Universidad de Oviedo
Universidá d'Uviéu
University of Oviedo

Programa de Doctorado de Investigación en Cirugía y Especialidades Médico-Quirúrgicas (RD 1393/2007)

Análisis de Resultados de la Implantación de Anillos Intracorneales de Ferrara en Pacientes con Queratocono en Brasil

Trabajo de investigación realizado por

D. Guilherme Hermeto Ferrara de Almeida Cunha

para optar por el grado de Doctor.

Director: Dr. Jesús M Merayo Lloves

Oviedo, 10 de Abril de 2017

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RESUMEN DEL CONTENIDO DE TESIS DOCTORAL

1.- Título de la Tesis	
Español: Análisis de Resultados de la Implantación de Anillos Intracorneales de Ferrara en Pacientes con Queratocono en Brasil	Inglés: Outcome Analysis of Ferrara Intrastromal Ring Segments in Keratoconus Patients in Brazil

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Programa de Doctorado: Programa de Doctorado de Investigación en Cirugía y Especialidades Médico-Quirúrgicas (RD 1393/2007)	
Órgano responsable: Universidad de Oviedo	

RESUMEN (en español)

Los segmentos de anillos intracorneales de Ferrara (ICRS) se llevan aplicando desde hace más de 30 años para la corrección del queratocono y como alternativa al trasplante de cornea o queratoplastia y su empleo se basa en la experiencia clínica de los cirujanos. Esta tesis doctoral evalúa los resultados de la aplicación de ICRS en pacientes con queratocono con el volumen y tiempo de seguimiento más amplio publicado tanto en la población general como en niños y evalúa los resultados de la aplicación de ICRS para la corrección del astigmatismo en las queratoplastias. Los ICRS en los pacientes estudiados mejoran la agueza visual con y sin corrección, remodelan la cornea mediante la reducción de los valores queratométricos y la regularización de valores topográficos con un procedimiento que preserva el eje visual. Además, influyen sobre la progresión de la enfermedad retrasando o evitando la queratoplastia. Se precisan estudios prospectivos y multicéntricos (ensayos clínicos) para estandarizar y personalizar la estrategia de implante y analizar los resultados con mayor fuerza que en los estudios observacionales.

RESUMEN (en Inglés)

Ferrara Intrastromal Ring Segments (ICRS) has been successfully used in the correction of keratoconus based on surgeon clinical practice for more than 30 years as an alternative to corneal transplant. The research work presented as a doctoral thesis develop an outcome analysis of ICRS in patients with keratoconus (general population and children) and also evaluate the role of ICRS in the correction of astigmatism after keratoplasty. The cohort of patients with ICRS analyzed improves visual acuity (expontaneus and corrected). ICRS is a procedure that, preserving the central part of the cornea, makes a reduction of the keratometric values and improves the corneal topography pattern. ICRS alter the progression of the disease delaying, or avoiding, the indication of keratoplasty. There are necessary clinical trials (multicentric and prospective studies) to Asses the customization and standardization of the implant protocols and to study the outcome of ICRS with more power than in observational studies

SR. PRESIDENTE DE LA COMISIÓN ACADÉMICA DEL Programa de Doctorado de Investigación en Cirugía y Especialidades Médico-Quirúrgicas (RD 1393/2007)

Agradecimientos

Agradezco al Dr. Merayo, director de mi tesis, por la amistad, y por me haber acogido en cuanto estuve lejos de casa. Muchas gracias por toda la ayuda, por la trasmisión de sus conocimientos y por fomentar mi crecimiento personal y profesional.

Al Dr Alfonso, por las enseñanzas, la inversión de tiempo en mi formación y por la oportunidad y confianza.

A Don Luis Fernandez-Vega por me haber permitido tener una experiencia única de aprendizaje en el Instituto durante mi estada en Oviedo.

A toda la equipo del Departamento de Segmento Anterior del IOFV, con especial mención al Dr. Lisa y al Dr. Abdel por los momentos juntos en la clínica.

A todos los compañeros del Grupo de Cirugía Refractiva y Calidad Visual del IOBA y después a los miembros del Grupo de Superficie Ocular de la FIO, por la recepción y intercambio de conocimientos; a Nacho, por la acogida, apoyo y amistad.

A los compañeros del Instituto y de la FIO, por la amistad y por la acogida; a Carlos por su amistad.

A Leo Torquetti, por todo su apoyo y ayuda, por toda dedicación a los estudios de los anillos de Ferrara y a todo el equipo que me ha ayudado en Brasil

A mi madre, Beatriz por su apoyo incondicional, siempre presente en los momentos difíciles; a mi padre, Paulo, ejemplo de dedicación y ética, por las oportunidades que tengo. Por toda experiencia y conocimiento aportados en el día a día en la clínica, además de nuestras charlas.

A mi mujer, Camila, siempre presente, amiga y compañera, siempre me apoyando en mis decisiones; a mis dos hijos, Bernardo y Arthur, por su amor y inspiración.

ÍNDICE

1. Motivación, Pregunta de Investigación y Estructura de la Tesis.

El queratocono es una patología de la estructura transparente del ojo, la cornea, que cursa con un progresivo adelgazamiento y aumento irregular de curvatura con resultado de perdida de la agudeza visual. Si la enfermedad avanza, la cornea pierde la trasparencia y se corre el riesgo de destrucción del tejido y perforación. Para su corrección se han empleado diversos tratamientos que se revisan en la introducción entre los que destacan los segmentos de anillos intracorneales (ICRS) desarrollados por el padre del autor. Si bien se tiene experiencia clínica con este tipo de prótesis desde hace más de 30 años y se han realizado trabajos en modelos experimentales, el desarrollo de la técnica y el análisis de resultados no ha tenido apenas soporte en publicaciones científicas y se ha basado fundamentalmente en datos empíricos de la experiencia clínica. Este hecho motivó el realizar un trabajo de investigación que revisara los resultados del implante de ICRS en la clínica del Dr. Paulo Ferrara para poder conocer el comportamiento de los ICRS a largo plazo con gran volumen de pacientes operados. El doctorando después de terminar la especialidad de oftalmología en Brasil se vino a España a realizar un largo periodo de formación postgraduada en investigación traslacional en ciencias de la visión (Universidad de Valladolid), master en superficie ocular, cornea, catarata y cirugía refractiva y el programa de doctorado (Universidad de Oviedo) y empezó la tarea de analizar los resultados del implante de los ICRS, fruto del cual se han realizado las publicaciones que soportan esta tesis.

La Tesis se presenta como un compendio de artículos con una parte común (Introducción, Justificación, Hipótesis de Trabajo, Objetivos, Discusión y Conclusiones) y los capítulos correspondientes a los diferentes trabajos y publicaciones: **Capitulo I** dedicado al análisis de resultados de la implantación de segmentos de anillos a largo plazo, **Capitulo II** dedicado al estudio de la progresión del queratocono, **Capitulo III** dedicado al análisis del efecto de los ICRS en el astigmatismo en los pacientes con queratoplastias y el **Capitulo IV** dedicado al análisis de resultados del implante de ICRS en niños con queratocono. Como en el momento de escribir esta memoria el artículo que soporta este capítulo está en fase de revisión se ha de considerar como un "trabajo en realización" hasta que esté aceptada su publicación.

A Mis Padres Beatriz e Paulo, Mi mujer Camila

e mis hijos, Bernardo e Arthur

2. Resumen.

Los segmentos de anillos intracorneales de Ferrara (ICRS) se llevan aplicando desde hace más de 30 años para la corrección del queratocono y como alternativa al trasplante de cornea o queratoplastia y su empleo se basa en la experiencia clínica de los cirujanos. Esta tesis doctoral evalúa los resultados de la aplicación de ICRS en pacientes con queratocono con el volumen y tiempo de seguimiento más amplio publicado tanto en la población general como en niños y evalúa los resultados de la aplicación de ICRS para la corrección del astigmatismo en las queratoplastias. Los ICRS en los pacientes estudiados mejoran la agueza visual con y sin corrección, remodelan la cornea mediante la reducción de los valores queratométricos y la regularización de valores topográficos con un procedimiento que preserva el eje visual. Además, influyen sobre la progresión de la enfermedad retrasando o evitando la queratoplastia. Se precisan estudios prospectivos y multicéntricos (ensayos clínicos) para estandarizar y personalizar la estrategia de implante y analizar los resultados con mayor fuerza que en los estudios observacionales.

Ferrara Intrastromal Ring Segments (ICRS) has been successfully used in the correction of keratoconus based on surgeon clinical practice for more than 30 years as an alternative to corneal transplant. The research work presented as a doctoral thesis develop an outcome analysis of ICRS in patients with keratoconus (general population and children) and also evaluate the role of ICRS in the correction of astigmatism after keratoplasty. The cohort of patients with ICRS analyzed improves visual acuity (expontaneus and corrected). ICRS is a procedure that, preserving the central part of the cornea, makes a reduction of the keratometric values and improves the corneal topography pattern. ICRS alter the progression of the disease delaying, or avoiding, the indication of keratoplasty. There are necessary clinical trials (multicentric and prospective studies) to Asses the customization and standardization of the implant protocols and to study the outcome of ICRS with more power than in observational studies

3. Acrónimos.

AV: Agudeza visual

CDVA: Agudeza visual con corrección

CXL: Crosslinking

DALK: Deep anterior lamellar keratoplkasty

ICRS: Intracorneal ring segments

IL-1: Interleucina 1

IL-6: Interleucina 6

K: Queratometría

Lasik: Laser in situ keratomileusis

LCRGP: Lentes de contacto semirrígidas permeables al gas

MMP: metaloproteinasas

PKP: Trasplante penetrante de córnea

PRK: keratectomia foto refractiva

Q: Asfericidad corneal

TIMP 1: Tissue Inhibitors of metalloproteinases 1

TNF- α: Factor de necrosis tumoral α

UDVA: Agudeza visual sin corrección

RK: Queratotomía radial

SD: Standard Deviation

SE: equivalente esférico

4. Introducción.

4.1. Córnea

La córnea constituye la primera lente del ojo, responsable por el 70% del poder refractivo del sistema óptico humano (entre 40 y 44 Dioptrías) (ALDER, 1950).[1] Se trata de una estructura transparente, avascular, ricamente inervada, y que funciona como barrera química y mecánica entre el interior del ojo y su exterior. (WARING, 1884 & KLYCE & BEUERMAN, 1988).[2,3] Su forma y transparencia dependen de la organización de las fibras de colágeno del estroma, que se mantienen ordenadas y paralelas entre ellas (MEEK ET AL, 2005 & MEEK ET AL, 2003).[4,5] Tiene su espesor más delgado en el centro (520 y 550 μm), y que aumenta hacia el limbo. Alteraciones en su geometría pueden alterar de manera significativa su poder óptico (NEJAD; FOSTER; GONDAL, 2014).[6]

4.1.1. Anatomía

La córnea está estructurada clásicamente en 5 capas: el epitelio, con un grosor de aproximadamente 50 μm, está formado por 5 a 7 capas de células. Posee la función de barrera frente al medio exterior y, juntamente con la lágrima, constituye una superficie homogénea para la refracción. La capa de Bowman está situada entre el estroma corneal y la membrana basal. Está constituida por colágenos tipo I, III, V, VII y XIII y proteoglicanos. El estroma corneal constituye el 90% del espesor corneal, formado por 78% de hidratación, 15% de fibras de colágeno entrelazadas, 7% de proteoglicanos, glicoproteínas y sales inorgánicos (MAURICE, 1984 & KRACHMER ET AL, 1984).[7,8] La capa de DUA ha sido descrita recientemente (DUA ET AL, 2013)[9] como una capa acelular en la región pre Descemet. Su reconocimiento puede tener un impacto considerable sobre el entendimiento de la biomecánica corneal. El endotelio es una estructura de gran importancia para el metabolismo corneal, responsable por la nutrición de la córnea, así como por la excreción de los productos finales del metabolismo y de su deturgescencia.

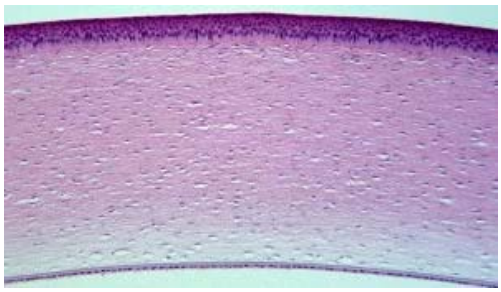


Figura 1: Histología de la córnea

4.1.2. Concepto de Asfericidad Corneal

Actualmente se cree que el contorno de la córnea se acerca a una sección cónica, descrita por la asfericidad (Q) y por el radio de curvatura (GONZÁLEZ-MÉIJOME ET AL, 2007).[10] Se cree que la forma asférica de la córnea se mantiene constante durante toda la vida.

Podemos abordar la forma de una superficie como esférica, asférica prolada o asférica oblada. La superficie esférica es redonda (Q=0) FIGURA A. Una superficie asférica es más curva en el centro y más plana hacia la periferia (Q negativo) FIGURA B. Una superficie asférica oblada es más plana en el centro y más curva en la periferia (Q positivo).

Cuándo un haz de luz paralelo pasa por una lente esférica, los rayos centrales enfocan más posteriores, mientras los rayos periféricos enfocan más anteriores. El valor de Q es cero y la aberración es discretamente positiva. En una superficie prolada, más curva en el centro y más plana en la periferia, los rayos periféricos enfocan más posteriores y coinciden con los rayos centrales. El valor de Q y la asfericidad serán negativos, en este caso. Eso hace que la calidad de la visión sea buena, pues todos los rayos luminosos van hacia un único foco. En una superficie oblada, más plano en el centro que en la periferia, los rayos periféricos enfocan más anteriores que los rayos centrales. El valor de Q y la aberración esférica serán positivos. En este caso, la aberración esférica inducida hace con que la calidad visual sea degradada y la sensibilidad al contraste disminuya (PHILIPPINE JOURNAL OF OPHTHALMOLOGY, 2011).[11]

La mayoría de los estudios está de acuerdo de que la asfericidad corneal en humanos varía de -0,01 a -0,80 (ASBELL; UCAKHAN, 2001; COLIN; VELOU, 2003).[12,13] El valor más comúnmente aceptado en adultos jóvenes es de, aproximadamente, -0,23 ± 0,08 en la zona óptica de 4,5 mm (SIGANOS, C. S. et al, 2002).[14]

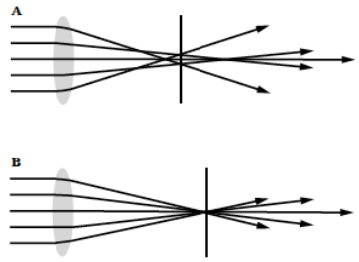


Figura 2: Córnea esférica (A) y asférica (B).
Fuente: Robert Edward T Ang, 2011

La asfericidad corneal es distinta cuando comparamos córneas sanas y córneas ectásicas. En la córnea ectásica, la curvatura puede presentarse bastante más elevada en el centro cuando se la compara a una córnea normal (hiperprolada), o más plana en el centro que una córnea normal (oblada), situación que ocurre en el queratocono inferior y en la degeneración marginal pelúcida.

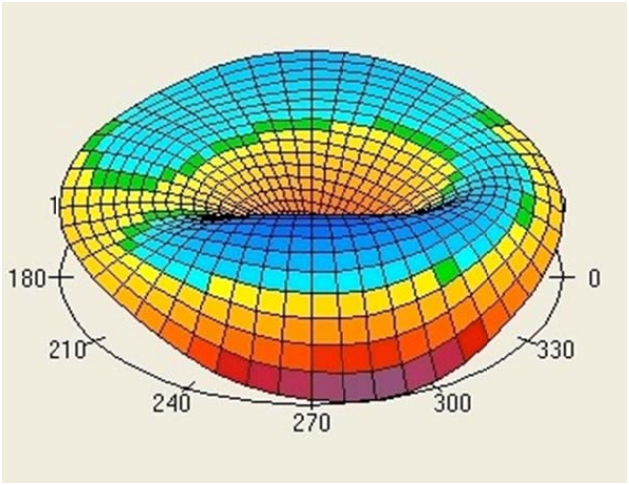


Figura 3: córnea oblata

4.2. Queratocono

El queratocono es la patología ectásica más frecuente en el paciente joven. Cursa con adelgazamiento progresivo de la córnea, seguida por el aumento progresivo de su curvatura y protrusión, que resultan en astigmatismos irregulares, miopía, además de elevados índices de aberraciones de alto orden y, consecuentemente, a un comprometimiento importante de la agudeza visual (TORQUETTI ET AL 2009).[15] Aunque sea considerada como una patología no inflamatoria, diversos estudios han demostrado marcadores de la inflamación elevados en esta patología (LEMA ET AL 2004; LEMA ET AL 2008; GALVIS ET AL 2015).[16,17,18]

Los síntomas del queratocono pueden variar, dependiendo de su etapa evolutiva (RABINOWITZ, 1998).[19] En grados iniciales, puede que sea difícil diferenciar el queratocono de otras condiciones refraccionales, como el astigmatismo, y su diagnóstico puede pasar desapercibido. Con la evolución del queratocono, el desenfoque visual creciente y la dificultad de la realización de la refracción nos hace sospechar de la patología.

La forma frustra de queratocono fue primeramente descrita por Amsler en 1961, y luego citada por otros autores (Klyce et al, 2009).[20] Esta forma de la patología puede aparecer en cualquier momento de la vida, con patrones queratométricos extremamente sutiles y sin presentar los signos clínicos de la enfermedad. Lo que diferencia la forma frustra de queratocono del queratocono manifiesto es que la primera no progresa.

La incidencia de queratocono se hace más frecuente en los centros de cirugía refractiva, cuando se la compara con la población en general. Su detección precoz es de gran preocupación en el "screening" de pacientes candidatos a la cirugía refractiva, dado que el procedimiento causa debilidad de la estructura de la córnea y predispone a la aparición de la ectasia corneal (Kleyce, 2009).[20] La forma frustra de queratocono es la principal causa de ectasia post Lasik (Randleman et al, 2008).[21]

4.2.1. Epidemiología

El queratocono comienza, en general, en la segunda década de vida y puede progresar hasta la tercera o cuarta década (RABINOWITZ 1998).[19] Se ha observado que el queratocono progresa más rápidamente en personas más jóvenes cuanto más temprana la edad de aparición (OWEN ET AL 2003).[22] La incidencia del queratocono depende de otros factores, como el grupo étnico analizado y los criterios de diagnóstico utilizados. El frotamiento ocular y la presencia de enfermedades sistémicas como síndrome de los parpados laxos, alergias, eczema e historia familiar también fueron relacionados con la aparición del queratocono (PIÑERO ET AL, 2012)[23], aunque su aparición no esté relacionada con otro factor de riesgo en la mayoría de los casos.
La incidencia del queratocono, según diferentes autores, oscila entre 50-230 para cada 100.000 habitantes (1 de cada 2000 en la población general) (PIÑERO ET AL, 2012).[23] Se ha aceptado al queratocono como una patología con igual distribución en ambos sexos.

4.2.2. Patogenia

La presentación más frecuente del queratocono ocurre en su forma aislada, sin otra patología sistémica u ocular detectable a la evaluación clínica. Patologías como el síndrome de Down y amaurosis congénita de Leber presentan alta incidencia con el queratocono. Su asociación con el queratocono se hace por la alta incidencia de frotación de los ojos en estos pacientes.

La disposición de las fibras de colágeno en córneas con queratocono no es la misma que en córneas normales (Radner et al, 1998).[24] La reducción del número de queratocitos y del número de lamelas, con degradación de fibroblastos en córneas con queratocono, ha sido descrita por Romero-Jiménez en 2010, así como las alteraciones en la organización de las lamelas de colágeno, con distribución desigual de las lamelas del colágeno por Meek, en 2005. Estas alteraciones estructurales pueden resultar en debilidad estromal, con subsecuente adelgazamiento y protrusión de la córnea.

Los aspectos bioquímicos subyacentes al desarrollo del queratocono parecen desempeñar un papel importante en su patogénesis, aunque no sean totalmente conocidos, a pesar de la intensa investigación realizada en este campo.

Los estudios bioquímicos e inmunohistoquímicos de córneas con queratocono sugieren que existe una degradación de la matriz extracelular debido al aumento de enzimas proteolíticas y otras enzimas catalíticas: enzimas lisosomales como la gelatinasa, la fosfatasa ácida, las catepsinas B y G y varias metaloproteasas como la MMP-2; y/o disminución de los niveles de las enzimas inhibidoras de las proteasas, como los TIMP-1 (Inhibidores tisulares de las metaloproteinasas-1), inhibidoras de la alpha 1 antiproteasa y la alpha 2 macroglobulina.[25]

Los hallazgos histológicos han demostrado una disminución del número de queratocitos en el estroma anterior , probablemente causada por un aumento de la apoptosis celular en córneas con queratocono (Wilson et al, 1996).[26] Los queratocitos de las córneas con queratocono presentan un número 4 veces superior de receptores para interleuquina-1, una citocina relacionada con la apoptosis de queratocitos y la liberación de otras citocinas.

Los microtraumas corneales decurrentes del frotamiento ocular y/o por el uso de lentes de contacto, permiten que la IL-1 producido por el epitelio y endotelio corneal tenga contacto con los queratocitos hipersensibles, resultando en su apoptosis y gradual disminución del colágeno.

En lágrimas de pacientes con queratocono y portadores de lentes de contacto se han encontrado sobreexpresados marcadores proinflamatorios como IL-1, IL-6, TNF α y otras metaloproteasas. La hipótesis de que factores externos, como las lentes de contacto, la atopia y el frotamiento crónico desencadenarían una inflamación crónica a nivel molecular, con progresiva degradación del estroma corneal, quedaría justificada (Lema et al, 2008; Lema et al, 2009).[17,27]

Los niveles bajos de antioxidantes, como aldehído deshidrogenasa y superóxido dismutasa, enzimas responsables de la eliminación de especies reactivas de oxígeno,

pueden resultar en elevados niveles de radicales libres y peróxido de hidrógeno, con el aumento del estrés oxidativo y la consiguiente toxicidad celular secundaria.

4.2.3. Diagnóstico Clínico y de Imagen

El queratocono es la patología ectásica más común de la córnea y se manifiesta, en general, en la segunda o tercera década de vida. El signo más precoz es el adelgazamiento paracentral del estroma, con protrusión apical y astigmatismo miópico asimétrico (Duke Elder y Leigh, 1965).[28] Las alteraciones inducidas en la córnea resultan en disminución de la calidad visual, además de perdida de líneas de visión. Factores ambientales pueden estar asociados con el desarrollo de la patología, como atopia, frotamiento de los ojos y lentes de contacto semirrígidas permeables al gas mal adaptadas. Además, las ectasias pueden tener un carácter progresivo.

4.2.3.1. Síntomas

En general, los primeros síntomas ocurren en la pubertad. Atopia y frotamiento de los ojos son frecuentes en estos pacientes. Empeora de la visión, cambios frecuentes de la graduación de las gafas por el aumento de la miopía y del astigmatismo, y por cambios el eje del astigmatismo, ocurren en visitas rutineras al oftalmólogo.

Con la progresión de la ectasia, el paciente puede referir imágenes muy distorsionadas, deslumbramientos, halos y poliopia, con importante compromiso de la agudeza visual. La adaptación de lentes de contacto en genera, es compleja en estos pacientes, incluso en los grados iniciales.

4.2.3.2. Signos Clínicos

En las fases iniciales, es posible observar sombras en tijera a la esquiascopia, además del signo de la gota de aceite de “Charleux” por retroiluminación, con la pupila dilatada. El aspecto de la córnea a la lámpara de hendidura suele ser normal en grados iniciales del queratocono.

Con la progresión de la ectasia, los nervios se vuelven visibles, seguido de la visualización del anillo de Fleischer, una línea color ocre-marronácea en forma de arco o anillo que rodea la base del cono, y las estrías de Vogt, líneas finas verticales en el estroma profundo y la membrana de Descemet, paralelas al eje del cono. Suelen suceder opacidades superficiales en el vértice del cono relacionadas con roturas en la capa de Bowman y cicatrización secundaria y las opacidades secundarias a la cicatrización en respuesta al estrés.

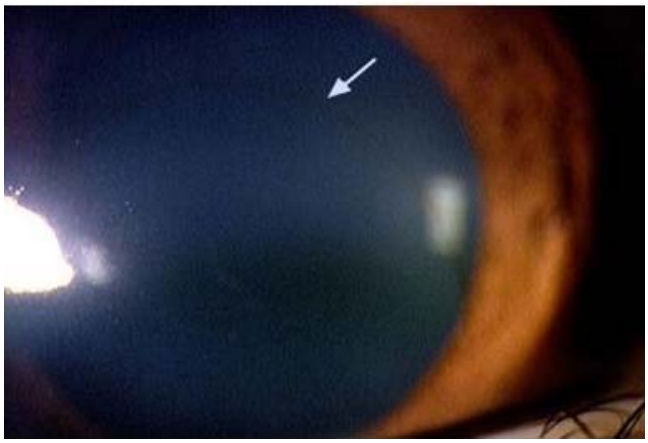


Figura 4: Anillo de Fleischer (Flecha)

En fases más avanzadas, el adelgazamiento y la ectasia se hacen más severas, provocando la pérdida de la visión. En este momento es posible observar el signo de Munson, que consiste en la deformación en V del párpado inferior cuando el paciente mira hacia abajo, y el signo de Rizzuti, que consiste en la aparición de un reflejo luminoso en el limbo nasal cuando se ilumina desde el lado temporal. La hidropsia aguda consiste en el aumento abrupto del espesor corneal (edema) resultante de roturas en la membrana de Descemet, con entrada de humor acuoso hacia el interior de la misma. Dolor y opacidad corneal secundaria al edema, con disminución de la agudeza visual, ocurren como consecuencia de este fenómeno. Al cabo de semanas, el cuadro se resuelve con la absorción del edema y la restauración de la trasparencia corneal. Ocurre cicatrización de la rotura y se forma un leucoma central.

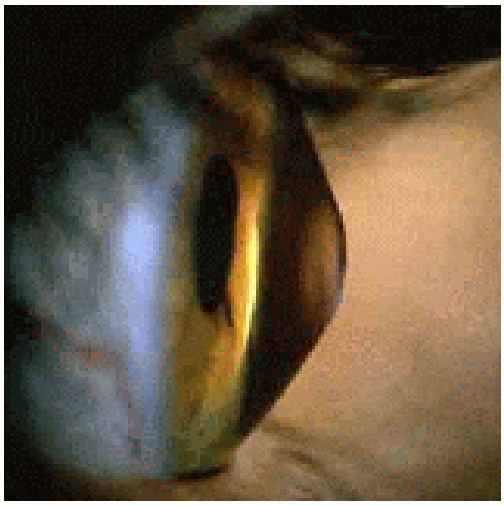


Figura 5: Queratocono

4.2.3.3. Criterios de diagnóstico

4.2.3.3.1. Topografía de córnea

Aunque el queratocono sea una patología que cursa con adelgazamiento e incremento de la curvatura corneal, ninguno de estos parámetros, ni la curvatura, ni la paquimetría o la regularidad de la superficie corneal es, de forma aislada, útil para el diagnóstico de queratocono.

La topografía de córnea basada en el disco de Placido proporciona abundante información sobre el contorno corneal. En ella se pueden reconocer los patrones de regularidad corneal, bien como los índices cuantitativos generados por este sistema. Las alteraciones de estos parámetros, asociadas a los datos clínicos del paciente, nos llevan a la sospecha del diagnóstico del queratocono.

Los patrones considerados sospechosos son aquellos que presentan áreas aisladas de encorvamiento; asimetría inferior-superior; desviación de eje entre los hemimeridianos de la córnea, o bien la asociación de estos patrones. También se han desarrollado varios índices destinados a auxiliar en el diagnóstico del queratocono, como el Rabinowitz-McDonnell, el índice KISA% y el Klyce-Maeda-Smolek, con elevada sensibilidad y especificidad para su diagnóstico.

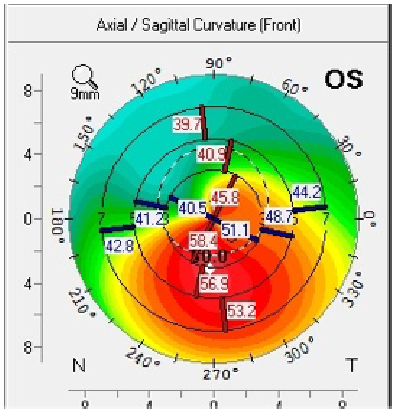


Figura 6: Topografía de córnea de un paciente con queratocono

4.2.3.3.2. Tomografía de córnea

La tomografía corneal hace la reconstrucción tridimensional de las estructuras de la cámara anterior del ojo para proveer datos de la superficie corneal —tal como funciona el topógrafo de córnea—, de elevación anterior y posterior, así como mapas diferenciales, además de la variación del espesor en toda la superficie de la córnea (mapa paquimétrico).

La utilización del tomógrafo de córnea (Pentacam; Oculus Optikgeräte, Wetzlar, German) posibilita un estudio profundizado de la córnea y de las alteraciones inducidas por el queratocono. Los datos proporcionados por el Pentacam® nos permite también evaluar los cambios inducidos en córneas ectásicas después del implante de los anillos de Ferrara.

En corneas normales, el mapa de elevación anterior y posterior guarda una relación entre sí. Las alteraciones de la elevación posterior pueden ocurrir antes que las alteraciones en la superficie anterior de la córnea. Un estudio realizado por Schlegel et al (2008)[29] sugiere que las alteraciones del mapa de elevación posterior de la córnea preceden las alteraciones del mapa anterior, probablemente debido al remodelamiento del epitelio corneal que enmascara o disminuye las alteraciones topográficas iniciales en pacientes sospechosos de queratocono, incluso antes de la aparición de los síntomas visuales.

El espesor corneal empieza a tener especial importancia en los pacientes que serán sometidos a la cirugía refractiva (Ambrosio et al; 2003),[30] como también la caracterización de la distribución del espesor corneal (Ambrosio et al, 2011).[31] La combinación de la caracterización del espesor corneal juntamente con los mapas de elevación nos permite evaluar e identificar anormalidades en los patrones corneales.

