

INTRODUCTION

Corneal transplantation or keratoplasty is an operation in which abnormal corneal host tissue is replaced by healthy donor cornea. A corneal graft may consist of partial-thickness (anterior or posterior lamellar) or full-thickness (penetrating) keratoplasty (PKP). Indications for keratoplasty may be either optical, tectonic, therapeutic or cosmetic (**Kanski and Bowling, 2011**).

Ametropia and astigmatism following successful keratoplasty can seriously impact a patient's quality of vision (**Kuryan and Channa, 2010**). Indeed, a significant percentage of patients fail to achieve emmetropia after anatomically successful keratoplasty. High degrees of myopia, astigmatism and occasionally hyperopia are frequently encountered refractive errors occurring after corneal transplantation (**Vajpayee et al., 2003**). Most studies evaluating post-keratoplasty refractive outcomes document a mean cylinder value of 4-5 dioptres (D). Postoperative astigmatism has been reported in the range of 2-8 D while spherical equivalents range from 2-12 D (**Pearlman, 1981**).

Spectacles are only appropriate in cases of anisometropia or astigmatism less than 4.0 D. A significant majority of patients who cannot be rehabilitated with spectacles are able to achieve adequate vision correction with contact lenses (**Price et al., 1991**). However, many patients are intolerant to spectacles

and contact lenses and suffer from aniseikonia (**Kuryan and Channa, 2010**). A considerable group of patients with significant astigmatism cannot be adequately corrected by contact lenses. Other patients find difficulty in proper handling and maintenance of contact lenses especially in the older age groups (**Hardten and Lindstrom, 1997**).

Patients who have failed non-surgical visual correction should be considered as candidates for surgical refractive intervention (**Vajpayee et al., 2003**). All candidates should be evaluated to ensure refractive and tectonic stability. The available options for surgical refractive correction after corneal transplantation include laser in-situ keratomileusis (LASIK), photorefractive keratectomy (PRK), corneal relaxing incisions, wedge resections, compression sutures, insertion of intrastromal corneal ring segments and intraocular lens implantation. There is no consensus regarding the appropriate time interval between keratoplasty and refractive intervention. Most studies recommend waiting at least 12 months after the transplant. There is general agreement that waiting 3-6 months after suture removal is an appropriate time interval (**Forseto et al., 1999**).

Many studies have consistently demonstrated superior outcomes when LASIK is used to treat residual refractive errors and astigmatism in patients with prior penetrating keratoplasty. Therefore, LASIK is the refractive surgery of choice for addressing visual complaints in post-keratoplasty patients

(Forseto et al., 1999). In five year follow-up studies, visual acuity was 20/40 or better in 86-98% of eyes and 50-85% were within 1 D of intended correction **(Buzard et al., 2004).** Corneal remodeling may occur after creation of the cut which could change the biomechanics of the cornea and alter the host-graft interface. Therefore, some have advocated for a two-step LASIK approach especially in high errors. In this approach, the flap is cut and replaced followed by months of topography and keratometry measurements before a second procedure is done to perform ablation **(Donnenfeld et al., 2002).** Flap-related complications remain the main disadvantage of post-keratoplasty LASIK procedures **(Forseto et al., 1999).**

Photorefractive keratectomy (PRK) is effective in the management of spherical errors after keratoplasty. It is less effective and less predictable than LASIK for treating astigmatic errors. The main advantage of PRK over LASIK is avoiding flap-related complications. However, patients with previous keratoplasty tend to experience significantly more corneal haze than does the general population **(Bilinghan et al., 2000).** The use of mitomycin C is associated with improved outcomes and less haze, however, results are still less optimal than LASIK **(Carones et al., 2002).**

Relaxing incisions are highly effective at addressing post-keratoplasty astigmatism, but do not address spherical abnormalities. They can be done manually by diamond knife or using femtosecond laser. Their effect can be augmented by

combining with compression sutures. They are associated with a higher incidence of wound dehiscence and variable wound healing, as well as alterations in corneal topography, refraction and keratometry (*Arffa, 1988*).

