Incidence and Reasons for Intrastromal Corneal Ring Segment Explantation

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• PURPOSE: To determine the main causes of intrastromal corneal ring segment (ICRS) explantation and define the incidence rate.

• DESIGN: Multicenter, observational consecutive case series.

• METHODS: Consecutive cases of ICRSs explanted in the last 10 years were reviewed. Clinical data included age of the patients at explantation, reasons for implantation and explantation, date of implantation and explantation, tunnel creation technique, and ICRS type. Main outcomes measures were the reasons for ICRS removal and the incidence rate.

• RESULTS: During the study period, 121 ICRSs (119 patients) were explanted, with an explantation rate of 5.60%. Functional failure (74 eyes, 61.16%) represents the main cause for ICRS removal: of them, 48 (39.67%) ICRSs were removed for refractive failure and 26 (21.49%) in the setting of a keratoplasty related to poor visual performance of the implanted eye. In addition, 47 eyes (38.84%) had ICRS removal for anatomic failure: among them, 36 (29.75%) were explanted for spontaneous extrusion (overall extrusion rate: 1.58%), 7 (5.79%) for suspected infectious keratitis, 3 (2.48%) for corneal melting, and 1 (0.83%) for corneal perforation. Mild cases of keratoconus were more prone to be explanted because of a loss of the initial improved visual acuity, whereas spontaneous extrusion happened often in advanced cases of keratoconus.

• CONCLUSIONS: We report the largest series of ICRS explantation as of this writing. The main cause of explantation was functional refractive failure followed by spontaneous extrusion of the ICRS, that is, correlated to an anatomic failure at the site of implantation in an advanced disease. (Am J Ophthalmol 2021;222:351–358. © 2020 Elsevier Inc. All rights reserved.)

Accepted for publication Sep 23, 2020.

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INTRASTROMAL CORNEAL RING SEGMENT (ICRS) IMplantation was designed originally as a refractive technology to correct low myopia.[1,2] ICRSs do this refractive adjustment by flattening the central cornea by an arc-shortening effect on the corneal lamellae structure, which improves the optical quality of the cornea, with consequent improvement in visual acuity,[3] and it has been reported to be a safe and effective method for low-myopia correction but not predictable enough for refractive surgeries.[4] Currently, indications for ICRS implantation have been extended to manage ectatic corneal conditions such as keratoconus, pellucid marginal degeneration, and post–laser in situ keratomileusis corneal ectasia.[5,6]

This surgical technique has been reported to have many advantages in this issue, such as favorable visual and refractive results, decreased corneal surface irregularity, and delay or elimination of the need for keratoplasty.[7] Nevertheless, ICRS implantation might not be able to halt the progression of the keratoconus: our research group showed a regression at 5 years, suggesting that implantation of ICRSs does not significantly influence progressive keratoconus in young patients with confirmed progression of the disease.[8] The 3 main ICRS technologies used are Intacs (Addition Technology, Inc), Ferrara (Ferrara Ophthalmics Ltd), and Keraring (Mediphacos Ltd), which is essentially similar to Ferrara but with a different arc length to achieve superior astigmatic correction.[9]

The introduction of femtosecond-laser technology made the tunnel creation for ICRS implantation much easier and safer, and largely replaced the previous manual dissection technique because of numerous advantages like increased accuracy of tunnel creation (depth, width, and centering), faster recovery, and fewer intraoperative complications.[10-12] Recently, to improve the predictability of the results after ICRS implantation and provide the best topographic outcome, the investigational group of Alio had successfully developed an artificial neural network that guides the implantation of the ring in keratoconic eyes.[13]

Although ICRS implantation is an effective tool in managing corneal ectatic disease, several postoperative complications may occur and necessitates ICRS removal. It was reported that the main causes of explantation are extrusion and refractive failure.[14] We present the largest series of patients who had ICRS explantation over a 10-year observation period in a multicenter

