

Management of Keratoconus With Intacs

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- **PURPOSE:** To prospectively study the effects of the use of Intacs microthin prescription inserts for the management of keratoconus.
- **DESIGN:** Prospective nonrandomized clinical trial.
- **METHODS:** Thirty-three eyes of 26 keratoconus patients (17 males and 9 females) ages 21 to 51 years (mean age, 32 ± 9.7 years) were included in the current study. All patients had clear central corneas and contact lens intolerance. Patients were excluded if any of the following criteria applied after the preoperative examination: previous intraocular or corneal surgery; history of herpes keratitis; diagnosed autoimmune disease; and systemic connective tissue disease. Two Intacs segments of 0.45-mm thickness were inserted in the cornea of each eye, aiming at embracing the keratoconus area to try to achieve maximal flattening. Preoperative examination included uncorrected visual acuity (UCVA), best-corrected visual acuity (BCVA), manifest refraction, keratometric data, and corneal topography.
- **RESULTS:** Intacs were successfully implanted in all eyes. In one eye Intacs were removed after 3 months because of their improper (superficial) placement. The follow-up ranged from 1 to 24 months (mean: 11.3 months). The mean UCVA significantly improved from 0.13 ± 0.14 (range, counting fingers [CF]-0.5) to 0.39 ± 0.27 (range, CF-1.0) ($P < .01$). Of 33 eyes, 2 eyes lost 1 line of UCVA, and 3 eyes maintained the preoperative UCVA, whereas the rest (28 eyes) experienced a 1- to 10-line gain. The mean BCVA also improved from 0.47 ± 0.31 (range, CF-1.0) to 0.64 ± 0.26 (range, 0.1-1.0) ($P < .01$). Of 33 eyes, 4 eyes experienced 1- to 2-line loss of BCVA, 4 eyes maintained the preoperative BCVA, whereas the rest (25 eyes), experienced a 1- to 6-line gain. Of 3 patients (3 eyes) with unsatisfactory results, 1 patient improved with one segment removal and in 2 patients the segments were

permanently removed. One of these eyes underwent successful PKP.

- **CONCLUSIONS:** With mean follow-up of 11.3 months, intracorneal ring segments implantation improved UCVA and BCVA in the majority of the keratoconus patients. Even though the results are encouraging, concern still exists regarding the predictability as well as the long-term effect of such an approach for the management of keratoconus. (Am J Ophthalmol 2003; 135:64-70. © 2003 by Elsevier Science Inc. All rights reserved.)

TO DATE, THE THERAPEUTIC OPTIONS FOR PATIENTS with keratoconus are limited to spectacles and contact lenses, while in the advanced stages of the disease the accepted approach is penetrating keratoplasty (PKP).^{1,2} Despite the good results of PKP, the scientific community has not slowed down the investigations of applying new methods to treat keratoconus. These attempts were encouraged by the postcorneal transplantation complications, such as allograft rejection, significant endothelial cell loss (especially when the life expectancy is long), irregular astigmatism, and side effects from long use of topical corticosteroids (such as secondary cataract and glaucoma).^{3,4}

Several attempts at alternative methods to treat keratoconus are reported in the literature, such as thermal keratoplasty, epikeratoplasty, photorefractive keratectomy, laser in situ keratomileusis (LASIK), and deep lamellar keratoplasty.⁵⁻⁸

Intastromal corneal ring segments (Intacs; Addition Technology Inc., Fremont, California, USA) were designed to achieve a refractive adjustment by flattening the central corneal curvature while maintaining clarity in the central optical zone.^{9,10} Several studies have demonstrated the efficacy of Intacs in correcting low myopia, while preliminary studies reported encouraging results in post-LASIK corneal ectasia and in keratoconic eyes.¹¹⁻¹⁶

The objective of our study was to prospectively evaluate the safety, efficacy, and optical effects of Intacs implantation in keratoconic eyes.

Accepted for publication Aug 21, 2002.

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METHODS

IN THIS PROSPECTIVE NONRANDOMIZED CLINICAL TRIAL, 26 keratoconus patients (33 eyes), 17 males (65%) and 9 females (35%), 21 to 51 years (mean age was 32 ± 9.7 years) were included. All patients had clear central corneas and contact lens intolerance, whereas patients were excluded if any of the following criteria applied after the preoperative examination: previous intraocular or corneal surgery; history of herpes keratitis; diagnosed autoimmune disease; and systemic connective tissue disease.

