

Intracorneal Implants for Keratoconus and Ectasia

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Welcome to part two of our three-part series highlighting corneal ectasia. This installment discusses intracorneal implants, a novel approach to stabilizing keratoconus and reversing corneal ectasia after LASIK and PRK. Over the past decade, our experience with these pathologies has shown that, despite our best intentions and careful planning, living tissue does not always react kindly to surgical intervention. Because keractasia is the bane of the LASIK surgeon, our armamentarium must include treatment options that can reverse its debilitating effect.

When I started working with Intacs (Addition Technology, Inc., Des Plaines, IL) in 1997, I followed the pioneering research of David Schanzlin, MD; Penny Asbell, MD; Joseph Colon, MD; and Ricardo Guimaraes, MD. All of these doctors investigated Intacs for the treatment of myopia and keratoconus. Early on, I recognized the value of intracorneal rings as an alternative to penetrating keratoplasty for keratoconus. By modulating the stresses on the cornea, these inserts create a hammock effect that reduces the biomechanical force exerted by the aqueous and thus prevent further steepening of the cornea.

My colleagues and I faced several challenges as we tried to find a market for the relatively safe and reversible procedure. The mechanical dissection system with which we created the intrastromal channels required a significant amount of skill to master, and patients recovered their vision more slowly than desired secondary to corneal trauma. We were also hindered by our inability to predict with absolute certainty the channels' final diameter or the depth at which the inlays were implanted.

The advent of femtosecond laser technology, and its incorporation into the implantation of intracorneal segments, allows us to create channels of appropriate depth and diameter with significant accuracy. Consequently, patients enjoy a speedy visual recovery and overall satisfaction with the vision provided by intracorneal implants.

I hope you enjoy this installment of "Peer Review" and encourage you seek out and review the articles in their entirety at your convenience.

—Mitchell C. Shultz, MD, Section Editor

Intracorneal inserts were originally approved by the FDA in 1999 for the correction of low-level myopia.¹ In 2004, the FDA granted a humanitarian device exemption to Addition Technology, Inc., that allowed ophthalmologists to implant the company's Intacs intracorneal segments into keratoconic eyes. More recently, surgeons have begun using Intacs and other intracorneal implants such as the Ferrara Ring (Ferrara Ophthalmics, Belo Horizonte, Brazil; not available in the United States) and the Keraring (Mediphacos, Belo Horizonte, Brazil; not available in

the United States) to stabilize and halt the progression of corneal ectasia after LASIK.

MECHANISM OF ACTION

Unlike penetrating keratoplasty—previously the definitive surgical treatment for keratoconus—intracorneal implants reshape abnormal corneas without permanently removing tissue.² Surgeons can therefore reverse the topographic and refractive effects of intracorneal implants at any time by explanting the devices.

Histopathologic analysis of eight corneal buttons

removed from keratoconic eyes with a history of Intacs showed focal epithelial hypoplasia immediately adjacent to the intrastromal tunnel. The investigators also noted a lower density of keratocytes in the area surrounding the tunnel than in other areas of the cornea. These changes appeared to be reversed in eyes from which the inserts were explanted several months before they underwent penetrating keratoplasty.²

THE INTRASTROMAL CHANNEL

Before the introduction of femtosecond laser technology approximately 9 years ago, surgeons exclusively used hand-held instruments to create intrastromal tunnels for corneal implants. A retrospective analysis of 10 eyes prepared with a mechanical spreader (data collected at 6 months) versus 20 eyes prepared with the IntraLase femtosecond laser (Abbott Medical Optics Inc., Santa Ana, CA; data collected at 1 year) showed that both groups had comparable improvements in UCVA (3.63 ± 2.67 vs 4.13 ± 3.02 lines), BSCVA (1.63 ± 3.58 vs 3.92 ± 2.40 lines), and average keratometry (2.52 ± 2.21 D vs 2.91 ± 2.45 D). More patients in the femtosecond group (85%), however, could tolerate wearing contact lenses postoperatively than in the mechanical group (70%).³

