Mechanical Stability of Microkeratome-Assisted Intracorneal Keratoprosthesis Implantation

Melanie H. Erb, MD; Mehran Taban, MD; Charles A. Barsam, MD; Paula M. Sweet, MT; Roy S. Chuck, MD, PhD

Objective: To develop a laboratory model to study intracorneal keratoprosthesis implantation.

Methods: A combination microkeratome and artificial anterior chamber system was used to create a hinged lamellar keratectomy on 13 human corneas. After reflecting the flap, the posterior stroma was trephined at either 2.5 or 3.0 mm. A model keratoprosthesis was positioned in the bed. The flap was sutured closed. Intrachamber pressure was increased, and wound leak pressure was recorded. The anterior corneal lamella was trephined at either 3.0 or 3.5 mm to expose the keratoprosthesis. Leak pressure was again determined.

Results: After keratoprosthesis placement and prior to anterior trephination, all 13 corneas were watertight at maximum attainable intrachamber pressures. With posterior/anterior trephination combinations of 2.5/3.0 mm, 2.5/3.5 mm, or 3.0/3.5 mm, mean±SD wound leak pressure occurred at 95±12 mm Hg, 32±7 mm Hg, or 59±12 mm Hg, respectively (P<.01).

Conclusions: With a posterior trephination of 2.5 mm, there is significant keratoprosthesis-cornea interface destabilization between a 3.0- and 3.5-mm anterior trephination. For an anterior trephination of 3.5 mm, interface destabilization improves by increasing the posterior trephination to 3.0 mm.

Clinical Relevance: An intracorneal keratoprosthesis may be implanted using microkeratome assistance. Our laboratory model provides a useful method for examining a range of posterior and anterior trephination diameters and their effects on the mechanical stability of intracorneal keratoprosthesis placement.

Arch Ophthalmol. 2004;122:1839-1843

Penetrating keratoplasty is the most frequently performed and most successful human transplantation operation.1 The Eye Bank Association of America estimates that more than 46000 transplant procedures were performed in 2000.2 The success rate of penetrating keratoplasty is greater than 90% for certain diseases, such as keratoconus.3 Overall, 5-year survival rates for primary corneal transplants range from 46.5% to 93%, depending on the preoperative diagnosis.2-18

Failure rates for corneal transplantation vary significantly depending on the cause of the disease. There remains a subset of patients whose corneal disorders make a successful outcome from penetrating keratoplasty highly unlikely and who generally carry a poor prognosis, usually because of previous or ongoing chronic inflammation. Causes of poor outcome include Stevens-Johnson syndrome, chemical burns, ocular cicatricial pemphigoid, severe keratoconjunctivitis sicca, stem cell deficiencies, and severe vascularization from other causes.18 Patients with recurrent graft failures also carry a poorer prognosis for favorable outcome following penetrating keratoplasty.20 A potential alternative for restoring vision in these high-risk patients is implantation of an artificial cornea, or keratoprosthesis.21

The concept of an artificial cornea was first suggested in 1789 by Guillaume Pellier de Quengsy. More recently, since the 1950s, 2-piece collar-button keratoprostheses, which are maintained in position by anterior and posterior plates, have been researched, designed, and implanted in a few select patients. The Dohlman-Doane,19 Strampelli,22 and Cardona23 keratoprostheses have become the most familiar models. Over the past 25 years, these collar-button keratoprostheses have had some success, but they are fraught with a high incidence of complications, including extrusion, corneal melting, infection, retroprosthetic membrane formation, and glaucoma.20 In the 1990s, new-generation keratoprostheses made with biomaterials with improved biological integration of the prosthetic material were introduced.24

Author Affiliations: Department of Ophthalmology, College of Medicine (Drs Erb, Taban, Barsam, and Chuck and Ms Sweet) and Department of Biomedical Engineering (Dr Chuck), University of California, Irvine. Dr Chuck is currently affiliated with the Wilmer Ophthalmological Institute, Johns Hopkins University, Baltimore, Md.

