ADDITION TECHNOLOGY

Professional Use Information Manual for Correction of Myopia with Intacs® Corneal Implants

Physician Booklet

RESTRICTED DEVICE: U.S. Federal Law restricts this device to sale, distribution and use by or on the order of a physician.

This document provides information concerning the intended use of Intacs Corneal Implants. For additional information, refer to the Intacs® Surgeon Training Manual.

Carefully read all instructions prior to use. Observe all contraindications, warnings and precautions noted in these instructions. Failure to do so may result in patient complications.

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General Warnings

- RESTRICTED DEVICE: U.S. Federal Law restricts this device to sale, distribution and use by or on the order of a physician.

- Specific training is required before a physician is qualified to perform the Intacs Corneal Implants procedure. Physicians must successfully complete an Addition Technology-approved training program and read and understand this booklet and the Intacs® Surgeon Training Manual, prior to performing the procedure.

- Performance of the Intacs Corneal Implants procedure, other than as specified in this booklet and the Intacs® Surgeon Training Manual, may result in an undesirable outcome.

- All patients must be given the opportunity to read and understand the Patient Information Booklet, entitled "Facts You Need to Know About Intacs® Corneal Implants for Nearsightedness," and to have you answer all their questions to their satisfaction before giving consent for the Intacs procedure.

I. Device Description

Intacs® Corneal Implants, also known as INTACS prescription inserts, are an ophthalmic medical device designed for the reduction or elimination of myopia from -1.00 to -3.00 diopters. When placed in the corneal stroma, outside of the patient's central optical zone, the product reshapes the anterior surface of the cornea. Intacs segments are designed to be placed in the periphery of the cornea, at approximately two-thirds depth, and are surgically inserted through a small radial incision in the corneal stroma. The Intacs product has been designed to allow removal or replacement.

Intacs Corneal Implants are composed of two clear segments, each having an arc length of 150° (see diagram below). They are manufactured from polymethylmethacrylate (PMMA) and are available in five thicknesses, 0.250 mm, 0.275 mm, 0.300 mm, 0.325 mm and 0.350 mm. The degree of correction is determined by the thickness of the Intacs Corneal Implants. The two segments are designated as clockwise (CW) and counterclockwise (CCW) to correspond to their orientation within the intrastromal tunnel. The product is designed with a fixed outer diameter and width. Intacs Corneal Implants have two positioning holes, located at each end of the segment, to aid in surgical manipulation.

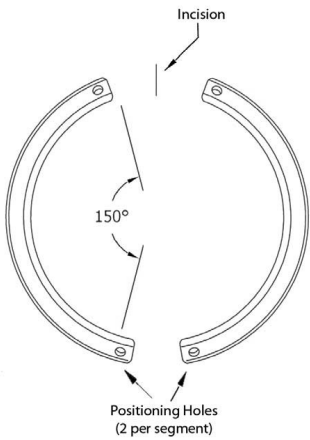


Diagram of Intacs Corneal Implants

Based on the U.S. clinical trial results, a continuous but non-overlapping recommended prescribing range was initially created for the 0.250 mm, 0.300 mm and 0.350 mm Intacs Corneal Implants. The 0.275 mm and 0.325 mm Intacs Corneal Implants were subsequently developed to provide for smaller correction increments between Intacs Corneal Implants thicknesses. The recommended prescribing range for the 0.275 mm and 0.325 mm Intacs Corneal Implants has been created by using an Intacs performance model which is based upon an interpolation of the existing clinical data. The recommended prescribing range for all thicknesses is shown below.

Intacs Corneal Implants Thickness	Predicted Nominal Correction	Recommended Prescribing Range
0.250	-1.3 D	-1.00 to -1.50 D
0.275	-1.7 D	-1.625 to -1.75 D
0.300	-2.0 D	-1.875 to -2.125 D
0.325	-2.3 D	-2.25 to -2.50 D
0.350	-2.7 D	-2.625 to -3.00 D

II. Indication For Use

Intacs® Corneal Implants are intended for the reduction or elimination of mild myopia (-1.00 to -3.00 diopters spherical equivalent at the spectacle plane) in patients:

- who are 21 years of age or older;
- with documented stability of refraction as demonstrated by a change of less than or equal to 0.50 diopter for at least 12 months prior to the preoperative examination; and
- where the astigmatic component is +1.00 diopter or less.

III. Contraindications

Intacs Corneal Implants are contraindicated:

- in patients with collagen vascular, autoimmune or immunodeficiency diseases;
- in pregnant or nursing women;
- in the presence of ocular conditions, such as keratoconus, recurrent corneal erosion syndrome or corneal dystrophy, that may predispose the patient to future complications; or
- in patients who are taking one or more of the following medications: isotretinoin (Accutane[1]); amiodarone (Cordarone[2]); sumatriptan (Imitrex[3]).

[1] Accutane® is a registered trademark of Roche Pharmaceuticals.
[2] Cordarone® is a registered trademark of Wyeth-Ayerst Laboratories.
[3] Imitrex® is a registered trademark of Glaxo-Wellcome, Inc.

