Biomicroscopic Findings and Management of Anterior Stromal Necrosis After Long-term Implantation of Intacs

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• PURPOSE: **We sought to evaluate the visual, refractive, and biomicroscopic findings pre- and posttreatment of observed anterior stromal necrosis (ASN) after long-term Intacs intracorneal ring segment (ICRS) implantation.**

• DESIGN: **Consecutive interventional case series.**

• METHODS: **All consecutive patients implanted with Intacs ICRS at a single center by 1 of the authors between October 2006 and October 2011 with a minimum follow-up time of 5 years were included. All Intacs were implanted using the Prolate system console and instrumentation from Addition Technology Inc (Chicago, Illinois, USA). The slit lamp, refractive, and visual findings and the management of those patients are described in detail. The primary outcome measures included the size of the epithelial defect overlying the Intacs body, the intended implantation depth measured by high-magnification slit lamp photography, and the management of the cases described in detail. The percentage of eyes with ASN out of those that reached the 5-year follow-up is reported.**

• RESULTS: **One hundred twenty-seven eyes (84 patients) were implanted with 215 ICRSs during the study period, and 77.16% (98/127) eyes had a follow-up of ≥5 years, out of which 9 eyes (7 patients) had ASN corresponding to at least 9.18% (95% confidence interval 4.29%-16.72%). The mean ± standard deviation time between implantation and ASN diagnosis was 10.5 ± 1.3 years.**

• CONCLUSION: **After 5 years of implantation, INTACS-treated eyes could present with an ASN over the ICRS body. Longer-term follow-up of patients implanted with INTACS is important to monitor if this complication keeps occurring over time. (Am J Ophthalmol 2020;220:170–176. © 2020 Elsevier Inc. All rights reserved.)**

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INTRASTROMAL CORNEAL RING SEGMENTS (ICRSS) WERE first implanted by Blevatskaya in 1966 in a superficial manner[1] and now are made of polymethyl methacrylate and are implanted deeper (70%-80% of the corneal depth). Intacs ICRS (Addition Technology Inc, Chicago, Illinois, USA) were first used in 1991 for the treatment of myopia[2] and have been used since 1996 for the treatment of keratoconus (KC)[3] to decrease myopia, astigmatism, and irregular astigmatism. Early postoperative complications include infectious keratitis, neovascularization, ring migration, and ring removal because of refractive failure or anterior stromal necrosis (ASN).[4,5]

INTACS are the only ICRS available for implantation in the United States. There are some 5-year follow-up studies that describe the refractive and topographic results after INTACS implantation.[6–8] In a retrospective case series, aseptic keratitis with signs of inflammation around the segment was reported as the main medical complication requiring explantation, however, the time from implantation to the onset of inflammatory signs was not reported.[9] Four cases of late ASN occurring between 5 and 20 years of INTACS implantation have been reported in the literature.[10–12] However, the incidence of such ASN is not known.

The aim of this study is to describe the biomicroscopic, refractive, and visual characteristics of patients with ASN after 5 years of implantation in a group of patients operated by a single surgeon in a single center.

METHODS

THIS PROSPECTIVE LONGITUDINAL STUDY INCLUDED ALL PAtients with KC who received an Intacs ICRS implant (Addition Technology Inc, Chicago, Illinois, USA) at a single center (Clínica Oftalmológica de Antioquia, Medellín, Colombia) by the same corneal specialist (J.C.A.) between October 2006 and October 2011. The present study adhered to the tenets of the Declaration of Helsinki and it was approved by the investigation and review board of Universidad Pontificia Bolivariana (Medellín, Colombia). Written informed consent was obtained from all participants.

