



New and Emerging Techniques - Surgical

Horizon Scanning Report

Endokeratoplasty for Decompensated Corneal Endothelium

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Endokeratoplasty for Decompensated Corneal Endothelium

The Australian Safety and Efficacy Register of New Interventional Procedures – Surgical (ASERNIP-S) in conjunction with the Royal Australasian College of Surgeons has undertaken a Horizon Scanning Report to provide advice on the state of play of the introduction and use of endokeratoplasty.

This report is based on information available at the time of research and cannot be expected to cover any developments arising from subsequent improvements to health technologies. This report is based on a limited literature search and is not a definitive statement on the safety, effectiveness or cost-effectiveness of the health technology covered. Before relying on the information in this report, users should carefully evaluate its accuracy, currency, completeness and relevance for their purposes. This report is not intended to be used as medical advice and it is not intended to be used to diagnose, treat, cure or prevent any disease, nor should it be used for therapeutic purposes or as a substitute for a health professional's advice. The Commonwealth does not accept any liability for any injury, loss or damage incurred by use of or reliance on the information.

Though every effort has been made to include all scientific research available, other relevant research results may have been reported since completion of this report. Please contact ASERNIP-S on the address provided below if you are aware of relevant research results that should inform the report or would like further information.

This Horizon Scanning Report was prepared by Rebecca Morgan from the NET-S Project, ASERNIP-S for the Health Policy Advisory Committee on Technology (Health PACT), on behalf of the Medical Services Advisory Committee (MSAC) and the Australian Health Ministers' Advisory Council (AHMAC).

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Background

Background to the Condition

The Cornea

The cornea is the transparent dome-shaped membrane that forms the front of the eye (Figure 1). Incoming light is refracted as it passes through the cornea and lens to form a focussed image on the retina. The cornea is the chief refractory structure of the eye; hence any cloudy or opaque areas inhibit the ability of the eye to form clear images on the retina (National Eye Institute 2001).

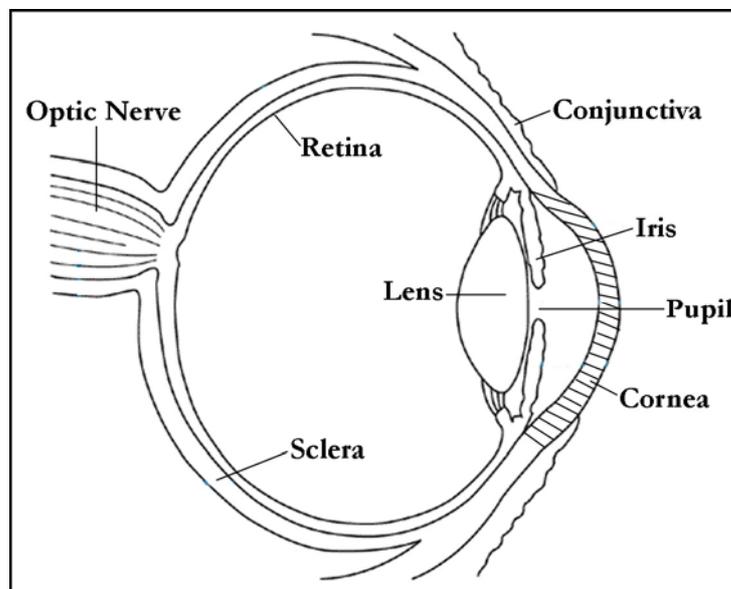


Figure 1: Diagrammatic representation of a median section through the eye. Light passes through the cornea, pupil and lens to the retina. As no light is reflected by the pupil, it appears black. The coloured part of the eye, the iris, controls how much light is received by the retina.

The cornea is comprised of five basic layers: epithelium, Bowman's layer, stroma, Descemet's membrane and endothelium (Figure 2). The *epithelium* is the outermost (anterior) layer, and is only 5-6 cell layers thick. If the epithelium is damaged, it grows back within a few days without scarring.

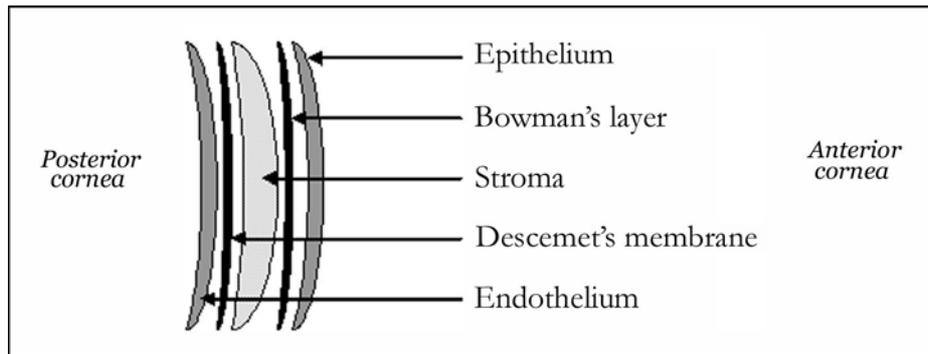


Figure 2: Diagrammatic representation of the corneal layers.

Directly beneath the epithelium is *Bowman's layer*. The strong layered collagen fibres maintain the shape of the cornea. Damage to the Bowman's layer can result in scar formation.

The middle layer of the cornea is the *stroma*. This layer consists mostly of water and collagen fibres. The arrangement of these fibres is critical to the refractive function of the cornea.

Posterior to the stroma is *Descemet's membrane*. It serves as a protective barrier to infectious organisms and injury, but allows water and nutrients to pass. This membrane is composed of collagen fibres (different from those of the stroma) which are manufactured by the underlying endothelium. It is readily regenerated after injury.

The most posterior layer is the *endothelium*. It is one cell layer thick and performs the vital function of pumping excess fluid out of the stroma. Endothelial cells do not regenerate once they are damaged by injury, surgery, disease or aging (National Eye Institute 2001; St Lukes Eye 2003).

Diseases of the Endothelium

Fuchs' endothelial dystrophy (FED) and (aphakic and pseudophakic) bullous keratopathy are examples of conditions resulting from a diseased endothelium. In Fuchs' endothelial dystrophy, the endothelium deteriorates at a higher rate than normal, reducing its functional capacity. Aphakic and pseudophakic bullous keratopathy result from endothelial damage which may be incurred during other ocular surgery (Aquavella 2001). Damage to the endothelium compromises its ability to pump water out of the stroma. Fluid accumulates in the stroma and epithelium, distorting the cornea's normal curvature. Untreated, both conditions can exhibit fluid filled subepithelial and epithelial bullae (blisters) and a swollen and cloudy cornea. Patients experience reduced visual acuity and pain (National Eye Institute 2001; Bergmanson *et al.* 1999).



Description of the Technology

The Procedure

There are several names given to this procedure: endokeratoplasty (Al-Fayez 2003; Arffa 2003; Busin *et al.* 2000; Shiuey and Moshirfar 2001), endothelial lamellar keratoplasty (Jones and Cuthbertson 1998), grafting of the posterior cornea (Ehlers *et al.* 2000), posterior keratoplasty (Azar *et al.* 200; Perez *et al.* 2003), posterior lamellar keratoplasty (Guell *et al.* 2003; Li *et al.* 2002; Melles *et al.* 1998; Seitz *et al.* 2003) and deep lamellar endothelial keratoplasty (Terry and Ousley 2001). For the purpose of this review, the procedure will be referred to as endokeratoplasty (EKP).

Endokeratoplasty involves transplanting donor posterior cornea consisting of posterior stroma, Descemet's membrane and endothelium, while retaining the patient's anterior cornea (epithelium, Bowman's layer and anterior stroma) (Melles *et al.* 1998).

Currently, there are two surgical methods for EKP that differ in their approach to the posterior cornea. The first utilises a microkeratome or laser to create an anterior flap, allowing the procedure to be conducted in an 'open sky' fashion, while the second involves access to the posterior cornea via a scleral incision.

1. 'Open Sky' Endokeratoplasty (Figure 3)

Donor Preparation

First the donor anterior cornea is removed (Azar *et al.* 2001; Busin *et al.* 2000; Ehlers *et al.* 2000; Guell *et al.* 2003; Shiuey and Moshirfar 2001) and the remaining donor cornea is placed endothelial side up on a trephine block and cut with a trephine (trephined) to create a posterior cornea donor button (Figure 3a,b).

Recipient Bed Preparation and Transplantation

A recipient anterior corneal flap is created using a microkeratome (Azar *et al.* 2001; Busin *et al.* 2000; Ehlers *et al.* 2000; Guell *et al.* 2003; Shiuey and Moshirfar 2001) or excimer laser (Seitz 2003). The flap is lifted to allow trephination of the diseased posterior cornea. The donor 'button' is then transplanted into the recipient bed and the hinged corneal flap is floated over the donor tissue and allowed to seal into place (Figure 3c-e). Most authors suture both the donor button and recipient flap; however, Azar *et al.* (2001) recently conducted a modified procedure, only suturing the flap.

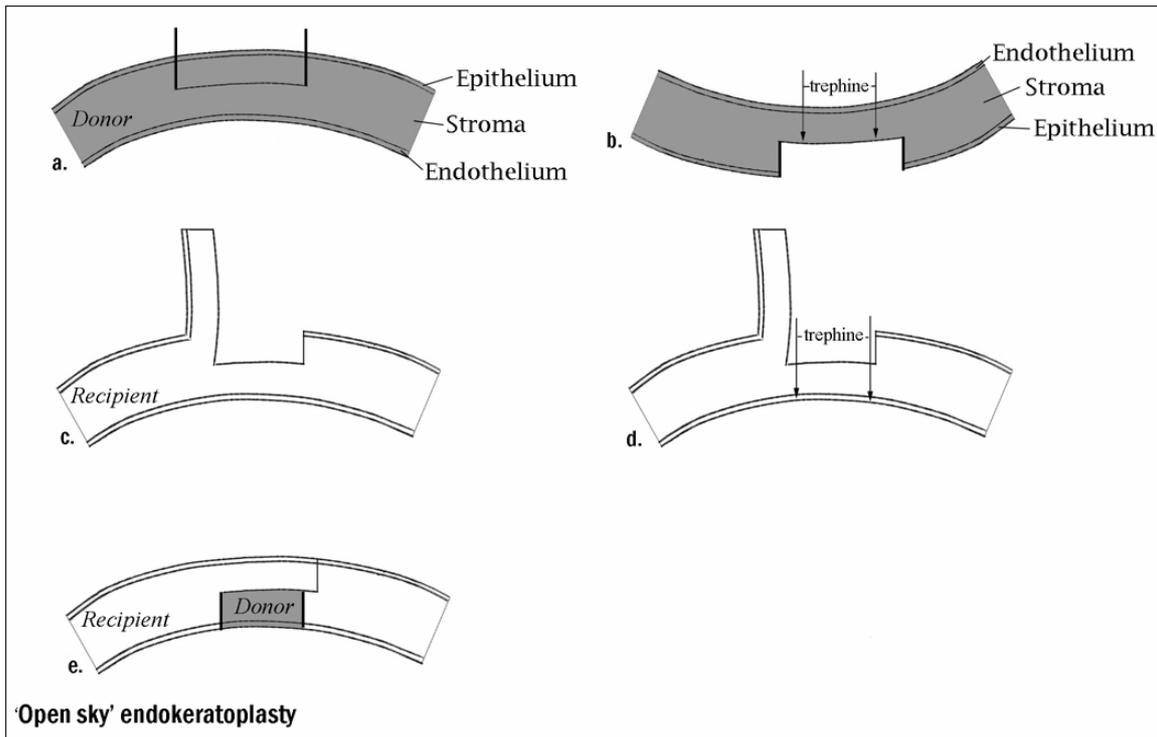


Figure 3: Diagrammatic representation of 'open sky' EKP. Anterior cornea is removed (a) and a posterior donor button trephined (b). An anterior flap is created in the anterior cornea (c), the posterior cornea removed (d) and the donor button inserted (e).

