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Department of Health and Ageing



Australia and New Zealand Horizon Scanning Network

ANZHSN

AN INITIATIVE OF THE NATIONAL, STATE AND
TERRITORY GOVERNMENTS OF AUSTRALIA
AND THE GOVERNMENT OF NEW ZEALAND

Horizon Scanning Technology Prioritising Summary

Artificial Corneas

November 2010



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PRIORITISING SUMMARY

REGISTER ID: 000519

NAME OF TECHNOLOGY: ARTIFICIAL CORNEAS

PURPOSE AND TARGET GROUP: CORNEAL REPLACEMENT IN PATIENTS
CONSIDERED HIGH RISK FOR CONVENTIONAL
KERATOPLASTY

STAGE OF DEVELOPMENT (IN AUSTRALIA):

- | | | | |
|-------------------------------------|--------------------|--------------------------|--|
| <input type="checkbox"/> | Yet to emerge | <input type="checkbox"/> | Established |
| <input type="checkbox"/> | Experimental | <input type="checkbox"/> | Established <i>but</i> changed indication or modification of technique |
| <input checked="" type="checkbox"/> | Investigational | <input type="checkbox"/> | Should be taken out of use |
| <input type="checkbox"/> | Nearly established | | |

AUSTRALIAN THERAPEUTIC GOODS ADMINISTRATION APPROVAL

- | | | |
|-------------------------------------|----------------|-------------|
| <input type="checkbox"/> | Yes | ARTG number |
| <input checked="" type="checkbox"/> | No | |
| <input type="checkbox"/> | Not applicable | |

In 2004 the AlphaCor™ was listed on the Australian Register of Therapeutic Goods (ARTG no. 83042, product ID 154882), however this listing is no longer current.

INTERNATIONAL UTILISATION:

COUNTRY	LEVEL OF USE		
	Trials Underway or Completed	Limited Use	Widely Diffused
Germany	✓		
Australia	✓		
Canada	✓		
United States	✓		

IMPACT SUMMARY:

In 2004, the ANZHSN wrote a brief summary on the use of the AlphaCor artificial cornea (see end of this summary) for patients considered at risk for conventional keratoplasty. Preliminary evidence indicated that the AlphaCor was likely to be effective in a small group of patients who have no other treatment alternatives. Further safety and effectiveness evidence was sought for this technology in 2005, however no new evidence had been published. This current summary is therefore an update on the AlphaCor and other artificial corneas.

BACKGROUND

The cornea focuses light onto the retina and therefore injury or disease that can cause opacification of the cornea may lead to visual impairment and in some cases,

blindness. In addition, the cornea acts as a barrier, providing protection to the intraocular structures and therefore needs to have strength as well as transparency. Currently the only routine treatment for corneal blindness is corneal transplantation with human donor corneas (Griffith et al 2002).

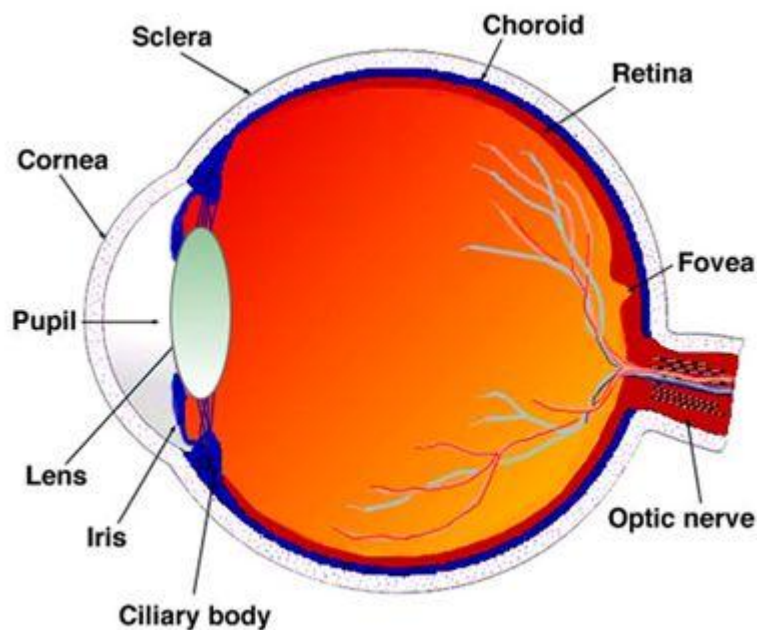


Figure 1 The human eye © Webvision (printed with permission (Kolb et al 2009))