En córneas ectásicas, la protrusión anterior genera un aumento de la prolacidad asociada a la negativización del valor de Q (asfericidad) (Piñero et al. 2012).[23] La asfericidad marcadamente más negativa para la superficie anterior de la córnea fue relatada en un estudio por Piñero et al. (2010)[32] comparando algunas características topográficas en una muestra de ojos normales con aquellos encontrados en córneas con queratocono grados I y II (Amsler-Krumeich).

4.2.4. Prevención y Tratamiento Médico

La presencia de alergias y del frotamiento ocular son frecuentemente asociados a la aparición y a la progresión del queratocono, además de cuadros variables de ojo seco. Esas condiciones afectan no solo el curso de la enfermedad, sino también a la adaptación de lentes de contacto en estos pacientes. El tratamiento clínico de estos síntomas es el primer paso para lograr rehabilitar al paciente desde el punto de vista de su corrección visual, como también para frenar la evolución del queratocono.

El objetivo mayor en el tratamiento del queratocono es la rehabilitación visual. La elección del tratamiento puede variar de acuerdo con el estadio de la patología y de los síntomas que presenta el paciente.

En casos iniciales, la corrección con gafas suele ser satisfactoria. Con la progresión del cuadro clínico, las gafas no son capaces de proporcionar una visión adecuada, y las lentes de contacto semirrígidas al gas (LCRGP) pasan a desempeñar un papel importante para el mantenimiento de la visión de estos pacientes. Las LCRGP no

detienen la progresión de la ectasia e incluso, en algunos casos, pueden estar relacionadas a ella.

El uso de las lentes de contacto semirrígidas permeables al gas constituye una de las modalidades más eficaces para la mejora de la agudeza visual en estos pacientes (MAGUIRE, 1988).[33] Las LCRGP neutralizan las aberraciones ópticas y las distorsiones de la superficie anterior de la córnea, mejorando la agudeza visual, incluso en queratoconos más avanzados. Algunos casos difíciles también pueden beneficiarse de lentes especiales con diseño multicurva, como ocurre en las lentes Rose K® y Menicom KRC® .

Hay pacientes que se vuelven intolerantes a las LCRGP. Una alternativa de tratamiento para estos pacientes es la técnica de Piggy Back, que consiste en la adaptación de una LCRGP encima de una lente de contacto blanda. Esa modalidad de adaptación mejora la tolerancia del paciente al uso de las lentes y proporciona una buena agudeza visual. Nuevos materiales con mayor permeabilidad al oxígeno amplían aún más la gama de opciones para el tratamiento de la visión en el paciente portador de queratocono con lentes de contacto. Las lentes de apoyo escleral nos permiten la adaptación incluso en pacientes con queratoconos muy avanzados. El hecho de que esas lentes no tocan la córnea, además de ser muy estables, proporcionan gran comodidad y buena calidad visual.

4.2.6. Tratamiento Quirúrgico

El queratocono es una patología del paciente joven, y su diagnóstico se lleva a cabo cada vez más temprano en los días actuales. Se ha observado que su progresión ocurre más rápidamente en personas más jóvenes, y que más rápido puede progresar cuanto más temprana sea la edad de aparición. Por eso resulta imprescindible el seguimiento cercano de estos pacientes, así como la pronta actuación del oftalmólogo frente a la progresión de la ectasia es fundamental para su desenlace.

El crosslinking (CXL) para el tratamiento del queratocono fue primeramente propuesto por Theo Seiler y Wollensak en 2003 (Wollensak G, Spoerl E, Seiler T.).[34]

Muchos trabajos en la literatura también preconizan su utilización para el tratamiento de las ectasias de córnea, como en queratocono (Padmanabhan et al, 2017)[35] y ectasias de córnea post lasik (Hafezi et al, 2007).[36]

La técnica de Crosslinking altera la biomecánica corneal, haciéndola más dura. Este tratamiento induce el entrecruzamiento de las fibras de colágeno del estroma y, para que esto ocurra, se aplica riboblavina sobre la córnea desepitelizada, seguido de irradiación con luz ultravioleta como mediadores (Sporel et al, 1999).[37] Su potencial terapéutico fue establecido en un estudio previo publicado por Wollensak et al.[34]

La mejor recomendación del CXL es en queratoconos iniciales, dado que su principal objetivo es el endurecimiento de la córnea, con poca influencia en su forma. Algunos estudios preconizan su utilización en pacientes jóvenes después de diagnosticado el queratocono, ya que su progresión sucede más rápidamente en personas más jóvenes y más rápido cuanto más temprana sea la edad de aparición.

La asociación del implante de los anillos, a efectos de mejorar la agudeza visual y disminuir los valores de la queratometria, con el crosslinking, para aumentar la estabilidad del tratamiento, ha sido propuesto por muchos (Ibrahim et al, 2016; Xuan-Li Liu, 2014)[38,39] con buenos resultados.

Las limitaciones de la técnica de CXL son los casos avanzados, la baja agudeza visual corregida con gafas y los elevados valores queratométricos, además de las corneas delgadas, con un espesor inferior a 400 μm.

Los implantes de segmentos intracorneales (ICRS) para la corrección de altas miopías fue primeramente descrito en la década de 1950 por Barraquer (Barraquer 1966)[40]. Ferrara empezó en 1986 sus estudios para la corrección de altos grados de miopía con los anillos intraestromales (Anillos de Ferrara) y en 1991 hizo el primer implante en un paciente humano. En 1996 empezó sus estudios en pacientes con queratocono.

El implante de segmentos intracorneales, propuesto para la corrección del queratocono, es un tratamiento menos invasivo y ha sido utilizado con éxito para disminuir la

queratometria, además de regularizar la superficie corneal y mejorar la agudeza visual (Siganos, 2002; Colin, 2003).[14,13]

Para nuestro grupo de investigación, los anillos intracorneales son la primera alternativa de tratamiento destinada a pacientes que presentan progresión del queratocono, bien como aquellos que presentan agudeza visual por debajo de 20/30 usando gafas. En nuestra experiencia, un 5% de los pacientes terminan en queratoplastia, a pesar de los implantes.

Se han llevado a cabo implantes de segmentos intracorneales exitosos para el tratamiento de las ectasias corneales como el queratocono (Ferrara 1995; Siganos 2002)[41,14], con el objetivo de disminuir las deformidades corneales, la curvatura corneal, el astigmatismo irregular y la mejora de la agudeza visual, con un índice bajo de complicaciones (Ferrara 2011).[42] Estudios han demostrado la reducción de la miopía y del astigmatismo irregular con el implante de los anillos intracorneales en queratoconos iniciales y moderados (Rodrigues 2014)[43], como también en queratoconos moderados y avanzados (Fahd 2012).[44] La seguridad del procedimiento, la estabilidad, la reversibilidad y el hecho de que el implante de los segmentos intracorneales no afecta el eje visual son las principales ventajas de su utilización (Torquetti 2014).[45] El mejor momento para el implante de los anillos intracorneales es todavía un tema polémico.

Las contraindicaciones para el implante de los anillos intracorneales son: opacidades corneales importantes, hidropesía, atopia severa, además de cualquier proceso infeccioso, local o sistémico (Ferrara; Torquetti 2011).[42] El espesor corneal inferior a 300 μm en el trayecto del anillo también es una contraindicación absoluta para la implantación de los segmentos.

El trasplante de córnea es la última alternativa de tratamiento para pacientes portadores de queratocono. El trasplante consiste en la sustitución de la porción central de la córnea enferma, parcial (Deep anterior lamellar keratoplasty – DALK) o en su totalidad (trasplante penetrante), por otra córnea donante sana. Se trata de un procedimiento más invasivo y con mayor índice de complicaciones.

Las complicaciones del trasplante penetrante pueden ser preoperatorias, como la hemorragia expulsiva y los daños intraoculares (iris y lente) o bien postoperatorias, como rechazo agudo y tardío, infecciones, glaucoma, catarata, además de recidiva del queratocono en el injerto trasplantado. Sin embargo, las complicaciones de esta técnica han disminuido en los últimos años, probablemente por la mejora en la técnica empleada (Mascaro et al, 2007).[46] Aunque los resultados visuales sean satisfactorios, la rehabilitación puede ser lenta, y el astigmatismo irregular generado por la intervención puede restringir el pronóstico visual (Marcomini et al, 2011).[47]

La técnica de trasplante parcial (DALK) consiste en la retirada del estroma corneal, preservando la capa de Descemet y el endotelio, los principales responsables de la falencia del trasplante penetrante, el rechazo endotelial. Las complicaciones relacionadas a esta técnica son: perforación de la córnea en el preoperatorio, pseudocámara anterior y proliferación en el interface del trasplante (Fernandez; Albertazzi, 2010).[48]

4.3. Corrección del queratocono con cirugía aditiva de la córnea: las bases de los anillos de Ferrara

4.3.1. Primeros estudios: JI Barraquer y Blavatskaya

Barraquer, en 1949,[49] describió la "Ley de los Espesores de Barraquer" que determinaba el comportamiento de la córnea cuando era sometida a la cirugía refractiva. Su postulado dice que cuando se añade tejido a la periferia de la córnea, o se retira tejido de su centro, ocurre el aplanamiento de la misma. De manera reversa, cuando se añade tejido al centro de la córnea o se retira tejido de su periferia, ocurre su encorvamiento. La primera citación de implantes de anillo corneal en la literatura es referida en el libro publicado por Barraquer en 1989.[50]

Bock y Maumenee[51] estudiaron el mecanismo de transporte de nutrientes a través de la córnea, utilizándose de membranas impermeables de polietileno. Krwawiscs,[51] en 1960, realizó implantes intraestromales a través de la creación de una lamela estromal, con su remoción después de diez días, con mantenimiento de los resultados refractivos por algún tiempo. Belau et al.[53] estudiaron la biocompatibilidad de materiales plásticos, como la silicona y el PMMA, observando su tolerancia durante largos periodos de tiempo. También describieron la correlación linear de las alteraciones refractivas y la dimensión de los implantes.

Choyce[54,55] empleó implantes corneales de acrílico PERSPEX CQ con 8 mm de diámetro y 0,2 mm de espesor para el tratamiento de distrofia endotelial, proporcionando alivio de los síntomas de la queratopatía bullosa.

En 1966, Blavatskaya (apud Barraquer)[49], realizó diversos experimentos en conejos con el objetivo de estudiar los efectos refractivos inducidos por implantes de discos, pequeñas lentes y tejido corneal implantados en la córnea, a través de la técnica de disección manual. Con el implante de anillos de tejido corneal, Blavatskaya logró corregir hasta 21 dioptrías de miopía. En aquel momento se demostró que la corrección obtenida a través del implante de los anillos era directamente relacionada a su espesor e inversamente relacionada a su diámetro. Así, los anillos de diámetro más pequeño y de mayor espesor producen mayor corrección.

Espesor del Anilo mm.	Modificación Diotrías
0.29-0.30	18.0-21.0
0.15-0.17	9.00-12.0
0.10-0.12	6.00-8.00

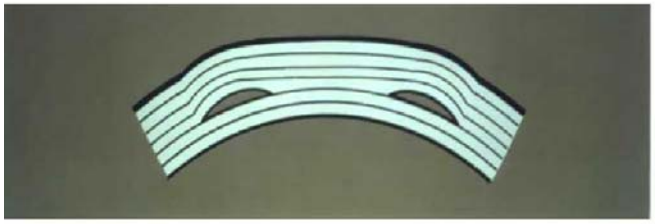
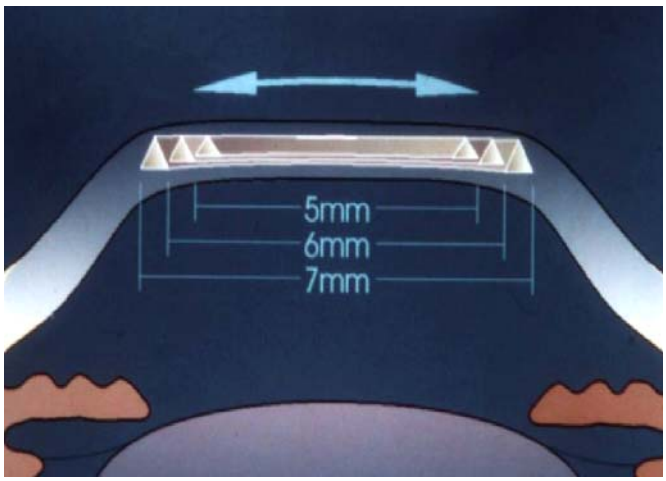


Fig. 1-54 Efecto de la inclusión intracorneal de un anillo. (Blavatskaya)



Figuras 7 y 8: Leyes de Blavatskaya respecto del espesor y diámetro de los segmentos.

Zhivostovsky y Vishnevetsky (apud Barraquer)[49] utilizaron anillos de plástico con diámetro externo de 7 mm y diámetro interno de 5 mm para la corrección de miopía con buenos resultados, dos años más tarde.

Maurice[56,57] sugirió que los problemas causados por los materiales impermeables podrían ser resueltos por materiales permeables al agua, como los hidrogeles. Dohlman y Brown[58] también obtuvieron buenos resultados con la utilización de hidrogel y glicerilmetacrilato.

McCarey y Andrews[59] estudiaron implantes con 71% de hidratación. Ellos observaron que los bordes mal acabados de los implantes ocasionaron la erosión de la córnea, con eventual extrusión de los implantes.

Maurice[56] en 1969, determinó que el estroma anterior al implante recibe nutrientes por difusión, y que la nutrición es proporcional al diámetro y a la profundidad del implante. De esta manera, ortesis con diámetro mayor que 5 mm implantada a menos de un 50% de espesor corneal seguramente será extruida.

La utilización de polisulfonas en ojos humanos demostró su poca tolerancia, a pesar de los resultados refractivos positivos (Choyce).[55]

4.3.2. Anillos de Ferrara

Los estudios con los implantes intracorneales se iniciaron en 1986, teniendo como objetivo la corrección de miopías moderadas y elevadas, una vez que las técnicas existentes hasta este momento permitían apenas la corrección de pequeñas miopías, hasta 6,00 dioptrías. En dicho momento no se disponía de una estructura fabril para producir los anillos y, por lo tanto, las dimensiones de las ortesis no eran precisas.

Otros estudios realizados por Burris T.E. (1993,1994),[60,61] Schanzlin (1997),[62] Nose W (1996)[63] y Fleming (1998)[64] también confirmaron la eficacia de los anillos para la corrección de la miopía baja o moderada.

El objetivo de la investigación, en aquella época, era definir la tolerancia de la córnea a la ortesis, sus dimensiones, forma y la profundidad de implantación, ya que los datos de la literatura disponibles hacían referencia sólo a los implantes lenticulares de hidrogel y polisulfona.[55,59]

Se han realizado estudios histopatológicos de varios segmentos implantados en ojos de conejos albinos, a los 3, 6, 9 y 12 meses. Los resultados obtenidos demostraron la ausencia de reacción inflamatoria perianular importante, así como ausencia de alteraciones de las estructuras adyacentes, como epitelio y endotelio.

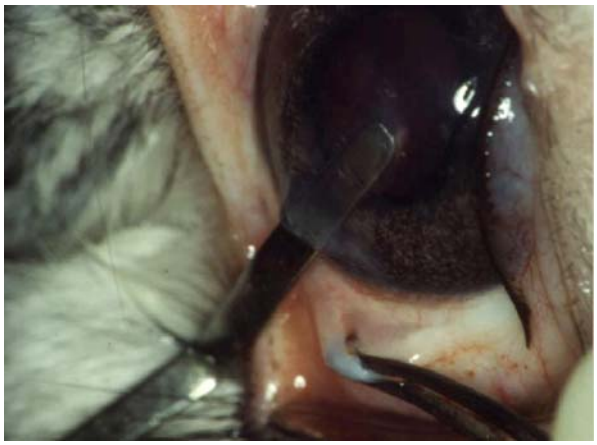


Figura 9: Creación de lamela estromal en ojo de conejo

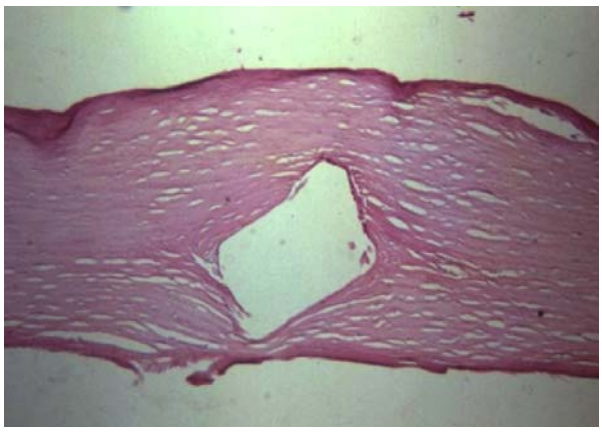


Figura 10: Corte histopatológico de ojo de conejo

En 1991, establecidas las dimensiones y la forma de la ortesis, la adquisición del torno informatizado permitió la producción de ortesis de dimensiones estandarizadas. A partir de ese momento fue posible la definición de un nomograma. Se hizo, entonces, el primer implante en un paciente ambliope y anisométrope utilizando la técnica de queratectomía parcial con microquerátomo. En dicha ocasión no había todavía segmentos de anillos. Los resultados de este estudio fueron presentados en 1994 en el Congreso Internacional realizado en Sao Paulo.[65]

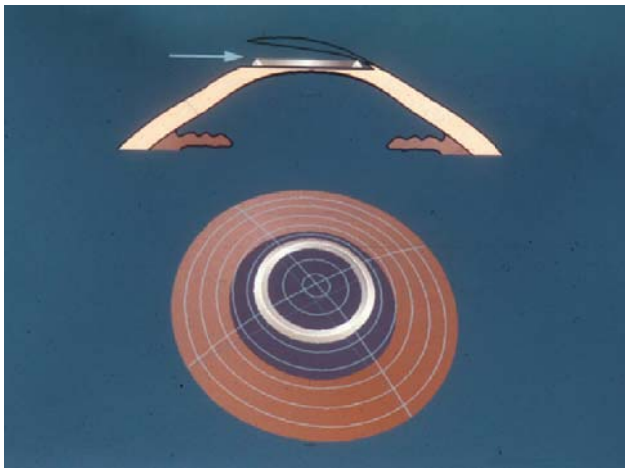
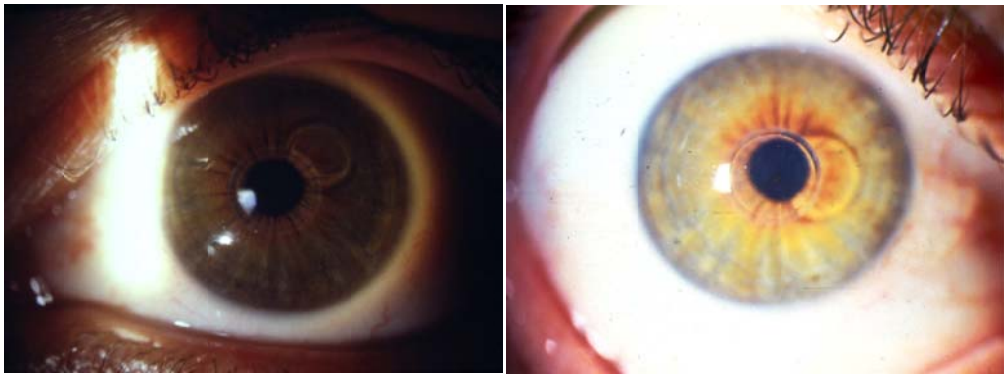


Figura 11: Diseño esquemático de la creación de flap estromal con microquerátomo



Figuras 12 y 13: Ojo humano implantado con Anillo de Ferrara

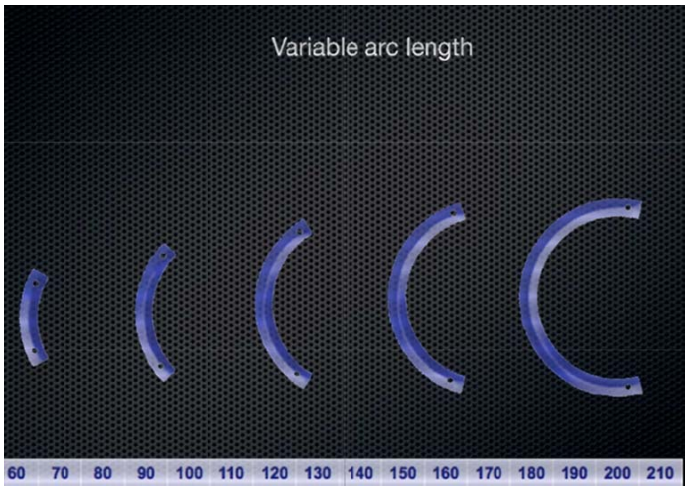


Figura 14: Anillos con diferentes segmentos de arco

4.3.2.1. Evolución de los anillos de Ferrara

Con el objetivo de evitar el eje visual se hizo necesario el desarrollo de una nueva técnica, la técnica de tunelización (1994), la misma que se utiliza en la actualidad. Con ella se desarrolló también la primera generación de segmentos de anillos. Estos tenían 350 grados de arco.

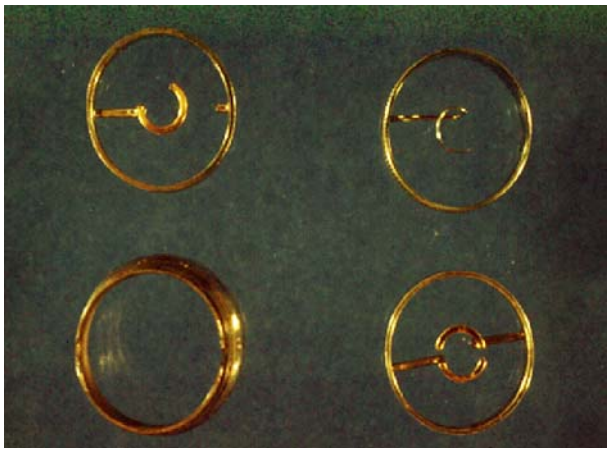


Figura 15: Primeros instrumentales para el implante de los Anillos de Ferrara, hechos en oro, por un orives.

Figura 16: Primera generación de los anillos de Ferrara

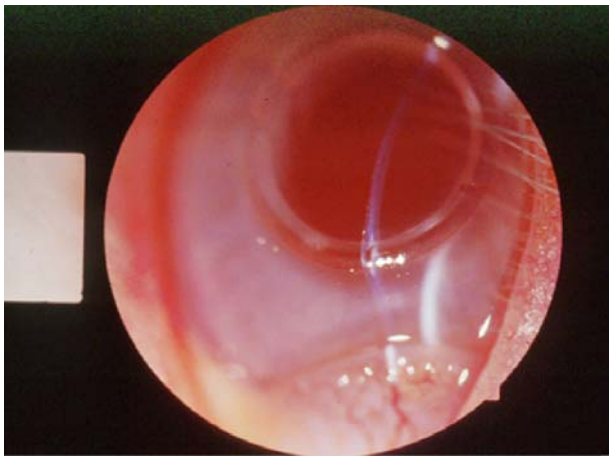


Figura 17: Foto de un ojo de conejo implantado con la primera generación de los anillos de Ferrara

El primer anillo utilizado en paciente post queratoplastia de córnea y queratotomía radial fue implantado en 1995. Esta paciente fue referida al Servicio de Córneas del Hospital São Geraldo de la Universidad Federal de Minas Gerais (UFMG), para un retrasplante. Se intentó el implante del segmento, como alternativa al trasplante, tras la firma del consentimiento informado de la cirugía. El resultado fue satisfactorio, con corrección de la ametropía y perfecta tolerancia de la ortesis por parte del tejido corneal. Después de 6 años de seguimiento, la paciente se presentaba bien, con la córnea compensada y la refracción estable.

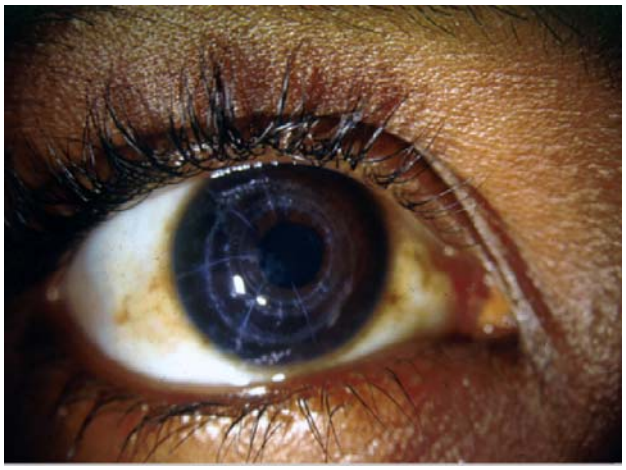


Figura 18: Paciente post queratoplastia y queratotomía radial implantado con anillo de Ferrara (1995)

El implante de estos segmentos de primera generación era difícil. La proximidad de las puntas del segmento de anillo a la incisión impedía su cicatrización, así como causaba la extrusión de los segmentos, en muchos casos. Estos problemas llevaron al desarrollo de la segunda generación de segmentos de anillos: los de 160 grados de arco. Estos

segmentos eran implantados a partir de la creación de 2 incisiones opuestas entre sí. El acabado de estos segmentos era pobre, además de no disponer de los agujeros en la extremidad de los segmentos, presentes en los segmentos actuales.

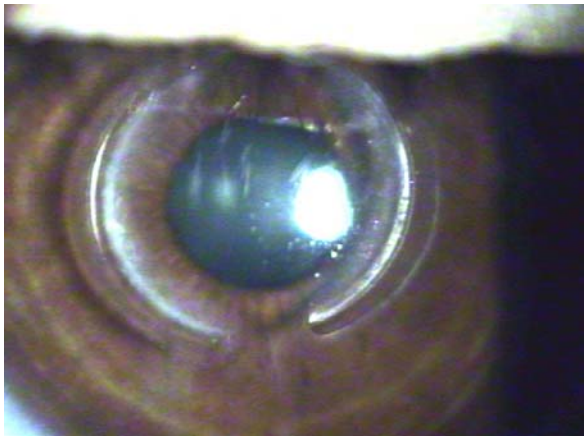
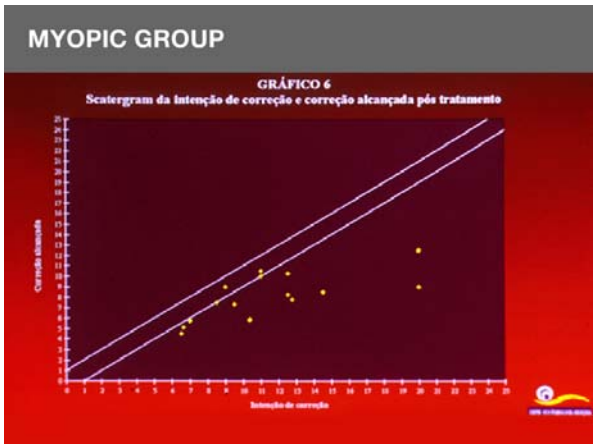
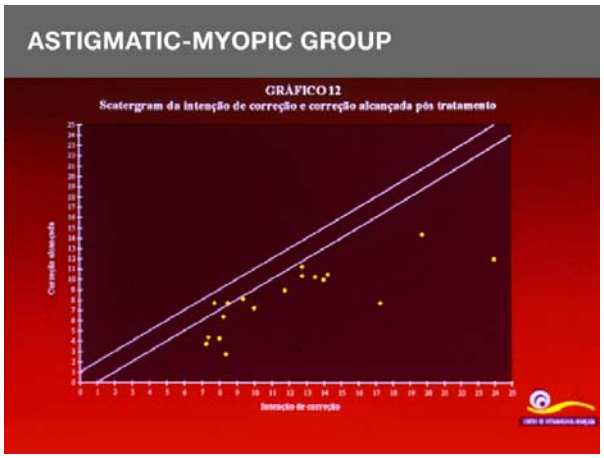


Figura 19: Segunda generación de los Anillos de Ferrara

El implante de 2 segmentos simétricos, además de causar el aplanamiento de la córnea, también resultaba en la reducción del astigmatismo corneal y refraccional.

Los anillos con objetivo refractivo se mostraron poco predecibles, a pesar de presentar resultados estables y un buen rendimiento visual.



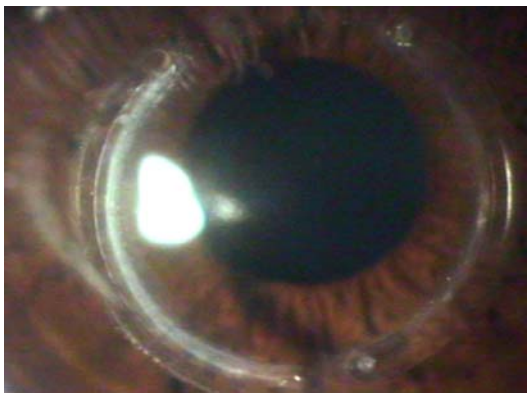


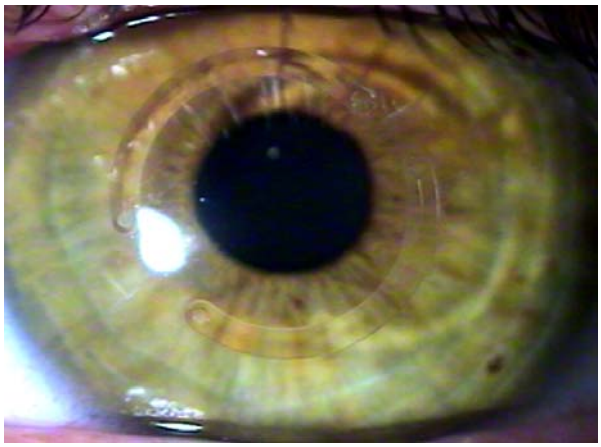
Figuras 20 y 21: Baja predictibilidad de los implantes para la corrección de la miopía y del astigmatismo corneal.

Sin embargo, los resultados de este implante fueron animadores, y la tolerabilidad del órgano al implante dio la seguridad necesaria para aplicar la técnica en córneas con queratocono. De esa manera, a partir de 1996, se decidió implantar los anillos en pacientes con queratocono, intolerantes a lentes de contacto y con indicación para trasplante de córnea.

Colin, en 1997,[66] publicó los primeros estudios de anillos intracorneales de gran diámetro en paciente con queratocono inicial.

