Intacs for keratoconus

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Purpose of review
The use of Intacs as a therapeutic modality in contact lens intolerant patients with mild to moderate keratoconus is increasingly gaining acceptance in the ophthalmic community.

Recent findings
During the past year we have gleaned significant new information about patients who are appropriate candidates, the location and relative placement of segment sizes and long-term safety and stability after Intacs placement. Another new and exciting development which will make this procedure safer and more commonly acceptable is the use of the femtosecond laser to create the channels to insert the Intacs, which has been described for the first time this year. This technology allows for accurate depth of inserting, improved outcomes and less complications due to superficial placement. New reports about Intacs revision surgery also allows us to retreat many patients who would otherwise have been considered surgical failures.

Summary
The new advances described this past year will improve outcomes and ultimately contribute to an increase in the amount of physicians performing this procedure and the number of patients requesting it.

Keywords
complications, femtosecond laser, Intacs, keratoconus, stability

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Abbreviations

BSCVA	best spectacle corrected visual acuity
I–S	ratio inferior–superior ratio
LASEK	laser-assisted subepithelial keratectomy
LASIK	laser in-situ kertomileusis
OCT	optical coherence tomography
UCVA	uncorrected visual acuity

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Introduction

Intacs (Addition Technology, Des Plaines, Illinois) as a treatment modality for keratoconus was first described by Colin *et al.* in 2001 [1] as an alternative to penetrating keratoplasty in contact lens intolerant patients with moderate disease. In his study he reported on 10 patients and demonstrated flattening of the cornea accompanied by return to contact lens tolerance as well as improved best spectacle corrected (BSCVA) and uncorrected visual acuity (UCVA).

Between 2001 and 2005 other investigators demonstrated similar outcomes using a varying combination of segment sizes in a more diverse group of patients. The results of these studies are summarized in a recent review article in *International Ophthalmology Clinics* [2••,3–5].

During this past year, studies have given us new information about the safety and efficacy of Intacs, candidacy, long-term stability, the number of segments to be placed, the relative placement of thick versus thinner segments, use of the femtosecond laser to create channels, adjustments to improve results in failures, contact lens fitting, LASEK after Intacs to improve unaided acuity, patients at risk for complications, histopathology and use of optical coherence tomography (OCT) to ensure adequate stromal depth to prevent corneal erosion of Intacs.

Ideal candidates for Intacs

Patients with mild to moderate keratoconus appear to be the best candidates for Intacs, as illustrated by two reports this past year, one by Alio *et al.* [6••] and one by Colin [7•], while those with more advanced disease are more prone to complications, as illustrated in a report by Kannellopoulos *et al.* [8•].

The results of Alio *et al.*'s study suggest that the best candidates are those with clear central corneas, low spherical equivalents and average keratometry readings of less than 53 D, while those with more advanced disease and average keratometry readings in excess of 55 D were poor candidates. In a retrospective study of 25 patients [6••], the authors noticed that at 6 months eyes with an average keratometry reading of less than 53 D gained more than three lines of BSCVA while those with average keratometry readings of greater than 55 D lost one line of BSCVA. In the first group, the preoperative mean BSCVA was 0.43 (20/50) and the postoperative mean BSCVA was 0.82 (20/20) ($P \leq 0.0001$). In the second group the preoperative mean BSCVA was 0.36 (20/63) and the postoperative mean BSCVA was 0.24 (20/80) ($P \leq 0.02$).

Colin [7•] reported on 57 patients with moderate disease who were contact lens intolerant who underwent Intacs and were followed for up to 1 year. At the 6 month examination, 78% of patients showed improvement of two lines or more in UCVA ($P < 0.001$). BSCVA of 20/40 or better improved from 53% of patients preoperatively to 74% of patients postoperatively ($P \leq 0.033$). Manifest refraction and spherical equivalent improved by 3 D while keratometry was reduced by a mean of 4 D. At 6 months, there were no adverse events and no decrease in central corneal thickness. In 12% of eyes Intacs were removed due to dissatisfaction with visual symptoms with no sequelae.