Artificial corneas are indicated for patients who are not suitable candidates for donor grafts. The indications for corneal transplant include:

- The restoration of the shape of the cornea. Conditions such as keratoconus, a cone-like protrusion of the surface of the cornea, resulting in a loss of shape of the cornea, leading to a loss of focusing power and resulting in blindness.
- Restoration of clarity. Conditions such as bullous keratopathy form painful ulcers on the surface of the cornea preventing light from entering the eye, resulting in vision loss.
- Restoration of the integrity of the cornea after the removal of infected corneal tissue (microbial keratitis) which could ulcerate and perforate. Corneal replacement may be required after corneal perforation after sharp trauma (CERA 2010).

Possible reasons for excluding a donor graft option include poor ocular surface quality, degree of deep vascularisation and previously failed grafts¹ (Griffith et al 2002).

The specific conditions that can be indications for corneal transplantation (in order of prevalence in Australia) include: keratoconus, bullous keratopathy, failed previous corneal transplant, corneal dystrophy (e.g. Fuch's dystrophy), herpetic eye disease, corneal scars and opacities, corneal ulcers (not due to herpes), accidental injury,

¹ Repeated corneal grafts are less likely to succeed with each successive graft, particularly in the face of high risk factors such as vascularisation. The study by Bersudsky et al (2001) reported that graft survival was 0% by the fourth graft.

bacterial, fungal, parasitic or viral eye infections other than herpes, interstitial keratitis, descemetocoele and congenital abnormalities such as Peter’s anomaly (CERA 2010).

The Australian Corneal Graft Registry has the outcomes of more than 20,000 transplants registered. Transplant outcomes usually depend on the initial indication for transplantation. The majority of all corneal transplant failures are due to immunologic causes seemingly independent of HLA² matching as the cornea appears to have a unique immunological response compared to other transplanted organs that is not yet fully understood. Although corticosteroids can suppress immune rejection it still occurs in approximately 15 per cent of transplanted donor corneas. A high risk transplant is defined by the degree of inflammation and vascularisation in the eye irrespective of HLA matching. The success rates of corneal transplantation using data from the Australian Corneal Graft Registry are summarised in Table 1 (CERA 2010).

Table 1 Success of corneal transplantations, 2007

	1 year	5 years	10 years	15 years
All indications	86%	73%	61%	50%
Keratoconus	96%	93%	87%	75%
Burns	73%	57%	22%	n/a

As artificial corneas are synthetic, patients do not require long term systemic immune-suppressant therapy. The development of artificial corneas would enable a consistent supply for transplantation, reduce disease transmission and reduce post-transplantation complications (Griffith et al 2002).

An artificial cornea would have to provide strength, transparency and refractive power similar to that of a human cornea, in addition to being oxygen and nutrient permeable, and should not elicit any immune or inflammatory response. The structural material of the cornea is primarily type I collagen. Synthetic polymers including hydrogels, that are hydrophilic and water-retaining, and silicon based polymers have been used to attempt to mimic the natural properties of the cornea. The ideal artificial cornea would have a flexible, transparent optical core surrounded by a porous “skirt”, which would be implanted in the same way as a penetrating keratoplasty. Firm anchorage and integration with host eye tissue should be achieved by fibroblast ingrowth and deposition of collagen, which would be made possible by the porous nature of the skirt. In addition, the outer surface of the artificial cornea should be capable of inhibiting cellular proliferation and attachment to prevent opacification of the membrane (Griffith et al 2002).

The AlphaCor™ (Addition Technology Inc) is a core-and-skirt hydrogel artificial cornea that satisfies all of these criteria. Implantation of the device is a two-stage procedure. The recipient cornea is first dissected to form a 7mm intra-stromal pocket and the device is placed into the pocket after the central 3mm of the posterior lamella is removed. This pocket is closed up and a conjunctival flap is formed to cover the anterior surface of the cornea. After 12-weeks the layers anterior to the device are removed over the central 3mm, exposing the device as a full thickness corneal replacement (Hicks et al 2006).

