Title

Complications and Explantation Reasons in Intracorneal Ring Segments (ICRS): A Systematic Review

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Abstract

Purpose

To review the intraoperative and postoperative intracorneal ring segment complications and to report the explantation rate among the available scientific literature.

Method

Three different databases, namely, PubMed, Web of Science and Scopus, were assessed from January 1995 to June 2019. The keywords used were: ring, rings, ICRS (intracorneal rings segments), segment, segments or Intacs, complication, explantation, explanted, retired and removal.

Results

The selection process of this systematic review study is described in a flow diagram. A total of 39 studies published between 1995 and 2019 were included in this systematic review. Sixteen studies were case reports, twenty-one were case series studies and two were chart analysis works. This study enrolled 1946 subjects, and 2590 eyes were included.

The postoperative complications described in most papers included migration, ring extrusion, corneal thinning, corneal melting and some type of infective keratitis. These complications together with glare, halos, fluctuating vision, neovascularization, foreign body sensation or pain represented most of the causes. The percentage rate of explantation ranged from 0.5 up to 83.3%. If we analyze those articles with a high number of implantations (2124 eyes), an explantation rate between 0% and 1.4% was obtained.

Conclusions

The complication rate and explantation ratio in segments of the intracorneal rings analyzed in the available scientific literature are minimal. Therefore, patient selection, surgery planning and postoperative follow-up are critical to the success of surgery.

Introduction

Intracorneal ring segments (ICRS) were used in the 1970s[1] for low and moderate myopia correction, and anterior cornea curvature flattening occurred by placing ICRS on the stroma. Previous studies reported that it was a safe, effective and stable method to correct low myopia.[2] Currently, the method has been extended to various pathologies, such keratoconus (KC), pellucid marginal degeneration (PMD) or iatrogenic corneal ectatic.[3] Three types of ICRS are available: INTACS ® (Addition Technology, Sunnyvale, CA, USA), Ferrara ® (Mediphacos, Belo Horizonte, Brazil) and Kerarings ® (Mediphacos, Belo Horizonte, Brazil). Classic ICRS channel creation by implanting the segments via mechanical dissection is currently being replaced by femtosecond lasers. In addition to being less annoying to the patient, the use of femtosecond lasers is faster and provides greater control of the depth, width and centering of the tunnel as well as increased accuracy. In addition, epithelial tissue changes are minimal, and recovery after surgery is faster.[4,5] Channel creation by both methods yields similar visual and refractive results. Nevertheless, increased intraoperative complications occurred with mechanical ICRS implantation.[6,7]

ICRS involves intraoperative complications, such incomplete tunnel creation, cornea surface perforation or anterior chamber perforation. In the first case, the complication can be resolved by mechanical dissection. The perforation rates are low, which is one of the most serious complications.[8,9] Another intraoperative complication is vacuum loss, which occurs during femtosecond suction; however, it is possible to recreate the same corneal plane and the intrastromal channel. Among postoperative complications, segment migration can occur, which may be due to an excessive ICRS width in a thin cornea. Coskunseven et al.[8] and Mounir et al.[10] reported a high ring migration rate. ICRS implantation near the incision implies a great risk of corneal melting, and ICRS should be explanted immediately in these

cases.[11] Another reason for explantation reported in current literature is poor visual acuity or fluctuations in visual quality. The first to describe an explantation for this reason was Asbell et al.[12] He got glare, halos and fluctuating vision. Recently other authors[13-19] have also reported poor visual acuity as a reason for explantation.

One of the main goals of ICRS surgery is to treat keratoconus or post-LASIK ectasia. . The use of a permanent suture at the incision site and avoiding eye rubbing have been proposed.[20] Infection risk is noted with ICRS implantation. Multiple microorganisms have been as causative agents of this complication, and both bacteria and fungi can cause infectious keratitis. For example, *Staphylococcus aureus*[21] appears in up to 25% of cases followed by *Pseudomonas* sp. and *Streptococcus pneumoniae* among others.[22,23]

Several factors have been detected in relation to the onset of this complication, such as previous traumas, use of contact lenses, or systemic diseases, such as diabetes mellitus.[24] The most efficient method to treat infectious keratitis after ICRS implantation is topical antibiotic therapy. Bourcier et al.[25] reported that topical antibiotic therapy alone was sufficient to treat the infection. On the other hand, in some publications, ICRS explantation was considered as the first therapeutic option to treat this complication. Deep corneal neovascularization is another complication that can be caused by the implant and is not associated with the surgical wound. Treatment with topical corticoid agents and surgical removal of the ring may induce vessel regression.[26]

This systematic review aims to report intraoperative and postoperative intracorneal ring segment complications and to report explantation rates among the available scientific literature.

