Membrane by injecting air into the deep stroma to create a large bubble between the stroma and the Descemet's membrane [9].

Approximately about 12–20 % of the keratoconus patients may require a corneal transplantation [10]. The Australian Graft Report of 2012 shows that keratoconus, with almost 1/3 of the corneal grafts performed, was the first reason for keratoplasty, followed by bullous keratoplasty and failed previous grafts. The 2012 Eye Banking statistical Report published by the Eye Banking Associations of America finds that keratoconus was the reason for penetrating keratoplasty in 18 % of the cases, and in 40 % of the DALK cases. Surprisingly penetrating keratoplasty represented almost 80 % of the total grafts, while DALK only accounted for 3 % of the total keratoplasties done, meaning that time consuming and surgical experience are still a factor reducing the popularity of DALK in the United States of America. Increasingly, however, DALK is becoming the preferred surgical option, largely thanks to improvements in operative technique, and now representing 10–20 % of all transplants for KC and 30 % when eyes with previous hydrops are excluded [11]. In the UK, the percentage of transplants for keratoconus in which DALK was used increased from 10 % in 1999–2000 to 35 % in 2007–2008 [12].

While the scope of this article is mainly corneal grafting as treatment of keratoconus, it is important to point out that the main goal of treatment of keratoconus has changed over the last few years from that aiming to improve visual acuity with keratoplasty to a number of relatively new procedures focused on the prevention of the progression of the disease or to restore or support contact lens tolerance by making wear more comfortable. These include ultraviolet crosslinking (UV-CXL), intracorneal ring segments (ICRS), and a newly proposed type of "corneal transplant" known as Bowman Layer (BL) transplantation described by Gerrit Melles [13].

23.2 Indications of Corneal Graft in Keratoconus

Corneal graft is the traditional recourse for advanced keratoconus. There are many different grading schemes for keratoconus from scales based on outdated indices such as the Amsler-Krumeich scale, to scales using a variety of detailed metrics of corneal structure provided by anterior segment optical coherence tomography and Pentacam imaging. Other scales (RETICS classification) include functional parameters (corrected distance visual acuity—CDVA) in order to assess the severity of the disease. All these different scales do not always correlate well with disease impact. While there are eyes with milder disease that may exhibit contact lens (CL) intolerances, there are other eyes with severe disease that obtain good functional vision with contact lenses.

Therefore, although there is no precise definition for advanced disease, most specialists would agree that a keratoconus patient is eligible for corneal transplant, when spectacle correction is insufficient, continued CL wear is intolerable, and visual acuity has fallen to unacceptable levels [11]. Nevertheless, there has been a strong push to extend other treatment modalities such UV-CXL and ICRS, both of which were originally meant for mild to moderate disease, to treat advanced disease. In 2014, BL transplantation was also described for advanced KC with extreme thinning/steepening [13]. These less troublesome therapeutic alternatives will seek to arrest disease progression, reenable comfortable contact lens, or improve visual acuity to some extent, although rarely do the visual gains exceed one or two lines in advanced disease. These techniques would permit PK or DALK to be postponed or avoided entirely [11].

Nowadays, despite the excellent outcomes of PK, DALK may be preferred in patients with keratoconus because of the absence of risk of endothelial rejection, earlier tapering of steroids, decreased risk of secondary glaucoma, and increased wound strength [14]. The advantage of DALK is even more evident in patients with mental retardation in which PK has a higher incidence of postoperative complications such as globe rupture, corneal ulceration, and graft rejection; in phakic patients; and in corneas with significant peripheral thinning [11].

PK would be considered more suitable in cases in which endothelial dysfunction is present, or when deep corneal scarring affects severely the visual axis up to the Descemet membrane level (such as in previous hydrops). It is not unusual for KC to coexist with endothelial dysfunction that might be underestimated as stromal thinning of KC may mask the corneal edema. Fuchs endothelial dystrophy is the most common of such disorders, but also includes posterior polymorphous dystrophy a peculiar condition of endothelial depletion and guttae excrescences that may be the product of the KC itself rather than a distinct entity [15]. If central deep corneal scarring is present PK will provide a better visual acuity than DALK, but with a higher risk. In some instances, safety of DALK can outbalance the better visual acuity of PK. In fact, when corneal scars arise from previous hydrops, PK outcomes tend to be worse as the risk of graft rejection is higher [11]. In these cases, manual lamellar dissection for DALK is a good choice as Anwar big bubble technique is contraindicated owing to the high risk of perforation during surgery.

23.3 Penetrating Keratoplasty in Keratoconus

Penetrating keratoplasty (PKP/PK) has traditionally been the surgery of choice for keratoconus, but nowadays lamellar techniques are the gold standard for patients with mild to moderate disease. Currently, an elective PK is reserved for those advanced cases where the Descemet membrane (DM) and endothelium appear splitted due to a previous corneal hydrops. Frequently a previous hydrops is not clearly reported by the patient but, in absence of an obvious endothelial split, deep stromal scars involving the DM are observed. In such cases, a lamellar technique can still be attempted, mainly if these scars are not affecting the visual axis, but as the integrity of the DM is not intact anymore this layer has a great tendency to rupture through the area of the scar (mainly if a Big Bubble technique is used) and the surgery will require to be converted into a PK intraoperatively if a big tear is observed (longer than 2–3 clock hours).

Penetrating keratoplasty technique for keratoconus does not differ significantly from the technique used for other etiologies, but some considerations should be taken into account:

23.3.1 Donor Size

A 7.5–8.5 mm host trephine (in relation with the corneal horizontal diameter) is often used and centered with the optical axis. However, in keratoconus the cone is often inferiorly displaced and should be fully removed to avoid residual or recurrent disease [16]. Therefore, the extent of the cone should be well known before surgery and thinning mapped out by slit lamp examination, as this will be difficult to discern with the operating microscope. Fleischer iron ring formation, which usually circumscribes the cone, may assist on its delineation. Corneal topography is not reliable in advanced scarred conus and should not be considered for surgical planning. Donor size will have then to be adjusted in relation with the host limbal white-to-white measurement and conus extension, so larger grafts than 8.5 mm may occasionally be needed in severe conus, as well as its partial decentration respecting the optical axis in cases of very advanced conus with a severe thinning up to the perilimbal area. On the other hand, the risk of rejection increases with grafts larger than 8.5 mm in diameter and as the graft–host junction moves closer to the limbus, so this should be considered into the postoperative treatment and management [17, 18]. Decentered grafts can as well induce a significant irregular astigmatism into the visual axis, requiring rigid lenses for the visual rehabilitation of the patient and occasionally a second centered graft for visual purposes.

The donor tissue trephine is routinely sized 0.25 mm larger than the host trephine because, using current techniques, donor corneal tissue cut with a trephine from the endothelial surface measures approximately 0.25 mm less in diameter than host corneal tissue cut with the same diameter trephine from the epithelial surface [19]. Keratoconus patients may benefit from using same-diameter trephines for both donor and host tissue, which in effect undersizes the donor button and helps to reduce postoperative myopia (reducing donor size by 0.25 mm causes the mean postoperative refractive error to shift toward hyperopia by approximately 2 D) [20, 21], but the surgeon should be aware that obtaining watertight wound closure with an undersized donor tissue can be challenging and may require additional sutures. Moreover, a flattened corneal contour could complicate contact lens fitting in the anisometropic patient and also laser excimer ablation for correction of a significant residual hyperopia after PK may not be possible as it is not as predictable and efficient as it is with residual myopia, thus requiring phakic or pseudophakic piggyback intraocular lenses for patients who are intolerant of spectacles and contact lenses, always once suture removal has been completed [22]. Considering this, despite undersizing the donor cornea may provide better visual outcome in patients with keratoconus, it should be selected carefully in PK. Axial length can be an important factor in the refractive error outcome following PK [23]. Ultrasound axial length measured from the anterior lens capsule to retina reveals a broad range in length from 18.77 to 25.65 mm. Reducing donor size, in a relatively short eye, could result in significant postoperative hyperopia, so same-size donor and host corneal buttons should not be used when the anterior lens-to-retina length is less than 20.19 mm, the mean length for nonkeratoconic individuals with emmetropia.