0002-9394/$36.00
https://doi.org/10.1016/j.ajo.2020.09.041

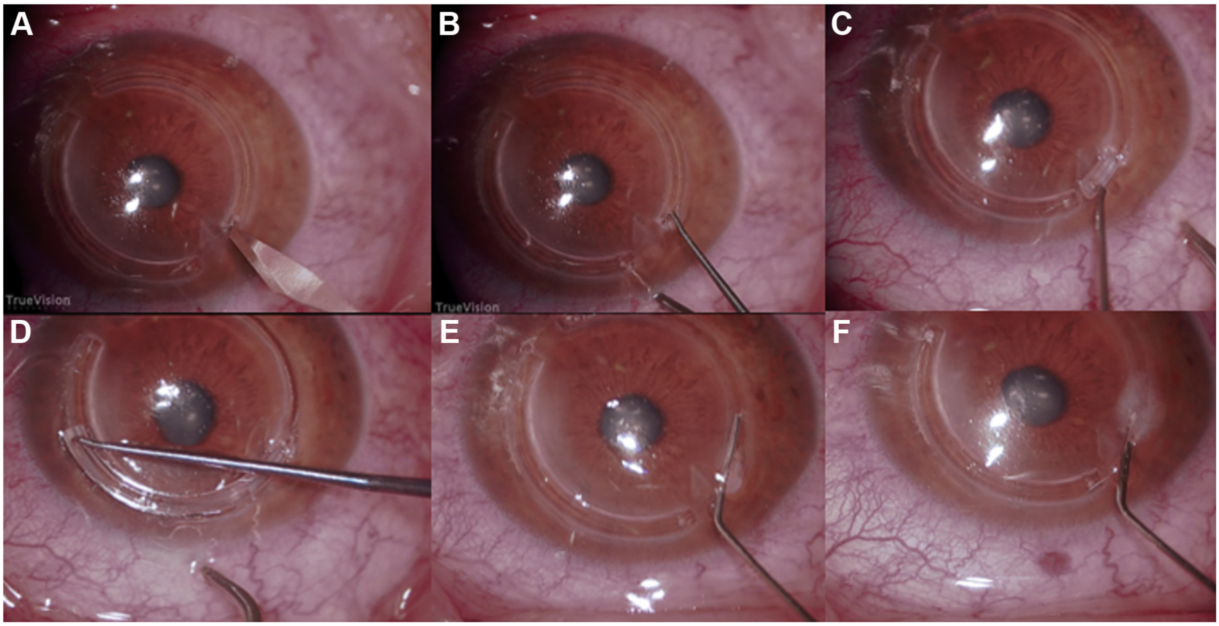

FIGURE 1. Intracorneal ring segment (ICRS) removal technique performed by JLA, under topical anesthesia. A. A 15° knife was used to make an incision over the edge of the segment. B-D. Next, a Sinskey hook was introduced to grab the segment at its distal end near the wound. Then, the ring was pulled out of the channel while gently breaking the adhesions of the ring to the stroma. E. Cefuroxime at the end of the surgery was used to wash the empty tunnel. F. A stromal hydration was eventually performed to close the entry incision.

study, investigating the motivating reasons and the incidence rates.

METHODS

RETROSPECTIVE, MULTICENTER, CONSECUTIVE STUDY performed for evaluation of ICRSs that were explanted between January 2009 and December 2019. The cases in this study came from 8 centers that belong to a cooperative network for ophthalmic research subsidized by the Spanish Ministry of Health. These collaborating centers sent the explanted material to IBERIA Biobank, one of the milestones in the current RETICS project. All the eyes included in this retrospective analysis had only ICRS placement ± CXL. The surgeries were performed by different surgeons under topical anesthesia. After performing an incision over the edge of the tunnel, a Sinskey hook was introduced to grab the segment and gently pull it out of the channel. Cefuroxime at the end of the surgery was used to wash the empty tunnel, and a stromal hydration was eventually performed to close the entry incision (Figure 1). In cases explanted after more than 1 year, some difficulties were funded in terms of attachment of the distal part of the segment, because of a healing process more evident in that sector. The mobilization of the segment was then necessary to be completed with hydro-dissection of the tunnel or even the use of knife dissection in the area in which the adherence was stronger. Thereafter, with the forceps used for the purpose of ICRS implantation, the explantation was finally performed. A radial cut was also performed through the tunnel in order to expose greater areas of the segment to finalize the explantation. All patients received postoperative treatment consisting of a combination of antibiotic and steroid eyedrops for 5 days and artificial tears for 1-3 months and were instructed not to rub their eyes. In case of removal due to infection, the treatment consisted in fortified antibiotics followed by ring removal. Information about each case was obtained from the donating surgeon using a standard questionnaire form that requested patient data (age, gender), reasons for implantation and explantation, date of implantation and explantation, tunnel creation technique, and ICRS type. The cause of explantation was identified as being related to either a functional failure, as in those cases requiring ICRS removal for a drop in the visual acuity or presence of halo/diplopia or poor visual outcomes, or anatomic failure requiring urgent explantation due to extrusion, infection, melting or endothelium perforation.