2. Endokeratoplasty via a Scleral Incision (Figure 4)

Donor Preparation

A peripheral corneal or scleral incision is made and a stromal pocket dissected across the cornea at a visually controlled depth. In most cases a trephine is inserted into this stromal pocket and a posterior disc excised (Figure 4a). Two authors report inversion of the cornea followed by full thickness or superficial trephination of the disc from the endothelial to the epithelial side (Terry and Ousley 2001; Melles *et al.* 2002 respectively, Figure 4b). The posterior button is placed endothelial side down on a spatula or a spoon shaped glide.

Recipient Bed Preparation

A peripheral corneal or scleral tunnel incision is made at a controlled depth and a stromal pocket dissected. The posterior corneal disc is cut with a custom-made flat trephine and/or micro-scissors inserted into the stromal pocket (Figure 4c-e). The posterior disc is removed with fine forceps. Variations in the location and length of the scleral incision were reported.

Transplantation

The donor button is inserted via the scleral incision and allowed to adhere to the recipient bed. One author sutured the button in place (Melles *et al.* 2003), while another three sutured the scleral incision (Melles *et al.* 1999; Melles *et al.* 2000; Terry and Ousley 2003).

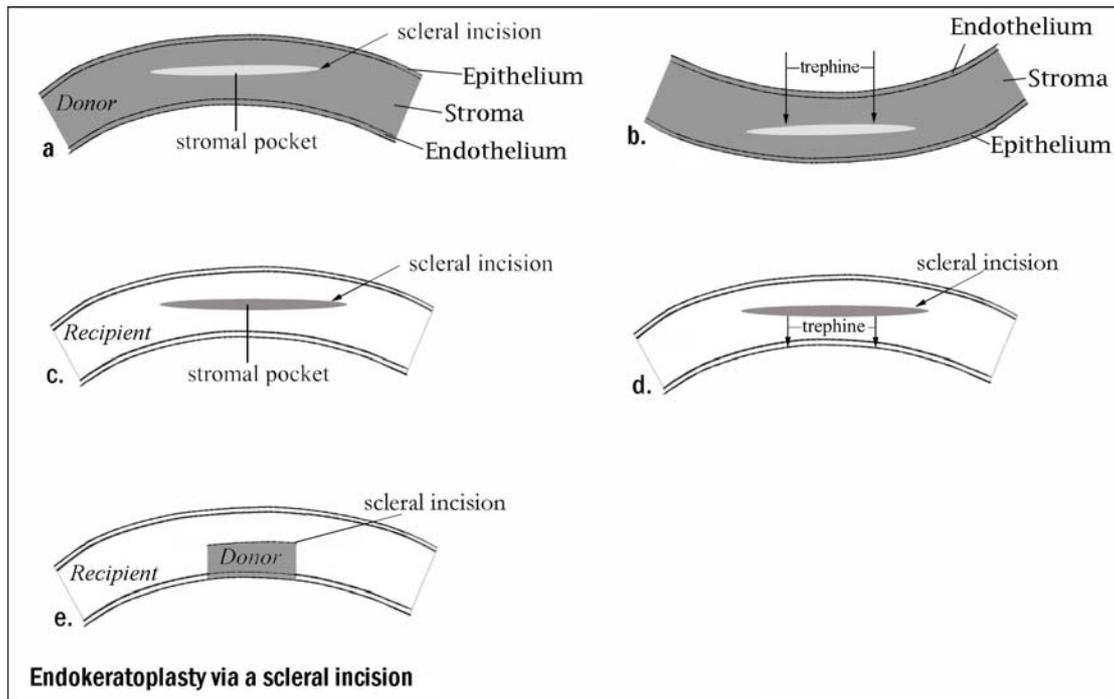


Figure 4: A stromal pocket is created in the donor cornea (a). The posterior button is excised either from the stromal pocket or from the endothelial side (b). A posterior corneal disc is excised from a stromal pocket (c,d) and the button inserted via the sclerocorneal incision.

Intended Purpose

Penetrating keratoplasty (PK) is the current surgical method for improving vision in individuals with a diseased corneal endothelium. Endokeratoplasty was developed so that only the diseased, posterior portion of the patient's cornea is replaced, leaving the patient with their own anterior cornea.

Endokeratoplasty has the potential to reduce surgical time, intraoperative complications, astigmatism, visual recovery time, suture-induced complications, risk of wound dehiscence, and the number of follow-up visits required. It may also allow more efficient use of donor corneas (Busin et al., 2000; Melles *et al.*, 1999).

Clinical Need and Burden of Disease

The number of endothelial cells on the posterior cornea naturally decreases with age. Trauma during surgery can also reduce the number of these cells. As endothelial cells do not regenerate, the incidence of decompensated endothelium-related conditions increases with age (McDonald 2001b). Corneal transplant is only required for patients in advanced stages of corneal decompensation (McDonald 2001a).



Fuchs' endothelial dystrophy is most common in women between 50 and 70 years of age. It is generally considered to be an inherited autosomal disorder. Attrition of the endothelial cells occurs at a greater rate than normal resulting in an abnormally hydrated and swollen cornea. Left untreated, blister-like structures (bullae) form on the epithelial surface. Once this stage has been reached the condition is termed bullous keratopathy (Bergmanson *et al.* 1999; McDonald 2001a).

Pseudophakic (natural lens replaced with intraocular lens (IOL)) and aphakic (no natural lens or IOL) and bullous keratopathy can result following cataract extraction. Surgical trauma to the endothelium can reduce the number and health of the endothelial cells (Aquavella 2003; McDonald 2001b). More females develop aphakic and pseudophakic bullous keratopathies than men (Maeno *et al.* 2000).

Endokeratoplasty is suitable for patients with a diseased corneal endothelium or Descemet's membrane and a normal anterior cornea. The Australian Corneal Graft Registry reports 14 649 corneal grafts have been performed in Australia from its inception in 1985 to 2003. Almost a third of penetrating corneal transplants performed in Australia are intended to treat bullous keratopathy or FED (4434/13831, 32.1%) (Williams *et al.* 2004). The New Zealand Corneal Transplant Registry reports 2 146 penetrating keratoplasty procedures have been performed from 1991 to 2003. About a fifth of these are for bullous keratopathy or FED (467/2146, 21.8%) (Corneal Transplant Registry, 2004).

Stage of Development

Endokeratoplasty remains in a developmental stage. While some good results have been achieved, several steps in the procedure are being modified in attempt to maximise the efficacy of the procedure.

Treatment Alternatives

Existing Comparators

The main goal of non-invasive treatment is to attempt to reduce swelling. This may be attempted with saline eye drops or ointments and glaucoma medications. Soft contact lenses may provide some comfort for patients. These measures are only suitable for patients in the early stages of Fuchs' dystrophy and bullous keratopathy. For those in the more advanced stages of endothelial decompensation, corneal transplant is usually indicated (Bergmanson *et al.* 1999; McDonald 2001a; McDonald 2001b).

Corneal transplantation involves replacing the diseased cornea with a healthy donor cornea. Conventional penetrating keratoplasty (PKP) is suitable for the treatment of a wide range of corneal diseases and involves replacing the full thickness of the cornea (Figure 5). As a result, wound healing is prolonged and sutures are removed after one year. There is a risk

of increasing astigmatism, loss of corneal clarity and considerable visual impairment. Graft rejection can also occur (Azar *et al.* 2001; Ehlers *et al.* 2000).

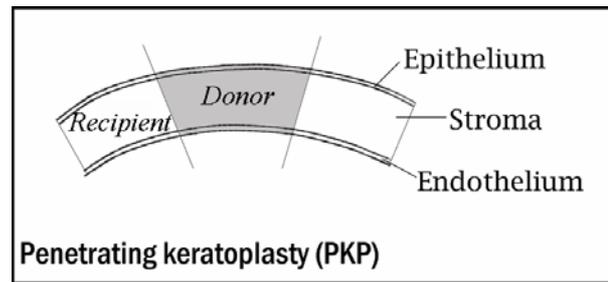


Figure 5: Penetrating keratoplasty involves transplantation of the full thickness cornea.

Recently a modified PKP has been developed with the aim of reducing the undesirable outcomes of conventional PKP and retaining the benefits of EKP. So far this has only been used on 8 patients with a very short follow up period (Busin 2003).

Clinical Outcomes

Results from seventeen studies of EKP were obtained; two randomised trials (conference abstract), ten case series and five case reports.

Effectiveness

There are several parameters used to assess vision. The five most reported parameters from the articles retrieved are best (spectacle) corrected visual acuity (B(S)CVA), uncorrected visual acuity (UCVA), spherical equivalent, astigmatism and keratometry.

Visual Acuity

Visual acuity is determined by asking the patient to read a Snellen eye chart viewed at 20 feet. 'Normal' acuity is 20/20, that is an individual can determine letters approximately one inch high from 20 feet away (or 6/6 in metres). If patient 1 has 20/40 vision, he or she can read an object from 20 feet that patient 2, with 20/20 vision, could read at a distance of 40 feet. Thus patient 2 would have two times better vision than patient 1 (Anand 2003; Holladay 2004). Visual acuity is sometimes reported as counting fingers or hand movements. These results can be converted to an approximate Snellen equivalent. Patient 3, able to count fingers at 20 feet, would have approximately 20/200 vision. Patient 4, able to count fingers at 2 feet, would have approximately 20/2000 vision. Patient 5, unable to count fingers at 20 feet but able to detect hand movements from that distance, would have approximately ten times worse vision than patient 3 (able to count fingers), hence would have a visual acuity of 20/2000 (Holladay 2004).



The improvement in visual acuity following EKP varied substantially.

Good visual results were reported in 5 out of 10 case series. Arffa (2003) reported BSCVA of 20/60 or better in 16 of 28 patients 6 months after surgery. Azar *et al.* 2001 performed EKP on one patient, with BSCVA of 20/50, six months after surgery. Busin *et al.* (2000) reported an improved UCVA to at least 20/400 in each of seven patients one month after surgery, usually not possible at one month postoperative in PKP patients. All patients exhibited BCVA of at least 20/100 at four to seven months postoperatively, with one patient recording 20/30. Melles *et al.* (2000) reported an improvement in visual acuity in all six patients, with the postoperative figures ranging from 20/80 to 20/20. Terry and Ousley (2003a) reported BSCVA ranging from 20/30 to 20/70 at six months postoperative. For one of the nine patients, BSCVA was worse 6 months postoperatively than preoperatively. Twelve months postoperative BSCVA ranged from 20/30 to 20/60, available for four of the nine patients.