La mejora de la técnica quirúrgica y de los conocimientos sobre el mecanismo de acción de los anillos permitió el desarrollo de nomogramas basados en el análisis estadístico. De esa manera se crea la tercera generación de los segmentos, dotada de mejoras en la superficie y la inclusión de un agujero en la punta de la extremidad del segmento.





Figuras 22 y 23: Tercera generación de los Anillos de Ferrara

La utilización de los segmentos intracorneales para la corrección de ectasias de córnea post Excimer Laser se inició en 1999. A partir de 2000 es posible encontrar trabajos en la literatura haciendo referencia al uso de estos implantes para la misma finalidad (Lovisolo).[67]

4.3.2.2. Evolución del nomograma de los anillos de Ferrara

4.3.2.2.1. Primera Generación

Al principio (1997 – 2002), la indicación de los segmentos ocurría de acuerdo con el grado del queratocono, y siempre se implantaban 2 segmentos (tabla I). En queratoconos avanzados, en los cuales las córneas son más delgadas, y que se utilizaban segmentos más gruesos, su extrusión ocurría con alguna frecuencia.

Nomograma

La selección del anillo depende de la ametropía y, tratándose del queratocono, del grado evolutivo del mismo.

Diámetro 5,00 mm	Grosor	Dioptría a ser corregida
	0,150 mm-2,00 a -4,00	
Cono I	0,200 mm	-4,25 a -6,00
Cono II	0,250 mm	-6,25 a -8,00
Cono III	0,300 mm	-8,25 a -10,00
Cono IV	0,350 mm	-10,25 a -12,00

El uso de este nomograma permite asociar a ambos: el grado evolutivo del queratocono y la ametropía existente. De esa forma, si tenemos un paciente con cono incipiente y alta miopía, utilizaremos un anillo de 350 micras, y así sucesivamente.

Figura 24: Primera generación del nomograma de Ferrara

4.3.2.2.2. Segunda Generación

La segunda generación del nomograma (2002 – 2006) llevaba en consideración la distribución del área ectásica, además del equivalente esférico para la selección de los anillos. Los pacientes con elevado equivalente esférico tenían implantados segmentos más gruesos. Sin embargo, en muchos pacientes con queratocono, la miopía no era inducida por la ectasia, sino por el crecimiento anteroposterior del ojo. Por eso, en muchos casos se observaba una hipercorrección debido al implante de segmentos gruesos en queratoconos iniciales.

Map	Distribution of Ectasia	Description
	0 % / 100%	All the ectatic area is located at one side of the cornea
	25 % / 75%	75% of the ectatic area is located at one side of the cornea
	33 % / 66%	66% of the ectatic area is located at one side of the cornea
	50 % / 50%	The ectatic area is symmetrically distributed on the cornea

Figura 25: Segunda generación del nomograma de Ferrara

4.3.2.2.3. Tercera Generación

En la tercera generación del nomograma (2006 – 2009), la selección del segmento dependía de otros factores: distribución del área ectásica en la córnea, del astigmatismo topográfico y del espesor corneal. En este momento, el segmento pasa a ser considerado como procedimiento ortopédico, o sea, pasa a buscar la disminución de la deformidad de la córnea, y la refracción deja de ser importante para la selección de los segmentos. En dicho momento se determinó que el espesor del segmento no debe exceder el 50 % del espesor corneal en el trayecto del anillo (ley de los espesores).

4.3.2.2.4. Cuarta Generación

La cuarta generación del nomograma (de 2009 hasta hoy) está focalizada en la asfericidad corneal, tema discutido anteriormente. La mayoría de los estudios está de acuerdo en que el valor de la asfericidad (Q) normal, en la zona óptica de 4,5 mm, puede variar de -0,01 a -0,80 (Silva et al, 2000).[68] El valor más aceptado actualmente como normal en poblaciones de individuos adultos es de aproximadamente -0,23 ± 0,08 (Yebra-Pimentel et al, 2004).[69] El seguimiento de un elevado número de casos posibilitó evaluar las alteraciones inducidas en el valor de la asfericidad por combinaciones de diferentes segmentos con diferentes espesores.

Los resultados obtenidos con este nomograma han sido satisfactorios (Ferrara et al, 2011)[42], además de reproductibles. Se utilizan ahora segmentos más delgados que antes a fin de obtener resultados iguales o mejores a los que se tenía utilizando los nomogramas anteriores. Además, la elección de los segmentos ahora es más simple, pues depende de un solo parámetro.

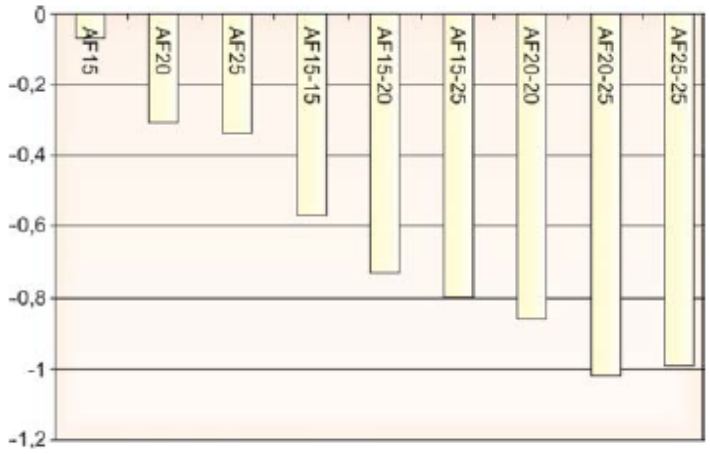


Figura 26: Cuarta generación del nomograma de Ferrara - Variación de la asfericidad según segmento o par de segmentos implantados.

	Q	K	Cyl
140 (arc)	↑	↓	↓↓↓
160 (arc)	↑↑	↓↓	↓↓
210 (arc)	↑↑↑	↓↓↓	↓

Cuadro 1: Relación de las modificaciones inducidas por los segmentos con relación a la asfericidad, al astigmatismo y a la queratometría de acuerdo con el segmento implantado.

4.3.2.3. Características de los Anillos de Ferrara

El anillo de Ferrara presenta las siguientes características:

- confeccionado en Acrílico CQ
- diámetro total (externo) de 6,2 mm
- sección triangular
- base de 600 micras
- espesuras variables
- segmentos de 140, 160, 210 y 320 grados de arco
- 1 orificio en cada extremidad

4.3.2.4. Mecanismo de acción de los Anillos de Ferrara

El anillo corneal obedece a los postulados de Barraquer y Blavatskaya, según los cuales la adición en la periferia de la córnea resulta en aplanamiento de la misma, y el diámetro del anillo determina cuánto la córnea será aplanada. De esa manera, cuanto más tejido adicionado (espesor del anillo) y cuanto menor el diámetro, mayor será la corrección miópica obtenida.[49,50]

De sus estudios resultan observaciones adicionales:

- Aplanamiento central y periférico de la córnea, preservando su asfericidad;

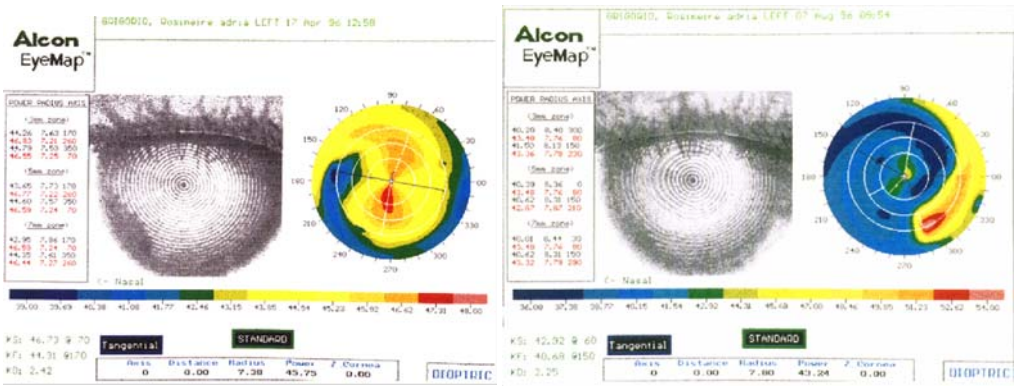


Figura 27: aplanamiento de la córnea después del implante del Anillo de Ferrara

- Disminución de la altura de la cámara anterior, demostrado por la biomicroscopía ultrasónica (UBM);

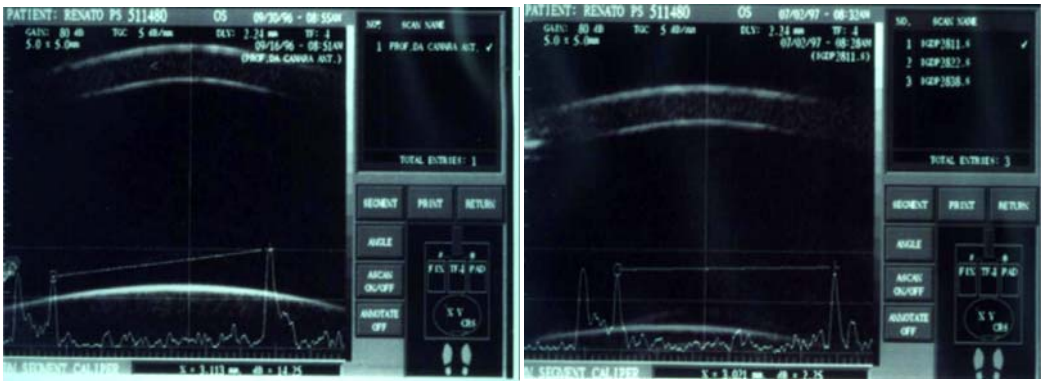


Figura 28: Disminución de la altura de la cámara anterior después del implante de los Anillo de Ferrara.

- Regularización de la superficie de la córnea a través de un movimiento de báscula de los segmentos, provocado por la superficie plana de la base del anillo. Ese movimiento resulta en un aplanamiento de la córnea en las puntas de los segmentos y en un encorvamiento de la misma en la región correspondiente al cuerpo del anillo;

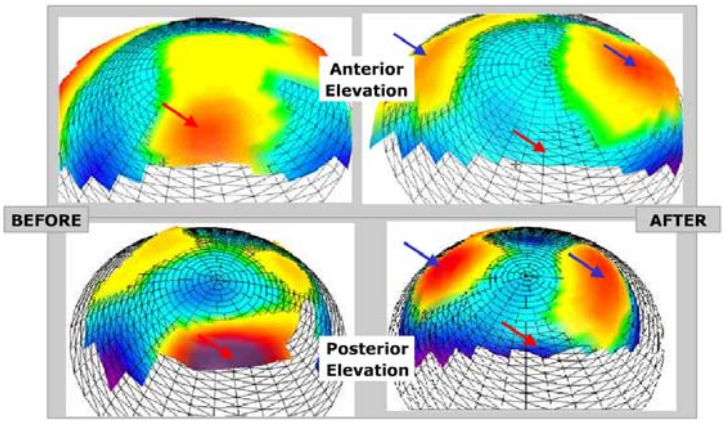


Figura 29: Mapas de elevación anterior y posterior en 3D. Las flechas en rojo indican la región de la incisión (inferior) y las flechas en azul muestran la elevación de las puntas de los anillos.

- Paralización de la evolución del queratocono, disminución de las opacidades presentes en el ápice del cono, reducción de síntomas como prurito, fotofobia, dolor ocular y/o incomodidad;

- Falta de correspondencia entre agudeza visual sin corrección postoperatoria y ametropía residual. Algunas veces es posible observar pacientes con buena visión, a pesar de los valores elevados de refracción;

*Datos del Software

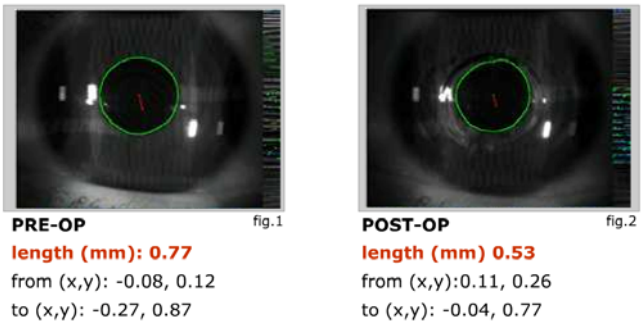


Figura 30: Modificación del reflejo de fijación con relación al centro de la pupila, antes y después del implante de los anillos de Ferrara.

- El efecto prismático generado por la sección triangular disminuye los fenómenos de halos y ofuscamiento que podrían resultar del pequeño diámetro de la ortesis.

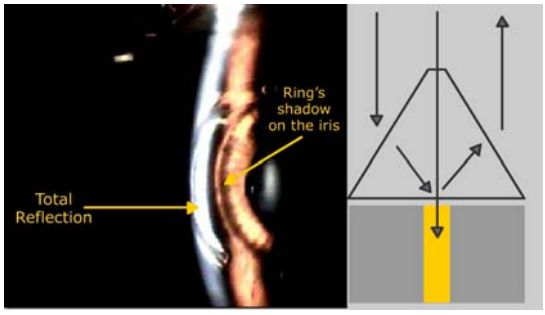


Figura 31: Efecto prismático del segmento.

4.3.2.5. Indicaciones y Contra-indicaciones de los Anillos de Ferrara

4.3.2.5.1. Indicaciones

El implante de los anillos de Ferrara está indicado para las siguientes situaciones:

1. Miopías moderadas y elevadas hasta 11 dioptrías;
2. Queratocono;

3. Degeneración Marginal Pelúcida
4. Astigmatismos irregulares elevados post trasplante de córnea;
5. Astigmatismos irregulares post queratotomía radial;
6. Ectasia corneal post Excimer Laser

El pequeño diámetro del anillo, además de permitir correcciones bastante elevadas, tanto de miopía como de astigmatismo, lo hace adecuado para la corrección de patologías oculares como queratocono, astigmatismos irregulares de cualquier etiología y ectasias corneales post Excimer Laser. Con respecto al queratocono, debe ser considerado el grado evolutivo, su tolerancia, o no, a lentes de contacto semirrígidas permeables al gas, y la estabilidad, o no, del queratocono.

4.3.2.5.2. Contraindicaciones

El implante de los anillos de Ferrara es contraindicado en las siguientes situaciones:

1. Conos muy avanzados, con curvaturas superiores a 75 dioptrías y opacidades apicales importantes;
2. Hidropsía;
3. En los casos de astigmatismos elevados post trasplante de córnea, el anillo no deberá ser implantado si la córnea donada se encuentra muy descentrada;
4. Pacientes con atopia intensa deberán ser tratados previamente;
5. Cualquier proceso infeccioso en actividad, local o sistémico.

4.3.2.6. Cirugía del implante de los anillos de Ferrara

4.3.2.6.1. Instrumental

Para la realización de la cirugía son necesarios los siguientes instrumentos:

- espátula doble y simples de Ferrara,
- Suarez spreader,
- marcador de zona óptica de 3,5,7 mm,

- marcador de incisiones radiales de 8 mm,
- gancho de Sinskey de 0.20 mm,
- micrómetro de diamante con lámina de Ferrara.

Figura 32: Instrumentales para el implante de los Anillos de Ferrara

4.3.2.6.2. Técnica Quirúrgica

Anestesia: la cirugía se hace con anestesia tópica después de la miosis con pilocarpina a 2%.

Se hace la marcación del eje visual con base en el reflejo del filamento de la lámpara del microscopio en la córnea, independientemente de la pupila. Es necesario tener en cuenta que, en el queratocono, el ápice suele estar a menudo desplazado inferiormente, y el anillo deberá quedar situado en la base del cono, donde sea que se encuentre.

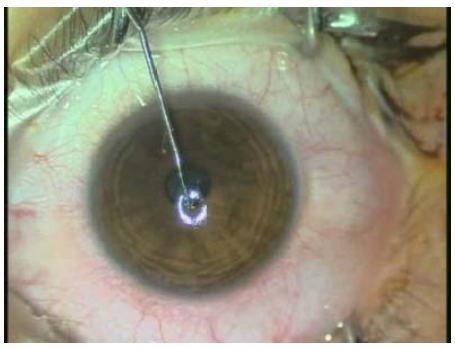


Figura 33: Marcación del eje visual en el primero reflejo de Purkinje en la córnea

Se delimita la zona óptica de 5,00 mm con violeta genciana y se marca el eje más curvo de la córnea, donde será realizada la incisión radial, con bisturí apropiado y calibrado

para un 80% de la espesura de la córnea en el local de la incisión. A seguir, se aplica el delaminador de córnea para realizar el bolso por donde será introducida la espátula de Ferrara para la confección del túnel. La introducción de los segmentos es simples y la cirugía termina con el posicionamiento adecuado de estos segmentos dentro de los túneles.

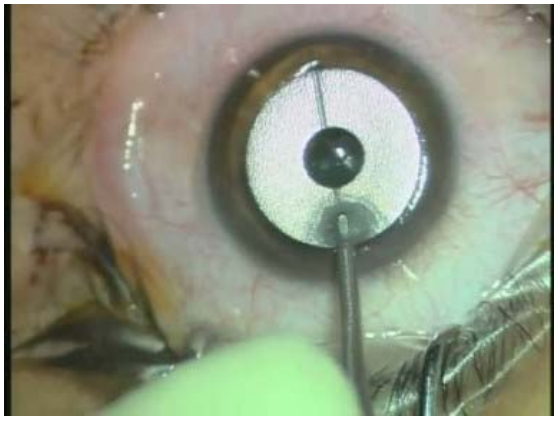


Figura 34: Marcación de la zona óptica de 5 mm.

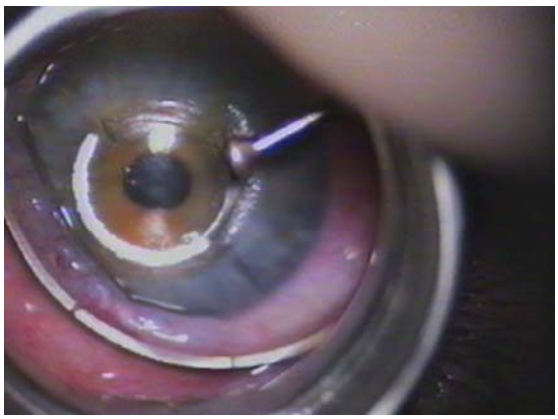


Figura 35: Creación del túnel estromal.

4.3.2.7. Complicaciones

La incidencia de complicaciones después de la curva de aprendizaje es muy baja. Las principales complicaciones son:

4.3.2.7.1. Infección: pueden ocurrir en dos situaciones: en el postoperatorio inmediato, o tardíamente asociado al uso de lentes de contacto blandas. En el primer caso, la conducta consiste en remover el

segmento del túnel acometido e instituir terapia intensiva con antibióticos. En las infecciones tardías puede o no haber necesidad de remover el segmento, dependiendo de la pérdida o no de sustancia corneal y de la intensidad de la infección.

Figura 36: Infección en la punta del Anillo.

4.3.2.7.2. Migración: habitualmente los pacientes portadores de queratocono son atópicos y presentan prurito intenso. El acto de rascarse los ojos puede desplazar los segmentos, llevándolos hacia cerca de las incisiones y posibilitando la extrusión de los mismos;

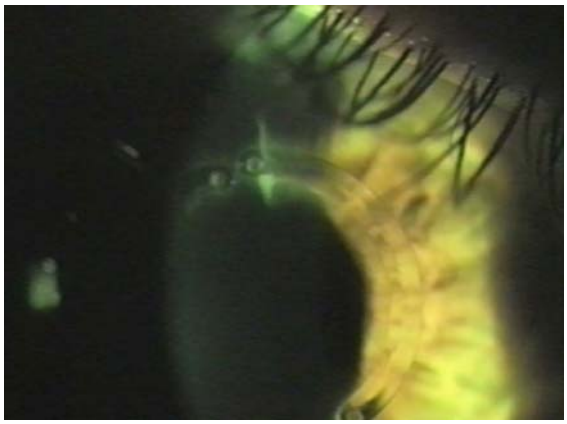


Figura 37: Migración de la punta del Anillo por debajo de la incisión.

4.3.2.7.3. Extrusión: resulta de una implantación superficial o de la migración de los segmentos. Esta situación se puede prevenir a través de los exámenes de rutina, removiendo el segmento antes que el mismo se exponga y reimplantándolo después de algún tiempo.

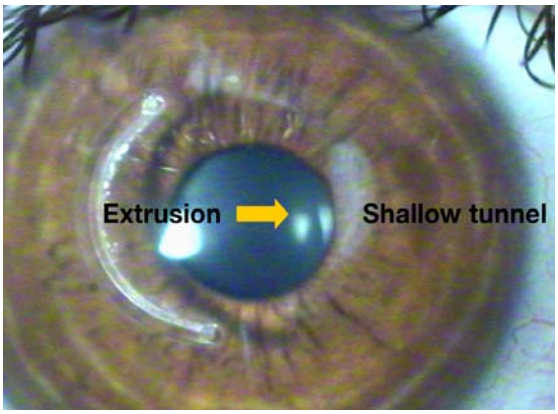


Figura 38: Extrusión del segmento, secundario a la confección de túnel superficial.

4.3.2.7.4. Descentralización: el anillo deberá estar situado, obligatoriamente, en la base del cono. Por lo tanto, la centralización del procedimiento deberá ser realizada siempre llevando en cuenta el reflejo.

4.3.2.7.5. Halos y Reflejos: pueden estar presentes en los primeros meses, mas raramente son referidos por los pacientes. Cuando y sí es necesario, se pueden prescribir mióticos suaves. La incidencia de pacientes con esta queja es muy pequeña. En la mayoría de los caso, el paciente sólo relata este fenómeno cuando se le pregunta;

4.3.2.7.6. Hipo e Hipercorrección: son complicaciones relativas si consideramos que el objetivo principal de la cirugía es ortopédico y que la corrección visual final deberá ser realizada utilizando los métodos convencionales. La mayoría de los casos queda hipo corregido, si es analizado el componente esférico. Los astigmatismos, en general, son híper corregidos con la inversión del eje del astigmatismo;

4.3.2.7.7. Opacidades perianulares; son pequeños depósitos blancos, opacos, que se depositan a lo largo de la fase interna del anillo. No tienden a crecer y no perjudican el desempeño visual, siendo sólo antiestéticos al examen a la lámpara de hendidura.

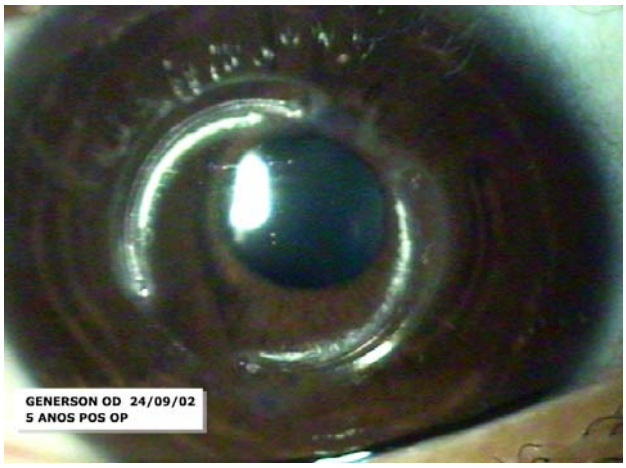


Figura 38: opacidades perianelares

5. Justificación

El queratocono es una enfermedad que puede llevar a la ceguera en las edades más productivas de la vida. Aunque cada vez se conoce mejor su fisiopatología, no tiene etiología conocida y los tratamientos se basan en prevenir los factores de riesgo y en medidas de corrección quirúrgica. Respecto a la corrección con cirugía, el queratocono sigue siendo una de las principales indicaciones de trasplante de cornea y se están evaluando alternativas al trasplante, como el entrecruzamiento del colágeno corneal con luz ultravioleta y el implante de ICRS. La clínica del Dr. Paulo Ferrara tiene una larga experiencia de más de 20 años en el implante de ICRS y cuenta con las historias clínicas y bases de datos que pueden ser soporte para el análisis de resultados con masa crítica suficiente de pacientes y seguimiento adecuado. Por ello, queda justificado el intentar analizar los resultados del implante de ICRS con objeto de conocer los efectos de los mismos sobre la agudeza visual, cambios en las medidas corneales, con especial atención al astigmatismo y en la progresión del queratocono.

6. Hipótesis de Trabajo

El implante de segmentos de anillos intraestromales en los pacientes con queratocono (adultos y niños) permite mejorar la agudeza visual, cambiar los valores de medidas corneales y alterar la evolución de la enfermedad. Además, como aplicación práctica en queratoplastias, pueden ser empleados para el manejo del astigmtismo.

7. Objetivos

1. Evaluar los resultados a largo plazo del implante de anillos de Ferrara en cuanto a los cambios en la agudeza visual y los cambios en valores de las medidas corneales con especial atención al astigmatismo y los valores queratométicos;

2. Evaluar el efecto de los ICRS en la evolución del queratocono;

3. Evaluar el efecto de los ICRS en la corrección del astigmatismo tras queratoplastia;

4. Evaluar los resultados de los ICRS implantados en niños con queratocono.

8. Pacientes, Material de Trabajo y Método

8.1. Diseño del Estudio

Estudio observacional, retrospectivo, de análisis de resultados de los pacientes con queratocono intervenidos de cirugía de ICRS y de pacientes con queratoplastia a los que se ha implantado ICRS para el control del astigmatismo

8.2. Pacientes

Las cirugías de los pacientes con queratocono fueron realizadas en los pacientes que acudieron a la clínica de Ojos Dr. Paulo Ferrara, en Belo Horizonte, Minas Gerais, Brasil, y se incluyeron pacientes desde julio de 1996 a Abril de 2014.

El estudio sobre la corrección del astigmatismo post trasplante de córnea en pacientes implantados con los ICRS fue realizado en los pacientes que acudieron a la clínica de Ojos Dr. Enio Coscarelli, en Belo Horizonte, Minas Gerais, Brasil, en el periodo de mayo de 2005 a septiembre de 2009

8.3. Clasificación del Queratocono

El queratocono fue clasificado de acuerdo con la clasificación de Amsler-Krumeich,[70] que combina efecto refractivo inducido por la ectasia, lecturas queratométricas , signos clínicos y paquimetría.

8.4. Indicación del implante de ICRS en queratocono

8.4.1. Criterios de inclusión

La principal indicación para el implante de los ICRS fue intolerancia a las lentes de contacto semirrígidas y/o progresión de la ectasia , definida por empeora de la agudeza visual con y sin corrección, intolerancia progresiva a las lentes de contacto y empeora progresiva de la curvatura corneal documentada por topografía de córnea (aumento del promedio de la queratometría de 1 D en un año)

8.4.2. Criterios de Exclusión

Los criterios de exclusión fueron queratoconos avanzados con la queratometría mayor que 60 D, opacidades apicales significantes, cicatrices, hidropsía, córneas delgadas con paquimetría inferior a 300 µm en el trayecto del anillo, atopia intensa o proceso infeccioso activo, local o sistémico.

8.5. Implante de ICRS en queratoplastias

8.5.1. Criterios de inclusión

Se incluyeron en el estudio pacientes sometidos al implante de los ICRS para la corrección del astigmatismo post trasplante de córnea.

Los criterios de inclusión fueron enjerto trasparente, con astigmatismos entre 2,5 y 8D, intolerantes a lentes de contacto. Todos los pacientes tenían mas de dos años de post operatorio de trasplante de córnea en el momento del implante de los anillos intracorneales, y por los menos 1 año de seguimiento de pos operatorio después de haber implantado los anillos

8.5.2. Criterios de Exclusión

Los criterios de exclusión fueron queratometría mayor que 60D, opacidades apicales significantes, cicatrices, córneas delgadas con paquimetría inferior a 300µm en el trayecto del anillo, atopia intensa o proceso infeccioso activo, local o sistémico.

8.6. Técnica Quirúrgica y estrategia de implante de ICRS

Todos los pacientes fueros operados por la técnica manual y por el mismo cirujano, Dr. Paulo Ferrara, con excepción de los pacientes del estudio de queratoplastia y astigmatismo, que fueron operados por el mismo cirujano, Dr Sandro Coscarelli, por la técnica manual.

La cirugía se hace con anestesia tópica después de la miosis con pilocarpina a 2%.

Se hace la marcación del eje visual con base en el reflejo del filamento de la lámpara del microscopio en la córnea, independientemente de la pupila (primero reflejo de Purkinje), utilizándose del Sinkey hook. Se delimita la zona óptica de 5,00 mm con violeta genciana y marcamos el eje más curvo de la

córnea, donde será realizada la incisión radial, con bisturí apropiado y calibrado para 80% de la espesura de la córnea en el local de la incisión. A seguir, se aplica el delaminador de córnea para realizar el bolso por donde será introducida la espátula de Ferrara para confección del túnel. La introducción de los segmentos es simples y la cirugía termina con el posicionamiento adecuado de estos segmentos dentro de los túneles. La técnica fue la misma en todos los pacientes operados.

La selección del espesor y del tamaño del arco de los anillos se hizo de acuerdo con el nomograma de Ferrara vigente en el momento de la cirugía tal y como se describe en la introducción. El nomograma tenía en cuenta la posición del área de la ectasia en la córnea, el astigmatismo topográfico y la paquimetría corneal en el trayecto del anillo.

8.7. Análisis de los resultados:

Los parámetros evaluados fueron agudeza visual con corrección, sin corrección, queratometría, paquimetría central. La asfericidad y volumen corneal también fueron estudiados. Los datos fueron obtenidos a través del topógrafo de córnea y del Pentacam®.

Los parámetros evaluados en el estudio astigmatismo y queratoplastia fueron agudeza visual con corrección, sin corrección, queratometría, equivalente esférico, astigmatismo topográfico y valores de k mínimo y máximo. Los datos fueron obtenidos a través del topógrafo de córnea (CT4000 Corneal Topographer, Eyetech, Inc.).

El análisis estadístico fue realizado con la utilización del GraphPad Instat 3 para Macintosh (versión 3,1ª; GraphPad Software, Inc., La Jolla, CA). El test t de Student para pares pareados fue utilizado para comparar los datos pre y post operatorios.