All patients were appropriately informed before their participation in the study, and gave their written informed consent in accordance with institutional guidelines, according to the Declaration of Helsinki.

A complete ophthalmologic examination was performed preoperatively to exclude other ocular disease, and the preoperative as well as postoperative follow-up evaluation included uncorrected visual acuity (UCVA; decimal scale), best corrected visual acuity (BCVA; decimal scale), manifest refraction, keratometric data, and corneal topography. Postoperative visits were scheduled for days 1, 3, 15, and 30, and every 3 months thereafter.

- **SURGICAL PROCEDURE:** Operations were performed by two surgeons (C.S.S., I.G.P.). The surgical procedure was done under topical anesthesia. Two Intacs segments of 0.45-mm thickness were inserted so as to embrace the steepest keratoconus meridian, according to the topographic image, aiming at maximal flattening.

There were 19 eyes (57%) with topographically inferior corneal ectasia and 14 eyes (43%) with central corneal ectasia. In the first group two Intacs segments (0.45 mm) were inserted superiorly–inferiorly (embracing the steep axis; Figure 1), whereas in eyes with central keratoconus Intacs (0.45 mm) were inserted in the location used for low myopia procedure (nasally–temporally).

The corneal thickness was measured intraoperatively at the incision site and peripherally in the cornea along the ring placement markings with ultrasonic pachymetry (Sonogage, Cleveland, Ohio, USA). Using a diamond knife, set at 70% of the thinnest corneal measurement, a 0.9-mm radial incision was formed, and corneal pockets were created using two Sinsky hooks and a Suarez spreader. Two corneal tunnels were then formed using clockwise and counterclockwise dissectors under suction created by a vacuum-centering guide. The two polymethyl methacrylate (PMMA) segments (0.45-mm thickness) were implanted in the respective corneal tunnels, maintaining a space of approximately 2.0-mm between their ends and 1.5 mm between the opposite edge of each segment and the edge of the incision.

The incision site was sutured using a single 10/0 nylon stitch. All procedures were uneventful. Postoperatively, all eyes received antibiotic/corticosteroid combination eye