Methods

This review is registered at the PROSPERO International prospective registry. The study

was performed according to the PRISMA statement recommendations. PubMed, Web of Science and Scopus data based were searched from January 1995 to June 2019. The keywords used were ring, rings, ICRS (intracorneal rings segments), segment, segments or Intacs, complication, explantation, explanted, retired or removal. Experts identified and evaluated the articles selected according by inclusion and exclusion criteria. Two independent reviewers extracted and selected studies. Duplicate articles were assessed by authors. Among the inclusion criteria were: (1) Case reports, case series, chart analysis and randomized controlled trials reporting intraoperative and postoperative complication in ICRS implantation; (2) ICRS explantation papers as well as the reasons; (3) There was no restrictions on publication type (conference abstract versus full article) and (4) abstracts were included only if they fulfill our eligibility criteria and if no subsequent study has been published. Among the exclusion criteria: (5) We excluded narrative reviews, systematic reviews, letters to the editor and correspondences; (6) animal studies were also excluded and (7) non-English publication and non-index publication. The authors designed the tables to extract the study data.

Systematic review data were extracted according to studies characteristics and main outcomes measures. Among the first part, extracted data items included (1) authors and publication year; (2) study design (case report or retrospective case series); (3) conflict of interest declaration (yes or no; which, if yes); (4) subject inclusion and exclusion criteria; (5) period of total patient follow-up from the first complication to its total resolution expressed in weeks; (6) percentage of male subjects involved in the study; (7) number of subjects and eyes involved in the study; (8) ICRS type, manual or femtosecond implantation and ICRS brand and / or design; (9) number of segments per eye, i.e., one, two or both numbers were provided if one and two ICRS implantations were reported among different subjects; and (10) mean subject age expressed in years. Amongst the outcome's measures, the following data items were reported: (11) previous eye history, such previous treatments, ocular pathologies or eye surgeries; (12) intraoperative and (13) postoperative complications were

reported and the percentage of total eyes in this study were expressed in brackets; (14) explantation rate and (15) explantation reasons. Finally, (16) treatment used to resolve the complications was recorded. In this case, the treatment reported was the one that was ultimately effective. In-between unsuccessful treatments were avoided.

To determine the individual studies risk of bias, two reviewers with adequate reliability worked independently and blindly to create a summary chart (Table 1) based on the Quality Assessment Tool for Case Series Studies from the National Heart, Lung, and Blood Institute.[27] For disputes between the two reviewers, a third non-blinded reviewer resolved the issue. Questions included in the tool were as follows: (1) Was the study question or objective clearly stated?, (2) Was the study population clearly and fully described, including a case definition?, (3) Were the cases consecutive?, (4) Were the subjects comparable?, (5) Was the intervention clearly described?, (6) Were the outcome measures clearly defined, valid, reliable, and implemented consistently across all study participants?, (7) Was the length of follow-up adequate?, (8) Were the statistical methods well described? and (9) Were the results well described? This analysis did not result in the elimination of any article. Articles with a high risk of bias had a lower weight for data synthesis. The primary summary measures used in this systematic review were incidence percentage of complications and explantations among all included studies. Furthermore, the average changes in terms of visual acuity and mean keratometry were also reported. Finally, we also included ICRS design and implantation technique with more complications and common treatments used in complication resolution as summary measures.

Results

This systematic review study selection process is described by a flow diagram (Figure 1). A total of 39 studies published between 1995 and 2019 were included in this systematic review. Sixteen studies were case reports, twenty-one were case series studies and only two

were chart analysis works. Only three studies reported conflicts of interest. Chhadva et al.[17] reported that Dr. Yoo is an AMO (Advanced Medical Optics) consultant. Said et al.[28] reported that Dr. Ibrahim is a Carl Zeiss Meditec consultant. Nguyen et al.[29] reported that Dr. Hersh receives speaker fees from Addition Technology, Inc. The inclusion criteria included subjects with grade I, II, and grade III keratoconus; residual myopia post LASIK; ICRS explantation; keratitis infection; post LASIK ectasia; contact lens intolerance; ICRS migration; atopic keratoconus or ICRS surgery simultaneously with crosslinking. Regarding exclusion criteria, most studies omitted ICRS implantation cases without complications. Others authors excluded studies for different reasons: corneal scarring[30], leucoma[31], keratitis[8,32], non-INTACS ICRS[15], manual ICRS implantation[17] or corneal hydrops[10,28] in grade IV keratoconus. The post-surgery follow-up ranged from two weeks to two hundred and forty weeks. The mean follow-up for the reported studies was 56.9 weeks. This systematic review enrolled 1946 subjects. In total, 62.34% of these subjects were male, and 2590 total eyes were included. The mean age of subjects was 33.45 years. Many of the studies report that surgery was performed manually or with a femtosecond and the type of segment but do not report the percentage of each type of surgery. Therefore, a quantitative analysis could not be performed using the studies. Detailed study characteristics were reported in Table 2.