Ehlers *et al.* (2000) reports a moderate best corrected visual acuity following EKP. In a study on three people, a significant improvement in BCVA from preoperative to postoperative was reported in all three (preoperative BCVA ranged from 0.05 (20/400) to the ability to discern hand movements, while postoperative BCVA ranged from 0.16 (20/125) to 0.05 (20/400) at 12 months). The results from the conference abstract of the only randomised trial report no significant difference between the groups in BCVA following EKP or PKP (Al-Fayez 2003).

Guell *et al.* 2003 reported the results from a case series with three patients who had received EKP via the 'open sky' method. No improvement in visual acuity was noted. Two of the three patients exhibited worse visual acuity than before the operation.

Spherical Equivalent

The refractive error, thus degree of correction required to normalise vision, is expressed as spherical equivalent and astigmatism. A spherical equivalent figure, measured in diopters (D), indicates how nearsighted (myopia) or farsighted (hyperopia) a person is. The higher the integer, the more correction required. Myopia is represented as a negative value, whereas hyperopia is given as a positive value (Laservision 2002).

A very high spherical equivalent was noted (+16 D) in a case report using the 'open sky' method and suturing of both the button and the flap (Azar *et al.* 2001). Melles *et al.* (2000) performed EKP via the scleral incision method, and also reported a high post operative spherical equivalent figure (+11.5 D) in one of seven patients (range 11.5 to -2.0D). Shiuey and Moshirfar (2001) reported moderate postoperative spherical equivalent in a single patient (-4.5 D at 2 months following EKP). Other authors report low postoperative spherical equivalent. Melles *et al.* (2002b), using the scleral incision method, reported spherical equivalent results in a single patient as -2.25 D preoperatively and -1.5 D at 1 year postoperatively. Busin *et al.* (2000) using the 'open sky' method in a series of seven patients, reported results that range from -1.00 to -4.00 D at one month postoperative to between -2.75 to 1.5 D four to seven months postoperatively. Terry and Ousley (2003c)



report 70% (19 of 27) patients were within 1 diopter of their preoperative spherical equivalent results at 6 months postoperatively and 67% (12 of 18) at 12 months postoperatively.

Astigmatism

The degree of astigmatism in an individual is an expression of how aspherical the cornea is. The amount of astigmatism varies greatly between individuals, and can be altered due to surgical intervention. Regular astigmatism can be corrected with spectacles. Astigmatism is expressed in diopters (D) (Anand 2003).

Many factors contribute to surgically induced astigmatism, including the incision method, length and shape of the corneal incision, location and distance of the incision from the corneal centre, suture material, tension and time of removal (Woo and Lee 2003; Dursun *et al.* 2002). As a result, many different suturing techniques have been employed following EKP to minimize the impact on postoperative astigmatism.

For 'open sky' EKP, the best postoperative astigmatism results were reported by Arffa (2003), ≤ 4.5 D in 24 of 28 patients. Postoperative astigmatism reported by Busin *et al.* 2000 ranged from 1.5 to 3.75 D at one month, and 1.5 to 5.0 D at four to seven months (seven patients), by Guell *et al.* (2003) from -3.5 to -6.0 D at 12 months (three patients) and by Shiuey and Moshirfar (2001) to 8.0 D at two months (one patient). Busin *et al.* (2000) used dissolvable sutures to secure the transplant in place while Guell *et al.* (2003) and Shiuey and Moshirfar (2001) used nylon sutures.

The postoperative astigmatism reported by authors that performed EKP via a scleral incision is generally less than the 'open sky' technique. Melles and Kamminga (2003) report an average astigmatism of 2.1 D {0.7 D} (16 patients) using nylon sutures to close the incision and the postoperative astigmatism reported by Melles *et al.* (2002b) was -1.0 D at one week and -1.75 at one year using no sutures (one patient). Melles *et al.* (2000) reported average postoperative astigmatic error as 1.54, [0.81 D] (seven patients). In this study, the stromal pocket dissection was conducted at 80% corneal depth instead of the 50% previously used, in an attempt to reduce the amount of surgically induced astigmatism. The average astigmatism reported by Terry and Ousley (2003a) six months postoperatively was 2.28 D {1.03 D}, with an average change in astigmatism of 1.13 D {1.50 D} (P=0.06). Twelve months postoperative average astigmatism was 2.31 D, {0.38 D} (four patients), with an average change in astigmatism from before surgery as 0.81 D, {0.55 D} (P= 0.06).

In a randomised trial of 32 patients, postoperative astigmatism was significantly better in the EKP group than the PKP group (P<0.05) (Al-Fayez 2003).

Keratometry

Keratometry measures the corneal curvature. An average K-reading is between 42-44 D, and expressed in diopters (Fedor 2002). Often two curves are measured. When the steepest and flattest curves are measured, the keratometry reading is expressed with the meridian (in



degrees) to indicate the orientation of the curve measured. Alternatively two curves 90 degrees apart are measured (St Luke's Eye 2003; Laservision 2002).

Following 'open sky' keratometry, results ranged from 45.25 D to 48.50 D (six patients, Busin *et al.* 2000). Following EKP via a scleral incision, Terry and Ousley (2003a) report the average change in corneal power as -0.4 D {1.7 D} after six months (eight patients), not statistically significant from preoperative (P=0.34). After 12 months, the average change in corneal power from preoperative was -1.3 {0.4 D} (P=0.34). Melles *et al.* (1999) report postoperative K-readings in one patient were reported as 41.05 D x175°/45.00 D x80° (three months), Melles *et al.* (2002b) as 42.75 D x100°/45.00 D x10° (one week) and 42.25 D x80°/44.25 D x10° (one year), and results from Melles *et al.* (2000) range from 41.25 D/43.00 D to 44.75 D/47.50 D at six or 12 months (six patients).

Safety

Interface Scarring

Mild interface scarring or haze was reported following EKP (Azar *et al.* 2001; Melles *et al.* 2000; Melles and Kamminga 2003; Terry and Ousley 2003). Deeper corneal dissection, or use of an excimer laser for cutting donor and recipient tissue, may minimize the incidence of this (Azar and Jain 2002; Seitz *et al.* 2003; Terry and Ousley 2003). The use of a laser for cutting donor tissue may also reduce excessive corneal flattening (Azar *et al.* 2001).

Donor Button Size

Azar and Jain (2002) hypothesise the diameter and thickness of the donor buttons, plus the tension of the button and flap sutures, influence postoperative hyperopia (farsightedness). Donor buttons of different sizes have been implanted in attempt to optimise postoperative vision. In penetrating keratoplasty, poorer outcomes with relatively large and small grafts have been observed, with the best outcome with grafts ranging from 7.5 to 8.5 mm (Williams *et al.* 2000). So far in EKP, the use of oversized donor grafts had no statistically significant influence on astigmatism, but the impact on K-readings was significant. The optimum sized graft was oversized by 0.5mm (Li *et al.* 2002). Transplantation of a large graft allows the maximum number of endothelial cells to be transplanted, hence quicker resolution of the stromal oedema. Melles *et al.* (2002) report the use of a 9.0mm diameter graft.

Perforation

There is significant risk of perforation of the stromal bed during dissection (Seitz *et al.* 2003). Perforation has only been recorded in EKP via the scleral incision method; 1 of 7, 1 of 16 and 1 of 9 patients respectively (Melles *et al.*, 2000; Melles and Kamminga 2003; Terry and Ousley, 2003).



Interface Epithelial Growth

From all the included data, six patients developed interface epithelial growth that required intervention (Busin *et al.* 2000; Ehlers *et al.* 2000; Perez *et al.* 2003). Five cases were resolved by aspiration or cell removal with forceps and the remaining case was resolved by removing the recipient flap. The incidence of epithelial ingrowth is expected to be reduced with lamellar transplants.

Infection

Despite the administration of topical and subcutaneous antibiotics following EKP, one case of infection with *Mycobacteria chelonae* occurred between the donor and recipient tissue 2 weeks after the operation. In this case the eye bank preservative medium was the source of this relatively rare infection (Busin *et al.* 2003).

Wound Healing

Most penetrating corneal transplantations typically require 12-18 months until suture removal (Ehlers *et al.* 2000). In EKP, wound healing is horizontal, tissue strength is minimally impaired and sutures, when employed, can be removed after three to four months (Busin *et al.* 2000; Melles and Kamminga 2003). Only one case of separation between the anterior flap and the edge of the corneal recipient eye donor was reported when superior sutures were removed.

Rejection

Postoperative epithelial defects, abnormalities and epithelial rejection that may occur after PKP may be reduced with EKP as the corneal flap is the patient's own. The reduced risk of graft rejection is speculative at this time and clinical studies are needed to ascertain whether EKP does reduce graft rejection (Melles *et al.* 1998). Potentially the risk of rejection may also be reduced with the use of cultured endothelium grown onto a corneal button or synthetic carrier (Melles *et al.* 2002; Terry and Ousley 2003).

There are several additional safety issues that could arise when performing endokeratoplasty, such as donor disc displacement, phototoxicity to the retina and loss of contrast sensitivity (Fraenkel 2004, personal communication). None of the included studies reported these complications. In fact one study reported loosening or dislocation of the donor transplant did not occur, even when an air bubble escaped from the anterior chamber into the vitreous cavity within the first postoperative hour (Melles *et al.*, 2000).



Potential Cost Impact

Cost Analysis

The cost of EKP in Australia is unknown at this time. According to the Medicare Benefits Schedule (July 2004), the reimbursement fee for transplantation of a full thickness cornea is \$1 112.35. The fee for transplantation of a superficial or lamellar cornea is \$749.90. The fee for a running corneal suture is \$117.95 (Medicare Benefits Schedule 2004). The Australian Corneal Graft Registry reports 14 649 grafts (full or partial thickness) have been performed in Australia from 1985 to 1999 (Williams *et al.* 2004). Currently there is one surgeon performing EKP in Australia.

Ethical Considerations

Informed Consent

For most studies, patients are enrolled in studies following review board approved informed consent (Melles *et al.* 2000). Some studies do not require institutional review board approval, however the potential risks and benefits are discussed with the patient (Shiuey and Moshirfar 2001). Donor corneas are obtained from eye bank eyes.

Access Issues

At the present time, use of the procedure has been restricted to research institutes in the USA, Europe, Denmark, Saudi Arabia and Australia. Only two procedures have been performed in Australia (Coster 2004; personal communication).

Training and Accreditation

Training

Trephination, transplantation and suturing are all common procedures for the corneal surgeon. While full thickness and anterior lamellar (layered) corneal transplants have been available for nearly 100 years, posterior lamellar corneal transplantation is a recent development (Terry and Ousley 2003). Endokeratoplasty is more technically demanding than the standard procedure, especially EKP via a scleral incision (Ehlers *et al.* 2000; Terry and Ousley 2003; Terry and Ousley 2001). Ongoing refinements and modifications to trephines and insertion devices ensure the most suitable devices are used.



Clinical Guidelines

Clinical guidelines will need to be developed once consistent beneficial results have been obtained following EKP. The procedure would initially be performed in patients with bullous keratopathy with proven visual potential. Post-operatively, guidelines would include assessment by established methods, such as visual acuity, keratometry, topography and microscopy (Fraenkel 2004, personal communication).

Limitations of the Assessment

Methodological issues and the relevance or currency of information provided over time are paramount in any assessment carried out in the early life of a technology.

Horizon scanning forms an integral component of Health Technology Assessment. However, it is a specialised and quite distinct activity conducted for an entirely different purpose. The rapid evolution of technological advances can in some cases overtake the speed at which trials or other reviews are conducted. In many cases, by the time a study or review has been completed, the technology may have evolved to a higher level leaving the technology under investigation obsolete and replaced.

