

Incidence of Lens Opacities and Clinically Significant Cataracts With the Implantable Contact Lens: Comparison of Two Lens Designs

Donald R. Sanders, MD, PhD; John A. Vukich, MD;
for the ICL in Treatment of Myopia (ITM) Study Group

ABSTRACT

PURPOSE: To compare the incidence of anterior subcapsular lens opacities, clinically significant cataracts, secondary lens-related surgical reinterventions, and vaulting characteristics of the now discontinued V3 and currently used V4 Staar Surgical Implantable Contact Lens (ICL) phakic intraocular lens designs.

METHODS: In this non-randomized prospective clinical trial, 87 eyes were implanted with the V3 and 523 eyes with the V4 ICL as part of the U.S. FDA clinical trial for myopia. LOCS III assessment of lens opacities, clinically significant cataract, ICL vaulting (clearance between ICL and crystalline lens), and secondary ICL-related surgeries were the main outcome measures. Mean follow-up in the V3 series was 30.7 ± 10.0 months (range 10.8 to 49.3 mo) and in the V4 series, 17.3 ± 6.9 months (range 0.25 to 38.5 mo).

RESULTS: Incidence of anterior subcapsular opacities was significantly higher with the V3 vs. V4 ICL (12.6% vs. 2.9%, $P < .001$). The difference was largely due to the higher rate of late-appearing opacities (≥ 1 year after surgery; 9.2% vs. 0.6%, $P < .001$). The V3 group had a greater proportion of eyes with poor vault (23.6% vs. 4.3%, $P < .001$) and the presence of poor vault was highly associated with the development of late anterior subcapsular opacities ($P < .001$). Clinically significant cataract was more frequent in the V3 vs. V4 ICL (9.2% vs. 0.8%, $P < .001$), as was cataract extraction (6.9% vs. 0.2%, $P < .001$), and need for ICL replacement (5.7% vs. 1.1%, $P < .001$). Differences in opacity rate between the V3 and V4 designs were not due to differences in postoperative follow-up.

CONCLUSION: Implantation of the currently used V4 Staar Surgical model ICL resulted in significantly less anterior subcapsular opacities, clinically significant cataracts, and secondary ICL-related surgery. [*J Refract Surg* 2002;18:673-682]

Initial studies on anterior chamber and iris-fixated phakic intraocular lenses (IOLs) have proven them to have good efficacy and predictability, with an initial low incidence of complications.^{1,2} Similar studies on the Implantable Contact Lens (ICL, Staar Surgical, Monrovia, CA)³⁻¹³, including the interim results of the U.S. FDA trial of the version 4 (V4) cohort of cases¹⁴, have shown the ICL to be equally promising. However, each type of phakic IOL has its own area of unique concern. Anterior chamber and iris fixated phakic IOLs have been reported to be associated with aqueous flare measurements in the range associated with uveitis as late as 18 months and 24 months after surgery.^{15,16} They have furthermore been reported to demonstrate ongoing continuing endothelial cell loss as late as 5 years after surgery¹⁷⁻¹⁹, although with some design changes the newer anterior chamber lenses appear to have less cell loss over time.^{18,20,21} Pupil ovalization has been characteristic of angle-supported phakic IOLs²² and recently premature development of nuclear cataract has been reported.²³

With posterior chamber phakic IOLs, because of their close proximity to the crystalline lens, the development of clinically significant cataract is clearly a concern. This report documents the incidence, time course of development, and severity of lens opacities noted with the current V4 cohort of eyes, and compares it to that seen in the now discontinued V3 ICL design. We also compare clinical vaulting characteristics and incidence of secondary ICL surgery as well as describe other studies on lens transparency and an analysis of risk of visual loss associated with cataract development after ICL implantation.

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Correspondence: Darcy Smith, STAAR Surgical Company, 1911 Walker Avenue, Monrovia, CA 91016.

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PATIENTS AND METHODS

The U.S. multi-center Food and Drug Administration (FDA) clinical study of the STAAR Implantable Contact Lens (ICL; STAAR Surgical Company, Monrovia, CA) for myopia was designed as a prospective, non-randomized clinical trial intended to evaluate the safety and efficacy of the ICL to treat moderate to high myopia.¹⁴ Fourteen clinical sites across the U.S. enrolled 523 eyes of 291 patients implanted with the version 4 (V4) ICL between November 11, 1998 and July 25, 2001. Basic enrollment criteria included myopia between -3 and -20 diopters (D), ≤ 2.50 diopters (D) of refractive cylinder, and patient age ≤ 45 years. This group represented the Phase III U.S. FDA cohort.

The earlier version 3 (V3) ICL lens design was implanted in 87 eyes in the U.S. between November 18, 1997 and December 22, 1998 as part of the Phase II portion of the FDA study, before being discontinued. The basic difference between the V3 and V4 ICL is in the vaulting characteristics; the V4 lens had an additional 0.13 to 0.21 mm of anterior vault, depending on dioptric power (Fig 1).