Table 3 describes the complications caused by the ICRS and the explantation provided in the revised studies. In relation to the previous ocular history of the patients, we found: eight articles with post-LASIK ectasia.[14,15,19,22,29,30,33,34] Six articles in low and moderate myopia. [12,14,18,23,24,35] Two with pellucid marginal degeneration.[14,33] And only one article with keratoplasty. [14] In addition, atopic asthma and blepharoconjunctivitis,[36] lagophthalmos and dry eye,[37] herpetic keratitis[38] and blepharitis[39] were described in the previous eye history.

Intraoperative complications were described in five publications: some epithelial damage at the incision site;[35] perforation of the anterior chamber (only 5% of the 20 eyes);[20] difficult insertion in one case and intraoperative suction loss;[28] incomplete tunnel creation, misdirection of the ring segment, perforation into anterior chamber, decentration of ring segments, inverted implanted rings, broken ring segments, broken and orifice of ring;[10] galvanometer lag error and endothelial perforation[8].

Postoperative complications were described in most papers: migration, ring extrusion, corneal thinning, corneal melting and type of infective keratitis (bacterial, *Staphylococcus aureus*, *Streptococcus mitis*, *Staphylococcus epidermidis*, annular herpetic and *Aspergillus fumigatus*). These complications together with glare, halos, fluctuating vision, neovascularization, foreign body sensation or pain account for 100% of the rings explanted in 50% of the articles. The percentage rate of explantation ranged from 0.5 up to 83.3%. If we analyze those articles with a high number of implantations [8,10,28,33,40] (2124 eyes), an explantation rate between 0% and 1.4% was obtained.

According ICRS type reviewed, Ferrara – Keraring ICRS reported a one percent explantation rate, and INTACS reported a nineteen percent explantation rate. Only four papers reported no explantation in the case.[28,38,41,42] The most commonly used treatments are antibiotics in those articles in which it is described. Some articles do not report it, and two of the articles recommended suture of the incision.[42,17]

Risk of bias assessment within the studies was grouped into three outcome levels: low evidence level (between zero and three yeses), medium evidence level (between four and six yeses) and high evidence level (between seven and nine yeses). The following studies obtained a low evidence level: Quantock et al.[43], Asbell et al.[12], Bourges et al.[23], McAlister et al.[36], Galvis et al.[37], Cosar et al.[11], Ibáñez-Alperte et al.[44], Chalasani et al.[45], Rayward et al.[38],

Jarade et al.[42], García de Oteyza et al.[46], Oatts et al.[18], Chan and Hersh[19] and Elbaz et al.[47]. The following studies obtained a medium evidence level: Shehadeh et al.[22], Güell et al.[35], Alió et al.[48], Hofling-Lima et al.[24], Ferrer et al.[14], Mulet et al.[33], Kugler et al.[40], Shihadeh[49] Bali et al.[15], Yeung et al.[16], Neira et al.[39], López-Ferrando and Medrano-Ruiloba[41] and Nguyen et al.[29]. The following studies obtained a high evidence level: Kwitko and Severo[50], Kanellopoulus et al.[20], Carrasquillo et al.[30], Zare et al.[31], Alió et al.[13], Coskunseven et al.[8], Chhadva et al.[17], Said et al.[28], Abdelmassih et al.[32], Mounir et al.[10], Iqbal et al.[51] and Tabatabaei et al.[34].

Discussion

Mechanical technique complications comprise anterior or posterior perforation by manual spreader, epithelial defects, decentration, and incision enlargement to the limbus or central cornea due to surgeon manipulation. Most cases of extrusion and final removal of ICRS were experimental in manual ICRS implantation. During ICRS implantation surgery, keratocyte activation[52] and apoptosis are noted. Twa et al.[53] demonstrated lipid formation and increased keratocyte density following ICRS implantation. Kugler et al.[40] postulated that additional trauma to the incision and tunnel results in increased keratocyte apoptosis, major tissue degradation, and a subsequently increased number of complications, such corneal melting. Femtosecond laser ICRS channel creation is less aggressive. Femtosecond laser is associated with reduced complications for corneal melting. Corneal confocal microscopy has been used for assessment after manual[54] and femtosecond[55] ICRS implantation; however, to our knowledge no studies have been reported keratocyte activation scores in femtosecond versus manual techniques.