The degree of postoperative myopia is determined by both corneal curvature and axial length. Lanier et al. [23] found a mean and range of axial length in keratoconic eyes to be fairly close to those observed in emmetropic eyes. Mean corneal curvature and anterior chamber depth, however, are consistently greater than in other eyes [20, 24]. As keratoconic corneas are steeper, with an increased anterior chamber depth, trephination leaves a peripheral corneal rim that is longer (ellipsoid shape) and steeper than normal (mainly if the base of the cone is not completely excised). Thus, placement of a normally sized donor results in a steep cornea and deeper anterior chamber, reasons for part of the postoperative myopia and astigmatism. Placement of a relatively small diameter donor can counteract this by rotating the peripheral rim downwards, reducing the final keratometry and anterior chamber depth, and so, the postoperative myopia. However, if the steepening is asymmetric, which commonly is the case in keratoconus, the length and steepness of the peripheral rim vary around its circumference. Therefore, the bed is not round, and placement of a round donor, even if undersized, will not result in a spherical cornea, leaving significant irregular astigmatism in spite of reducing the postoperative myopia.

A suggested alternative to reduce the postoperative astigmatism as well as the myopia after PK in patients with keratoconus is to cauterize the vertex of the recipient cornea [25]. Cauterization of the cornea (thermokeratoplasty) of patients with keratoconus was introduced by Gasset and Kaufman [26] in the 1970s with the purpose of flattening the cone by shrinking the surrounding corneal tissue. The effect of this procedure, although often remarkable, was limited in time and the technique was abandoned. In 1998 Busin et al. recovered this technique with the theory that this induced corneal shrinkage could flatten the keratoconus and "regularize" the corneal shape of the recipient rim before trephination during PK surgery [25]. They superficially cauterized a central area of 6 mm in diameter with bipolar forceps until whitening and shrinkage of corneal tissue was observed. Their results show a significant decrease in the postoperative spherical equivalent and keratometric astigmatism before and after suture removal compared with the control group, subsequently improving the postoperative uncorrected and best-corrected visual acuity results. The cauterization of the apex should be avoided during DALK as it will induce a severe adherence of the DM to the overlying stroma as well as the damage or perforation of the endothelium, compromising severely any attempt of lamellar keratoplasty.

23.3.2 Suturing Technique

Once the four cardinal 10-0 nylon sutures have been placed the surgeon can use the preferred suture technique: interrupted sutures (IS), combined continuous and interrupted sutures (CCIS), single continuous suture (SCS), or double continuous suture (DCS). IS should be always the closure method of choice in cases where a partial or complete suture removal in one region of the graft is likely to be necessary at some point during the postoperative period: pediatric keratoplasty (as sutures become loose quickly); vascularization in the host cornea (occasionally seen after a hydrops episode or contact lens-related keratitis); multiple previous rejections, or other inflammatory concomitant conditions that may predispose to localized vascularization, rejection, or ulceration of the donor tissue. Also large and decentered grafts that are placed close to the limbal area present, as already discussed, an increased risk of rejection, being necessary the use of IS for its closure.

However, most of the keratoconic eyes do not present any additional risk for graft rejection or infection, so a SCS or DCS are generally preferred by most surgeons. The advantages of a continuous suture are ease of placement, the ease with which the suture can be removed at a later date, and the potential for suture adjustment intra- (with an intraoperative keratometer) and postoperatively to reduce astigmatism. With DCS a 12-bite 10-0 nylon suture placed with bites at approximately 90 % depth and a second continuous suture (10-0 or 11-0 nylon) placed with bites alternating between each of the original suture's bites for 360° at approximately 50–60 % corneal depth are used. The second suture is tied with only enough tension to take up slack in the suture. The second suture permits early removal or adjustment of the 10-0 nylon first suture for astigmatism control in 2–3 months; the second suture acts as a safety net if the deep suture breaks during the adjustment and is generally left in place for 12–18 months postoperatively (Fig. 23.1).

Interrupted sutures, CCIS, and a single continuous suture (SCS) have shown comparable postoperative astigmatism [27]. In addition, a comparison of astigmatism in keratoconus patients utilizing a single continuous versus a double continuous suture showed that after suture removal, astigmatism was comparable (DCS −4.6 D, SCS −5.2 D) between the two groups [28]. Therefore, it is apparent that all methods of suture closure can work well. The ultimate choice rests with the surgeon.

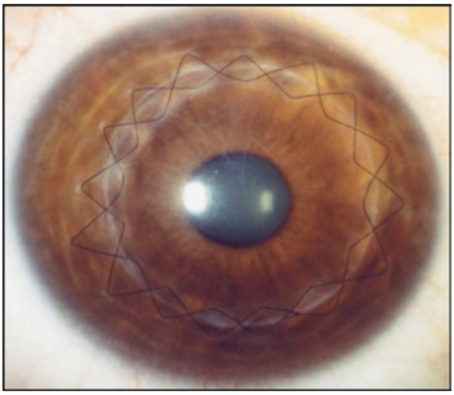


Fig. 23.1 Clinical picture of a keratoconic eye after penetrating keratoplasty with a double continuous 10/0 Nylon suture

Regardless of the preferred method, it is very important to have clear concepts of each suture technique. As a basic idea for standard graft suturing, the needle is passed 90 % depth through the donor cornea and then through the host cornea. The ideal bite is as close to Descemet's membrane as possible, and there should be an equal amount of tissue purchased in the donor and host cornea in order to approximate Bowman's layer in both the donor and host. Discrepancies frequently exist in the thickness of the donor and host cornea if donor corneas are thick due to the hyperosmolar glycosaminoglycans in the preservation medium, or fresh donor tissue is used in patients with severe corneal edema. In keratoconic eyes this scenario is frequent, where the graft is sutured to a relatively thin host cornea. Closing Bowman's layer to Bowman's layer should always be attempted to avoid steps in the graft–host junction and subsequent exposed sutures, so in areas where the recipient cornea presents thin (assessed preoperatively by slit lamp examination) partial thickness bites (50–70 % depth) in the donor tissue should be in relation with deep bites (95 % depth) in the host thin stroma (Fig. 23.2).

The postoperative astigmatism management and elective suture adjustment/removal for PK in

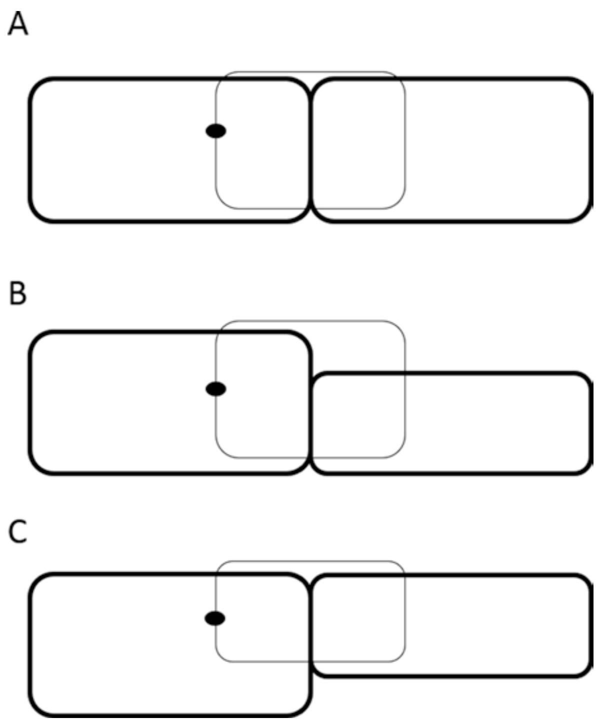


Fig. 23.2 Normal appearance of the graft–host junction with correct aligning of Bowman's layer of the donor and host corneas, with needle passed at a 90 % depth in both sides (**a**). If care is not taken in cases of a thin recipient cornea, steps will remain at the graft–host junction, leaving an irregular astigmatism and exposed sutures that need to be replaced (**b**). To avoid this, a partial thickness bite (50–70 % depth) should be performed at the donor side (**c**)

cases of previous keratoconus does not differ from other PK indications, with a complete suture removal generally recommended after 12–15 months.