El análisis estadístico para el estudio de queratoplastia y astigmatismo incluyó el test t de Student, transformación de Welch, testes no paramétricos de de Mann-Whitney, utilizándose del Instat 3 para Macintosh (versión 3,1ª;

GraphPad Software, Inc., La Jolla, CA). El análisis vectorial fue realizado utilizándose del SigmaPlot software (SSP Inc.) el análisis del seguimiento clínico fue realizado con el software basado en internet de análisis refractiva (Zubisoft GmbH).

En cada capitulo y en las publicaciones se detalla la metodología empleada en en cada caso.

9. CAPITULO I. Resultados a largo plazo de la implantación de anillos de Ferrara en pacientes con queratocono

Se resumen a continuación los trabajos de investigación clínica relacionados con el análisis de resultados a largo plazo del implante de ICRS y que han sido objeto de publicación en las siguientes publicaciones que se adjuntan:

1. Ferrara G, Torquetti L, Ferrara P, Merayo-Lloves J. Intrastromal cornal ring segments: visual outcomes from a large case series. Clinical Experiment Ophthalmol 2012;40(5):433-439
2. Torquetti L, Ferrara G, Almeida F, Ferrara P, Merayo-Lloves J. Clinical outcomes after intrastromal corneal ring segments reoperation in keratoconus patients. Int Ophthalmol 2013;6(6):796-800
3. Torquetti L, Ferrara G, Ferrara P. Predictors of Clinical Outcomes after Intraestromal corneal Ring Segments Implatation. Int Keratoco Ectatic Corneal Dis 2012;1(1):26-30
4. Torquetti L, Ferrara G, Almeida F, Cunha L, Araujo LPN, Machado AP, Lyra JM, Merayo-Lloves J, Ferrara P. Intrastromal Corneal Ring Segment Implantation in Patients with Keratoconus: 10-Year Follow-Up. J Refract Surg 2014;30(1)22-6

El queratocono es una patología bilateral y asimétrica, no inflamatoria por definición, que cursa con adelgazamiento progresivo de la córnea, seguido por el aumento de su curvatura y protrusión, resultando en elevados grados de astigmatismo irregular y miopía y, consecuentemente, baja de la agudeza visual. Su presentación es variable, y ocurre en general en la segunda década de vida, pudiendo progresar hasta la tercera o cuarta década de vida (Rabinowitz 1998).[71]

Las primeras indicaciones de los anillos intracorneales fueron para la corrección de miopías moderadas y elevadas (FERRARA, 1991, NOSE W, 1996)[41,63], pero como el objetivo refractivo resultó poco predecible, en 1996 (FERRARA, 1996) se cambió la indicación de los anillos por la corrección de córneas irregulares. Se ha utilizado, desde entonces, el implante de los anillos intracorneales para el tratamiento de las ectasias corneales, principalmente en el queratocono. Los ICRS actúan disminuyendo las

irregularidades corneales y los valores de queratometría, además de aumentar los valores de asfericidad y del espesor corneal. Es un procedimiento seguro y poco invasivo que preserva el eje visual.

Los resultados de las alteraciones inducidas por los implantes intracorneales en la córnea enferma son la mejora de la calidad visual, añadida de la mejora de la agudeza visual con y sin corrección. Otro efecto benéfico que se pudo observar en los pacientes portadores de queratocono implantados con los anillos intracorenales fue la estabilización de la patología, además de la mejora de los síntomas del paciente, como la fotofobia, el prurito y el lagrimeo.

Muchos estudios fueron realizados con la finalidad de se evaluar a largo plazo los resultados del implante de los anillos de Ferrara. El estudio Intrastromal cornal ring segments: visual outcomes from a large case series[42] presentó los resultados visuales y topográficos de 1073 ojos de 810 pacientes implantados con los anillos de Ferrara para la corrección de queratocono. Los criterios de inclusión fueron la evidencia de progresión de la ectasia e intolerancia a lentes de contacto semirrígidas permeables al gas. Se excluyeron del estudio a los pacientes con queratoconos muy avanzados, con curvaturas mayores que 62 dioptrías, opacidades apicales o bien espesor corneal por debajo de 300 μm.

Los pacientes fueron separados en 2 grupos, de acuerdo con el fenotipo del queratocono: paracentral (oval) (grupo I) o central (pezón o nipple) (grupo II). El número, tamaño de arco y espesor de los anillos fue determinado por el nomograma previamente descrito.[41,72]

El promedio de seguimiento de los grupos I y II fue de 23,8 y 22,9 meses, respectivamente. (Tabla I). La agudeza visual ―con y sin corrección― de los dos grupos mostró una mejora estadísticamente significativa. Se observó un aumento del espesor de la córnea, como también de la asfericidad en todos los pacientes, estadísticamente significativo. El equivalente esférico también disminuyó en el postoperatorio. (Tabla 2)

	Group 1	Group 2
Eyes (*n*)	972	101
Age (years)	29.4 ± 9.4 (range 17 to 59)	30.2 ± 8.7 (range 14 to 64)
Sex (male/female)	57/43	51/49
Follow-up (months)	23.8 ± 12.2	22.9 ± 15.1

Tabla 1: Grupo I de pacientes implantados con segmentos de 160° de arco, y Grupo II de pacientes implantados con segmentos de 210° de arco

	Group 1			Group 2			Unpaired *t*-test (between groups)
	Preoperative	Postoperative	*P*†	Preoperative	Postoperative	*P*‡	*P*
UCVA	20/220	20/80	0.00001	20/350	20/130	0.001	0.038
BCVA	20/100	20/40	0.00023	20/110	20/60	0.0003	0.0034
Asphericity	−0.88 ± 0.52	−0.35 ± 0.55	0.00004	−1.17 ± 0.47	−0.56 ± 0.56	0.00004	0.0031
Spherical equivalent (D)	−3.99 ± 4.22	−2.26 ± 3.09	0.0002	−8.52 ± 5.63	−4.14 ± 4.37	0.0002	0.0010
Keratometry (D)	49.18 ± 4.42	45.72 ± 3.72	0.00003	51.92 ± 5.91	48.10 ± 4.96	0.0001	0.0001
Pachymetry (µm)	448 ± 44.8	465 ± 49.2	0.0001	418 ± 53.4	435 ± 56.6	0.0002	0.0001

Tabla 2: Preoperatorio y ultimo postoperatorio de pacientes implantados con los anillos de Ferrara

Las complicaciones observadas en el postoperatorio fueron pocas (3,82%), y la principal fue la hipo corrección (16 ojos). (Tabla 3).

Complication	Treatment	Eyes (%)
Undercorrection	Implantation of additional segment	16 (1.49)
Overcorrection	Segment removal and reimplantation	11 (1.02)
Extrusion	Segment removal	6 (0.56)
Malposition	Segment repositioning	4 (0.37)
Progressive corneal steepening	Keratoplasty	2 (0.18)
Ring neovascularization	Bevacizumab	2 (0.18)
Total		41 (3.82)

Tabla 3: Complicaciones después del implante de anillos de Ferrara

Los pacientes que presentaron complicaciones fueron sometidos a una nueva cirugía para el implante de un segmento adicional (16 ojos) en hipo correcciones, la remoción de segmentos en caso de hipercorrección (6 ojos), sustitución de segmentos (11 ojos) y reposicionamiento (4 ojos). Se observó una mejora de estos pacientes recuperados estadísticamente significativa (Tabla 4).

	Preoperative	Postoperative	*P*
UCVA	20/300	20/80	0.005
BCVA	20/160	20/50	0.0002
Asphericity	–0.84 ± 0.74	–0.35 ± 0.81	0.15
Spherical equivalent (D)	–4.64 ± 4.87	–3.04 ± 3.45	0.137
Keratometry (D)	49.33 ± 4.19	46.16 ± 3.90	0.0001
Pachymetry (µm)	450 ± 42.9	469 ± 40.8	0.0001

Tabla 4: Preoperatorio y último postoperatorio de pacientes sometidos a reimplante, retiro o cambio de ICRS.

El estudio Clinical outcomes after intrastromal corneal ring segments reoperation in keratoconus patients[73] fue realizado con la finalidad de evaluar los resultados de estos pacientes sometidos a la reoperación. El promedio de intervalo de tiempo entre la primera cirugía y la reoperacion fue de 8,4 meses, y el promedio de tiempo de seguimiento tras la reoperación fue de 30,5 meses.

Se observó una mejora del promedio de la agudeza visual sin corrección post operatoria de 20/300 para 20/80 (p=0.005), una mejora del promedio de la agudeza visual con corrección de 20/160 para 20/50 (p=0.0002), el promedio de la queratometría disminuyo de 49.33 D para 46.16 D (p=0.0001), el aumento del promedio de la paquimetría en el punto más delgado de 450 µm para 469 µm (p=0.0001). Se observó una mejora de los valores de asfericidad y de equivalente esférico , pero esas alteraciones no fueron estadísticamente significativas.

En el estudio Predictors of Clinical Outcomes after Intraestromal corneal Ring Segments Implatation, Torquetti et al,[74] con el mismo grupo de pacientes, hizo otras dos evaluaciones independientes del comportamiento del implante de los ICRS, de acuerdo con la edad de los pacientes y con el grado evolutivo del queratocono.

Los pacientes fueron divididos en 4 grupos de acuerdo con la edad: < de 20 años, de 21 a 30 años, de 31 a 40 años y mayores de 40 años. (Tabla 5). Los pacientes también fueron divididos en 4 grupos de acuerdo con el grado evolutivo del queratocono, de acuerdo con el promedio de K: Grado I (Km < 46D), grado II (46 < Km < 52D), grado III (52 < Km < 60D) o grado IV (Km > 60 D). Los mismos criterios fueron utilizados para este estudio.

Age (years)	*Eyes (n)*	*Age (Y)—(range)*	*Sex (F/M)*
<20	98	17 ± 2.25 (10-19)	68/30
20-30	546	23 ± 3.93 (20-29)	224/302
30-40	292	33 ± 2.96 (30-39)	107/195
>40	142	47 ± 6.85 (40-74)	88/59

Tabla 5: Datos de los pacientes estudiados

El promedio del seguimiento de los pacientes fue de 23,8 ± 12,2 meses. La mayoría de los pacientes tenían entre 21 y 30 años. Los pacientes más jóvenes presentaban valores más negativos de asfericidad, aunque los de queratometría fueran semejantes en todos los grupos. El aplanamiento de la queratometría, así como el aumento de los valores de la asfericidad fueron más acentuados en los pacientes con menos de 20 años. (Tabla 6). La reducción de la queratometría fue estadísticamente significativa en todos los grupos.

Age (years)	*Preoperative Km (D)*	*Postoperative Km (D)*	*p-value*	*ΔKm (D)*	*Preoperative Q (μm)*	*Postoperative Q (μm)*	*p-value*	*ΔQ (μm)*
<20	49.75 ± 4.83	45.80 ± 3.80	<0.01	3.95	–1.09 ± 0.63	–0.36 ± 0.63	<0.01	–0.73
21-30	49.43 ± 4.54	45.86 ± 3.82	<0.01	3.57	–0.90 ± 0.45	–0.38 ± 0.51	<0.01	–0.52
31-40	49.51 ± 4.13	46.11 ± 3.62	<0.01	3.40	–0.85 ± 0.48	–0.39 ± 0.55	<0.01	–0.46
>40	49.54 ± 4.60	46.40 ± 4.30	<0.01	3.14	–0.77 ± 0.57	–0.29 ± 0.70	<0.01	–0.48

p-values = mean ± SD

Tabla 6: Datos pre y postoperatorios de acuerdo con los valores de K y Q

El promedio de la agudeza visual con y sin corrección mejoró en todos los grupos (p<0,001, Tabla 7). La mejora de la AV con corrección fue más acentuada en los pacientes entre 21 y 30 años de edad y en los pacientes con queratocono grado I.

Age (years)	*Preoperative* UDVA	*Postoperative* UDVA	*p-value*	*Preoperative* CDVA	*Postoperative* CDVA	*p-value*
>20	20/240	20/100	<0.01	20/110	20/55	<0.01
21-30	20/240	20/80	<0.01	20/105	20/40	<0.01
31-40	20/170	20/70	<0.01	20/110	20/47	<0.01
>40	20/270	20/70	<0.01	20/105	20/50	<0.01
Grades						
I	20/210	20/60	<0.01	20/60	20/35	<0.01
II	20/220	20/80	<0.01	20/94	20/40	<0.01
III	20/250	20/100	<0.01	20/400	20/55	<0.01
IV	20/800	20/200	<0.01	20/400	20/90	<0.01

p-values = Mean ± SD

Tabla 7: Datos pre y postoperatorios de la UCVA y CDVA, de acuerdo con la edad y el grado de queratocono

Torquetti et al[15] (2009) publicaron un estudio con pacientes operados con ICRS para el tratamiento de queratocono. Los pacientes operados presentaban evidencias de progresión de la ectasia y/o intolerancia a lentes de contacto semirrígidas permeables al gas. Se excluyeron del estudio los casos de queratoconos muy avanzados, con curvaturas mayores que 62 dioptrías, opacidades apicales o bien espesor corneal por debajo de 300 μm.

Se estudió en este trabajo la agudeza visual con y sin corrección y la queratometría pre y postoperatoria. Las cirugías fueron realizadas por el mismo cirujano (Paulo Ferrara), y la selección de los anillos fue determinada por el nomograma previamente descrito. [41,72]

El seguimiento de los pacientes varió entre 5 y 12 años de postoperatorio e incluyó 35 ojos de 28 pacientes. Se observó un aplanamiento de todos los ojos a la topografía de córnea, estadísticamente significativa. (Figura 1) La agudeza visual sin corrección mejoró hasta el cuarto año postoperatorio y después permaneció estable hasta el quinto año postoperatorio. La agudeza visual mejoró hasta el tercer año postoperatorio, permaneciendo estable hasta en quinto año postoperatorio. (Figura 2).

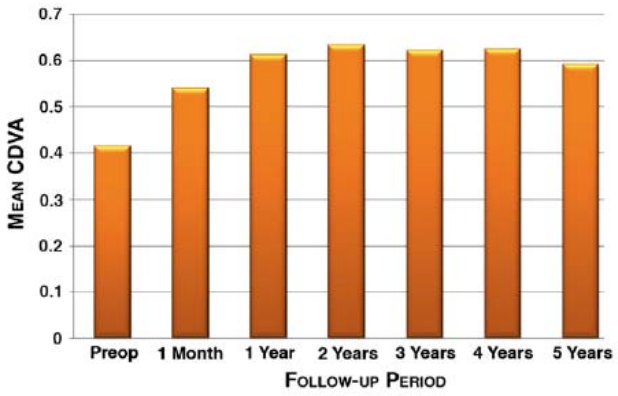


Figura 1: Agudeza visual con corrección a lo largo de los 5 años de seguimiento

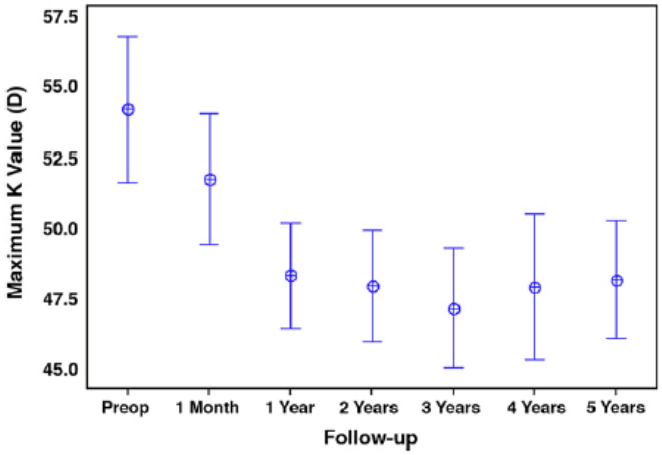


Figura 2: Promedio de K máximo a lo largo de los 5 años de seguimiento

La estabilidad a largo plazo encontrada en este trabajo puede ser comparada a otros estudios de implante de ICRS en la literatura. (Tabla 8)

Table 4. Comparison of Ferrara and Intacs ICRS studies with long-term results.

	Mean ± SD								
	Preoperative			Postoperative					
				1 Year			2 Years		
Parameter	Present Study (Ferrara)	Alio et al.[23] (Intacs)	Colin and Mallet[25] (Intacs)	Present Study (Ferrara)	Alio et al.[23] (Intacs)	Colin and Mallet[25] (Intacs)	Present Study (Ferrara)	Alio et al.[23] (Intacs)	Colin and Mallet[25] (Intacs)
Maximum K (D)	54.07 ± 7.34	51.07 ± 3.62	53.6 ± 5.8	48.22 ± 4.73	47.84 ± 3.73	48.5 ± 5.6	47.84 ± 4.98	47.69 ± 3.80	48.7 ± 5.2
Minimum K (D)	48.49 ± 5.06	45.84 ± 3.48	46.7 ± 6.6	43.89 ± 4.59	43.76 ± 3.59	44.3 ± 5.4	44.01 ± 3.83	44.10 ± 2.55	44.9 ± 4.9
Mean K (D)	51.27 ± 5.91	48.46 ± 3.27	50.1 ± 5.6	45.88 ± 4.52	45.80 ± 3.52	46.4 ± 5.3	45.71 ± 4.20	45.90 ± 2.38	46.8 ± 4.9
UDVA	0.15 ± 0.15	NA	0.10*	0.29 ± 0.17	NA	0.20*	0.29 ± 0.19	NA	0.20*
CDVA	0.41 ± 0.25	0.46 ± 0.20	0.35*	0.61 ± 0.24	0.66	>0.50*	0.63 ± 0.22	0.66	>0.50*

CDVA = corrected distance visual acuity; K = keratometry reading; NA = not available UDVA = uncorrected distance visual acuity
*Approximate data; mean not given in the original study, only the range reported

Tabla 8: Comparación de resultados de implante de anillos de Ferrara e Intacs a largo plazo

En 2014, Torquetti et al[45] publicó Intrastromal Corneal Ring Segment Implantation in Patients with Keratoconus: 10-Year Follow-Up, con seguimiento a los 5 y 10 años de post operatorio de pacientes implantados con ICRS para el tratamiento de queratocono. Los pacientes operados tenían intolerancia a lentes de contacto semirrígidas permeables al gas y/o presentaban progresión de la ectasia. Se excluyeron del estudio los casos con curvaturas mayores que 60 dioptrías, opacidades apicales o bien espesor corneal por debajo de 300 µm.

Fueron evaluados en este trabajo la agudeza visual con y sin corrección, la queratometría pre y postoperatoria, así como la variación del espesor corneal después del implante de los ICRS. Las cirugías fueron realizadas por el mismo cirujano (Paulo Ferrara), y la selección de los anillos fue determinada por el nomograma previamente descrito. [41,72]

Treinta y seis ojos de 30 pacientes operados entre junio de 1996 y enero de 2002 fueron evaluados. Se observó una disminución de los valores de la queratometría y del espesor corneal a los 5 años de seguimiento, además de una mejora de la agudeza visual estadísticamente significativa. Sin embargo, cuando comparamos los resultados a los 5 años de seguimiento con los resultados a los 10 años, observamos que las variaciones de los valores estudiados no fueron estadísticamente significativos. (Tabla 9) (Figura 3). El 56,5% de los pacientes ganó 2 o más líneas de visión a los 5 años, mientras que el 66,7 % de los pacientes ganó 2 o más líneas de visión a los 10 años de seguimiento.

TABLE 1
Preoperative and 5- and 10-Year Follow-up Examination Data of Eyes Implanted With Ferrara Intrastromal Corneal Ring Segments

Parameter	Preoperative	5-Year Postoperative	*P*	5-Year Postoperative	10-Year Postoperative	*P*
K1 (D)	48.85 ± 5.70	46.90 ± 5.08	< .05	46.90 ± 5.08	47.12 ± 4.22	.945
K2 (D)	54.99 ± 6.33	50.58 ± 5.11	< .05	50.58 ± 5.11	50.65 ± 4.70	.873
Km (D)	51.83 ± 5.66	48.70 ± 5.02	< .05	48.70 ± 5.02	48.82 ± 4.38	.953
UDVA (logMAR)	1.01 ± 0.28	0.71 ± 0.38	< .05	0.71 ± 0.38	0.67 ± 0.25	.735
CDVA (logMAR)	0.45 ± 0.45	0.24 ± 0.19	< .05	0.24 ± 0.19	0.29 ± 0.09	.292
Pach (μm)	457.42 ± 58.21	421.34 ± 74.12	< .05	421.34 ± 74.12	434.32 ± 77.65	.427

K1 = minimum keratometry; D = diopters; K2 = maximum keratometry; Km = mean keratometry; UDVA = uncorrected distance visual acuity; CDVA = corrected distance visual acuity; Pach = pachymetry

Tabla 9: Comparación de resultados de implante de anillos de Ferrara a los 5 y 10 años de seguimiento.

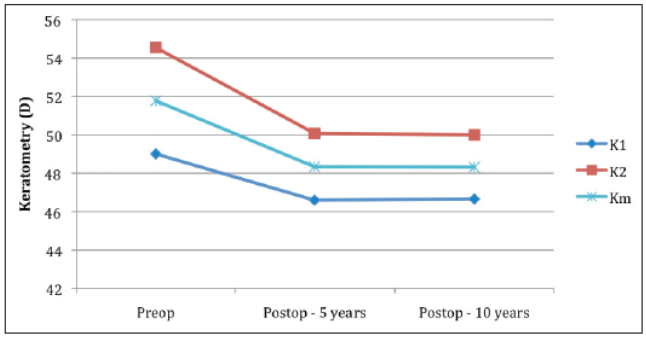


Figura 3: Valores preoperatorios de K a los 5 y 10 años de seguimiento

De acuerdo con el nomograma de Ferrara, la escoja del arco de anillo se hace de acuerdo con la morfología del queratocono a ser tratado. Para queratoconos centrales, con astigmatismo bajo, el segmento de elección es el de 210 grados de arco, pues induce importante aplanamiento corneal, disminución de los valores de queratometría y aumento de la asfericidad, sin alterar de manera significativa el astigmatismo. Para queratoconos paracentrales, los segmentos de elección son los de 160 grados de arco. Estos segmentos aplanan la córnea y disminuyen su queratometría con menor intensidad, pero actúan de manera más importante en la reducción del astigmatismo corneal En el estudio Intrastromal cornal ring segments: visual outcomes from a large case series, 2 grupos fueron separados según su morfología, si central (Nipple), o paracentral (Oval).

Los resultados en los 2 grupos demostraron mejora significativa de la UDVA y en la CDVA, con aumento significativo del espesor corneal. El valor de la asfericidad aumentó, de manera significativa, después del implante de los ICRS. El promedio del valor en el pos operatorios del grupo I (tipo Oval) fue de -0.35, y en el grupo II (tipo Nipple) fue de -0.56. La asfericidad es considerada como uno de los marcadores de la calidad de la visión. La mayoría de los estudios esta de acuerdo que los valores de asfericidad en la córnea humana varia de -0.01 a -0.80.[68]

Para todos los parámetros mensurados, los resultados fueron mejor en el grupo I. Una posible explicación es que el grupo de queratocono central presentaba grados más avanzados de queratocono, con valores pre operatorios más alterados.

La incidencia de complicaciones fue baja en el estudio (3,82% de los ojos tratados). Eso puede ser explicado por la pericia del cirujano y por la evolución del nomograma. La principal complicación del estudio fue la hipo corrección.

Además de pocas las complicaciones observadas en el post operatorio del implante de los anillos, la mayoría de ellas puede ser fácilmente resuelta, debido a la reversibilidad y ajustabilidad de la técnica. Los pacientes que necesitaron ser reoperados presentaron mejora de la AV y de los valores topográficos tras la reintervención en el periodo estudiado.

Hipo e hipercorrección fueron los principales motivos de reoperación en el grupo estudiado. Las causas no son totalmente conocidas, probablemente estén relacionadas a las propiedades biomecánicas de la córnea. Córneas con patrones topográficos semejantes pueden tener distintas respuestas al implante de los anillos, debido a que la rigidez y la viscoelasticidad pueden variar entre los pacientes.

Chan y Khan[75] evaluaron resultado de pacientes que tuvieron los segmentos sustituidos, con mejora de visión (mejora de la AV sin corrección de por lo menos 1 línea de visión) en todos los pacientes. Los autores de los ensayos clínicos fase II y fase III realizados por el FDA (Food and Drug Administration)[76] en los Estados Unidos concluyeron que la remoción de los ICRS (Intacs) es segura, efectiva y fácil de ser realizada, con retorno los parámetros pre operatorios después de 3 meses de la retirada del segmento.

Las alteraciones corneales inducidas por los segmentos pueden ocurrir hasta el sexto mes post operatorio, motivo por lo cual las reintervenciones solamente ocurrieron después de ese periodo. La remoción de los implantes ocurrió en 6 pacientes. El grupo de pacientes que presentaron peor agudeza visual, con y sin corrección, fueron aquellos que presentaron híper corrección en el post operatorio. El aplanamiento excesivo de la córnea inducida por los segmentos es una de las causas de insatisfacción del paciente en el post operatorio. Por lo tanto, la selección correcta de los anillos en el pre operatorio es de suma importancia.

En el estudio Predictors of Clinical Outcomes after Intraestromal corneal Ring Segments Implatation,[74] la mayoría de los pacientes tenían entre 21 y 40 años de edad. Los grupos fueron divididos de acuerdo con la edad. No presentaron diferencias estadísticamente significativas de la variación del promedio de la queratometría, del volumen corneal y del espesor corneal entre ellos. La asfericidad presentó mayor variación en los pacientes menores de 21 años, cuando comparamos los valores pre y post operatorios. La asfericidad es el parámetro considerado como más confiable para demostrar el remodelamiento corneal. Pacientes más jóvenes, por el hecho de que tienen la cornea menos rígida, presentan mayor efecto tras el implante de los anillos.

No fue observado diferencia estadísticamente significativa entre los grupo, con relación a la agudeza visual con y sin corrección, de acuerdo con la edad. Entretanto, la agudeza

visual con corrección fue mejor en pacientes entre 21 y 30 años de edad. Con relación al estadio del queratocono, cuanto más inicial el queratocono, mejor la respuesta al tratamiento, con mejora de la agudeza visual final.

Nuestros resultados están de acuerdo con otros estudios en la literatura. Alió et al. [77] relataron haber tenido buenos resultados en un grupo de estudio con un promedio de edad de 29,5 años de edad. Los factores relacionados con los buenos resultados fueron queratocono inicial, valores de K bajos (< 53D), buena agudeza visual preoperatoria y bajos valores de miopía y astigmatismo.

La variación de la biomecánica corneal con la edad puede desempeñar un papel en los diferentes resultados clínicos tras el implante de los ICRS, cuando comparamos grupos de diferentes edades. Elsheikh et al.[78] realizaron un estudio experimental para se determinar el comportamiento del tejido corneal sometido al estrese, y como varia de acuerdo con la edad. Demostraron con ese estudio que hay una fuerte relación de la edad con la rigidez corneal.

Otro estudio relacionando el espesor y biomecánica corneal con la edad de los pacientes, demuestra que no hay cambios del espesor corneal con la edad, pero hay alteraciones de los parámetros biomecánicos, independientes del espesor corneal central, lo que sugiere cambios estructurales resultantes del crosslinking del colágeno relacionados a la edad.[79]

Hay pocos trabajos que evalúen resultados a largo plazo del implante de los anillos intracorneales en la literatura. Intrastromal Corneal Ring Segment Implantation in Patients with Keratoconus: 10-Year Follow-Up[45] es el estudio con mayor tiempo de seguimiento publicado hasta los días de hoy. Los resultados del estudio refuerzan la reproductibilidad y eficacia de la técnica.

En un estudio de 2 años de seguimiento, Colin y Malet[80] describieron una mejora de la agudeza de pacientes con queratocono implantados con Intacs de 1 línea de visión el primer año de postoperatorio en el 61% de los ojos operados, mientas que la mejora, al segundo año de postoperatorio, fue en el 68,3% de los ojos.

Los ICRS aplanan la córnea y su efecto persiste por un largo periodo de tiempo. Alio et al.[78] realizaron un estudio retrospectivo con más de 2 años de seguimiento en pacientes implantados con Intacs para el tratamiento del queratocono. La agudeza visual mejoró de manera significativa ($p<.01$), de 0.46 (20/50) en el preoperatorio para 0.66 (20/30) a los 6 meses de postoperatorio. El promedio de K redujo 3,13D ($p<.01$). La comparación a los 6 meses y a los 36 meses demostró una estabilidad en los resultados.

El implante de los ICRS es un tratamiento mínimamente invasivo para el tratamiento del queratocono. Observamos una mejora importante de los valores de la agudeza visual en los pacientes de nuestros estudios, sobre todo en aquellos operados precozmente. Los valores de queratometría han bajado de manera significativa, así como han aumentado los valores de la asfericidad y del espesor corneal de manera significativa en la evaluación postoperatoria.

Las principales ventajas del procedimiento son la seguridad, la reversibilidad y la estabilidad de los resultados que proporciona a los pacientes con queratocono. El éxito de la técnica depende de muchos factores, como la técnica quirúrgica, el implante centrado en el centro óptico del ojo, la simetría de los implantes y la profundidad adecuada.

Nuestros estudios denostaron que los implantes de ICRS inducen una mejora de la regularidad corneal y de la visión en pacientes con queratocono. Se puede observar que, a los diez años de seguimiento, la mayoría de los pacientes evaluados mantuvieron estables las medidas corneales de la K, de la Q y del espesor corneal, además de la agudeza visual, confirmando en el grupo estudiado que los anillos fueron capaces de retrasar, o incluso frenar, la progresión del queratocono.