A Horizon Scanning Report maintains a predictive or speculative focus, often based on low level evidence, and is aimed at informing policy and decision makers. It is not a definitive assessment of the safety, effectiveness, ethical considerations and cost effectiveness of a technology.

In the context of a rapidly evolving technology, a Horizon Scanning Report is a 'state of play' assessment that presents a trade-off between the value of early, uncertain information, versus the value of certain, but late information that may be of limited relevance to policy and decision makers.

This report provides an assessment of the current state of development of EKP, its present and potential use in the Australian health system, and future implications for the use of this technology.

Search Strategy Used for Report

A search of All EBM reviews, CINAHL, EMBASE, Ovid MEDLINE In-Process and other non-indexed citations, Ovid MEDLINE (R), PubMed and Google was conducted from the date of inception of the databases until March 2004. The search terms used were endokeratoplasty, keratoplasty and posterior, keratoplasty and endothelial, keratoplasty and lamellar, keratoplasty and lamellar and posterior. The American Academy of Ophthalmology website, in particular posters and programs from past annual scientific meetings, was also searched. There was no language restriction imposed on the searches.



Availability and Level of Evidence

Twelve published studies (seven case series and five case reports) and five conference abstracts (two prospectively randomised trials and three case series) were retrieved that specifically related to EKP in living human recipients. There is probably patient overlap between the two randomised trial conference abstracts and between two of the case series conference abstracts and one published paper. Suspected overlap has been noted in the safety and efficacy tables (appendix A).

List of Studies Found

Total number of studies included:	17
Prospectively randomised trial	2 (2 conference abstracts)
Case series	10 (7 published, 3 conference abstracts)
Case reports	5 (5 published)
Excluded studies	6

Several studies used EKP in cadaver eye bank eyes. The data from these studies were not included in this report. One case report detailed a patient who had undergone EKP which was converted to PKP. This study was also excluded (appendix B).

Sources of Further Information

A paper and poster presented at the 2002 and 2003 American Academy of Ophthalmology Annual Meetings respectively, reports the results of a prospectively randomised trial that compares the safety and efficacy of EKP to PKP for pseudophakic bullous keratopathy. At the time of writing this report, only the abstracts were available. The poster and paper were titled *Endokeratoplasty vs penetrating keratoplasty for pseudophakic bullous keratopathy* and the senior author was Dr Mashoor F Al-Fayez (Associate Professor of Ophthalmology, King Abdul Aziz University Hospital).

Impact Summary

Endokeratoplasty or posterior lamellar keratoplasty is a new surgical procedure for patients who have diseased corneal endothelium, such as with Fuchs' endothelial dystrophy and bullous keratopathy.

The majority of authors report good improvements in visual acuity following endokeratoplasty. Results vary from excellent, for example Melles *et al.* (2000) reports one patient improved from a preoperative BSCVA of 20/50 to postoperative 20/20 with no induced change in spherical equivalent and a normal K-reading after 12 months. Another patient from the same study improved from a preoperative BSCVA of 20/150 to



postoperative 20/25 with a change in spherical equivalent from -1.75 to 0.25 D with K-readings of 46.00/46.25.

Several authors report results that are not as encouraging. Shiuey and Moshirfar (2001) report one patient who improved in BSCVA from 20/200 preoperatively to 20/100 at two months postoperative, but with a spherical equivalent of -4.5D and 8D astigmatism. Terry and Ousley (2003a) report one patient with a preoperative BSCVA of 20/60 and at six months postoperatively 20/70. The patient also reported 2.25 D induced astigmatism and an unchanged K-reading.

Overall the current final optical quality remains lower than initially anticipated, however ongoing modifications in methods and devices are being made in attempt to improve these results (Ehlers *et al.* 2000). Some maculopathy is to be expected in the elderly population, who make up the majority of patients undergoing endokeratoplasty. This partially explains why few patients have 20/20 vision following the procedure. In addition, Terry and Ousley (2003) raise the point that although fewer patients have achieved 20/20 vision following endokeratoplasty, the level of astigmatism is generally lower than following PKP.

Conclusions

The technique of endokeratoplasty has undergone several refinements since its initial experimentation on eye bank eyes (Melles *et al.* 1998). While the visual acuity results varied between authors, most consider the procedure advantageous in regards to visual acuity and recovery time. Available results infer endokeratoplasty may be an effective alternative to penetrating keratoplasty (Terry and Ousley 2003).

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Tabulated studies are highlighted in bold.

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cataract surgery. *J Cataract Refract Surg* 2003; 29(12):2401-2406.

***List of Abbreviations Used***

ABK	Aphakic bullous keratopathy
B(S)CVA	Best (spectacle) corrected visual acuity
CF	Counting fingers
D	Diopters
EKP	Endokeratoplasty
FED	Fuchs' Endothelial Dystrophy
HM	Hand movements
K-reading	Keratometry reading
L	Left eye
NR	Not reported
PBK	Pseudophakic bullous keratopathy
PKP	Penetrating keratoplasty
Preop	Preoperative
Postop	Postoperative
PVA	Preoperative visual acuity
R	Right eye
RA	Refractive astigmatism
SD	Standard deviation
SE	Spherical equivalent
UCVA	Uncorrected visual acuity
VA	Visual acuity
[x]	Standard deviation
{x}	Variance not stated



Appendix A: Table of Key Efficacy and Safety Findings

Study Details	Key Efficacy Findings	Key Safety Findings	Appraisal / Comments
Randomised controlled trial			
Al-Fayez 2003, Saudi Arabia (conference abstract) 32 patients, all with PBK Prospectively randomised: PKP (n=17) EKP (n=15) 24 months minimum follow up	24 months minimum follow up: BCVA: No significant difference between groups Visual recovery, postoperative astigmatism: better in EKP group ($P<0.05$)	24 months minimum follow up: All grafts clear in both groups	<u>Potential for bias:</u> Full study details not available. Conference abstract only. <u>Outcome measures and their validity:</u> Well validated outcomes used. <u>Other comments:</u> No peer reviewed publication available.
Al-Fayez 2002, Saudi Arabia¹ (conference abstract) 23 patients, all with PBK Prospectively randomised: PKP (n=12) EKP (n=11) 12 months minimum follow up	12 months minimum follow up: BCVA: No significant difference between groups Visual recovery, postoperative astigmatism: better in EKP group ($P<0.05$)	12 months minimum follow up: All grafts clear in both groups	<u>Potential for bias:</u> Full study details not available. Conference abstract only. <u>Outcome measures and their validity:</u> Well validated outcomes used. <u>Other comments:</u> No peer reviewed publication available.

¹ Probably patient overlap with Al-Fayez 2003.



Study Details	Key Efficacy Findings	Key Safety Findings	Appraisal/Comments
<p>Case series</p> <p>Arffa 2003, USA (conference abstract)</p> <p>28 patients, all with endothelial decompensation</p> <p>Follow up: 6 months</p> <p><u>Sutures:</u> No suturing of donor button to recipient bed</p> <p>Flap sutures removed by 6 months postoperative</p>	<p>6 months postop:</p> <p><u>BSCVA</u> ≥ 20/60 in 16/28 patients</p> <p><u>Refractive astigmatism</u> ≤ 4.5 D in 24/28 patients</p>		<p><u>Potential for bias:</u> Full study details not available. Conference abstract only.</p> <p><u>Outcome measures and their validity:</u> Well validated outcomes used.</p> <p><u>Other comments:</u> No peer reviewed publication available.</p> <p>“...EKP appears to achieve good visual and refractive results in a shorter postoperative time than conventional keratoplasty.”</p>