23.3.3 Outcomes

Penetrating keratoplasty offers good long-term visual rehabilitation for keratoconus patients, and compared with other indications for PK there is a relatively low rate of graft failure and long mean graft survival. Rejection rate has been reported to be 5.8–41 % with a long-term follow-up, where most rejections occurred in the first 2 years [29–33]. Larger host trephine size, male donor gender, and nonwhite donor race have been associated with increased rejection hazard [29]. Despite this observed rejection rate, only a 4–6.3 % graft failure rate has been reported with a mean follow-up of 15 years, with an estimated 20-year probability of 12 % [29, 30, 34]. Fukoka et al. reported a cumulative probability of graft survival at 10, 20, and 25 years after PK of 98.8 %, 97.0 %, and 93.2 %, respectively, while Pramanik et al. estimated a graft survival rate of 85.4 % at 25 years after initial transplantation [30, 34]. Summarizing, the existing evidence shows that the graft survival rate gradually decreases after 20 years post-PK.

An average best-corrected visual acuity (BSCVA) in logarithm of the minimum angle of resolution (LogMAR) at preoperation, 10, 20, and 25 years after surgery of 1.54 ± 0.68, 0.06 ± 0.22, 0.03 ± 0.17, and 0.14 ± 0.42, respectively, has been reported [30]. Best spectacle-corrected visual acuity (BSCVA) of 0.14 ± 0.11 LogMAR has been reported with a mean period of 33.5 months, while a BSCVA of 20/40 or better with a mean follow-up of 14 years was observed in 73.2 % of patients [33, 34].

An open angle glaucoma rate of 5.4 % with a mean follow-up of 14 years has been reported [34].

Claesson et al. reported a poorer survival and worse visual outcome of regrafts compared with first grafts in patients where the original indication was keratoconus: the failure rate was three times higher with regrafts and the observed visual acuity with preferred correction was ≥ 0.5 in 69 % of first grafts, while only 55 % of regrafts achieved that level [35].

23.4 Deep Lamellar Anterior Keratoplasty in Keratoconus

The goal of deep lamellar anterior keratoplasty in keratoconus is to achieve a depth of dissection as close as possible to the Descemet Membrane (DM). There are various ways to create a plane of separation between DM and the deep stromal layers, mainly variations of the two basic strategies: the Anwar big bubble method and the Melles manual dissection.

23.4.1 Surgical Techniques

23.4.1.1 The Big Bubble Method

Anwar based the big bubble method on a discovery in 1998 that intrastromal injection of balanced salt solution (BSS) was often effective at establishing cleavage plane just above the DM [36], taking advantage of the loose adhesion between DM and the posterior stroma. Anwar and Teichman described the current big bubble procedure in 2002 using air instead of BSS [9].

After a partial trephination of 70–80 % of the corneal stroma, pneumatic pressure is used to detach DM by injecting air into the deep stroma with a 30G needle. The air injected into the stroma produces a dome-shaped detachment of the DM that is seen under the surgical microscope as a ring meaning that the big bubble has been formed. The stromal tissue above the DM plane is removed with spatula and scissors, making first sure to exchange the air in the supradescemetic plane with viscoelastic to avoid inadvertent puncture of the DM. When all of the stromal tissue is successfully removed, the DME membrane exposed is characteristically smooth (Fig. 23.3).

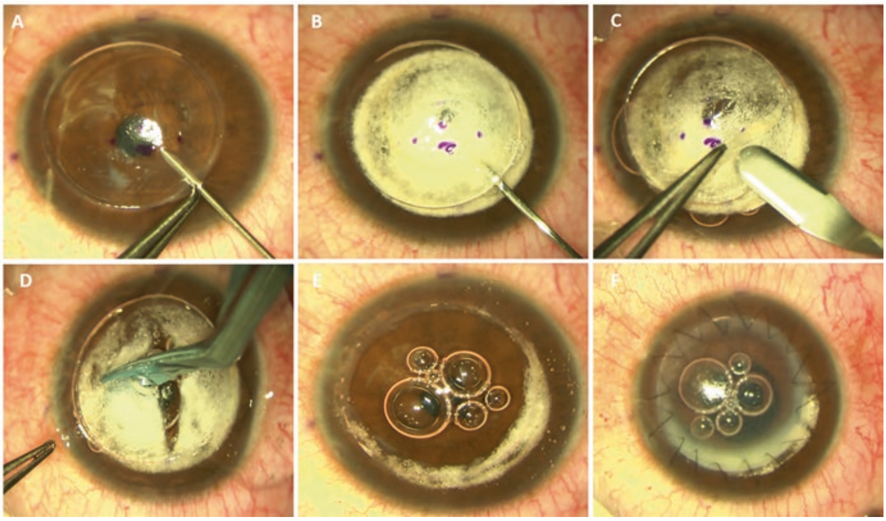


Fig. 23.3 DALK Big Bubble Technique: after a partial trephination of 70–80 % of the corneal stroma, pneumatic pressure is used to detach DM by injecting air into the deep stroma with a 27G needle (**a**). Once the air is injected it produces a dome-shaped detachment of the DM that is seen under the surgical microscope as a ring meaning that the big bubble has been formed (**b**). Then a lamellar dissection with a Crescent blade of the anterior stroma is performed (**c**) followed by the removal of the stromal tissue above the DM plane with spatula and scissors (**d**), making first sure to exchange the air in the supradescemetic plane with viscoelastic to avoid inadvertent puncture of the DM. When all of the stromal tissue is successfully removed, the DME membrane exposed is characteristically smooth (**e**), and the donor cornea without its DM and endothelium is then sutured with the preferred suture technique (**f**)

23.4.1.2 Melles Manual Method

This technique is based on the air–endothelium interface [8]. First the anterior chamber is filled with air. Then, using a series of curved spatulas through a scleral pocket, the stroma is carefully dissected away from the underlying DM. The difference in refractive index between the air and the corneal tissue creates a reflex in front of the surgical spatulas, and the distance between the instrument and the reflex is used to judge the amount of remaining tissue. Viscoelastic is injected through the scleral incision into the stromal pocket. Once the desired plane is reached, the superficial stroma is removed using trephine and lamellar dissection (Fig. 23.4).

Since the original descriptions, there have been many variations to the standard technique. Lamellar dissection can be made with diamond knife, nylon wire, microkeratome [37], or femtosecond laser. To help guiding the dissection plane trypan blue, ultrasound pachymetry [38] or real time optical coherence tomography [39] (OCT) has been tried. Partharsathy et al. describe the "small bubble" technique for confirming the presence of the big bubble [40].

For corneas with extreme peripheral thinning, a modified procedure has been proposed dubbed "tuck-in lamellar keratoplasty" [41, 42]. In this technique, the central anterior stromal disc is removed and a centrifugal lamellar dissection is performed using a knife to create a peripheral intrastromal pocket extending 0.5 mm beyond the limbus. The donor cornea is prepared in such a way that it has a central full thickness graft with a peripheral partial thickness flange. The edges of a large anterior lamellar graft are tucked in below to add extra thickness.