Both series followed the identical protocol and utilized the same method to determine length sizing before surgery. Patients were examined at 1 day, 1 week, 1, 3, 6, 12, and 24 months following ICL implantation. This report compares the two groups with regard to lens opacity analysis²⁴ (LOCS III), the incidence of clinically significant cataracts (defined as a loss of ≥ 2 lines of best spectacle-corrected visual acuity (BSCVA), a significant increase in glare compared to before surgery, or the necessity for ICL removal, cataract extraction, and IOL implantation), the degree of vaulting or clearance between the ICL and the crystalline lens as estimated by the investigator at the slit lamp, and ICL-related secondary surgical interventions. For estimations of vaulting the investigators were instructed to estimate the distance between the posterior surface of the ICL and the anterior surface of the crystalline lens as a percentage of the central corneal thickness at each postoperative examination. Consistent measurements of 10% or less (approximately 50 μm) in an eye were considered to be a case with poor vault. A series of 40 eyes at one site underwent examination with a P40 ultrasonic biomicroscope (Paradigm Medical, Salt Lake City, UT) and clinical assessment of vault. The investigator identified eyes measured to have poor vault by biomicroscopy as having poor vault by clinical estimation. Conversely, no eyes measured and determined to have adequate vault by biomicroscopy

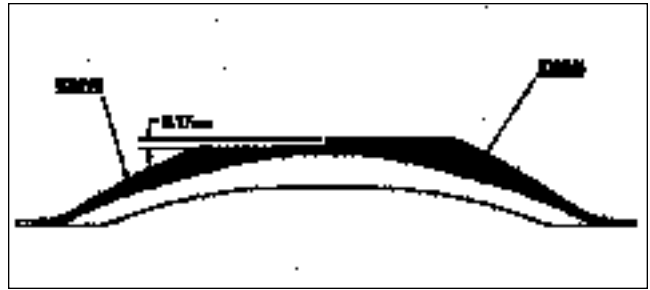


Figure 1. Schematic demonstrates the difference in vaulting characteristics between V3 and V4 designs. In this -14.50-D ICL sectioned along the long axis, the V4 design demonstrated 0.17 mm more vault compared to the V3 design.

were clinically assessed to have poor vault (John Vukich, MD, personal communication).

Statistical Analysis

The V3 and V4 ICL designs were compared with regard to continuous variables by *t*-tests and binomial variables by Fisher's exact test. To compensate for any potential differences in follow-up between the V3 and V4 ICLs, Kaplan-Meier survival analysis was used to compare rates of anterior subcapsular opacification and development of clinically significant cataract.²⁵

RESULTS

Percent accountability (a measure of adequacy of follow-up used in U.S. FDA clinical trials) defined as [available for analysis divided by (enrolled minus discontinued minus not yet eligible for a specific reporting interval)] was over 90% at all examinations reporting intervals through 24 months after surgery for the V4 series. It was over 93% for all periods through 1 year and 87.5% at 2 years for the V3 series. Mean follow-up in the V3 series was 30.7 \pm 10.0 months (range 10.8 to 49.3 mo) and in the V4 series was 17.3 \pm 6.9 months (range 0.25 to 38.5 mo).

There were no statistically significant differences between the V3 and V4 series with regard to mean preoperative spherical equivalent refraction (V3 = -10.70 D, V4 = -10.00 D, $P=.11$), patient age at the time of enrollment (V3 = 36.6 yr, V4 = 36.4 yr, $P=.80$), or population gender (% female V3 = 60.3%, V4 = 60.5%, $P=.54$).

In neither group was there a significant change in nuclear, cortical, or posterior subcapsular opacities from before surgery to after surgery.

Tables 1 and 2 provide detailed information on all anterior subcapsular LOCS opacities >trace noted in the V3 and V4 series, respectively, and Table 3

Table 1
Anterior Subcapsular (AS) Opacities in the Series of 87 Cases Receiving the V3 ICL