IV. Warnings

- Some patients with large dilated pupil diameters (≥7.0 mm) are predisposed to low light visual symptoms postoperatively and should be appropriately advised.
- The long-term effect of Intacs Corneal Implants on endothelial cell density has not been established. Central endothelial cell density loss for eyes implanted with INTACS inserts was 1.3% ± 3.9% (n=94) during the first postoperative year and 2.0% ± 3.2% (n=94) during the second postoperative year. Additional long-term data are being collected.
- Under mesopic conditions, patients may experience some loss in contrast sensitivity at low spatial frequencies (1.5 cycles per degree).

V. Precautions

- Use of the Vacuum Centering Guide subjects the eye to increased intraocular pressure. **Continuous application of vacuum should be limited to 3 minutes or less and to no more than 750 mBar.** If it is necessary to reapply the Vacuum Centering Guide, wait 5 minutes to allow normal vascular perfusion of the eye to occur before reestablishing suction.
- Patients who receive the 0.350 mm Intacs Corneal Implants may experience a reduced outcome as compared to patients who receive other Intacs Corneal Implants thicknesses. Additionally, there may be an increased removal rate for 0.350 mm patients due to dissatisfaction with their outcomes. (See section entitled “Safety and Efficacy Results.”)
- Patients with myopia of -1.00 diopter are more likely to be overcorrected.
- Intacs Corneal Implants are not recommended in patients with systemic diseases likely to affect wound healing, such as insulin-dependent diabetes or severe atopic disease.
- Intacs Corneal Implants are not recommended in patients with a history of ophthalmic *Herpes simplex* or *Herpes zoster*.
- A temporary decrease in central corneal sensation has been noted in some patients. No clinical consequences were demonstrated in the U.S. clinical trials.
- The safety and effectiveness of alternative refractive procedures following the removal of Intacs Corneal Implants have not been established.
- Intacs Corneal Implants are intended for single use only; do not reuse or resterilize.

- The safety and effectiveness of Intacs Corneal Implants have **NOT** been established:
  - in patients with progressive myopia or astigmatism, nuclear sclerosis or other crystalline lens opacity, corneal abnormality, or previous corneal surgery or trauma;
  - for patients under 21 years of age;
  - for corneas that are steeper than 46 diopters or flatter than 40 diopters;
  - for corneas with a central thickness less than 480 microns or peripheral thickness less than 570 microns;
  - in patients with greater than -3.50 diopters of myopia or with astigmatism greater than +1.00 diopter; or
  - in long-term use.

VI. Adverse Events

A total of 452 patients were enrolled in the U.S. Phase II and Phase III clinical trials for the 0.250 mm, 0.300 mm and 0.350 mm Intacs Corneal Implants. Intacs segments were successfully placed in 449 eyes out of 454 surgical attempts.

A. Adverse Events

Adverse events (AEs) were defined in the protocols as those observations that, if left untreated or undetected, were considered to be serious and potentially sight-threatening or could have permanent sequelae associated with them.

A total of five AEs, one in each of five patients, were reported for an overall cumulative AE incident rate of 1.1% (See Table 1). All patients recovered without clinically meaningful sequelae.

TABLE 1: Adverse Events

Description of Event	Incidence n/N	Incidence %
Infectious keratitis—Both segments removed	1/454	0.2%
Shallow placement of temporal segment—One segment removed	1/454	0.2%
Loss of 2 lines of BSCVA at two consecutive exams—BSCVA regained later	1/454	0.2%
Anterior chamber perforation during initial procedure—Intacs segment not placed	1/454	0.2%
Anterior chamber perforation during exchange procedure—Intacs segment not replaced	1/454	0.2%
Total	5/454	1.1%

BSCVA = Best Spectacle-Corrected Visual Acuity

B. Ocular Complications

Ocular complications were defined in the protocols as those findings that had the potential to be clinically significant but were likely to resolve without permanent sequelae and would not result in injury to the eye.

There were four incidents of intraoperative complications where Intacs Corneal Implants were not placed: corneal surface perforation (3) and chemosis (1). None of these intraoperative complications was related to the Intacs Corneal Implants.

Table 2 provides a summary of the ocular complications associated with Intacs Corneal Implants that occurred at Month 6 and Month 12. A total of 64 patients at Month 6 and 45 patients at Month 12 experienced ocular complications. The complication categories are listed in order of frequency at Month 12.

TABLE 2: Summary of Ocular Complications

	Month 6		Month 12	
Description	**n/N**	**%**	**n/N**	**%**
Reduction of Central Corneal Sensation ≥20 mm[1]	24/259	9.3%	13/237	5.5%
Induced Cylinder: > 1 D to 2 D	19/437	4.3%	15/410	3.7%
> 2 D	1/437	0.2%	0/410	0%
Neovascularization: Pannus	2/438	0.5%	6/410	1.5%
Deep	5/438	1.1%	5/410	1.2%
Loss ≥ 10 Letters or ≥ 2 Lines BSCVA[2]	7/436	1.6%	4/410	1.0%
Persistent Epithelial Defect	2/435	0.5%	1/410	0.2%
Iritis/Uveitis	2/438	0.5%	1/410	0.2%
Noninfectious Infiltrate (no loss of BSCVA)	2/438	0.5%	0/410	0%

[1]Subgroup test.
[2]Protocol defines BSCVA loss as an Adverse Event only if present at 2 or more consecutive exams.

