INTACS Inserts for Treating Keratoconus

One-year Results

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Objective: To evaluate the use of INTACS micro-thin prescription inserts (Kera Vision, Inc., Fremont, CA) for the treatment of keratoconus.

Design: Prospective, nonrandomized (self-controlled) comparative trial.

Participants/Intervention: Ten patients from our prospective clinical study who had completed 12 months of follow-up were evaluated. All patients had keratoconus with clear central corneas and were contact lens intolerant. After reviewing corneal pachymetry and topography of individual patients, INTACS inserts of 0.45-mm thickness were placed in the inferior cornea to lift the cone and INTACS of 0.25-mm thickness were inserted superiorly to counterbalance and flatten the overall anterior corneal surface.

Main Outcome Measures: Differences between preoperative and postoperative uncorrected visual acuity, best spectacle-corrected visual acuity, manifest refraction, and keratometry values were statistically assessed. Changes in corneal ectasia were evaluated by reviewing corneotopographic maps.

Results: No intraoperative complications occurred in this series of patients. Spherical equivalent error and refractive astigmatism were reduced with INTACS inserts treatment. Postoperative month 12 uncorrected visual acuity (logarithm of the minimum angle of resolution [logMAR] mean, 0.35, standard deviation [SD], 0.16 [20/50, 2 lines]) was significantly better than preoperative (logMAR mean, 1.05; SD, 0.33 [20/200, 3 lines]; P ≤ 0.05). Average best spectacle-corrected visual acuity at postoperative month 12 was improved by approximately two lines compared with baseline (logMAR mean, 0.22; SD, 0.12 [20/32, 1 line]; logMAR mean, 0.38; SD, 0.13 [20/50, 1 line], respectively). Topographic corneal shape (size and height of the cone) was improved for all subjects after insert placement.

Conclusions: INTACS micro-thin prescription inserts seem to provide a viable method for treating clear corneal keratoconus for patients who are contact lens intolerant. The corneal steepening and astigmatism associated with keratoconus were reduced, and visual acuity was improved with treatment in almost all eyes. Ophthalmology 2001;108:1409–1414 © 2001 by the American Academy of Ophthalmology.

Keratoconus is a noninflammatory, progressive ectatic and thinning disease of the cornea. In its early stages, spectacles and contact lenses are the usual treatment modalities. As keratoconus progresses and severe astigmatism is developed, thinning of the central cornea occurs, penetrating keratoplasty (PK) becomes the only option for restoring normal visual function. In many of these keratoconus cases, however, when the cornea has remained transparent and the patient is contact lens intolerant, both surgeon and patient are often reluctant to take the final PK step. Although good visual acuity results are usually achieved with the corneal graft procedure, there is moderate to high risk for intraoperative and perioperative complications. In addition, significant endothelial cell loss occurs within the donor corneal button while performing the graft, and accelerated cell loss continues over time, an important issue to consider, especially when the patient is young.

In an effort to prevent or extend the time leading to PK, benefits of various refractive procedures for treating keratoconus have been explored. These procedures can be generally classified as subtractive, including radial keratotomy, asymmetric keratotomy, photorefractive keratectomy, photo astigmatic refractive keratectomy, phototherapeutic keratoplasty, and laser in situ keratomileusis, 1–5 or additive, including epithelial keratooplasty 6–9 and lamellar keratoplasty. 10 None of these techniques are currently widely accepted as efficacious because of the progressive nature of the disease, or their implementation requires use of donor tissue.