² HLA = human leukocyte antigen: HLAs are proteins expressed on the surface of cells which are used by the immune system to differentiate self from non-self (Wikipedia 2010).

In the long-term it is hoped that cell-based, tissue-engineered corneal replacements that would more closely mimic the natural cornea will be able to be used to meet all corneal transplant requirements (Griffith et al 2002). Early animal studies have been conducted on artificial corneas composed of 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide and N-hydroxysuccinimide mixed with either porcine type I collagen (10%) (Liu et al 2006) or recombinant human collagen (13.7%) (Merrett et al 2008). Both of these studies reported good results 6-12 months post-implantation, with stable integration and maintenance of optical clarity. The second of these prototypes is the basis for the most recent generation of biosynthetic corneas described below (Fagerholm et al 2010).

CLINICAL NEED AND BURDEN OF DISEASE

Keratoprosthesis is not designed to replace corneal transplantation as a first option for corneal disease, and thus organ donation rates will not reflect the true need for this technology. However, due to the difficulty in estimating the number of patients who would require keratoprosthesis a simple overview of the number of corneal transplants is given.

In Australia and New Zealand the most common condition requiring corneal transplantation is keratoconus, with transplantation usually in individuals aged 15-30 years. Keratoconus has an unknown aetiology but may have a genetic basis. Due to the prevalence of keratoconus more than half of all corneal transplant recipients are under 50 years of age (CERA 2010).

Although organ donation rates are low in Australia compared to many developed countries, the rate of corneal donations at just over 60 per million population compares favourably with other countries. In 2009 there were 1,032 donors in Australia and New Zealand resulting in 1,679 corneal transplants. The waiting list may have up to 500 patients waiting for corneal transplantation in Australia and New Zealand. Although the waiting list has not increased markedly over the past few years, indicating that requirements for Australia and New Zealand are almost being met by donation, there is still a shortage of organs. This shortage may increase with an increase in the number of patients requiring transplantation. However due to the ease of matching patients with corneas compared to other organs, the Australia and New Zealand Eye Bank Association has ensured that since 1991, in an emergency situation, no eye has been lost for want of a corneal transplant (CERA 2010)

The Australia and New Zealand Organ Donation Registry records all donations of corneas from solid organ donors and does not include cases of cornea only donation. In 2009 there were a total of 247 and 43 corneal donors in Australia and New Zealand, respectively. In Australia, no request for corneal donation was made in 36 of these cases and consent was not received in a further 62 cases. Of the remaining 149 potential donors, 97 corneas were not retrieved, leaving a total of 201 retrieved corneas. Of these, 13 were not used and 188 were sent to the eye bank and transplanted at a later date. The majority of the 96 donors whose corneas were transplanted were aged 45-54 years (24%) and 55-64 years (26%). In New Zealand, no request for corneal donation was made in 28 of the 43 cases and consent was not received in only one case. Of the remaining 14 potential donors, 2 corneas were not retrieved, leaving a total of 26 retrieved corneas, which were all sent to the eye bank and transplanted at a later date. The majority of the 13 donors whose corneas were transplanted were aged 55-64 years (46%) (ANZOD Registry 2010). Data collected by the Australian Corneal Graft Registry for all corneal transplants since its inception

indicate that the median age of recipients was 59 years with peaks at 20-40 and 60-80 years (Figure 2) (Williams et al 2007).