Wedge resections can be used to correct high errors of astigmatism following keratoplasty (*Troutman RC, 1983*). A wedge of corneal tissue including the recipient and/or donor cornea is excised from the flatter corneal meridian to correct high astigmatism (usually higher than 10.0 D) after penetrating keratoplasty. The length and width of a wedge resection and its proximity to the central cornea determine the amount of astigmatism to be corrected. The procedure results in an increase in overall graft curvature, hence a myopic shift will generally be encountered (*Lugo et al., 1987*). Difficulty in manually excising the exact amount of tissue may account for the low predictability of the technique. Recently, femtosecond laser has been used as a safe and effective alternative to the manual technique to perform a corneal wedge resection. It allows for more precise and controlled tissue excision (*Ghanem and Azar, 2006*).

Insertion of intrastromal corneal ring segments can significantly correct post-keratoplasty irregular astigmatism and improve corneal topography. However, several complications were encountered during and after implantation including small dehiscence of graft-host interface during stroma tunnel dissection, an inflammatory infiltrate around the segment

immediately after operation, stromal channel vascularization leading to ring explantation, and night halos (*Arriola et al., 2009*).

In cases of high astigmatism after penetrating keratoplasty, implantation of a toric intraocular lens (tIOL) offers a promising alternative to arcuate keratotomies with or without compression sutures. Viestenz et al. reported that cylinder values could be reduced from 7.0 ± 2.6 D to 1.63 ± 1.5 D after tIOL implantation. They recommended, however, regular and symmetric corneal topography for successful implantation of tIOL (*Viestenz et al., 2005*).

Repeat keratoplasty should be considered as the last option for treating intractable high or irregular post-keratoplasty astigmatism in clear corneal grafts when the above interventions fail. Szentmary et al. observed a significant decrease in central graft power and an improvement in astigmatism with sutures in place. However, astigmatism increased significantly after second suture removal. They concluded that final suture removal should be postponed as long as possible in such eyes (*Szentmary et al., 2005*).

AIM OF THE WORK

Reviewing the literature regarding the different types of refractive errors occurring after corneal transplantation and the various surgical methods of their correction.

KERATOPLASTY

Corneal transplantation is the oldest, most common and most successful transplantation in humans overall. Corneal transplantation refers to surgical replacement of a full-thickness or lamellar portion of the host cornea with that of a donor eye (*Seitz et al., 2005*).

General indications of keratoplasty include: optical keratoplasty (**Figure 1**) done to improve vision as in keratoconus, tectonic keratoplasty done to restore or preserve corneal integrity as in descemetocoele, therapeutic keratoplasty (**Figure 2**) to remove infected corneal tissue in cases unresponsive to antimicrobial therapy and cosmetic keratoplasty to improve the appearance of the eye which is a rare indication (*Seitz et al., 2005*).



Figure (1): Optical penetrating keratoplasty for macular corneal dystrophy (*Kanski and Bowling, 2011*).

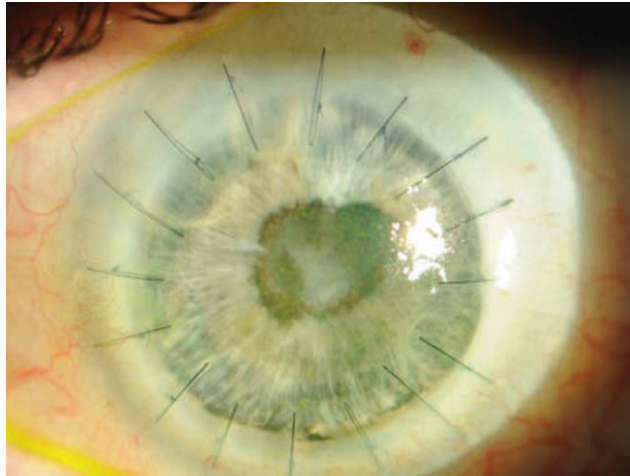


Figure (2): Therapeutic penetrating keratoplasty for pseudomonas keratitis (**Kanski and Bowling, 2011**).