10. CAPITULO II. Progresión del queratocono con o sin los anillos de Ferrara.

Se resumen a continuación los trabajos de investigación clínica relacionados con la progresión del queratocono con y sin anillos de Ferrara y que han sido objeto de publicación en las siguientes publicaciones que se adjuntan:

1. Torquetti L, Arce C, Merayo-Lloves J, Ferrara G, Ferrara P, Signorelli B, Signorelli A. Evaluation of anterior and posterior surfaces of the cornea using a dual Scheimpflug analyser in keratoconus patients implanted with intrastromal corneal rings. ***Int Ophthalmol*** 2016;9(9):1283-1288
2. Torquetti L, Ferrara G, Almeida F, Cunha L, Araujo LPN, Machado AP, Lyra JM, Merayo-Lloves J, Ferrara P. Intrastromal Corneal Ring Segment Implantation in Patients with Keratoconus: 10-Year Follow-Up. J Refract Surg 2014;30(1)22-6

El queratocono es una patología caracterizada por el adelgazamiento progresivo de la córnea, de causa indeterminada, en la cual la córnea asume una forma cónica. El implante de los anillos intracorneales proporciona buenos resultados visuales, con mejora de los patrones de la regularidad corneal, de la visión con y sin corrección, además de frenar, o incluso evitar, la progresión del queratocono.[45,81] El procedimiento para el implante de los segmentos es mínimamente invasivo, además de reversible.[45]

El volumen de la córnea fue recientemente correlacionado como factor adicional en el "screening" del queratocono, y se relataron diferencias entre córneas normales y córnea de pacientes con queratocono. "Intrastromal Corneal Ring Segments Implantations in Patients With Mild Keratoconus"[43] describe los resultados de 50 pacientes que fueron sometidos al implante de anillos intracorneales para el tratamiento de queratocono leve a moderado. El estudio describe que hay un remodelamiento del estroma corneal con aumento de su volumen en un 60% de los casos implantados con los anillos intracorneales. Estos hallazgos sugieren una reorganización de las lamelas del estroma corneal por parte de los ICRS, aportando a la mejora de la queratometría, la asfericidad y la agudeza visual. El mismo hecho fue descrito por otro estudio, que demostró la

formación de colágeno y otros componentes de la matriz extracelular después de la implantación de los ICRS.[82]

En el estudio "Evaluation of anterior and posterior surfaces of the cornea using a dual Scheimpflug analyser in keratoconus patients implanted with intrastromal corneal rings" Torquetti *et al*.[81] describió el aumento del grosor de la córnea de pacientes con queratocono después del implante de los anillos intracorneales. Este hecho también puede ser explicado por la teoría del remodelamiento del colágeno de la córnea inducido por el implante de los ICRS. Actuando como espaciadores, los arcos de los anillos pueden interferir en la renovación del colágeno corneal, con el consecuente aumento del espesor corneal.[83] La redistribución de la curvatura corneal resulta en la redistribución del estrés corneal, interrumpiendo el ciclo biomecánico de progresión del queratocono.[84]

Hemos realizado un estudio para evaluar los resultados a largo plazo de la estabilidad, así como de la agudeza visual, de pacientes jóvenes implantados con los ICRS. Se evaluaron 58 ojos de 37 niños con queratocono tratados con los ICRS, retrospectivamente, por un periodo mínimo de 6 meses. Catorce ojos permanecieron sin tratamiento y 2 ojos fueron tratados con trasplante de córnea debido a las alteraciones del queratocono avanzado antes del inicio del estudio. El promedio de edad de los pacientes tratados fue de 13 años de edad. (unpublished data).

De los pacientes operados, 16 pacientes tuvieron un ojo operado, mientras 21 pacientes tuvieron los dos ojos operados. De los 21 pacientes con los dos ojos operados, 18 de ellos tuvieron la cirugía de los dos ojos realizada con un intervalo de tiempo entre uno y 3 meses, mientras en 3 pacientes, el tiempo entre la cirugía del primer ojo y del segundo varió entre 6 y 22 meses.

La principal indicación para el implante de los anillos en este estudio fue la intolerancia a las LCRGP y/o progresión de la ectasia. Todas las cirugías fueron realizadas por el mismo cirujano (Dr. Paulo Ferrara), como previamente descrito. [15,42,43,73,85] Los segmentos fueron implantados de acuerdo con el nomograma de Ferrara, descrito anteriormente. [68,72]

Los datos pre y postoperatorios de la AV con y sin corrección, de la asfericidad, la queratometría y del espesor corneal fueron colectados de todos los pacientes. El promedio de la AV sin corrección preoperatoria fue de 0,45 LogMAR, y de la AV con corrección fue de 0,41 LogMAR. En el primer mes de postoperatorio hubo una mejora de la AV sin corrección para 0,31 LogMAR y de la AV con corrección para 0,20 LogMAR. En el primer año de postoperatorio, el promedio de la AV sin corrección permaneció estable, mientras que el promedio de la AV con corrección mejoró para 0,17 LogMAR. La topografía evidenció el aplanamiento de la córnea en todos los ojos. El promedio del K mínimo y del K máximo disminuyó en todos los pacientes, de la misma manera que los valores de Q y del espesor corneal aumentaron en todos los pacientes. Un paciente tuvo que ser sometido al CXL y un paciente fue sometido al trasplante de córnea, debido al empeoramiento de su queratocono, a pesar del implante del ICRS. La k mínima disminuyó entre el periodo preoperatorio y el periodo postoperatorio, y sus valores se mantuvieron estables a los 2 años de seguimiento. La K máxima disminuyó entre el periodo preoperatorio y el periodo postoperatorio, pero sus valores aumentaron en un promedio de 0,3 dioptrías al año. Los valores de la asfericidad y del espesor corneal aumentaron entre el periodo preoperatorio y el primer mes postoperatorio, y se mantuvieron constantes a los 2 años de seguimiento.

En otro estudio retrospectivo con 5 años de seguimiento realizado por Torquetti et al,[15] se evaluó el implante de los anillos intraestromales para la corrección del queratocono en 37 ojos de 28 pacientes. Todos los pacientes fueron operados por el mismo cirujano (Dr. Paulo Ferrara). Siete de los 28 pacientes operados tuvieron el ojo contra lateral operado entre el primer día y el tercer año de post operatorio, según la evolución de la patología.

La principal indicación para el implante de los ICRS fue la progresión de la ectasia, además de intolerancia a las lentes de contacto semirrígidas permeables al gas. Se observó en el estudio una mejora de la agudeza visual sin corrección hasta el cuarto año postoperatorio, con estabilidad del resultado en el quinto año de postoperatorio. La agudeza visual con corrección mejoró hasta el tercero año postoperatorio, permaneciendo estable hasta el 5 año postoperatorio. Los valores de la queratometría postoperatoria disminuyeron en todos los pacientes operados (0=.000) (tabla 1)

Table 2. Preoperative and postoperative data.

	Mean ± SD						
		Postoperative					
Parameter	Preoperative	1 Month	1 Year	2 Years	3 Years	4 Years	5 Years
Maximum K (D)	54.07 ± 7.34	49.36 ± 6.66	48.22 ± 4.73	47.84 ± 4.98	47.06 ± 4.90	47.83 ± 6.56	48.09 ± 5.92
Minimum K (D)	48.49 ± 5.06	45.27 ± 5.39	43.89 ± 4.59	44.01 ± 3.83	43.12 ± 4.82	44.14 ± 5.75	44.45 ± 5.97
Mean K (D)	51.27 ± 5.91	47.29 ± 5.91	45.88 ± 4.52	45.71 ± 4.20	44.78 ± 4.55	45.97 ± 6.21	46.24 ± 5.89
UDVA	0.15 ± 0.15	0.25 ± 0.19	0.29 ± 0.17	0.29 ± 0.19	0.33 ± 0.17	0.30 ± 0.22	0.31 ± 0.23
CDVA	0.41 ± 0.25	0.56 ± 0.24	0.61 ± 0.24	0.63 ± 0.22	0.62 ± 0.20	0.62 ± 0.16	0.59 ± 0.19

CDVA = corrected distance visual acuity; K = keratometry reading; NA = not available; UDVA = uncorrected distance visual acuity

Tabla 1: Datos pre y postoperatorio

En "Intrastromal Corneal Ring Segment Implantation in Patients with Keratoconus: 10-Year Follow-Up",[45] 36 pacientes implantados con los ICRS para el tratamiento de queratocono, a los 5 años y a los 10 años de seguimiento, fueron evaluados. De éstos, 15 pacientes han tenido los 2 ojos tratados. Los resultados postoperatorios fueron satisfactorios, el 70% de los pacientes ganó 2 o más líneas de visión sin corrección y el 56,5% de los pacientes ganó 2 o más líneas de visión corregida a los 5 años de seguimiento, mientras que el 66,7% de los pacientes ganó 2 o más líneas de visión corregida a los 10 años de seguimiento. (Tabla 2)

TABLE 1

Preoperative and 5- and 10-Year Follow-up Examination Data of Eyes Implanted With Ferrara Intrastromal Corneal Ring Segments

Parameter	Preoperative	5-Year Postoperative	*P*	5-Year Postoperative	10-Year Postoperative	*P*
K1 (D)	48.85 ± 5.70	46.90 ± 5.08	< .05	46.90 ± 5.08	47.12 ± 4.22	.945
K2 (D)	54.99 ± 6.33	50.58 ± 5.11	< .05	50.58 ± 5.11	50.65 ± 4.70	.873
Km (D)	51.83 ± 5.66	48.70 ± 5.02	< .05	48.70 ± 5.02	48.82 ± 4.38	.953
UDVA (logMAR)	1.01 ± 0.28	0.71 ± 0.38	< .05	0.71 ± 0.38	0.67 ± 0.25	.735
CDVA (logMAR)	0.45 ± 0.45	0.24 ± 0.19	< .05	0.24 ± 0.19	0.29 ± 0.09	.292
Pach (μm)	457.42 ± 58.21	421.34 ± 74.12	< .05	421.34 ± 74.12	434.32 ± 77.65	.427

K1 = minimum keratometry; D = diopters; K2 = maximum keratometry; Km = mean keratometry; UDVA = uncorrected distance visual acuity; CDVA = corrected distance visual acuity; Pach = pachymetry

Tabla 2: Datos postoperatorios a los 5 y 10 años de seguimiento

Cuando comparamos los datos preoperatorios con los resultados a los 5 años de cirugía, observamos que las variaciones de los valores de K, de la agudeza visual con y sin corrección y del espesor corneal fueron estadísticamente significativas. Sin embargo, cuando comparamos los resultados a los 5 años de seguimiento con los resultados a los 10 años, observamos que las variaciones de los valores estudiados no fueron estadísticamente significativos.

El queratocono en una patología bilateral, aunque en muchos pacientes la manifestación de los signos y de los síntomas ocurra en un ojo solamente. En los estudios realizados con nuestros pacientes, muchos tuvieron los dos ojos operados en un corto periodo de tiempo, mientras que otros tuvieron el ojo contralateral operado hasta 3 años después del primer ojo. La progresión del queratocono en el ojo contralateral, con estabilidad de la ectasia en el ojo operado con el anillo, sugiere que el ICRS tiene influencia en la estabilidad de la esctasia.[15] También, en el análisis de los resultados de anillos implantados en niños, tres de los 37 niños operados necesitaron que se les implantara el ICRS en el ojo contralateral después de, por lo menos, 6 meses, lo que indica un progresión del queratocono en el ojo no tratado, mientras que, en el ojo tratado, el queratocono se mantuvo estable.

En la evaluación a los diez años de seguimiento, donde se estudió el comportamiento del queratocono después de haberse implantado los anillos intracorneales, se observó a los 5 años de postoperatorio una mejora de la regularidad de la superficie corneal, la reducción de los valores de los valores de queratometría y la mejora de la agudeza visual con y sin corrección, además de un incremento del espesor corneal entre el periodo preoperatorio y el periodo postoperatorio. Sin embargo, la comparación de los resultados de K, de la agudeza visual y del espesor corneal entre el quinto año y el décimo año de seguimiento no fueron estadísticamente significativos, lo que significa que los pacientes evaluados permanecieron estables entre el quinto y el decimo año post operatorio. [45]

Nuestros estudios están de acuerdo con otros estudios. Alió et al[77] publicaron los resultados de un estudio retrospectivo con 48 meses de seguimiento en el que pacientes portadores de queratocono fueron sometidos al implante de anillos intraestromales para la corrección de queratocono, con mejora de la agudeza visual y reducción de los valores de queratometría estadísticamente significativa (P<,01). La comparación de los resultados a los 6 meses con los resultados a los 36 meses de evolución demostró una estabilidad refractiva y topográfica de los pacientes tratados con los ICRS.

Los anillos intraestromales tienen como objetivo disminuir las irregularidades corneales y mejorar la visión del paciente además de frenar, o incluso evitar, la progresión del queratocono.[15,42,73] Beniz et al[86] realizaron un estudio retrospectivo de 18 pacientes portadores de queratocono avanzado con indicación de trasplante de córnea, implantados con anillos intraestromales como alternativa al trasplante. En su estudio, el 84,2% de los pacientes mantuvo la agudeza visual corregida a los 2 años de seguimiento, el 52,6% con gafas y el 31,6% de los pacientes con LCRGP. Tres de los 18 pacientes necesitaron el trasplante de córnea, a pesar del implante de los ICRS. De acuerdo con Beniz,[86] el implante de los anillos intraestromales puede efectivamente frenar, o incluso eliminar, la necesidad del trasplante de córnea en un grupo de pacientes con indicación para esta modalidad de tratamiento.

En el estudio de 10 años de seguimiento, el promedio de la edad de los pacientes fue de 39 años. El hecho de que el queratocono tiende a mantenerse estable después de los 30 años de edad puede influir en los resultados del estudio. Por tanto, no podemos asegurar que la estabilidad de los resultados no hayan sido influenciados por la edad de los pacientes.[45]

De modo contrario, el estudio retrospectivo realizado con niños entre 8 y 16 años de edad (en proceso de realización) demostró que el implante de los anillos logró frenar la evolución de queratocono en pacientes jóvenes. De acuerdo con nuestra experiencia, el 5% de los pacientes requiere de trasplante de córnea debido a progresión del queratocono a pesar del implante de los anillos intracorneales.

En conclusión, los anillos intracorneales disminuyen la irregularidad de la superficie corneal, disminuyen los valores de las queratometrías, aumentan los valores de la asfericidad y del espesor corneal y, consecuentemente, mejoran la agudeza visual en pacientes con queratocono. Otro efecto benéfico de los anillos es el de frenar la evolución de la patología, impidiendo el empeoramiento de la visión del paciente.

Futuros estudios con un seguimiento más largo y con un número mayor de pacientes es necesario para confirmar estos resultados.

11. CAPITULO III. Otras Aplicaciones de los Anillos de Ferrara: Corrección del astigmatismo tras queratoplastia.

Se resume a continuación el trabajo de investigación clínica sobre astigmatismo y queratoplastia

1. Coscarelli S, Ferrara G, Alfonso SJ, Ferrara P, Merayo-Lloves J, Araujo LPN, Machado AP, Lyra JM, Torquetti L. Intrastromal Corneal Ring Segment Implantation to correct astigmatism after penetrating keratoplasty. J Cataract Surg 2012;38:1006-1013.

El astigmatismo postoperatorio asociado al trasplante de córnea es una condición frecuente en la clínica medica.[87] La causa de esta condición se debe a factores relacionados a la córnea receptora, como ocurre por ejemplo en traumas corneales previos o en pacientes con queratocono.[88] Otras causas pueden estar relacionadas a la técnica quirúrgica, edad del paciente y remoción precoz de las suturas.[89]

El astigmatismo irregular postoperatorio es el responsable de la disminución de la agudeza visual. Aunque las gafas puedan corregir la ametropía del paciente, en general las lentes de contacto semirrígidas permeables al gas son la mejor opción para esos pacientes, pues les permite tener una mejor agudeza visual.[87]

Las alternativas quirúrgicas para el tratamiento del astigmatismo post trasplante de córnea, como la resección en cuña,[90-92] LASIK,[93,94] bien como el implante de lentes intraoculares fáquicas[95,96] han sido propuestas con buenos resultados.

El implante de segmentos intracorneales fue primeramente propuesto para la corrección de la miopía, pero debido a la baja previsibilidad de los resultados obtenidos, dejaron de ser utilizados con este propósito. El implante de los anillos se mostró una técnica poco invasiva, reversible y ajustable. Es un tratamiento que ha sido utilizado con éxito para disminuir la queratometría, regularizar la superficie corneal y mejorar la agudeza visual (Siganos, 2002; Colin, 2003).[13,14]

El objetivo del presente estudio es evaluar los resultados de la CDVA, el equivalente esférico (SE) y la queratometría mínima y máxima en pacientes con astigmatismo residual postrasplante de córnea, sometidos al tratamiento con implante de los anillos intracorneales.

En el estudio Intrastromal Corneal Ring Segment Implantation to correct astigmatism after penetrating keratoplasty[97] fue realizado una análisis retrospectiva con pacientes consecutivos que fueron implantados con ICRS para llevar a cabo la corrección de astigmatismo residual post queratoplastia penetrante de córnea, entre los meses de mayo de 2005 y septiembre de 2009.

En los criterios de inclusión constaron el injerto trasparente, con astigmatismos que variaban entre 2,5 y 8,0 dioptrías, e intolerancia a lentes de contacto rígidas permeables al gas. Todos los pacientes completaron, por lo menos, 2 años de postoperatorio del trasplante de córnea antes del implante de los segmentos de anillos intracorneales, además de por lo menos 6 meses después de haber removido las suturas. Todas las cirugías fueron realizadas por el mismo cirujano, Dr. Sandro Coscarelli, por la técnica manual, como descrito previamente.[15]

El seguimiento de los pacientes se realizó de la siguiente forma: primero y séptimo día postoperatorio, primero y sexto mes postoperatorio, cada año sucesivamente. En cada visita postoperatoria se evaluó a la lámpara de hendidura y se efectuó la refracción de los pacientes, la medición de la AV y la topografía de córnea, además de tonometría y fundoscopia. Se realizó el análisis aritmético del astigmatismo y de su eje a través de un análisis vectorial.[98]

El análisis estadístico incluyó el test *t* de Student, la transformación de Welch y el test non paramétrico de Mann-Whitney, utilizándose del Instat para Macintosh software (versión 3.1ª, Graphpad Software). Asimismo, se realizó el análisis vectorial a través del Sigmaplot software (SPSS Inc.). A efectos de realizar el "outcome" y el análisis de los resultados se utilizó el Software de análisis refractivo (Zubisoft GmbH).

El estudio incluyó 59 ojos de 54 pacientes implantados con ICRS. El promedio de edad fue 36,01 ± 11,02 años (SD) (19 a 72 años). (Tabla1). Todos los pacientes completaron

1 año de seguimiento. El astigmatismo corneal preoperatorio ha variado de 3 a 5 dioptrías. Las figuras 1 y 2 muestran la CDVA pre y postoperatoria. No hubo pérdida de líneas de visión en ninguno de los pacientes. La agudeza visual, el equivalente esférico y el error refractivo fue estadísticamente significativo (p<.0001).

Table 1. Preoperative and last follow-up examination data.

Parameter	Preoperative	Postoperative	*P* Value
Eyes (n)	59	—	—
Patients (n)	54	—	—
Sex (n)			
Male	26	—	—
Female	28	—	—
Mean age (y)	36.01 ± 11.02	—	—
Mean follow-up (mo)	14	—	—
CDVA (logMAR)			.001
Mean ± SD	0.45 ± 0.17	0.30 ± 0.17	
Range	0.18, 1.00	0.00, 1.00	
SE (D)			.001
Mean ± SD	−6.34 ± 3.40	−2.66 ± 2.52	
Range	0.37, −16.50	0.87, −10.50	
Spherical refractive error (D)			.001
Mean ± SD	−7.10 ± 3.07	−3.46 ± 2.05	
Range	2.15 to 16.68	0.88 to 10.79	
Mean TA at 3.0 mm (D)	3.37 ± 1.51	1.69 ± 1.04	.001
Mean maximum K (D)	48.09 ± 2.56	44.17 ± 2.67	.001
Mean minimum K (D)	44.90 ± 2.54	42.46 ± 2.63	.001

CDVA = corrected distance visual acuity; K = keratometry; SE = spherical equivalent; TA = topographic astigmatism

Tabla 1: Datos del preoperatorio y el último examen postoperatorio.

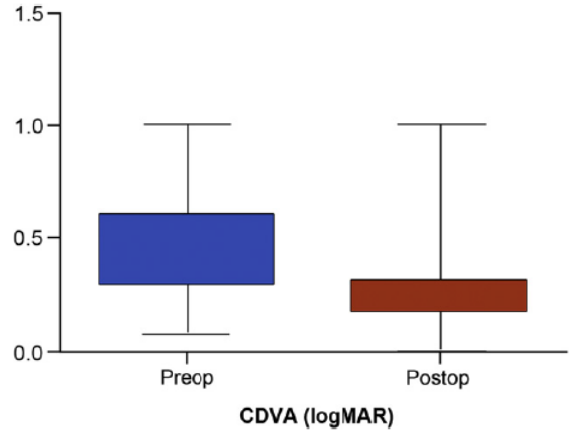


Figura 1: CDVA antes y después del implante del ICRS (datos no pareados)

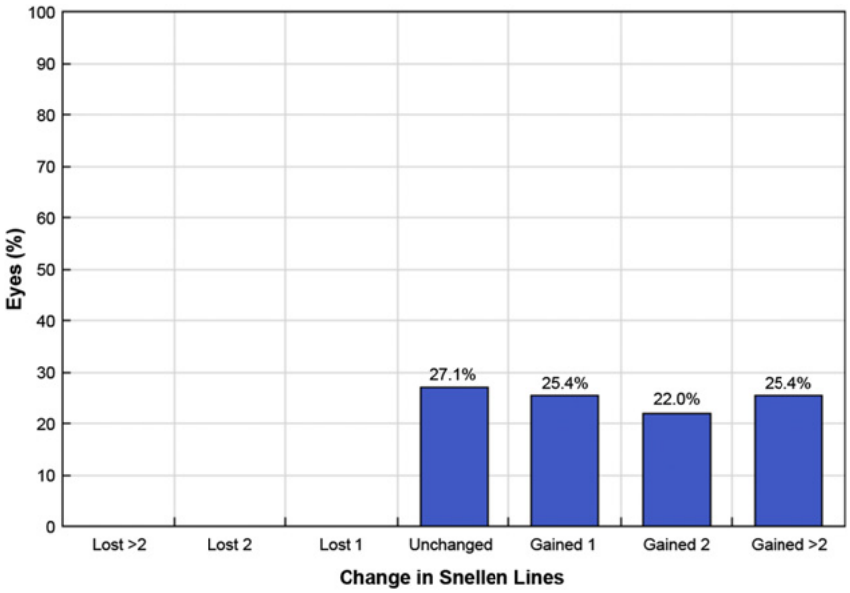


Figura 2: 28 (47,4%) de los pacientes ganaron 2 o más líneas de visión. Ningún paciente perdió líneas de visión.

En relación a la previsibilidad de la cirugía, 43 ojos (72,8%) presentaron hipocorrección, y 9 (15,2%) de los ojos presentaron hipercorrección del equivalente esférico (SE). Solamente 7 ojos (13%) tuvieron la corrección esperada. La reducción del astigmatismo en el postoperatorio fue estadísticamente significativo ($p<.001$)

Se observó una disminución del promedio del astigmatismo topográfico de 3 D del pre para el post operatorio ($p<.0001$).

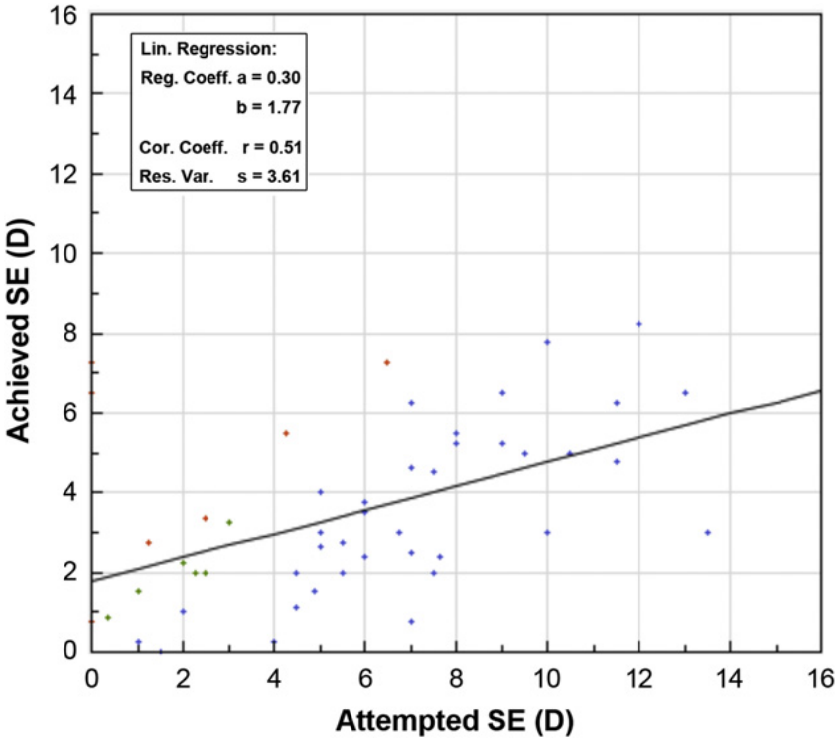


Figura 3: Previsibilidad de la corrección del SE. Los puntos azules representan hipocorrección, los puntos verdes, corrección total, y los puntos rojos representan hipercorrección.

La topografía evidenció un aplanamiento de la córnea estadísticamente significativo en todos los ojos (p<.0001). (Tabla 1). El análisis vectorial mostró que la mayoría de los ojos ha tenido un reducción del error refractivo esfero cilíndrico estadísticamente significativo (Figura 4).

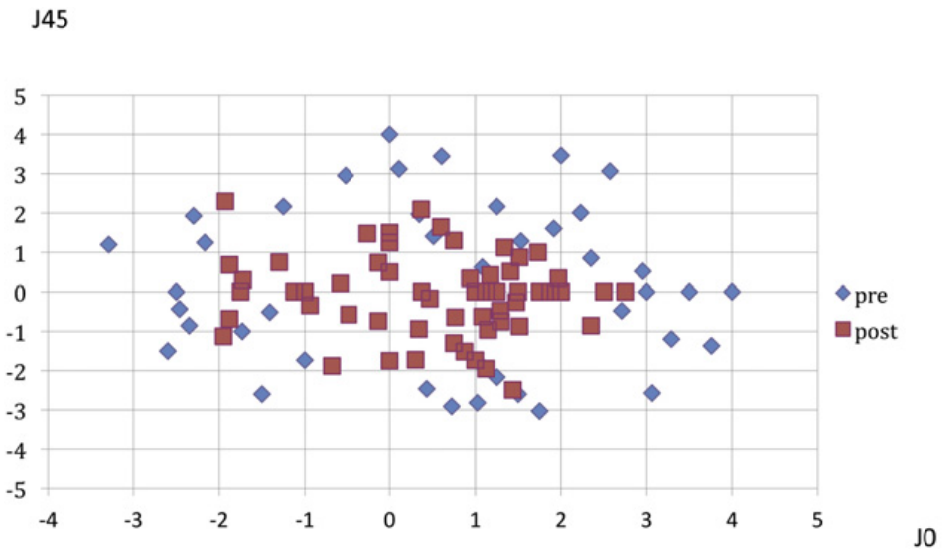


Figura 4: Vectores astigmáticos (J_0 y J_{45}) antes y después del implante de los ICRS. Los puntos rojos más cercanos al centro (postoperatorio) representan una reducción del astigmatismo en el postoperatorio del implante de los anillos.

El Double-angled Plot nos proporciona una visión general de la magnitud (dioptrías) del cilindro y de su eje (grado). Después del implante del ICRS, el centroide del astigmatismo refractivo se situó 1,0 dioptría más cercano al cero. (Figura 5).

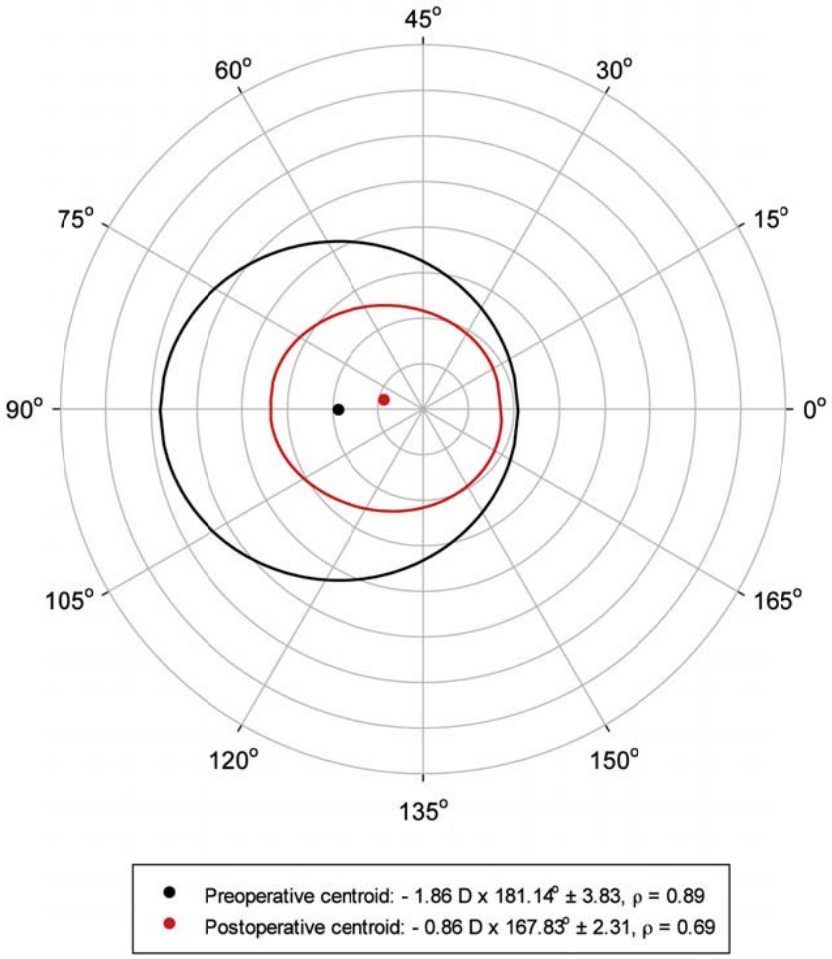


Figura 5: La reubicación del centroide más cercano al origen (punto rojo) y la contracción de la elipse (en rojo) en el Double-angled Plot muestran el grado de mejora.

Ninguno de los pacientes presentaron complicaciones post operatorias. En 3 pacientes (5%), la cirugía ha tenido que ser interrumpida por dehiscencia de junción entre el injerto y la córnea receptora, a pesar del periodo entre el trasplante de córnea y el implante del anillo (por lo menos 2 años).