Inclusion criteria for the study were patients with KC diagnosis that had Intacs ICRS implantation between October 2006 and October 2011 that visited the clinic for some

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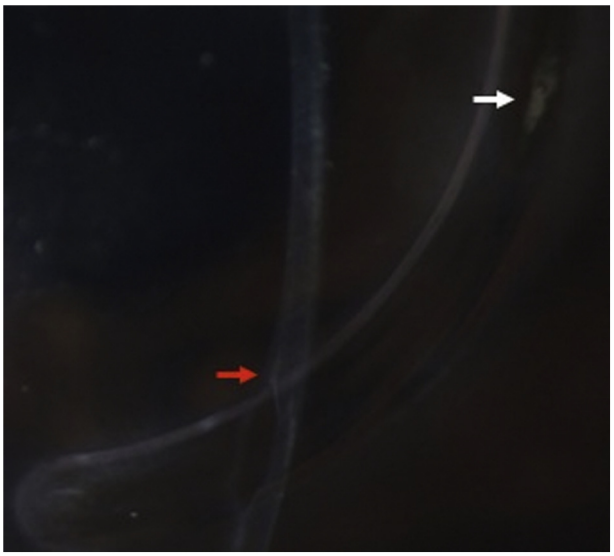

FIGURE 1. Case 3. Intacs of the left eye with a linear epithelial/stromal defect overlying it in the temporal region (white arrow). Inferior part of the same segment showing an implantation depth of about 80% (red arrow) measured by using high magnification of the split slit beam.

TABLE 1. Cumulative Anterior Stromal Necrosis Incidence According to Follow-up Time

Follow-up Time (y)	Cumulative Eyes, *n*	Cumulative ASN Cases, *n*	Cumulative Incidence
5	11	0	0%
6	14	0	0%
7	23	0	0%
8	42	1	2.38%
9	61	2	3.27%
10	82	6	7.32%
11	95	8	8.42%
12	98	9	9.18%

ASN = anterior stromal necrosis.

complication related to the ICRS after 5 years of implantation. Patients were examined at presentation and after management of the complication. The following variables were assessed: symptoms, biomicroscopic signs, history of eye rubbing, uncorrected visual acuity, best-corrected visual acuity (BCVA), subjective refraction, longitudinal linear erosion, and estimated actual implantation depth.

Longitudinal linear erosion was measured over the Intacs body with the help of a fluorescein strip and blue cobalt light, the length was measured in millimeters and its width as <0.5 mm if so, or if greater, its magnitude in millimeters. Actual implantation depth was measured using microphotographs that were taken with the slit lamp IM 900 (Haag Streit, Köniz, Switzerland) as close as possible to the stromal defect and enlarged to measure the distance from the bottom part of the ICRS to corneal surface and dividing it by the distance from the endothelial to the epithelial surface, hence obtaining an estimate of the actual implantation depth (Figure 1).

All Intacs were implanted in patients with KC using the Prolate system console and instrumentation from Addition Technology (Chicago, Illinois, USA). The segments were intended to be implanted at 70% of the ultrasonically measured corneal thickness using the Sonogage pachymeter (Sonogage Inc, Cleveland, Ohio, USA) at the site of incision by adjusting the double-pass diamond blade to that amount.

• **STATISTICAL ANALYSIS:** Data were extracted from clinical charts and transferred to Excel (Microsoft Corp, Redmond, Washington, USA). Qualitative variables were expressed by their relative and absolute frequencies, and quantitative variables as median and interquartile range (P25-P75), and mean and standard deviation (SD). The percentage of ASN was estimated as the cumulative incidence of ASN with the 95% confidence interval. For the change in variables before and after removal of the segments, the paired mean difference test was performed, and $P < .05$ was considered statistically significant. Statistical analysis was conducted with Epidat software (available at https://www.paho.org/english/sha/epidat.htm).

RESULTS

DURING THE DEFINED PERIOD, A TOTAL OF 215 INTACS ICRSS were implanted in 127 eyes of 84 patients. More than half (58.33%) were male (49/84) and the mean ± standard deviation (SD) age at implantation was 29.44 ± 10.9 years. In 51.19% (43/84) the procedure was bilateral. Of 127 implanted eyes, 66 (51.97%) were left eyes and in 88 eyes (69.3%) 2 ICRSs were implanted. The mean ± SD number of months of follow-up was 86.5 ± 86.3.