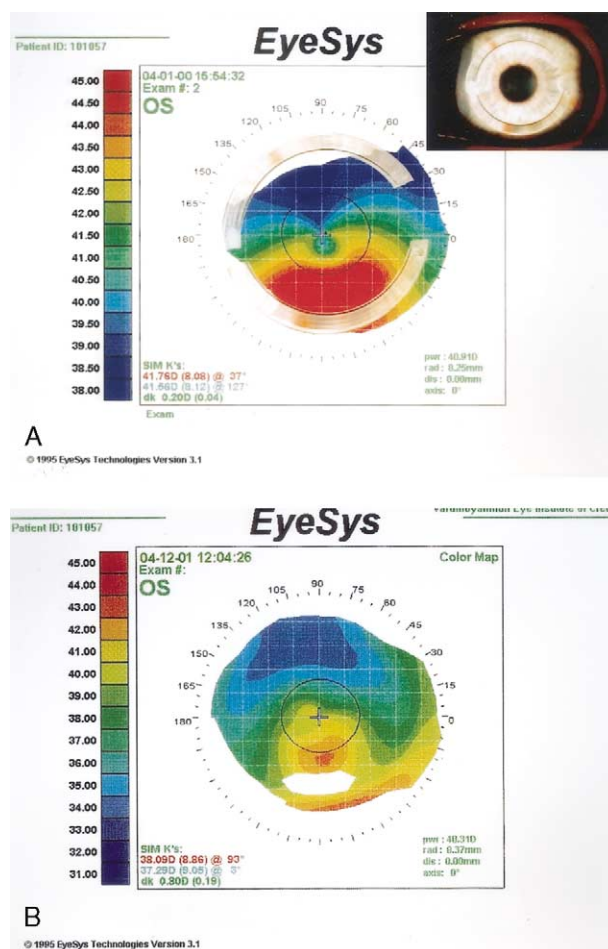


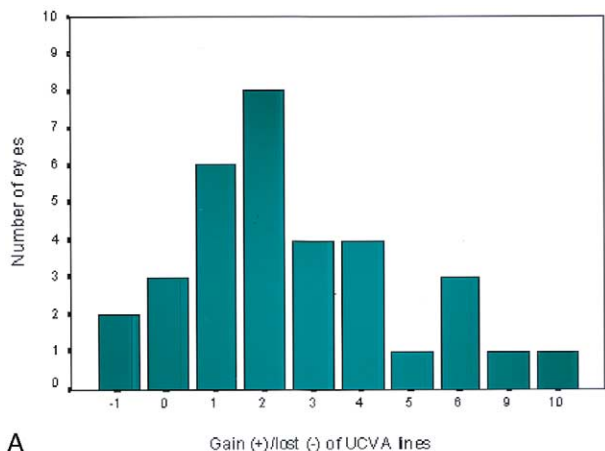
FIGURE 1. Preoperative illustration: (A) Intacs position of insertion indicated (top right) and 12-month postoperative (B) topographies of a case of left eye keratoconus.

drops four times daily for 2 weeks. In addition, all patients were instructed to avoid rubbing and to use preservative-free artificial tears frequently. The sutures were removed 2 weeks after surgery.

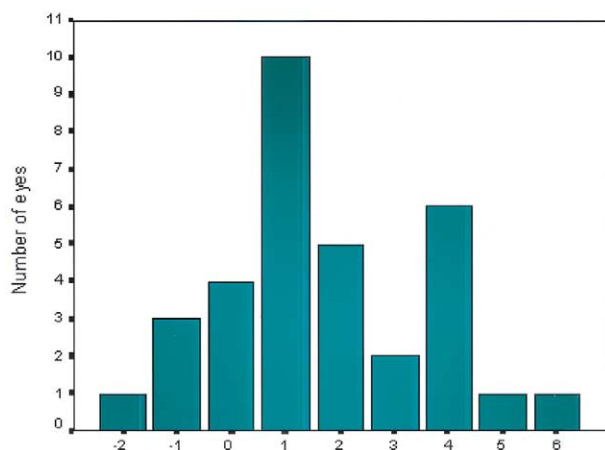
- **STATISTICAL ANALYSIS:** Group differences for continuous variables were tested using the unpaired and paired Student *t* tests and one-way analysis of variance (ANOVA) for normally distributed data. Results are presented as means \pm standard deviation [SD]. A *P* value less than .05 was regarded as statistical significance.

RESULTS

INTACS WERE SUCCESSFULLY IMPLANTED IN ALL EYES, ALTHOUGH IN ONE EYE THEY WERE REMOVED AFTER 3 MONTHS BECAUSE OF THEIR IMPROPER (SUPERFICIAL) PLACEMENT. IN ADDITION, ONE PATIENT'S INTACS WERE REMOVED AFTER 3 MONTHS OF FOLLOW-UP DUE TO PATIENT'S DISSATISFACTION, FOLLOWED BY A SUBSEQUENT PENETRATING KERATOPLASTY 3 MONTHS LATER. THE



A



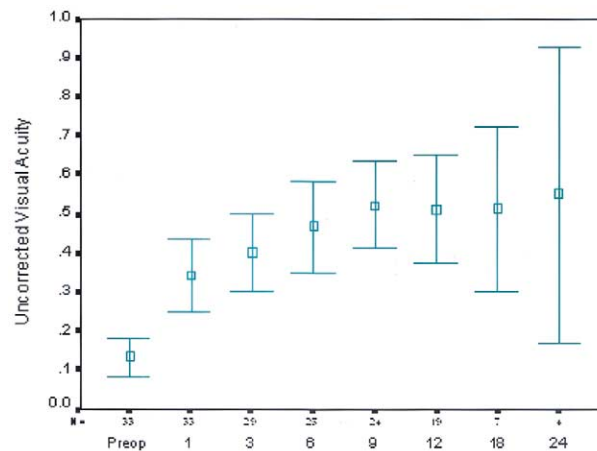
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FIGURE 2. Change in (A) uncorrected visual acuity (UCVA) and (B) best-corrected visual acuity (BCVA) (lines in decimal scale) between preoperative and the last postoperative follow-up.