Nevertheless, the femtosecond laser introduced new complications to ICRS. All these complications were intraoperative, including incomplete channel creation, galvanometer lag error or vacuum loss. Incomplete tunnel creation was solved by completing the channel

using a mechanical separator; thus, complications of manual segment implantation were also noted. Other authors, such as Coskunseven et al.,[8] have proposed increasing the energy level of the femtosecond or reducing the space between spots. The false channel causes difficulty in implantation. As described by Jacob et al.[56] The situation can be overcome by removing the segment and turning it around so it is inserted in the opposite direction through the entry incision. It is then advanced using the second segment as an intrachannel instrument. On one hand, when galvanometer error does occur, the surgical procedure must be suspended. During the second surgery, the same cone should be used. The tunnel channel depth must be 30 μm above the original tunnel.[8] If an error occurred during incision formation, the cut should be continued with the knife-edge. On the other hand, if vacuum loss occurs during incision, it is possible to create the vacuum again at the same conjunctival and corneal plane.[8]

One of the main reasons for the extrusion of the ICRS is segment migration. In this sense, the depth at which the segment is placed is key. Femtosecond laser tunnel creation is faster, easier and more reproducible and offers accurate tunnel dimensions (width, diameter and depth).[57] This implies more control of intraoperative and postoperative complications.[58] With mechanical dissectors, segment depth may be near the corneal surface, which increases late spontaneous ICRS extrusion risk.[58] The femtosecond procedure generates more precise stromal separation compared with manual tunnel creation, which is based on the surgeon's skills. For both manual and femtosecond ICRS implantation, a suture can be placed in cases of segment migration that prevents the segment from migrating again.[42]

Of the thirty-nine articles analyzed in this review, two did not report the type of implanted ring. Specifically, sixteen INTACS (448 eyes), thirteen Keraring or Ferrara (1804 eyes) and eight cases with two both are reported without specifying how many eyes there are of each type. The number of eyes with reported explantation is greater with INTACS (19%) compared with Keraring (1%) despite the fact than INTACS was implanted in a considerably

smaller number of eyes. Most INTACS[13,15-17,19,29] were explanted for low quality vision reasons.

Keraring and Ferrara are more effective in the treatment of keratoconus compared with INTACS.[59] Piñero et al.[60] reported that astigmatism correction in ectatic cornea was more limited with INTACS, demonstrating that it increases the spherical corneal aberration. This finding implies a worsening of the visual quality, increasing the haloes and glare. This notion is justified by a larger INTACS diameter, which induces minimal corneal central flattening.[61]

Among the limitations of this systematic review, the authors of the majority of cases in the case report only indicate the number of segments with complications and do not report the total number of segments implanted successfully. Thus, given that this information is not present in the published literature, it is not possible to establish the real prevalence of intra- and postoperative complications.

In conclusion, the femtosecond laser has reduced postoperative complications related to migration and corneal melting but has introduced new intraoperative complications, such as incomplete channel or vacuum loss. If patient selection is adequate and exhaustive, surgery planning can be implemented and intraoperative and postoperative complications will be minimized, representing the results of unpredictable surgery in most cases.