Study Details	Key Efficacy Findings	Key Safety Findings	Appraisal/Comments																																																																																																																																
<p>Case series</p> <p>Busin et al. 2000, Italy</p> <p>7 patients with ABK, PBK or FED</p> <p>Follow up: 4 to 7 months</p> <p><u>Recipient:</u> Microkeratome cut anterior stromal flap, 160µm thick, 9.5mm diameter</p> <p>Posterior cornea excised with 6.5mm diameter trephine</p> <p><u>Donor:</u> Patients 1-4: Button punched with 7.0mm trephine. Entire thickness of cornea transplanted. Epithelium later removed.</p> <p>Patients 5-7: Anterior 160µm removed, 7.0mm diameter button trephinated</p> <p><u>Sutures:</u> All patients: Button: 4 cardinal 10-0 nylon sutures, running 8-bite antitorque 8-0 polygalactin suture around circumference.</p> <p>Patients 1-4: Epithelium removed.</p>	<p><u>Patient data:</u></p> <table border="1" data-bbox="506 344 1379 501"> <thead> <tr> <th>Patient</th> <th>1</th> <th>2</th> <th>3</th> <th>4</th> <th>5</th> <th>6</th> <th>7</th> </tr> </thead> <tbody> <tr> <td>Age</td> <td>67</td> <td>72</td> <td>76</td> <td>69</td> <td>58</td> <td>73</td> <td>74</td> </tr> <tr> <td>Sex</td> <td>M</td> <td>F</td> <td>F</td> <td>M</td> <td>M</td> <td>F</td> <td>M</td> </tr> <tr> <td>Condition diagnosed</td> <td>PBK</td> <td>ABK</td> <td>PBK</td> <td>PBK</td> <td>PBK</td> <td>FED</td> <td>ABK</td> </tr> <tr> <td>PVA</td> <td>HM</td> <td>CF</td> <td>HM</td> <td>CF</td> <td>HM</td> <td>20/400</td> <td>CF</td> </tr> </tbody> </table> <p><u>1 month postop:</u></p> <table border="1" data-bbox="506 549 1379 730"> <tbody> <tr> <td>UCVA</td> <td>20/200</td> <td>20/400</td> <td>20/100</td> <td>20/200</td> <td>20/400</td> <td>20/200</td> <td>20/200</td> </tr> <tr> <td>BCVA</td> <td>20/60</td> <td>20/60</td> <td>20/80</td> <td>20/80</td> <td>20/100</td> <td>20/40</td> <td>20/60</td> </tr> <tr> <td>SE (D)</td> <td>-2.75</td> <td>-4.00</td> <td>-2.00</td> <td>-2.00</td> <td>-1.50</td> <td>-1.00</td> <td>-1.50</td> </tr> <tr> <td>RA (D)</td> <td>2.00</td> <td>3.75</td> <td>3.25</td> <td>3.00</td> <td>2.00</td> <td>1.50</td> <td>2.50</td> </tr> <tr> <td>Mean K-reading (D)</td> <td>48.50</td> <td>46.25</td> <td>48.00</td> <td>46.50</td> <td>45.75</td> <td>46.00</td> <td>45.75</td> </tr> </tbody> </table> <p><u>At time of review:</u></p> <table border="1" data-bbox="506 778 1379 1011"> <tbody> <tr> <td>Months postop</td> <td>7</td> <td>6</td> <td>6</td> <td>5*</td> <td>4</td> <td>4</td> <td>4</td> </tr> <tr> <td>UCVA</td> <td>20/200</td> <td>20/200</td> <td>20/100</td> <td>20/400</td> <td>20/400</td> <td>20/80</td> <td>20/200</td> </tr> <tr> <td>BCVA</td> <td>20/40</td> <td>20/60</td> <td>20/60</td> <td>20/100</td> <td>20/100</td> <td>20/30</td> <td>20/80</td> </tr> <tr> <td>SE</td> <td>-1.75</td> <td>-2.75</td> <td>-2.00</td> <td>1.50</td> <td>-1.00</td> <td>-1.25</td> <td>-1.50</td> </tr> <tr> <td>RA</td> <td>2.25</td> <td>3.00</td> <td>3.50</td> <td>5.00</td> <td>3.00</td> <td>1.50</td> <td>2.00</td> </tr> <tr> <td>Mean K-reading (D)</td> <td>46.00</td> <td>45.50</td> <td>47.00</td> <td>41.50</td> <td>45.25</td> <td>46.00</td> <td>45.00</td> </tr> </tbody> </table> <p>RA readings: medium-low * Corneal flap removed after 3 month postoperative examination. Data in table refers to examination 2 months post flap removal.</p> <p>Regular astigmatism from topographical analysis</p>	Patient	1	2	3	4	5	6	7	Age	67	72	76	69	58	73	74	Sex	M	F	F	M	M	F	M	Condition diagnosed	PBK	ABK	PBK	PBK	PBK	FED	ABK	PVA	HM	CF	HM	CF	HM	20/400	CF	UCVA	20/200	20/400	20/100	20/200	20/400	20/200	20/200	BCVA	20/60	20/60	20/80	20/80	20/100	20/40	20/60	SE (D)	-2.75	-4.00	-2.00	-2.00	-1.50	-1.00	-1.50	RA (D)	2.00	3.75	3.25	3.00	2.00	1.50	2.50	Mean K-reading (D)	48.50	46.25	48.00	46.50	45.75	46.00	45.75	Months postop	7	6	6	5*	4	4	4	UCVA	20/200	20/200	20/100	20/400	20/400	20/80	20/200	BCVA	20/40	20/60	20/60	20/100	20/100	20/30	20/80	SE	-1.75	-2.75	-2.00	1.50	-1.00	-1.25	-1.50	RA	2.25	3.00	3.50	5.00	3.00	1.50	2.00	Mean K-reading (D)	46.00	45.50	47.00	41.50	45.25	46.00	45.00	<p>1 case of interface epithelial growth in patient that received full thickness graft. Corneal flap subsequently removed. Donor button resutured.</p> <p>All corneas cleared</p> <p>Re-epithelialisation completed in all patients by 4 weeks postop.</p>	<p><u>Potential for bias:</u> The method of patient selection was not stated, therefore it could not be assessed whether the patient sample was biased.</p> <p><u>Outcome measures and their validity:</u> Well validated outcomes used. Note: mean K-reading without meridian used to report keratometry.</p> <p><u>Other comments:</u> “...All patients could be refracted as early as one month after surgery, a time when this is not usually not possible for PK (penetrating keratoplasty) patients.”</p> <p>“...a regular medium- to low-degree astigmatism was present in all patients, making it possible for them to improve their uncorrected vision considerably simply by spectacle correction.”</p>
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<p>All patients: Cardinal sutures removed, flap replaced and properly aligned.</p> <p>Flap: running 8-bite antitorque 10-0 nylon suture.</p> <p>Polygalactin suture dissolved by end of second postoperative month in all cases. 10-0 nylon running suture removed between 3 and 4 months postop.</p>			
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Study Details	Key Efficacy Findings	Key Safety Findings	Appraisal/Comments																														
<p>Case series</p> <p>Ehlers et al. 2000, Denmark</p> <p>3 patients, 4 eyes; all with PBK</p> <p>Follow up: 12 months</p> <p><u>Recipient:</u> Microkeratome cut anterior stromal flap, 200µm thick, 9.0mm diameter</p> <p>Posterior cornea excised with 7.0mm diameter trephine</p> <p><u>Donor:</u> Epithelium removed. Anterior 200µm removed, 7.0mm diameter button punched.</p> <p><u>Sutures:</u> Button: 16 10-0 absorbable vicryl sutures. Flap: interrupted 10-0 nylon sutures with buried knots.</p> <p>Nylon sutures removed when loose or after 6 months. Intrastromal vicryl sutures disappeared within 6 months.</p>	<p>12 months postop:</p> <table border="1" data-bbox="506 344 1368 528"> <thead> <tr> <th>Patient</th> <th>1 (L)</th> <th>2a (L)</th> <th>2b (R)</th> <th>3 (R)</th> </tr> </thead> <tbody> <tr> <td>Age</td> <td>79</td> <td>71</td> <td>72</td> <td>78</td> </tr> <tr> <td>Sex</td> <td>F</td> <td>M</td> <td>M</td> <td>M</td> </tr> <tr> <td>Condition diagnosed</td> <td>PBK</td> <td>PBK</td> <td>PBK</td> <td>PBK</td> </tr> <tr> <td>Pre-op BCVA</td> <td>0.05 (20/400)</td> <td>HM</td> <td>1/60 (20/1200)</td> <td>1/60 (20/1200)</td> </tr> <tr> <td>Post-op BCVA</td> <td>0.16 (20/125)</td> <td>0.10 (20/200)</td> <td>0.05 (20/400)</td> <td>0.10 (20/200)</td> </tr> </tbody> </table>	Patient	1 (L)	2a (L)	2b (R)	3 (R)	Age	79	71	72	78	Sex	F	M	M	M	Condition diagnosed	PBK	PBK	PBK	PBK	Pre-op BCVA	0.05 (20/400)	HM	1/60 (20/1200)	1/60 (20/1200)	Post-op BCVA	0.16 (20/125)	0.10 (20/200)	0.05 (20/400)	0.10 (20/200)	<p>Epithelial island aspirated from flap-graft interface at 1 month post operative (all patients) and 2 months (patient 2b).</p> <p>All corneas clear at 12 months postop.</p> <p>No wound dehiscence.</p> <p>No sign of immunologic rejection.</p>	<p><u>Potential for bias:</u> The method of patient selection was not stated, therefore it could not be assessed whether the patient sample was biased.</p> <p><u>Outcome measures and their validity:</u> Well validated outcomes used.</p> <p><u>Other comments:</u> “...new technique has so far been more time consuming than the established technique and technically more demanding.”</p>
Patient	1 (L)	2a (L)	2b (R)	3 (R)																													
Age	79	71	72	78																													
Sex	F	M	M	M																													
Condition diagnosed	PBK	PBK	PBK	PBK																													
Pre-op BCVA	0.05 (20/400)	HM	1/60 (20/1200)	1/60 (20/1200)																													
Post-op BCVA	0.16 (20/125)	0.10 (20/200)	0.05 (20/400)	0.10 (20/200)																													



Study Details	Key Efficacy Findings	Key Safety Findings	Appraisal/Comments																																																																
<p>Case series</p> <p>Guell et al. 2003, Spain</p> <p>3 patients, FED</p> <p>Follow up: 12 to 14 months</p> <p><u>Recipient:</u> Microkeratome cut anterior flap, 250µm thick, 8.5mm diameter.</p> <p>Posterior cornea excised with 7.0mm trephine</p> <p><u>Donor:</u> Anterior 250µm removed, 7.0mm diameter button trephinated.</p> <p><u>Sutures:</u> Button: 6 10-0 nylon interrupted sutures Flap: 6 interrupted 10-0 nylon sutures, buried knots.</p> <p>All nylon sutures removed before 6 months.</p>	<p><i>Patient data:</i></p> <table border="1" data-bbox="506 344 1368 451"> <thead> <tr> <th>Patient</th> <th>1 (R)</th> <th>2 (L)</th> <th>3 (L)</th> </tr> </thead> <tbody> <tr> <td>Age</td> <td>36</td> <td>57</td> <td>57</td> </tr> <tr> <td>Sex</td> <td>F</td> <td>M</td> <td>M</td> </tr> <tr> <td>Condition diagnosed</td> <td>FED</td> <td>FED</td> <td>NR</td> </tr> </tbody> </table> <p><i>BSCVA:</i></p> <table border="1" data-bbox="506 499 1368 754"> <thead> <tr> <th>Pre-op</th> <th>0.5 (20/40)</th> <th>0.63 (20/32)</th> <th>CF to 0.5m (20/2400)</th> </tr> </thead> <tbody> <tr> <td>2 weeks postop</td> <td>CF to 1m (20/1220)</td> <td>0.1 (20/200)</td> <td>CF to 0.5m (20/2400)</td> </tr> <tr> <td>3 weeks postop</td> <td>0.1 (20/200)</td> <td>0.3 (20/70)</td> <td>CF to 0.5m (20/2400)</td> </tr> <tr> <td>6 months postop</td> <td>0.1 (20/200)</td> <td>0.3 (20/70)</td> <td>HM to 0.5m (20/2400)</td> </tr> <tr> <td>9 months postop</td> <td>0.32 (20/63)</td> <td>0.3 (20/70)</td> <td>HM to 0.5m (20/2400)</td> </tr> <tr> <td>12 months postop</td> <td>0.5 (20/40)</td> <td>0.5 (20/40)</td> <td>HM to 0.5m (20/2400)</td> </tr> </tbody> </table> <p><i>Astigmatism (D):</i></p> <table border="1" data-bbox="506 802 1368 962"> <thead> <tr> <th>Pre-op</th> <th>-0.75</th> <th>-2.00</th> <th>-0.5</th> </tr> </thead> <tbody> <tr> <td>2 weeks postop</td> <td>-7.00</td> <td>-3.00</td> <td>-3.00</td> </tr> <tr> <td>3 weeks postop</td> <td>-7.50</td> <td>-4.00</td> <td>-4.00</td> </tr> <tr> <td>6 months postop</td> <td>-8.50</td> <td>-4.00</td> <td>-4.00</td> </tr> <tr> <td>9 months postop</td> <td>-9.50</td> <td>-3.50</td> <td>-3.50</td> </tr> <tr> <td>12 months postop</td> <td>-6.00</td> <td>-3.50</td> <td>-3.50</td> </tr> </tbody> </table>	Patient	1 (R)	2 (L)	3 (L)	Age	36	57	57	Sex	F	M	M	Condition diagnosed	FED	FED	NR	Pre-op	0.5 (20/40)	0.63 (20/32)	CF to 0.5m (20/2400)	2 weeks postop	CF to 1m (20/1220)	0.1 (20/200)	CF to 0.5m (20/2400)	3 weeks postop	0.1 (20/200)	0.3 (20/70)	CF to 0.5m (20/2400)	6 months postop	0.1 (20/200)	0.3 (20/70)	HM to 0.5m (20/2400)	9 months postop	0.32 (20/63)	0.3 (20/70)	HM to 0.5m (20/2400)	12 months postop	0.5 (20/40)	0.5 (20/40)	HM to 0.5m (20/2400)	Pre-op	-0.75	-2.00	-0.5	2 weeks postop	-7.00	-3.00	-3.00	3 weeks postop	-7.50	-4.00	-4.00	6 months postop	-8.50	-4.00	-4.00	9 months postop	-9.50	-3.50	-3.50	12 months postop	-6.00	-3.50	-3.50	<p>Transparent cornea</p> <p>No signs of rejection</p> <p>Patient 1: When superior sutures removed (3 months postoperatively), separation between anterior cap and edge of corneal recipient eye observed. Two interrupted 10-0 nylon sutures placed for 3 more months</p>	<p><i>Potential for bias:</i> The method of patient selection was not stated, therefore it could not be assessed whether the patient sample was biased.</p> <p><i>Outcome measures and their validity:</i> Well validated outcomes used.</p> <p><i>Other comments:</i> “...recovery time was slower when compared with PK.”</p> <p>“...from a functional perspective penetrating keratoplasty has been a much better and faster approach...”</p>
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Study Details	Key Efficacy Findings	Key Safety Findings	Appraisal/Comments
<p>Case series</p> <p>Melles and Kaminga 2003, Netherlands</p> <p>16 consecutive patients, all with FED or PBK</p> <p>Follow up: 6,12,24,36,48, 60 months</p> <p>One of three procedures performed</p> <p>1) <i>11 patients:</i> 9.0mm scleral incision intracorneal trephine, spoon shaped glide, insert 7.5mm donor disc</p> <p>2) <i>4 patients:</i> 5.0mm scleral tunnel folded 8.5mm donor posterior disc</p> <p>3) <i>1 patient</i> 4.0mm scleral incision Descemet's membrane + endothelium selectively excised, 9.0mm donor inserted</p> <p><u>Sutures:</u> 1) Scleral incision sutured with 10-0 nylon 2) none 3) none</p>	<p><i>BSCVA</i> average: 0.56 (20/36) {0.26} Range: CF - 1.0 (20/20) (n=14)</p> <p>Patients without concomitant ocular disease: <i>BSCVA</i> average: 0.78 (20/26) {0.13} Range: 0.7 (20/29) -1.0 (20/20) (n=9)</p> <p><i>Astigmatism</i> average: 2.1 D {0.7 D} (n=14) Maximum: 3.5 D</p>	<p>2 patients: iridocorneal adhesiolysis within several days postop</p> <p>1 patient: residual viscoelastic adherence at donor-recipient interface, penetrating keratoplasty performed 1 month postop</p> <p>1 patient: developed significant interface haze, penetrating keratoplasty performed 13 months post op</p> <p>1 patient: perforation during dissection of recipient cornea</p> <p>All donor buttons adhered to recipient without sutures.</p>	<p><i>Potential for bias:</i></p> <p><i>Outcome measures and their validity:</i> Well validated outcomes used.</p> <p>Value for CF could not be calculated, as distance from which measurement taken was not reported.</p> <p><i>Other comments:</i> All patients were operated on by the same surgeon.</p> <p>Authors comment BSCVA can be tested much sooner than with PKP.</p>