Additional clinical data were obtained accessing the clinical history of each case. Postoperative clinical data were obtained at 3 months following the definition of failure episode. Keratoconus patients were divided into 5 different groups according to the RETICS grading system based on the preoperative visual impairment.[15]

• **STATISTICAL ANALYSIS:** Patient's data and clinical data were gathered and organized in a Microsoft Office Excel

TABLE 1. Demographics of the Study Population

Parameter	Mean ± SD or n (%)
Age, y, mean ± SD	34 ± 11
Gender	
Male	66 (55.46)
Female	53 (44.54)
Eye	
Right	52 (42.98)
Left	54 (44.63)
NA	15 (12.40)
ICRS model	
Keraring	37 (30.58)
Ferrara	36 (29.75)
Intacs	35 (28.93)
Myoring	6 (4.96)
Vissumring	4 (3.31)
NA	3 (2.48)
Providing center	
Vissum Instituto Oftalmologico, Alicante	62 (51.24)
Centro de Oftalmología Barraquer, Barcelona	48 (39.67)
Vissum Miranza, Albacete	4 (3.31)
Hospital Clinico San Carlos, Madrid	2 (1.65)
Hospital Ramón y Cajal, Madrid	2 (1.65)
IOBA Valladolid	1 (0.83)
Clinica Novovisión Murcia	1 (0.83)
Clinica Universitaria de Navarra	1 (0.83)
Reasons for ICRS removal	
Refractive failure	48 (39.67)
Extrusion	36 (29.75)
Setting of a keratoplasty	26 (21.49)
Infection	7 (5.79)
Melting	3 (2.48)
Cornea perforation	1 (0.83)

ICRS = intrastromal corneal ring segment, n (%) = absolute frequency (relative frequency), NA = information not available.

file. The data were analyzed using SPSS for Windows software (version 22.0, SPSS, Inc). Quantitative data were described using mean and standard deviation, as well as minimum and maximum. For time-independent variables, χ^2 test were estimated to determine differences, and the error type I was fixed in 5%.

RESULTS

DURING THE STUDY PERIOD, 1,644 ICRS IMPLANTATIONS (not including centers contributing 1 or 2 cases) were performed and 121 ICRSs (119 patients; 53 women, 66 men) were explanted, with an estimated explantation rate of 5.60% and a relative extrusion rate of 1.58%. Mean age of the patients at the time of explantation was 34 years (SD 11; range 13-63). Of the 121 eyes, 97 (80.17%) had primary keratoconus, 14 (11.57%) had ectasia after laser in situ keratomileusis, 4 (3.31%) had astigmatism, and 1 (0.83%) had myopia. Information was not available for 4 cases (3.31%). The most explanted ICRSs in our sample were the following: 37 Keraring (30.58%), 36 Ferrara (29.75%), 35 Intacs (28.93%), 6 Myoring (4.96%), 4 Vissumring (3.31%), and not available in 3 cases (2.48%) (Table 1). Tunnel creation in the ICRS explantation cases was made by femtosecond laser in 96.78% of eyes. All ICRSs were inserted to 70% corneal depth (the exact measurement after the implantation was not taken). In addition, 54.8% of patients had history of atopy or eye rubbing. 63 eyes (52.1%) had adjunctive corneal crosslinking (CXL): 33 (52.4%) had both procedures at the same time, 25 (39.7%) had ICRS placement first and CXL thereafter, and 5 (7.9%) had CXL first and ICRS after. CXL was not significantly correlated with the ICRS explantation ($P = .881$).