Donor tissue preparation

Donor tissue should be removed within 12-24 hours of death. The optimal death-to-preservation time is 12-18 hours. There is an attempt to age-match donors and recipients. Corneas from infants (3 years and under) are used only very occasionally, even for pediatric transplants, as they are associated with surgical, refractive and rejection problems. Most surgeons do not use corneas from donors younger than 24 months, as these corneas are extremely flaccid and can result in high corneal astigmatism and myopia postoperatively. Most eye banks establish a lower donor age limit of 24 months and an upper age limit of 70 years, as older corneas tend to have lower endothelial cell counts (**Gal et al., 2008**).

Most corneas are stored in coordinating eye banks prior to transplantation, where pre-release evaluation includes

medical history review, donor blood screening to exclude contraindications and microscopic examination of the cornea including endothelial cell count determination. Corneas are preserved in hypothermic storage at 2-6 °C (up to 7-10 days) or organ culture medium at 30-37 °C (up to 4 weeks) until needed; culture allows extended testing for infective contamination (*Pels et al., 2008*).

Contraindications to ocular tissue donation include death of unknown cause, infectious diseases such as HIV, viral hepatitis, syphilis, congenital rubella, tuberculosis, septicaemia and active malaria. Most hematological malignancies, diseases of the central nervous system such as Creutzfeldt-Jakob disease, Alzheimer's disease, dementia, multiple sclerosis and motor neuron disease are contraindications to ocular tissue donation as well. Other contraindications include recipients of transplanted organs, prior ocular surgery and ocular diseases that are likely to compromise the graft outcome as inflammation and malignancy (*Seitz et al., 2005*).

The donor tissue is routinely inspected by slit-lamp biomicroscopy and the endothelial cell count is determined by specular microscopy. A cornea suitable for transplantation should display an intact epithelial layer, a stroma free of opacities or folds and a viable and regular endothelium with a cell density above 2000-2200 cells/mm² (*Wiffen et al., 1995*).

Table (1): Indications of penetrating, anterior lamellar and endothelial keratoplasty by frequency (*2014 Eye Banking Statistics Report. www.restoresight.org*).

INDICATION	FREQUENCY (%)
Penetrating Keratoplasty (total number of eyes: 38,919)	
Keratoconus	16
Repeat corneal transplant	11.3
Post-cataract surgery corneal edema	8.7
Corneal dystrophies and degenerations	3.1
Fuch's dystrophy	3.1
Trauma	2.9
Microbial keratitis	2.1
Congenital opacities	2.1
Other causes	14.1
Unknown, unreported or unspecified	36.6
Anterior Lamellar Keratoplasty (total number of eyes: 1,953)	
Keratoconus	38.8
Corneal dystrophies and degenerations	5.5
Trauma	2.4
Microbial keratitis	1.6
Congenital opacities	1.5
Repeat corneal transplant	1.4
Post-refractive surgery	0.5
Other causes	9.8
Unknown, unreported or unspecified	38.5
Endothelial Keratoplasty (total number of eyes: 28,961)	
Fuch's dystrophy	47.7
Post-cataract surgery corneal edema	17.8
Repeat corneal transplant	8.2
Other causes	10.7
Unknown, unreported or unspecified	15.6

Penetrating Keratoplasty

The first successful total penetrating keratoplasty (PKP) was performed by Eduard Zirm in 1905. Penetrating keratoplasty remains the most commonly performed corneal transplantation procedure, largely because lamellar surgery is difficult and time-consuming, and because interface irregularity can limit visual outcome. Depending on the age and patient's cooperation, corneal transplant surgeries may be performed under local or general anaesthesia (*Seitz et al., 2005*).