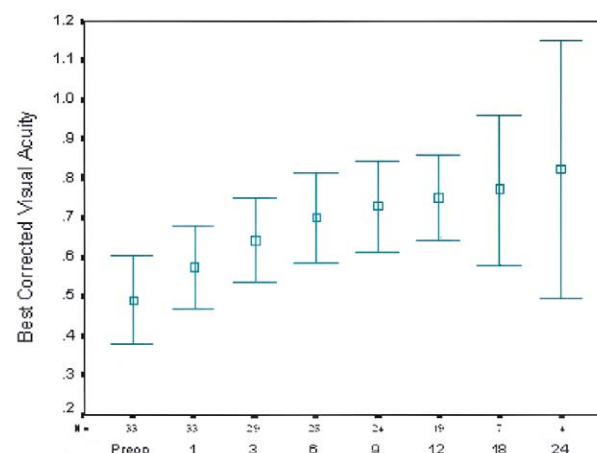
mean follow-up was 11.3 ± 6.5 months (range, 1–24 months).

• **VISUAL ACUITY:** The mean UCVA significantly improved after Intacs implantation from 0.13 ± 0.14 (range, CF-0.50) to 0.39 ± 0.27 at the last follow-up (range, CF-1.00) ($P < .01$, paired t -test). Of 33 eyes, 2 eyes lost 1 line of UCVA, and 3 eyes maintained the preoperative UCVA, whereas the rest (28 eyes) experienced 1- to 10-line gain. The mean difference between preoperative and postoperative UCVA was a gain of 2.5 lines (range, loss of 1 line to a gain of 10 lines, Figures 2A and 3A).

Best-corrected visual acuity also significantly changed from 0.47 ± 0.31 (range, CF-1.00) to 0.64 ± 0.26 (range, 0.10-1.00) ($P < .01$, paired t -test). Of 33 eyes, 4 eyes experienced a 1- to 2-line loss of BCVA and 4 eyes maintained the preoperative BCVA, whereas the rest (25 eyes) experienced a 1- to 6-line gain. The mean difference between preoperative and last follow-up BCVA was a gain



A

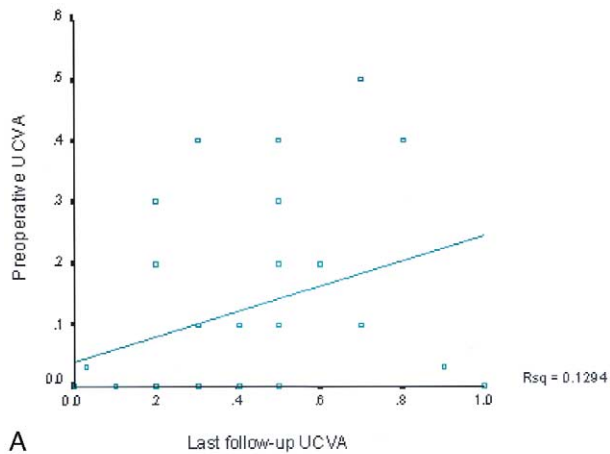


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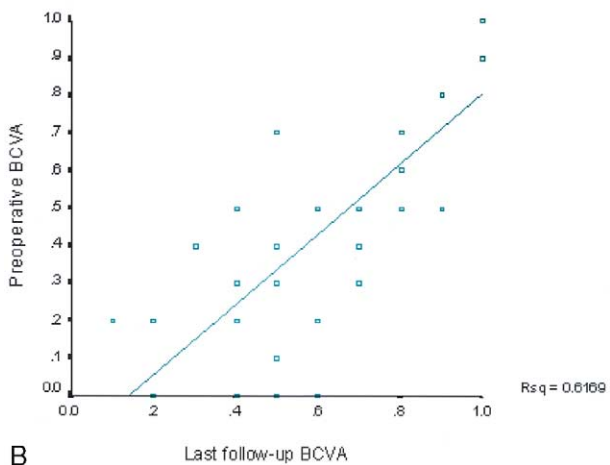
FIGURE 3. Mean (A) uncorrected visual acuity (UCVA) and (B) best-corrected visual acuity (BCVA) (decimal scale) after Intacs implantation. The error bars indicate 95% confidence intervals for the means.

of 1.7 ± 1.9 lines (range, loss of 2 lines to gain of 6 lines; Figures 2B and 3B). In parallel, the correlation between preoperative and last follow-up BCVA indicates a sufficiently invariable improvement (observable as the offset on the horizontal axis) ($rsq = 0.62$), while no similar effect was observed for the UCVA ($rsq = 0.13$; Figure 4A and 4B).