23.4.2 Outcomes

Most studies have found equivalent visual and refractive results between PK and DALK provided stromal dissection reaches the level or

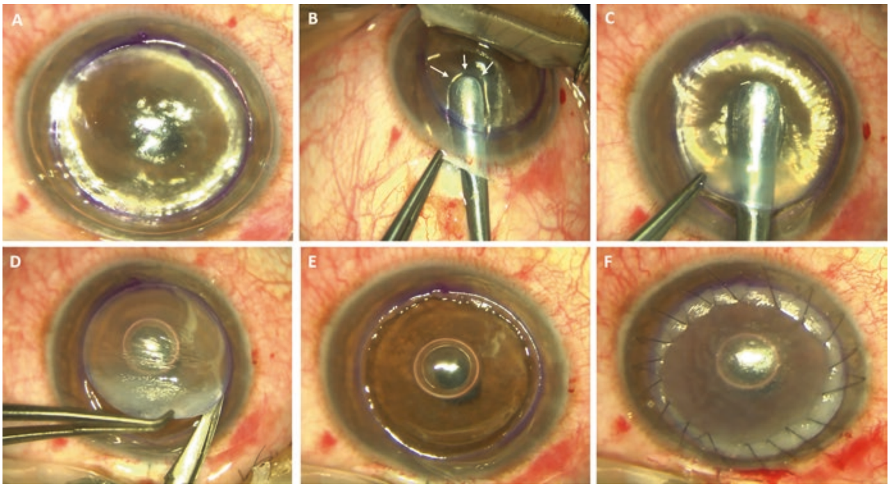


Fig. 23.4 DALK Melles Technique: first the anterior chamber is filled with air and a partial trephination of 70 % of the corneal stromais performed (**a**). Then, using a series of curved spatulas through a scleral pocket, the stroma is carefully dissected away from the underlying DM (**b**). The difference in refractive index between air and corneal tissue creates a reflex of the surgical spatulas, and the distance between the instrument and reflex is used to judge the amount of remaining underlying tissue (**b**, *arrows*). Viscoelastic is injected through the scleral incision into the stromal pocket and the dissection can be completed through the trephination edge (**c**). Once it is completed, the superficial stroma is removed (**d**), the DME membrane exposed, (**e**) and the donor cornea sutured (**f**)

close to the DM [12, 43–48], although 20/20 vision seems more likely after PK [12, 48]. For instance, in a recent study from Australian patients including 73 consecutive patients with keratoconus, the mean BCVA was not significantly different for DALK (0.14 logMAR, SD 0.2) versus PK (0.05 logMAR, SD 0.11) [12, 44]. A review of published literature that included 11 comparative studies on DALK and PK found that visual and refractive outcomes are comparable if the residual bed thickness in DALK cases is between 25 and 65 μm [14].

In those studies where the visual outcomes of DALK were inferior to PK [49], the dissection plane was "predescemetic" and the incomplete stromal dissection and the not fully baring of the DM had a negative impact in the results [49]. The problem seems to be related to the depth of the undissected stromal bed rather than to its smoothness as predescemetic DALKs performed by laser ablation did not outperform those dissected manually.

The recently published Australian graft registry data compared the outcomes of PKs and DALKs performed for KC over the same period of time and found that overall, both graft survival and visual outcomes were superior for PK. In a recent study from the UK, Jones et al. compared the outcomes after PKP and DALK for keratoconus [12]. The risk of graft failure for DALK was almost twice that for PKP. Probably, in the day-to-day clinical practice, visual outcomes with DALK, although comparable with PK, may be just slightly inferior or less predictable compared with PK, given surgical inexperience, and unpredictable issues regarding residual stromal thickness and DM folds. Nonetheless, elimination of risk of endothelial rejection compensates for this difference.

Lastly, one of the important advantages of DALK is a lower rate of endothelial loss compared with PK. The reported endothelial cell loss is as high as 34.6 % after PK, whereas it was 13.9 % after DALK [50].

23.4.3 Complications

Allograft reactions are less frequent in DALK than in PK and less likely to result in graft failure if correct treatment is initiated. Subepithelial and stromal rejection after DALK has been reported in the range of 3–14.3 % whereas in PKP ranges from 13 to 31 % in the first 3 years after surgery [11]. Endothelial rejection is not an issue in DALK.

Increases in IOP following DALK has been reported to be only 1.3 % of operated eyes, compared with 42 % of eyes after PK [50]. Development of glaucoma may also be up to 40 % less [51]. It is attributed to the lower steroid requirement of DALK [52].

Urrets–Zavalia Syndrome first reported following PK in KC and causing fixed, dilated pupil with iris atrophy is a rare entity following DALK [53].

There are also a few complications that are unique to DALK and the presence of a donor–host interface. One of the major problems with DALKs is intraoperative DM perforation, which may occur in 0–50 % of the eyes [11]. Surgeon's inexperience, corneal scarring near the DM, and advanced ectasias with corneal thickness less than 250 μm increase the risk [54, 55]. Depending on the size of the perforation, conversion to PK may be required to avoid double anterior chamber and persistent corneal edema, especially when the rupture leads to the collapse of the anterior chamber (macroperforation). Incidence of pseudoanterior chamber or double anterior chamber is in the range of 1 % [56]. It can occur because of retention of fluid secondary to breaks in the DM, or, because of incomplete removal of viscoelastic in the interface [57]. Large pseudo chambers must be managed surgically by drainage of the fluid and anterior chamber injection of air or gas [58]. The presence of DM folds caused by a mismatch between donor button and the recipient bed is usually transient and disappear over time, but interface wrinkling when central and persistent may affect quality of vision [59]. Occasionally an eye with anatomically correct DALK may require a reoperation secondary to interface haze and poor visual acuity, usually stemming from incomplete or predescemetic stromal dissection [11]. Interface keratitis is a serious complication of DALK and it is caused mainly by Candida [60] but Klebsiella pneumonia [61], and nontuberculous mycobacteria [62] have also been isolated in several cases. Conservative treatment is usually unsuccessful and most cases need a therapeutic PK [60]. Interface vascularization can occur because of inflammatory, infective, and traumatic episodes and can be treated with injection of bevacizumab [63].

23.5 Femtosecond Laser-Assisted Keratoplasty for Keratoconus

The capability of femtosecond laser energy to create different cutting patterns with a controlled level of biological interaction and minimal tissue trauma has provided a new possibility for corneal surgeons in both penetrating and nonpenetrating keratoplasty procedures. From case to case the cutting profile can be more convenient in one specific shape, what was impossible to be made before with the manual trephination techniques. The potential advantages of femtosecond laser-assisted keratoplasy are the following [64, 65]:

1. More precise and regular cuts
2. No risk of injury for intraocular structures
3. Perfect donor–recipient size matching
4. Less injury to donor endothelium
5. Customization of the cutting pattern
6. More donor–host tissue interaction promoting better wound healing
7. Potentially less induction of surgically induced astigmatism
8. Shorter visual rehabilitation time
9. Stronger and probably more stable wounds with earlier suture removal

23.5.1 Femtosecond-Assisted Keratoplasty Incision Profiles

Intralase (AMO) provides the more sophisticated and complex patterns when compared to the other technologies. The combination of simpler incisions (posterior side cut, anterior side cut, and lamellar cut) can be combined in limitless number of complex edge profile graft combinations [66] with a very high level of precision in dimensions and concentration which is not possible with other techniques [67].

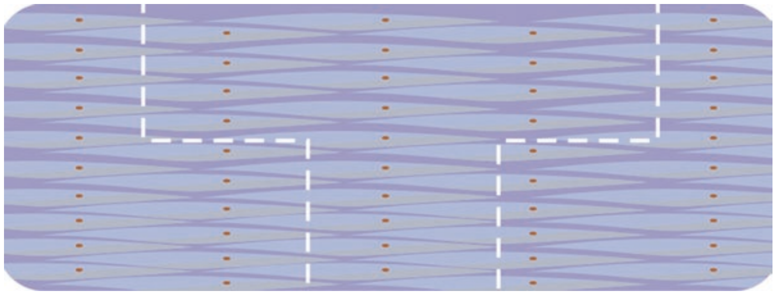


Fig. 23.5 Mushroom-based edge profile

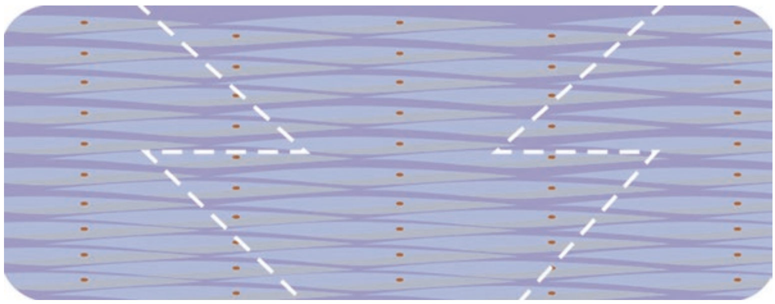


Fig. 23.6 Zigzag-based edge profile

- *Top-hat-based edge profile*
- This type of architecture maximizes the posterior tissue to be transplanted. Not suitable for keratoconus.
- *Mushroom-based edge profile*
- The inverted version of a top-hat is known as mushroom (Fig. 23.5) and is often used for anterior surface surgery, being composed of a narrower posterior side cut and a wider anterior side cut both intersected by the ring lamellar cut. The broader anterior section maximizes the anterior stroma area to be transplanted, what makes it suitable for keratoconus.
- *Zigzag-based edge profile*
- Zigzag profile (Fig. 23.6) is composed of a slanted anterior and posterior side cuts connected by the ring lamellar cut. It can be adapted to maximize either anterior or posterior surface, which makes it suitable to a wide variety of situations, including keratoconus.