• **REASONS FOR ICRS EXPLANTATION:** The main cause of explantation was functional failure (74 eyes, 61.16%): among them, refractive failure happened in 48 eyes (39.67%), followed by ICRS explantation in the setting of a keratoplasty, which was indicated because poor visual performance (23 eyes [19.07%] underwent deep anterior lamellar keratoplasty, 3 [2.48%] penetrating keratoplasty). Forty-seven eyes (38.84%) had ICRS removal for anatomic failure: among them, spontaneous extrusion occurred in 36 eyes (29.75%), suspected infection (keratitis) in 7 eyes (5.79%), and corneal melting in 3 (2.48%); in addition, there was 1 case (0.83%) of corneal perforation (segment perforated the endothelium). Table 2 shows the number of ICRSs explanted by year of explantation, causes of explantation, and ICRS model.

A χ^2 test of independence was performed to examine the relation between time-independent clinical variables (sex, laterality, history of trauma or eye rubbing, history of atopy or allergy) and ICRS explantation, and the relation between these variables was found to be significant only with history of atopy/allergy ($P = .022$).

Table 3 showed the percentage of ICRS removal in the different groups, according to the preoperative visual impairment (Group 1, corrected distance visual acuity [CDVA] < 0.05 logMAR; Group 2, CDVA between 0.05 and 0.19; Group 3, CDVA between 0.19 and 0.40; Group 4, CDVA between 0.40 and 0.7; Group PLUS, CDVA > 0.7 logMAR).[15]

• **FUNCTIONAL FAILURE:** Refractive failure was defined as an effort to improve the quality of vision of the patients, when a worsening in visual acuity or the development of subjective optical symptoms (eg, halo and monocular diplopia) where evident after the initial improvement. Patients that experienced a refractive failure underwent ICRS explantation without any prior refractive surgery. Table 4 shows the drop of the visual acuity in the refractive failure group before explantation (UDVA 0.81 ± 0.43 and CDVA

TABLE 2. Number of Intrastromal Corneal Ring Segments (ICRS) Explanted by Year of Explantation, Cause of Explantation and ICRS Model

		Explantation Cause						ICRS Model					
		Functional Failure		Anatomic Failure									
Year of Explantation	ICRS Explants	RF	K	E	I	M	CP	Keraring	Ferrara	Intacs	Myoring	Vissumring	NA
2009	4	2	2	—	—	—	—	—	2	2	—	—	—
2010	18	6	5	5	2	—	—	4	5	8	1	—	—
2011	17	9	1	4	2	1	—	9	3	4	1	—	—
2012	14	6	3	3	2	—	—	5	1	6	2	—	—
2013	12	7	4	1	—	—	—	5	5	1	1	—	—
2014	11	4	3	3	—	—	1	3	5	2	—	1	—
2015	12	3	1	7	—	1	—	4	3	2	—	2	1
2016	9	1	3	4	1	—	—	3	2	1	1	1	1
2017	8	4	3	1	—	—	—	—	4	4	—	—	—
2018	13	4	1	7	—	1	—	4	3	6	—	—	—
2019	3	2	—	1	—	—	—	—	3	—	—	—	—

CP = corneal perforation, E = spontaneous extrusion, I = suspected infectious keratitis, ICRS = intrastromal corneal ring segment, K = keratoplasty, M = melting, NA = information not available, RF = refractive failure.

0.4 ± 0.33) despite an initial improvement after the implant of the ring (UDVA 0.69 ± 0.28 and CDVA 0.29 ± 0.22). Mean time from implantation to explantation was 19 ± 24 months (Figure 2). Refractive failure often happened following ICRS implantation in mild cases of keratoconus (Table 3).

Keratoplasty was defined as the necessity of a subsequent keratoplasty in those patients that did not achieve the desired optical outcome after the initial surgery (CDVA before explantation was limited to 0.51 ± 0.22, Table 4). In these cases, a keratoplasty has been necessary to improve the visual acuity and the ICRS has been removed in the setting of this surgery.

A χ^2 test of independence revealed significant differences for both female sex (P = .026) and history of allergy/atopy (P = .034) and functional failure.

• **ANATOMIC FAILURE:** Of extrusion cases, 29 had tunnel creation by femtosecond laser and 1 by mechanical dissection; information about the tunnel creation technique was not available in 6 cases. Mean time from implantation to explantation was 25 ± 38 months (Figure 2). Extrusion of the rings frequently happened in the context of ICRS implantation in advanced cases of keratoconus (Table 3). Among them, 12 (33.3%) were Keraring, 11 (30.6%) Ferrara ring, 8 (22.2%) Intacs, 3 (3.8%) VissumRing, 1 (2.8%) Myoring, and not available in 1 case (2.8%). A χ^2 test of independence revealed no significant differences between Keraring and Ferrara ring extrusion ($P > .05$).

