Effect of Tissue Fit on Corneal Shape after Transplantation

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Postkeratoplasty astigmatism is now a major problem preventing visual recovery. Certain postopertive topographic characteristics are felt to be dictated by the fit of the donor corneal button in its recipient bed. Deficient tissue at the wound is predicted to contribute to the location of the steep meridian and excess tissue to the location of the flat meridian. In an eight-cat sample using our Fit Assessment Method and Photogrammetric Index Method, the authors tested the relationship between button fit in recipient bed and resulting corneal curvature at approximately 42, 161, and 289 postoperative days. Corneal symmetry improved between the first and second postoperative periods. Deficient tissue led to steepened curvature and ample tissue to flattened curvature in the first measurement period. When buttons fit poorly, deficient tissue led to steepness in the first postoperative period, but led to flattened curvature 90 deg away from the deficient tissue meridian in the second and third periods. The relationship between ample tissue and flattest postoperative curvature did not depend on the magnitude of button-bed disparity in any period. Corneal elasticity appeared to influence the way tissue disparity affected postoperative topography. Our findings support Troutman's balloon mode. When there was a large amount of uncompensated tissue disparity, the tissue deficiency exerted a force that shortened the translimbal chord. This produced both steepened curvature parallel to this chord soon after surgery and flattened curvature at 90 deg to the chord in the stable postoperative cornea. Invest Ophthalmol Vis Sci 25:1226–1231, 1984

Since microsurgical techniques and postoperative management have led to increased production of clear corneal transplants, postkeratoplasty astigmatism that prevents visual recovery is a major concern. The fit of a donor corneal button in its recipient bed seems a likely contributor to postoperative corneal astigmatism. When the button is positioned in the bed, dissimilar shapes and orientations of button and bed produce meridians with excess and deficient corneal tissue at the wound. The mechanics described by Troutman and Patton dictate that postoperative topography will reflect the amount of available corneal tissue at the wound.[1,2] Along a meridian, deficient tissue at the wound will shorten the translimbal chord, steepening the corresponding postoperative meridian. Corneal flattening will be seen along the meridian of excess tissue. Using our Fit Assessment Method (FAM) in a cat population, we tested the predictions that the meridian with the relatively greatest amount of tissue at the wound would become the direction of the flattest postoperative meridian, and the meridian with the relatively least amount of tissue at the wound would become the direction of the steepest postoperative meridian.

Materials and Methods. *Animal surgery:* The same surgeon performed penetrating keratoplasties upon the right eyes of young adult, domestic cats. Animals were included in the study if there were no preoperative, biomicroscopic, anterior segment, ocular abnormalities, and preoperative keratometric astigmatism was less than 0.5 D. Only animals with clear grafts and no postoperative complications were retained, and eight study cats resulted.

The transplants were oversized (7.5 mm recipient/8.0 mm donor). Prior to use, all trephines were inspected for defects under the operating microscope. Donor corneas with scleral rims were placed endothelial side up on a teflon block and trephined with new, unused, disposable trephines attached to a corneal press. After centering the trephines on the recipient corneas, the anterior chambers were entered by hand trephination and the corneal excisions completed with razor blade knives and corneal scissors. Identifying the 12:00 in vivo directions on donor and recipient buttons were 9-0 silk marking sutures. Donor buttons were positioned by aligning their 12:00 positions with the 12:00 positions of the recipient beds, and the marking sutures were removed. Wounds were closed with 16, evenly spaced, interrupted, 9-0 nylon sutures and an additional suture in the 8:00 position. All sutures were removed after 2 weeks. Animal care and surgical technique were otherwise as recommended[3] and adhered to the ARVO Resolution on the Use of Animals in Research.