Financial Disclosure: None.
These new-generation keratoprostheses are 1-piece, intracorneal designs.

Recently, Hicks et al21 and Crawford et al25 have reported clinical trial results of their artificial cornea, the Chirila Keratoprosthesis, now renamed AlphaCor (Argus Biomedical, Perth, Australia). The AlphaCor keratoprosthesis has recently been approved by the Food and Drug Administration and is now commercially available in the United States. The AlphaCor is made from poly (2-hydroxyethyl methacrylate) (PHEMA) and has a fused optic-and-skirt design. The optic core is transparent. The peripheral sponge skirt is opaque and porous and allows biointegration into the host cornea by ingrowth of stromal fibroblasts.20,21,26,27

The AlphaCor keratoprosthesis is implanted in a corneal stromal lamellar pocket.21,24 A 360° conjunctival peritomy is made, and the epithelium is debrided. A superior 180° paralimbal incision is extended at 50% depth into the corneal stroma to create a corneal flap over the superior half of the cornea. The dissection is continued as an intralamellar pocket of 3.5-mm radius within the inferior cornea. The flap is retracted, and a central trephination is made in the posterior bed. The AlphaCor is placed in the bed, and the superior paralimbal incision is closed with interrupted 10-0 nylon sutures. A Gunderson conjunctival flap is created to cover the entire corneal surface. After 8 to 12 weeks, the conjunctiva and anterior corneal lamella are trephined to expose the AlphaCor optic.

As with any new procedure, the optimal parameters for the surgical technique are continually being refined. We have developed a laboratory model to study the implantation of an intracorneal keratoprosthesis using an artificial anterior chamber. With this laboratory model, we investigate a new surgical technique for keratoprosthesis implantation utilizing microkeratome assistance. Additionally, we examine a range of posterior and anterior trephination diameters and their effects on the mechanical stability of intracorneal keratoprosthesis placement.

METHODS

A combination manual microkeratome and artificial anterior chamber system (ALTK System; Moria/Microtech, Doylestown, Pa) was used to perform the hinged anterior lamellar keratectomy (Figure 1). The operation of the system has been previously described.28 A normal saline solution infusion system was connected via a 3-way connection to the artificial anterior chamber and a digital manometer (Netech Corp, Hicksville, NY). After a corneoscleral rim was secured onto the artificial anterior chamber, the intrachamber pressure was raised or lowered by raising or lowering the infusion bottle.

Our laboratory keratoprosthesis (Flexlens X-Cel; Walman Co, Duluth, Ga) has the same dimensions as the AlphaCor keratoprosthesis and is made of a similar polymer; however, the rim is not porous. The material of our laboratory keratoprosthesis is methafilcon A, a hydrophilic random copolymer of 2-hydroxyethyl methacrylate (HEMA) and methacrylic acid cross-linked with ethylene glycol dimethacrylate. The model keratoprosthesis’ dimensions are diameter of 7 mm, thickness of 0.3 mm, base curve of 8.5 mm, refractive index of 1.4153, and power of +42 diopters (Figure 2).

After approval by the University of California, Irvine institutional review board/ethics committee, 13 corneoscleral rims not suitable for corneal transplantation and preserved in Optisol were obtained (Donor Network of Arizona, Phoenix). The mean±SD age at the time of death of the 4 women and 9 men was 67±10 years (range, 42-75 years).

The corneoscleral rims were mounted on the artificial anterior chamber with a digital manometer. Prior to the hinged anterior lamellar keratectomy, the intrachamber pressure was raised or lowered by raising or lowering the infusion bottle.