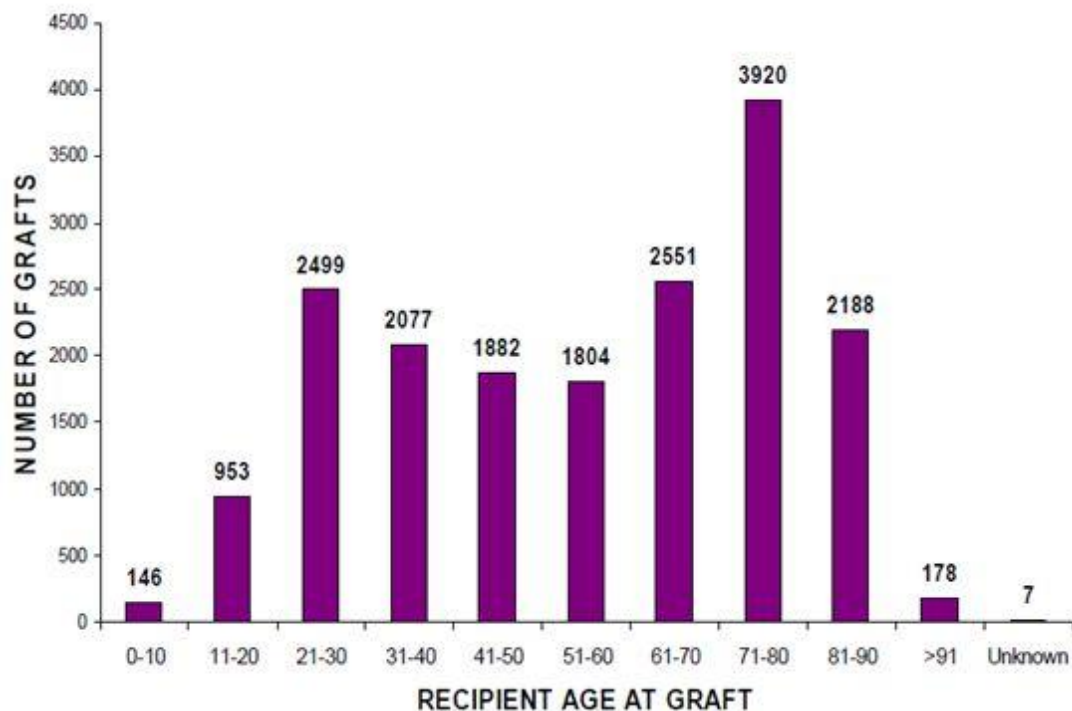


Figure 2 Summary of recipient age at cornea graft for all individuals who have undergone corneal transplantation in Australia and New Zealand (Williams et al 2007)

The total number of full thickness and superficial corneal transplant procedures in all Australian hospitals (public and private) for the year 2007-08 was 888 and 168, respectively (AIHW 2010).

The majority of corneal grafts are penetrating grafts requiring a full-thickness corneal transplant (94%). Approximately five per cent of grafts are lamellar grafts, where the superficial layers of an opaque cornea are replaced by a thin layer of clear cornea from a donor eye and a small percentage of grafts are limbal stem cell transplants. Five-year survival rates for penetrating corneal, lamellar corneal and limbal allograft transplants are 73, 69 and 42 per cent, respectively. The median survival time for penetrating corneal, lamellar corneal and limbal allograft transplants is 16, 14 and four years. During the immediate post-operative period less than one per cent of all corneas failed to function (Williams et al 2007).

Over 93 per cent of all transplanted corneas were retrieved from non-beating heart donors and 6 per cent from multi-organ donors. Multi-organ donors tended to be younger and were more likely to have died from strokes/haemorrhage or from traumatic or accidental death. Corneas donated from multi-organ donors had better survival rates than those from cadaveric donors.

DIFFUSION

Artificial corneas are not currently in routine clinical use in Australia or New Zealand. The AlphaCor™ artificial cornea was originally developed by the Lions Eye Institute in Western Australia and was manufactured by Argus Biomedical Pty Ltd in Perth, however it would appear that this company is no longer trading and that Addition Technology Inc (USA) now own the AlphaCor™ product. The evaluators attempted to contact Addition Technology Inc to no avail.

COMPARATORS

Conventional transplantation using corneas harvested from donors is the only alternative treatment option, however as indicated above, the artificial cornea would be indicated for those patients who are not suitable candidates for donor grafts and therefore have no other alternative.

SAFETY AND EFFECTIVENESS ISSUES

Fagerholm et al (2010) reported the 2-year follow-up results of the Phase I study of a cell-free biosynthetic artificial cornea made from 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide and N-hydroxysuccinimide cross linked recombinant human collagen. The implant is 500µm thick, optically clear (white light transmittance of $95.1 \pm 0.5\%$) with a refractive index of 1.35. Ten patients (mean age 43.8 years, range 18-75 years) were implanted by anterior lamellar keratoplasty in one eye with the implant held in place by sutures which were removed after 6.5 ± 3 weeks (level IV intervention evidence). Immuno-suppressants were stopped at this point, however antibiotics were continued for another 5.4 ± 3 weeks.