Fit assessment method (FAM): Each button was coated with McCarey-Kaufman medium (Aurora Biologicals, Ltd.; Buffalo, NY), placed endothelial side up on sterile nonglare glass, and photographed through the operating microscope with the 12:00 position adjacent to a 0.10 mm scale. The microscope was focused on the endothelial button edge that was illuminated by an oblique light source. The nonglare glass containing both scale and button was rotated and photographed in eight positions. The photograph that most clearly represented the entire endothelial edge was enlarged, and the edge was traced manually from a Kail opaque projector image. Tracings were enlarged to the same scale. Projector distortion was found to be 0.5 mm in 95 mm.[4] Tracings were stream-digitized at 0.1-inch intervals on a Tektronix

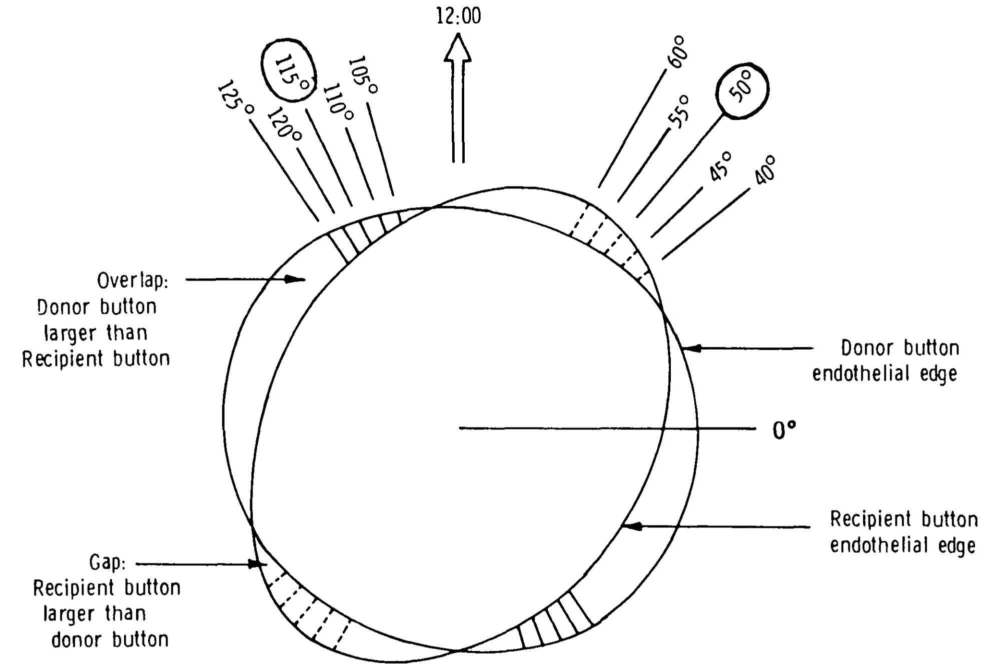

Fig. 1. Overlaid endothelial edge tracings of paired donor and recipient button photographs. **A**, *top*, Computation of the average amount of overlap or gap along a meridian. Distances between donor and recipient button endothelial edges, measured at both ends of a meridian, were added to give a measure of available tissue for each meridian. Gap (-----) was represented by negative and overlap (——) by positive numbers. These measures for five adjacent meridians at 5-deg intervals were averaged, and that mean was assigned to the central of these five meridians (circled). Means were assigned to all meridians at 5-deg intervals between 0 and 180 deg.