For treating keratoconus it is most logical to reinforce the cornea using an additive technique, in contrast to weakening its structural integrity using incisions or ablation. Several studies have demonstrated efficacy and effectiveness of INTACS micro-thin prescription inserts (KeraVision, Inc., Fremont, CA) for correcting mild to moderate myopia, 11–13 and preliminary investigation has demonstrated their potential for treating astig-
maturity and myopia concurrent with astigmatism. INTACS inserts are placed into the corneal periphery through a small (1.2 mm) radial incision in the superior cornea and correct myopia by flattening the center of the cornea by an “arc shortening” effect. The procedure for placement of INTACS inserts is performed outside of the central visual axis, and INTACS inserts can be removed or replaced if the desired outcome is not achieved. The keratoconic corneal tissue has a thinner structure and is potentially more easily flattened compared with normal myopic eyes. INTACS inserts offer a unique surgical alternative for treating contact lens-intolerant patients with clear cornea keratoconus as an attempt to delay or avoid PK altogether.

The objective of our prospective interventional trial was to evaluate INTACS inserts for treatment of keratoconus. Our treatment goal was to reshape keratoconic corneas using two inserts of different thickness. Inserts were applied to lift the inferior ectasia and flatten the soft keratoconic corneal tissue to decrease the asymmetric astigmatism induced by keratoconus. Preliminary results from 10 patients with clear cornea keratoconus and contact lens intolerance who were treated with INTACS inserts and have reached postoperative month 12 in our ongoing prospective clinical trial are presented.

Patients and Methods

All patients included in this study were referred to our institution for PK to treat keratoconus. Enrolled patients had keratoconus with clear central cornea and were contact lens intolerant. Patients had best spectacle-corrected visual acuity of 20/100 or better in the treatment eye and corneal thickness of 400 μm or more at the location where INTACS inserts were to be placed. When both eyes of a patient were eligible for study enrollment, the eye with the worse visual acuity was included for analysis. Informed consent was obtained from all patients before study enrollment.

Preoperative and postoperative evaluation included slit-lamp examination, collection of manifest refraction, uncorrected and best spectacle-corrected visual acuity (decimal chart), and videokeratography (TMS-2, Tomey, New York, NY). Central and peripheral corneal thickness were measured using ultrasonic pachometry (DGH 1000, DGH Technology, Inc., Exton, PA). Patients were examined with a Scheimpflug photographic camera (Nidek, Tokyo, Japan) at all examination time points for evaluating depth of INTACS inserts.

INTACS inserts are made of polymethyl methacrylate, have a crescent-shaped arc length of 150°, and are designed to have an inner diameter of 6.8 mm and outer diameter of 8.1 mm when placed in the cornea. Refractive effect is modulated by INTACS thickness (0.25 mm to 0.45 mm, in 0.05-mm increments), and current designs have a predicted myopic range of correction from −1.00 to −4.10 diopters.

Surgical procedure for treating keratoconus with INTACS inserts was similar to that used for correction of low myopia, except for location of incision site. After the patient was prepared for normal anterior segment surgery and placed under topical anesthesia, a small corneal incision (~1.8 mm in length) was made temporally at the edge of the 7-mm optical zone (Fig 1). Two intrastromal tunnels (clockwise and counterclockwise) were created using the same specialized instruments developed for the myopia procedure. Special care was taken when making the inferior tunnel, where the cornea is relatively thinner. In all patient eyes, a 0.45-mm INTACS insert was placed inferiorly to lift the conus, and a 0.25-mm INTACS insert was placed superiorly to flatten the cornea and decrease baseline keratoconic asymmetric astigmatism.

The same procedure for placing INTACS inserts was followed in all cases. The corneal wound was gently hydrated during INTACS inserts placement, and edges of the stroma were approximated to prevent epithelial ingrowth. The incision was closed with one 10–0 nylon suture. A topical antibiotic/steroid combination was applied postoperatively and a clear shield put on the eye for recovery. The suture was removed 1 to 4 weeks after the surgery, on a case-by-case basis at discretion of the surgeon (JC).

Outcomes for 10 eyes of 10 patients enrolled in our ongoing prospective study were evaluated. Follow-up visits were conducted at postoperative months 1, 3, 6, and 12. All patients included in this analysis had completed follow-up to postoperative month 12 and were not missing data for more than one postoperative time point, excluding month 12.