Determination of graft size can be done preoperatively using slit-lamp biomicroscopy with a variable slit beam, and operatively by trial placement of multiple trephines with different diameters or by measurement with a caliper. Grafts measuring 8.5 mm in diameter or more are prone to postoperative anterior synechiae formation, vascularization and increased intraocular pressure. An ideal graft size is 7.5 mm; grafts smaller than this may give rise to flatter curvature, higher astigmatism and more topographic irregularity (*Seitz et al., 2003*).

Trephination and excision of donor tissue should always precede that of host cornea. Donor tissue is prepared by trephining a previously excised corneoscleral button. This button is usually trephined to be about 0.25 mm larger in diameter than the planned diameter of the host opening to facilitate watertight closure, minimize postoperative flattening and reduce the

possibility of postoperative glaucoma. Mechanical trephination is the standard method although newer non-mechanical laser techniques are more accurate and are preferred by some surgeons when available (*Gaster et al., 2012*).

After donor tissue preparation is done, excision of the diseased host tissue is performed taking care not to damage other ocular structures like the iris and the lens (**Figure 3**). Different methods for recipient trephination are available. It can be done simply by freehand or with motorized suction trephine systems that stabilize the globe and ensure that the angle of trephination is perpendicular to the surface. Femtosecond laser-assisted trephination systems are also available. Then fixation of the donor tissue to the recipient bed is done using 10-0 monofilament nylon sutures (*Bahar et al., 2009*).

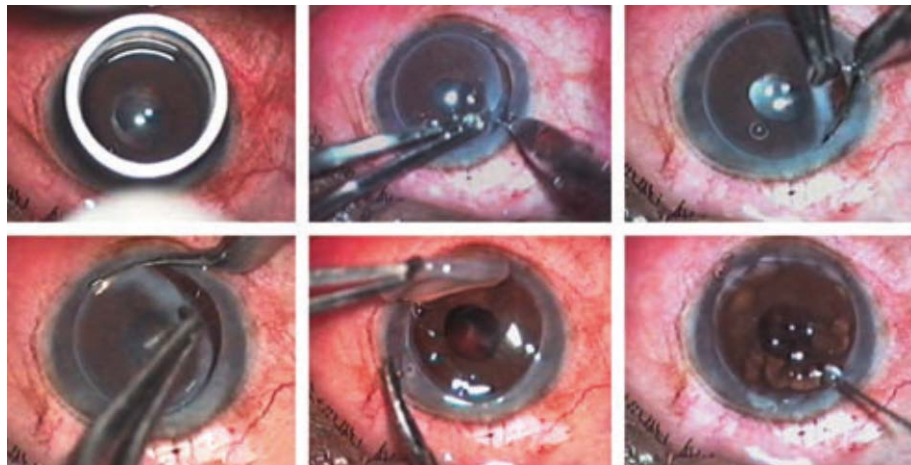


Figure (3): Penetrating Keratoplasty: Excision of host tissue by partial-thickness trephination; incision into the anterior chamber; completion of excision; and injection of viscoelastic (*Kanski and Bowling, 2011*).

The depth of the sutures must typically involve about 90% of the corneal tissue thickness. Four cardinal sutures are first placed at positions 12, 6, 3 and 9 o'clock. The rest of the sutures are either a combination of interrupted and running sutures or solely interrupted sutures (*Seitz et al., 2005*).

Interrupted sutures are suitable for vascularized or thinned cornea as subsequent selective removal may be necessary to prevent the advancement of vessels or to control astigmatism. Running sutures, on the other hand, have the advantage of speedy placement intraoperatively and better tension distribution and healing (**Figure 4**). The running sutures may be adjusted intraoperatively by using a keratoscope to project a circular image onto the donor cornea (*Belmont et al., 1993*).