Seventy-seven percent of implanted eyes (98/127) had a minimum follow-up of 5 years. Twenty-nine eyes (23%) were excluded from the analysis because they were lost to follow-up and 3 eyes were excluded because the ICRS was removed during the first 5 years after implantation. Of 98 eyes that had a 5-year follow-up, 9 cases (9.18% [95% confidence interval 4.29%-16.72%]) had a spontaneous linear ASN over the ICRS body. Table 1 shows the cumulative ASN incidence according to follow-up time. All cases occurred after 9 years of implantation with a mean time between implantation and ring exposure diagnosis of >10 years (126 ± 15.6 months).

Table 2 describes the characteristics of the eyes and ICRS with ASN: 100% (9/9) of the eyes were 130° in arc length; in 89% (8/9 eyes) the ASN was located in the inferotemporal area and in 11.1% (1/9) in the temporal area; regarding diameter, 77.8% (7/9) were 7.0 mm and

TABLE 2. Characteristics of Eyes and Implanted Intacs Intrastromal Corneal Ring Segments in Cases of Anterior Stromal Necrosis

Case No.	Thickness at the Incision Site (μm)[a]	Flattest K	Steepest K	Axis (Degrees)	Diameter of ICRS (mm)	Thickness of ICRS (μm)	Arc Length of ICRS (Degrees)	Segment Location	Time to Extrusion (y)
1	580	42.5	48.8	150	7	450	130	IT	10
2	495	44.6	46.2	7	7	250	130	T	10
3	525	43.8	49.1	128	7	250	130	IT	10.1
4	466	45.4	48.3	132	6	450	130	IT	8.6
5	421	45.4	48.4	42	7	450	130	IT	9
6	490	43.1	45.6	46	6	450	130	IT	11.7
7	523	43.0	47.8	33	7	450	130	IT	11.3
8	529	46.1	50.3	21	7	450	130	IT	12.5
9	533	43.6	48.6	65	7	450	120	IT	10.9

ASN = anterior stromal necrosis; ICRS = intrastromal corneal ring segment; IT = inferotemporal; K =keratometries.
[a]Determined by intraoperative ultrasonic pachymetry.

hexagonal in cross-section and 22.2% (2/9) were 6.0 mm and oval in cross-section. Cases 1 and 7 and cases 3 and 8 were bilateral with a difference of 16-24 months in the occurrence of ASN between eyes.

Table 3 shows the symptoms, signs, and management in each case. The main complaint of ASN was a foreign body sensation in 100% (9/9). There was no trauma or discharge history and no corneal infiltrate was found on clinical examination in neither eye. Only 1 of 9 cases with stromal necrosis reported eye rubbing before the event (case 6). The segment exposures were linear in 89% (8/9) of the cases, the length of the ASN was between 1 and 3 mm in 100% of the cases (9/9), its width was <0.5 mm in 66.7% (6/9) and 0.7 mm in 22.2% (2/9), and it overlaid the midbody of the Intacs ICRS segment. Figure 2 shows slit lamp photography of the ASN. Figure 3 shows that the stromal defects were partially covered by epithelium that was enlarged after gentle debridement with a cellulose sponge.

After removing the offending Intacs ICRS, we elected to fill the virtual gap of the removed segment tunnel in the first case with amniotic membrane (glycerin-preserved, see Methods) to try to better preserve the corneal contour. This type of amniotic membrane took >2 years to attain transparency and it did not seem to prevent the ensuing myopization and increase in astigmatism. From the second case on, we have removed the ICRS without any additional surgical manipulation (aside from the occasional end-to-end suture), leaving a bandage contact lens for a month or so without any adverse side effects and spontaneous closure of the ICRS tunnel and the ASN.

The clinical presentation in 3 cases that had delayed removal of the segment point to the indolent nature of this stromal necrosis. Case 3 lived overseas and consulted several months after the initiation of symptoms; he had a wider stromal defect and had developed corneal neovascularization by the time of ICRS removal. Cases 7 and 9 are still waiting to have the segments removed (1 of them for more than a year). They occasionally complain of a foreign body sensation and are being managed by a bandage contact lens and prophylactic antibiotics.