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<p>Case series</p> <p>Melles et al. 2000, Netherlands</p> <p>7 patients; PBK, ABK FED</p> <p>Follow up: 6 or 12 months</p> <p><u>Recipient:</u> Scleral incision 9.0mm, deep stromal pocket dissected. 7.0mm or 7.5mm diameter flat trephine excised posterior disc.</p> <p><u>Donor:</u> Donor posterior disc, same size as excised disc trephinated, inserted with spoon shaped glide.</p> <p><u>Sutures:</u> Button: none Scleral incision: 10-0 monofilament nylon sutures.</p>	<p><u>Patient data:</u></p> <table border="1"> <thead> <tr> <th>Patient</th> <th>1</th> <th>2</th> <th>3</th> <th>4</th> <th>5*</th> <th>6</th> <th>7</th> </tr> </thead> <tbody> <tr> <td>Age</td> <td>75</td> <td>57</td> <td>82</td> <td>70</td> <td>84</td> <td>70</td> <td>68</td> </tr> <tr> <td>Sex</td> <td>F</td> <td>M</td> <td>M</td> <td>F</td> <td>F</td> <td>F</td> <td>F</td> </tr> <tr> <td>Condition diagnosed</td> <td>PBK</td> <td>PBK</td> <td>FED+ PBK</td> <td>FED+ PBK</td> <td>FED+ ABK</td> <td>FED+ PBK</td> <td>FED+ PBK</td> </tr> </tbody> </table> <p><u>Efficacy:</u></p> <table border="1"> <thead> <tr> <th>Follow up (months)</th> <th>12</th> <th>6</th> <th>12</th> <th>12</th> <th>6</th> <th>6</th> <th>6</th> </tr> </thead> <tbody> <tr> <td colspan="8">BSCVA</td> </tr> <tr> <td>Preop</td> <td>CF</td> <td>CF</td> <td>20/50</td> <td>20/150</td> <td>NR</td> <td>20/80</td> <td>20/200</td> </tr> <tr> <td>Postop</td> <td>20/80</td> <td>20/80</td> <td>20/20</td> <td>20/25</td> <td>NR</td> <td>20/40</td> <td>20/40</td> </tr> <tr> <td colspan="8">SE (D)</td> </tr> <tr> <td>Preop</td> <td>0.0</td> <td>0.0</td> <td>0.0</td> <td>-1.75</td> <td>NR</td> <td>0.5</td> <td>-0.75</td> </tr> <tr> <td>Postop</td> <td>0.0</td> <td>11.5</td> <td>0.0</td> <td>0.25</td> <td>NR</td> <td>0.5</td> <td>-2.0</td> </tr> <tr> <td>K-reading</td> <td>45.50/ 47.00</td> <td>43.25/ 45.00</td> <td>41.25/ 43.00</td> <td>46.00/ 46.25</td> <td>NR</td> <td>45.25/ 46.50</td> <td>44.75/ 47.50</td> </tr> </tbody> </table> <p>*converted to penetrating keratoplasty</p> <p>Astigmatic error average 1.54 D [0.81D]</p>	Patient	1	2	3	4	5*	6	7	Age	75	57	82	70	84	70	68	Sex	F	M	M	F	F	F	F	Condition diagnosed	PBK	PBK	FED+ PBK	FED+ PBK	FED+ ABK	FED+ PBK	FED+ PBK	Follow up (months)	12	6	12	12	6	6	6	BSCVA								Preop	CF	CF	20/50	20/150	NR	20/80	20/200	Postop	20/80	20/80	20/20	20/25	NR	20/40	20/40	SE (D)								Preop	0.0	0.0	0.0	-1.75	NR	0.5	-0.75	Postop	0.0	11.5	0.0	0.25	NR	0.5	-2.0	K-reading	45.50/ 47.00	43.25/ 45.00	41.25/ 43.00	46.00/ 46.25	NR	45.25/ 46.50	44.75/ 47.50	<p>Intra/post operative complications (3/7 patients):</p> <ul style="list-style-type: none"> Elevated intraocular pressure, trabeculectomy performed 1 month postop Continuous vitreous pressure during surgery, peripheral anterior synechiae formed, later loosened Perforation of recipient's stromal bed occurred during stromal pocket dissection, procedure converted to penetrating keratoplasty <p>6/7 patients: all transplants remained <i>in situ</i> without sutures, complete apposition of donor to recipient tissues.</p> <p>All transplants cleared</p> <p>Normal degree of inflammation</p> <p>Minimal scarring</p> <p>Normal healing response</p>	<p><u>Potential for bias:</u> The method of patient selection was not stated, therefore it could not be assessed whether the patient sample was biased.</p> <p><u>Outcome measures and their validity:</u> Well validated outcomes used. Note: two curves reported when measuring keratometry, but no meridian reported.</p> <p><u>Other comments:</u> "...Compared with penetrating keratoplasty, posterior lamellar keratoplasty may have the advantages of less postoperative astigmatism and faster visual recovery, less risk of late wound dehiscence, and elimination of all corneal suture related complications."</p>
Patient	1	2	3	4	5*	6	7																																																																																												
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<p>Case series</p> <p>Terry and Ousley 2003a, USA</p> <p>9 patients, all FED and pseudophakia</p> <p>Follow up: 6 or 12 months</p> <p><u>Recipient:</u> Scleral incision 9.0mm, deep stromal pocket dissected. 7.5 or 8.0mm trephine excised posterior disc.</p> <p><u>Donor:</u> Donor posterior disc, same diameter as excised. Recipient disc inserted on spatula.</p> <p><u>Sutures:</u> Button: none Scleral incision: several interrupted 10-0 nylon sutures.</p>	<p><i>BSCVA:</i></p> <table border="1"> <thead> <tr> <th>Patient</th> <th>1</th> <th>2</th> <th>3</th> <th>4</th> <th>5</th> <th>6</th> <th>8</th> <th>9</th> </tr> </thead> <tbody> <tr> <td>Preop</td> <td>20/50</td> <td>20/200</td> <td>20/60</td> <td>20/100</td> <td>20/40</td> <td>20/200</td> <td>20/200</td> <td>20/200</td> </tr> <tr> <td>Postop 6 months</td> <td>20/40</td> <td>20/40</td> <td>20/70</td> <td>20/70</td> <td>20/30</td> <td>20/70</td> <td>20/70</td> <td>20/50</td> </tr> <tr> <td>Postop 12 months</td> <td>20/40</td> <td>20/40</td> <td>N/R</td> <td>20/60</td> <td>20/30</td> <td>N/R</td> <td>N/R</td> <td>N/R</td> </tr> </tbody> </table> <p><i>UCVA:</i></p> <table border="1"> <thead> <tr> <th>Preop</th> <th>20/100</th> <th>20/200</th> <th>20/80</th> <th>20/200</th> <th>20/70</th> <th>20/200</th> <th>20/200</th> <th>20/200</th> </tr> </thead> <tbody> <tr> <td>Postop 6 months</td> <td>20/60</td> <td>20/70</td> <td>20/200</td> <td>20/200</td> <td>20/50</td> <td>20/200</td> <td>20/200</td> <td>20/200</td> </tr> <tr> <td>Postop 12 months</td> <td>20/100</td> <td>20/70</td> <td>N/R</td> <td>20/200</td> <td>20/200</td> <td>N/R</td> <td>N/R</td> <td>N/R</td> </tr> </tbody> </table> <p><i>Astigmatism (D):</i></p> <table border="1"> <thead> <tr> <th>Preop</th> <th>1.75</th> <th>1.75</th> <th>0.00</th> <th>1.00</th> <th>1.50</th> <th>0.25</th> <th>2.00</th> <th>1.00</th> </tr> </thead> <tbody> <tr> <td>Postop 6 months</td> <td>1.00</td> <td>2.00</td> <td>2.25</td> <td>1.25</td> <td>1.75</td> <td>3.75</td> <td>2.50</td> <td>3.75</td> </tr> <tr> <td>Postop 12 months</td> <td>2.75</td> <td>2.00</td> <td>N/R</td> <td>2.50</td> <td>2.00</td> <td>N/R</td> <td>N/R</td> <td>N/R</td> </tr> </tbody> </table> <p><i>Power of cornea (D): (measured by TMS-topography unit)</i></p> <table border="1"> <thead> <tr> <th>Preop</th> <th>46.4</th> <th>45.4</th> <th>44.4</th> <th>44.5</th> <th>44.3</th> <th>40.4</th> <th>40.3</th> <th>46.1</th> </tr> </thead> <tbody> <tr> <td>Postop 6 months</td> <td>45.3</td> <td>43.3</td> <td>44.4</td> <td>45.3</td> <td>42.8</td> <td>40.9</td> <td>42.8</td> <td>43.6</td> </tr> <tr> <td>Postop 12 months</td> <td>45.4</td> <td>43.9</td> <td>N/R</td> <td>43.5</td> <td>42.6</td> <td>N/R</td> <td>N/R</td> <td>N/R</td> </tr> </tbody> </table> <p>6 months postop: Average astigmatism: 2.28 D {1.03 D} Average change in astigmatism: +1.13 D {0.50 D} (<i>P</i>=0.06) Average change in corneal power: -0.4 D {1.7 D} (<i>P</i>=0.34)</p> <p>12 months postop: All patients noted improved vision compared to preop Average astigmatism: 2.31 D {0.38 D} Average change in astigmatism: +0.81 D {0.55 D} (<i>P</i>=0.06) Average change in corneal power: -1.3 D {0.4 D} (<i>P</i>=0.34)</p>	Patient	1	2	3	4	5	6	8	9	Preop	20/50	20/200	20/60	20/100	20/40	20/200	20/200	20/200	Postop 6 months	20/40	20/40	20/70	20/70	20/30	20/70	20/70	20/50	Postop 12 months	20/40	20/40	N/R	20/60	20/30	N/R	N/R	N/R	Preop	20/100	20/200	20/80	20/200	20/70	20/200	20/200	20/200	Postop 6 months	20/60	20/70	20/200	20/200	20/50	20/200	20/200	20/200	Postop 12 months	20/100	20/70	N/R	20/200	20/200	N/R	N/R	N/R	Preop	1.75	1.75	0.00	1.00	1.50	0.25	2.00	1.00	Postop 6 months	1.00	2.00	2.25	1.25	1.75	3.75	2.50	3.75	Postop 12 months	2.75	2.00	N/R	2.50	2.00	N/R	N/R	N/R	Preop	46.4	45.4	44.4	44.5	44.3	40.4	40.3	46.1	Postop 6 months	45.3	43.3	44.4	45.3	42.8	40.9	42.8	43.6	Postop 12 months	45.4	43.9	N/R	43.5	42.6	N/R	N/R	N/R	<p>9 patients initially enrolled.</p> <p>Patient 7 had microperforation during initial recipient pocket dissection. Converted to penetrating keratoplasty, data not included.</p> <p>First postoperative day: Intact corneal epithelium in all patients.</p> <p>First postoperative day: Considerable clearing of cornea.</p> <p>Moderate interface haze present in several patients.</p>	<p><i>Potential for bias:</i> The method of patient selection was not stated, therefore it could not be assessed whether the patient sample was biased.</p> <p><i>Outcome measures and their validity:</i> Well validated outcomes used. Note: power of cornea reported when measuring corneal curvature.</p> <p><i>Other comments:</i> “...Is a 20/20 result with 5D of astigmatism after penetrating keratoplasty actually better than a 20/30 visual result with no astigmatism after DLEK surgery? Moreover, the risks and complications of penetrating keratoplasty in the short and long term ...inherently are avoided by DLEK surgery. A BSCVA after DLEK surgery of ‘only’ 20/30 in this elderly population may be a desirable tradeoff to 20/20 vision if the potential disasters of penetrating keratoplasty can be avoided securely.”</p>
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Terry and Ousley 2003b, USA² (conference abstract) 23 patients, FED Follow up: 12 months	<i>BSCVA</i> Average: improved from 20/142 preop to 20/48 at 12 months postop <i>SE</i> Average: -0.35 D postop Not significantly different from preop <i>Astigmatism</i> Average: 2.04 D postop Not significantly different from preop		<i>Potential for bias:</i> Full study details not available. Conference abstract only. <i>Outcome measures and their validity:</i> Well validated outcomes used. <i>Other comments:</i> Probable patient overlap with another study.
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² Probably patient overlap with Terry and Ousley 2003a and 2002.