• **TOPOGRAPHIC FINDINGS (KERATOMETRIC VALUES:** A significant reduction in keratometric values was found at the last follow-up examination. Mean preoperative keratometry from 50.86 diopters ± 6.62 diopters (range, 41.67 diopters–71.00 diopters) significantly changed to 47.63 diopters ± 5.41 diopters (range, 37.54–57.56 diopters; $P < .01$) at last follow-up with a mean reduction of 1.94 diopters ± 3.51 diopters (range, +4.56 diopters to –13.75 diopters; Figure 5A). The preoperative mean keratometric



A



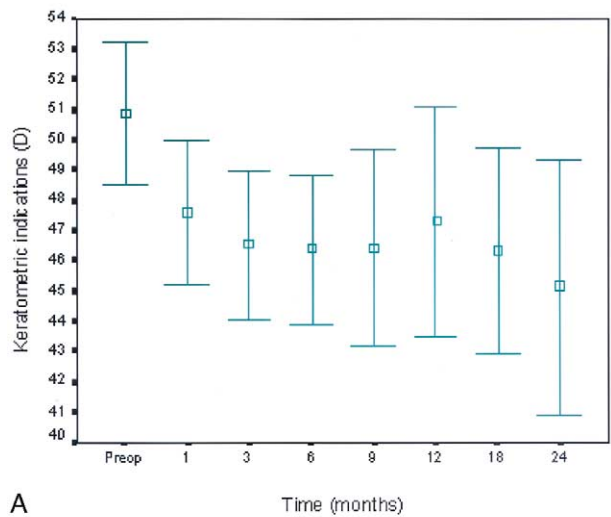
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FIGURE 4. Correlation between preoperative and postoperative (A) uncorrected visual acuity (UCVA) and (B) best-corrected visual acuity (BCVA).

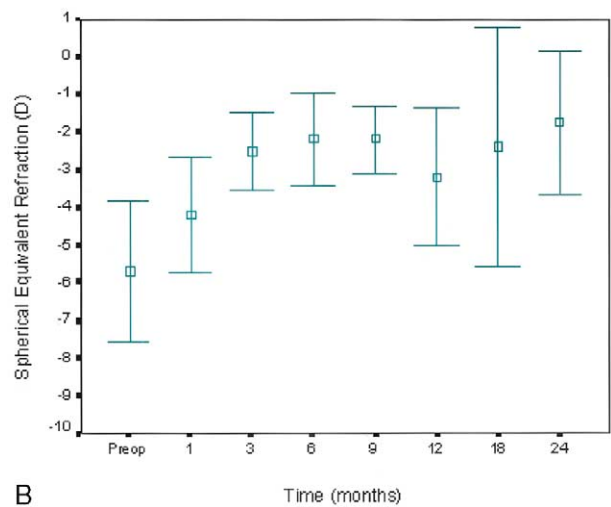
astigmatism was 3.33 ± 2.10 and the postoperative one was 3.06 ± 2.14 . These differences were not statistically significant ($P = .44$)

- **VISUAL ACUITY VERSUS KERATOMETRIC DATA:** An attempt was made to correlate the results of UCVA with the keratometric data. Eyes with a loss in or unchanged UCVA after Intacs (5 eyes) when compared with those with improved UCVA (28 eyes) were found to have preoperatively higher mean keratometric values (53.53 diopters ± 10.24 diopters compared with 50.38 diopters ± 5.91 diopters, $P = .34$) as well as preoperatively higher average keratometric astigmatism (4.65 diopters ± 2.37 diopters compared with 4.05 diopters ± 4.29 diopters, $P = .77$).

- **REFRACTIVE OUTCOME:** Preoperative and last follow-up mean values for spherical equivalent refraction revealed a statistically significant reduction ($P = .05$) from -5.67 diopters ± 4.87 diopters (range, 0 to -22.25 diopters) to -4.28 diopters ± 3.86 diopters (range, 0 to



A



B

FIGURE 5. Changes in mean (A) keratometric indications and (B) spherical equivalent refraction during the follow-up period. The error bars indicate 95% confidence intervals for the means.