23.5.2 Basics on Femtosecond Graft Architecture

Regardless of the profile being used, it is important to understand the basics of femtosecond incisions and stepped graft architecture [64].

- *Incision intersection*
  Femtosecond laser-assisted keratoplasty is formed by a combination of straight incisions that need to interact with each other in order to obtain a clear and continuous graft cutting profile that is easy to dissect, handle, and be later extracted. The overlapping degree is generally set between 10 and 30 μm.
- *Lamellar cut depth*
  As a thumb rule, lamellar cut depth is set at 50 % of average pachymetry in both donor and recipient corneas.
- *Oversizing*
  Femtosecond laser is able to create identical sized grafts in terms of diameter regardless of the keratometry readings, which has led to recommend using the exact same diameter in donor and recipient corneas [66, 68]. It is then up to the surgeon to decide oversizing primarily just in terms of postoperative spherical refraction needs.
- *Deepest posterior point*
  When designing the donor graft in PKP, posterior depth must be set below the maximum pachymetric reading in the incision area in order to assure a clean and full thickness incision. On the other hand, recipient might be

moved from laser room to the main surgical operating room. In these cases, patient movement makes advisable to intentionally avoid performing a full thickness incision to prevent any pressure leaking during transportation from the Lasik room to the suturing surgical theater. Thus, posterior depth is generally set 70 μm above the thinnest pachymetric reading in the incision area, which is generally enough tissue to prevent wound leakage [69].

23.5.3 Surgical Technique

Donor: an artificial anterior chamber (AAC) is required to hold the donor tissue in proper position and pressure similar to a real patient during a lasik procedure; *Recipient*: as previously described, it is necessary to leave a safety gap of posterior noncut tissue on the recipient cornea which prevents any aqueous humor leakage during transportation [69]; *Graft manipulation*: a Sinskey hook is used to dissect the different incisions being the procedure identical in both donor and recipient corneas. However, recipient cornea partial thickness cut will be completed with a diamond blade and curved scissors.

23.5.4 Femtosecond-Assisted Penetrating Keratoplasty

The initial published evidence comparing manual and femtosecond laser-assisted PK (f-PK) showed a faster visual rehabilitation together with an improved best corrected visual acuity, and a lower refractive and topographic astigmatism in the laser group [70–73]. Nevertheless, these papers had a limited follow-up of the cases, generally shorter than a year. Little evidence still exists about the long-term outcomes of f-PK: Chamberlain et al. published their results with 2-year follow-up and using a "zig-zag" edge profile [74]. They could demonstrate a topographic astigmatism significantly lower in the f-PK group but only during the first 6 postoperative months. Afterward no significant differences were observed regarding the refractive or topographic astigmatism and visual acuity. Only a few papers have been published comparing the different cutting edge profiles [75]. Our impression is that there are not significant differences in the visual or refractive outcomes regarding the preferred edge profile, although studies comparing the "zig-zag" and "mushroom" profiles in keratoconus are still required (Fig. 23.7).

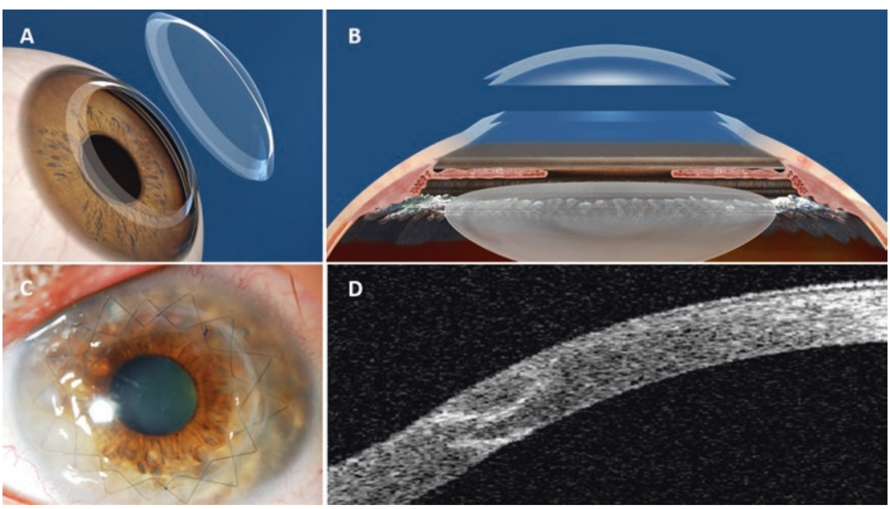


Fig. 23.7 Femtosecond laser-assisted penetrating keratoplasty with a "Zig-Zag" edge profile (**a**, **b**; courtesy of Abbott Medical Optics, USA). Postoperative clinical picture (**c**) and an anterior segment OCT capture (**d**) where it is possible to appreciate the zig-zag edge profile at the host–donor interface with a perfect coalescence of the edges

23.5.5 Femtosecond-Assisted Deep Anterior Lamellar Keratoplasty

The use of the femtosecond laser in DALK (f-DALK) avoids manual trephination and allows more precise identification of tissue depth and insertion of the air needle by following the plane between the lamellar and posterior laser side cuts. As variability in stromal thickness in eyes with advanced keratoconus, ectasia, or dense and deep stromal scars may limit the ability of the femtosecond laser to produce a uniform lamellar plane, we use the laser only to create the side cut both in donor and recipient cornea, while leaving a minimal amount of residual corneal tissue. With this we try to control the potential risk of creating a DM perforation with the femtosecond laser.

Femtosecond laser mushroom configuration is the preferred profile for DALK (Fig. 23.8). For the side cut a full thickness mushroom configuration cut is made on the donor cornea first and then a nonpenetrating mushroom configuration on the recipient. In the recipient cornea, the depth of the anterior side cut is about 60 % of the thinnest corneal pachymetry, the depth of the posterior side cut about 80 % of the thinnest corneal pachymetry, leaving a ring lamellar cut of 1 mm (Fig. 23.9). In the donor cornea, the Descemet's membrane (DM) and endothelium is debrided assisted by trypan blue dye.

Femtosecond laser-assisted DALK might have an advantage in keratoconus cases because it provides a larger amount of donor–recipient tissue to interact for the purpose of corneal wound healing consistency, and it has been demonstrated recently by our group that f-DALK shows a more active wound healing leading to leucomatous wounds [76]. We established a grading for the side cut corneal healing pattern as observed by slit lamp examination (Table 23.1), and we could observe that 52 % of f-DALK cases

Fig. 23.9 Mushroom DALK configuration: the depth of the anterior side cut is about 60 % of the thinnest corneal pachymetry, the depth of the posterior side cut about 80 % of the thinnest corneal pachymetry, leaving a ring lamellar cut of 1 mm