El astigmatismo postoperatorio es una condición frecuente en pacientes sometidos al trasplante de córnea, y su corrección sigue siendo un reto para los clínicos. Muchas son las causas del astigmatismo residual post trasplante de córnea, y factores relacionados al paciente, a la córnea receptora, a la técnica quirúrgica y a la conducción del postoperatorio pueden influir en el astigmatismo residual. Los trastornos periféricos, como el queratocono, pueden persistir en la córnea receptora, resultando en astigmatismos irregulares. Este hecho puede explicar la alta prevalencia de pacientes con queratocono en nuestro estudio.

Entre las alternativas para la corrección del astigmatismo postoperatorio están las lentes de contacto y la corrección refractiva con el láser de excímeros. Sin embargo, deben ser considerados los frecuentes problemas en estos pacientes, como síndrome de ojo seco, neovascularización corneal y rechazo del injerto,[99] así como también las contraindicaciones para el PRK y el LASIK, como altas ametropías, córneas delgadas y la edad de los pacientes, en general, jóvenes.

La utilización de lentes fáquicas para la corrección de los errores refractivos fue evaluado por algunos autores (Alfonso *et al.*[100] y Morshirfar *et al.* [101]) demostrando ser un procedimiento seguro, con resultados previsibles y estables. Alfonso *et al.*[100] describió la seguridad, previsibilidad y eficacia de los implantes de Implantable Collamer Lens (ICL) para la corrección del error refractivo en 15 ojos de 15 pacientes post queratoplastia. Se observó una mejora importante del error refractivo, con mejora de la agudeza visual corregida. Morshirfar *et al.*[101] evaluó el resultado del implante de Artisan para la corrección de alta miopía en pacientes post queratoplastia, con mejora de la agudeza visual – con y sin corrección. Después de 6 meses de seguimiento, no fue observado disminución significativa de la densidad de células endoteliales.

El estudio "Intrastromal Corneal Ring Segment Implantation to correct astigmatism after penetrating keratoplasty"[97] describe los resultados de 59 ojos de 49 pacientes sometidos al implante de los ICRS para corrección de astigmatismos irregulares en pacientes trasplantados de córnea. Los astigmatismos irregulares y elevados pueden perjudicar los resultados de la cirugía, a pesar de una cicatrización adecuada.

El "outcome" en nuestro estudio fue satisfactorio. La CDVA no se alteró en el postoperatorio de 16 ojos (27,2%), mientras que 43 ojos (72,8%) mejoraron, por lo menos, una línea de visión. El promedio del equivalente esférico disminuyó de -6,34 ± 3,40 D a -2,66 ± 2,52 D, y los valores de K disminuyeron, mejorando la regularidad corneal.

Nuestro estudio está de acuerdo con los resultados de otros trabajos. Coskunseven et al.[102] defiende el implante de los ICRS para la corrección de altos astigmatismos post queratoplastia. Para Coskunseven, córneas delgadas y con queratocono recurrente son inadecuadas para la realización de corrección con laser de excímeros. Arriola-Villalobos *et al*.[103] publicó un estudio con 9 ojos demostrando la mejora de la agudeza visual corregida en todos los ojos, además de la disminución de los valores de la queratometría máxima y mínima, concluyendo que los anillos son una buena opción para la correcion de altos astigmatismos post trasplante de córnea. Chang y Hardten[104] sugiere que no se haga el implante de los anillos por, por lo menos, un año después de la realización del trasplante de córnea y por lo menos 3 meses después de la remoción de la sutura.

En nuestro estudio, la realización del implantes ocurrió después de, por lo menos, 2 años de la queratoplastia y, por lo menos, 6 meses después de la remoción de la sutura de córnea a fin de se evitar daño en la junción de la córnea donante con la córnea receptora, por la tracción inducida por el tunelizador durante la realización de la cirugía por la técnica manual. El implante de los segmentos tuvo que ser postergado en un 5% de los casos (3/59 pacientes) por dehiscencia en la región de la cicatriz entre el injerto y la córnea receptora durante la confección del túnel estromal. En estos casos está indicada la utilización del láser de Femtosegundo pues facilita la confección del túnel estromal y previene ese tipo de complicación.[105,106]

La utilización de anillos de 5 mm de diámetro es preferible en pacientes post PKP. Su diámetro menor promueve un mayor aplanamiento de la córnea central, dado que el resultado refractivo es inversamente proporcional a su diámetro. El segundo beneficio de estos segmentos es que su diámetro pequeño asegura una distancia mayor de la junción del injerto con la córnea receptora, lo que reduce el riesgo de dehiscencia del injerto y de la neovascularización del túnel por neovasos provenientes del limbo o de la

cornea receptora. La desventaja de los segmentos de zona óptica pequeña son los halos y el deslumbramiento, sobre todo en condiciones de baja luminosidad.
Los resultados del implante de los segmentos intraestromales en pacientes con trasplante de córnea presentaron resultados diferentes cuando se los comparó con los resultados de anillos implantados para el tratamiento del queratocono. Las córneas con queratocono presentan biomecánica distinta a las córneas trasplantadas, pues las primeras son más delgadas y elásticas que las últimas, más rígidas, con espesor y elasticidad normales. En la teoría, ese hecho puede explicar la hipo corrección en nuestros resultados.

El objetivo principal de la indicación del implante de los anillos intracorneales es la regularización de la superficie corneal, con mejora de la AV. La reducción de la refracción debe ser considerada como un efecto secundario de los anillos.

Muchas son las ventajas del tratamiento del astigmatismo corneal con los segmentos intracorenales. En primero lugar, los ICRS evitan el centro de la córnea, y no causan alteraciones de trasparencia en el eje visual, como puede ocurrir con el láser de excímeros, lo que podría comprometer nuestro resultado. Por tratarse de una técnica reversible, se puede volver atrás cuando no se obtiene el resultado esperado. De la misma manera, se puede ajustar el resultado mediante el cambio de los segmentos por otros más gruesos, o delgados, con el objetivo de mejorar los resultados visuales. Por último, los segmentos corneales evitan las complicaciones de un procedimiento intraocular.

Los resultados de nuestro estudio sugieren que los ICRS constituyen un tratamiento promisor para pacientes con astigmatismo residual post PK, sobre todo en aquellos con irregularidades corneales, pues resulta en reducción de la refracción, mejora de la AV y de los patrones topográficos. Es necesario llevar a cabo unos estudios en el futuro con miras a evaluar mejor los resultados de esta técnica destinada a la corrección de astigmatismos irregulares post PKP.

12. Trabajos en realización

12.1. Resultados de la implantación de anillos de Ferrara en niños

Se resume a continuación el trabajo de investigación clínica relacionado con los resultados de la implantación de anillos de Ferrara en niños. El artículo está enviado en fase de revisión y pendiente de aceptación.

Ferrara G[1], Merayo-Lloves J[2], Ferrara P[1]. Torquetti L[1,3].Intrastromal corneal ring segments in children with keratoconus. Int J Kerat Ect Cor Dis Submitted April 5 2017.

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El queratocono es la patología ectásica más frecuente en el paciente joven. Se inicia, en general, en la segunda década de vida, pudiendo progresar hasta la tercera o cuarta década (RABINOWITZ 1998).[19] Se ha observado que el queratocono progresa más rápidamente en personas más jóvenes, y más rápido cuanto más temprana la edad de aparición (OWEN ET AL 2003).[22] Hay una fuerte correlación entre pacientes atópicos, frotamiento ocular y el queratocono.

Se ha empleado los ICRS para la corrección de las ectasias con el objetivo de disminuir las irregularidades corneales y mejorar la agudeza visual. [12,13,14,66,107,108] Además de disminuir el astigmatismo y los valores de queratometría, los ICRS pueden ser, también, una alternativa quirúrgica para frenar la evolución del queratocono, si no, eliminar la necesidad de un trasplante de córnea.

Hemos realizado el estudio "Intrastromal Corneal Ring Segments in Children with Keratoconus" donde se evaluó los resultados del implante de los ICRS en 58 ojos de 37 niños entre 8 a 16 años, con diagnostico de queratocono, con 2 años de seguimiento. Todos los pacientes tenían por lo menos 6 meses de seguimiento postoperatorio. Fueran estudiados la variación de la agudeza visual, de los valores de queratometría, paquinetría y de la asfericidad corneal tras el implante de los ICRS.

La principal indicación para el implante de los anillos fue intolerancia a las LCRGP y/o progresión de la ectasia. La progresión de la ectasia fue definida por el empeoramiento

de la AV sin y con corrección y encorvamiento progresivo de la córnea documentada por la topografía de córnea. Se excluyó del análisis a los pacientes con queratocono muy avanzado, con opacidades apicales importantes y/o cicatrices, hidropsía, córneas delgadas con el espesor corneal inferior a 300 μm en el trayecto del anillo y pacientes con atopia, así como también a los pacientes con procesos infecciosos de carácter local o sistémico.

El análisis estadístico incluyó la agudeza visual con y sin corrección, queratometría, paquimetría y asfericidad corneal. Todos los datos fueron extraídos del Pentacam (Oculus Pentacam®, Germany). El análisis estadístico fue realizado por el MINITAB software (versión 3.3.1). El test *t* de Student´s para datos pareados fue utilizado para comparar los valores del pre y del postoperatorio.

Todas las cirugías fueron realizadas por el mismo cirujano (Dr. Paulo Ferrara), como previamente descrito.[15] Los segmentos fueron implantados de acuerdo con el nomograma de Ferrara descrito anteriormente. [68,72]

Fueron estudiados 58 ojos de 37 pacientes implantados con ICRS. 14 ojos permanecieron sin tratamiento y 2 ojos fueron tratados con trasplante de córnea debido a las alteraciones del queratocono avanzado antes del inicio del estudio. El promedio de edad de los pacientes tratados fue de 13 ± 2.1 años de edad (8 a 16 años). No hubo ninguna complicación peri ni post operatoria.

Los datos pre y post operatorios de la AV con y sin corrección, de la asfericidad, y de la queratometría fueron colectados de todos los pacientes. El promedio de la AV sin corrección preoperatoria fue de 0,41 LogMAR, y de la AV con corrección fue de 0,36 LogMAR. En el primer mes de postoperatorio hubo una mejora de la AV sin corrección para 0,29 LogMAR y de la AV con corrección para 0,20 LogMAR. En el segundo año de postoperatorio, el promedio de la AV sin corrección fue 0,25, mientras el promedio de la AV con corrección fue 0,16 LogMAR. (Tabla 1)

Pre and Post operative data

	Post operative			
Pre operative	1st month	p	2nd year	p

UCVA	0,41	0,29	0,004	0,25	0,262
CDVA	0,36	0,2		0,16	0,983

Tabla 1. Reducción de los valores de la AV (LogMAR) con y sin corrección tras el implante de los ICRS

La topografía evidenció el aplanamiento de la córnea en todos los ojos. El promedio del K mínimo y del K máximo disminuyeron en todos los pacientes, de la misma manera que los valores de Q y paquimetría aumentaron en todos ellos. Un paciente tuvo que ser sometido al CXL y uno al trasplante de córnea debido al empeoramiento de su queratocono, a pesar del implante del ICRS.

La queratometría mínima disminuyó en un promedio de 4 unidades entre el periodo preoperatorio y el postoperatorio (p-value <0.001). Los resultados se mantuvieron estables a los 2 años de seguimiento (p-value 0,412). (Grafico 1)

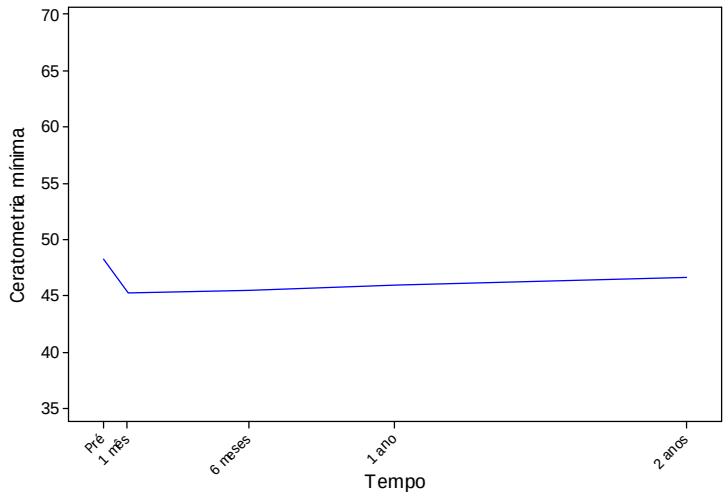

Grafico 1. Reducción de los valores de la queratometría mínima tras el implante de los ICRS

La queratometría máxima disminuyó en un promedio de 6 unidades entre el periodo preoperatorio y el postoperatorio (p-value <0.001). Los valores de K máximo aumentaron en un promedio de 0,7 dioptrías al año (p-value = 0,002). (Grafico 2)

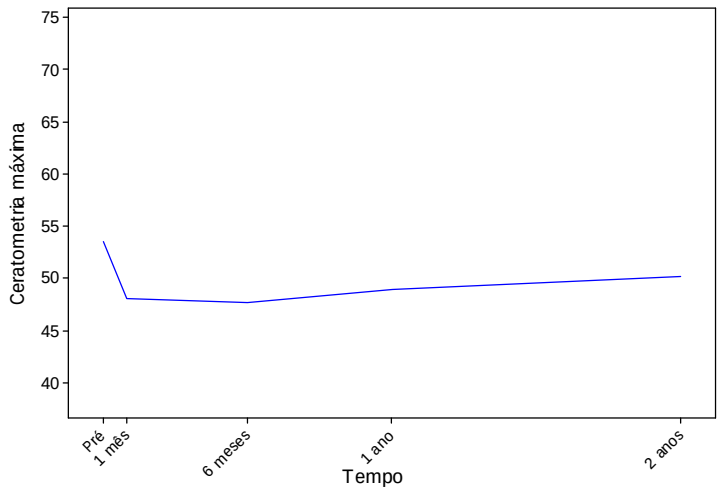

Grafico 2. Reducción de los valores de la queratometría máxima tras el implante de los ICRS

Los valores de la asfericidad aumentaron en un promedio de 0,61 unidades (0,44 a 0,79) entre el periodo preoperatorio y el primer mes postoperatorio (p-value <0,001), y se mantuvieron constantes a los 2 años de seguimiento (p-value = 0,275). (Grafico 3)

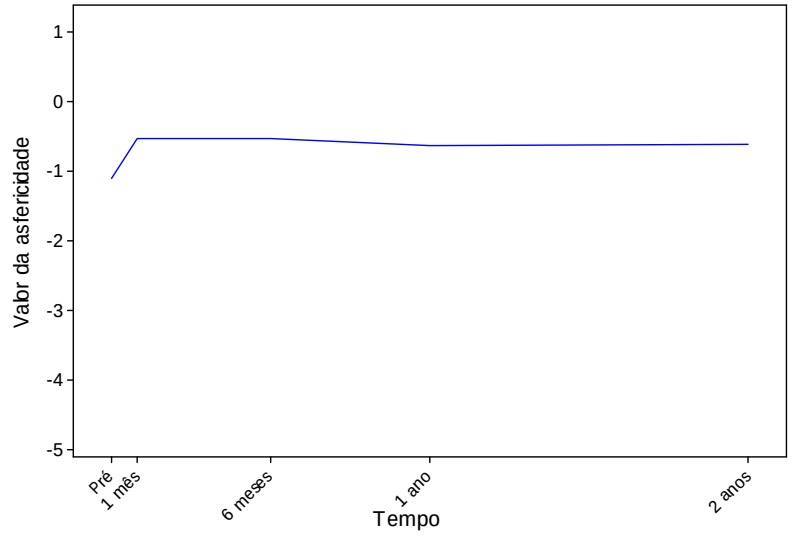

Grafico 3. Aumento de los valores de la asfericidad corneal tras el implante de los ICRS

Los valores de la paquimetría aumentaron un promedio de 8.5 unidades (p-values = 0.05) entre el periodo preoperatorio y el primer mes postoperatorio, y se mantuvieron estables a los 2 años de seguimiento (p-value = 0.112). (Grafico 4)

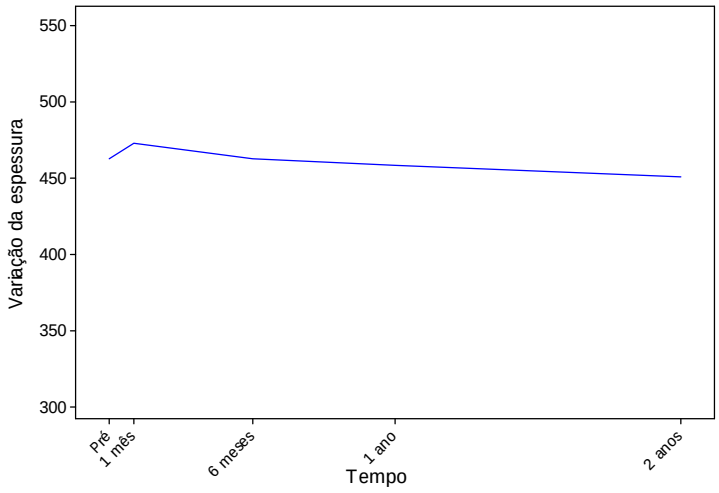

Grafico 4. Variación de la paquimetría a lo largo del tiempo, tras el implante de los ICRS

Estudios anteriores han demostrado que los ICRS son eficaces para corregir los astigmatismos y los astigmatismos miópicos[49], con preservación de la AV, y estables a lo largo del tiempo[41]. El objetivo de la técnica de adicción es reforzar la córnea, disminuyendo su irregularidad y mejorando la AV de los pacientes afectados.

En el presente estudio, concluimos que los valores de queratometría - mínima y máxima - han reducido entre la evaluación pre operatoria y la evaluación en el primer mes postoperatorio, mientras que los valores de la paquimetría y de la asfericidad aumentaron en ese mismo periodo.

Entre el primer mes y el segundo año postoperatorio, observamos que la K mínima no se alteró, y que la K máxima sufrió pequeños cambios a lo largo del tiempo. Aunque hubo un ligero aumento de la queratometría máxima durante el periodo estudiado (un promedio de 0,7 dioptrías al año), ese aumento no tuvo significancia clínica. Los valores de asfericidad y de paquimetría no variaron entre el primero mes y el segundo año de seguimiento, de manera significativa.

Estudios similares han demostrado resultados parecidos al nuestro. Miranda *et al.* [109] observaron una reducción del promedio de la curvatura corneal central en el postoperatorio en sus estudios. La agudeza visual con y sin corrección mejoraron en el 80,56% y en el 77,78% de los pacientes, respectivamente. Siganos *et al* [14] presentaron una mejora del promedio de la agudeza visual sin corrección de 0.07 $\pm$ 0.08 en el pre

operatorio a 0.20 ± 0.13 y 0.30 ± 0.21 después de uno y seis meses de post operatorio, respectivamente, y una mejora del promedio de la agudeza visual con corrección de 0.37 ± 0.25 en el pre operatorio a 0.50 ± 0.43 en el post operatorio. Kuitko y Severo [16] reportaron una mejora de la agudeza visual con corrección del 86,4% de los ojos operados, mantenimiento de la visión en el 1,9% y el 11,7%, empeoramiento de la visión corregida en el periodo postoperatorio, después de haber implantado los ICRS. Con relación al agudeza visual sin corrección, el 86,4% de los ojos mejoraron, el 7,8% se mantuvo sin alteraciones y el 5,8% de los ojos empeoró. El promedio de la curvatura corneal central disminuyó de 48.76 ± 3.97 a 43.17 ± 4.79.

Alió et al.[77] realizaron un estudio retrospectivo para evaluar los resultados a largo plazo (hasta 48 meses) tras la implantación de Intacs en pacientes con queratocono. Se encontró que el promedio de la agudeza visual con corrección aumenta significativamente ($p < 0,01$) de 0,46 (20/50) preoperatoriamente a 0,66 (20/30) 6 meses después de la implantación. También la media del valor de K disminuyó significativamente ($p < 0,01$) por 3,13 D. La comparación de los resultados 6 meses y 36 meses después de la implantación mostró refracción y topografía estables. Kymionis et al.[110] estudiaron 17 ojos de pacientes con queratocono que tenían implante de Intacs para aplanar la córnea. Encontraron que el agudeza visual sin corrección pre-Intacs era 20/50 o peor en todos los ojos, mientras que en el último examen de seguimiento el 59% tenía agudeza visual sin corrección de 20/50 o mejor. La mayoría de los ojos (59%) experimentó una ganancia de una a 8 líneas de agudeza visual. Estudios anteriores demostraron que el anillo intracorneal aplana la córnea y mantiene este efecto durante un largo período de tiempo. No hay en adultos un re-encorvamiento significativo de la córnea con el tiempo.

Encontramos que los valores de queratometría pre operatoria fueron mayores en nuestro estudio en comparación con estudios similares[77,80,110]. Además, la agudeza visual - con y sin corrección - pre operatorios fueron peores en nuestro estudio. Esto puede explicarse por el comportamiento más agresivo del queratocono en niños. De esta manera, cuando la cirugía fue indicada, la enfermedad se encontraba en un estadio evolutivo más avanzado.

En nuestro estudio, dos pacientes (5,4%) se sometieron a queratoplastia, y un paciente (2,7%) se sometió a crosslinking corneal debido a la progresión del queratocono. De acuerdo con nuestra experiencia personal, aproximadamente el 5% de los pacientes tiene que someterse a la queratoplastia penetrante o lamelar, debido progresión del queratocono, a pesar de la implantación adecuada del ICRS. Es importante destacar que la implantación de los anillos en estos pacientes usualmente tuvo lugar en fases muy avanzadas de la enfermedad, lo que no significa necesariamente una evolución del queratocono, sino un resultado visual insatisfactorio.

Hubo mejoría de todos los parámetros en nuestro estudio. El patrón de reducción de los parámetros de la queratometría fue similar a otros estudios. En cuanto a la agudeza visual, hubo mejora en la agudeza visual sin corrección y en la agudeza visual con corrección, pero no tan acentuada como ocurre en adultos.

El implante de anillo intracorneal juega un papel importante con miras a retrasar la progresión del queratocono y pospone una cirugía de trasplante corneal. El presente estudio demostró que los anillos de Ferrara, a pesar de la pequeña muestra de pacientes, podría ser una valiosa herramienta para proporcionar mejora de la topografía corneal y visual en niños con queratocono. La realización de estudios adicionales, con muestras más grandes y períodos de seguimiento más largos, se hacen necesarios para confirmar los resultados presentados.

13. Discusión

Las primeras indicaciones de los anillos intracorneales de Ferrara fueron para la corrección de miopías moderadas y severas (1991). Como el objetivo refractivo resultó poco predecible, en 1996 se cambió la indicación del implante de los anillos por la corrección de córneas irregulares.

Se han utilizado, desde entonces, los ICRS para el tratamiento de las deformidades corneales, como en los casos de queratocono, ectasia post Lasik, ectasia post queratotomía radial, astigmatismos irregulares y miopía, obteniéndose una mejora de la agudeza visual con y sin corrección.

La principal indicación de los ICRS es para la corrección del queratocono. El objetivo de la técnica aditiva de la córnea es reforzar su estructura y disminuir las deformidades, mejorando así la visión funcional de los pacientes y, de esta manera, postergar o incluso eliminar la necesidad del trasplante de córnea. Las principales ventajas de los ICRS son la seguridad y la reversibilidad, dado que la cirugía no afecta el eje visual ni la estabilidad de los resultados obtenidos.

Las alteraciones inducidas por los implantes de anillos intracorneales pueden ser previstas por la ley de los espesores de Barraquer, es decir, cuando el material es adicionado a la periferia de la córnea, o igual cantidad de material es sustraído del centro de la córnea, inducimos el aplanamiento de la misma. Los resultados de la corrección varían en relación directa con el espesor de los anillos y en relación inversa al diámetro de los anillos. Así, cuanto más espeso el anillo y cuanto más pequeño su diámetro, mayor será el resultado obtenido.

Los ICRS inducen el aplanamiento central y periférico de la córnea, preservando su asfericidad, además de disminuir la altura de la cámara anterior. El movimiento de báscula provocado por los segmentos resulta en un aplanamiento de la córnea en las puntas de los segmentos y en un encorvamiento de la misma en la región correspondiente al cuerpo del anillo. Además, se observa la reducción de síntomas de los pacientes, como el prurito, la fotofobia, y el dolor ocular, probablemente por la regularización de la superficie corneal.

El queratocono es la patología ectásica más frecuente del paciente joven, y su diagnóstico tiene lugar, en general, en la segunda década de vida. La baja calidad de la visión de estos pacientes fue demostrada por Aydin et al. Su progresión puede causar una debilidad visual importante, lo cual ocasiona un importante impacto en la calidad de vida de los pacientes, ya que afecta sus

actividades laborales en las edades más productivas de la vida. Por esa razón se hace necesaria la intervención precoz de estos pacientes a fin de restaurar la visión y evitar su progresión.

El empleo de los ICRS para el tratamiento de estos pacientes proporciona una rápida rehabilitación visual, además de ser poco invasivo, posibilitando un rápido regreso a sus actividades habituales. Los anillos disminuyen las irregularidades corneales, el astigmatismo irregular y los valores de queratometría, mejorando de esta manera la agudeza visual de los pacientes. En su estudio, Freitas Santos Paranhos J et al.[111] demostraron la mejora de la calidad de vida de los pacientes tras el implante de los ICRS. Esta mejora también fue relatada por Sahebjada S et al.[112]

La rigidez de la córnea aumenta con la edad, hecho que puede interferir en los resultados de los implantes de ICRS. Además de la edad del paciente, el estadio evolutivo de la enfermedad también interfiere en el resultado final, donde esperamos resultados menos efectivos en queratoconos avanzados cuando los comparamos con los casos iniciales.

Demostramos en nuestros estudios que la mejora de la AV con corrección fue más acentuada en los pacientes entre 21 y 30 años de edad y en los pacientes con queratocono grado I.[74] Alió et al.[113] relataron que, en pacientes mayores, los resultados fueron peores que en pacientes más jóvenes, con mayor índice de complicaciones. Los factores relacionados con buenos resultados en su estudio fueron la edad joven, queratocono inicial, valores de K bajos (< 53D), buena agudeza visual preoperatoria, bajos valores de miopía y astigmatismo. Rodrigues P et al.[43] demostraron la eficiencia del implante de los ICRS en pacientes con queratoconos iniciales y moderados.

Cuanto más joven es el paciente en el momento del diagnóstico de queratocono, mayor es la probabilidad de un mal pronóstico. En estos casos, se espera una rápida progresión de la enfermedad, con comprometimiento importante de la visión. La intervención precoz se hace necesaria, con objeto de evitarse, o postergar, la necesidad del trasplante de córnea.

La evaluación de los resultados del implante de los ICRS en 58 ojos de 37 niños con queratocono (en realización), demostró que los pacientes operados presentaron una disminución de los valores de la queratometría y un aumento de los valores del espesor corneal y asfericidad, además de mejorar la AV en el postoperatorio de manera estadísticamente significativa. A lo largo de dos años de seguimiento, la AV con y sin corrección, los valores del K mínimo, del espesor corneal y asfericidad se mantuvieron estables, mientras que el promedio del K máximo aumentó de manera significativa (0.3D al año). A pesar del aumento del promedio del K

máximo de manera estadísticamente significativa, éste no lo fue clínicamente. En este estudio, 2 pacientes (5,4%) se sometieron a queratoplastia, y un paciente (2,7%) se sometió a crosslinking corneal, debido a la progresión del queratocono, al final de 5 años de seguimiento.

La evaluación de 1073 ojos de 810 pacientes operados consecutivamente entre enero de 2006 y julio de 2008, realizada por nuestro grupo de investigación, demostró la mejora de la AV con y sin corrección, el aumento del volumen corneal y el incremento de la asfericidad tras el implante de los ICRS.[42] Los pacientes que alcanzaron los mejores resultados fueron aquellos que presentaban queratocono tipo oval, con menores valores de K y córneas menos proladas. Torquetti et al.[15] observaron en su estudio con 35 ojos de 28 pacientes y un seguimiento mínimo de 5 años (5 y 12 años) de postoperatorio, la disminución de la queratometría en todos los ojos, de manera estadísticamente significativa. La mejora gradual de la agudeza visual sin corrección ocurrió hasta el cuarto año postoperatorio permaneciendo estable hasta el quinto año postoperatorio. La agudeza visual con corrección mejoró hasta el tercer año postoperatorio y permaneció estable hasta el quinto año postoperatorio. En lo que respecta al "follow-up" de 10 años de pacientes implantados con los anillos de Ferrara, se evaluaron 36 ojos de 30 pacientes operados entre junio de 1996 y enero de 2002.[45] Se realizó el seguimiento de estos pacientes implantados con ICRS a los 5 años y a los 10 años de postoperatorio. Se observó una disminución de los valores de la queratometría a los 5 años de seguimiento, además de una mejora de la agudeza visual estadísticamente significativa. El 70% de los pacientes ganó 2 o más líneas de visión sin corrección, mientras que un 10% de ellos perdió 2 o más líneas de visión sin corrección en el postoperatorio. Todos los pacientes que perdieron líneas de visión presentaban queratocono grado III y grado IV, o habían sido sometidos a una reoperación para efectuar el reposicionamiento, la remoción o el cambio de segmentos de ICRS, demostrando como descrito anteriormente, que los queratoconos más avanzados presentan un pronóstico visual peor después de la cirugía. (Rodrigues P, Torquetti L y Alió JI).[15,45,113] El 56,5% de los pacientes ganó 2 o más líneas de visión corregida a los 5 años, mientras que el 66,7% de los pacientes ganó 2 o más líneas de visión a los 10 años de seguimiento. Sin embargo, cuando comparamos los resultados a los 5 años de seguimiento con los resultados a los 10 años, observamos que las variaciones de la queratometría, AV con y sin corrección y espesor corneal no fueron estadísticamente significativas. El implante de los anillos genera una redistribución de la curvatura corneal, lo que resulta en redistribución del estrés, interrumpiendo el ciclo de progresión del queratocono.[84]

Las alteraciones estructurales relacionadas con la edad del paciente resultan en el entrecruzamiento del colágeno y pueden ocasionar alteraciones en la biomecánica corneal,[79] desacelerando o incluso frenando la evolución del queratocono. Estas variaciones pueden influir

en algunos de nuestros resultados, ya que parte de nuestros pacientes tenía más de 30 años en el momento de la cirugía.