Study Details	Key Efficacy Findings	Key Safety Findings	Appraisal/Comments																																																																																																																																
<p>Case series</p> <p>Terry and Ousley 2003c, USA</p> <p>27 patients, FED</p> <p>Follow up: 6 and 12 months</p> <p>Methods from Terry and Ousley 2003a.</p> <p><u>Recipient:</u> Scleral incision 9.0mm, deep stromal pocket dissected. 7.5 or 8.0mm trephine excised posterior disc.</p> <p><u>Donor:</u> Donor posterior disc, same diameter as excised. Recipient disc inserted on spatula.</p> <p><u>Sutures:</u> Button: none Scleral incision: several interrupted 10-0 nylon sutures.</p>	<p><i>SE (D):</i></p> <table border="1" data-bbox="506 344 1308 525"> <thead> <tr> <th>Patient</th> <th>1</th> <th>2</th> <th>3</th> <th>4</th> <th>5</th> <th>6</th> <th>7</th> </tr> </thead> <tbody> <tr> <td>Preop</td> <td>0.375</td> <td>-0.375</td> <td>0.000</td> <td>-1.250</td> <td>-2.000</td> <td>-0.375</td> <td>*</td> </tr> <tr> <td>Postop 6 months</td> <td>0.000</td> <td>-0.250</td> <td>-0.625</td> <td>-1.375</td> <td>-1.125</td> <td>0.625</td> <td></td> </tr> <tr> <td>Postop 12 months</td> <td>0.875</td> <td>0.000</td> <td>deceased</td> <td>-0.750</td> <td>-1.000</td> <td>2.000</td> <td></td> </tr> </tbody> </table> <table border="1" data-bbox="506 555 1308 678"> <thead> <tr> <th>8</th> <th>9</th> <th>10</th> <th>11</th> <th>12</th> <th>13</th> <th>14</th> <th>15</th> </tr> </thead> <tbody> <tr> <td>6.00</td> <td>0.250</td> <td>0.000</td> <td>-1.250</td> <td>0.625</td> <td>4.750</td> <td>1.125</td> <td>-0.500</td> </tr> <tr> <td>0.750</td> <td>1.125</td> <td>1.500</td> <td>-1.250</td> <td>0.875</td> <td>-4.000</td> <td>0.500</td> <td>-0.375</td> </tr> <tr> <td>1.250</td> <td>2.000</td> <td>0.000</td> <td>-1.875</td> <td>0.375</td> <td>-2.500</td> <td>0.250</td> <td>-1.500</td> </tr> </tbody> </table> <table border="1" data-bbox="506 708 1308 831"> <thead> <tr> <th>16</th> <th>17</th> <th>18</th> <th>19</th> <th>20</th> <th>21</th> <th>22</th> <th>23</th> </tr> </thead> <tbody> <tr> <td>-0.500</td> <td>-0.375</td> <td>-5.750</td> <td>-0.250</td> <td>□</td> <td>0.000</td> <td>-0.250</td> <td>2.375</td> </tr> <tr> <td>-0.375</td> <td>2.750</td> <td>-5.000</td> <td>0.000</td> <td></td> <td>-2.250</td> <td>-0.500</td> <td>2.250</td> </tr> <tr> <td>-0.250</td> <td>NA</td> <td>-3.750</td> <td>-0.250</td> <td></td> <td>-2.625</td> <td>-0.125</td> <td>NA</td> </tr> </tbody> </table> <table border="1" data-bbox="506 861 1308 984"> <thead> <tr> <th>24</th> <th>25</th> <th>26</th> <th>27</th> <th>28</th> <th>29</th> <th>Mean</th> <th>SD</th> </tr> </thead> <tbody> <tr> <td>-2.625</td> <td>1.000</td> <td>0.500</td> <td>-5.500</td> <td>0.000</td> <td>-1.500</td> <td>-0.204</td> <td>2.376</td> </tr> <tr> <td>-5.00</td> <td>-2.375</td> <td>0.250</td> <td>-0.750</td> <td>-0.500</td> <td>-1.125</td> <td>-0.435</td> <td>1.673</td> </tr> <tr> <td>NA</td> <td>NA</td> <td>NA</td> <td>NA</td> <td>NA</td> <td>NA</td> <td>-0.438</td> <td>1.567</td> </tr> </tbody> </table> <p>*converted to penetrating keratoplasty because of difficulties during recipient lamellar dissection □converted to penetrating keratoplasty following perforation in to the anterior chamber</p>	Patient	1	2	3	4	5	6	7	Preop	0.375	-0.375	0.000	-1.250	-2.000	-0.375	*	Postop 6 months	0.000	-0.250	-0.625	-1.375	-1.125	0.625		Postop 12 months	0.875	0.000	deceased	-0.750	-1.000	2.000		8	9	10	11	12	13	14	15	6.00	0.250	0.000	-1.250	0.625	4.750	1.125	-0.500	0.750	1.125	1.500	-1.250	0.875	-4.000	0.500	-0.375	1.250	2.000	0.000	-1.875	0.375	-2.500	0.250	-1.500	16	17	18	19	20	21	22	23	-0.500	-0.375	-5.750	-0.250	□	0.000	-0.250	2.375	-0.375	2.750	-5.000	0.000		-2.250	-0.500	2.250	-0.250	NA	-3.750	-0.250		-2.625	-0.125	NA	24	25	26	27	28	29	Mean	SD	-2.625	1.000	0.500	-5.500	0.000	-1.500	-0.204	2.376	-5.00	-2.375	0.250	-0.750	-0.500	-1.125	-0.435	1.673	NA	NA	NA	NA	NA	NA	-0.438	1.567	<p>39 patients enrolled in study. Results from first consecutive 27 patients to receive DLEK surgery with at least the 6 month postoperative time gate reported.</p> <p>Text in paper reports procedure converted to penetrating keratoplasty in patients 7 and 21. Table reports conversion conducted in patients 7 and 20.</p>	<p><i>Potential for bias:</i> The method of patient selection was not stated, therefore it could not be assessed whether the patient sample was biased.</p> <p><i>Outcome measures and their validity:</i> Well validated outcomes used. Corneal curvature measured with topographic analysis, therefore not comparable to other included studies.</p> <p><i>Other comments:</i> All surgeries performed by same surgeon.</p> <p>“...The need for contact lenses, relaxing incisions, and LASIK to treat unexpected ametropias after transplantation in our elderly Fuch’s population will be reduces, if not eliminated entirely, by the DLEK technique.”</p>
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Study Details	Key Efficacy Findings	Key Safety Findings	Appraisal/Comments
<p>Case series</p> <p>Terry and Ousley 2002, USA³ (conference abstract)</p> <p>24 patients, FED</p> <p>Follow up: 6 and 12 months</p>	<p><i>Average Visual Acuity:</i> Preop: 20/200 6 months postop: 20/66 12 months postop: 20/49</p> <p><i>Average Astigmatism:</i> 6 and 12 month results within 1 D of preop</p> <p><i>Average SE:</i> 6 and 12 month results within 1 D of preop</p>		<p><i>Potential for bias:</i> Full study details not available. Conference abstract only.</p> <p><i>Outcome measures and their validity:</i> Well validated outcomes used.</p> <p><i>Other comments:</i> Probable patient overlap with another study.</p>

³ Probably patient overlap with Terry and Ousley 2003a and 2003b.