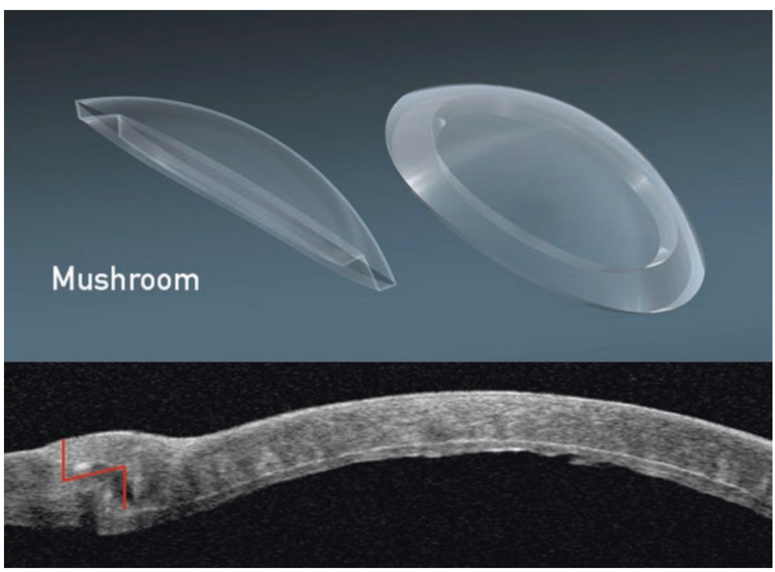
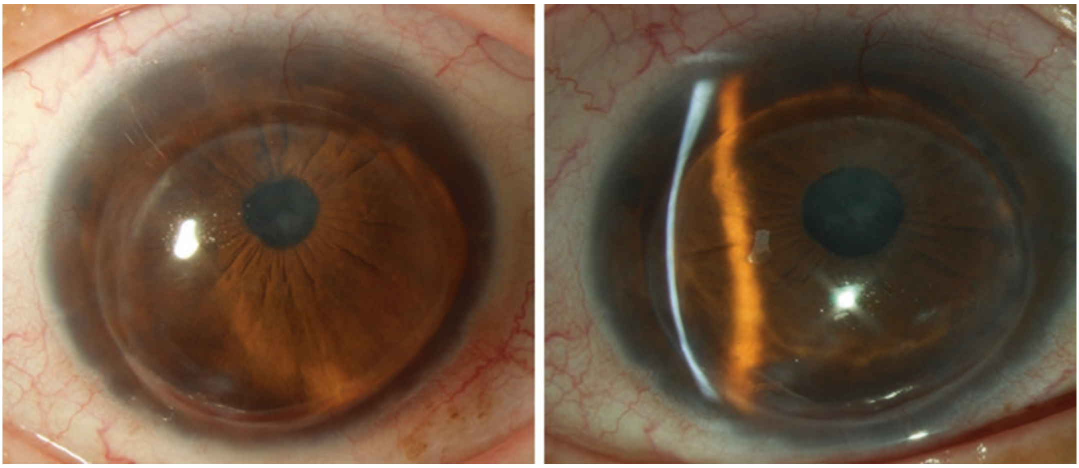


Fig. 23.8 Femtosecond laser-assisted DALK with a "Mushroom" edge profile (*up*: courtesy of Abbott Medical Optics, USA). Postoperative anterior segment OCT capture (*down*) where it is possible to appreciate the mushroom edge profile at the host–donor interface

Table 23.1 Analysis of femtosecond laser side cut corneal wound healing pattern



Keratoconus recurrence 17 years after a penetrating keratoplasty (*left*). Observe the severe thinning of the recipient stroma at the graft–host junction (*right*)

showed a healing pattern grade 3 or 4 [76]. The reasons for this could be either due to the larger area of contact between the donor and recipient tissues and/or to femtosecond laser-related biological activation of the corneal tissues, which should be related to the level of energy used for the creation of the side cut.

Equivalent to f-PK, f-DALK accelerates the visual rehabilitation, showing a better visual result during the immediate postoperative period, but without significant differences after the sixth postoperative month [77]. In a recent study of our group, we could not demonstrate significant differences regarding the visual or refractive outcomes after 1-year follow-up. However, we demonstrated a faster visual rehabilitation in the f-DALK group versus manual DALK as well as significant differences in the wound healing pattern between groups, being more intense in the f-DALK group [76].

Summarizing, and regarding the current evidence, femtosecond laser accelerates the visual rehabilitation after PK or DALK compared with the manual technique, obtaining better refractive and visual results along the immediate postoperative period; however, these benefits are lost later in the follow-up, not being able to improve the refractive or visual outcomes in the long term. Considering the high costs of this technology, these results do not justify its use as a gold standard for keratoplasty. Nevertheless, if available, femtosecond laser offers important intraoperative (easy wound closure) and perioperative (faster rehabilitation) advantages, together with a stronger surgical wound that allows a faster suture removal (depending on the wound healing pattern) and probably less risk of dehiscence against an ocular trauma in the long term.

23.6 Keratoconus Recurrence After Corneal Transplantation

We have already discussed the good long-term results of the different options of corneal grafting for keratoconus. Nevertheless, de Toledo et al. observed a progressive increase of keratometric astigmatism in 70 % of their cases from 10 years after suture removal, following an initial phase of refractive stability during the first 7 years after PK for keratoconus (4.05 ± 2.29 D 1 year after suture removal, 3.90 ± 2.28 D at year 3, 4.03 ± 2.49 D at year 5, 4.39 ± 2.48 D at year 7, 5.48 ± 3.11 D at year 10, 6.43 ± 4.11 D at year 15; 7.28 ± 4.21 D at year 20, and 7.25 ± 4.27 D at year

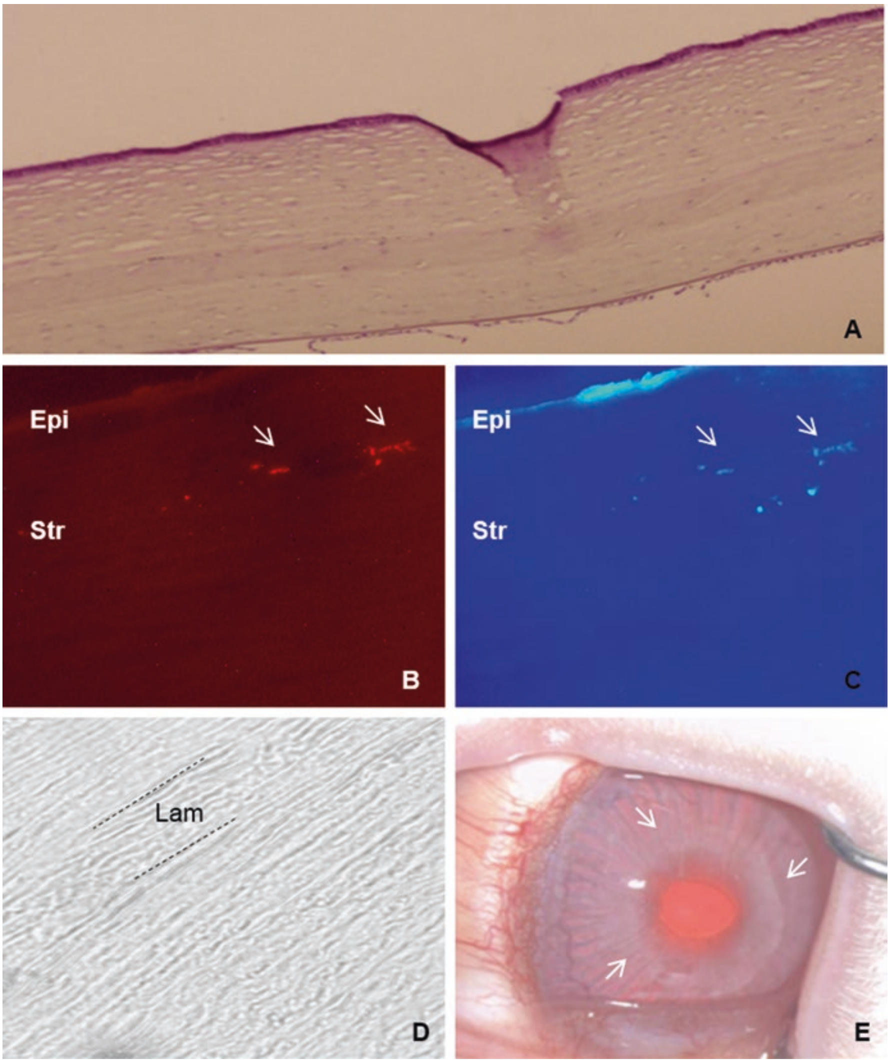


Fig. 23.10 Reconstruction of corneal stroma. (**a**) Hematoxylin–eosin staining of a rabbit cornea with an implanted graft of decellularized human corneal stroma with h-ADASC colonization: hypocellular band of ECM without vessels or any inflammatory sign (magnification ×200); (**b**) human cells labeled with CM-DiI around and inside the implant that express (**c**) human keratocan (human adult keratocyte specific marker; magnification ×400), confirming the presence of living human cells inside the corneal stroma and their differentiation into human keratocytes (*arrows*); (**d**) phase-contrast photomicrographs showing a morphologically unaltered corneal stroma (magnification ×400); (**e**) the graft remains totally transparent after 12 weeks of follow-up (magnification ×2) (*arrows* point to the slightly visible edge of the graft). *Epi* epithelium, *Str* stroma, *Lam* Lamina

25), so a late recurrence of the disease may occur with an increasing risk over time [16]. Actually, a 20 year post-PK probability of 10 % has been reported previously, with a mean time to recurrence of 17.9–21.9 years, so given the younger age at which keratoconus patients undergo corneal transplantation, these long-term findings should be explained to patients and incorporated into the preoperative counseling [29, 34, 78] (Fig. 23.10).