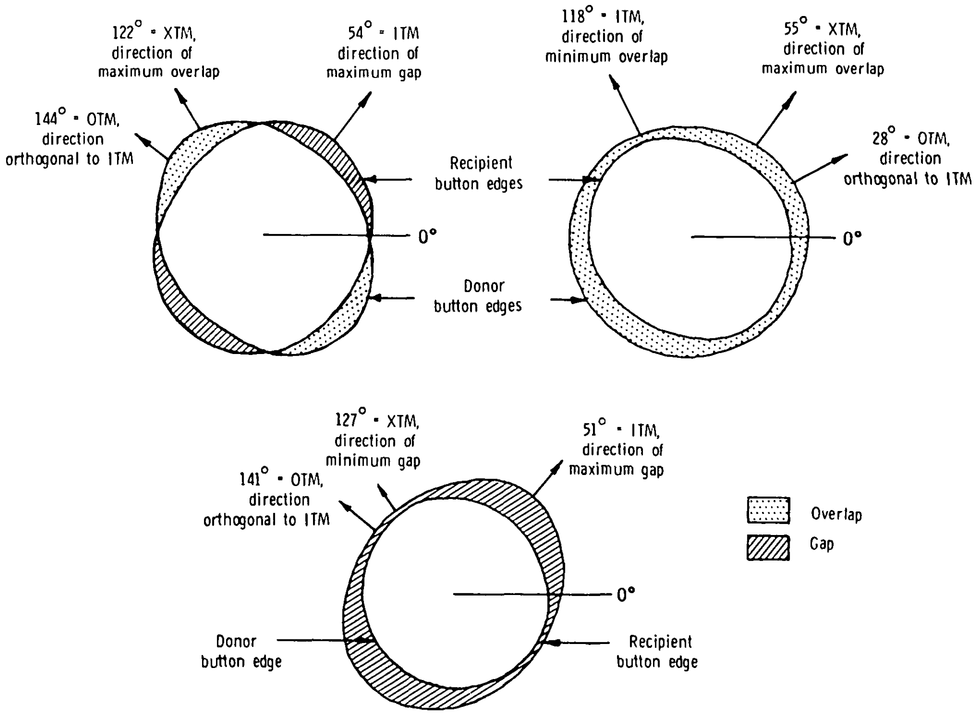

Fig. 1. B, *bottom*, Three examples of tracing overlays. The maximum tissue meridian (XTM) was the meridian with the highest mean value. This mean could represent the area of greatest overlap, a positive number, or least gap, a negative number. The minimum tissue meridian (ITM) had the lowest mean value, which could represent the area of least overlap or greatest gap. OTM was a meridian located 90 deg away from ITM. Net tissue difference (NTD) was the difference between the highest mean and the lowest mean.

4956 Digitizer. A center of each edge outline was defined as the mean center of minimum enclosing rectangles constructed at 5-deg intervals.

Our FAM computer program overlaid corresponding pairs of donor and recipient button tracings, representing the size and shape of the donor button endothelial margin and the size and shape of each recipient bed endothelial margin and matching their cardinal orientations and centers. Across some meridians, the traced donor button edge was outside the traced recipient button edge, indicating that the donor button was wider than the recipient bed. The area between the tracing edges represented a likely excess of tissue at the wound when the button was positioned in the bed. Along other meridians, the recipient button edge was inside the donor button edge, and