Results

The average age of the patients was 30.9 ± 6.1 years. No intraoperative complications occurred in this patient series; both inferior and superior intrastromal tunnels for placement of INTACS inserts were made without any technical problems. INTACS inserts were removed 2 months postoperatively from one patient eye currently enrolled in our prospective clinical series (n = 23) because of superficial placement. INTACS inserts were removed easily under topical anesthesia, after opening the original incision with a Sinskey hook. Refractive error, visual acuity, and corneal topography values for the patient returned to preoperative status 1 month after INTACS inserts removal.

Mean values for preoperative and postoperative pachymetry at the corneal center and at the 7.0-mm diameter optical zone for the

<table>
<thead>
<tr>
<th>Zone</th>
<th>Mean Thickness (Standard Deviation)*</th>
<th>Range</th>
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<tbody>
<tr>
<td>Central</td>
<td>479 (32)</td>
<td>420–515</td>
</tr>
<tr>
<td>Superior</td>
<td>653 (44)</td>
<td>570–720</td>
</tr>
<tr>
<td>Temporal</td>
<td>602 (52)</td>
<td>530–700</td>
</tr>
<tr>
<td>Inferior</td>
<td>623 (54)</td>
<td>550–700</td>
</tr>
<tr>
<td>Nasal</td>
<td>608 (38)</td>
<td>550–730</td>
</tr>
</tbody>
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*Microns.
series of 10 eyes are shown in Table 1. It is interesting to note that
the average value for central corneal thickness is thinner than that
commonly observed in normal eyes, but in all patient cases,
preoperative inferior corneal thickness was greater than 500 µm.

Postoperative clinical aspects of treating keratoconus with IN-
TACS inserts are presented in Figure 2. Mild to moderate intrala-
mellar channel deposits at the superior edge of the inferior segment
were exhibited by most eyes.

The anterior corneal surface change induced by INTACS in-
serts in a case study keratoconic cornea was demonstrated by
photographs collected using the eye analyzer system (Fig 3 A, B).
Eye analyzer system photos show the corneal flattening effect
obtained by placement of INTACS inserts. Relative insert depth
and thickness are illustrated by the postoperative photograph.

Mean preoperative and postoperative uncorrected visual acuity
(logarithm of the minimum angle of resolution [logMAR]) values,
with confidence intervals (95%) are shown for the 10 patients in
Figure 4. Mean preoperative uncorrected visual acuity was approx-
imately 20/200 in Snellen visual acuity units (mean logMAR, 1.05;
standard deviation [SD], 0.33). Uncorrected visual acuity at all
postoperative time points was improved over baseline (month 1
logMAR mean, 0.54; SD, 0.22 [~20/63, 2 lines]; month 3 log-
MAR mean, 0.54; SD, 0.31 [~20/63, 2 lines], month 6 logMAR
mean, 0.64; SD, 0.37 [~20/80, 4 lines], month 12 logMAR mean,
0.35; SD, 0.16 [~20/50, 2 lines]. Improvement was statistically
significant (P ≤ 0.05) at all time points except month 6, when data
were missing for two patients.

Average preoperative best spectacle-corrected visual acuity for
the 10 patients approximated Snellen visual acuity of 20/50 (log-
MAR mean, 0.38, SD, 0.13 [−1 line]; Fig 5). Mean values for
postoperative best spectacle-corrected visual acuity improved pro-
gressively over time, and at postoperative month 12 corrected
visual acuity was two lines better than baseline (month 1 logMAR
mean, 0.35; SD, 0.19 [~20/50, 2 lines]; month 3 logMAR mean,
0.30; SD, 0.31 [~20/40, 3 lines], month 6 logMAR mean, 0.30;
SD, 0.21 [~20/40, 2 lines], month 12 logMAR mean, 0.22; SD,
0.12 [~20/32, 1 line]).
Preoperative and postoperative mean values (with 95% confidence intervals) for manifest refraction cylinder are shown in Figure 6. Average preoperative astigmatism was approximately 4 diopters (SD, 1.9). Refractive astigmatism was reduced after placement of INTACS inserts. At postoperative month 12 the improvement was statistically significant ($P < 0.05$), with mean value of 1.3 diopters (SD, 1.4).