It is well known how other corneal stromal dystrophies, like granular or lattice dystrophy, tend to recur into the donor cornea, due to either colonization of the new stroma by the abnormal host keratocytes or epithelial secretion in early stages. In keratoconus this host keratocyte invasion has not been well stabilized as the main etiology for the post graft recurrent ectasia, but is likely in relation with the early keratoconic changes observed in the histology of explanted donor buttons after regrafting [78–80]. Postgraft ectasia is often preceded by thinning of the recipient stroma at the graft–host junction, so the disease progression at the host stroma is likely to be the underlying reason for these cases of recurrent ectasia and progressive astigmatism over time [16, 78]. In such cases, a mean keratometric sphere and cylinder increase of 4D and 3D, respectively, between final suture removal and diagnosis can be observed [78].

The management of recurrent ectasia after corneal grafting should be spectacle adjustment if low astigmatism levels are induced and rigid/hybrid gas permeable contact lenses with higher levels of astigmatism or significant anisometropia. For more advanced cases, scleral lenses may be considered before a surgical approach. If a second corneal transplant is required either a new full thickness PK versus lamellar keratoplasty can be considered. Large grafts are usually necessary as the whole area of thinning should be included within the graft limits in order to excise the whole cone to avoid a new recurrence and also to avoid suturing through a thin recipient cornea. As large grafts are associated with increased risk of rejection and glaucoma, lamellar techniques by manual dissection of the host and donor corneal stroma are always preferable as far as the donor endothelium presents healthy without signs of failure. If femtosecond dissection of the lamellar bed is chosen, gentian violet and cyanoacrylate glue can be used in the area of thinning as masking agents to minimize the risk of perforation [81]. Limbus may have to be recessed while suturing very large grafts that sit close to the limbus in order to avoid passing the suture through the conjunctiva at the host side. Recurrence after regrafting has also been reported, event that it may require a third graft for visual rehabilitation [78].

Keratoconus recurrence after DALK has not been described, being currently available very little evidence about its real incidence and impact. Feizi et al. reported a case where keratoconus recurred only 49 months after DALK [82]. They suggested that the time interval from transplantation to recurrence may be shorter after DALK than after PK, but this has not been supported or confirmed by other authors [83]. Further research analyzing the long-term outcomes after DALK for keratoconus is required in order to investigate its real incidence.

23.7 A Glance at the Future

Keratoconus is a corneal disease that affects primary the corneal stroma and Bowman layer. Current research and future therapeutic directions are focusing in the regeneration of corneal stroma by less or no invasive procedures that could avoid the common complications that we still see even with lamellar keratoplasty techniques.

Melles at al. recently described a new technique where an isolated Bowman layer is transplanted into a mid-stromal manually dissected corneal pocket in patients with an advanced (Stage III-IV) keratoconus [84]. They observed a modest improvement in the maximum keratometry and BSCVA but an unchanged best contact lens corrected visual acuity (BCLVA). This is a new interesting approach that it could have its indication for those advanced keratoconus non-suitable for corneal collagen crosslinking or intracorneal ring segments and intolerant to contact lenses but without visually significant corneal scars and therefore good BCLVA. In such cases Bowman's transplant could avoid or postpone the necessity of keratoplasty if the mild observed corneal flattening enables continued contact lens wear and the cone is stabilized (as it has been reported to happen but with only a sample of 20 eyes and a short mean follow-up of 21 months). Further research by alternative authors with a larger sample and longer follow-up is needed before introducing this technique into the routine clinical practice.

As discussed, Bowman's transplantation could have some benefits in cases of advanced keratoconus, but even if these results are finally confirmed by other authors, they offer a mild improvement to these patients without a significant functional/anatomical rehabilitation, so further techniques may focus on attempting the subtotal regeneration or substitution of the corneal stroma in order to achieve better results. Different types of stem cells have been used in various ways in several research projects in order to find the optimal procedure to regenerate the human corneal stroma: Corneal Stromal Stem Cells (CSSC), Bone Marrow Mesenchymal Stem Cells (BM-MSCs), Adipose Derived Adult Mesenchymal Stem Cells (ADASCs), Umbilical Cord Mesenchymal Stem Cells (UCMSCs), Embryonic Stem Cells (ESCs) [85]. These approaches can be classified into four techniques:

1. *Intrastromal injection of stem cells alone*

   Direct injection of stem cells inside the corneal stroma has been assayed in vivo in some studies, demonstrating the differentiation of the stem cells into adult keratocytes without signs of immune rejection. Our group demonstrated the production of human extracellular matrix when human ADASCs (h-ADASC) were transplanted inside the rabbit cornea [86]. Du et al. reported a restoration of the corneal transparency and thickness in lumican null mice (thin corneas, haze, and disruption of normal stromal organization) 3 months after the intrastromal transplant of human CSSCs. They also confirmed that human keratan sulfate was deposited in the mouse stroma and the host collagen lamellae were reorganized, concluding that delivery of h-CSSCs to scarred human stroma may alleviate corneal scars without requiring surgery [87]. Very similar findings were reported by Liu et al. using human UMSCs in the same animal model [88]. Recently, Thomas et al. found that, in a mice model for mucopolysaccharidosis, transplanted human UMSC participate both in extracellular glycosaminoglycans (GAG) turnover and enable host keratocytes to catabolize accumulated GAG products [89]. In our experience, the production of human extracellular matrix by implanted mesenchymal stem cells occurs, but not quantitatively enough to be able to restore the thickness of a diseased human cornea. However, the direct injection of stem cells may provide a promising treatment for corneal dystrophies including keratoconus, by regulating the abnormal host keratocyte collagen production, enabling collagen microstructure reorganization, and corneal scarring modulation.

2. *Intrastromal implantation of stem cells together with a biodegradable scaffold*

   In order to enhance the growth and development of the stem cells injected into the corneal stroma, transplantation together with biodegradable synthetic extracellular matrixes has been performed. Espandar et al. injected h-ADASCs with a semisolid hyaluronic acid hydrogel into rabbit corneal stroma, reporting better survival and keratocyte differentiation of the h-ADASCs when compared to their injection alone [90]. Ma et al. used rabbit ADSCs with a polylactic-co-glycolic (PLGA) biodegradable scaffold in a rabbit model of stromal injury, observing newly formed tissue with successful collagen remodeling and less stromal scarring [91]. Initial data show that these scaffolds could enhance stem cell effects over corneal stroma, although more research is required.

3. *Intrastromal implantation of stem cells with a nonbiodegradable scaffold*

   At the present time, no clinically viable human corneal equivalents have been produced by tissue engineering methods. The major obstacle to the production of a successfully engineered cornea is the difficulty with reproducing (or at least simulating) the stromal architecture. The majority of stromal analogs for tissue engineered corneas have been created by seeding human corneal stromal cells into collagen-based scaffoldings, which are apparently designed to be remodeled (see Ruberti et al. 2008 for a general review of corneal tissue engineering) [92]. The major drawback of these analogs is their lack of strength, thus unable to restore the normal mechanical properties of the cornea. New and improved biomaterials compatible with human corneas and with enhanced structural support have been developed leading to advanced scaffolds that can be used to engineer an artificial cornea (keratoprosthesis) [85]. The combination of these scaffolds with cells can generate promising corneal stroma equivalents, and some studies have already been published that use mainly corneal cell lines providing positive results regarding adhesion and cellular survival in vitro [93]. Our opinion is that stem cells do not differentiate properly into keratocytes in the presence of these synthetic biomaterials, losing their potential benefits and not resolving the major drawbacks with such substitutes: their relatively high extrusion rate and lack of complete transparency [94].