Patient	Series	Sex	Age	Pre-op SE	Last SE	Time Opacity First Seen	Initial LACRHS Grade	Last LACRHS Grade	Time CP Last Vis	Observation	Pre-op BCVA	Last BCVA	Δ BCVA (±1 SD)	Pre-op UCVA	Last UCVA	Treatment	Comment	
ANTERIOR SUBCAPSULAR OPACITIES - 1 (0.0%)																		
DW	1	M	48	M	-11.75	-0.1	3	0.5	3.0	34	Good*	20	20	0	CF	40	ICL Removed Cataract Extraction ICL Implantation 30 Min Post-op	
DL	1	M	43	M	-11.75	0.00	1	1.0	1.5	37	None	20	20	+3	CF	20	ICL 3 Min Post-op	
DW	2	M	43	F	-9.5	+0.00	1	1.0	1.0	30	Good*	20	20	-1	CF	20	ICL Removed Cataract Extraction ICL Implantation 30 Min Post-op	
LATRAL CRACKING - 1 (0.0%)																		
DL	3	M	44	F	-4.00	+0.25	24	1.0	1.0	34	Good*	15	20	-1	CF	20	Observation	ICL removed and reinserted at surgery
DL	1	M	38	F	-14.00	-1.0	24	1.0	1.0	24	Good*	20	20	0	CF	20	Observation	Four Visits
AR	4	M	43	F	-12.50	-0.5	24	1.0	1.0	26	Good*	20	20	0	CF	20	Observation	Four Visits
FF	5	M	33	F	-10.00	+1.25	32	0.5	1.0	31	Last BCVA*	20	20	-1	CF	20	ICL, Ruptured 31 Min Post-op ICL, Ruptured Cataract Extraction ICL Implantation 31 Min Post-op	Four Visits
JT	5	M	35	F	-10.00	-0.5	28	0.5	1.0	29	None	20	20	+1	CF	25	ICL, Ruptured 15 Min Post-op	Four Visits ICL removed and reinserted at surgery
CH	6	M	34	F	-11.00	-0.50	34	0.5	1.0	28	Good*	20	20	0	CF	20	ICL, Ruptured Cataract Extraction ICL Implantation 31 Min Post-op	Four Visits
DM	6	M	48	F	-10.75	-0.25	34	1.0	0.5	35	Good*	20	20	+1	CF	20	ICL, Ruptured Cataract Extraction ICL Implantation 30 Min Post-op	Four Visits
PA	6	M	32	F	-6.75	0.00	26	0.5	0.5	32	None	20	20	+1	CF	25	ICL, Ruptured 31 Min Post-op	Four Visits

* Good = Best Corrected Visual Acuity (BCVA) = 20/20 or better; SE = Spherical Equivalent; BCVA = Best Corrected Visual Acuity; UCVA = Uncorrected Visual Acuity; CF = Clear Vision

summarizes the major differences between these series.

There were 11 of 87 (12.6%) anterior subcapsular opacities in the V3 series, vs. 15 of 523 (2.9%) in the V4 series ($P < .001$). Figure 2 shows that after correcting for differences in follow-up between the V3 and V4 series with Kaplan-Meier survival analysis, there was a statistically significant difference between the V3 and V4 lens designs with regard to development of anterior subcapsular opacities ($P = .016$).

A total of 18 eyes in the V3 and V4 series required ICL removal and reinsertion during surgery or on the same day of surgery as a result of the ICL being implanted upside down. Eight of the eighteen eyes (44.4%) developed anterior subcapsular opacities while only 18 of the 592 (3.0%) not undergoing removal and reinsertion developed anterior subcapsular opacities ($P < .001$). Although 7 of 87 (8%) of the V3 eyes required removal and reinsertion at surgery, only 11 of 523 (2.1%) of the V4 eyes required it ($P = .006$). Of the eight eyes developing anterior subcapsular opacities after removal and reinsertion,

four (50%) of the anterior subcapsular opacities were seen within the first week after surgery and six (75%) were seen within 90 days after surgery.

The incidence of early anterior subcapsular opacities (occurring within 90 days of surgery) was similar with the V3 and V4 lens designs (3.4%, vs. 2.3%, $P = .21$, Fig 3). Eight of the 12 early anterior subcapsular opacities in the V4 series (67%) were first observed during the first week after surgery.

The difference in rate of opacities in the V3 and V4 series was largely due to the high incidence of late-appearing (≥ 12 mo after surgery) anterior subcapsular opacities in the V3 series (8 of 87, 9.2%), compared to the V4 series (3 of 523, 0.6%, $P < .001$, Fig 3).

Vaulting was assessed clinically in 72 of 87 (83%) of the V3 lens eyes and of these, 17 (23.6%) had poor vault or little clearance between the ICL and the crystalline lens. Vaulting was assessed clinically in 509 of 523 (97%) of the V4 eyes and vaulting was assessed to be poor in 22 of these 509 V4 eyes (4.3%). The difference in vaulting characteristics between the V3 and V4 designs was statistically significant

Table 2
Anterior Subcapsular (AS) Opacities in the Series of 523 Cases Receiving the V4 ICL