Average values for preoperative and postoperative minimum and maximum keratometry are presented in Figure 7. Preoperative average minimum keratometry was 48.0 diopters (SD, 4.1) and ranged from 44.2 to 54.1 diopters; average maximum keratometry was 53.2 diopters (SD, 3.0) and ranged from 50.2 to 58.2 diopters. Minimum and maximum keratometry was reduced at all postoperative time points after placement of INTACS inserts. At postoperative month 12, average minimum keratometry was 44.4 diopters (SD, 2.4) and ranged from 40.3 to 48.1 diopters; average maximum keratometry was 48.6 (SD, 2.8) and ranged from 46.0 to 53.4 diopters. Keratometry was missing for 3 of 10 patients followed to postoperative month 12, because it was too difficult to obtain in these cases.

Corneotopographic maps qualitatively demonstrated reduction of corneal ectasia (Fig 8). Extent of the corneal ectasia and height of the cone were improved in all cases, similar to the one shown. Corneal topography surface quality indices suggested that surface regularity is similar preoperatively and postoperatively; however, surface asymmetry was reduced with treatment (Table 2). Simulated keratometry values were similar preoperatively and postoperatively. Postoperative minimum simulated keratometry readings were approximately 4 diopters less than baseline.

In subjects with keratoconus, it has been demonstrated previously that best-corrected visual acuity is related to degree of myopia and astigmatism. Because INTACS inserts are designed to correct myopia, we plotted the relationship between postoperative month 12 residual myopia (manifest refraction spherical equivalent) and best spectacle-corrected visual acuity in individual cases (Fig 9). With increased postoperative residual myopia, best spectacle-corrected visual acuity was diminished. The scatterplot demonstrated that this patient cohort may have been composed of two distinct sample subsets. Preliminary analysis indicated that patient subsets did not differ by level of preoperative myopia, cylinder, keratometry, or postoperative achieved correction, suggesting that further study is necessary for refining postoperative outcomes. The relationship between preoperative myopia and uncorrected visual acuity was not as clearly apparent.

**Discussion**

The objective of using INTACS inserts for treating keratoconus is not to eliminate the corneal disease but to decrease corneal abnormality associated with it and improve visual acuity in affected patients to satisfactory levels. An important potential benefit of treating keratoconus with INTACS inserts is to delay or eliminate the need for a corneal graft.

Postoperative results of our series of patients demonstrated that spherical equivalent error and astigmatism were significantly reduced and visual acuity was improved in almost all cases over baseline measures. INTACS inserts seemed to be a minimally invasive technique for effectively reducing the corneal steepening and astigmatism associated with keratoconus and improving visual acuity.

Previous study has indicated that risk factors may exist that increase the likelihood in some patients with keratoconus for “earlier” surgical intervention (PK). Principal risk factors include low baseline corrected visual acuity (worse than 20/40), relatively steep corneal curvature (>55 diopters), and contact lens intolerance. Preliminary results of our series of patients, who were contact lens intolerant and referred to receive PK, indicated that treating keratoconus with INTACS inserts is an effective treatment modality for improving visual acuity and extending the time between onset of advanced keratoconus and undergoing PK. Twelve months after treatment with INTACS inserts, 8 of 10 (80%) patients had 20/40 or better best spectacle-corrected visual acuity, and 100% had 20/50 or better. In addition, uncorrected visual acuity was significantly improved. Five of ten patients (50%) had 20/40 or better with treatment, and 7 of 10 had 20/50 (70%) or better. Preoperatively, all patients had uncorrected visual acuity of 20/80 or worse (6 of 10 had 20/400 or worse).