C. Secondary Surgical Interventions

A cumulative total of 17/449 (3.8%) Intacs Corneal Implants patients had a secondary surgical intervention performed during the twelve month reporting period. The surgical interventions included: cyst/plug removal (3/449), filament removal (2/449), foreign body/iron rust ring removal (1/449), punctal plug/punctal occlusion (5/449), wound revision (1/449) and Intacs Corneal Implants repositioning (5/449). Only three of the surgical interventions were considered to be clinically meaningful. Two patients had a new tunnel dissected to improve the position of the Intacs segments and one patient had a "relaxing incision" to reduce their induced cylinder.

D. Other Ocular Findings

Deposits were observed in the intrastromal tunnel, including the incision area, at the Month 12 exam for 213/312 (68%) of Phase III patients. The magnitude was graded as "Trace" for 115/312 (36.9%), as "+1" for 87/312 (27.9%), as "+2" for 10/312 (3.2%) and as "+3" for 1/312 (0.3%).

The specific origin and etiology of the deposits have not yet been conclusively established. The prevalence and level of deposits remained stable from the Month 6 to the Month 12 postoperative exams. In all cases, the deposits were confined to the intrastromal tunnel with no visual consequence.

E. Patient Reported Visual Symptoms

Among the 39 Intacs Corneal Implants removals during the reporting period, 19/39 (49%) were due to the patients' dissatisfaction with visual symptoms. (See section entitled "Removals and Exchanges.")

The tables that follow include patient reported visual symptoms for those patients who completed their Month 12 exam. Table 3 provides a summary of the visual symptoms for patient eyes with a frequency of "Always" and a magnitude of "Severe." All patients who reported these visual symptoms had a BSCVA of 20/20 or better. No patient who reported these visual symptoms lost 10 or more letters or 2 or more lines of BSCVA.

TABLE 3: Visual Symptoms at Month 12

	Response of "Always" & "Severe"	
Visual Symptoms	**n/N**	**%**
Difficulty with Night Vision	15/314	4.8%
Blurry Vision	9/314	2.9%
Diplopia	5/314	1.6%
Glare	4/313	1.3%
Halos	4/312	1.3%
Fluctuating Distance Vision	3/313	1.0%
Fluctuating Near Vision	1/313	0.3%
Photophobia	1/314	0.3%

Table 4 provides a summary of visual symptoms that were reported for the initial implant eye at the Month 12 exam as occurring "often" or "always" by Intacs Corneal Implants thickness.

Table 4: Frequency of Visual Symptoms at Month 12 by Intacs Thickness*

	0.250 mm				0.300 mm				0.350 mm			
	Often		Always		Often		Always		Often		Always	
Visual Symptoms	**n/N**	**%**	**n/N**	**%**	**n/N**	**%**	**n/N**	**%**	**n/N**	**%**	**n/N**	**%**
Difficulty with Night Vision	9/109	8.3%	9/109	8.3%	7/110	6.4%	8/110	7.3%	7/110	6.4%	17/110	15.5%
Blurry Vision	5/109	4.6%	8/109	7.3%	5/110	4.5%	6/110	5.5%	7/110	6.4%	9/110	8.2%
Diplopia	2/109	1.8%	2/109	1.8%	3/110	2.7%	3/110	2.7%	3/110	2.7%	9/110	8.2%
Glare	8/109	7.3%	2/109	1.8%	9/110	8.2%	3/110	2.7%	5/110	4.5%	5/110	4.5%
Halos	6/109	5.5%	4/109	3.7%	11/110	10%	4/110	3.6%	8/109	7.3%	6/109	5.5%
Fluctuating Distance Vision	1/109	0.9%	0/109	0%	1/110	0.9%	1/110	0.9%	3/110	2.7%	5/110	4.5%
Fluctuating Near Vision	1/109	0.9%	1/109	0.9%	2/110	1.8%	0/110	0%	4/110	3.6%	4/110	3.6%
Photophobia	5/109	4.6%	5/109	4.6%	3/110	2.7%	2/110	1.8%	7/110	6.4%	1/110	0.9%

*Data collected for Phase III patients only.

The visual symptoms that were reported for the initial implant eye at the Month 12 exam with a magnitude of "moderate" or "severe" are provided in Table 5.

Table 5: Magnitude of Visual Symptoms at Month 12 by Intacs Thickness*

	0.250 mm				0.300 mm				0.350 mm			
	Moderate		Severe		Moderate		Severe		Moderate		Severe	
Visual Symptoms	**n/N**	**%**	**n/N**	**%**	**n/N**	**%**	**n/N**	**%**	**n/N**	**%**	**n/N**	**%**
Difficulty with Night Vision	19/131	14.5%	3/131	2.3%	20/130	15.4%	2/130	1.5%	19/131	14.5%	12/131	9.2%
Blurry Vision*	13/106	12.3%	3/106	2.8%	9/103	8.7%	2/103	1.9%	18/105	17.1%	5/105	4.8%
Diplopia	7/131	5.3%	1/131	0.8%	6/130	4.6%	3/130	2.3%	16/131	12.2%	4/131	3.1%
Glare	19/131	14.5%	1/131	0.8%	18/129	14.0%	3/129	2.3%	17/131	13.0%	5/131	3.8%
Halos	14/131	10.7%	2/131	1.5%	20/129	15.5%	6/129	4.7%	20/130	15.4%	5/130	3.8%
Fluctuating Distance Vision	5/131	3.8%	0/131	0%	12/129	9.3%	0/129	0%	15/131	11.5%	4/131	3.1%
Fluctuating Near Vision*	6/106	5.7%	0/106	0%	5/102	4.9%	0/102	0%	8/105	7.6%	1/105	1.0%
Photophobia	19/131	14.5%	1/131	0.8%	14/130	10.8%	0/130	0%	16/131	12.2%	1/131	0.8%

*Data collected for Phase III patients only.