Carrasquillo et al observed comparable refractive outcomes between eyes with intrastromal tunnels that were created mechanically ($n = 17$) or with the IntraLase femtosecond laser ($n = 16$). At mean follow-up of 10.3 months, UCVA and BSCVA in the mechanical group had improved from 20/200 to 20/100 and 20/40 to 20/30, respectively. During the same period, UCVA and BSCVA in the femtosecond group had improved from 20/158 to 20/63 and 20/40 to 20/25, respectively. The investigators stated, however, that they were able to implant Intacs more deeply with femtosecond versus mechanical dissection.⁴

A retrospective study by Ertan et al showed a statistically significant relationship between the size of the intrastromal channel and visual improvement among 159 keratoconic eyes of 103 patients. The eyes were randomized to receive channels measuring 6.7 X 8.2 mm (approximately 1.3 mm wide; $n = 97$) or 6.6 X 7.6 mm (approximately 1 mm wide; $n = 62$). All of the intrastromal tunnels were created with the IntraLase femtosecond laser. At 6 months, more eyes in the narrow-channel group showed significant improvement in UCVA and BSCVA from baseline (72.5% and 75.8%) than in the wide-channel group (63.9% and 70.1%). The investigators observed a higher incidence of complications with narrow versus wide channels, however, including epithelial plugs (26 vs 12 eyes), yellow deposits (29 vs 10 eyes), haze in the tunnel (nine vs two eyes), and an upward displacement of the implant (four vs zero eyes).⁵

When using the IntraLase to create intrastromal tunnels, surgeons must be sure to center the laser's appplanation plate over the pupil. In a retrospective case series, Ertan and Karacal found that the Intacs in 59 eyes of 39 patients were temporally decentered by a mean of 788.33 ± 500.34 μm . The investigators hypothesized that the pressure exerted on keratoconic corneas by the laser's appplanation plate may dilate the pupil and shift its geometric center, thus leading to the creation of decentered intrastromal tunnels. Strategies for avoiding the decentration of Intacs include properly positioning the patient's head, lifting the plate before readjusting its position, and marking the pupil's center preoperatively.⁶

POSTOPERATIVE RESULTS

Table 1 summarizes the refractive and keratometric outcomes with intrastromal rings from a series of peer-reviewed studies published between 2006 and 2008.^{4,7-12} These retrospective^{8,10,12} and prospective^{7,9,11} case series all show that intracorneal implants are a safe, viable alternative to penetrating keratoplasty for the treatment of keratoconus and corneal ectasia. Of all of these studies, however, the retrospective case series from Ertan and Ozkiliç is unique, because it divided the participants into three age groups (13 to 19, 20 to 35, and 35 to 56 years). Because the investigators did not detect a statistically significant difference in outcomes between the age groups, they concluded that age-related changes in corneal stiffness did not affect the Intacs' ability to reshape the cornea and stabilize keratoconus. In addition, they wrote, "Intacs treatment in adolescent patients with keratoconus is a safe, effective, minimally invasive alternative technique [to treating keratoconus] as it is for patients of other ages who are intolerant of gas permeable contact lenses and who have clear central corneas."¹²

Uceda-Montanes et al showed that the Keraring improved the visual acuity and corneal topography of a 31-year-old woman who developed ectasia after LASIK. Ten months after the patient received symmetric 0.35-mm rings in her left eye and asymmetric rings (0.20 mm superior and 0.25 mm inferior) in her right eye, her BSCVA had improved by four lines bilaterally. During the same period, the patient's apical keratometry had improved from 55.00 to 46.00 D OD and 52.00 to 45.00 D OS.¹³

POSTOPERATIVE COMPLICATIONS

The potential complications of intracorneal implants include the induction of astigmatism,¹ the migration of the segment in the intrastromal tunnel, extrusion, and infection.

Extrusion

The reported rate of extrusion for the Ferrara ring ranges from 10% to 19.6%.¹⁴ In a case described by Liu et