ICL Design	Eye	Age	Sex	Pre-op SE (D)	Last SE (D)	Time Since Last Exam	Initial Lens Haze Grade	Last Lens Haze Grade	Time of Last Exam	Reason	Pre-op BCVA SnV	Last BCVA SnV	Δ BCVA (+ = Gain)	Pre-op UCVA SnV	Last UCVA SnV	Treatment	Comment
EARLY ANTERIOR SUBCAPSULAR OPACITIES (N = 15/523)																	
ICL	R	50	F	-12.25	-12.25	3 Mo	0.5	1.5	27	Other Last BCVA+	20	20	0	CF	200	ICL Removed (1st Exam) ICL Replaced 26 Mo Post-op	Mitotic cells preservation indicated at AC-surgery. ICL removed and reinserted at surgery.
ICL	R	48	F	-12.00	-12.25	1 Day	0.5	0.5	13	Mitosis	20	13	+1	CF	20	Observation	ICL removed and reinserted at surgery.
ICL	R	45	M	-12.25	-12.50	1 Day	1.5	1.5	24	Mitosis	20	20	+1	CF	60	Observation	ICL removed and reinserted at surgery.
ICL	R	45	F	-8.25	0.00	1 Yr	0.5	1.5	30	Mitosis	20	20	0	CF	20	ICL Replaced 26 Mo Post-op	ICL removed and reinserted at surgery. Poor Vault
ICL	R	40	M	-12.00	0.00	1 Yr	1.0	1.0	24	Mitosis	20	20	0	CF	20	Observation	ICL removed and reinserted at surgery.
ICL	R	40	F	-9.25	-9.25	3 Mo	1.0	0.5	24	Last BCVA+	15	20	-5	CF	20	Observation	ICL removed and reinserted at surgery.
ICL	R	40	M	-12.00	-12.00	7 Mo	0.5	1.0	13	Last BCVA+	20	20	-1	CF	100	Observation	
ICL	R	39	M	-12.00	-12.00	1 Day	1.0	2.0	27	Mitosis	20	20	-1	CF	20	Observation	
ICL	R	42	F	-8.00	-10.00	1 Day	0.5	0.5	24	Mitosis	20	12	+1	CF	20	Observation	
ICL	R	42	F	-10.00	0.00	1 Yr	1.0	0.5	24	Mitosis	20	20	0	CF	20	Observation	
ICL	R	42	F	-8.00	-8.00	2 Mo	0.5	1.0	24	Mitosis	20	20	0	CF	20	Observation	
ICL	R	44	M	-12.25	-8.00	2 Mo	0.5	1.0	24	Other*	20	20	-1	CF	70	Observation	
LATE ANTERIOR SUBCAPSULAR OPACITIES (N = 2/523)																	
ICL	R	49	M	-8.00	-3.25	1 Yr	1.5	1.5	14	Mitosis	40	40	0	CF	200	ICL Removed 16 Mo Post-op	
ICL	R	38	M	-8.25	-7	26 Mo	1.5	1.0	30	Mitosis	20	20	0	CF	CF	ICL Replaced 26 Mo Post-op ICL Removed 26 Mo Post-op	Poor Vault
ICL	R	38	F	-8.50	-12.25	1 Yr	0.5	1.5	18	Mitosis	20	20	+1	CF	30	ICL Replaced (1st Exam) ICL Replaced 16 Mo Post-op	Poor Vault

* = Clinically Significant Cataract BCVA = Best Corrected Visual Acuity UCVA = Uncorrected Visual Acuity CF = Crossed

Table 3
Comparison of Outcomes Between V3 and V4 ICL Designs

	V3 ICL no. (%)	V4 ICL no. (%)	P-value
Anterior Subcapsular Opacities >Trace			
Total	11/87 (12.6)	15/523 (2.9)	<.001
Early anterior subcapsular opacities	3/87 (3.4)	12/523 (2.3)	.21
Late anterior subcapsular opacities	8/87 (9.2)	3/523 (0.6)	<.001
ICL Removed and Reinserted at Surgery	7/87 (8.0)	11/523 (2.1)	.006
Poor Vault	17/72 (23.6)	22/509 (4.3)	<.001
Clinically Significant Cataract	8/87 (9.2)	4/523 (0.8)	<.001
Secondary Surgeries			
Cataract extraction	6/87 (6.9)	1/523 (0.2)	<.001
ICL replacement	5/87 (5.7)	6/523 (1.1)	.01
ICL removals	0/87 (0)	2/523 (0.4)	.73

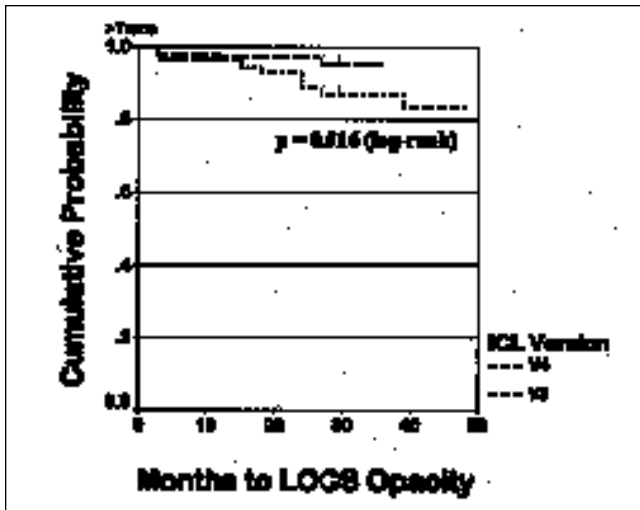


Figure 2. Kaplan-Meier survival analysis curve demonstrates the cumulative probability of not developing an anterior subcapsular (AS) LOCS opacity >trace in the V3 vs. V4 series of eyes.

($P < .001$). Poor vaulting was associated with 9 of the 11 eyes (81.8%) with late anterior subcapsular opacities in both series, while poor vaulting only occurred in 30 of the 570 eyes (5.3%) evaluated for vault in both series that did not demonstrate late anterior subcapsular opacities ($P < .001$).