The corneoscleral rims were mounted on the artificial anterior chamber with an attached manometer. Prior to the hinged anterior lamellar keratectomy, the intrachamber pressure was increased to more than 65 mm Hg by raising the infusion bottle (mean±SD, 71±3 mm Hg). The hinged-flap anterior lamellar kera-
tectomy was made using a manual microkeratome (LSK One; Moria/Microtech) with a 300-µm-thick head and a blade angle of 25°. From our previous work with the combination artificial anterior chamber and manual microkeratome system, the actual mean±SD depths of the cut with a 300-µm head are 244.4±38.3 µm and 296.5±31.3 µm at intrachamber pressures of 53.5±2.7 mm Hg and 95.8±4.8 mm Hg, respectively.28,29

The flap was reflected after the diameter was measured with calipers. A handheld trephine with a diameter of either 2.5 or 3.0 mm was centered in the posterior stromal bed. The trephine was advanced until perforation. The posterior lamellar button was excised using forceps and corneal scissors (Figure 3). The flap was replaced, and 2 cardinal 10-0 nylon sutures were placed at 180° and 90° from the hinge.

The model keratoprosthesis was then positioned in the bed (Figure 4). A third cardinal 10-0 nylon suture was placed at 270° from the hinge. The flap was secured with a total of 15 interrupted 10-0 nylon sutures to assure watertight wound closure. Intrachamber pressure was increased to a maximum by slowly raising the height of the infusion bottle, which was eventually limited by ceiling height. All 13 corneas were watertight at the maximum attainable mean±SD intrachamber pressure of 103±8 mm Hg (range, 81-110 mm Hg).

The intrachamber pressure was then reset to approximate physiologic levels, 17 to 21 mm Hg, by lowering the height of the infusion bottle. A handheld trephine with a diameter of either 3.0 or 3.5 mm was centered on the anterior corneal lamella and advanced. The anterior lamellar button was excised using forceps and corneal scissors to expose the keratoprosthesis (Figure 5). Intrachamber pressure was again elevated progressively by raising the height of the infusion bottle while the cornea was observed for leaks. The leak pressure was recorded.

For comparison between groups, t test was used. A P value <.05 was considered statistically significant.

## RESULTS

After hinged anterior lamellar keratectomy, posterior lamellar trephination, keratoprosthesis placement, and sutured flap, and prior to anterior trephination, all 13 corneas maintained watertight seals at the maximum attainable mean±SD intrachamber pressure of 103±8 mm Hg (range, 81-110 mm Hg). The maximum pressure was limited by the ceiling height when elevating the infusion bottle.

With a posterior trephination of 2.5 mm and an anterior trephination of 3.0 mm (n=4), mean±SD leak pressure occurred at 95±12 mm Hg (range, 81-109 mm Hg). These corneas with keratoprostheses were extremely stable, with 3 of 4 corneas exhibiting no leakage at the maximum intrachamber pressure of 81 mm Hg or more and 1 of 4 corneas leaking at 92 mm Hg. In comparison, with the posterior trephination maintained at 2.5 mm and the anterior trephination increased to 3.5 mm (n=4), the corneas and keratoprostheses were much less stable and the leak pressure much lower, occurring at a mean±SD of 32±7 mm Hg (range, 25-40 mm Hg; P<.001). Finally, when the anterior trephination was maintained at 3.5 mm while the posterior trephination was increased to 3.0 mm (n=5), the mean±SD leak pressure increased to 59±12 mm Hg (range, 39-68 mm Hg; P=.004). Although the anterior trephination of 3.5 mm was less stable than 3.0 mm for a posterior trephination of 2.5 mm, stability could be improved by increasing the posterior trephination from 2.5 to 3.0 mm (Table).