Study Details	Key Efficacy Findings	Key Safety Findings	Appraisal/Comments
Case report			
<p>Azar DT <i>et al.</i> 2001, USA</p> <p>1 patient; 94 year old female, PBK</p> <p>Follow up: 2 years</p> <p><u>Recipient:</u> Microkeratome cut anterior stromal flap, 130µm thick, 8.5mm diameter</p> <p>Posterior cornea excised with 6.0mm diameter trephine</p> <p><u>Donor:</u> Anterior 130 µm removed, button punched with 6.0mm trephine</p> <p><u>Sutures:</u> Button: 15 interrupted 10-0 nylon sutures Flap: 5 interrupted 10-0 nylon sutures</p>	<p><i>6 months postop</i> Spherical equivalent +16.0 D BSCVA 20/50</p> <p><i>2 years postop</i> UCVA 20/100</p>	<p><i>6 months postop</i> Extremely flattened cornea</p> <p><i>2 years postop</i> Graft recipient interface showed mild haze</p>	<p><u>Potential for bias:</u> The method of patient selection was not stated, therefore it could not be assessed whether the patient sample was biased.</p> <p><u>Outcome measures and their validity:</u> Well validated outcomes used.</p> <p><u>Other comments:</u> “...Melles <i>et al.</i> (1998) ...using a scleral tunnel incision to create a midstromal pocket followed by excision of a posterior lamellar disc... This approach has potential benefits (i.e., reduced surgical time; less risk of suture-induced vascularisation and wound dehiscence). However, endothelial injury may occur during the positioning of the donor disc, a surgical manoeuvre that is avoided in our approach.”</p>



Study Details	Key Efficacy Findings	Key Safety Findings	Appraisal/Comments
Case report			
<p>Melles et al. 1999a, Netherlands</p> <p>1 patient; 64 year old female, PBK (pre-existing maculopathy)</p> <p>Follow up: 3 months</p> <p><u>Recipient:</u> Scleral tunnel incision 9.0mm, midstromal pocket dissected. 7.0mm diameter flat trephine excised posterior disc.</p> <p><u>Donor:</u> Donor posterior disc, 7.0mm diameter, placed with spoon shaped glide.</p> <p><u>Sutures:</u> Button: none Scleral incision: running 10-0 monofilament nylon suture.</p>	<p><i>Three months post-op</i> (Sutures still in place) K-reading: 41.05 x175° / 45.00 x 80° Astigmatic error: 3.5 D BCVA: 20/80</p>	<p><i>1 day postop</i> Minimal stromal oedema Some folds in Descemet's membrane Complete apposition of donor and recipient stromal surfaces</p>	<p><u>Potential for bias:</u> The method of patient selection was not stated, therefore it could not be assessed whether the patient sample was biased.</p> <p><u>Outcome measures and their validity:</u> Well validated outcomes used. Note: Two keratometry values given with meridian.</p> <p><u>Other comments:</u> "...Compared with full-thickness keratoplasty performed for posterior corneal disorders, posterior lamellar keratoplasty may have several advantages..."</p>



Study Details	Key Efficacy Findings	Key Safety Findings	Appraisal/Comments
Case report			
<p>Melles et al. 2002b, Netherlands</p> <p>1 patient; 62 year old male, PBK</p> <p>Follow up: 12 months</p> <p><u>Recipient:</u> Scleral tunnel incision 5.0mm, midstromal pocket dissected, visually controlled depth. 8.5mm diameter posterior disc excised with microscissors.</p> <p><u>Donor:</u> Full thickness posterior disc, 8.5mm diameter, folded and placed with custom made inserter.</p> <p><u>Sutures:</u> Button: none Scleral incision: none</p>	<p><i>Preop</i> VA: 0.4 (20/50) SE: -2.25 D Astigmatism: -1.25 D (x110°)</p> <p><i>1 week postop</i> BCVA: 0.8 SE: -1.0 D Astigmatism: -1.0 D (x85°) K-readings: 42.75 D x100° / 45.00 D x 10°</p> <p><i>1 year postop</i> BCVA: 0.8 (20/25) SE: -1.5 D Astigmatism: -1.75 D (x80°) K-readings: 42.25 D x 80° / 44.25 D x 10°</p>	<p><i>1 day postop</i> Minimal stromal edema</p> <p><i>1 week postop</i> Transplant cleared</p> <p><i>1 year postop</i> Minimal scarring between donor and recipient stromal surfaces</p>	<p><u>Potential for bias:</u> The method of patient selection was not stated, therefore it could not be assessed whether the patient sample was biased.</p> <p><u>Outcome measures and their validity:</u> Well validated outcomes used. Note: Two keratometry values given with meridian.</p> <p><u>Other comments:</u> “...Compared to full thickness keratoplasty performed for posterior corneal disorders, posterior lamellar keratoplasty may have an advantage because a fast visual recovery with a relatively stable refractive error of the eye may be achieved within the first few weeks after surgery”</p> <p>“...Donor tissue may be used more efficiently”</p>



Study Details	Key Efficacy Findings	Key Safety Findings	Appraisal/Comments
Case report			
<p>Perez et al. 2003, USA</p> <p>1 patient; 79 year old female, PBK</p> <p>Follow up: 12 months</p> <p><u>Recipient:</u> Microkeratome cut anterior flap, 150µm thick, 9.5mm diameter</p> <p>Posterior cornea excised with 6.0mm trephine and corneal scissors</p> <p><u>Donor:</u> Excimer laser ablated cornea to 350µm thickness. Button trephined (6.5mm diameter).</p> <p><u>Sutures:</u> Button: interrupted 10-0 nylon sutures Flap: sutured with 8 interrupted 10-0 nylon sutures</p>	<p>Preop UCVA: left eye 20/200</p> <p>7 months postop UCVA: left eye 20/125</p> <p>12 months postop BCVA: left eye 20/70 With contact lens: 20/40</p>	<p>5 months postop Island of epithelial cells between host and donor tissue noted</p> <p>7 months postop Corneal flap lifted, epithelial cells removed</p>	<p><u>Potential for bias:</u> The method of patient selection was not stated, therefore it could not be assessed whether the patient sample was biased.</p> <p><u>Outcome measures and their validity:</u> Well validated outcomes used.</p> <p><u>Other comments:</u> “...The 2 surgical approaches have been shown as effective in visual restoration and in survival of the transplanted posterior stroma and endothelium in preliminary clinical studies performed in Europe and the United States. However, long-term follow-up studies are needed to determine whether these techniques will become safe and effective alternatives to PKP.”</p>



Study Details	Key Efficacy Findings	Key Safety Findings	Appraisal/Comments																																								
Case report																																											
<p>Shiuey and Moshirfar 2001, USA</p> <p>1 patient; 70 year old male, FED Has intraocular lens.</p> <p>Follow up: 2 months</p> <p><u>Recipient:</u> Microkeratome cut 300µm flap. 5.5mm diameter trephine excised posterior disc.</p> <p><u>Donor:</u> Thinned using laser to 350µm. 6.0mm diameter button trephinated.</p> <p><u>Sutures:</u> Button: 8-bite running 10-0 nylon suture. Flap: 3 sets tension sutures passed over flap.</p> <p>One tension suture removed on the third postoperative day. Remaining 2 sutures removed 1 week postoperative.</p>	<table border="1" data-bbox="499 352 1173 563"> <thead> <tr> <th></th> <th><i>BSCVA</i></th> <th><i>UCVA</i></th> <th><i>SE</i></th> <th><i>Astigmatism</i></th> </tr> </thead> <tbody> <tr> <td>Preop</td> <td>20/200</td> <td>NR</td> <td>NR</td> <td>NR</td> </tr> <tr> <td>Postop</td> <td></td> <td></td> <td></td> <td></td> </tr> <tr> <td>1 day</td> <td>NR</td> <td>20/400</td> <td>NR</td> <td>NR</td> </tr> <tr> <td>3 days</td> <td>NR</td> <td>20/400</td> <td>NR</td> <td>NR</td> </tr> <tr> <td>1 week</td> <td>NR</td> <td>20/400</td> <td>NR</td> <td>NR</td> </tr> <tr> <td>1 month</td> <td>20/200</td> <td>NR</td> <td>-5.0 D</td> <td>8.00 D x90°</td> </tr> <tr> <td>2 months</td> <td>20/100</td> <td>NR</td> <td>-4.5 D</td> <td>8.00 D x60°</td> </tr> </tbody> </table>		<i>BSCVA</i>	<i>UCVA</i>	<i>SE</i>	<i>Astigmatism</i>	Preop	20/200	NR	NR	NR	Postop					1 day	NR	20/400	NR	NR	3 days	NR	20/400	NR	NR	1 week	NR	20/400	NR	NR	1 month	20/200	NR	-5.0 D	8.00 D x90°	2 months	20/100	NR	-4.5 D	8.00 D x60°	<p>Intact epithelium from day 1 postoperative.</p> <p>No displacement of flap</p> <p>No inflammation at stromal interface</p> <p>Donor button showed 3+ oedema with Descemet's folds on day 1, decreasing to trace oedema with resolution of Descemet's folds by 2 months postop</p>	<p><u>Potential for bias:</u> The method of patient selection was not stated, therefore it could not be assessed whether the patient sample was biased.</p> <p><u>Outcome measures and their validity:</u> Well validated outcomes used.</p> <p><u>Other comments:</u> "...The use of infant donor corneas has 2 potential advantages. The first is that these corneas are rich in endothelial cells...Theoretically, having a higher endothelial cell count translates into faster resolution of corneal oedema and greater longevity of the graft...The second potential advantage is that infant corneas represent a new source of tissue that was previously unusable."</p>
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Appendix B: *Included and Excluded Studies*

Author	Study Design	BSCVA	UCVA	Spherical Equivalent (D)	Refractive Astigmatism (D)	Keratometry Reading (D)	Central Corneal Thickness	Endothelial Cell Count	SRI	SAI	Axis
Al-Fayez 2003	Prospectively randomised trial (n=32)	✓(desc)			✓(desc)			✓(desc)			
Al-Fayez 2002	Prospectively randomised trial (n=23)	✓(desc)			✓(desc)			✓(desc)			
Arffa 2003	Case series (n=28)	✓(sum)			✓(sum)						
Azar <i>et al.</i> 2001	Case report	✓	✓	✓							
Behrens <i>et al.</i> 2003	Cadaver study				✓						
Busin <i>et al.</i> 2003	Case report	✓ ⁴									
Busin <i>et al.</i> 2000	Case series (n=7)	✓	✓	✓	✓	✓(ave)					
Ehlers <i>et al.</i> 2000	Case series (n=3)	✓					✓				
Guell <i>et al.</i> 2003	Case series (n=3)	✓			✓			✓			
Li <i>et al.</i> 2002	Eye bank eyes				✓(Δ)	✓(Δ)					
Melles and Kamminga 2003	Case series (n=16)	✓(ave)			✓(ave)			✓(ave)			
Melles <i>et al.</i> 2002a	Eye bank eyes				✓(ave)						
Melles <i>et al.</i> 2002b	Case report	✓		✓	✓	✓					✓
Melles <i>et al.</i> 2000	Case series (n=7)	✓		✓		✓	✓	✓			
Melles <i>et al.</i> 1999a	Case report	✓				✓	✓				
Melles <i>et al.</i> 1998	Eye bank eyes				✓(ave)			Cell death			
Perez <i>et al.</i> 2003	Case report	✓	✓								
Shiuey and Moshirfar 2001	Case report	✓	✓	✓	✓						
Terry and Ousley 2003a	Case series (n=8)	✓	✓		✓	✓(ave)	✓	✓	✓	✓	
Terry and Ousley 2003b	Case series (n=23)	✓(ave)		✓(ave)	✓(ave)			✓(ave)			
Terry and Ousley 2003c	Case series (n=27)			✓(actual, ave)							
Terry and Ousley 2002	Case series (n=24)	✓(ave)		✓(ave)							
Terry and Ousley 2001	Eye bank eyes				✓(actual, Δ)	✓(ave, Δ)					✓

⁴ Reported results after procedure converted to penetrating keratoplasty