There were no complications reported with the implants, no signs of rejection and no reports of patient discomfort. One patient underwent unrelated cataract surgery in the implanted eye with no adverse events on the implant reported. Intraocular pressure in all operated eyes was unaffected by the surgery and was normal at 24-months with a range of 9-20 mmHg. Thickness of the cornea initially decreased post-operatively, however corneal thickness increased by 3-months ($404 \pm 87 \mu\text{m}$) and remained stable at 24-months ($403 \pm 109 \mu\text{m}$), with the thinnest cornea at follow-up being 211 µm. Epithelial cells began to migrate over the implants immediately post-operatively, however the presence of the sutures prevented this migration to some extent. Once sutures were removed cell migration was almost complete with the exception of a few discrete regions. At 24-months there was good visualisation of the retina by fundus photography indicating that the implants remained transparent. Normal tear production of >15mm in five minutes was observed in 7/10 eyes with the remaining three eyes producing 8, 9 and 10mm (Fagerholm et al 2010).

Best spectacle corrected visual acuity (BSCVA) improved from post-operative values in six patients, remained the same in two and decreased in two patients. These values are summarised in Table 2. A BSCVA of 0.2 equates to 20/100 vision, that is the patient can see at 20 feet the same detail as a person with normal vision can see at 100 feet. The mean of these BSCVA values (0.18) was compared to 60 historical patients who had undergone conventional corneal transplants. These patients had a significantly higher BSCVA (0.46, $p < 0.001$), however pre-operative values for these patients were not given (Fagerholm et al 2010).

Table 2 Pre and post-operative best spectacle corrected visual acuity values

BSCVA pre-operative		BSCVA 24-months		
CF 2m		0.1	20/200	Increase
0.2	20/100	0.2	20/100	Same
0.2	20/100	0.1	20/200	Decrease
<0.1	<20/200	0.4	20/50	Increase
CF 1m		0.2	20/100	Increase
0.3	20/60	0.1	20/200	Decrease
0.3	20/60	0.4	20/50	Increase
0.3	20/60	0.3	20/60	Same
<0.1	<20/200	0.1	20/200	Increase
0.1	20/200	0.2	20/100	Increase

A value of CF 2m indicates that the individual can count fingers at 2 metres

Hicks et al (2006) reported on the outcomes of all adult patients (n=322) who had been implanted with the AlphaCor™ device since its inception (level IV intervention evidence). Mean follow-up was 15.5 months (median 12.6 months, range 0.5 to 7.4 years), however only 69 (21.1%) of the implants have a follow-up exceeding 2-years. Although the AlphaCor™ was developed in Australia and has been in use in 11 countries, the majority of implants have taken place in the United States, accounting for 70 per cent of all implantations. Implantations were performed by a total of 84 surgeons who implanted one to 24 devices each. Thirteen patients had undergone a failed penetrating keratoplasty and all patients had complex ocular histories with multiple pathologies including trauma (n=77), infection (n=66), dystrophy (n=66) and bullous keratopathy (n=123). Cataract surgery was performed concurrently with AlphaCor™ implantation in 14 cases.

A total of 322 AlphaCor™ devices were implanted into 304 eyes of 302 individuals with only two patients undergoing bilateral implantation. Peri-operative complications included the opening of an old graft wound (8.7%), perforation of the posterior lamella (4.7%), perforation of the anterior lamella (4.7%), damage to the AlphaCor™ device (0.3%), vitreous loss (0.9%) and perforation of the sclera (0.6%). Explantation was required in 18 cases. Of these a new device was implanted in 18.2³ per cent of cases and 78.2 per cent reverted to penetrating keratoplasty and to a pre-implantation stage. Four eyes (1.3%) were enucleated or eviscerated, three of which were due to complications with the AlphaCor™ device. Over the follow-up period, vision was permanently lost in a total of six eyes, equating to an annual risk per eye of 0.014. Stromal thinning or loss (stromal melting⁴) occurred in 85 cases (26.4%) and accounted for the explantation of 12 devices. Infection with herpes did not increase the risk of stromal melting; this risk was decreased with the administration of topical medroxyprogesterone. Intraoptic deposits were noted in 27 cases (8.4%) with one case requiring explantation. Overall, 148 (46.0%) cases had one or more mild or severe complications, with a mean time to complication onset of 12.3 months (Hicks et al 2006).