VII. Clinical Trial Results

A. Introduction

Two prospective, nonrandomized, unmasked, multicenter U.S. clinical trials (Phase II and Phase III) were conducted to determine the safety and efficacy of Intacs Corneal Implants. Three thicknesses (0.250 mm, 0.300 mm and 0.350 mm) of Intacs Corneal Implants were evaluated with approximately the same number of eyes in each group. The patient's nonoperative fellow eye served as a control during the first 6 months postoperatively, however the fellow eye was eligible for Intacs Corneal Implants placement six months after the initial eye procedure. Eligibility criteria required: eyes from -1.00 D to -3.50 D of myopia spherical equivalent at the spectacle plane with +1.00 D or less of astigmatism; being at least 21 years of age; having a stable manifest refraction as documented by a 1.00 D change or less within the previous six months; and best spectacle-corrected visual acuity of 20/20 or better in both eyes.

Out of 454 surgical attempts, Intacs Corneal Implants were successfully placed in 449 (98.9%) eyes. Complete follow-up data at the Month 12 exam were available for 410/420 (97.6%) of the eligible initial implant eyes.

The demographics and the preoperative parameters for the cohort of 449 patients are presented in Table 6 and Table 7. Patients who underwent the procedure ranged in age from 21 to 65 years, with a mean age of 39.4 years.

TABLE 6: Demographics

	n/N	%
Gender		
Female	228/449	51%
Male	221/449	49%
Race		
Caucasian	373/449	83%
Hispanic	32/449	7%
Black	22/449	5%
Asian	12/449	3%
Other	10/449	2%

TABLE 7: Preoperative Parameters		
Manifest Refraction (D)	**Mean ± SD (D)**	**Range (D)**
Spherical Equivalent	-2.24 ± 0.69	-0.75, -4.125
Sphere	-2.40 ± 0.71	-1.00, -4.50
Cylinder	+0.31 ± 0.30	0, +1.00
UCVA	**n/N**	**%**
20/125 or worse	194/448	43%
20/50 to 20/100	196/448	44%
20/25 to 20/40	55/448	12%
≤ 20/20	3/448	1%

SD = Standard Deviation
UCVA = Uncorrected Visual Acuity

B. Safety and Efficacy Results

Table 8 presents a summary of the key safety and efficacy results for all evaluated patient eyes through the Month 24 exam. The primary clinical outcome assessment was performed at the Month 12 postoperative exam.

TABLE 8: Summary of Key Safety and Efficacy Variables								
	Month 3		**Month 6**		**Month 12**		**Month 24**	
Variables	**n/N**	**%**	**n/N**	**%**	**n/N**	**%**	**n/N**	**%**
UCVA 20/16 or better	218/442	49%	212/438	48%	**216/410**	**53%**	32/51	63%
UCVA 20/20 or better	316/442	71%	303/438	69%	**303/410**	**74%**	41/51	80%
UCVA 20/25 or better	379/442	86%	374/438	85%	**356/410**	**87%**	44/51	86%
UCVA 20/40 or better	427/442	97%	421/438	96%	**396/410**	**97%**	49/51	96%
MRSE ± 0.50 D	298/442	67%	295/437	68%	**284/410**	**69%**	34/51	67%
MRSE ± 1.00 D	406/442	92%	397/437	91%	**377/410**	**92%**	47/51	92%
MRSE Stability ±0.50 D[1]	310/437	71%	363/435	83%	**356/392**	**91%**	39/47	83%
MRSE Stability ±1.00 D[1]	395/437	90%	421/435	97%	**386/392**	**98%**	46/47	98%
Loss of ≥10 Letters or ≥2 Lines BSCVA	13/442	3%	7/436	2%	**4/410**	**1%**	0/51	0%
BSCVA worse than 20/40	0/442	0%	0/436	0%	**0/410**	**0%**	0/51	0%
Increased Cylinder >2.00 D	0/442	0%	1/437	0.2%	**0/410**	**0%**	0/51	0%

[1]Stability was assessed as the change in MRSE from the previous scheduled exam.
MRSE = Manifest Refraction Spherical Equivalent

1. Stability of Refractive Effect

Stability of refractive effect is defined as the proportion of patients with a change in manifest refraction spherical equivalent (MRSE) of 1.00 D or less between two refractions taken three months apart. As highlighted in Table 9, stability was first established for the Month 3 to Month 6 interval. A statistically significant difference was seen in the stability results among the INTACS inserts thicknesses, with the best results seen for the 0.250 mm thickness with 100% of patients achieving stability in this interval. (See Table 10). The stability results for the 0.300 mm and 0.350 mm thicknesses were slightly less than the 0.250 mm thickness, with 95.2% for both.