The incidence of clinically significant cataract was 8 of 87 (9.2%) in the V3 series and 4 of 523 (0.8%) in the V4 series ($P < .001$). Figure 4 shows that after correcting for differences in follow-up between the V3 and V4 series with Kaplan-Meier survival analysis, there was a statistically significant difference with regard to the development of clinically significant cataract ($P = .018$). The V3 and V4 series diverged 2 years after surgery with the V3 cohort demonstrating more late cataracts.

Looking at the opacities from both the V3 and V4 series, only 3 of the 15 (20%) early anterior subcapsular opacities required secondary ICL surgery to treat the opacities, compared to 8 of the 11 (72.7%) late opacities ($P = .008$). Conversely, 80% of the early anterior subcapsular opacities compared to 27.3% of the late opacities required only observation.

Although 6 of 87 (6.9%) V3 eyes required cataract extraction, the procedure was performed in only 1 of 523 (0.2%) V4 eyes ($P < .001$). Similarly, 5 of 87 (5.7%) V3 eyes required ICL replacement while 6 of 523 (1.1%) were replaced in the V4 series ($P = .01$). Four of the five (80%) ICL replacements in the V3 series and three of the six (50%) in the V4 series were to implant longer lenses to treat poor vault.

The overall incidence of lens opacities >trace in

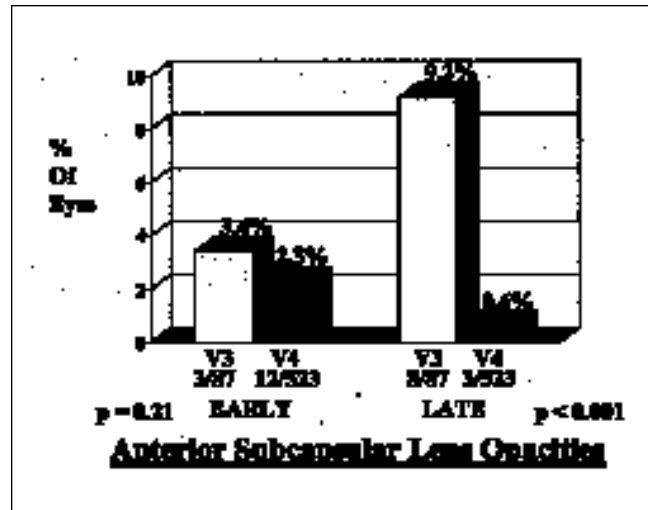


Figure 3. Incidence of early and late anterior subcapsular opacities >trace on LOCS score in the V3 and V4 series.

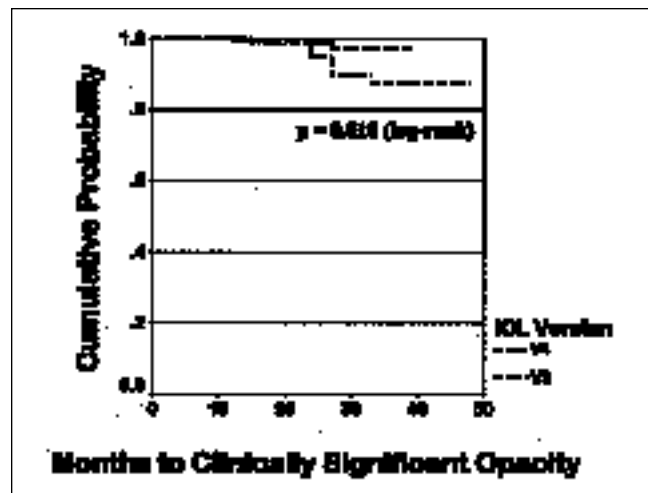


Figure 4. Kaplan-Meier survival analysis curve demonstrates the cumulative probability of not developing a clinically significant cataract in the V3 vs. V4 series of eyes.

the V4 series was 15/528 (2.8%). There were a total of 19 investigators who participated in the enrollment of the cohort. To determine the effect of surgeon experience, we compared the incidence of opacities in the first seven implants of each investigator (two investigators did less than seven) to later eyes. In the initial implantations of each surgeon, 9 of 124 (7.3%) developed anterior subcapsular opacities, compared to 6 of 399 (1.5%) in the later implantations ($P = .002$).

Two investigators (investigator number 1 and

investigator number 5, Table 2) out of a total of 19 were responsible for the majority of observed lens opacities. Although these two investigators implanted only 85 of 523 eyes (16%) in the V4 cohort, they produced 8 of the 15 (53%) opacities >trace. Although their incidence of opacities was 8 of 85 (9.4%), the remainder of the investigators had an incidence of 7 in 438 (1.6%, $P<.001$). Furthermore, these two investigators had an incidence of clinically significant lens opacities of 3 of 85 (3.5%), while the remainder of the investigators had an incidence of 1 in 438 (0.2%, $P=.001$).