³ Although the paper refers to cases as being a device implanted, 18.2% of 18 explants equates to 3.3 cases.

⁴ The integrity of the cornea can be compromised by both inflammatory and non-inflammatory conditions, which may lead to stromal thinning, melting, and perforation. Progression may be slow over months to years, or may be rapid over hours to days. Treatment should be directed locally at the cornea and systemically to address the underlying systemic inflammatory process, aiming decrease corneal melting and to promote re-epithelialisation of the corneal surface.

Visual acuity pre- and post-implantation is summarised in Table 3. Mean pre-operative visual acuity was perception of hand movement and post-operative values demonstrated a mean improvement of two lines on Snellen visual acuity chart.

Table 3 Best corrected visual acuity values pre- and post-implantation with the AlphaCor™ device

BCVA	Minimum	Maximum	Mean
Best VA obtained with previous graft before it failed (n=240)	LP	20/20	20/200
VA prior to AlphaCor implantation (n=322)	LP	20/200	HM
6-months post-implantation (n=108)	LP	20/20	20/400
12-months post-implantation (n=64)	NLP	20/20	20/200
18-months post-implantation (n=36)	NLP	20/20	20/400
24-months post-implantation (n=228)	NLP	20/20	20/400
30-42-months post-implantation (n=14)	NLP	20/20	CF
Best BCVA at any time post-operatively (n=192)	LP	20/20	20/200
Current VA (n=161)	NLP	20/20	20/300

VA = visual acuity, BCVA = best corrected visual acuity, LP = light perception: ability to perceive any light, NLP = no light perception: inability to see any light, total blindness, HM = hand motion: ability to distinguish a hand if it is moving or not in front of the patient's face, CF = counting fingers: ability to count fingers at a given distance

Several case reports have reported on complications of implantation with the AlphaCor™ device. A patient with pseudo-exfoliation glaucoma and pseudophakic bullous keratopathy had experienced graft failures after penetrating keratoplasty, with a BCVA of counting fingers. Ten months post-implantation the patient presented with severe eye pain and a BCVA of hand movement in the implanted eye. One month later the patient had no light perception in the implanted eye. The prosthesis was removed and a penetrating keratoplasty was performed. Histopathology revealed invasion of the prosthesis by fibroblasts and multi-nucleated foreign-body giant cells and stromal melting. Possible risk factors for poor implantation outcomes with the AlphaCor™ device include a previous history of cataract surgery with a retained lens, African-American origins, diabetes and hypertension. However, the advantages of the AlphaCor™ device unlike other prostheses, is that a reversal to penetrating keratoplasty is possible without the loss of the eye (Chalam et al 2007). A similar outcome was reported by Chow et al (2007) with fibrosis and inflammation in the peripheral skirt of the device in a foreign-body reaction pattern resulting in the exposure of the skirt and its eventual explantation two years after implantation. Similarly three cases reported by Coassin et al (2007) were explanted after corneal melting with histopathology of the skirt of the device demonstrating signs of inflammatory cytokine expression and infiltration of fibroblasts. The authors suggest that further research into improving the bio-integration of the device is required.

COST IMPACT

A cost-effectiveness analysis has been performed on the use of the Boston Keratoprosthesis (Kpro), which has been developed by the Massachusetts Eye and Ear Infirmary. This device is not a true artificial cornea as it is made of two curved plates of polymethylmethacrylate (PMMA) sandwiched around a corneal *autograft or*

allograft.⁵ The Boston Keratoprosthesis is a commonly used prosthetic cornea with more than 3,000 devices implanted worldwide. Eighty-two patients underwent keratoprosthesis surgery for a number of indications including penetrating keratoplasty graft failure (n=59), infection (n=10) and trauma (n=4). Of these, 63 patients experienced improvement in their best corrected visual acuity at two years, 13 experienced no improvement, and six had worse visual acuity. A total discounted incremental QALY gain of 0.763 was obtained for the keratoprosthesis and the total discounted cost associated with this utility was US\$12,315. The univariate sensitivity analysis resulted in a range of incremental cost-effectiveness ratios from US\$13,242 to \$20,697 per QALY (Ament et al 2010).