TABLE 9: Stability of Refractive Effect

Change in MRSE	Month 1 to Month 3	Month 3 to Month 6	Month 6 to Month 9	Month 9 to Month 12	Month 12 to Month 18	Month 18 to Month 24
Within ± 0.50 D	310/437 (71%)	363/435 (83%)	336/409 (82%)	356/392 (91%)	63/68 (93%)	39/47 (83%)
Within ± 1.00 D	395/437 (90%)	421/435 (97%)	398/409 (97%)	386/392 (98%)	68/68 (100%)	46/47 (98%)
Mean Difference ± SD	0.21 ± 0.64	0.04 ± 0.44	-0.00 ± 0.44	-0.01 ± 0.36	-0.03 ± 0.33	-0.05 ± 0.45
95% CI	0.15 to 0.27	0.00 to 0.09	-0.05 to 0.04	-0.04 to 0.03	-0.11 to 0.05	-0.18 to 0.08

CI = Confidence Interval

2. Performance by Thickness

A summary of the performance for key safety and efficacy variables by Intacs Corneal Implants thickness is provided in Table 10. Overall, the 0.250 mm and 0.300 mm Intacs Corneal Implants had better outcomes than the 0.350 mm thickness. Statistically significant differences ($p \leq 0.05$) were seen among thicknesses for the proportion of subject eyes that had a UCVA of 20/20 or better ($p < 0.001$), 20/40 or better ($p = 0.028$), a manifest refraction outcome within 0.50 D of predicted ($p = 0.004$) and within 1.00 D of predicted ($p = 0.005$), stability of manifest refraction within 1.00 D ($p = 0.011$), the proportion of eyes with an induced cylinder greater than or equal to 1.00 D ($p = 0.018$) and the rate of removals ($p = 0.004$). In all cases, the protocol-defined safety and efficacy endpoints were met for the 0.350 mm thickness.

TABLE 10: Performance by Intacs Corneal Implants Thickness at Month 12								
	Total		**0.250 mm**		**0.300 mm**		**0.350 mm**	
Variables	**n/N**	**%**	**n/N**	**%**	**n/N**	**%**	**n/N**	**%**
UCVA 20/20 or better	303/410	73.9%	113/135	83.7%	107/138	77.5%	83/137	60.6%
UCVA 20/40 or better	396/410	96.6%	134/135	99.3%	134/138	97.1%	128/137	93.4%
MRSE ± 0.50 D	284/410	69.3%	94/135	69.6%	108/138	78.3%	82/137	59.9%
MRSE ± 1.00 D	377/410	92.0%	129/135	95.6%	131/138	94.9%	117/137	85.4%
MRSE Stability ±1.00 D[1]	421/435	96.8%	144/144	100%	138/145	95.2%	139/146	95.2%
Loss of ≥10 Letters or ≥2 Lines BSCVA	4/410	1.0%	2/135	1.5%	1/138	0.7%	1/137	0.7%
BSCVA worse than 20/40	0/410	0%	0/135	0%	0/138	0%	0/137	0%
Induced Cylinder ≥1.00 D	30/410	7.3%	4/135	3.0%	10/138	7.3%	16/137	11.7%
Induced Cylinder >2.00 D	0/410	0%	0/135	0%	0/138	0%	0/137	0%
Removals[2]	34/449	7.6%	5/148	3.4%	9/150	6.0%	20/151	13.3%

[1] Stability was assessed as the change in MRSE from the Month 3 to Month 6 exam.
[2] Removal data are cumulative and extend beyond the Month 12 exam.

3. Performance Based on Recommended Prescribing Range

Table 11 provides a summary of the Intacs Corneal Implants performance at Month 12, stratified by thickness, for patients with preoperative refractive errors within the recommended prescribing range.

TABLE 11: Performance Based on Recommended Prescribing Range*								
	Intacs Corneal Implants Thickness (Preoperative CRSE)							
	0.250 mm (-1.00 to -1.50 D)		**0.300 mm (-1.875 to -2.125 D)**		**0.350 mm (-2.625to -3.00 D)**		**Total**	
Variables	**n/N**	**%**	**n/N**	**%**	**n/N**	**%**	**n/N**	**%**
UCVA 20/16 or Better	65/101	64.4%	37/68	54.4%	35/72	48.6%	137/241	56.8%
UCVA 20/20 or Better	84/101	83.2%	55/68	80.9%	47/72	65.3%	186/241	77.2%
UCVA 20/40 or Better	100/101	99.0%	68/68	100.0%	69/72	95.8%	237/241	98.3%
CRSE ± 0.50 D	75/100	75.0%	53/68	77.9%	42/72	58.3%	170/240	70.8%
CRSE ± 1.00 D	94/100	94.0%	63/68	92.6%	59/72	81.9%	216/240	90.0%
MRSE ± 0.50 D	78/101	77.2%	51/68	75.0%	41/72	56.9%	170/241	70.5%
MRSE ± 1.00 D	97/101	96.0%	64/68	94.1%	60/72	83.3%	221/241	91.7%

CRSE = Cycloplegic Refraction Spherical Equivalent
* Based on the recommended prescribing range for the 0.250 mm, 0.300 mm and 0.350 mm Intacs Corneal Implants contained in Section I, entitled "Device Description."

4. Additional Studies

Endothelial Cell Counts

Tables 12A and 12B provide the endothelial cell density percent changes from the Preoperative exam at Month 12 and Month 24, respectively. The changes in endothelial cell density were statistically significant among the 0.250 mm and 0.350 mm Intacs Corneal Implants thicknesses for all three regions at Month 12 and were statistically significant among the three Intacs segments thicknesses for all three regions during the Month 12 to Month 24 time period. For the central region, the largest decreases were observed for the 0.250 mm Intacs segments during the first postoperative year (-1.7%) and second postoperative year (-2.2%). The 0.350 mm Intacs segments also had a decrease of 2.2% during the second postoperative year.