Alio *et al.*'s study suggesting that patients with more advanced disease do not do as well is also illustrated in a report by Kannellopoulos *et al.* [8•], who reported on a series of 20 eyes with more advanced disease who had a 40% complication rate: one anterior chamber perforation, one dense corneal infiltrate and six eyes with ring exposure secondary to corneal thinning over the implants at 3–6 months postoperatively, despite improvements in UCVA and BSCVA which remained stable till the 12-month follow-up visit. All three of these studies were performed inserting Intacs with a mechanical spreader.

Femtosecond laser to create channels for Intacs insertion

Many of the problems encountered when inserting Intacs using the mechanical spreader could potentially be overcome with a new technique described by Rabinowitz *et al.* [9••] – a femtosecond laser (IntraLase; IntraLase Corp., Irvine, California) used to create the channels. This procedure is easier for the surgeon, more patient friendly and ensures accurate depth of placement of the Intacs, which cannot be guaranteed using the mechanical spreader.

In their study, Rabinowitz *et al.* [9••] reported on 10 eyes using the mechanical spreader to create the channels and subsequently on another 20 eyes using the femtosecond laser. Data were collected at 6 months (femtosecond group), and 1 year (mechanical group). Both groups showed significant reduction in average keratometry, spherical equivalent refraction, BSCVA, UCVA, surface regularity index (SRI), and surface asymmetry index (SAI). The laser group performed better in all parameters except change in SRI. The results of the laser versus the mechanical spreader were as follows: reduction in spherical equivalent refraction (3.98 versus 2.96), change in average keratometry (2.91 versus 2.52), improvement in UCVA (4.13 versus 3.63), improvement in BSCVA (3.92 versus 1.63), change in SRI (0.37 versus 0.64), and change in SAI (1.00 versus 0.70). Statistical analysis, however, did not reveal any statistically significant differences between the two groups for any single parameter studied. The biggest improvement in the laser group versus the mechanical group was BSCVA ($P = 0.09$). Overall success, defined as contact lens or spectacles tolerance, was 85% in the laser group and 70% in the mechanical group.

Ertan *et al.* [10], in a subsequent report on a larger group of 118 eyes with keratoconus, demonstrated that Intacs implantation with the femtosecond laser was safe and effective. At the end of the first postoperative year, 81.3% of eyes had improved UCVA and 73.7% had improved BSCVA. The mean keratometry decreased from 51.56 to 47.66 D, and the mean refractive spherical equivalent decreased from −7.57 to −3.72 D.

Long-term follow up

Patients often ask about the long-term results of Intacs for keratoconus; this past year there are three studies which answer that question:

Colin and Malet [11] reported on 100 eyes with 2-year follow up. The UCVA and BSCVA improved in 80.5% and 68.3% of eyes, respectively ($P < 0.001$). The proportion of eyes with a BSCVA of at least 0.5 (20/40) increased from 22.0% at baseline to 51.2% and 53.7% at 1 and 2 years, respectively ($P < 0.001$). The manifest refraction spherical equivalent improved from a mean ± SD of -6.93 ± 3.91 D preoperatively to -4.01 ± 3.16 D at 1 year and -3.80 ± 2.73 D at 2 years ($P < 0.001$). The mean keratometry readings decreased from 50.1 ± 5.6 D preoperatively to 46.4 ± 5.3 D at 1 year and 46.8 ± 4.9 D at 2 years ($P < 0.001$). Contact lens tolerance was restored in over 80% of cases. The segments were removed from four eyes without complications or sequelae.

Alio *et al.* [12] reported on 13 eyes whose outcomes were evaluated at 6, 12, 24 and 36 months in all eyes and at 48 months (six eyes). Mean BSCVA increased from 0.46 (20/50) preoperatively to 0.66 (20/30) postoperatively ($P \leq 0.001$). Mean decrease of inferior–superior (I–S) asymmetry was 2.81 D ($P \leq 0.02$), and the average keratometry value was 3.13 D ($P \leq 0.001$). Mean difference between 6 and 36 months (stability) showed no significant difference regarding BSCVA ($P \leq 0.5$) and I–S asymmetry ($P \leq 0.6$). Although a significant increase was noticed in the average keratometry by 1.67 D ($P \leq 0.002$), at 36 months it did not reach the initial preoperative values.