-16.50 diopters) with a mean reduction value of 1.82 ± 3.30 diopters at the last follow-up (Figure 5B).

- **VISUAL ACUITY VERSUS REFRACTION:** An attempt was made to correlate the results of UCVA with refraction. Eyes with a loss in or unchanged UCVA after Intacs (5 eyes) when compared with those with improved UCVA (28 eyes) were found to have statistically significant higher preoperative values of spherical equivalent (7.88 ± 9.81 compared with 5.31 ± 3.84 , $P = .01$).

- **VISUAL ACUITY VERSUS SITE OF INTACS PLACE-
MENT:** There were no statistically significant differences in changes of UCVA and BCVA between patients with central (temporally and nasally placed segments) and inferior cone (superiorly and inferiorly placed segments) after Intacs implantation (UCVA: gain 3.50 ± 3.03 vs

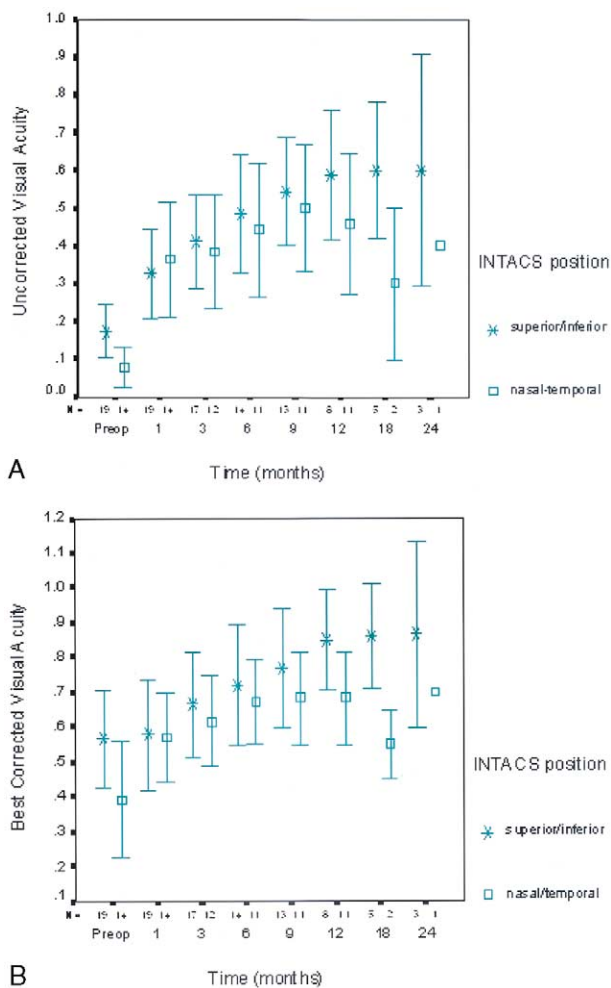


FIGURE 6. Correlation between changes in (A) uncorrected visual acuity (UCVA), (B) best-corrected visual acuity (BCVA), and Intacs placement (according to the area of cone; mean \pm SD).

2.16 \pm 2.04 lines, $P = .19$; BCVA: gain 2.50 \pm 1.70 vs 1.36 \pm 1.88 lines, $P = .08$; Figure 6A and B).

• **ADVERSE EFFECTS AND POSTOPERATIVE COMPLICATIONS.** In one eye, 6 months after Intacs implantation, a significant decrease in UCVA (from 0.4 to CF) and BCVA (from 0.8 with contact lens to 0.2) and increases in topographic irregularity were observed (Figure 7A and B). We decided to remove the superior segment and to advance the inferior segment to further embrace the keratoconus area. Three months later, the patient had a remarkable and unexpected increase in UCVA (0.8), BCVA (0.9) and in the topographic findings, which remained stable at the last follow-up 10 months later (Figure 7C and D).

In another eye (with central cone), due to superficial placement of one segment and lack of improvement of the patient's data, we decided to remove the segments after 3

months of follow-up. No significant alterations in the preoperative data were found after this manipulation.