TABLE 12A: Endothelial Cell Density
Percent Change at Month 12 from Preoperative*

Region		0.250 mm	0.300 mm	0.350 mm	Total
Central	n	36	31	27	94
	Mean ± SD	-1.7% ± 3.5%	-0.7% ± 4.8%	-1.5% ± 3.2%	-1.3% ± 3.9%
6:00 Peripheral	n	33	31	27	91
	Mean ± SD	-3.1% ± 5.6%	-0.6% ± 5.0%	-2.4% ± 6.8%	-2.1 ± 5.8%
10:00 Peripheral	n	34	31	26	91
	Mean ± SD	-2.9% ± 4.8%	0.0% ± 4.2%	-5.0% ± 6.4%	-2.5% ± 5.4%

*Data from one of the four Phase III subgroup sites have been excluded due to specular microscopy technique-related factors at this site.

TABLE 12B: Endothelial Cell Density
Percent Change From Month 12 to Month 24*

Region		0.250 mm	0.300 mm	0.350 mm	Total
Central	n	36	31	27	94
	Mean ± SD	-2.2% ± 3.3%	-1.5% ± 3.2%	-2.2% ± 3.3%	-2.0% ± 3.2%
6:00 Peripheral	n	33	31	27	91
	Mean ± SD	-2.3% ± 4.8%	-2.6% ± 4.7%	-2.7% ± 4.9%	-2.5% ± 4.8%
10:00 Peripheral	n	34	31	26	91
	Mean ± SD	-1.4% ± 4.7%	-3.5% ± 3.7%	-2.9% ± 5.1%	-2.5% ± 4.6%

* Data from one of the four Phase III subgroup sites have been excluded due to specular microscopy technique-related factors at this site.

Contrast Sensitivity
The mean change in contrast sensitivity, performed under mesopic conditions with and without a glare source, at Month 6 and Month 12 relative to preoperative levels was less than 0.1 log unit for all spatial frequencies. Without glare, the proportion of initial implant eyes with a functional decrease at Month 6 was greater than that of the non-operated fellow eyes at 1.5 cycles per degree ($p = 0.013$) and at 6 cycles per degree (not statistically significant). With glare, no statistically significant differences were found between eyes at any spatial frequency.

5. Patient Satisfaction

Responses to the postoperative patient satisfaction survey at Month 12 indicated that 90% of patients with unilateral Intacs segments and 95% of those with bilateral Intacs segments were "somewhat" or "strongly" satisfied with their Intacs Corneal Implants.

C. Removals and Exchanges

Intacs Corneal Implants have been removed from 34 initial implant eyes and 5 contralateral eyes for a total of 39 patient eyes during the reporting period. Intacs segments can be easily removed in a brief, outpatient procedure. Reasons for removals included: one for infection, 15 for patient dissatisfaction with correction achieved (undercorrection, overcorrection or induced astigmatism), 19 for patient dissatisfaction with visual symptoms (glare, halos, difficulty with night vision, etc.) and four for other reasons (1 non-monovision correction, 2 FAA restrictions, 1 deferred exchange). There have been no clinically significant complications associated with Intacs Corneal Implants removal procedures. The removal results demonstrate that:

- The refractions returned to preoperative levels by three months following removal, in most instances. Best spectacle-corrected visual acuity was 20/20 or better in all cases.
- The central cornea remained clear in all eyes. Slit lamp findings were limited to stromal haze and deposits within the peripheral tunnels.
- A small percentage of patients reported more frequent and/or more severe visual symptoms three months following removal than was documented prior to placement of Intacs Corneal Implants.

Table 13 provides a summary of the refractive status of the 29 patient eyes with three months postremoval data available.

TABLE 13: Refractive and Visual Acuity Change from Preoperative to Month 3 Postremoval Exam

Variables	n/N	%	95% CI
MRSE ± 0.50 D	25/29	86%	68%, 96%
MRSE ± 1.00 D	29/29	100%	88%, 100%
MRSE Stability ±1.00 D[1]	20/20	100%	83%, 100%
Loss of ≥5 Letters or ≥1 Line BSCVA	2/29	7%	1%, 23%
Loss of ≥10 Letters or ≥2 Lines BSCVA	0/29	0%	0%, 12%
Cylinder ±0.50 D	27/29	93%	77%, 99%
Cylinder ±1.00 D	29/29	100%	88%, 100%

[1] Stability was assessed as the change in MRSE from Month 1 to Month 3 postremoval. Only patients with results within the specified time window for both exams were included in the analysis.

Visual symptoms were also assessed at the Month 3 Postremoval exam. Table 14 summarizes visual symptoms reported at a frequency greater than the Preoperative exam. Table 15 provides a similar summary for the reported magnitude of visual symptoms. Table 16 provides a summary of visual symptoms reported as "severe" at the Month 3 Postremoval exam.

TABLE 14: Increase in Frequency[1] of Visual Symptoms Preoperative vs. Month 3 Postremoval

	Results		
Visual Symptom	**n/N**	**%**	**95% CI**
Blurry Vision	8/19	42%	20%, 67%
Photophobia	5/19	26%	9%, 51%
Glare	2/19	11%	1%, 33%
Difficulty with Night Vision	2/19	11%	1%, 33%
Diplopia	2/19	11%	1%, 33%
Halos	0/19	0%	0%, 18%
Fluctuating Near Vision	0/19	0%	0%, 18%
Fluctuating Distance Vision	0/19	0%	0%, 18%

[1] Data collected for Phase III patients only.