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442 **Figure legends**

443 Figure 1. Study selection process according to the PRISMA statement

444 **Table legends**

445 Table 1. Quality Assessment Tool for Case Series Studies

446 Table 2: Study characteristics and patient population

447 Table 3: Data extraction for complications and explantations

448

Table 1. Quality Assessment Tool for Case Series Studies

Author (year)	Q 1	Q 2	Q 3	Q 4	Q 5	Q 6	Q 7	Q 8	Q 9
Quantock et al.[39] (1995)	Yes	Yes	No	No	Yes	No	No	No	No
Asbell et al.[31] (1999)	Yes	Yes	No	No	Yes	No	No	No	No
Bourges et al.[16] (2003)	Yes	Yes	No	No	Yes	No	No	No	No
Shehadeh et al.[15] (2004)	Yes	Yes	NA	NA	Yes	No	No	NA	Yes
Güell et al.[33] (2004)	Yes	No	No	Yes	Yes	No	Yes	Yes	Yes
Alió et al.[44] (2004)	Yes	Yes	No	Yes	Yes	Yes	No	No	Yes
Hofling-Lima et al.[17] (2004)	Yes	Yes	No	Yes	No	No	Yes	No	No
Kwitko and Severo[48] (2004)	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes
Kanellopoulus et al.[13] (2006)	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes
McAlister et al.[34] (2006)	NA	CD	NA	NA	Yes	Yes	Yes	NA	NA
Galvis et al.[35] (2007)	NA	CD	NA	NA	Yes	Yes	Yes	NA	NA
Carrasquillo et al.[24] (2007)	Yes	Yes	NR	Yes	Yes	Yes	Yes	Yes	Yes
Zare et al.[25] (2007)	Yes	Yes	NR	Yes	Yes	Yes	Yes	Yes	Yes
Cosar et al.[11] (2009)	NA	CD	NA	NA	Yes	Yes	Yes	NA	NA
Ibáñez-Alperte et al.[40] (2010)	Yes	Yes	NA	NA	No	No	NR	NA	No
Alió et al.[49] (2010)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Ferrer et al.[29] (2010)	Yes	No	No	NR	Yes	Yes	Yes	NA	Yes
Mulet et al.[30] (2010)	Yes	Yes	No	NA	Yes	Yes	No	NA	Yes
Chalasani et al.[41] (2010)	NA	CD	NA	NA	Yes	Yes	Yes	NA	NA
Kugler et al.[45] (2011)	Yes	No	No	No	Yes	No	Yes	NA	Yes
Rayward et al.[36] (2011)	NR	No	NA	NA	No	No	NR	NA	No
Coskunseven et al.[8] (2011)	Yes	Yes	No	Yes	Yes	Yes	Yes	No	Yes
Shihadeh[46] (2012)	Yes	Yes	NA	NA	No	No	Yes	NA	Yes
Bali et al.[27] (2012)	Yes	Yes	No	No	Yes	Yes	Yes	No	Yes
Yeung et al.[47] (2013)	Yes	Yes	No	No	Yes	Yes	Yes	NA	Yes
Jarade et al.[38] (2013)	Yes	No	No	Yes	Yes	NR	CD	NA	NR
Neira et al.[12] (2014)	NR	Yes	No	Yes	Yes	Yes	NR	NA	Yes
Chhadva et al.[21] (2015)	Yes	Yes	No	Yes	Yes	Yes	Yes	NA	Yes
López-Ferrando and Medrano-Ruiloba[37] (2016)	NR	No	No	No	Yes	Yes	Yes	NA	Yes
Said et al.[22] (2016)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Abdelmassih et al.[26] (2017)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
García de Oteyza et al.[42] (2017)	NA	CD	NA	NA	Yes	NA	NA	NA	Yes
Oatts et al.[32] (2017)	NA	CD	NA	NA	Yes	NA	NA	NA	Yes
Chan and Hersh[28] (2017)	NA	CD	NA	NA	Yes	NA	NA	NA	Yes
Mounir et al.[10] (2018)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Elbaz et al.[43] (2018)	NA	CD	NA	NA	Yes	NA	NA	NA	Yes
Nguyen et al.[23] (2019)	Yes	No	Yes	NA	Yes	No	NA	NA	Yes
Iqbal et al.[50] (2019)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Tabatabaei et al.[51] (2019)	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes

Question 1: Was the study question or objective clearly stated?; Question 2: Was the study population clearly and fully described, including a case definition?; Question 3: Were the cases consecutive?; Question 4: Were the subjects comparable?; Question 5: Was the intervention clearly described?; Question 6: Were the outcome measures clearly defined, valid, reliable, and implemented consistently across all study participants?; Question 7: Was the length of follow-up adequate?; Question 8: Were the statistical methods well-described?; Question 9: Were the results well-described?; Q: Question; CD: Cannot determine; NA: Not applicable; NR: Not reported; Rater #1 initials: MJBLL; Rater #2 initials: JMSG.