Table 4 presents the uncorrected visual acuity, objective refraction, and BCVA at the time of ASN diagnosis and 1 month after the ICRS was removed (2 cases have not had removal of the exposed segment yet: case 7 declined removal and case 9 is waiting for approval from the insurance company). Before and after removal of the ICRS, there was a statistically significant difference in the magnitude of the cylinder ($P = .021$) and no statistically significant difference in the value of the sphere ($P = .425$). All eyes had worsening the uncorrected visual acuity after ICRS removal and 22.22% (2/9) cases had worsening the BCVA after removal ICRS segment. Loss of ≥2 Snellen lines on BCVA was observed in none of the eyes.

DISCUSSION

KYMIONIS AND ASSOCIATES[6] PUBLISHED A 5-YEAR (RANGE 4.9-6.5 years) follow-up study of 17 Intacs ICRSs for KC with a 55% follow-up with no reported cases of ASN. Kang and associates[7] reported a 5-year follow-up study of 87 eyes implanted with Intacs for KC with a 34% follow-up with only 1 case of ASN that occurred before 5 years of implantation. Bourges and associates[11] reported 1 case of aseptic ASN of the temporally located Intacs segment 5 years after implantation for myopia. Oatts and associates[12] reported linear ASN over the temporally located segment in 3 eyes of 2 patients 7, 17, and 20 years postimplantation, respectively, for the correction of myopia with the same indolent clinical features as seen in our patients. The metanalysis by Bautista-Llamas and associates[10] describes a greater number of ASNs seen in Intacs as opposed to Ferrara-type implants, but because the total number of implanted segments was unknown no incidence could be

TABLE 3. Clinical Presentation and Management of Reported Cases of Anterior Stromal Necrosis

		Biomicroscopic Findings							Resolution		
Case No.	Symptoms	LLE	Oval-Shaped Erosion	Measure of Stromal Defect	Halo Around the Tunnel	Neovascularization	Punctate Keratitis	ICRS depth at ASN Diagnosis	ICRS Explanted	Complication Related to the ICRS Explantation	Special Management
1	FBS	Yes	No	L: 2 mm W: <0.5 mm	No	No	Yes	63%	Yes	No	Glycerin-preserved amniotic membrane inside the tunnel
2	FBS, tearing	Yes	No	L: 1.5 mm W: <0.5 mm	No	No	Yes	70%	Yes	No	
3	FBS	No	Yes	L: 3 mm W: 2.2 mm	No	Yes	No	75%	Yes	No	
4	FBS	Yes	No	L: 1.7 mm W: <0.5 mm	Yes	No	No	74%	Yes	No	
5	FBS, itching	Yes	No	L: 1.3 mm W: <0.5 mm	No	No	Yes	66%	Yes	No	
6	FBS, itching and eye rubbing	Yes	No	L: 1.3 mm W: <0.5 mm	No	No	No	80%	Yes	No	Conservative management[a]; after waiting 11 months,[b] ICRSs were removed
7	FBS	Yes	No	Sup: L: 1 mm W: 0.7 mm Inf: L: 3 mm W: <0.5 mm	No	No	No	66%	No		After 1.5 years[b] the linear defect has remained constant, not increased in size, or closed spontaneously
8	FBS	Yes	No	L: 1 mm W; 0.7 mm	No	No	No	77%	Yes	No	
9	FBS	Yes	No	L: 2.4 mm W: <0.5 mm	Yes	No	No	75%	No		Surface therapy management[a,b]

ASN = anterior stromal necrosis; FBS = foreign body sensation; ICRS = intrastromal corneal ring segment; Inf = inferior defect; L = length; LLE = longitudinal linear erosion; Sup = superior defect; W = width.

[a]Topical lubricants, antihistamines, and contact lenses.

[b]Waiting for insurance approval for ICRS removal.