Suspected infection presented with keratitis with signs of inflammation around the segment. In all but 1 case of corneal melting, the clinician observed melting before extrusion occurred and extracted the ICRS to prevent further melting.

A χ^2 test of independence revealed no significance for all the time-independent clinical variables and the anatomic failure of the segment ($P > .05$ for all the parameters).

DISCUSSION

THE GOAL OF OUR STUDY WAS TO DEFINE THE MOTIVATING factors related to ICRS failure, either functional or anatomic. To our knowledge, this is the largest series published to date of explanted ICRSs: our series allows for determining the incidence of complications leading to segment removal following the latest surgical procedures. In our study, the total incidence rate of explantation was 5.60%. It was calculated considering only those centers providing more than 2 cases and after deleting the number of patients referred from outside clinics that have not been implanted in the same center (explantation rate calculated among the centers Vissum Instituto Oftalmologico, Alicante; Centro de Oftalmologia Barraquer, Barcelona; and Vissum Miranza, Albacete), resulting in 92 ICRSs explanted among a total of 1,644 implantations. Among the implanted ICRSs, 618 (37.6%) were Keraring, 614 (37.3%) Ferrara ring, 329 (20%) Intacs, and to a lesser extent the other types of ICRSs presented in the study. All the ICRS implantations have been performed using the manufacturer's nomograms. In this way, we have tried not to overestimate the explantation rate.

The reasons for ICRS explantation have changed over time, according to the change in ICRS designs, as well as changes in surgical technique for tunnel creation. Reported postoperative complications of ICRS implantation include segment extrusion, refractive failure, corneal

TABLE 3. Percentage of Reasons for Intrastromal Corneal Ring Segment Explantation in Cases of Keratoconus Classified According to Preoperative Visual Impairment

		Functional Failure		Anatomic Failure	
Keratoconus Grade	All, %	Refractive Failure, %	Keratoplasty, %	Extrusion, %	Others[a], %
Grade I	6.98	17.65	—	—	—
Grade II	27.91	41.17	12.5	20	33.3
Grade III	32.56	17.65	25	53.33	33.3
Grade IV	20.93	17.65	37.5	20	—
Grade PLUS	11.63	5.88	25	6.67	33.3

[a]Others causes of anatomic failure included: suspected infectious keratitis, corneal melting, and corneal perforation.

neovascularization, infectious keratitis, mild deposits around the ICRS, segment migration, and corneal melting. However, ICRS explantation is not necessary in some cases. In a large review of 850 eyes with Keraring implantation, complications were reported in 25 eyes and only 2 ICRSs were explanted for corneal melting.[16]

Ferrer and associates[11] performed a multicenter retrospective review of 250 ICRS implantations; of these, 58 were removed. The most common reason for explantation included segment extrusion in 28 cases, followed by poor refractive outcomes in 22, keratitis in 4, corneal melting in 3, and corneal perforation in 1. Pinero and associates[5] reviewed 146 eyes implanted with Intacs or Kerarings. They found that extrusion was the principal reason for explantation in 8 eyes, corneal melting in 3, and corneal neovascularization in 2. In another study of Intacs, Boxer Wachler and associates[12] reported 5 explantations in 74 eyes; segment migration was found in 1 eye and chronic foreign body sensation in 4 eyes. A recent study reported 35 ICRSs explanted from 572 eyes implanted (6.01%), stratified into medically motivated, and those who were electively removed: specifically, 15 were removed for medical complications and 20 for refractive and topographic considerations.[17] A recent systematic review[14] obtained an explantation rate between 0% and 1.4%, analyzing those articles with a high number of implantations.

Our retrospective analysis of 121 ICRSs explanted in the period 2009-2019 revealed that the main reason for explantation was functional failure, mainly refractive failure (39.67%)—drop in visual acuity was correlated to the ring implanted, and these patients were treated by explantation of the ICRS without any additional refractive surgery—and explantation performed in the setting of a keratoplasty being necessary for a poor visual outcome (21.49%), followed by natural extrusion of the ring (29.75%). The high rates of anatomic failure of ICRSs are related to mechanical technique complications, which are nowadays overpassed using femtosecond laser during the tunnel creation. One of the motivating reasons for the extrusion of the ICRS is segment migration, and the femtosecond laser gives a more reproducible, accurate, and safer solution for tunnel creation, leading to perfect control in stromal separation, width, and depth of the tunnel.[18,19] In the present study, the incidence rate of extrusion, calculated as a percentage of all the implantations performed during the study period, is 1.58%. To our knowledge, this is the first article to extract the incidence rate of spontaneous extrusion in such a large group of cases.