Table 2

Author (year)	Design	Conflict	Inclusion criteria	Exclusion criteria	Follow-up (weeks)	Subjects (% Male)	N (eyes)	ICRS Type	ICRS per eye	Age
Quantock et al.[39] (1995)	CR	No	NA	NA	32	1(100%)	1	Manual Keraring	1	46
Asbell et al.[31] (1999)	CR	No	NA	NA	40	1 (NR)	1	Manual Keraring	2	28
Bourges et al.[16] (2003)	CR	No	NA	NA	240	1 (0%)	1	Manual INTACS	2	41
Shehadeh et al.[15] (2004)	CR	No	Ectasia	No complications	12	1 (100%)	1	Manual INTACS	2	53
Güell et al.[33] (2004)	CS	No	Myopia PL	NA	12-40	8 (NR)	13	Manual INTACS	2	NR
Alió et al.[44] (2004)	CA	No	ICRS explanted	NA	48	4 (NR)	5	Manual INTACS	1/2	32, 51 (50% NR)
Hofling-Lima et al.[17] (2004)	CS	No	Keratitis	NA	88	8 (37.5%)	8	Ferrara (87.5%) INTACS (12.5%)	NR	32
Kwitko and Severo[48] (2004)	CS	No	KC	NA	52	47 (NR)	51	Manual Ferrara	2	NR
Kanellopoulus et al.[13] (2006)	CS	No	KC	NA	48	15 (40%)	20	Manual INTACS	2	30.2
McAlister et al.[34] (2006)	CR	No	NA	NA	3	1(100%)	1	Manual Ferrara	2	34
Galvis et al.[35] (2007)	CR	No	NA	NA	16	1(0%)	1	Manual Ferrara	2	42
Carrasquillo et al.[24] (2007)	CS	No	KC and PLE	Corneal scarring	6-49	29(55%)	33	50% Manual 50% FS INTACTS	1/2	39
Zare et al.[25] (2007)	CS	No	KC and CLI	Leucoma	24	22 (77%)	30	FS INTACTS	1/2	26
Cosar et al.[11] (2009)	CR	No	NA	NA	144	1 (100%)	1	Manual INTACS	2	33
Ibáñez-Alperte et al.[40] (2010)	CR	No	KC	NA	≈7	1 (NR)	1	Manual INTACS	2	36
Alió et al.[49] (2010)	CS	No	KC and ICRS explanted	NR	24	21 (NR)	21	Manual / FS INTACTS and Keraring	1/2	36
Ferrer et al.[29] (2010)	CS	No	ICRS explanted	NR	336	47 (51%)	57	Manual / FS INTACTS and Keraring	1/2	37
Mulet et al.[30] (2010)	CS	No	Keratitis	NR	4	149 (59%)	212	Manual / FS INTACTS and Keraring	1/2	35
Chalasani et al.[41] (2010)	CR	No	NA	NA	12	1 (0%)	2	Ferrara	1	40
Kugler et al.[45] (2011)	CS	No	Ectasia	Non complications	≈28	279 (NR)	279	FS INTACS	1/2	44.25
Rayward et al.[36] (2011)	CR	No	KC G II	NA	2	1 (100%)	1	NR	1	26
Coskunseven et al.[8] (2011)	CA	NR	KC G II – III CT > 350 µm	Herpes or keratitis	NR	531 (NR)	850	FS Keraring	NR	28.32
Shihadeh[46] (2012)	CR	No	KC moderate myopia	NA	≈ 20	1 (100%)	2	NR	1	34
Bali et al.[27] (2012)	CS	No	KC (4) Ectasia (6)	Non INTACTS surgeries	48	9 (66.6%)	10	FS INTACTS	1/2	44.5
Yeung et al.[47] (2013)	CS	No	KC	NA	12	3 (66.6%)	6	INTACTS	2	21.6
Jarade et al.[38] (2013)	CS	No	ICRS Migration	No surgery complications	24	2 (NR)	2	INTACTS / Keraring	1	NR
Neira et al.[12] (2014)	CS	NR	Atopic Dermatitis AKC	No surgery complications	NR	5 (40%)	5	Manual INTACS	1/2	32.6
Chhadva et al.[21] (2015)	CS	Yes [a]	KC	Manual Implantation	48.5	8 (50%)	10	FS INTACTS	2	38
López-Ferrando and Medrano-Ruiloba[37] (2016)	CS	NR	KC	NA	36-168	35 (NR)	50	Manual Ferrara	1/2	NR
Said et al.[22] (2016)	CS	Yes [b]	KC, CLI CT> 450 µm	Haze Hydrops Infection	24	100 (43%)	160	FS Keraring	1/2	21,77
Abdelmassih et al.[26] (2017)	CS	No	ICRS + CXL	Keratitis or IOL	24-208	12 (83.35%)	17	FS Keraring and INTACS	1/2	12.3
García de Oteyza et al.[42] (2017)	CR	No	NA	NA	NR	1 (100%)	1	FS Ferrara	2	13
Oatts et al.[32] (2017)	CR	No	NA	NA	84-240	2 (50%)	3	Manual INTACS	2	33
Chan and Hersh[28] (2017)	CR	No	NA	NA	8-104	3 (33%)	3	FS INTACS	1/2	49,67
Mounir et al.[10] (2018)	CS	No	KC G II – III CT > 350 µm	PLE Hydrops KC G IV	52	417 (49,4%)	623	FS Keraring	1/2	22,27
Elbaz et al.[43] (2018)	CR	No	NA	NA	16	1(100%)	1	Manual Ferrara	2	37
Nguyen et al.[23] (2019)	CS	Yes [c]	KC PLE	NA	NR	31 (71,4%)	35	FS INTACTS	1/2	41
Iqbal et al.[50] (2019)	CS	No	KC G I, II or III	NA	72	37(NR)	63	FS Keraring	1/2	9-17
Tabatabaei et al.[51] (2019)	CR	NR	NA	NA	26	11 (72,7%)	11	Keraring, Intacs, Myoring and AICI	NR	29