DISCUSSION

This report demonstrates anterior subcapsular lens opacities that appear early (≤ 90 days after surgery) following implantation of an ICL are frequently asymptomatic and most likely due to surgically induced trauma. The strong association between anterior subcapsular opacities and removal and reinsertion of the ICL on the day of surgery strongly suggests surgical trauma as a factor in their development. Early anterior subcapsular opacities occurred in approximately 2% to 3.5% of patients, but resulted in clinically significant cataracts in under 1% of eyes. The strong association between surgeon experience and lens opacity, and the fact that 2 of 19 surgeons accounted for a majority of the opacities in the V4 series also points to surgical trauma as a major factor.

Of even greater concern than these early opacities are lens opacities that appeared late (≥ 1 year after surgery). Late opacities occurred in 9.2% of the V3 series. To date, only three late opacities (0.6%) have occurred in the V4 cohort of eyes and almost half of the series (258 eyes) have already been examined 2 years after surgery.¹⁴

Development of late opacities is clearly associated with poor vault or clearance between the ICL and crystalline lens centrally. The V3 series had 23.6% of eyes with poor vault and seven of eight (89%) late opacities that developed were associated with this finding. The V4 series of eyes had only 4.3% of eyes with poor vault and two of the three (67%) late opacities that developed were associated with it. The improvement in vault with the V4 lens would be expected given the change in design characteristics and represents an improvement in preventing the late development of lens opacities.

The previous V3 design of the ICL, which had substantially less vaulting away from the crystalline lens, had more late anterior subcapsular opacities than the V4 design (9.2% vs. 0.6%, $P<.001$)

and required more secondary surgery to improve the vault (ICL replacements with longer lenses) and treat the opacities (cataract extraction). Survival analysis (Figs 2 and 4) demonstrates that the differences in lens opacities between V3 and V4 series were not due to differences in follow-up in the two series.

The incidence of lens opacities and clinically significant cataracts in published series of ICL implantation for myopia is given in Table 4. Menezo et al³ reported on five V4 lenses with no lens opacities, and three opacities in seven eyes (43%) with earlier ICL designs. Gonvers et al⁶ reported a lens opacity in 1 of 13 eyes (7.7%) with the V4 lens and the authors commented that it was the only V4 lens with no vault. They also reported on a 21% incidence of lens opacities with the V3 design. None of the opacities reported were clinically significant. None of the other published series specifically reported on V4 lenses, although the other reports had relatively low incidences of lens opacities and clinically significant cataracts.

Methods other than clinical assessment by slit-lamp observation have been used to attempt to quantitate lens transparency with the ICL. In two studies^{11,12}, microdensitometric analysis utilizing Scheimpflug photography²⁸ showed no loss of transparency in a total of 31 eyes followed for an average of 12 months after surgery.

One ICL study⁹, utilizing the technique of autofluorescence developed by Van Best, Tjin, and Tsoi et al²⁹, demonstrated a statistically significant decrease in lens transmittance after surgery. There was no statistically significant difference between the 6-month and the 18- and 24-month measurement, indicating that the transmittance did not continue to decrease during the entire follow-up period, although the authors concluded otherwise.

Interestingly, Perez-Santonja, Hernandez, and Benitez del Castillo et al³⁰ demonstrated a statistically significant decrease in lens transmittance at 3, 6, and 14 months after implantation of the Worst-Fechner (iris-claw) phakic iris-supported lens, and Benitez del Castillo, Hernandez, JL, Iradier, MT et al³¹ also found a statistically significant decrease in lens transmittance 6 months after implantation with the Baikoff anterior chamber phakic IOL. The magnitude of the changes in lens transmittance was similar, with all three types of phakic IOLs (posterior chamber, anterior chamber, and iris-supported) in spite of the fact that these phakic IOLs differ with regard to proximity to the crystalline lens.