Kymionis *et al.* [13••] reported on 17 eyes with 5 years of follow up. At 5 years, the spherical equivalent error was statistically significantly reduced (pre-Intacs mean ± SD, -5.54 ± 5.02 D, range −12.50–3.63; -3.02 ± 2.65 D, range −8.25–1.88; $P = 0.01$). Pre-Intacs UCVA was 20/50 or worse in all eyes (range, counting fingers to 20/50), whereas, at the last follow-up examination, 10 (59%) of 17 eyes had UCVA of 20/50 or better (range, counting fingers to 20/32). Six eyes (35%) maintained the pre-Intacs BSCVA and one eye lost three lines of BSCVA, whereas the rest of the 10 eyes (59%) experienced a gain of one to eight lines. There was no evidence of progressive sight-threatening complications in this study.

Post laser in-situ kertomileusis ectasia

This past year, long-term data have also for the first time been reported on patients who have had Intacs for post laser in-situ kertomileusis (LASIK) ectasia. While most surgeons put in a single inferior ring through a temporal incision, Kymionis *et al.* [14••] reports on a 5-year follow up of eight eyes in which two segments were inserted vertically, as done in low myopia correction.

At 5 years, the spherical equivalent was statistically significantly reduced (pre-Intacs mean $\pm$ SD, -5.47 ± 2.66 D, range, -11.50 to -3.00) to -2.56 ± 3.44 D, range, -9.50–1.5; $P = 0.01$). At the end of the first postoperative year, refractive stability was obtained and remained stable during the follow-up period with no significant changes between the interval meantime ($P > 0.05$). Pre-Intacs UCVA was 20/100 or worse in all eyes (range, counting fingers 20/100), whereas at the last follow-up examination, six (75%) of eight eyes had UCVA of 20/40 or better (range, counting fingers 20/25). Two eyes (25%) maintained the pre-Intacs BSCVA, whereas the rest of the eyes (six eyes, 75%) experienced a gain of one or two lines. Refractive stability was maintained for up to 5 years and there was no evidence of progressive time-dependent corneal ectasia, late regression, or sight-threatening complications in this study.

Asymmetric segments

In Colin's initial report [7•] he inserted a 0.25 mm segment above and 0.45 mm segment below. Since then, however, there have been many variations on this, some of which have been reported on this year. These include a thicker segment above and thinner one below, a single inferior segment, or two vertical segments.

It appears that putting the thicker segment above and thinner one below is not a good idea, as illustrated by two case reports: one by Alio and Shabayek [15] and one by Chan and Wachler [16]. Both noticed poor vision and decreased BSCVA in patients who had thicker segments above and thinner ones below, with the vision improving dramatically when the segments were reversed with the thinner one being inserted above and the thicker one below, as in Alio's report, or both Intacs being removed and a single thicker segment inserted inferiorly, as in Chan's report.

Sharma and Boxer Wachler [17•] subsequently performed a study evaluating the efficacy of single-segment Intacs compared with double-segment Intacs in subjects with post-LASIK ectasia and keratoconus and concluded that single-segment Intacs improved both UCVA and BSCVA by differential flattening of inferior meridian and steepening of superior meridian, as reflected by a change in the I–S ratio. Thirty-seven eyes of patients with keratoconus and post-LASIK ectasia were classified into two groups: a single-segment group (17 eyes, 11 patients) and a double-segment group (20 eyes, 17 patients). Both groups were matched for age, visual acuity (UCVA and BSCVA), refractive error (sphere, cylinder, spherical equivalent), and keratometry value (flat, steep, average) by *t*-test for equality of means. There was more improvement in UCVA in the single-segment group (nine lines) than the double-segment group (2.5 lines), $P < 0.01$; in BSCVA in the single-segment group (2.5 lines) than the double-segment group (<1 line), $P < 0.01$; in steep keratometry values in the single-segment group (2.76 ± 2.68 D) than the double-segment group (0.93 ± 2.01 D), $P = 0.02$; and in I–S ratio in the single-segment group (9.51 ± 7.49) than the double-segment group (4.22 ± 4.82), $P = 0.01$; and greater cylinder decrease after Holladay vector analysis in the single-segment group (5.69 ± 3.10 D) than the double-segment group (1.58 ± 3.09 D), $P < 0.01$.

Ertan and Bahadir [18] reported on the successful outcomes of two cases of vertical implantation of asymmetric Intacs in two patients who had temporal cones, with the thicker segment being placed in the temporal area.