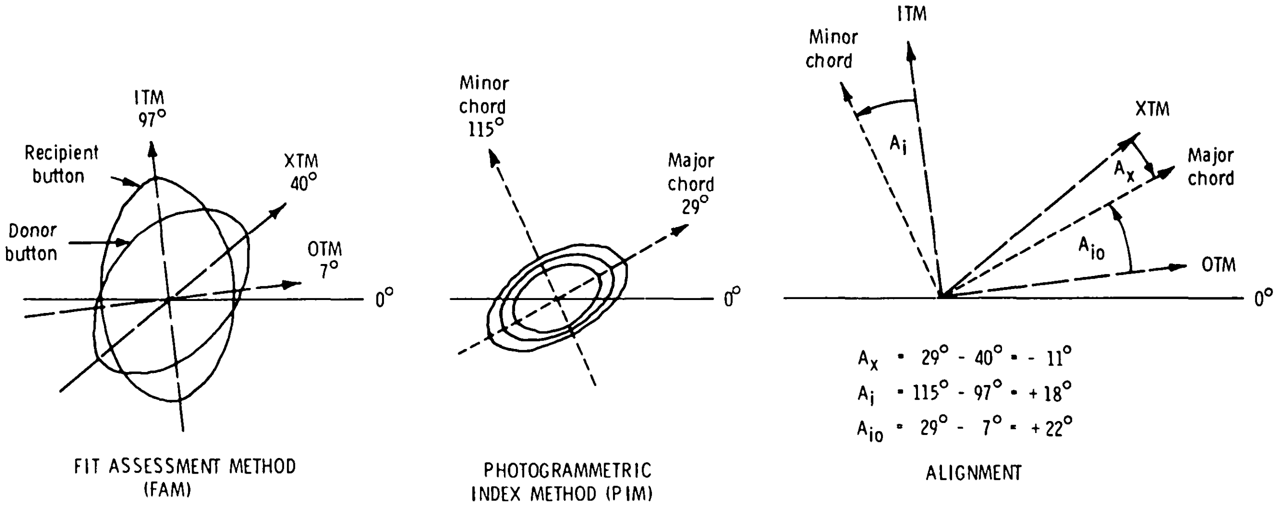

Fig. 2. The measurement of angles of alignment. The directions of tissue meridians found by the Fit Assessment Method (FAM) were compared with the directions of major and minor chords found by the Photogrammetric Index Method (PIM). The acute angle between the maximum tissue meridian (XTM) and the major keratographic chord was the angle of alignment for majors, A_x. The acute angle between the minimum tissue meridian (ITM) and the minor keratographic chord was the angle of alignment for minimums, A_i. The acute angle between the orthogonal tissue meridian (OTM) and the major keratographic chord was A_{io}. Keratographic chord directions clockwise from tissue meridians were negative alignment angles; if counterclockwise, the angles were positive.

this discrepancy represented the likelihood of insufficient tissue at the wound.

To determine amount of tissue in a given meridian, the distance between donor and recipient edge tracings at the wound was measured at both ends of meridians that passed through the center every 5 deg (Fig. 1A). Overlap, donor button larger than recipient bed, was quantified as positive and gap, bed larger than button, as negative distances. The distances at either end of a meridian were combined into a measure of available tissue for each meridian. These measures for five adjacent meridians were averaged, and the mean was assigned to the central meridian of the five. This method assigned mean values to meridians at 5-deg intervals between 0 and 180 deg.

Three tissue meridians of interest were selected for each cat (Fig. 1B). The meridian with the highest mean value was called the maximum tissue meridian (XTM), that with the lowest value was called the minimum tissue meridian (ITM), and the meridian 90 deg to ITM was called the orthogonal tissue meridian (OTM). The difference between the mean value at XTM and the mean value at ITM was called the net tissue difference (NTD) and was used to indicate the magnitude of button-bed disparity.

Assessment of postoperative curvature: Using the Reynolds' corneascope, keratographs of each cornea were taken at 41.9 ± 7.9 days, 160.8 ± 19.6 days, and 289.0 ± 9.8 days (mean ± standard error of the mean) postoperatively. After intramuscular injection of ketamine hydrochloride (5 mg/kg), Liquifilm Forte (Allergan Pharmaceuticals, Inc.; Irvine, CA) drops were applied to the eye, blotted from the conjunctival fornix, and keratographs were taken. Specula were not used. Keratographic rings were centered on the grafts. Central keratographic rings 2, 3, and 4 were processed by the Photogrammetric Index Method (PIM).[4] Major and minor chords that represented the flattest and steepest meridians, respectively, were located, and the Eccentricity index (E), which evaluates corneal symmetry was computed. Higher E values reflect more corneal symmetry.

Alignment: To discover correspondence between fit of the donor button in the recipient bed and postkeratoplasty topography, angles between the directions of selected tissue meridians (XTM, ITM, and OTM) and the directions of selected postoperative keratographic chords (major and minor) were measured (Fig. 2). For each cat's cornea, the acute angle between ITM and the keratographic minor chord, called the angle of alignment for minors (A_i), related the direction of deficient tissue to the direction of steepest postoperative curvature. The angle between XTM and the major chord, defined as the angle of alignment for majors (A_x), related the directions of ample tissue and flattest postoperative curvature. The angle between OTM and the major chord, defined as A_{io}, related the directions of deficient tissue and flattest postoperative curvature by measuring their orthogonality. Keratographic chord directions, which were clockwise from ITM, XTM, or OTM were negative alignment angles; if counterclockwise, the angles were positive. For each keratograph the separate alignments, A_i, A_x, and A_{io}, were averaged over rings,