Otros estudios ya habían demostrado que el aplanamiento corneal y el efecto de los implantes de ICRS se mantienen estables en la mayoría de los pacientes. Alió et al.[77] realizaron un estudio retrospectivo con más de 2 años de seguimiento, en el cual evaluaron los resultados del implante de ICRS (Intacs) en pacientes con queratocono. Después de 6 meses de follow-up, hubo una mejora de la agudeza visual sin corrección, además de una disminución de los valores queratométricos estadísticamente significativos. En un estudio de 2 años de seguimiento, Colin y Malet[80] describieron los resultados del implante de Intacs: mejora de la agudeza visual con corrección del 61% de los ojos con un año de follow-up, y del 68,3% de los ojos a los 2 años de seguimiento. El 14,63% de los ojos implantados perdieron una o más líneas de visión a los 2 años de seguimiento.

En muchos de los pacientes la manifestación del queratocono ocurre en solamente un ojo, mientras que, en otros, la manifestación ocurre en los 2 ojos. En la evaluación de niños con diagnóstico de queratocono tratados con los ICRS en nuestro servicio, observamos que 21 de los 37 niños operados necesitaron del implante del ICRS en el ojo contralateral. De éstos, 3 de los pacientes tuvieron el ojo contralateral operado después de por lo menos 6 meses del implante del primer ojo, lo que indica una progresión del queratocono en el ojo no tratado, mientras que en el ojo tratado el queratocono se mantuvo estable. En otro estudio con 5 años de seguimiento (Torqueti et al, 2009),[15] 7 de los 28 pacientes tuvieron el ojo contralateral operado hasta 3 años después del primer ojo.

En estos estudios, se indicaron los ICRS en los casos con evidencia de progresión del queratocono y/o intolerancia a las lentes de contacto. El hecho de que los ojos operados en el primero momento del diagnóstico no evidenciaron progresión después del implante, y la comprobación de la progresión en el ojo contralateral, con indicación de tratamiento quirúrgico, sugiere que los anillos intracorneales fueron efectivos para la paralización de la evolución de la ectasia durante el periodo estudiado.

El implante de los anillos de Ferrara es mínimamente invasivo, además de reversible. El resultado del implante de los ICRS depende de muchos factores, entre ellos, el implante correcto de los segmentos, centralizando el tratamiento en el eje visual (primer reflejo de Purkinge), en la zona óptica adecuada, y en la profundidad correcta del 80% del espesor corneal en el sitio de la incisión (técnica manual) o en una profundidad del 80% del espesor corneal en el punto más delgado de la córnea en el trayecto del anillo (técnica de Femtosegundo). La

incidencia de complicaciones es pequeña con el dominio de la técnica quirúrgica.

Las complicaciones, en general, están relacionadas a la técnica quirúrgica, al nomograma y a los anillos intracorneales. Las patologías sistémicas, como las enfermedades del colágeno, también pueden influir en los resultados y deben ser diagnosticadas antes de la indicación de la cirugía.

Inicialmente se utilizaron dos segmentos simétricos en todos los casos, y la indicación de los segmentos ocurría de acuerdo con el grado del queratocono. Se confeccionaba la incisión en el meridiano más curvo para sacar provecho del "efecto coupling" de los segmentos.

La segunda generación del nomograma tenía en cuenta la refracción del paciente para la selección de los anillos, además de la distribución del área de ectasia en la córnea. Se escogieron segmentos más gruesos y, como la miopía no era inducida por la ectasia, sino por el crecimiento anteroposterior del ojo, en muchos casos se observaba una híper corrección debido al implante de segmentos gruesos en queratoconos iniciales.

La tercera generación del nomograma pasó a considerar el procedimiento como tratamiento ortopédico, y la refracción dejó de tener importancia en la selección de los segmentos. Este nomograma tiene en cuenta la distribución del área ectásica en la córnea, el astigmatismo topográfico y el espesor corneal. Se determinó, en ese momento, que el espesor del segmento no debe exceder el 50% del espesor corneal en el trayecto del anillo.

El seguimiento de un número elevado de casos posibilitó llevar a cabo la evaluación de las alteraciones inducidas en el valor de la asfericidad (Q) por combinaciones de diferentes segmentos con diferentes espesores. La cuarta generación del nomograma fue desarrollada a partir de estos datos. Los resultados obtenidos con este nomograma han sido satisfactorios (Ferrara et al, 2011),[42] además de reproducibles. El valor de Q normal, en la zona óptica de 4,5 mm, puede variar de -0,01 a -0,80 (Silva et al, 2000),[68] y el valor más aceptado actualmente como normal en poblaciones de individuos adultos es de aproximadamente -0,23 ± 0,08 (Yebra-Pimentel et al, 2004).[69]

Actualmente se utilizan segmentos más delgados que antes para lograr resultados iguales o mejores a los que se obtenía utilizando los nomogramas anteriores. Además, la elección de los segmentos resulta ahora mucho más sencilla, pues depende de un solo parámetro.

En el estudio realizado con 1073 ojos de 810 pacientes (Ferrara G et al.),[42] las complicaciones observadas en el postoperatorio fueron hipo e hipercorrección, extrusión, descentramiento, neo

vascularización y progresión del queratocono, totalizando 41 ojos (3,82%). La principal complicación observada fue la hipocorrección, que ocurrió en 16 ojos, seguida de una hipercorrección ocurrida en 11 ojos.

La mejora de la técnica quirúrgica y de los conocimientos sobre el mecanismo de acción de los anillos permitieron el desarrollo de nomogramas basados en el análisis estadístico, mejorando la previsibilidad de los resultados. Incluso con la evolución del nomograma, todavía ocurren casos de hipo e hipercorrección, relacionados probablemente a alteraciones de la biomecánica corneal. La respuesta al implante de los anillos puede ser diferente entre pacientes con estándares topográficos similares, posiblemente debido a diferencias de viscoelasticidad y rigidez. Las córneas más elásticas tienden a responder mejor al implante de los anillos.

De las complicaciones relacionadas con la técnica quirúrgica, la extrusión es la más temida. Ella está relacionada al implante superficial de los anillos y al implante de segmentos muy gruesos (300µm), segmentos excluidos del nomograma actual. La paquimetría en el trayecto del anillo debe ser, por lo menos, el doble del espesor del segmento que se pretende implantar.

Los casos de infección pueden ocurrir en dos situaciones: en el postoperatorio inmediato o en el tardío asociado al uso de lentes de contacto blandas. Las infecciones en el postoperatorio inmediato requieren el explante de los segmentos, además de la administración de antibióticos tópicos, mientras que, en los casos tardíos, la utilización de los antibióticos suele ser suficiente.

La migración de los segmentos está relacionada con el prurito intenso en pacientes atópicos y el acto de rascarse el ojo puede desplazar los segmentos. La descentración y asimetría de los segmentos están relacionadas a la técnica quirúrgica. Todas las etapas de la cirugía deben ser seguidas a fin de evitar las complicaciones. Las incisiones superficiales pueden dificultar la confección del túnel escleral, generando implantes descentrados y/o asimétricos. Además, los implantes superficiales corren más riesgo de extrusión.

Los halos y los reflejos son complicaciones relacionadas a los anillos y pueden estarlo al tamaño de la pupila. Cuando son muy sintomáticos, los pacientes pueden beneficiarse de pilocarpina o tartarato de brimonidina, con el objetivo de cerrar la pupila y disminuir los reflejos no deseados. Se desarrollaron también los anillos amarillos, que filtran la luz azul, lo que mejora de manera significativa la queja de los halos y del reflejo.
Las opacidades perianulares son pequeños depósitos blancos, opacos, que se depositan a lo largo de la fase interna del anillo. Pueden ser observados en casos de trauma quirúrgico significativo, pero no perjudican el desempeño visual. La neovascularización del túnel es raro, y

puede ser tratada con inyección de bevacizumab subconjuntival.

Las complicaciones tales como descentración, extrusión e infección bacteriana fueron descritas por Kwitko y Severo.[114] Para ellos, la curva de aprendizaje del cirujano y los diferentes procesos de cicatrización en las córneas con queratocono pueden causar la mayoría de las complicaciones relacionadas a la técnica quirúrgica. Una vez dominado el procedimiento quirúrgico, la tasa de complicaciones es muy baja.

La incidencia de complicaciones en nuestros estudios ha sido prácticamente nula, lo que puede ser explicado por el dominio de la técnica quirúrgica, dado que todos los pacientes fueron operados por el Dr. Paulo Ferrara, experto cirujano del segmento anterior, y por los conocimientos adquiridos a lo largo del tiempo, además de la evolución del nomograma.

Para nuestro grupo de estudios, los anillos intracorneales son la primera alternativa de tratamiento para los pacientes que presentan una progresión del queratocono. La técnica puede asociarse, en casos de progresión, a la realización del CXL. En nuestra experiencia, un 5% de los pacientes terminan en queratoplastia, a pesar de los implantes. El trasplante de córnea sigue siendo la última alternativa de tratamiento para pacientes portadores de queratocono.

Además del queratocono, los implantes intracorneales han sido indicados para el tratamiento de astigmatismos irregulares secundarios a trasplante de córnea y ectasia post Lasik, con el objetivo de disminuir la queratometría, regularizar la superficie corneal y mejorar la agudeza visual

El astigmatismo irregular, asociado al trasplante de córnea, son responsables de la disminución de la agudeza visual en el postoperatorio de estos pacientes. El implante de segmentos intracorneales ha sido propuesto para el tratamiento de estos astigmatismos, con buenos resultados.

Un estudio retrospectivo de Coscarelli et al.[97] con 59 ojos de 54 pacientes implantados con ICRS para la corrección de astigmatismo residual postrasplante penetrante de córnea, evidenció el aplanamiento de la córnea y una reducción del error refractivo esfero cilíndrico estadísticamente significativo. La CDVA no se alteró en el postoperatorio de 16 ojos (27,2%), mientras que 43 ojos (72,8%) mejoraron, por lo menos, una línea de visión.

Otros estudios también han demostrado buenos resultados para la corrección del astigmatismo post PKP, con reducción de la refracción, mejora de la AV y de los resultados topográficos. (Coskunseven et al., Arriola-Villalobos et al., Chang y Hardten).[102,103,104]

En estos pacientes, es preferible el uso de segmentos de pequeño diámetro, pues tienen más efecto y promueven un mayor aplanamiento de la córnea, además de quedar lejos de la junción del injerto con la córnea receptora, lo que reduce el riesgo de dehiscencia del injerto y de neovascularización del túnel por neovasos provenientes del limbo o de la córnea receptora.

Las complicaciones del estudio fueron hipocorrección y dehiscencia de sutura. El 72,8% de los ojos (43 ojos) del estudio presentó hipocorrección. La causa de la misma se debe, probablemente, a diferencias en la biomecánica corneal, que es distinta entre córneas normales y córneas de pacientes con queratocono, pues presentan rigidez, espesor y elasticidad normales y, por consiguiente, menos responsivas al efecto de los implantes. El 5% de los casos (3/59 pacientes) han tenido que ser reoperados por dehiscencia en la región de la cicatriz entre el injerto y la córnea receptora durante la confección del túnel estromal. El advenimiento del láser de femtosegundo facilita la confección del túnel estromal y previene ese tipo de complicación.[105,106]

La ectasia de la córnea es una complicación infrecuente en la cirugía refractiva y ocurre más frecuentemente en pacientes sometidos al Lasik. Los tratamientos para la ectasia post Lasik incluyen lentes esclerales, CXL, trasplante de córnea y el ICRS.

Torquetti et al.[115] evaluaron 25 ojos de 20 pacientes que presentaron ectasia de la córnea tras la cirugía refractiva, de los cuales 20 ojos habían sido sometidos a la técnica de Lasik, 4 ojos habían sido sometidos a queratotomía radial y un ojo había sido sometido a PRK. El promedio de seguimiento fue de 39,8 meses. Se observó en el estudio una mejora del promedio de la agudeza visual con y sin corrección, un aumento del promedio de la asfericidad y de la paquimetría, además de la reducción de los valores del promedio de la queratometría, estadísticamente significativos.

Los pacientes que desarrollan ectasia post Lasik, en general presentan valores preoperatorios de Q superiores cuando se los compara con los pacientes portadores de queratocono. Al evaluar el aumento de la asfericidad en los resultados de pacientes operados de anillos intracorneales para el tratamiento de ectasia post lasik encontramos valores cercanos al de córneas normales. En

este estudio el promedio de la asfericidad postoperatoria fue de -0,23, considerado como valor normal de Q para la población en general.

Entre las ventajas de la técnica del implante de los ICRS sobre el trasplante de córnea se destacan la reversibilidad de la técnica, el hecho de que la técnica puede ser ajustada al resultado y, lo más importante, porque evita las complicaciones de una cirugía intraocular.

Las limitaciones del estudio de los segmentos en ectasia post Lasik fueron la pequeña muestra de pacientes, además de no poseer un grupo de comparación. En eses casos de ectasia post cirugía refractiva, los ICRS presentaron resultados satisfactorios.

Los anillos intracorneales se mostraron eficaces en el tratamiento del queratocono, así como para la corrección del astigmatismo irregular post queratoplastia y ectasia post cirugía refractiva, con mejora de la agudeza visual, valores queratométricos, aumento de la asfericidad corneal y paquimetría. El implante de los anillos intracorenales es una técnica mínimamente invasiva, segura y reversible. Los ICRS desempeñan un papel importante en la estabilización del queratocono, pudiendo postergar, o mismo evitar, el trasplante de córnea.

14. Futuros Proyectos de Investigación

i. Estudio a largo plazo del “outcome” del implante de los ICRS en niños.

ii. Seguimiento a largo plazo de un número mayor de pacientes implantados con los ICRS.

iii. Desarrollo de nuevos materiales, buscando mayor biocompatibilidad corneal y índices de refracción más cercanos a los índice corneales.

iv. Mejora del nomograma a partir de conocimientos de la biomecánica corneal

15. Conclusiones

1. El implante de ICRS en pacientes con queratocono, con las limitaciones de un estudio observacional y retrospectivo, regulariza la superficie de la cornea, disminuye los valores queratométricos – especialmente la queratometría máxima, disminuyendo el astigmatismo irregular - y mejora la agudeza visual con y sin corrección a los pacientes implantados.

2. Dentro de las limitaciones del estudio, el implante de ICRS estabiliza la cornea y detiene la progresión de la enfermedad.

3. El implante de ICRS en pacientes con queratoplastia disminuye el equivalente esférico, disminuye los valores queratométricos y el el astigmatismo topográfico, además de mejorar la agudeza visual con y sin corrección.

4. El análisis de resultados de implante de ICRS en niños muestra resultados similares a los de adultos con reducción de valores queratométricos, mejora de la agudeza visual y estabilidad refractiva a los dos años de seguimiento.

16. Referencias

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17. Publicaciones Científicas que avalan la presente tesis doctoral como "compendio de artículos"

"…Copia completa de los trabajos en la que conste el nombre y adscripción del autor y de todos los coautores, si los hubiere, así como la referencia completa de la revista o editorial en la que los trabajos hayan sido publicados o aceptados para su publicación, en cuyo caso se aportará justificante de la aceptación por parte de la revista o editorial. Informe con el factor de impacto de las publicaciones presentadas. En aquellas áreas en las que no sea aplicable este criterio se sustituirá por las bases relacionadas por la Comisión Nacional Evaluadora de la Actividad Investigadora (CNEAI) para estos campos científicos…"

1.
AUTOR: Ferrara G[1], Torquetti L[1], Ferrara P[1], **Merayo-Lloves J**[2].
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6.5. Ferrara G[1], Merayo-Lloves J[2], Ferrara P[1]. Torquetti L[1,3].Intrastromal corneal ring segments in children with keratoconus. Int J Kerat Ect Cor Dis Submitted April 5 2017. ***(articulo enviado y pendiente de aceptación en el momento de depositar la tesis)***

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Clinical and Experimental Ophthalmology 2011; ••: ••–•• doi: 10.1111/j.1442-9071.2011.02698.x

Original Article

Intrastromal corneal ring segments: visual outcomes from a large case series

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Abstract

Background: To evaluate the clinical safety and efficacy of implanted Ferrara intrastromal corneal ring segments in a large sample of patients with ectatic corneal disease.

Design: Retrospective, consecutive case series.

Samples: A total of 1073 eyes of 810 patients consecutively operated from January 2006 to July 2008 were evaluated.

Methods: Two groups were created according to the type of ring implanted: Group 1 – patients implanted with the 160° of arc ring – and Group 2 – patients implanted with the 210° of arc ring.

Main Outcome Measures: Uncorrected visual acuity, best-corrected visual acuity, keratometry, asphericity and pachymetry at the thinnest point of the cornea. All patients were evaluated using a corneal tomography (Pentacam, Oculus, Inc., Lynnwood, WA, USA).

Results: For Group 1 patients, uncorrected visual acuity increased to 20/80, best-corrected visual acuity increased to 20/40, asphericity decreased to −0.35, spherical equivalent decreased to −2.26 D and keratometry decreased to 45.72 D ($P < 0.001$ for each compared with preoperative values). For Group 2 patients, uncorrected visual acuity increased to 20/130, best-corrected visual acuity increased to 20/60, asphericity decreased to −0.56, spherical equivalent decreased to −4.14 D and keratometry decreased to 48.10 D ($P < 0.001$ for each compared with preoperative values). The 210° intrastromal corneal ring segments reduced keratometry and asphericity more than the 160° intrastromal corneal ring segments did. The complication rate was 3.82%.

Conclusions: Ferrara intrastromal corneal ring segments implantation is safe and effective and has a low complication rate. It can effectively reduce the corneal steepening and improve uncorrected visual acuity and best-corrected visual acuity in patients with keratoconus.

Key words: cornea, corneal topography, keratoconus.

Introduction

Ferrara pioneered the technique of intrastromal corneal ring segment (ICRS) implantation in keratoconus.[1] ICRS are polymethylmethacrylate devices that have now been successfully used for the management of keratoconus,[2–6] pellucid marginal degeneration,[7] postoperative corneal ectasia,[8,9] myopia[10,11] and high postkeratoplasty astigmatism.[12] ICRS implantation is a safe, reversible alternative to keratoplasty and does not affect the central visual axis of the cornea. The goal of ring segment implantation is to improve visual acuity and to delay or avoid corneal grafts in patients with keratoconus.

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Received 9 July 2011; accepted 15 August 2011.

Competing/conflicts of interest: No stated conflict of interest.

Funding sources: Dr Paulo Ferrara, Dr Guilherme Ferrara and Dr Jesús Merayo-Lloves have financial interest in the Ferrara Ring. Dr Leonardo Torquetti has no financial interest.

The changes in corneal structure induced by additive technologies can be roughly predicted by the Barraquer thickness law.[13,14] This law states that when material is added to the periphery of the cornea or an equal amount of material is removed from the central area, a flattening effect is achieved. In contrast, when material is added to the centre or removed from the corneal periphery, the surface curvature is steepened. The corrective result varies in direct proportion to the thickness of the implant and in inverse proportion to its diameter. The thicker and the smaller the diameter of the device, the higher the corrective result.[13,14]

The purpose of this study was to evaluate the visual and topographic outcomes of the Ferrara ICRS for the treatment of keratoconus and keratectasia in a large sample of patients.

Methods

This study was approved by the institutional review board of Dr Paulo Ferrara Eye Clinic, Belo Horizonte, MG, Brazil and followed the tenets of the Declaration of Helsinki. The procedures were fully explained to each patient, and each provided written informed consent.

In the present study, 1073 eyes of 810 consecutive surgical patients from January 2006 to July 2008 were retrospectively evaluated. The patients were divided into two groups according to the type of keratectasia and ring implanted. Patients with keratoconus and keratectasias of the oval- or bowtie-type[15,16] were designated as Group 1 ($n = 972$ eyes, Table 1) and implanted with ICRS with 160° of arc (160-ICRS, Ferrara e Hijos, Boecillo, Spain). Patients with the nipple-type keratectasia[15,16] were designated as Group 2 ($n = 101$ eyes) and were implanted with ICRS with 210° of arc (210-ICRS). Only cases of primary ectasias were included in this study.

Inclusion criteria were contact lens intolerance and/or evidence of ectasia progression as measured by worsening of uncorrected visual acuity (UCVA) and best-corrected visual acuity (BCVA), progressive intolerance to contact lens wear and progressive corneal steepening documented by topographical changes. Two or more lines of UCVA and/or BCVA worsening and at least 2 diopters (D) of increase in mean keratometry as measured with a Pentacam (Pentacam HR, Oculus, Inc., Lynnwood, WA, USA) were required to define progression of the disease. Exclusion criteria included any of the following discovered during the preoperative examination: advanced keratoconus with curvatures over 62 D, significant apical opacity and scarring, hydrops, corneas with thickness below 300 µm in the ring track as evaluated by Pentacam pachymetry, and intense unresolved atopia, which is more appropriately treated before implantation. Pregnant or nursing women and patients with evidence of any systemic disease that would increase the risk of surgery were also excluded from the study.

Table 1. Demographic data for Groups 1 and 2

	Group 1	Group 2
Eyes (*n*)	972	101
Age (years)	29.4 ± 9.4 (range 17 to 59)	30.2 ± 8.7 (range 14 to 64)
Sex (male/female)	57/43	51/49
Follow-up (months)	23.8 ± 12.2	22.9 ± 15.1

Group 1 patients were implanted with the 160° arc ring (160-instrastromal corneal ring segments [ICRS]), Group 2 patients were implanted with the 210° arc ring (210-ICRS). *P*-values >0.05 for all variables.

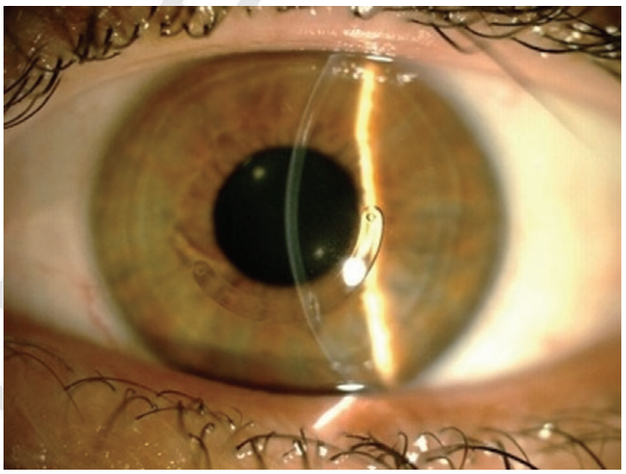

Figure 1. Day 1 postoperative slit-lamp examination.

Clinical measurements

A complete ophthalmologic examination was performed before surgery and included UCVA and BCVA assessment, biomicroscopy, fundoscopy, tonometry, corneal topography, pachymetric map and asphericity measurement using the Pentacam HR. All clinical examinations were performed in a standardized manner by an experienced examiner (PF).

On the first postoperative day, slit-lamp biomicroscopic examination was performed (Fig. 1). Healing of the wound and migration of the segments were evaluated. At the last follow-up examination, manifest refraction, UCVA, BCVA, slit-lamp and topographic examinations were performed.

Surgical technique

All surgeries were performed by the same surgeon (PF) using the manual technique. The arc and thick-

ness of the ICRS were selected according to a previously described nomogram that is based on the position of the keratoconus on the cornea, topographic astigmatism and the pachymetric map.[4,5] The nomogram determines the ring thickness to be implanted (Fig. 2). The surgery was performed under topical anaesthesia after miosis was achieved with 2% pilocarpine. An eyelid speculum was used to expose the eye, and 2.5% povidone-iodine eye drops were instilled onto the cornea and conjunctival cul-de-sac. The visual axis was marked by pressing a Sinskey hook on the central corneal epithelium while asking the patient to fixate on the corneal light reflex of the microscope light. Using a marker tinted with gentian violet, a 5.0-mm optical zone and incision site were aligned to the desired axis in which the incision would be made. This incision site was always the steepest topographic axis of the cornea given by the Pentacam.

A square diamond blade was set at 80% of corneal thickness as determined by the pachymetric map at the incision site. Using a 'stromal spreader', a pocket was formed in each side of the incision. Two 270° semicircular dissecting spatulas, clockwise and counterclockwise, were consecutively inserted through the incision and gently pushed with some quick, rotary 'back-and-forth' tunnelling movements. Following channel creation, the ring segments were inserted using a modified McPherson forceps. The rings were properly positioned with the aid of the Sinskey hook.

The postoperative regimen consisted of moxifloxacin 0.5% (Vigamox, Alcon, Fort Worth, TX, USA) and dexamethasone 0.1% (Maxidex, Alcon) eye drops four times daily for 2 weeks. The patients were instructed to avoid rubbing the eye and to frequently use preservative-free artificial tears (Oftane 0.4%, Alcon). The patients were examined postoperatively at 1 day, 1 month, 3 months, 6 months and 1 year after the surgery. After the first year, the patients were evaluated annually. The mean follow-up time was based on the time of the last visit.

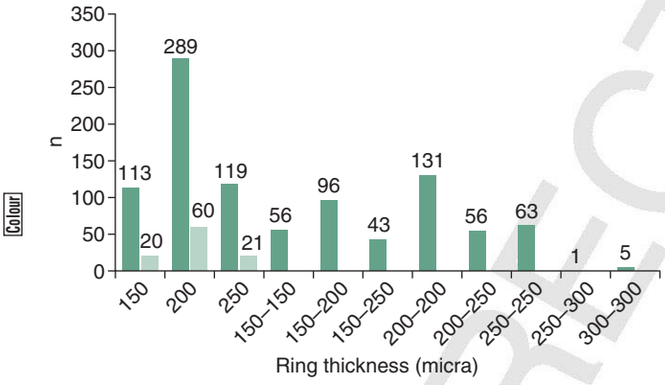

Figure 2. Distribution of implanted instrastromal corneal ring segment (ICRS) rings according to thickness and arc. Blue bars, 160–ICRS; Red bars, 210–ICRS.

Statistical analysis

The Statistical Package for the Social Sciences (SPSS, Chicago, IL, USA) was used for descriptive statistics, including means ± standard deviations, and to test group differences for continuous variables. Student's *t*-test for paired data was used to compare preoperative and postoperative data. Statistical analysis was done using independent sample *t*-tests to compare variables between Groups 1 and 2. *P*-values less than 0.05 were considered statistically significant.

Results

The mean follow-up times for Groups 1 and 2 were 23.8 ± 12.2 months and 22.9 ± 15.1 months, respectively (Table 1). The mean UCVA in Group 1 increased from 20/220 to 20/80 ($P = 0.00001$, Table 2). For Group 2, the mean UCVA increased from 20/350 to 20/130 ($P = 0.001$). The mean BCVA in Group 1 increased from 20/100 to 20/40 ($P = 0.00023$, Table 2), whereas in Group 2, it increased

Table 2. Preoperative and last follow-up examination data of patients implanted with the Ferrrara ICRS

	Group 1			Group 2			Unpaired *t*-test (between groups)
	Preoperative	Postoperative	*P*†	Preoperative	Postoperative	*P*‡	*P*
UCVA	20/220	20/80	0.00001	20/350	20/130	0.001	0.038
BCVA	20/100	20/40	0.00023	20/110	20/60	0.0003	0.0034
Asphericity	–0.88 ± 0.52	–0.35 ± 0.55	0.00004	–1.17 ± 0.47	–0.56 ± 0.56	0.00004	0.0031
Spherical equivalent (D)	–3.99 ± 4.22	–2.26 ± 3.09	0.0002	–8.52 ± 5.63	–4.14 ± 4.37	0.0002	0.0010
Keratometry (D)	49.18 ± 4.42	45.72 ± 3.72	0.00003	51.92 ± 5.91	48.10 ± 4.96	0.0001	0.0001
Pachymetry (μm)	448 ± 44.8	465 ± 49.2	0.0001	418 ± 53.4	435 ± 56.6	0.0002	0.0001

†Preoperative Group 1 *versus* Postoperative Group 1. ‡Preoperative Group 2 *versus* Postoperative Group 2. BCVA, best-corrected visual acuity; ICRS, intrastromal corneal ring segments; UCVA, uncorrected visual acuity.

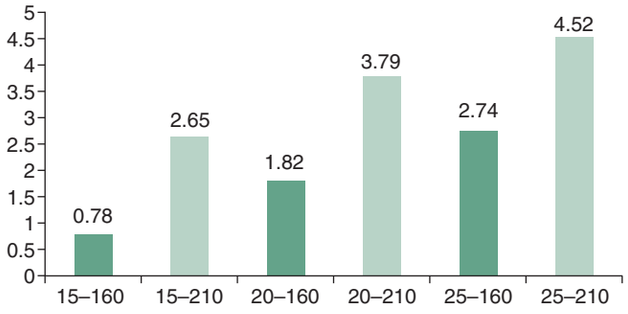

Figure 3. Effect of ring thickness on mean keratometry. The mean decrease in keratometry from preoperative to postoperative values at the last follow-up visit was greater for thicker rings. Blue bars, 160–instrastromal corneal ring segments (ICRS); Red bars, 210–ICRS. The numbers 15, 20 and 25 on the bottom of the chart, before the numbers 160 and 210, refer to ring thickness: 15 = 150 micra, 20 = 200 micra and 250 = 250 micra.

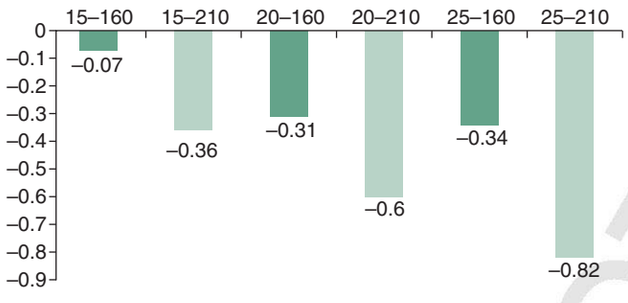

Figure 4. Effect of ring thickness on mean asphericity. The mean decrease in asphericity from preoperative to postoperative values at the last follow-up visit was greater for thicker rings. Blue bars, 160 – instrastromal corneal ring segments (ICRS); Red bars, 210 – ICRS and thickness implanted. The numbers15, 20 and 25 on the bottom of the chart, before the numbers 160 and 210, refer to ring thickness: 15 = 150 micra, 20 = 200 micra and 250 = 250 micra.

from 20/110 to 20/60 ($P = 0.0003$). Asphericity changed in Group 1 from −0.88 to −0.35 ($P = 0.001$) and from −1.17 to −0.56 in Group 2 ($P = 0.000$).