While considering the motivating reasons for extrusion, keratocyte activation and apoptosis should be considered.[20] Kugler and associates[21] have suggested that the additional trauma during tunnel creation might increase keratocyte apoptosis and to an increased number of complications, such as corneal melting over the ring that can eventually lead to the extrusion of the same. In this case, tunnel creation with femtosecond laser is less aggressive with reduced complications, as previously assessed with corneal confocal microscopy.[22,23]

Our clinical research group reviewed 146 keratoconic eyes that underwent ICRS implantation with either the mechanical or the femtosecond laser–assisted procedure and compared the complications between both groups, observing that no significant differences were present in the reposition, corneal neovascularization, corneal melting, extrusion, and infection rates. The explantation rate was higher in the mechanical subgroup (mechanical 20.83% vs femtosecond 10.53%), even if the differences did not reach statistical significance.[24] Considering the retrospective nature of this study, we were not able to collect information about tunnel creation technique in 27 cases, as these cases were implanted by unknown referral surgeons and no clinical report was available in any case about the type of surgical procedure performed. Nevertheless, in the remnant 94 cases, 91 of them had tunnel creation by femtosecond laser (96.81%).

Infectious keratitis is considered as a rare complication of this procedure, with an incidence rate reported to be 1.4%-6.8%, and the onset time has been reported to vary greatly, ranging from 3 days to 22 months.[11,25,26] In the present study, more than 121 ICRSs were removed over the last 10 years, and 7 rings (5.79%) were explanted because of infection, at a mean interval of 19 months (ranging from 5 days to

TABLE 4. Time-Dependent Variables According to Reason for Intrastromal Corneal Ring Segment Explantation