In one eye, because of patient's dissatisfaction, Intacs were removed followed by a PKP after 3 months. Penetrating keratoplasty was uneventful, and after 6 months of follow-up there was no evidence of any postoperative complications.

At 6 months the majority of eyes demonstrated mild channel deposits at the inner edge of the segments. In one eye superficial mild wound site neovascularization was found after 2 months, which remains stable during the follow-up of 11.3 months and without any changes in visual acuity or topographic findings.

DISCUSSION

THE PROCEDURE OF PKP FOR KERATOCONUS HAS SIGNIFICANTLY improved during the past few decades. Currently, PKP results in moderate regular and irregular astigmatism, which is easily managed by various surgical techniques.^{17,18} The complication rate (such as corticosteroid side effects and allograft reactions) has decreased during the last decade.¹⁹

In the year 2000, Colin and associates¹⁵ first published an article about their preliminary results regarding the management of keratoconus with Intacs. One year later, the same authors published a series of 10 keratoconic patients 1-year after Intacs implantation²⁰ where they support that Intacs reduced the corneal steepening and astigmatism, while visual acuity was improved in almost all eyes. The surgical procedure was similar to that for low myopia correction, except the Intacs segment thickness and location of incision site. The authors used a temporal incision in all patients while a 0.45-mm thickness segment was inserted inferiorly and a 0.25-mm segment superiorly to counterbalance and flatten the overall anterior corneal surface.

In our study we used a different surgical approach, in which two same-thickness segments (0.45-mm) were inserted in all eyes. We used this approach because we believe that the intended tectonical changes in the disarray keratoconic cornea should have the maximum effect. Despite the differences between the two methods, it seems that Intacs improve UCVA, BCVA, refraction, and topographic findings in keratoconic patients. In addition, in our study there were 14 keratoconic eyes with central keratoconus. In these patients Intacs were implanted in the same position as in the low myopia procedure (nasally-temporally) without significant differences in the effect of Intacs between these eyes and those implanted superiorly-inferiorly.

An important finding was that there were a few patients who did not show improvement of UCVA (3 eyes, 9%) and BCVA (4 eyes, 12%), whereas in another group of patients a reduction in UCVA (2 eyes, 6%) and BCVA (4

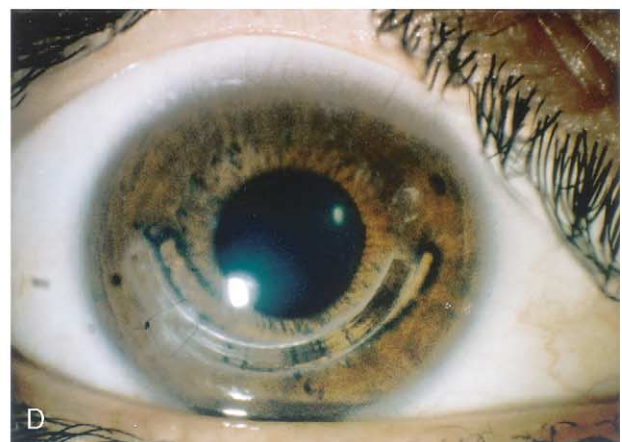
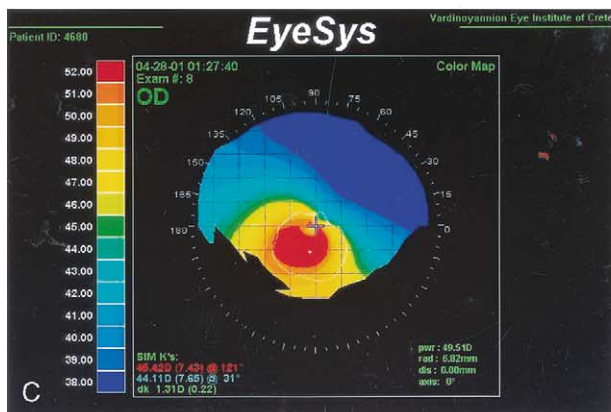
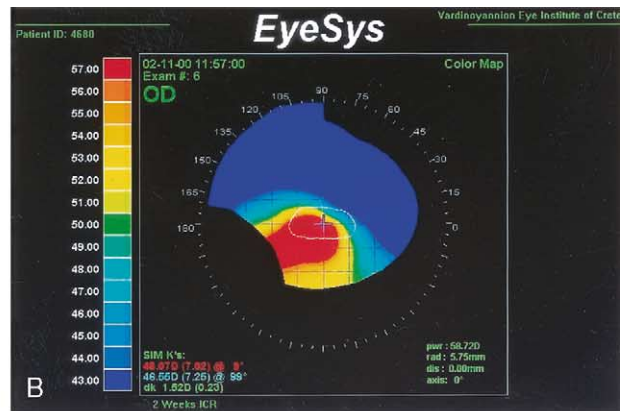
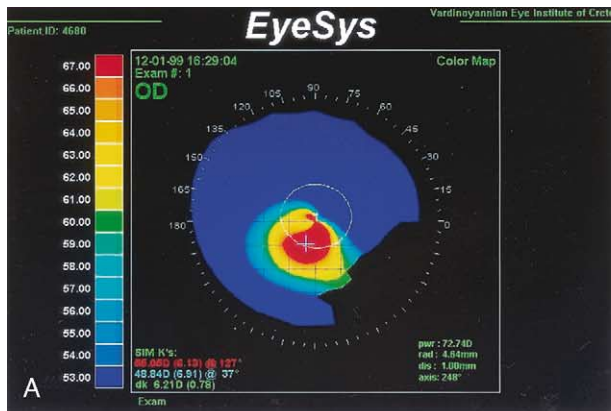