ICRS: Intracorneal ring segments; CR: Case report; NA: Not applied; CS: Case series; NR: Not Reported; PL: Post LASIK; CA: Chart analysis; KC: Keratoconus; PLE: Post-Lasik ectasia; FS: Femtosecond; CLI: Contact lens intolerant; G: Grade; CT: Corneal thickness; AKC: Atopic keratoconjunctivitis; CXL: Crosslinking; IOL: Intraocular lens; AMO: Advanced Medical Optics. [a] Dr. Yoo is AMO consultant. [b] Dr. Ibrahim is Carl Zeiss Meditec Consultant. [c] Dr. Hersh receives speaker fees from Addition Technology, Inc.

Table 3: Data extraction for complications and explantations

Author (year)	Previous eye history	Intraoperative complications	Postoperative complications	Explantation Yes / No (%)	Explantation reason	Treatment used
Quantock et al.[39] (1995)	Nonfunctional eye or glaucoma	None	Crescentic iron line	Yes (100%)	Study protocol	NR
Asbell et al.[31] (1999)	Myopia	None	Faint haze in stromal channel	Yes (100%)	Glare, halos, fluctuating vision	Tobramycin / dexamethasone
Bourges et al.[16] (2003)	Myopia	None	Lamellar channel deposits	Yes (100%)	Stromal thinning, extrusion	Bacitracin / polyvinyl alcohol
Shehadeh et al.[15] (2004)	PLE	None	Bacterial keratitis	Yes (100%)	Staphylococcus	Cefamezin / gentamicin
Güell et al.[33] (2004)	Residual myopia PL	Epithelial damage	Progressive stromal lysis	Yes (7.7%)	Progressive stromal lysis	NR
Alió et al.[44] (2004)	KC	None	Migration (100%), partial extrusion (80%), moderate melting (80%), corneal thinning (20%)	Yes (100%)	Segment migration and partial extrusion	NR
Hofling-Lima et al.[17] (2004)	KC and low myopia	None	Infectious keratitis	Yes (62.5%)	Infectious keratitis	NR
Kwitko and Severo[48] (2004)	KC	None	Ring decentration (3.9%), extrusion (19.6%), disciform keratitis (1.9%), bacterial keratitis (1.9%)	Yes (3.9%)	Extrusion after trauma	NR
Kanellopoulus et al.[13] (2006)	KC	AC Perforation (5%)	Movement, exposure and corneal thinning (30%), CM and infiltrate (5%)	Yes (35%)	Repeated exposure and / or corneal thinning	NR
McAlister et al.[34] (2006)	KC Atopic asthma and BC	None	White infiltrate and deposit formation	Yes (100%)	Infection keratitis	Dexamethasone chloramphenicol
Galvis et al.[35] (2007)	KC, lagophthalmos and dry eye	None	*Staphylococcus aureus*	Yes (100%)	Infection keratitis	Vancomycin, imipenem, amphotericin B and moxifloxacin
Carrasquillo et al.[24] (2007)	KC and PLE	None	Neovascularization and fungal infection	Yes (3%)	Herpes simplex keratitis	NR
Zare et al.[25] (2007)	KC	None	ICRS exposure	Yes (13%)	Extrusion (13%), bacterial keratitis (3%)	NR
Cosar et al.[11] (2009)	KC	None	Neovascularization	Yes (100%)	Neovascularization	FML / ciprofloxacin
Ibáñez-Alperte et al.[40] (2010)	NR	None	Corneal ulcer and hypopyon	Yes (100%)	Extrusion / bacterial keratitis	Vancomycin / ceftazidime
Alió et al.[49] (2010)	Keratoconus	None	ICRS extrusion and vascularization	Yes (100%)	Extrusion (33%), VA (57%), neovascularization (10%)	NR
Ferrer et al.[29] (2010)	KC (79%), PLE (12%), PMD (5%), KP (2%) and myopia (2%)	None	ICRS migration, keratitis, CM and corneal perforation	Yes 100%	Extrusion (48%), VA (38%), keratitis (7%), CM (5%) and perforation (2%)	NR
Mulet et al.[30] (2010)	KC (81%), irregular astigmatism (10%), PLE (5%) and PMD (4%)	None	*Streptococcus mitis* and *aureus*	Yes (1%)	Infection keratitis	Ceftazidime / amikacin, ofloxacin / vancomycin
Chalasani et al.[41] (2010)	Keratoconus	None	*Staphylococcus epidermidis*	Yes (50%)	Infection keratitis	Vancomycin / tobramycin
Kugler et al.[45] (2011)	NR	None	Corneal melt (1.4%)	Yes (1.4%)	Incision overlapping	BCL / steroids
Rayward et al.[36] (2011)	RGP CL and herpetic Keratitis	None	Annular herpetic keratitis	No (100%)	NA	Acyclovir / antibiotics
Coskunseven et al.[8] (2011)	None	Incomplete channel (2.6%), galvanometer lag (0.6%), endothelial perforation (0.6%), channel entrance (0.2%), vacuum (0.2%)	ICRS migration (0.8%), corneal Melting (0.2%) and corneal abscess (0.1%)	Yes (0.5%)	Melting corneal	Antibiotics
Shihadeh[46] (2012)	CL intolerance	None	*Aspergillus fumigatus*	Yes (100%)	Microbiological infection	Gatifloxacin / itraconazole
Bali et al.[27] (2012)	KC and PLE	None	Epithelial ingrowth (20%)	Yes (100%)	Poor VA / epithelial ingrowth	NR