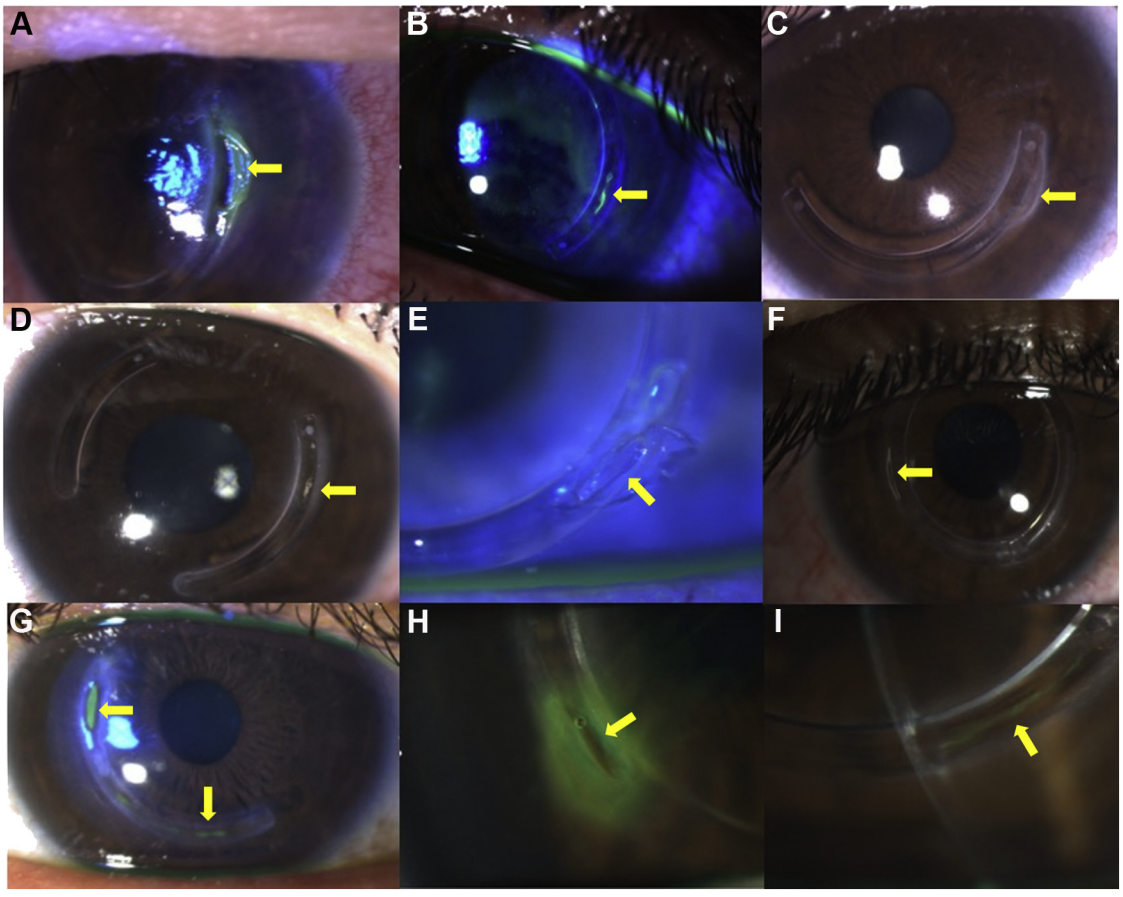

FIGURE 2. Cases of anterior stromal necrosis in order of presentation. (A) Case 1. Note the deep stromal defect that is discovered by removing the weak epithelium. (B) Case 2. Linear defect over the ring with associated punctate keratitis. (C) Case 3. Oval shaped stromal thinning deeper in the center, with infiltrated border and neovascularization toward the lesion. (D) Case 4. Localized thinning on the proximal end of the ring with inflammatory halo around the tunnel in the same location. (E) Case 5. Deep stromal defect exposing the ring segment, covered by weakened epithelium. (F) Case 6. Linear defect on the body of the temporal ring segment. (G) Case 7. Two areas of thinning on the anterior surface of the ring. One short and wide (superior) and the other linear (inferior), and inflammatory halo around the tunnel. (H) Case 8. Localized stromal defect reveals the anterior surface of the ring, surrounded by thinned stroma and poor-quality epithelium. (I) Case 9. Linear defect on the anterior surface of the ring which is located at 75% depth. Anterior stromal necrosis is indicated by the yellow arrows.

calculated. They also included cases caused by poor refractive results, shallow implantations, ASNs near the tips of the segments, infections, etc.