TABLE 15: Increase in Magnitude[1] of Visual Symptoms Preoperative vs. Month 3 Postremoval

	Results		
Visual Symptom	**n/N**	**%**	**95% CI**
Fluctuating Vision	1/8[2]	12%	0%, 53%
Halos	1/9	11%	0%, 48%
Difficulty with Night Vision	1/9	11%	0%, 48%
Diplopia	1/9	11%	0%, 48%
Glare	0/9	0%	0%, 34%
Photophobia	0/9	0%	0%, 34%

[1] Preoperative magnitude collected for Phase II patients only.
[2] One subject did not answer the question preoperatively.

TABLE 16: Magnitude of Visual Symptoms
Proportion "Severe" at the Month 3 Postremoval Exam

	Results		
Visual Symptom	**n/N**	**%**	**95% CI**
Blurry Vision[1]	1/12	8%	0%, 38%
Difficulty with Night Vision[2]	1/22	5%	0%, 23%
Diplopia[2]	1/22	5%	0%, 23%
Fluctuating Distance Vision	1/22	5%	0%, 23%
Glare	0/22	0%	0%, 15%
Halos	0/22	0%	0%, 15%
Photophobia	0/22	0%	0%, 15%
Fluctuating Near Vision[1]	0/12	0%	0%, 26%

[1]Data collected for Phase III patients only.
[2]The same patient reported both severe difficulty with night vision and diplopia.

Intacs Corneal Implants were exchanged for 12 patients in an attempt to improve their refractive outcome. Sufficient data are not currently available to determine the efficacy of exchanging Intacs Corneal Implants.

VIII. Patient Instructions, Registration and Reporting

Patients Instructions

- If patients wear contact lenses, they should be instructed to stop wearing them 2-3 weeks before their preoperative examination in order to obtain an accurate refraction.
- If patients wear eye makeup, they should be instructed to stop 2-3 days before the procedure to reduce the risk of infection.
- Patients should be instructed to not rub their surgery eye for the first six months after the procedure. This is important to promote proper healing of the incision.
- Patients should be instructed on the importance of using all medications as directed.
- Patients should be instructed to contact you immediately if they experience any pain, discomfort, feel that something is in their eye or experience a change in their vision after the initial postoperative recovery period (typically 7 days).
- Patients should be instructed to report any unusual symptoms that could be associated with prolonged topical steroid use, if applicable.

Registration

A Patient Registry Card and a Patient Identification Card are enclosed in the Intacs Corneal Implants product package. Please provide both cards to the patient at the time of surgery. Each patient who receives Intacs Corneal Implants must be registered with Addition Technology. Registration is accomplished by the patient completing the Patient Registry Card and mailing it to Addition Technology. Patient registration is essential for Addition Technology's long-term patient follow-up program and will assist Addition Technology in responding to Adverse Event Reports and/or potentially sight-threatening complications. The Patient Identification Card is intended as an implant card to be kept in the patient's wallet.

Medical Device Reporting

Adverse events and/or potentially sight-threatening complications that may reasonably be regarded as related to Intacs Corneal Implants and that were not previously expected in nature, severity or incidence rate should be reported to Addition Technology immediately. This information is being requested from all surgeons in order to document potential long-term effects of placement of Intacs Corneal Implants.

Physicians must report these events in order to aid in identifying any emerging or potential problems with Intacs Corneal Implants. Use the following toll-free number when reporting adverse events or potentially sight-threatening complications involving Intacs Corneal Implants:

1-877-888-5372

IX. Conformance to Standards

Intacs Corneal Implants have been designed, manufactured and distributed in conformance with requirements of the FDA Quality System Regulation (QSR), relevant ISO standards and the Medical Device Directive (MDD) 93/42/EEC.

X. How Supplied

Intacs Corneal Implants are supplied sterile and are nonpyrogenic. Intacs Corneal Implants are intended for single use only; do not reuse or resterilize. In the event that the packaging for Intacs Corneal Implants is damaged, do not use the product or attempt to resterilize. Contact Addition Technology regarding any products that are observed to be damaged. Properly dispose of all packaging materials and recycle when possible.

XI. Symbols and Their Explanations

"Attention, See Physician Booklet"

REF

"Model Number"

"Lot Number"

"Method of Sterilization Using Ethylene Oxide"

"Do Not Reuse"

"Use By"

XII. Directions For Use

Refer to Figure 1 for a flow chart of the Intacs® surgical procedure. The Intacs® Surgeon Training Manual contains detailed information regarding the surgical procedure, recommended equipment, medications and patient management.