4. *Intrastromal implantation of stem cells with a decellularized corneal stromal scaffold*

   The complex structure of the corneal stroma has not been yet replicated, and there are well-known drawbacks to the use of synthetic scaffold-based designs. Recently, several corneal decellularization techniques have been described, which provide an acellular corneal extracellular matrix (ECM) [95]. These scaffolds have gained attention in the last few years as they provide a more natural environment for the growth and differentiation of cells when compared with synthetic scaffolds. In addition, components of the ECM are generally conserved among species and are tolerated well even by xenogeneic recipients. Keratocytes are essential for remodeling the corneal stroma and for normal epithelial physiology [96]. This highlights the importance of transplanting a cellular substitute together with the structural support (acellular ECM) to undertake these critical functions in corneal homeostasis. To the best of our knowledge, all attempts to repopulate decellularized corneal scaffolds have used corneal cells [97–99], but these cells have major drawbacks that preclude their autologous use in clinical practice (damage of the donor tissue, lack of cells, and inefficient cell subcultures), thus the efforts to find an extraocular source of autologous cells. In a recent study by our group, we showed the perfect biointegration of human decellularized corneal stromal sheets (100 μm thickness) with and without h-ADASC colonization inside the rabbit cornea in vivo (Fig. 23.10a,b), without observing any rejection response despite the graft being xenogeneic [100]. We also demonstrated the differentiation of h-ADASCs into functional keratocytes inside these implants in vivo, which then achieved their proper biofunctionalization (Fig. 23.10c). In our opinion the transplant of stem cells together with decellularized corneal ECM would be the best technique to effectively restore the thickness of a diseased human cornea, like in keratoconus. Through this technique, and using extraocular mesenchymal stem cells from patients, it is possible to transform allergenic grafts into functional autologous grafts, theoretically avoiding the risk of rejection.

23.8 Conclusion

Treatment of keratoconus has experienced great advances in the last two decades. From being limited only to rigid gas permeable contact lens wear and penetrating keratoplasty for the most advanced cases, to have nowadays different therapeutic alternatives to treat not only the cone and postpone/avoid the necessity of a corneal transplant, but also being able to halt the progression of the disease with a very high rate of efficacy and safety [101] (Figs. 23.11 and 23.12). Also the advances in refractive surgery including surface corneal ablation treatments and phakic intraocu-

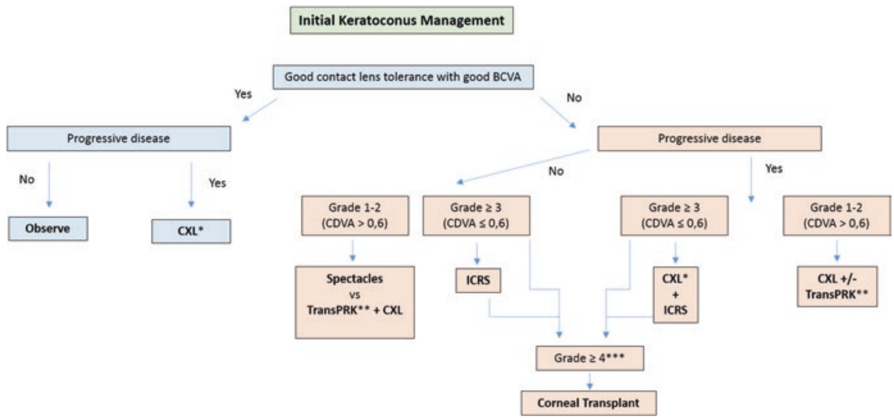


Fig. 23.11 Decision tree for intervention at presentation in keratoconus. Grading regarding the RETICS classification. *BCVA* best corrected visual acuity, *CDVA* corrected distance visual acuity, *CXL* corneal collagen crosslinking, *TransPRK* transepithelial photorefractive keratectomy, *ICRS* intracorneal ring segments (* if thinnest point > 370 μm; ** wavefront guided transPRK (limited treatment) to reduce coma-like aberrations and increase CDVA; *** if corneal scarring, insufficient corneal thickness for ICRS implantation or ICRS failure with persistent contact/scleral lenses intolerance and poor CDVA)

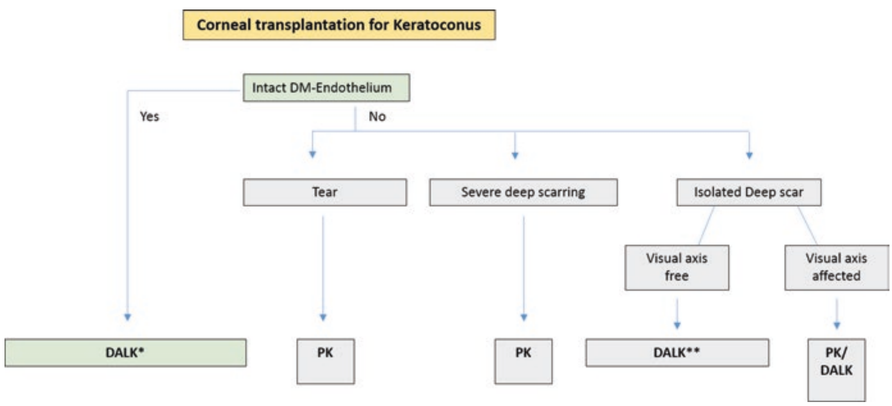


Fig. 23.12 Guideline for corneal transplant technique selection in cases of advanced keratoconus (*big bubble DALK as technique of choice due to its better visual performance; **assess manual DALK with "Melles" technique as big bubble technique will likely burst the Descemet membrane-endothelium layer)

lar lenses have allowed a better management and visual rehabilitation of these patients after a corneal transplant is required, being able to achieve, in many cases, a 20/20 unaided vision (Fig. 23.13). The future expected advances in transepithelial crosslinking, nanotechnology, and regenerative medicine predict an exciting future in this field and we will be looking forward to updating these guidelines.

Compliance with Ethical Requirements

Informed Consent: No human studies were carried out by the authors for this article.

Animal Studies: All institutional and national guidelines for the care and use of laboratory animals were followed.

Financial support or proprietary interest: None.
No conflicting relationship exists for any author.
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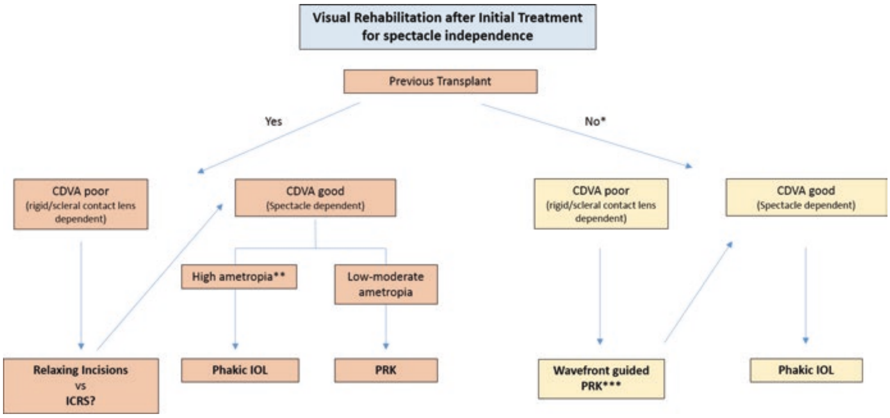

Fig. 23.13 Visual rehabilitation in order to achieve a spectacle independence for keratoconic eyes once the initial treatment has been completed and the stability of the disease has been confirmed (* gross shape correction with CXL ± ICRS; ** mainly in cases of high cylinder or moderate-high hyperopia; *** if previous CXL has been done and stability is confirmed)

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