The area of leak and destabilization always occurred at the keratoprosthesis–anterior trephination interface and not at the flap edge. The keratoprosthesis would dislocate anteriorly through the anterior trephine opening (Figure 6). The model keratoprosthesis is made of HEMA...
and is soft, flexible, and deformable. Although the keratoprosthesis diameter was 7 mm and the anterior trephination diameter was 3.0 or 3.5 mm, the increase in intrachamber pressure distorted the keratoprosthesis’ soft, flexible shape, thus allowing the keratoprosthesis to prolapse through the anterior trephination. The mean±SD flap diameter was 9.75±0.4 mm. Although corneal sutures served to reduce the effective diameter of the bed, there remained room for a small amount of lateral movement of the 7-mm keratoprosthesis in the bed. This lateral movement of the keratoprosthesis may have allowed the keratoprosthesis edge to migrate near the anterior trephine opening, thus enabling the keratoprosthesis to prolapse through the anterior trephine opening.

Over the past 25 years, the rigid collar-button keratoprostheses have had some success but have been fraught with a high incidence of complications, including extrusion, corneal melting, infection, retroprosthetic membrane formation, and glaucoma. In the 1990s, new-generation keratoprostheses made with biomaterials that improve the flexibility, biocompatibility, and hydrophilicity of the keratoprosthesis were introduced. These new-generation keratoprostheses are 1-piece, intracorneal designs.

Intracorneal keratoprostheses may have the following advantages over the collar-button designs: (1) the biointegration of the intracorneal keratoprosthesis with the host cornea in combination with a 1-piece optic-and-skirt design may prevent interface complications such as aqueous leakage, infection, extrusion, or epithelial downgrowth; (2) flexibility of the intracorneal keratoprosthesis may minimize mechanical stresses on the cornea and may allow possible tonometry in the future; (3) a larger optic allows ocular examinations, including fundus and optic nerve ophthalmoscopy, and enables a wider field of view to perform visual field testing; and (4) the non-adhesive nature of PHEMA and intracorneal placement may prevent retroprosthetic membrane formation.

The AlphaCor intracorneal keratoprosthesis has recently been approved by the Food and Drug Administration and is now commercially available. Multicenter clinical trials have been in progress for over 3 years in Australia and Southeast Asia, with outcomes reported in 40 eyes. Clinical implantation of the AlphaCor keratoprosthesis is just beginning in the United States. As with any new procedure, the optimal parameters for the surgical technique are

### Table. Comparison of Wound Leak Pressures With Varying Posterior and Anterior Trephination Diameters*

<table>
<thead>
<tr>
<th>Trephination Diameters</th>
<th>Sample</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>Mean</th>
<th>SD</th>
<th>Minimum</th>
<th>Maximum</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>2.5-mm Posterior/3.0-mm Anterior Trephination</strong></td>
<td>Maximum pressure</td>
<td>81</td>
<td>109</td>
<td>97</td>
<td>100</td>
<td>97</td>
<td>12</td>
<td>81</td>
<td>109</td>
</tr>
<tr>
<td>Wound leak pressure</td>
<td>81</td>
<td>109</td>
<td>97</td>
<td>92</td>
<td>95</td>
<td>12</td>
<td>81</td>
<td>109</td>
<td></td>
</tr>
<tr>
<td><strong>2.5-mm Posterior/3.5-mm Anterior Trephination</strong></td>
<td>Maximum pressure</td>
<td>107</td>
<td>110</td>
<td>100</td>
<td>97</td>
<td>104</td>
<td>6</td>
<td>97</td>
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<tr>
<td>Wound leak pressure</td>
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<td>26</td>
<td>40</td>
<td>32</td>
<td>7</td>
<td>25</td>
<td>40</td>
<td></td>
</tr>
<tr>
<td><strong>3.0-mm Posterior/3.5-mm Anterior Trephination</strong></td>
<td>Maximum pressure</td>
<td>108</td>
<td>108</td>
<td>109</td>
<td>108</td>
<td>108</td>
<td>0.4</td>
<td>108</td>
<td>109</td>
</tr>
<tr>
<td>Wound leak pressure</td>
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<td>62</td>
<td>39</td>
<td>63</td>
<td>68</td>
<td>59</td>
<td>39</td>
<td>68</td>
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</tbody>
</table>

*Data are presented as millimeters of mercury. Differences in wound leak pressure between each group was statistically significant with \( P<.01 \).
continually being refined. In clinical trials, the AlphaCor was implanted in a corneal stromal lamellapocket. The posterior trephination diameters ranged from 2.0 to 3.5 mm, and the anterior trephination diameters ranged from 2.0 to 4.0 mm, with posterior/anterior trephinations of 3.0/3.0 mm in the most recent report.