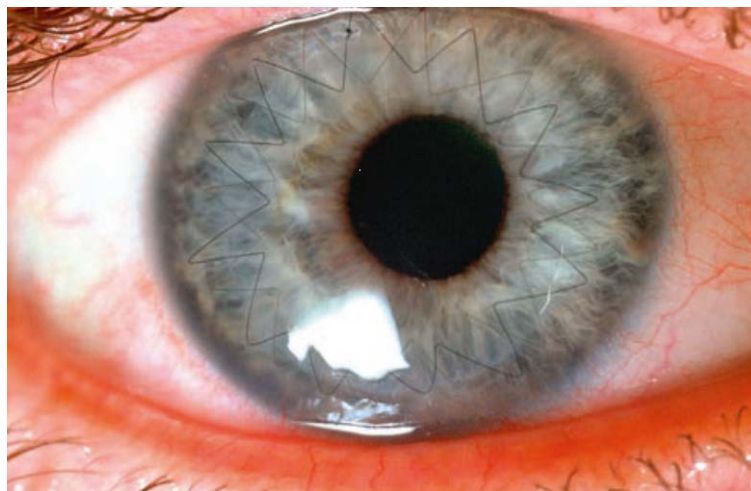


Figure (4): Penetrating keratoplasty secured by continuous sutures (*Kanski and Bowling, 2011*).

Because penetrating keratoplasty involves an “open sky” exposure of the intraocular contents, adequate reduction of intraocular pressure (IOP) prior to penetrating keratoplasty is an important step to avoid the risk of expulsive suprachoroidal hemorrhage (*Seitz et al., 2005*).

Lamellar Keratoplasty

Lamellar keratoplasty is a procedure in which a partial-thickness graft of donor tissue is used to provide tectonic stability and/or optical improvement. There are two types of lamellar keratoplasty: anterior lamellar and posterior lamellar keratoplasty (*Arenas et al., 2012*). In an anterior lamellar keratoplasty procedure, the transplanted tissue does not include corneal endothelium. This procedure avoids endothelial rejection and thus donor tissue may be obtained from older eyes. Superficial anterior lamellar keratoplasty is done when the corneal pathology involves the superficial layers of the corneal tissue (*Vajpayee et al., 2006*). Deep anterior lamellar keratoplasty (DALK) replaces corneal tissue almost to the level of the Descemet's membrane (DM). DALK is done when the corneal pathology involves deeper layers of the corneal stroma (*Anwar and Teichmann, 2002*).

Several methods can be used in DALK in an attempt to simplify the identification of DM or pre-Descemet's deep stromal plane, perform a complete and safe dissection of the overlying corneal stroma and obtain a smooth host surface of

uniform thickness. The basic technique of layer-by-layer manual dissection is technically challenging, time consuming, leaves a relatively rough surface and has a high rate of perforation of DM. Air-guided deep stromal dissection utilizes an air bubble in the anterior chamber to generate a mirror reflection of the spatula inserted into the stromal pocket aiding in determining the depth of dissection and locating DM. Anwar's big-bubble technique provides a planned, safe, quick and consistent exposure of DM by injection of air deep into the stroma. The surface of the DM appears smooth after successful stromal resection. Other techniques use balanced salt solution (hydrodelamination) or viscoelastic devices to achieve a cleavage plane over the DM (*Karimian and Feizi, 2010*).

On the other hand, in posterior lamellar (endothelial) keratoplasty, the anterior corneal surface is preserved hence maintaining its refractive character. It is performed in diseases affecting the corneal endothelium. The revolutionary success of endothelial keratoplasty was initiated by the insight of Gerrit Melles that partial-thickness grafts could stick to the back of the cornea without sutures (*Melles et al., 1998*).

Melles et al., 2004 proposed a simplified technique involving removal of the Descemet's membrane from the recipient cornea followed by placing a donor endothelial graft onto the back of the recipient posterior stroma. This technique was modified and popularized by *Price, 2005* and termed Descemet stripping endothelial keratoplasty (DSEK). DSEK