		Functional Failure		Anatomic Failure	
Variable	All, Mean ± SD	Refractive Failure, Mean ± SD	Keratoplasty, Mean ± SD	Extrusion, Mean ± SD	Others[a], Mean ± SD
UDVA (logMAR)					
Pre-implantation	1.22 ± 0.77	0.99 ± 0.49	1.63 ± 0.94	1.15 ± 0.63	1.1 ± 0.79
Post-implantation	0.71 ± 0.47	0.69 ± 0.28	1.18 ± 0.75	0.68 ± 0.38	0.47 ± 0.57
Pre-explantation	0.83 ± 0.41	0.81 ± 0.43	0.86 ± 0.47	0.85 ± 0.35	0.77 ± 0.5
Post-explantation	0.77 ± 0.46	0.65 ± 0.46	0.86 ± 0.38	0.88 ± 0.59	0.63 ± 0.06
CDVA (logMAR)					
Pre-implantation	0.48 ± 0.48	0.27 ± 0.22	0.84 ± 0.73	0.33 ± 0.22	0.53 ± 0.41
Post-implantation	0.47 ± 0.68	0.29 ± 0.22	0.58 ± 0.41	0.34 ± 0.23	0.37 ± 0.62
Pre-explantation	0.44 ± 0.28	0.4 ± 0.33	0.51 ± 0.22	0.42 ± 0.22	0.67 ± 0.55
Post-explantation	0.3 ± 0.24	0.26 ± 0.3	0.37 ± 0.26	0.3 ± 0.12	0.3 ± 0.1
Sphere (D)					
Pre-implantation	–2.77 ± 4.56	–1.31 ± 3.59	–4.25 ± 5.66	–4.03 ± 4.55	0 ± 4.58
Post-implantation	–0.54 ± 3.09	0.1 ± 2.59	–2 ± 5.24	0.98 ± 3.32	0.25 ± 0.5
Pre-explantation	–0.87 ± 3.43	0.06 ± 3.49	–1.55 ± 3.94	–1.3 ± 3.02	–1.75 ± 2.48
Post-explantation	–1.83 ± 4.45	–0.54 ± 4.48	–3.08 ± 3.21	–2.89 ± 5.17	–0.5 ± 4.51
Cylinder (D)					
Pre-implantation	–4.39 ± 2.54	–3.86 ± 2.17	–5.19 ± 3.23	–4.32 ± 2.59	–5.5 ± 2.29
Post-implantation	–3.44 ± 2.58	–4.54 ± 2.72	–3.5 ± 4.12	–3 ± 1.73	–1.25 ± 1.57
Pre-explantation	–4.06 ± 2.14	–4.68 ± 2.21	–3.77 ± 1.9	–3.37 ± 2.25	–3.12 ± 1.24
Post-explantation	–3.88 ± 3.12	–3.14 ± 2.31	–3.18 ± 2.03	–5.41 ± 4.54	–4.75 ± 1.52
K1 (D)					
Pre-implantation	46.49 ± 5.55	45.72 ± 2.17	46.77 ± 3.95	46.15 ± 4.96	50.57 ± 14.4
Post-implantation	45.12 ± 5.92	43.22 ± 4.78	46.45 ± 6.12	44.9 ± 4.77	48.04 ± 10.17
Pre-explantation	45.37 ± 5.71	44.62 ± 4.89	45.68 ± 5.73	44.31 ± 3.26	52.92 ± 14
Post-explantation	45.05 ± 3.56	44.97 ± 4.58	45.07 ± 2.71	45.7 ± 3.23	42.07 ± 1.76
K2 (D)					
Pre-implantation	53.06 ± 8.23	49.43 ± 4.31	60.67 ± 12.03	52.17 ± 4.38	55.44 ± 17.31
Post-implantation	51.12 ± 9.66	49.09 ± 6.74	53.88 ± 12.24	50.15 ± 7.61	54 ± 16.64
Pre-explantation	49.33 ± 7.18	48.49 ± 5.45	48.68 ± 9.06	49.43 ± 4.87	56.13 ± 14.21
Post-explantation	49.33 ± 4.47	48.94 ± 5.13	48.93 ± 2.74	50.75 ± 4.43	45.6 ± 1.21
KM (D)					
Pre-implantation	49.34 ± 6.07	47.35 ± 4.2	52.27 ± 6.75	48.77 ± 3.73	53.33 ± 15.86
Post-implantation	47.91 ± 7.25	45.82 ± 5.04	50.15 ± 8.41	47.46 ± 5.91	50.67 ± 12.73
Pre-explantation	47.45 ± 6.4	45.79 ± 6.44	48.23 ± 6.15	46.95 ± 3.72	54.52 ± 14.43
Post-explantation	47.04 ± 3.53	46.85 ± 4.49	46.94 ± 2.74	47.89 ± 3.23	44.09 ± 0.96
CCT (μm)					
Pre-implantation	446.25 ± 58.54	483.4 ± 45.31	420.14 ± 85.36	435 ± 44.82	428.33 ± 20.98
Post-implantation	442.89 ± 54.01	462.5 ± 43.41	476.5 ± 13.43	394.33 ± 57.57	—
Pre-explantation	420.5 ± 60.65	452 ± 45.86	411.56 ± 80.65	412.29 ± 47.03	395 ± 18.38
Post-explantation	451.05 ± 72.56	463.6 ± 48.54	543.2 ± 27.3	396.37 ± 3.23	408 ± 29.7
TP (μm)					
Pre-implantation	426.16 ± 43.45	441.67 ± 44.36	414 ± 45.32	426.12 ± 43.59	400 ± 39.34
Post-implantation	433.14 ± 47.77	435.33 ± 62.64	463.45 ± 16.26	398.5 ± 34.65	—
Pre-explantation	388.3 ± 63.11	418.6 ± 70.42	384.89 ± 75.21	381.71 ± 47.62	351 ± 33.94
Post-explantation	447.56 ± 72.06	459.67 ± 44.88	528.8 ± 21.99	389.67 ± 50.78	400 ± 31.11

CCT = central corneal thickness, CDVA = corrected distance visual acuity, D = diopters, K1 = corneal dioptric power in the flattest meridian in the central 3.0 mm zone, K2 = corneal dioptric power in the steepest meridian in the central 3.0 mm zone, KM = mean corneal power in the 3.0 mm zone, logMAR = logarithm of the Minimum Angle of Resolution, TP = corneal thickness at the thinnest point, UDVA = uncorrected distance visual acuity.