We established a tentative incidence of long-term (>5 years) ASN over Intacs ICRS of 9.18%. Since our follow-up was only 77%, our denominator was slightly lower. If we had used all the implanted eyes (127) as a denominator, our long-term incidence of ASN would have been 7.09%, so a conservative figure for the incidence of long-term ASN probably lies between 7.09% and 9.18%. Certainly, it would have changed if we had 100% follow-up of our patients. The time to ASN in our study was between 9.5 and 11.5 years (114-138.5 months), much longer than the previously mentioned medium-term follow-up series,[6–8] which could account for their lack of observed ASN.

Shallow implantation of the Intacs ICRS could be a cause of ASN, but according to our photographic record, the actual implantation depth (Table 3) was close to the intended implantation depth of 70%. Other possible causes of AST could be anterior lamellar compression by the either the hexagonal (Figure 4A) or oval (Figure 4B) Intacs body as the optical coherence tomography images of some random patients from these series show, poor tissue nutrition from the aqueous humor to the anterior corneal tissues by the space-occupying ICRS, ocular surface disease causing desiccation and local inflammation above the segments, or interruption of the normal flow of leukocytes from limbus to limbus traveling between the corneal lamellae getting clogged in the compressed upper lamella with activation of matrix metalloproteases and other lytic enzymes.

We do not think infection was responsible for the observed ASN since we did not see stromal infiltrates surrounding the epithelial defect or ocular discharge. We

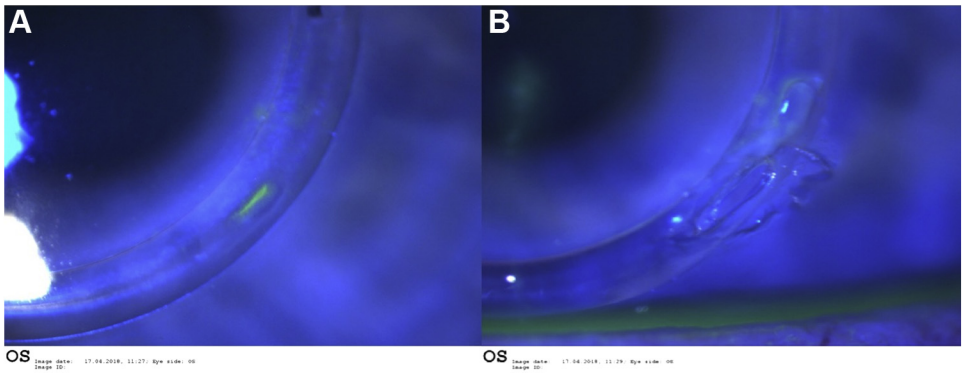

FIGURE 3. Case 5. Partially exposed inferotemporal Intacs in the left eye. Note the small linear epithelial defect evident by fluorescein staining (A) that reveals a much larger stromal defect overlying the Intacs body after careful dissection with a cellulose sponge (B).

TABLE 4. Refractive Change Before and After Intrastromal Corneal Ring Segment Removal in Reported Cases of Anterior Stromal Necrosis