Adjustments, laser-assisted subepithelial keratectomy and contact lenses

An initial poor outcome after Intacs implantation does not necessarily mean failure of the procedure; in some instances the Intacs can be adjusted to improve the visual outcomes, as illustrated in a report by Pokroy and Levinger [19••].

They noted that they were able to improve the results in seven of 58 patients who initially had a poor result. After the initial Intacs surgery, six of these eyes had UCVA $\leq$ 20/100 and one had UCVA of 20/50. After the final Intacs adjustment, three eyes achieved UCVA $\geq$ 20/40, five achieved UCVA $\geq$ 20/70, and two remained less than 20/200. The indications for Intacs adjustments were increased astigmatism in four eyes, induced hyperopia (overcorrection) in three, and undercorrection in one. One eye had both surgically induced astigmatism and hyperopia. Induced astigmatism and hyperopia were most often managed by removing the superior segment. The undercorrected eye, having initially received a single inferior segment, was treated by implanting a superior segment.

These authors concluded that approximately 10% of keratoconic eyes managed with Intacs may require Intacs adjustment surgery, which often has a good outcome.

Hirsh *et al.* [20] performed LASEK on four patients with stable keratoconus 6 months after Intacs implantation to correct residual myopia and astigmatism. The mean refraction prior to LASEK was myopia of −0.2 D and astigmatism of −2.71 D. The mean follow-up period after LASEK was 8 months. Prior to both surgeries, the mean UCVA was 6/240 (range, count fingers to 6/60) and at the final postoperative visit 6/12 (range 6/10–6/18). The preoperative mean BSVCA was 6/15 (range 6/10–6/24) and at the final postoperative follow-up visit 6/9 (range 6/8.5–6/12). They concluded that wavefront-guided LASEK for correction of residual myopia and astigmatism in keratoconus patients after Intacs insertion and stable refraction provided excellent visual outcome, with no loss of visual acuity and no complications.

Patients whose uncorrected vision is unsatisfactory after Intacs implantation may sometimes obtain adequate acuity after being fitted with a soft toric contact lens, as illustrated in a report by Ucakhan *et al.* [21]. They described a patient who underwent Intacs surgery with an unsatisfactory result and who refused to undergo an Intacs removal procedure. The patient's eye was satisfactorily fitted with a soft contact lens 5 months after Intacs placement.

Optical coherence tomography

Lai *et al.* [22] suggested that OCT provides a more precise measurement of ring segment depth than slit lamp evaluation and may help identify implants that pose a greater risk for depth-related complications in patients treated with Intacs.

In four patients, the slitlamp impression of intrastromal corneal ring segment implantation depth did not correlate well with OCT measurements. The position of the distal portions of the ring segments was shallower than that of the portion closer to the insertion site. Segments placed in the inferior cornea experienced more distal shallowing. The distal and inferior portions of intrastromal corneal ring segments tended to be placed at a shallower depth, putting them at higher risk for extrusion through the corneal stroma.

Histopathology

Samimi *et al.* [23] reported on the histopathological findings of keratoconus buttons at the time of keratoplasty following Intacs implantation. This retrospective study involved eight patients who had penetrating keratoplasty (PKP) after removal of Intacs inserts because of a poor refractive outcome or insert extrusion. Conventional histology showed hypoplasia of the epithelium immediately surrounding the channel. There was no evidence of an inflammatory response or foreign-body granuloma. Keratocyte density was decreased above and below the tunnel. All samples stained negatively with α-smooth muscle actin, indicating that myofibroblasts were not present. These changes were no longer visible when PKP was performed more than 6 months after Intacs explantation. They concluded that although histological changes seem to be entirely reversible after implant removal, longer follow up is necessary to determine whether implants accelerate corneal thinning.

Conclusion

The treatment of patients with keratoconus is improving as technology improves and as we learn more about the effects of these segments on keratoconic corneas. The ease and accuracy with which Intacs can be inserted with the femtosecond laser will likely lead to more clinicians and patients adopting this procedure. Long-term results appear to suggest that this is a safe procedure, indicating a moderate degree of stability over the long term, which is particularly evident in patients treated with Intacs for post-LASIK ectasia.

Acknowledgement

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References and recommended reading

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• of special interest
•• of outstanding interest
Additional references related to this topic can also be found in the Current World Literature section in this issue (p. 344).

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