The unit cost of the AlphaCor device could not be ascertained despite attempts by the evaluator to contact Addition Technology Inc. The cost of the device in 2004 was \$A11,922.73, excluding GST (AlphaCor™ 2004).

There are three Medicare Benefit item numbers associated with corneal transplants. The transplantation of a full thickness cornea (item number 42653) has an associated fee of \$1,265.00, second and subsequent transplantation procedures (item number 42656) has a fee of \$1,577.80 and the transplantation of a superficial of lamellar cornea (item number 42659) has a fee of \$852.80.

ETHICAL, CULTURAL OR RELIGIOUS CONSIDERATIONS

No issues were identified/raised in the sources examined.

OTHER ISSUES

No issues were identified/raised in the sources examined.

SUMMARY OF FINDINGS

Artificial corneas are intended to be used in patients who have no other treatment options available. They have the advantage that they do not have a cellular component and therefore do not elicit an immune response that requires the administration of immunosuppressants. For the majority of patients, these implants are an effective device which improves visual acuity compared to pre-implantation values however the complications reported to date raise questions about whether this technology is as yet appropriate for widespread dissemination.

RECOMMENDATION:

Based on the preliminary evidence of one device and the large cases series of the AlphaCor device, it would appear that artificial corneas offer an effective treatment option for patients with no other treatment alternatives. With the potential development of new artificial corneas made from different materials and further research into mechanisms to reduce complications may offer improved outcomes. Therefore it is recommended that the following be conducted:

⁵ Autograft = a tissue or organ that is transplanted from one part to another part of the same body, allograft = a homograft between allogeneic individuals

- | | |
|--|--|
| <input type="checkbox"/> Horizon Scanning Report | <input type="checkbox"/> Full Health Technology Assessment |
| <input checked="" type="checkbox"/> Monitor | <input type="checkbox"/> Archive |

HEALTHPACT ASSESSMENT:

NUMBER OF INCLUDED STUDIES

Total number of studies	5
Level IV intervention evidence	2
Case reports	3

REFERENCES:

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SEARCH CRITERIA TO BE USED:

Artificial Organs/adverse effects/contraindications
Cornea/surgery
Prostheses and Implants/adverse effects
Prosthesis Implantation
Hydrogel
Cornea
Corneal Diseases/physiopathology/surgery
Corneal Transplantation
Keratitis, Herpetic/physiopathology/surgery
Cataract Extraction/adverse effects

HEALTH PACT DECISION:

- | | |
|--|--|
| <input type="checkbox"/> Horizon Scanning Report | <input type="checkbox"/> Full Health Technology Assessment |
| <input type="checkbox"/> Monitor | <input type="checkbox"/> Archive |
| <input type="checkbox"/> Refer | <input type="checkbox"/> Decision pending |

PRIORITY RATING

- High** **Medium** **Low**

PRIORITISING SUMMARY 2004

REGISTER ID: 000059

NAME OF TECHNOLOGY: ALPHACOR™, ARTIFICIAL CORNEA

PURPOSE AND TARGET GROUP: CORNEAL REPLACEMENT IN PATIENTS
CONSIDERED HIGH RISK FOR CONVENTIONAL
KERATOPLASTY

STAGE OF DEVELOPMENT (IN AUSTRALIA):

- | | |
|--|--|
| <input type="checkbox"/> Experimental | <input type="checkbox"/> Established |
| <input type="checkbox"/> Investigational | <input type="checkbox"/> Established <i>but</i> changed indication
or modification of technique |
| <input checked="" type="checkbox"/> Nearly established | <input type="checkbox"/> Should be taken out of use |

INTERNATIONAL UTILISATION:

COUNTRY	LEVEL OF USE		
	Trials Underway or Completed	Limited Use	Widely Diffused
Australia	✓		

2004 IMPACT SUMMARY:

Argus Biomedical Pty Ltd is an Australian based company that manufactures AlphaCor™, an artificial cornea with the aim of replacing damaged or diseased corneas in patients. The technology is currently available through private practice in either public or private hospitals. The AlphaCor™ is listed on the Australian Register of Therapeutic Goods (ARTG no. 83042, product ID 154882).