The clinical relevance of these findings must be

Table 4
Incidence of Lens Opacities in Published Series of ICL for Myopia

Published Series	No. of Eyes (Patients)	No. of Cases	Lens Models	Clarity Measurement	Time To Opacity	Average Follow-Up (Months)	Comments
Manson, Fuchs-Matthies, Chansins, & Chant ²	7 (7)	1 (14%)	V2/V3	MR	20 months	4.3 mos.	No vitreous or ICL-related opacities.
	5 (5)	0 (0%)	V4	0 (0%)			
Keane & Clark ³	16 (17)	0 (0%)	V4	0 (0%)	30A	3-6 mos.	
Kalderer, Duvickić & Cankarac ⁴	134 (88)	9 (6%)	V3 or Bausher	0 (0%)	30A	11-4-6.3	No V4 Lenses studied.
Lawson, Okamoto-Okada, Sasaki, & Ishikawa ⁵	19	4 (21%)	V3	0 (0%)	TRK	7.4-2.8	
	15	1 (7%)	V4	0 (0%)	TRK		2000 vitreous V4 case with opacity. Remaining 13 V4 eyes had good vision.
Yoon & Linnar ⁶	39 (39)	2 (5%)	V3 or Bausher	1 (1.7%)	16 mos., 20 mos.	6.75 @ 2 yrs	2000 vitreous opacity eyes. No V4 eyes.
Tranbali, Aho, Rao, and Laatikainen ⁷	39 (39)	1 (2.6%)	V4	1 (2.6%)	1 Year	21.9 mos. (6-3.5)	Developed Secondary Trilaterality superior to the non-developing inferior.
Shewee, Almar, Reyes del Castillo, Ramos-Velazquez, et al. ⁸	20 (19)	0 (0%)	V4	0 (0%)	30A	16.3 to 3.1 mos. (12-20)	
Shawhan, Brown, Martin, et al. ⁹	10 (10)	0 (0%)	V3	0 (0%)	30A	1 (204) @ 6 mos.	
Yamada, Yamashita & Yamada ¹⁰	15 (14)	0 (0%)	V4	0 (0%)	30A	7.9 to 1.05 (3-13)	
Pavlenko & Chikmagalov & Pchelnykh ¹¹	19 (17)	0 (0%)	V4	0 (0%)	30A	12 (4-14)	
Case Reports of Cataract:							
Tranbali & Purohit ¹²	1	1	V4	1	6 mos.	6 mos.	58-Year-old patient.
Paul, Chou, & Hsu ¹³	3 (3)	1	V4	0 (0%)	4 mos., 13 mos., 13 mos.	NR	Edema in the macula in 2 eyes.

determined in reference to normal values obtained by this method. In their original paper, Van Best, Tjin, Tsoi et al²⁹ measured the transmittance values in 103 normal patients with age ranging from 11 to 83 years, with no evidence of lens opacities.

The best-fit curve approximating the normal transmittance values as a function of age [T (t)] was;

$$T(t) = T_0 [1 - \exp(t - t_0)/t_\eta)]$$

Where t = age (yr); T₀ = 0.96 (transmittance at age zero)

$$t_0 = 105.9 \text{ yr, and } t_\eta = 16.13 \text{ yrs.}$$

In the study demonstrating a decrease in lens transmittance with the ICL⁹, the mean age of the patients at enrollment was 32.3 years, so that the normal lens transmittance values expected during the 2-year course of the study obtained from the equation above were 0.949 to 0.950. The lens transmittance values obtained before and after ICL implantation ranged from 0.969 to 0.950, thus they were at or above the expected values for normal unoperated controls without lens opacities.

Similarly in the study of the Worst-Fechner

lens³⁰, before and after surgery values were at or above those expected in normal unoperated controls without lens opacities. In the Baikoff lens study³¹, transmittance values were only slightly below expected normal values.

Given that the changes after surgery are so small, and that range of phakic IOL values are so close to the age adjusted normal values for eyes without lens opacities, one must question the clinical relevance of these findings. Although not directly germane to our findings with regard to anterior subcapsular opacities, phakic IOLs in general do not appear to be cataractogenic when studied by lens transmittance in spite of statements to the contrary in the peer-reviewed literature.

It appears that by clinical observation the incidence of late development of anterior subcapsular opacities out to 2 years with the V4 ICL lens design is small, and both Scheimpflug photography and lens autofluorescence techniques do not demonstrate an ongoing decrease in lens transparency. In spite of this, concerns about the long-term development of lens opacities past the 2-year time frame with posterior chamber IOLs have been expressed.³²

Table 5
Comparison of U.S. ICL Study to FDA Approved PRK or LASIK Pre-market Approval Applications (PMAs) Summary of Safety and Effectiveness

Device/ Manufacturer	Procedure	Myopia Range (D)	Follow-up (mo)	Loss of >2 Lines Best Spectacle-corrected Visual Acuity	Percent (mo)
U.S. FDA ICL	ICL	-3.00 to -20.00 SE	12	Actual: 0.2% (12)	Theoretical Max.: = 1.4%
LaserSight ³⁴	PRK	-6.00 to -10.00 SE	6 and 12	0.9 (6)	3.3 (12)
Nidek ³⁵	PRK	≥-7.00 to -13.00 SE	6	3.5	(6)
Autonomous ³⁶	LASIK	≥-7.00 to -11.00 sph ≥0.50 to ≤ 6.00 cyl	3	4.5	(3)
Summit ³⁷	LASIK	-7.00 to -14.00 sph -0.50 to -5.00 cyl	6	3.3	(6)
Visx ³⁸	LASIK	≥-7.00 to -14.00 SE 0.25 to 6.00 cyl	6	0	(6)

One way to deal with this concern would be to determine the risk of visual loss in the patient population if more cataracts do indeed occur with time.

One can calculate the theoretical risk of visual loss due to the development of clinically significant cataract that requires ICL removal, cataract extraction, and IOL implantation, analogous to Javitt's analysis of the risk of visual loss following clear lens extraction for myopia.³³ This analysis involves calculating the additional risk of retinal detachment as a result of making a number of patients pseudophakic, calculating the risk of visual loss if retinal detachment occurs, and adding the risk of visual loss due to the secondary procedure even if retinal detachment does not occur. Using an extremely conservative model assuming an ultimate rate of clinically significant cataract of 10 times the current rate (approximately 10%), and including the actual visual loss that occurred in the U.S. FDA study of ICL implantation, the total actual and theoretical risk of visual loss in the study can be calculated to be approximately 1.4% (Sanders DR. Actual and theoretical risks of visual loss following use of the ICL for moderate to high myopia. Unpublished data). For every increase of 10% in cataract rate (for instance, an increase from 10% to 20%), the conservative model predicts an increased risk of visual loss of 0.5% to 0.6%. The total visual risk assuming a late cataract rate of 20% is close to 1.9%.