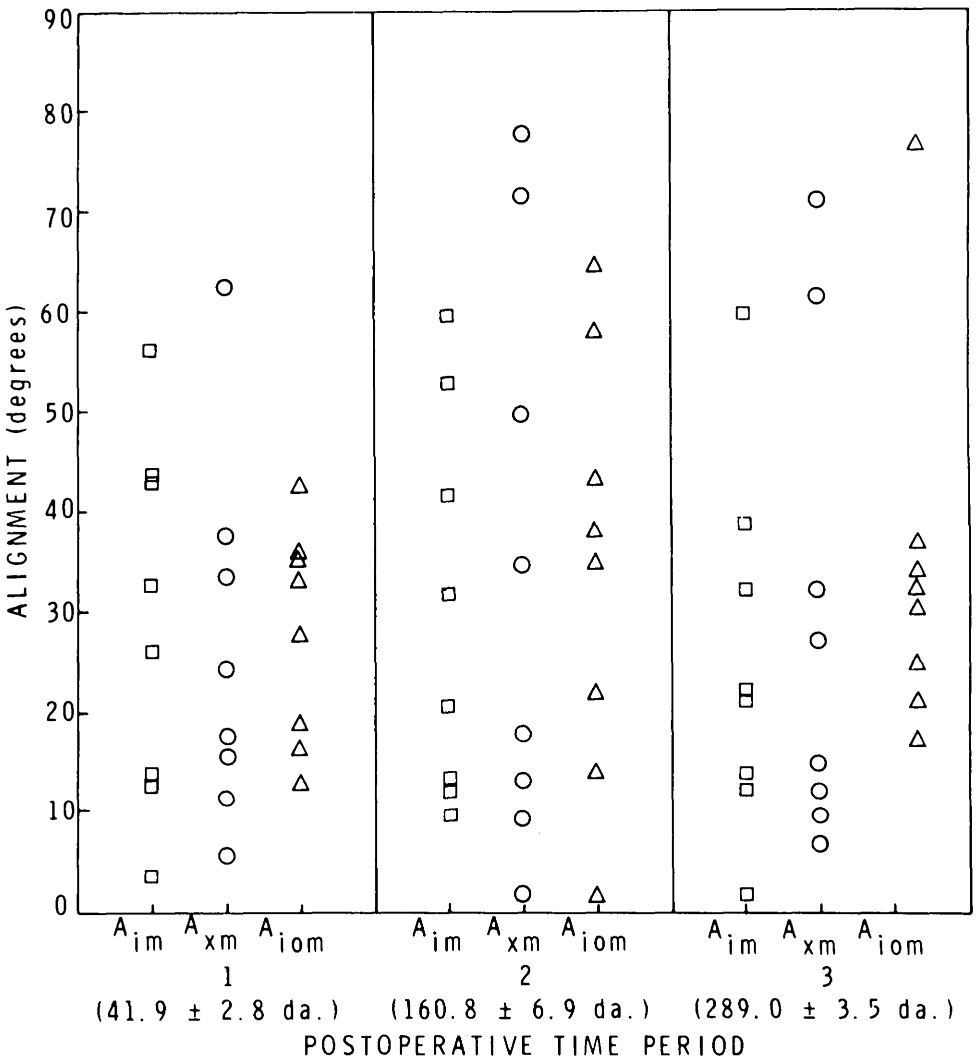

Fig. 3. Distributions of alignments, A_{im}, A_{xm}, and A_{iom}. Each alignment was averaged over rings 2, 3, and 4. The absolute values are shown for the three, postoperative time-periods.

and their means designated A_{im}, A_{xm}, and A_{iom}, respectively.

Alignment angles close to 0 deg would indicate that ITM, XTM, and OTM were in the same directions as the postoperative keratographic chords with which they were compared. Angles close to ±90 deg would indicate maximum divergency. For each ring, the distributions of these alignments for all cats were compared with a uniform distribution from 0 to 90 deg by the Kolmogorov-Smirnov Procedure.[5] If the amount of tissue along a meridian did not contribute to the resulting corneal curvature, the angles of agreement would be distributed uniformly over the 90-deg interval. If the distributions were skewed significantly by frequent small alignment values, the correspondence between amount of tissue at the wound and resulting curvature would be said to be better than chance. Spearman rank correlations were used to assess the associations between NTD and A_{im}, A_{xm}, and A_{iom} in each time period. Because the concept of alignment does not depend on the directions of the acute angles, tests of significance for distributions and correlations used the absolute values of alignments. One-sided Wilcoxin tests were used to assess increases in E from the first to the second and from the second to third time-periods.