The development of an artificial anterior chamber to support human corneoscleral rims has enabled corneal surgeons to experiment with surgical techniques in vitro. We have developed a laboratory model to study the implantation of a model intracorneal keratoprosthesis using an artificial anterior chamber. With this laboratory model, we investigated a new surgical technique for keratoprosthesis implantation using microkeratome assistance instead of manual dissection of a lamellar pocket. We found that a model intracorneal keratoprosthesis may be implanted using microkeratome assistance with relative ease.

We examined a range of posterior and anterior trephination diameters and their effects on the mechanical stability of intracorneal keratoprosthesis placement. With a posterior trephination of 2.5 mm, there is significant wound destabilization between a 3.0- and 3.5-mm anterior trephination. Although the anterior trephination of 3.5 mm was less stable, interface stabilization could be much improved by increasing the posterior trephination from 2.5 to 3.0 mm. Thus, it appears that a smaller mismatch between posterior and anterior trephination diameters may play a more significant role in stabilization of the keratoprosthesis-cornea interface than the absolute anterior trephination size. Additional studies of varying trephination diameters are currently under way for confirmation.

The major drawback of this ex vivo model is that it does not allow for biointegration of the keratoprosthesis. Thus, ex vivo, the keratoprosthesis-cornea interface will have less stability than in vivo. However, our laboratory model does provide insight into the mechanical stability of intralaminar keratoprosthesis placement, which may be applied to clinical situations. First, if the mechanical stability of the keratoprosthesis-cornea interface is maximized without any biointegration ex vivo, then in vivo, there will be reduced mechanical stresses to the system after biointegration. This may be beneficial for long-term wound stability and implant extrusion rates. Second, although the absolute trephination diameters may not be directly transferable to a clinical situation, the laboratory model gives us a method to easily vary and evaluate anterior and posterior trephination sizes. We found that mechanical stability decreases as the anterior trephination size increases. However, with the larger anterior trephination size, mechanical stability could be improved by increasing the posterior trephination size.

With our model, we can facilitate intelligent keratoprosthesis implantation by varying posterior and anterior trephination diameters and evaluating their effects on mechanical stability. The eventual goal is to maximize both anterior and posterior trephination sizes to allow maximal field of vision and adequate ocular examinations for optimalophthalmic management.

Correspondence: Roy S. Chuck, MD, PhD, Wilmer Ophthalmological Institute, Johns Hopkins University, 3-127 Jefferson Bldg, 600 N Wolfe St, Baltimore, MD 21287-9278 (rchuck1@jhmi.edu).

Funding/Support: This study was supported by grant EY00412-02A1 from the National Institutes of Health, Bethesda, Md (Dr Chuck).

Previous Presentation: This study was presented in part at the annual meeting of the American Society of Cataract and Refractive Surgery; May 2, 2004; San Diego, Calif.

Acknowledgment: We thank the Donor Network of Arizona, Phoenix, for providing the human corneas.

Submitted for Publication: September 26, 2003; final revision received March 29, 2004; accepted May 18, 2004.

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7. Volker-Dieten NU, D’Amore PA, Khan AS, Alperin JH. Mismatch between posterior and anterior trephination sizes. We found that mechanical stability could be improved by increasing the posterior trephination from 2.5 to 3.0 mm. Thus, it appears that a smaller mismatch between posterior and anterior trephination diameters may play a more significant role in stabilization of the keratoprosthesis-cornea interface than the absolute anterior trephination size. Additional studies of varying trephination diameters are currently under way for confirmation.

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