AlphaCor™ is indicated for patients who are not suitable candidates for donor grafts. Possible reasons for excluding a donor graft option include poor ocular surface quality, degree of deep vascularisation, number of previously failed grafts, previous glaucoma and lens status. In some cases the physical fitness of the patient is an indication for excluding the donor option as they may not tolerate the ongoing immunosuppressant medication required following graft surgery. AlphaCor™ is synthetic, so patients do not require long term systemic immunosuppressants. The surgical procedure involves removing part of the diseased cornea and inserting the AlphaCor™ lens. AlphaCor™ is a curved flexible plastic disc with a transparent central part that acts like a lens. The patient's own tissues grow into the rim of the disc thereby securing it into place. The procedure is completed by the formation of a flap of tissue from the conjunctiva that is used to cover the surface of the front of the eye and allows the AlphaCor™ to heal in place. This tissue is removed approximately three months after the initial surgery. The device has been trialled in several studies by its developers since 1998.

The first phase I human clinical trial (level IV evidence) assessed preliminary safety (retention, incidence of serious complications) and performance (visual acuity, comfort, appearance) in fourteen consecutive patients (Crawford et al 2002). The device was retained in 93% of patients, for up to 2.5 years. All but one patient maintained or improved their pre-operative level of visual acuity.

One published study (level IV evidence) describes outcomes of 38 patients who had the device implanted to November 2001, with follow up ranging from 2 weeks to 36 months (Hicks et al. 2003a). The percentage of patients who had previously received at least one donor graft prior to recruitment in this study was 85% (32) and the mean number of prior grafts was 1.6. The device had been retained in 83% (33) of patients, removed and replaced with donor tissue in 13% (5) and removed and replaced with a second AlphaCor™ in 5% (two) of cases. In this study 52% of the patients remained free of any complications requiring additional treatment. Pre-operative and best post-operative acuities (uncorrected and best-corrected) show that most patients displayed an improved visual acuity. Pre-operative visual acuity ranged from a perception of light (PL) to 6/60 (20/200) vision, whilst post-operative visual acuity ranged from PL to 6/6⁻¹ (20/20⁻²) vision.

The most common category (30%) of complication was that related to stromal melting adjacent or anterior to the device skirt and was strongly associated with a history of infection by ocular herpes simplex virus (HSV). The strong association between melt-related complications and device removals and history of ocular HSV is now considered a contraindication for AlphaCor™ surgery (Hicks et al 2003a).

The other main category of complication relates to optical surface spoilation or substance deposits within the hydrogel optic. This is attributed to patient use of topical medication and smoking, which discolours the optical surface and affects vision (Hicks et al 2003a).

The cost of corneal transplantation in Australia in 2003 for Medical Benefits Schedule item numbers 42653, 42656, 42659 was \$1,112.35, \$1,387.35 and \$749.90. The number of major corneal, scleral and conjunctival procedures undertaken in public hospitals was 2,896 in 2001-02 (AIHW, 2004).

A total of 119 AlphaCor™ devices have been implanted to the end of January 2004. This total comprises 48 implanted in American patients and 71 in either Europe, Australia and Singapore. The USA total does not include implants used in clinical trials, whereas the latter includes devices used in trials in Australia. The cost of the device is currently \$A11,922.73, excluding GST (AlphaCor™ 2004). Additional costs would include surgeon and anaesthetist fees. An AlphaCor™ marketing spokesperson indicated that several private health insurance companies in Australia cover the cost of this device (personal communication, Marketing Division AlphaCor™).

The AlphaCor™ device may serve a small proportion of the population who have no other alternative treatment. These patients are generally not suitable candidates for corneal transplants or may have religious beliefs that oppose donor transplants.

2004 RECOMMENDATION:

This technology has minimal low evidence available sourced from one group which suggests it may be effective; it is likely to be used by only a small group of potential patients, who have no existing treatment alternatives; and at considerable cost. It is recommended that the following be conducted:

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| <input type="checkbox"/> Horizon Scanning Report | <input type="checkbox"/> Full Health Technology Assessment |
| <input checked="" type="checkbox"/> Monitor | <input type="checkbox"/> Archive |

2004 REFERENCES

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