The flattening effect of INTACS inserts on the soft corneal keratoconic tissue seems to be greater than that produced in normal corneas. An average mean keratometric reduction of four diopters was achieved in our patient case series. Clinical trials for Food and Drug Administration premarket approval of INTACS inserts have demonstrated that mean keratometry change in subjects with simple myopia commonly ranged from no change for the 0.25-mm inserts to 3.5 diopters for the 0.45-mm inserts (KeraVision Inc., personal communication).

Stability is a critical issue for any surgical intervention.
conducted for treating keratoconus. In our prospective case series, three eyes have been followed for 24 months or more. Postoperative visual acuity, refraction, and keratometry readings were stable over 2 years in all three eyes.

It is unclear whether INTACS inserts will prevent progression of keratoconus or even ultimately eliminate the need for PK. Should PK become necessary after treatment with INTACS inserts, we advise that inserts be removed in a separate procedure before performing PK. Conducting PK at the time of INTACS inserts removal may induce some degree of undesirable postoperative astigmatism. No evidence of neovascularization was observed in any of our patients, even though most of them had worn contact lenses previously. This may be because the incision for treating keratoconus was made on the temporal meridian and was thus further from the limbus than is for the standard myopia procedure (commonly performed at the 12 o’clock position).

Treatment of keratoconus with INTACS inserts provides flexibility to improve outcomes for individual patients should the desired effect not be achieved with initial selection of insert thickness. Scatterplot analysis demonstrated a relationship between residual postoperative myopia and best spectacle-corrected visual acuity. Further study of the individual patient response to INTACS inserts treatment for

Figure 8. Preoperative (Preop) and postoperative (day 2, months 12 and 18) corneal topography of keratoconic patient eye before and after INTACS inserts placement. See Table 2 for corneal topography surface quality indices and simulated keratometry values.

Figure 9. Scatterplot demonstrating the relationship between postoperative month 12 manifest refraction spherical equivalent and best spectacle-corrected visual acuity in patients treated with INTACS inserts for keratoconus.
keratoconus and modulation of postoperative outcomes with INTACS inserts exchange is warranted. Use of a portable corneoscope or operating microscope–mounted topography unit during surgery may be valuable for refining the corrective effect achieved by INTACS inserts in individual cases. For cases in which there is apparent undercorrection or overcorrection, refractive adjustments can be made during the procedure by replacing the original INTACS inserts choice with thicker or thinner inserts. When unexpected corneal shape changes occur, INTACS inserts may be removed and/or exchanged with ones of a different thickness.

Further follow-up and additional cases are needed to draw final conclusions regarding the efficacy of this procedure for treating keratoconus. A European multicenter study has been initiated, and results of this larger scale study will be valuable. It is necessary to further refine this technique to determine optimal thickness inserts combinations for treating the various keratoconic deformations. We must also examine whether two inserts are always needed or whether one insert may be sufficient for treating some patients. Long-term study must be conducted to ascertain the impact INTACS inserts treatment has on the natural progression of keratoconus. Will INTACS inserts inhibit progression, accelerate it, or have no effect at all? Results of using INTACS inserts for treatment of keratoconus must be compared with those currently achieved by PK. A retrospective study of 123 eyes demonstrated that 17.9% (22 of 123) had at least one graft rejection, although episodes did not significantly influence the incidence of attaining 20/40 vision. The effect of INTACS inserts placement in the cornea toward increasing incidence of graft rejection or influencing the clinical outcome of penetrating keratoplasty should be considered.

This preliminary investigation has demonstrated promising results in applying INTACS inserts for treatment of keratoconus. Future study will include evaluating INTACS inserts for correction of keratoconus in subjects who can still tolerate contact lenses but would like to try an alternative treatment, as well as for correcting keratectasia after laser in situ keratomileusis.

References