	UCVA		Sphere		Cylinder		Axis		BCVA	
Case No.	Before	After[a]	Before	After	Before	After	Before	After	Before	After
1	20/25	20/30	1.25	−1.50	−2.00	−3.50	177	2	20/25	20/25
2	20/40	20/80	Plano	−1.25	−1.50	−1.50	26	13	20/30	20/40
3	20/50	20/60	0.50	1.25	−2.50	−3.00	149	132	20/30	20/30
4	20/60	20/80	1.75	2.25	−2.75	−4.75	179	176	20/25	20/25
5	20/60	20/50	−1.00	−1.50	−1.00	−1.25	90	133	20/25	20/30
6	20/200	20/400	−6.50	−8.25	−4.25	−5.00	25	30	20/40	20/40
7[b]	20/25	—	Plano	—	−1.25	—	59	—	20/20	—
8	20/60	20/100	−2.00	−3.00	−1.50	−2.25	14	30	20/60	20/60
9[b]	20/30	—	−0.25	—	−6.50	—	167	—	20/25	—

BCVA = best-corrected visual acuity; ICRS = intrastromal corneal ring segment; UCVA = uncorrected visual acuity.
[a]Values measured 1 month after ICRS removal.
[b]After values are not present because segments have not been removed.

covered all patients with topical moxifloxacin while they had an epithelial defect. We did not obtain corneal cultures in any patient.

After studying 8 corneal buttons submitted to penetrating keratoplasty for less than optimal refractive results in group of patients with KC who were implanted with Intacs ICRS, Samimni and associates[13] found epithelial thinning over the Intacs body and a diminished number of keratocytes both above and below the ICRS body, along with a probable chronic activation of metalloproteases that could allow for the long-term ASN. The reason why the stromal necrosis always seems to occur over the temporal area of the cornea might be related to exposure, frictional forces, or the fact that that is the weakest corneal area by as stated by Newton and Meeks.[14]

We should emphasize that this study pertains only to manual Intacs implantation using the Prolate system by and single surgeon and not to Intacs implanted using the femtosecond laser.

As the study of Oatts and associates[12] points out—and this study confirms—additional longer-term follow-up studies of patients implanted with Intacs are needed to see if these devices will be tolerated by the cornea, especially because they tend to be implanted in younger patients. Usually removal of the segments occurs without major disruption of BCVA and just a slight increase in myopia and astigmatism, but there could be midperipheral corneal neovascularization and partial melt (case 3) or cosmetic complaints because of permanent haze.[12]

In our practice we have stopped using Intacs ICRSs and have switched to triangular-shaped ICRSs of symmetric/asymmetric thickness because there is more corneal remodeling with less foreign material,[15] less disruption of the parallelism of the corneal lamellae over the ICRS, and

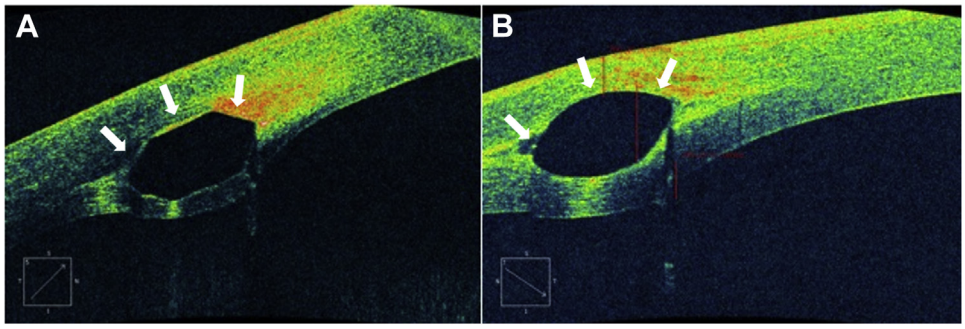

FIGURE 4. Anterior segment optical coherence tomography showing the profile of a hexagonal 7.0-mm Intacs intracorneal ring segment (ICRS) (A) and an oval 6.0-mm Intacs SK ICRS (B). There is some compression of the corneal lamellae above by these mass-occupying ICRSs, evidenced by the change in direction and the loss of parallelism of those lamellae (white arrows).

because the rate of ASN seems to be less than with Intacs ICRSs.[10] Triangular-shaped segments are the most commonly used type of ICRS worldwide, but in the United States the only ICRSs available are Intacs, and therefore it is important to know the odds of long-term ASN after implantation of this type of ICRS. Recently, Jacob and associates[16] have used corneal allogenic intrastromal ring segments (after having also observed ASN like ours), obtaining a flattening and astigmatic-diminishing effect using allogenic human cornea.[16]