[a]Others causes of anatomic failure included suspected infectious keratitis, corneal melting, and corneal perforation.

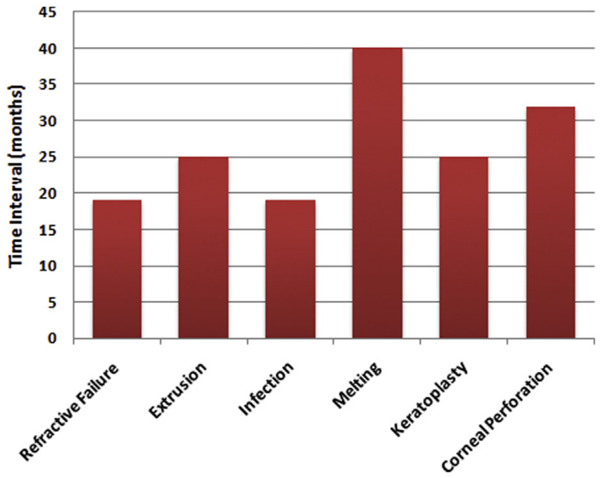

FIGURE 2. Mean time from implantation to explantation depending on the cause of intrastromal corneal ring segment removal.

61 months). In 2 of the cases with late infection, a history of eye trauma or rubbing was present, that can explain a possible epithelial disruption followed by infection.

In 2013, our research group concluded a multicenter, retrospective, interventional study analyzing the outcomes of ICRS implantation based on the preoperative visual acuity[15]: they found that the groups with more severe keratoconus are the ones with the highest success rate (gain more lines of CDVA) and, on the other hand, are the ones with the lowest failure rate (lose fewer lines of CDVA).[27] Similarly, as shown in Table 3, we found that mild cases of keratoconus were more prone to be explanted because of a loss of the initial improved visual acuity (groups I and II: 58.83% in the refractive failure group and 20% in the extrusion group); on the other hand, spontaneous extrusion happened often in advanced cases of keratoconus that is correlated to an anatomic failure at the site of implantation (grade III to PLUS: 41.17% in the refractive failure group and 80% in the extrusion group). In those cases of functional failure where a keratoplasty was eventually needed in the effort to provide a further improvement in the patient's quality of vision, the ICRS was implanted more frequently in very advanced cases (among them, 62.5% had a grade IV or PLUS of the disease).

Although this is a retrospective study, the large sample size makes its results reliable to show the ICRS explantation issue with current femtosecond laser use for tunnel creation. We strongly believe that our calculations of the incidence of explantation will provide valuable information to the scientific community.

Limitations of this retrospective analysis include the likelihood of patients lost to follow-up; it is possible that a patient had an ICRS explantation in a different hospital and we did not record it. However, patients with complications typically are motivated to return for examination to the same surgeon; thus, this effect might have been minimal. Furthermore, the retrospective character of this study does not reveal the pathomechanism of any of the complications mentioned.

In conclusion, based on our data, which represent the largest multicenter cohort of explanted ICRSs ever published in the literature, we can define the "real-world" incidence rate of explants and how the trend toward the different causes of removal has changed over time, especially thanks to the advent of the femtosecond laser. Explantation due to functional failure represents the main reason for ICRS removal that determines either a worsening of visual acuity more often in mild cases of keratoconus or the need of a keratoplasty to further improve the visual acuity in cases of very advanced disease; spontaneous extrusion of the ring represents the main cause of anatomic failure and happened in the scenery of implantations performed in advanced cases of keratoconus. Future investigations of ICRSs in the treatment of keratoconus to improve visual and refractive predictability, and both the functional and anatomic success of this type of keratoconus surgery, are warranted.

FUNDING/SUPPORT: THIS PUBLICATION HAS BEEN SUPPORTED IN PART BY RED TEMÁTICA DE INVESTIGACIÓN COOPERATIVA en Salud (RETICS), reference number RD16/0008/0012, financed by the Instituto Carlos III–General Subdirection of Networks and Cooperative Investigation Centers (R&D&I National Plan 2008-2011) and the European Regional Development Fund, European Union (Fondo Europeo de Desarrollo Regional FEDER), IBERIA Biobank. Financial Disclosures: The authors indicate no financial support or conflicts of interest. All authors attest that they meet the current ICMJE criteria for authorship.

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