Yeung et al.[47] (2013)	NR	None	ICRS migration (33.3%)	Yes (83%)	Poor VA / ICRS Migration	CXL
Jarade et al.[38] (2013)	NR	None	ICRS Migration	No (100%)	NA	Incision Suturing
Neira et al.[12] (2014)	Atopic Dermatitis, AKC, blepharitis and GPC	None	Corneal melting (100%)	Yes (100%)	Corneal melting	Topical steroids
Chhadva et al.[21] (2015)	NR	None	VA (80%), overlapping and VA (20%)	Yes (100%)	Overlapping and Visual quality	Incision suturing / PKP
López-Ferrando and Medrano-Ruiloba[37] (2016)	Eye Rubbing	None	Late breaks (6%), ICRS migration (4%), overlapping (2%)	No (100%)	NA	NR
Said et al.[22] (2016)	KC	Vacuum loss	ICRS broke / inverted ICRS	No (100%)	NA	Moxifloxacin / prednisolone
Abdelmassih et al.[26] (2017)	KC	None	Vascularization and corneal thinning	Yes (5,9%)	ICRS migration	Tobramycin / gatifloxacin
García de Oteyza et al.[42] (2017)	KC	None	Whitish infiltrate, hypopyon, CM	Yes (100%)	Staphylococcus aureus keratitis	Vancomycin, ceftazidime, moxifloxacin, tobramycin, dexamethasone and loteprednol
Oatts et al.[32] (2017)	Myopia	None	Epithelial defect, thinned cornea and extrusion	Yes (100%)	FBS, photophobia and VA	NR
Chan and Hersh[28] (2017)	KC and PLE	NR	VA, diplopia and haloes	Yes (83,3%)	Low vision quality	Antibiotic and corticosteroid
Mounir et al.[10] (2018)	KC	Vacuum loss, incomplete tunnel creation, ICRS migration, AC perforation, inverted ICRS, broken ICRS	ICRS migration, extrusion, Incision opacification, steroid-induced glaucoma, infectious keratitis, crystalline sterile keratitis, CM	Yes (0,8%)	ICRS migration, infectious keratitis and perforation into the anterior chamber	Moxifloxacin / prednisolone
Elbaz et al.[43] (2018)	KC	None	Spontaneous in situ breakage	Yes (100%)	Pain, redness and FBS	Antibiotics and corticosteroid
Nguyen et al.[23] (2019)	KC and PLE	NR	Microbial keratitis, photophobia, FBS and VA	Yes (6%)	Refractive / topographic considerations	Gatifloxacin and vancomycin
Iqbal et al.[50] (2019)	KC	NR	Migration (1,6%), extrusion (4,7%) and KC progression (6,4%)	Yes (6,3%)	ICRS migration and Extrusion	Gatifloxacin / prednisolone
Tabatabaei et al.[51] (2019)	PLE	NR	Keratitis	Yes (100%)	Keratitis	Cefazolin / amikacin / vancomycin

NR: Not reported; PLE: Post-LASIK ectasia; PL: Post LASIK; KC: Keratoconus; AC: Anterior chamber; CM: Corneal melting; BC: Blepharoconjunctivitis; ICRS: Intracorneal ring segment; FML: Fluorometholone; VA: Visual acuity; PMD: Pellucid marginal degeneration; KP: Keratoplasty; BCL: Bandage contact lens; RGP: Rigid gas permeable; CL: Contact lens; CXL: Crosslinking; AKC: Atopic keratoconus; GPC: Giant papillary conjunctivitis; PKP: Penetrant keratoplasty; FBS: Foreign body sensation

Figure 1

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