IN SUMMARY, WE DESCRIBE THE BIOMICROSCOPIC FINDINGS OF LONG-TERM ASN AFTER INTACS ICRS IMPLANTED FOR KC USing the Prolate system and report an estimated incidence of 9.18% (9/98) eyes 8.6 to 12.5 years after implantation. Longer-term follow-up studies (10-20 years) are needed to evaluate the real incidence of ASN after Intacs implantation.All authors have completed and submitted the ICMJE form for disclosure of potential conflicts of interest and none were reported. All authors attest that they meet the current ICMJE criteria for authorship.

REFERENCES

1. Blevatskaya ED. Intralamellar homoplasty for the purpose of relaxation of refraction of the eye. *Arch Soc Am Ophthalmol Optom* 1968;6:311–325.
2. Nose W, Neves RA, Burris TE, et al. Intrastromal corneal ring: 12-month sighted myopic eyes. *J Refract Surg* 1996; 12(1):20–28.
3. Colin J, Cochener B, Savary G, Malet F, Holmes-Higgin D. INTACS inserts for treating keratoconus: one-year results. *Ophthalmology* 2001;108(8):1409–1414.
4. Ferrer C, Alió JL, Montañés AU, et al. Causes of intrastromal corneal ring segment explantation: clinicopathologic correlation analysis. *J Cataract Refract Surg* 2010;36(6):970–977.
5. Kanellopoulos A, Pe LH, Perry HD, et al. Modified intracorneal ring segment implantations (INTACS) for the management of moderate to advanced keratoconus: efficacy and complications. *Am J Ophthalmol* 2006;141:604.
6. Kymionis GD, Siganos CS, Tsiklis NS, et al. Long-term follow-up of Intacs in keratoconus. *Am J Ophthalmol* 2007; 143(2):236–244.
7. Kang M-J, Byun Y-S, Yoo Y-S, Whang W-J, Joo C-K. Long-term outcome of intrastromal corneal ring segments in keratoconus: five-year follow up. *Sci Rep* 2019;9:315.
8. Alió JL, Shabayek MH, Artola A. Intracorneal ring segments for keratoconus correction: long-term follow-up. *J Cataract Refract Surg* 2006;32(6):978–985.
9. Nguyen N, Gelles JD, Greenstein SA, Hersh PS. Incidence and associations of intracorneal ring segment explantation. *J Cataract Refract Surg* 2019;45(2):153–158.
10. Bautista-Llamas M-J, Sánchez-González MC, López-Izquierdo I, et al. Complications and explantation reasons in intracorneal ring segments (ICRS) implantation: a systematic review. *J Refract Surg* 2019;35:740–745.
11. Bourges J-L, Than Trong T, Ellies P, Briat B, Renard G. Intrastromal corneal ring segments and corneal anterior stromal necrosis. *J Cataract Refract Surg* 2003;29(6):1228–1230.
12. Oatts JT, Savar L, Hwang DG. Late ASN of intrastromal corneal ring segments: a report of two cases. *Am J Ophthalmol Case Rep* 2017;8:67–70.
13. Samimi S, Leger F, Touboul D, Colin J. Histopathological findings after intracorneal ring segment implantation in keratoconic human corneas. *J Cataract Refract Surg* 2007;33(2):247–253.
14. Newton R-H, Meeks KM. The integration of the corneal and limbal fibrils in the human eye. *Biophysical J* 1998;75: 2508–2512.
15. Prisant O, Pottier E, Guedj T, Hoang Xuan T. Clinical outcomes of an asymmetric model of intrastromal corneal ring segments for the correction of keratoconus. *Cornea* 2020; 39(2):15–60.
16. Jacob S, Patel SR, Agarwal A, Ramalingam A, Saijimol AI, Raj JM. Corneal allogenic intrastromal ring segments (CAIRS) combined with corneal cross-linking for keratoconus. *J Refract Surg* 2018;34(5):296–303.