FIGURE 7. (A) Preoperative topography illustration. Postoperative topographies: (B) 2 weeks after two Intacs segments insertion; (C) 10-months after upper segment removal; (D) an illustration of right eye keratoconus where the upper segment was removed.

eyes, 12%) was observed. Loss of lines or unchanged BCVA did not necessarily correlate with patient dissatisfaction, because some of these patients experienced a significant gain of UCVA. Regarding UCVA, however, a statistically significant increase in preoperative mean spherical equivalent refraction and an increase in mean average keratometric values were found in eyes that Intacs implantation did not change or decreased UCVA in comparison with eyes with post-Intacs implantation improvement. It seems that Intacs have less effect in more advanced stages of disease, while encouraging results were found in early stages.

An advantage of this method is that Intacs are removable. One patient underwent Intacs removal, followed by PKP after 3 months (estimated by the authors to be sufficient period of time) without any complications. This one patient, however, certainly cannot eliminate the concern for the effect on the success rate of PKP after Intacs removal.

Several questions arise from complicated cases. We were surprised by the significant improvement in the patient who underwent superior segment removal. These findings support that we are indeed unable to predict the effect of Intacs in keratoconic patients.

Even though the sample of eyes that completed a 2-year follow-up is small (4 eyes), it seems that the major changes in visual acuity, refraction, and topographic findings took place during the first 9 months, while a trend for stable results was observed after this period. These results are in controversy with the results of Intacs implantation in low myopia patients, where stability in refraction and visual acuity after the third month are observed.¹⁴ This is very important when Intacs are used for keratoconus, where more time must probably be given to come out with final conclusions about the effect of Intacs in these eyes. How much time that will be, is a question to which the authors have no answer for to date.

The question that arises from our results and those of other investigators is whether Intacs can replace in selected cases PKP. We believe that the results of Intacs implantation are very preliminary, and despite the initial enthusiasm, as long as we do not have sufficient concrete data regarding patient selection and predictability of the procedure, Intacs could be considered as a new alternative minimally invasive method that is under investigation and, at the present time, cannot replace the importance of PKP in the treatment of these patients. Indeed, the assumption that Intacs can stabilize keratoconus and prevent its

progression is at this point anecdotal. Additionally, to rationalize the keratoconus patients' expectations and to protect this new method, the patients must be informed that Intacs are a new promising alternative therapy that has come to complement the keratoconic patients' treatment and not to replace PKP (at least for the present). This is essential because this method is under investigation with preliminary results. The possibility of not satisfying the exceeding patients' expectations could lead to a negative and mistrustful approach to any other therapeutic method.

In conclusion, after a mean follow-up of 11.3 months, Intacs seem to offer a minimally invasive alternative treatment before PKP for keratoconus patients with clear corneas and contact lens intolerance, especially in early stages of the disease with less topographic irregularities.

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