Results. Figure 3 shows the absolute values of A_{im}, A_{xm}, and A_{iom} for each cat at the three time-periods. By inspection, symbols appear more frequent toward 0 deg than toward 90 deg.

In Table 1, the alignments of the eight cats have been collected into distributions for each ring. Significant *P* values reflect one-sided departures from a uniform distribution, indicating that low alignment values were frequent. In the earliest time period, all departures are significant except A_i in ring 3 and A_x in ring 4. Only A_i for rings 3 and 4 were significant for the second time-period, and A_i for ring 2 and A_{io} for ring 3 in the third.

Table 2 shows the Spearman rank correlations between NTD, the magnitude of button-bed disparity and each kind of alignment, represented by the mean

Table 1. *P* values based on the Kolmogorov-Smirnov test[5] of H_0—that observations come from a uniform distribution over the interval 0–90 deg versus H_1—that observations come from a distribution skewed toward 0 deg

		Time-period		
Ring	Alignment	1	2	3
2	A_i	<0.050	n.s.*	<0.050
	A_x	<0.025	n.s.	n.s.
	A_{io}	<0.005	n.s.	n.s.
3	A_i	n.s.	<0.050	n.s.
	A_x	<0.025	n.s.	n.s.
	A_{io}	<0.025	n.s.	<0.050
4	A_i	<0.050	<0.050	n.s.
	A_x	n.s.	n.s.	n.s.
	A_{io}	<0.025	n.s.	n.s.

* n.s. = nonsignificant.

alignment over rings 2, 3, and 4. If R_s was high and positive, the selected tissue meridians aligned more closely with their corresponding keratographic chords when button-bed disparity was large than when disparity was small. There was a significant ($P < 0.01$) rank correlation between NTD and A_{im} during the first time period. NTD similarly correlated with A_{iom} ($P < 0.05$) in the second and third time-periods, and no correlation was seen between NTD and A_{xm} in any time-period.

Eccentricity, the PIM indicator of corneal symmetry, increased from the first to the second period ($p < 0.05$) and was unchanged from the second to the third.

Discussion. The postpenetrating keratoplasty topographic effects of donor cornea fit in the recipient bed are evident in Figure 3, which shows a greater concentration of good (close to 0 deg) alignments than poor (close to 90 deg) alignments in all postoperative time-periods. In our sample, good alignment between the most deficient tissue meridian and the steepest postoperative meridian appeared to be more frequent than poor alignment. Good alignment also appeared to be more frequent between the most ample tissue meridian and the flattest postoperative meridian, and between the meridian orthogonal to the most deficient tissue meridian and the flattest meridian. The higher frequency of close alignments suggests a relationship between the adequacy of tissue at the wound and postkeratoplasty topography.

Most alignment distributions had significantly large frequencies of good alignments in the earliest time-period, and this effect became less dramatic over time (Table 1). Table 2 illustrates a difference between results in the first time-period and in the second and third periods. We related alignment to the magnitude of uncompensated disparity between the shapes of the donor button and recipient opening. In the earliest time-period, the influence of deficient tissue on the location of steep postoperative curvature depended on the amount of button-bed disparity. In the last two time-periods, higher button-bed disparity increased the shortened translimbal chord's tendency to locate the flattest corneal meridian orthogonal to itself. When buttons fit poorly, deficient tissue led to steepness soon after surgery but led to flattened curvature 90 deg away in the stable postoperative cornea. Also from the first to the second time-periods, corneas became more symmetrical. Thus corneal elasticity, which allowed the postkeratoplasty cornea to approach its preoperative, symmetric shape, appeared to adjust the manner in which button-bed fit affected topography over time.

When all degrees of disparity of button-bed fit are considered, deficient tissue led to steepness, and ample tissue appeared to lead to flatness soon after surgery (Table 1). However, the relationship between ample tissue and flattest postoperative curvature did not depend on the magnitude of button-bed disparity in any time period (Table 2). Since large disparity between button and bed produced no better alignment of ample tissue with flatness than small disparity, ample tissue may not produce flatness. The good alignments between ample tissue and flatness seen soon after surgery may be geometric artifacts, which occur merely because there is usually excess tissue at 90 deg to the deficient tissue.