Figure 1: Intacs Corneal Implants Surgical Procedure Flow Chart (10-Step Prolate System)

Instruments/Materials

- Anesthesia Ring (for use with topical anesthesia)
- Inspection Gauge
- Povidone-Iodine 2.5% and 5% Solution
- Lid Speculum

- Sterile Marking Pen
- 11 mm Zone Marker
- Sinskey Hook

- Sterile Marking Pen
- Procedure Marker

- Calibrated Diamond Knife with 15° angled blade (or rectangular blade of 1 mm or less)

- Pocketing Hook

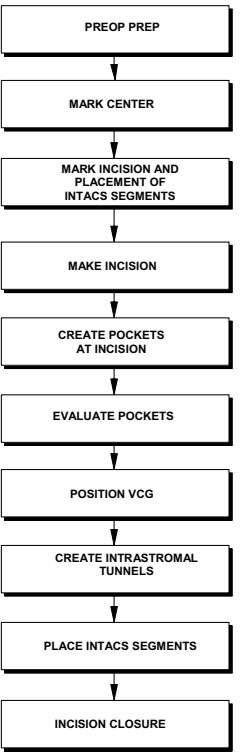
- Symmetric Glide

- Anesthesia Ring (Remove prior to placing VCG)
  Vacuum Centering Guide (VCG)
- Procedure Marker

- Symmetric Glide
- Corneal Separators (CW/CCW)
- Vacuum Centering Guide (VCG)

- Intacs Forceps
- Sinskey Hooks
- Intacs Carrier

- Ophthalmic Suture
  (11-0 or 10-0; 11-0 recommended)



Key Points	Warnings/Precautions
• Iodine preparation of eye • Avoid excessive manipulation or irritation of the conjunctiva • Use lint-free drapes & talc-free gloves • Mark the geometric center of the cornea • Reference off the geometric center mark • Incision mark is placed at 12:00 • Verify that the placement marks are at least 1 mm from the limbus	• Completely isolate eyelashes • Avoid overtightening the lid speculum • Frequently irrigate the cornea with balanced saline solution during the operative procedure • Chemosis may result if local anesthesia used • Avoid contacting the Intacs segments & instruments with the lids, lid margins, lashes & lacrimal fluid • Visually inspect instruments prior to use • Inspect Corneal Separators with Inspection Gauge • Pilocarpine to constrict pupil is not recommended
• Cut entire length of incision mark • Remove loose epithelium from incision area • Irrigate incision area	• Set diamond knife to 68% of pachometry reading at the incision site • Verify diamond knife setting • Stay 1 mm away from the limbus
• From the base of the incision, create a corneal pocket on each side of the incision using the Pocketing Hook • Pockets should be at the same depth across the full width of incision, within the same stromal plane and as long as the Symmetric Glide	• Create pockets at the full depth of the incision to avoid shallow implant depth
• Estimate pocket depth • Create deeper pockets, if necessary	
• Locate VCG & Procedure Marker on center mark • Apply vacuum at 400-500 mBar • Confirm proper placement • Increase vacuum to 600-667 mBar	• Position vacuum port temporally • Limit continuous VCG time to 3 minutes or less and applied vacuum to 750 mBar
• Insert Symmetric Glide into the first pocket • Rotate Corneal Separator blade tip under Symmetric Glide • Rotate Corneal Separator to create tunnel • Create intrastromal tunnel on the second side • Release vacuum, remove VCG	• Stop creating the tunnel if excessive resistance or “tissue wave” is encountered, consider creating a deeper pocket and tunnel • Stop the procedure in the event of a posterior chamber perforation or anterior corneal surface perforation
• Irrigate incision area • Insert one Intacs segment into each intrastromal tunnel • Align the outer edge of each segment under the appropriate placement mark	• Avoid contact of the Intacs segments with iodine and/or epithelial surface
• Approximate incision edges to ensure proper healing • Place one or two interrupted sutures, evenly spaced. Suture depth should be to the level of the stromal pocket • Suture knots should be buried	• Avoid epithelial ingrowth into stroma • Tension across the sutures should be evenly applied • Avoid overtightening sutures • Incision edges must be apposed at end of procedure

XIII. Return Goods Policy

Please return any damaged product to your Addition Technology representative. All products returned to Addition Technology must be accompanied by a Return Goods Authorization Number.

Call 1-877-888-5372 for return authorization and full policy information.

CAUTION: U.S. Law restricts this device to sale by or on the order of a physician.

The device, the surgical instruments and the method of use may be protected by one or more U.S. Patent Numbers: U.S. 5,824,086, U.S. 5,403,355, U.S. 5,843,105, U.S. 5,846,256 and U.S. 6,447,528.

WARRANTY AND LIMITATION OF LIABILITY

Addition Technology warrants that the product when delivered is free from defect in materials and workmanship and conforms to the manufacturer's then-current version of its published specifications. This warranty applies for the period of time up to and including the expiration date for the product. At its option, Addition Technology will repair, replace or provide a refund for any product manufactured by it and found to be defective, so long as the product is returned to Addition Technology according to the return goods policy. Addition Technology shall not be liable for any incidental or consequential loss, damage or expense, directly or indirectly arising from the use of, or inability to use, its product.

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About Addition Technology, Inc.
Addition Technology, a vision care company, was founded in 2001. Addition Technology purchased the Intacs technology, which is a new approach to treating vision problems. The Intacs technology is an additive platform that surgically reshapes the cornea by adding materials rather than cutting or permanently removing tissue like other refractive surgery techniques. Addition Technology is also developing potential applications of Intacs Corneal Implants for the treatment of hyperopia and astigmatism. It is estimated that over 50% of the world's population experience vision problems.

Located in Lombard, Illinois, Addition Technology works closely with a worldwide team of ophthalmic surgeons and scientists who are leaders in the fields of keratoconus and vision correction.