Even if the rate of clinically significant cataract approached 100%, the risk of visual loss due to subsequent cataract surgery would be approximately the risk of visual loss in clear lens extraction for high myopia, which Javitt has estimated to be 4.6%.³³

For comparison purposes, one can examine the actual reported visual loss in published safety and effectiveness summaries of the approved excimer

laser pre-market approval applications using photorefractive keratectomy (PRK) and laser in situ keratomileusis (LASIK), available from the FDA³⁴⁻³⁸ (Table 5). Only series are included where data have been stratified by the level of manifest spherical equivalent refraction (MRSE) to allow for a review specifically of moderate to high myopia (>-6.00 to >-7.00 D, depending on the study). This higher myopia data was selected for comparison to the ICL study since, in the latter, only 21.2% of eyes had preoperative myopia less than -7.00 D while 9.9% had more than -15.00 D; mean preoperative myopia in the ICL series was more than -10.00 D.

With the exception of one LASIK series that reported no loss of BSCVA, the actual visual loss and the combined actual plus calculated theoretical loss due to 10 or 20 times the current rate of cataract in the ICL series is lower than the actual rate of visual loss reported in the other four excimer series. Thus, from a safety standpoint, the risk of visual loss due to cataract development in the ICL series is well within the acceptable range of FDA approved refractive procedures that might otherwise be utilized.

ICL vaulting in the U.S. FDA trial was evaluated by slit-lamp examination rather than the use of a Scheimpflug camera²⁸, or an ultrasonic biomicroscope, because at the time of enrollment, user-friendly and/or cost effective units were unavailable to place in a 12-site clinical trial. Although a quantitative method of assessing vault would have been preferred, the small substudy of 40 eyes from one site comparing ultrasonic biomicroscopy to clinical assessment of vault, discussed in the methods section, demonstrated that clinical slit-lamp assessment was adequate to detect poor vault.

The overall length sizing of the ICL in the V3 and

V4 series was based on external measurement of horizontal white-to-white distance, which at the time of enrollment of these eyes was considered by the manufacturer to be the best available clinical method. It was part of the U.S. FDA clinical protocol. Subsequently, it has become clear that white-to-white measurements do not correlate well with sulcus-to-sulcus distance¹³ (Lovisolo CF, Fumagalli G, Paganoni C. High frequency echographic sizing of the ICL. Presented at the 1998 ESCRS Winter Meeting, Munich Germany). Given this information, it is remarkable that only 4.3% of the V4 series demonstrated poor vault, 0.4% had anterior subcapsular opacities associated with poor vault, 0.8% were replaced for a longer ICL¹⁴, and 0.4% were replaced for a shorter ICL.¹⁴ With the advent of new patient and physician-friendly high frequency ultrasonic devices³⁹, sulcus-to-sulcus measurements may result in even better ICL sizing with fewer eyes presenting with poor vault and fewer ICL replacements required.

Participants in the Implantable Contact Lens for Myopia (ITM) Study Group as of March 2002: Davis Duehr Dean Medical Center, Madison, WI—John A. Vukich, MD; Center for Clinical Research, Chicago, IL—Donald R. Sanders, MD, PhD, Kimberley Doney; The Barnett Dulaney Eye Center, Phoenix, AZ—Ronald Barnett, MD, David Dulaney, MD, Scott Perkins, MD; Rowen Laser Vision & Correction Center, Towson, MD—Sheri L. Rowen, MD; Advance Sight Medical Group, Los Angeles, CA—Douglas Steel, MD; Houston Microsurgery Center, Houston, TX—Ralph Berkeley, MD, Michael Caplan, MD, Paul Mann, MD; Shepard Eye Center, Santa Maria, CA—Stephen Bylsma, MD; Carolina Eye Associates, Southern Pines, NC—R. Gale Martin, MD; Eye Centers of Florida, Fort Myers, FL—David C. Brown, MD; Sarasota Cataract Institute, Sarasota, FL—Harry Grabow, MD; Williamson Eye Center, Baton Rouge, LA—Charles H. Williamson, MD; Shepherd Eye Center, Las Vegas, NV—John R. Shepherd, MD; Oregon Eye Surgery Center, Eugene, OR—I. Howard Fine, MD; Kruff Eye Institute, Chicago, IL—Manus Kruff, MD; Pacific Eye Institute, Upland, CA—Robert Fabricant, MD; Advanced Vision Correction Centers, Burbank, CA—Alan Berg, MD; STAAR Surgical—Monica Gaston, Nancy Hall, Darcy Smith.

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