Our findings support Troutman's balloon model.[6] When there was a large amount of uncompensated tissue disparity, the tissue deficiency exerted forces, which shortened the translimbal chord. This produced both steepened curvature parallel to this chord soon after surgery, and flattened curvature 90 deg away in the stable postoperative cornea.

Table 2. Spearman rank correlation coefficients, R_s, between net tissue difference (NTD) and mean alignments for rings 2, 3, and 4, A_{im}, A_{xm}, and A_{iom}, and the corresponding *P* values

	Time-periods					
	1		2		3	
Relationship	R_s	P	R_s	P	R_s	P
NTD vs A_{im}	0.833	<0.01	0.190	n.s.	0.405	n.s.
NTD vs A_{xm}	−0.452	n.s.	0.333	n.s.	−0.262	n.s.
NTD vs A_{iom}	0.548	n.s.	0.762	<.05	0.738	<0.05

n.s. = nonsignificant.

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Outflow Facility in Acute Experimental Ciliochoroidal Detachment

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Total outflow facility was measured by constant pressure perfusion in six cynomolgus monkey eyes with ciliochoroidal detachment and in fellow eyes following sham operation. Outflow facility in eyes with ciliochoroidal detachment was 0.22 ± 0.04 $\mu l/min^{-1}/mmHg^{-1}$ ($P < 0.05$). Since the spontaneous intraocular pressure following acute ciliochoroidal detachment was lower than the normal episcleral venous pressure, it is concluded that the increase in outflow facility in eyes with ciliochoroidal detachment actually may be a measure of the rate of fluid flow across the sclera out of the suprachoroidal space. Invest Ophthalmol Vis Sci 25:1231–1232, 1984

Ciliochoroidal detachment (CCD) and hypotony often coexist, yet the exact cause–effect relationship is unclear. Hypotony is one of the known risk factors leading to CCD in susceptible eyes.[1] Conversely, CCD also is thought to cause or potentiate hypotony. Originally, it was believed that CCD causes hypotony by a reduction in aqueous humor formation.[2] More recent experimental evidence in monkeys suggests that CCD causes mild hypotony due to an increase in unveoscleral outflow.[3] Theoretically, an increase in outflow facility or a decrease in episcleral venous pressure also could lead to mild hypotony. Therefore, the present study was designed to measure the total outflow facility in eyes with acute CCD.

Materials and Methods. Six cynomolgus monkeys, weighing 2–5 kg were used in this study. The animals were sedated with intramuscular ketamine hydrochloride, 10 mg/kg, and anesthetized with intravenous sodium pentobarbital, 10 mg/kg, supplemented as necessary. A CCD with autologous serum was created in the right eye of each animal, using a technique described in detail elsewhere.[3] Briefly, a conjunctival periotomy was performed inferiorly. A small radial sclerotomy was made 2 mm from the limbus and a tapered polyethylene cannula was inserted into the suprachoroidal space. Vitreous was aspirated through a separate sclerotomy in the adjacent quadrant. One milliliter of autologous serum was injected into the suprachoroidal space through the cannula, as vitreous was aspirated into a 19-gauge needle. This created a large multilobed, bullous CCD. The polyethylene tube and needle were removed, and the sclerotomies closed with 8-0 silk sutures. In the left eye of each animal, a sham operation was performed, consisting of vitreous aspiration and reinjection to simulate the operative trauma of the right eye. Only one sclerotomy was made in the sham eyes. A 23-gauge needle, attached to polyethylene tubing, was inserted into the anterior chamber of each eye. The tubing was attached to a pressure transducer and perfusion setup using mock primate aqueous humor.[4] The intraocular pressure (IOP) was allowed to stabilize for 2 hr.

Constant pressure perfusion then was carried out 10 mmHg above the spontaneous IOP, as described elsewhere.[4] The eye was allowed to equilibrate at the higher IOP for about 20 min, and flow measurements were made for about 10 min. Outflow facility was calculated from the rate of fluid flow into the eye at the higher IOP, divided by the difference between the