TABLE 1. REFRACTIVE AND KERATOMETRIC OUTCOMES WITH INTRACORNEAL IMPLANTS

Investigator	Number of Eyes	Implant/Indication	Channel Creation	Follow-up	Mean Outcomes
Carrasquillo et al ⁴	33	Intacs/keratoconus and ectasia	Mechanical (n = 17) IntraLase (n = 16)	10.8 months (mean for both groups)	UCVA: 20/200 to 20/80 ^a BSCVA: 20/40 to 20/30 ^a
Kanellopoulos et al ⁷	20	Intacs/keratoconus	Mechanical	6 months	UCVA: 20/154 to 20/28 ^a BSCVA: 20/37 to 20/22 ^a Keratometry: 49.45 to 46.35 D
Alió et al ⁸	13	Intacs/keratoconus	Mechanical	6 months	BSCVA: 20/50 to 20/30 ^a Keratometry: 48.46 to 45.32 D ^a
Shetty et al ⁹	14	Intacs /keratoconus	Mechanical	6 months	UCVA: 20/400 to 20/125 BSCVA: 20/40 to 20/30 Keratometry: 53.01 to 49.42 D
Kymionis et al ¹⁰	17	Intacs/keratoconus	Mechanical	5 years	UCVA: gain of 2.8 lines (Snellen) BSCVA: gain of 1.4 lines (Snellen) Keratometry: 49.59 to 48.02 D ^a
Coskunseven et al ¹¹	50	Keraring/keratoconus	IntraLase	15.6 months (mean)	UCVA: gain of 1.7 lines (Snellen) BSCVA: gain of 1.3 lines (Snellen) Keratometry: 50.63 to 47.56 D ^a
Ertan and Ozkilig ¹²	109, divided into three age groups (13 to 19, 20 to 35, and 35 to 56 years)	Intacs/keratoconus	IntraLase	1 year	Comparable statistically significant improvements in UCVA ($P = .930$), BSCVA ($P = .470$), and keratometry ($P = .545$) in all three age groups
^a Statistically significant result.					

al, the implant's extrusion occurred after a 31-year-old man was poked in the eye by his child. After removing the segment and examining the patient's eye, the investigators determined that "the Ferrara channels of our patient were superficially created and thus most likely contributed to the extrusion of the ring segment."¹⁴ To minimize the risk of extrusion, the cornea should be dissected to at least 370 μm deep for the entire length of the segment, and the proximal end of segment should be positioned at least 1 mm inside the channel.¹⁴

Infection

A case study published by Chalasani et al shows the importance of appropriately treating microbial infections associated with intracorneal rings. The factors that contribute to such infections include a breakdown of the epithelium over the implant, extrusion of the ring from the intrastromal channel, and the presence of multiple incisions. Because the 40-year-old woman described in the case did not respond to intensive therapy with topical antibiotics, the infection progressed to the beds of both channels, leading to the development of a hypopyon. The Ferrara segments were explanted from her left eye, and the superior and inferior channels were irrigated with vancomycin 5%. After additional therapy with topical vancomycin and tobramycin, the patient was discharged from the hospital. The strategy followed by Chalasani et al in this case reflects their recommendation that clinicians choose a treatment modality that depends on the extent and severity of the corneal infection.¹⁵

INTRACORNEAL IMPLANTS AND CORNEAL CROSS-LINKING

A retrospective, nonrandomized study showed that combining Intacs with corneal cross-linking improved corneal keratometry more effectively than Intacs alone. By approximately 100 days postoperatively, the steep and average keratometry in the Intacs/cross-linking eyes had changed by 1.94 ± 1.32 D and 1.34 ± 1.27 D, respectively. During the same period, keratometry had changed by 0.89 ± 2.07 D (steep) and 0.21 ± 2.70 D (average) in the Intacs-only group.

The investigators hypothesized that the greater degree of corneal flattening that they observed in the Intacs/cross-linking group was caused by an accumulation of riboflavin above the superior edge of the implant and a subsequent increase in corneal cross-linking at this site relative to other areas of the cornea.¹⁶

Kamburoglu and Ertan observed a similarly synergistic relationship between Intacs and corneal cross-linking in a 27-year-old man who underwent both procedures to sta-

bilize post-LASIK ectasia. Three days after the patient received Intacs SK segments in his right eye, his UCVA improved from 20/100 to 20/60. His vision slowly deteriorated to 20/100 over the next 8 months, however, and stabilized at 20/30 only after treatment with transepithelial cross-linking. The UCVA in the patient's left eye improved dramatically from 20/160 to 20/60 with Intacs, but because he underwent transepithelial cross-linking the next day, his vision did not regress before it stabilized at 20/25 7 months later. The investigators concluded, "Intacs SK implantation may be an alternative in the treatment of postoperative LASIK ectasia and [corneal cross-linking] may be considered as an additional treatment modality for preventing regression that may be seen after this treatment and for stabilization and reversal of its effect."¹⁷ ■

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