For Group 1 patients, the preoperative spherical equivalent, −3.99 D, was reduced to −2.26 D at the last postoperative examination and the keratometry decreased from 49.18 to 45.72 D (both $P < 0.001$, Table 2). Simultaneously, the pachymetry at the thinnest point increased from 448 to 465 μm ($P < 0.001$). For Group 2 patients, the spherical equivalent decreased from −8.52 to −4.14 D and the keratometric values decreased from 51.92 to 48.10 D (both $P < 0.001$, Table 2). Simultaneously, the pachymetry at the thinnest point increased from 418 to 435 μm ($P < 0.001$).

The mean keratometry values decreased between the preoperative and postoperative periods (Fig. 3), and the thicker rings induced larger reductions. The

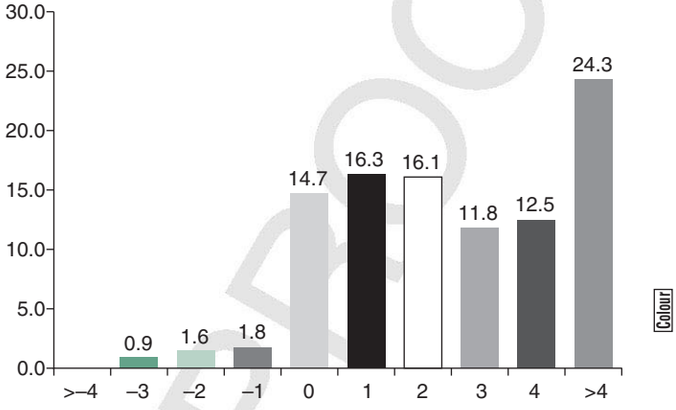

Figure 5. Best-corrected visual acuity lines gain/lost in Group 1 (%).

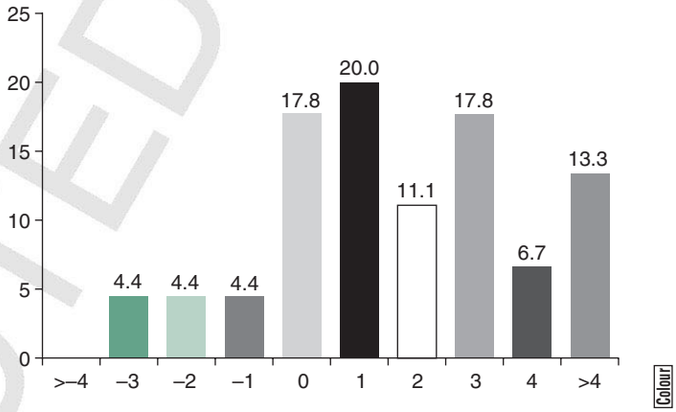

Figure 6. Best-corrected visual acuity lines gain/lost in Group 2 (%).

210-ICRS caused larger changes in mean keratometry than did the 160-ICRS (Table 2). Asphericity values changed between the preoperative and postoperative periods (Fig. 4), and the thicker the ring, the larger the asphericity change. Also, the 210-ICRS caused larger changes in asphericity than the 160-ICRS did (Table 2).

Patients in Group 1 had better preoperative and postoperative UCVAs and BCVAs than patients in Group 2 (Table 2). The changes in keratometry, asphericity, spherical equivalent and pachymetry were larger in Group 2 than in Group 1 (Table 2). Regarding lines gain/loss, 81% of patients of Group 1 gained at least two lines of BCVA. In Group 2, 49% of patients gained at least two lines of BCVA. (Figs 5,6).

Complications

The complication rate after Ferrara ICRS implantation was low, 3.82% (Table 3). The main com-

Table 3. Complication rate after ICRS implantation

Complication	Treatment	Eyes (%)
Undercorrection	Implantation of additional segment	16 (1.49)
Overcorrection	Segment removal and reimplantation	11 (1.02)
Extrusion	Segment removal	6 (0.56)
Malposition	Segment repositioning	4 (0.37)
Progressive corneal steepening	Keratoplasty	2 (0.18)
Ring neovascularization	Bevacizumab	2 (0.18)
Total		41 (3.82)

ICRS, intrastromal corneal ring segments.

Table 4. Preoperative and last follow-up examination data of patients who underwent follow-up surgery for removal, exchange or additional ICRS implantation

	Preoperative	Postoperative	*P*
UCVA	20/300	20/80	0.005
BCVA	20/160	20/50	0.0002
Asphericity	–0.84 ± 0.74	–0.35 ± 0.81	0.15
Spherical equivalent (D)	–4.64 ± 4.87	–3.04 ± 3.45	0.137
Keratometry (D)	49.33 ± 4.19	46.16 ± 3.90	0.0001
Pachymetry (μm)	450 ± 42.9	469 ± 40.8	0.0001

$n = 37$ eyes, 34 from Groups 1 and 3 from Group 2. BCVA, best-corrected visual acuity; ICRS, intrastromal corneal ring segments; UCVA, uncorrected visual acuity.

plication, 16 cases, was undercorrection, requiring implantation of an additional segment. One eye each of 37 patients (34 in Group 1 and 3 in Group 2) underwent follow-up surgery (Table 4) to remove ($n = 6$), exchange ($n = 11$), reposition ($n = 4$) or insert an additional ICRS ($n = 16$). For those patients, there were significant improvement between the preoperative values and the final follow-up values for UCVA, BCVA, keratometry and pachymetry. Asphericity and spherical equivalent for these patients did not improve significantly.

Discussion

Modern treatment of keratoconus and keratectasia includes the implantation of ICRS that can effectively reduce corneal steepening and improve UCVA and BCVA. The Ferrara ring nomogram requires the keratoconus type, oval, bowtie or nipple, to determine the arc segment, 160° or 210°, which will be implanted. Longer arc ring segments provide more keratometry reduction and less astigmatism reduction. In the nipple type of keratoconus, Group 2 in this study, the cornea is usually very steep with relatively low astigmatism. Therefore, for this type of keratoconus, the 210° ring segments are the most appropriate. They provide significant flattening without a large concomitant induction of astigmatism.[3]

Our postoperative results showed a significant improvement in UCVA and BCVA. These results are in concordance with most similar papers;[1,2,4,17–19] however, this is the first study to describe the clinical outcomes in a large sample of consecutive surgical patients. To the best of our knowledge, this study has the largest sample of patients implanted with ICRS ever published. Our data reinforce the reproducibility and efficacy of the technique.[20,21]

Miranda *et al*. obtained a significant reduction in the postoperative central corneal curvature, and the BCVA and UCVA improved in 87.1 and 80.6% of the eyes, respectively.[22] Siganos *et al*. showed an increase of the UCVA from 20/285 preoperatively to 20/100 and 20/60 after 1 and 6 months, respectively.[2] The BCVA improved from 20/55 preoperatively to 20/40 and 20/33 after 1 and 6 months, respectively. Kwitko and Severo reported that after implantation of Ferrara rings in keratoconus eyes, the BCVA improved in 86.4% of eyes, was unchanged in 1.9% and worsened in 11.7%.[3] The UCVA improved in 86.4% of eyes, was unchanged in 7.8% and worsened in 5.8%. The mean corneal curvature was reduced from 48.76 D to 43.17 D.

When comparing our results with studies using other types of ICRS (e.g. Intacs and Keraring), we found similar outcomes. Alio' *et al*. performed a retrospective study to evaluate the long-term (up to 48 months) results after Intacs implantation in patients with keratoconus.[23] After 6 months, the mean UCVA increased significantly ($P < 0.01$) from 0.46 (20/50) preoperatively to 0.66 (20/30), and the average keratometry decreased by 3.13 D. Coskunseven *et al*. evaluated the results Keraring ICRS in 50 eyes of patients with keratoconus.[20] Of these, 47 had UCVA of 20/40 (range: counting fingers to 20/30). At the last follow-up examination, 14 of the 50 eyes had a UCVA of 20/40 or better (range: counting fingers to 20/25). Nine eyes maintained the preoperative BCVA, whereas 39 eyes experienced a BCVA gain of one to four lines.

We found a significant increase in corneal thickness in both groups. In theory, this can be explained by corneal collagen remodelling induced by the implantation of the ICRS.[24,25] By acting as 'spacers', the ring segments could interfere with corneal collagen turnover, with consequent increases in the corneal pachymetry.

We found a significant decrease in asphericity values after implantation of the ICRS. The postoperative value was –0.35 for Group 1 and –0.56 for Group 2. Most studies agree that human cornea asphericity values range from –0.01 to –0.80.[26–28]

Currently, the most commonly accepted value in a young adult population is approximately –0.23.[29] The asphericity can be considered as one of markers of visual quality. Thus, returning it closer to 'normal' or at least reducing the excess prolateness usually found in keratoconus could be a predictor of improved visual quality.

For all the measured parameters, the results were better for Group 1 than Group 2. The type of keratoconus can explain the differences. The Group 2 patients had the nipple-type keratoconus that tends to be more aggressive and respond to the 'conventional' 160° ring segments with less efficacy than the oval-type keratoconus. Nipple-type keratoconus is better treated with long-arc ring segments, such as the 210° ring segments. Given the same thickness of ICRS, the 210° ring segments can provide greater changes in keratometry and asphericity than the 160° ring segments. The efficacy and safety of the 210° ring has been demonstrated.[3]

The incidence of complications found in this study was extremely low. This can be explained by two factors: (i) mastery of the technique; and (ii) nomogram evolution. After mastering the surgical technique, especially the deep incision and the well-constructed intrastromal tunnel, the technique-related complications become very infrequent. The nomogram has evolved based on the knowledge that thinner segments achieve the same or better results than the thicker segments used in the past.[4,22] In some cases, an undercorrection or overcorrection was found; the cause for these changes are not well understood but probably are related to corneal biomechanics. The reason for insertion of additional ICRS was usually undercorrection, that is, a suboptimal reduction of corneal steepening after implantation of a single ICRS. One of the most feared complications of ICRS, ring extrusion, is now rare because the 350-μm thick rings are no longer implanted. The pachymetry at the ring track must be at least double the ring thickness to be implanted.

We showed that the outcome of patients requiring follow-up surgery because of overcorrection or undercorrection, 3.4%, is acceptable. For these patients, there was improvement of UCVA, BCVA, keratometry and pachymetry. However, asphericity and spherical equivalent did not improve in these patients undergoing subsequent surgery, perhaps because of the scarring of corneal tissue and/or stroma secondary to the first procedure.

Kwitko and Severo reported Ferrara ICRS decentration in 3.9% of cases, segment extrusion in 19.6% and bacterial keratitis in 1.9%.[2] As the authors mentioned in their paper, the surgeon's learning curve and different healing processes in keratoconic corneas can cause the majority of complications related to the surgical technique. Once the surgical procedure is mastered, the complications rate related to the surgery itself is very low, as demonstrated in the present study. To avoid surgery-related complications, the steps must be followed carefully, including constructing the stromal tunnel with the adjustable diamond knife set at 80% of local corneal thickness. This reduces the chance of a shallow tunnel and subsequent ring extrusion.

Extrusion of the ICRS usually occurs in patients with little stroma, overlying the implanted segments and when the ring is located close to the incision. As a general rule, it must be assumed that the thickest portion of a pair of segments in the stromal bed cannot exceed half the thickness of the cornea. If the desired ICRS thickness exceeds half the thickness of the cornea, then a thinner diameter ICRS must be selected even if the correction is likely to be smaller than desired. This should be considered as the 'pachymetry law' for ICRS implantation. Since this rule began to be followed, the incidence of extrusion has decreased significantly.[30]

Kubaloglu *et al.* evaluated the clinical outcomes of keratoconus patients that had ICRS implantation in which the intrastromal tunnel was created manually, as we did in our study, and by femtosecond laser.[31] After 1 year, there was significant improvement in UCVA, BCVA, keratometry, spherical equivalent, manifest sphere and cylinder in both groups. Importantly, there were no significant differences between the two groups regarding the visual or refractive results. After mastering the manual technique, the incidence of perioperative complications is extremely low, and this technique is both very safe and effective.

In conclusion, Ferrara ICRS implantation is an effective treatment for keratoconus and keratectasia. The procedure is minimally invasive and yields good visual, refractive and keratometric outcomes. Moreover, it is a safe technique and does not preclude any future additional treatment if necessary.

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Intrastromal corneal ring segment implantation to correct astigmatism after penetrating keratoplasty

Sandro Coscarelli, MD, Guilherme Ferrara, MD, Jose F. Alfonso, MD, PhD, Paulo Ferrara, MD, PhD, Jesús Merayo-Lloves, MD, PhD, Luana P.N. Araújo, MD, Aydano P. Machado, PhD, João Marcelo Lyra, MD, PhD, Leonardo Torquetti, MD, PhD

PURPOSE: To evaluate the clinical outcomes of implantation of Ferrara intrastromal corneal ring segments (ICRS) in patients with astigmatism after penetrating keratoplasty (PKP).

SETTING: Private clinic, Belo Horizonte, Brazil.

DESIGN: Retrospective consecutive case series.

METHODS: Chart records of post-PKP patients who had ICRS implantation from May 2005 to September 2009 were retrospectively reviewed. The following parameters were studied: corrected distance visual acuity (CDVA), keratometry (K) values, spherical equivalent (SE), spherical refractive error, corneal topographic astigmatism, minimum K, and maximum K.

RESULTS: The study evaluated 59 eyes (54 patients). The mean CDVA (logMAR) improved from 0.45 ± 0.17 (SD) (range 0.18 to 1.00) to 0.30 ± 0.17 (range 0.00 to 1.00). The mean SE was −6.34 ± 3.40 diopters (D) (range 0.37 to −16.50 D) preoperatively and −2.66 ± 2.52 D (range 0.87 to −10.50 D) postoperatively. The mean spherical refractive error decreased from −7.10 ± 3.07 D (range 2.15 to 16.68 D) preoperatively to −3.46 ± 2.05 D (range 0.88 to 10.79 D) postoperatively. No patient lost visual acuity. The mean corneal topographic astigmatism decreased from 3.37 ± 1.51 D preoperatively to 1.69 ± 1.04 D postoperatively. The mean maximum K value decreased from 48.09 ± 2.56 D to 44.17 ± 2.67 D and the mean minimum K value, from 44.90 ± 2.54 D to 42.46 ± 2.63 D. All changes were statistically significant (P<.0001).

CONCLUSION: Intrastromal corneal ring segments effectively reduced corneal cylinder in patients with astigmatism after PKP.

Financial Disclosure: Drs. Ferrara and Merayo-Lloves have proprietary interest in the Ferrara ring. Drs. Coscarelli, Torquetti, and Alfonso have no financial or proprietary interest in any material or method mentioned.

J Cataract Refract Surg 2012; 38:1006–1013 © 2012 ASCRS and ESCRS

The postoperative astigmatism associated with penetrating keratoplasty (PKP) is a common condition in clinical practice. The reason for this could be related to factors inherent to the receptor, such as previous corneal trauma or keratoconus.[1] Additional contributing factors may include the trephination technique, inadequate fixation of the eye during surgery with compression or deformation of the ocular globe, the suture technique, and postoperative issues such as the patient's age and receptor corneal disease, time on topical corticosteroids, and early suture removal.[2]

Previous studies[2–4] report several risk factors that may increase the incidence of post-PKP astigmatism and its management. Contact lenses are a better choice than spectacles to correct astigmatism because they provide better quality of vision.[5,6] Moreover, the corrected distance visual acuity (CDVA) with contact lenses is usually better than with spectacles in this type of astigmatism. When optical methods fail to achieve satisfactory visual rehabilitation, surgical treatment may be necessary. Whereas some authors have published that incisions and wedge resection of the cornea could be useful to correct the

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doi:10.1016/j.jcrs.2011.12.037

astigmatism,[7–9] other authors report that laser in situ keratomileusis (LASIK)[10,11] or the implantation of toric phakic intraocular lenses (pIOLs) could achieve better and more predictable results.[12,13]

In the present study, we evaluated the use of intrastromal corneal ring segments (ICRS) as an alternative surgical option for the treatment of astigmatism in patients who had PKP for keratoconus, bullous keratopathy, radial keratotomy (RK), post-LASIK ectasia, or stromal scarring. The outcome analysis comprised the CDVA, spherical equivalent (SE), refractive error, corneal topographic astigmatism, and minimum and maximum keratometry (K) values. To our knowledge, this study has the largest sample of patients with ICRS implantation to correct post-PKP astigmatism in the literature.

PATIENTS AND METHODS

This retrospective study included consecutive post-PKP patients who had ICRS implantation (Ferrara ring, Ferrara e Hijos) from May 2005 to September 2009 to correct residual astigmatism. All patients were informed about the possible intraoperative and postoperative complications and gave written informed consent in accordance with institutional guidelines and the Declaration of Helsinki.

Inclusion criteria were a clear and transparent corneal graft, a minimum of 2.50 diopters (D) and a maximum of 8.00 D of astigmatism, and contact lens intolerance. All patients had at least 2 years of follow-up after PKP before ICRS implantation. Patients who did not meet the inclusion criteria were not evaluated in this study.

Surgical Technique

The same surgeon (S.C.) performed all surgeries using a manual technique as previously described.[14] The surgery was performed using topical anesthesia after miosis was achieved with pilocarpine 2.0%. The visual axis was marked by pressing a Sinskey hook on the central corneal epithelium while asking the patient to fixate on the corneal light reflex of the microscope light. Using a marker tinted with gentian violet, a 5.0 mm optical zone and incision site were aligned to the desired axis in which the incision would be made. This incision site was always at the steepest topographic axis of the cornea given by the topographer.

Submitted: May 23, 2011.
Final revision submitted: November 18, 2011.
Accepted: December 5, 2011.

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A square diamond blade was set at 80% of corneal thickness at the incision site, and this blade was used to make the incision. A pocket was formed in each side of the incision using a stromal spreader. Two (clockwise and counterclockwise) 270-degree semicircular dissecting spatulas were consecutively inserted through the incision and gently pushed with quick rotary back-and-forth tunneling movements. After channel creation, the ring segments were inserted using a modified McPherson forceps. The rings were properly positioned with the aid of a Sinskey hook.

Postoperative Regimen and Assessment

The postoperative regimen consisted of tobramycin 0.3% and dexamethasone 0.1% eyedrops 4 times a day for 1 week, after which the dose was tapered over 3 weeks. In addition, patients received topical lubricants 4 times a day for at least 3 months.

Postoperative examinations were performed at 1 and 7 days, after 1 and 6 months, and then every year. Measurement of CDVA, slitlamp evaluation, refraction, corneal topography, fundoscopy, and tonometry were performed at each control visit. Visual acuity was determined on a Snellen chart and then converted to logMAR notation. The K values were obtained by corneal topography (CT4000 Corneal Topographer, Eyetech, Inc.).

To evaluate the CDVA, refractive error, and corneal topographic astigmatism, the nonparametric Mann-Whitney test was used because at least 1 datum from the sample did not have a Gaussian distribution. The SE was corrected by Welch transformation because of significant difference between 2 standard deviations (SDs).

Analysis of Astigmatism

The astigmatism results were analyzed arithmetically (nonvector analysis) and with regard to the cylindrical axis using vector analysis. Although empirical changes in cylinders are commonly reported, they do not accurately reflect the true nature of the change in cylinder. Cylinders have a magnitude and an axis, which are related to the spherical power.[15] To take into account all 3 components, the data in this study were transformed into Cartesian coordinates (ie, x and y coordinates) to allow mathematic analyses. The result in the Cartesian coordinate form was then reconverted into polar coordinates (sphere, cylinder, axis). To distinguish the mean value of the cylinder calculated in this manner, the term *centroid* has been proposed.[16]

Refractions before and 12 months after ICRS insertion were assessed for astigmatism using the power vector method.[17] Any spherocylindrical refractive error was expressed by 3 dioptric powers: M, J0, J45, with M being the aspheric lens equal to the SE of the given refractive error and J0 and J45 being 2 Jackson cross-cylinders equivalent to the conventional cylinders. These numbers are the coordinates of a point in a 3-dimensional dioptric space, being the power vector from the origin of this space to the point (M, J0, J45). Thus, the length of the vector is a measure of the overall blurring strength of the spherocylindrical refractive error. Changes in refractive error induced by the surgery were computed by the ordinary rules of vector extraction.

The target astigmatism is the intended astigmatic correction in each individual eye. The ideal target astigmatism was zero (ie, intention to correct the full magnitude of the cylinder).

Statistical Analysis

Data reported here are from the 12-month examination after ICRS implantation. Statistical analysis included the Student *t* test, Welch transformation, and Mann-Whitney nonparametric test and was performed using Instat for Macintosh software (version 3.1a, Graphpad Software). Vectorial analysis was performed using SigmaPlot software (SPSS Inc.). Internet-Based Refractive Analysis software (Zubisoft GmbH) was used for clinical outcomes analysis.

RESULTS

This study included 59 eyes of 54 patients. The mean age of the 28 women (51.85%) and 26 men (48.14%) was 36.01 years ± 11.02 (SD) (range 19 to 72 years). The indications for PKP were keratoconus in 49 eyes, post-LASIK ectasia in 5 eyes, progressive hyperopia secondary to RK in 2 eyes, stromal scarring in 2 eyes, and bullous keratopathy in 1 eye. Forty-nine patients had a single eye treatment, whereas 5 patients had both eyes treated.

All patients completed at least 1 year of follow-up. The mean follow-up was 14 months.

Table 1 shows the preoperative and last follow-up examination data. The preoperative corneal astigmatism ranged from 3.00 to 5.00 D. Figures 1 and 2 show the preoperative and postoperative CDVA. No patient lost visual acuity. Of the patients, 28 (47.4%) gained 2 or more lines of CDVA (Figure 3). The improvements in CDVA, SE, and refractive error were statistically significant ($P < .0001$).

Table 1. Preoperative and last follow-up examination data.

Parameter	Preoperative	Postoperative	*P* Value
Eyes (n)	59	—	—
Patients (n)	54	—	—
Sex (n)			
Male	26	—	—
Female	28	—	—
Mean age (y)	36.01 ± 11.02	—	—
Mean follow-up (mo)	14	—	—
CDVA (logMAR)			.001
Mean ± SD	0.45 ± 0.17	0.30 ± 0.17	
Range	0.18, 1.00	0.00, 1.00	
SE (D)			.001
Mean ± SD	−6.34 ± 3.40	−2.66 ± 2.52	
Range	0.37, −16.50	0.87, −10.50	
Spherical refractive error (D)			.001
Mean ± SD	−7.10 ± 3.07	−3.46 ± 2.05	
Range	2.15 to 16.68	0.88 to 10.79	
Mean TA at 3.0 mm (D)	3.37 ± 1.51	1.69 ± 1.04	.001
Mean maximum K (D)	48.09 ± 2.56	44.17 ± 2.67	.001
Mean minimum K (D)	44.90 ± 2.54	42.46 ± 2.63	.001

CDVA = corrected distance visual acuity; K = keratometry; SE = spherical equivalent; TA = topographic astigmatism

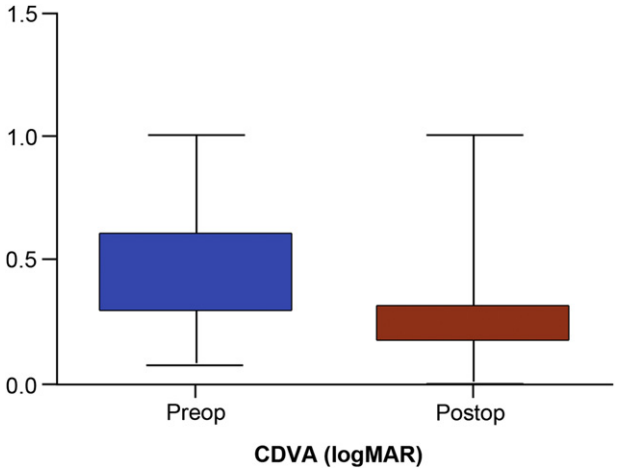

Figure 1. The CDVA (logMAR) before and after the ICRS implantation (unpaired *t* test) (CDVA = corrected distance visual acuity).

Intended Correction

Regarding the predictability of the postoperative SE, 43 eyes (72.8%) presented with undercorrection and 9 (15.2%) with overcorrection. There was concordance between the attempted refraction and achieved refraction in 7 eyes (13.0%) (Figure 4).

The decrease in the mean corneal topographic astigmatism at 3.0 mm from preoperatively to postoperatively was statistically significant ($P < .0001$). Most eyes had more than 3.0 D of refractive astigmatism preoperatively (Figure 5). Approximately half the eyes remained with more than 3.00 D of refractive astigmatism postoperatively; the rest had less than 3.00 D (Figure 6). The decrease in K values from preoperatively to postoperatively was

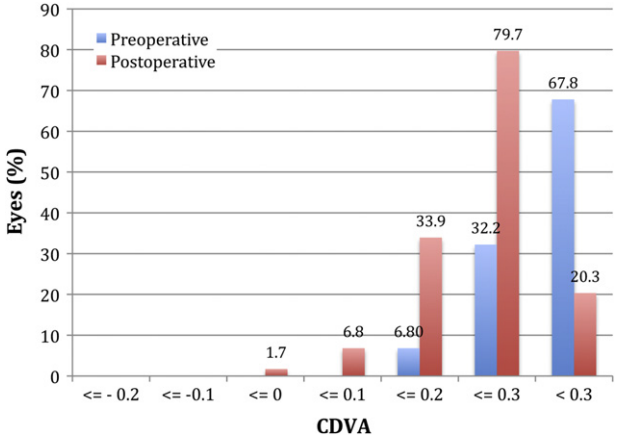

Figure 2. Preoperative and postoperative CDVA (logMAR) (CDVA = corrected distance visual acuity).

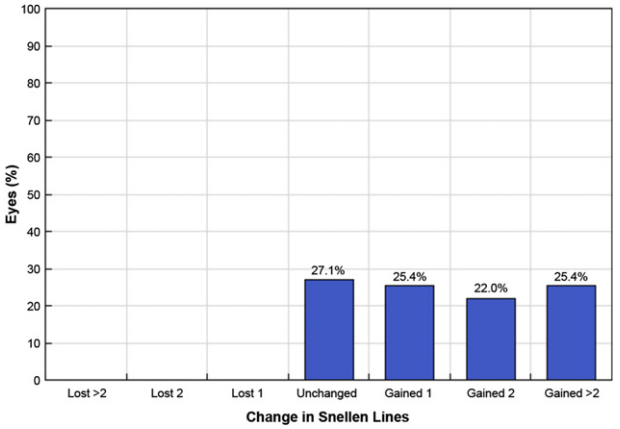

Figure 3. Lines of CDVA lost and gained.

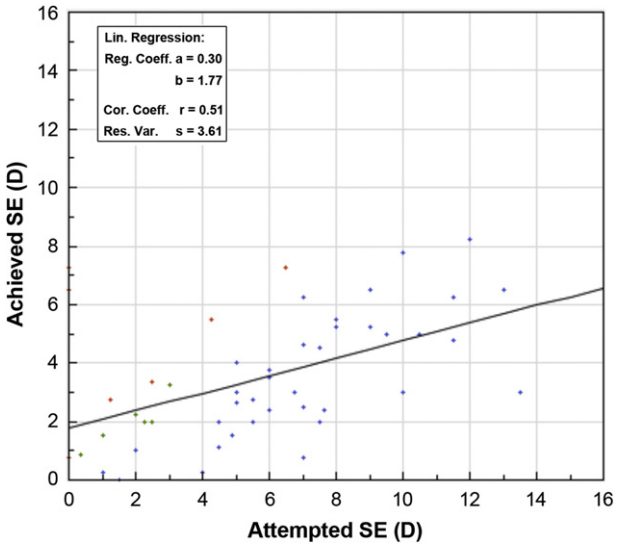

Figure 4. Predictability of SE correction. The blue dots represent undercorrection, the green dots represent full correction, and the red dots represent overcorrection (Cor. = correlation; Coeff. = coefficient; Lin. = linear; SE = spherical equivalent; Res. Var. = response variable).

statistically significant ($P < .0001$) (Table 1). Vectorial analysis showed that most eyes had a statistically significant reduction in spherocylinder refractive error (Figure 7).

Double-Angle Plot

Figure 8 shows the double-angle plots of the individual cylinders, providing an overview of the cylinder magnitude (diopter) and axis (degree) of each data point. The radius from the center of the plot to each individual point represents the magnitude of the cylinder. After ICRS implantation, the refractive astigmatism centroid was 1.00 D closer to zero and the SD of the astigmatism was reduced by a factor of 1.66 (3.83 D/2.31 D). The relocation of the centroid closer to the origin and the contraction of the ellipse on the doubled-angle plots show the amount of improvement.

Figure 9 shows the doubled-angle plot of the preoperative and postoperative keratometric astigmatism. Although there was a reduction in the mean keratometric astigmatism, it was considerably less than the reduction in refractive astigmatism.

There were no vision-threatening complications. The ICRS were deeply implanted in all eyes (Figure 10). In 3 eyes (5%), the surgical procedure was interrupted due to dehiscence of the inner layers of corneal transplantation, even 2 years after transplantation.

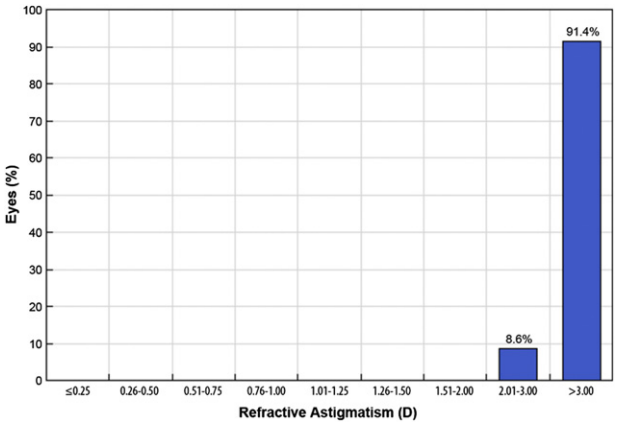

Figure 5. Preoperative refractive astigmatism.

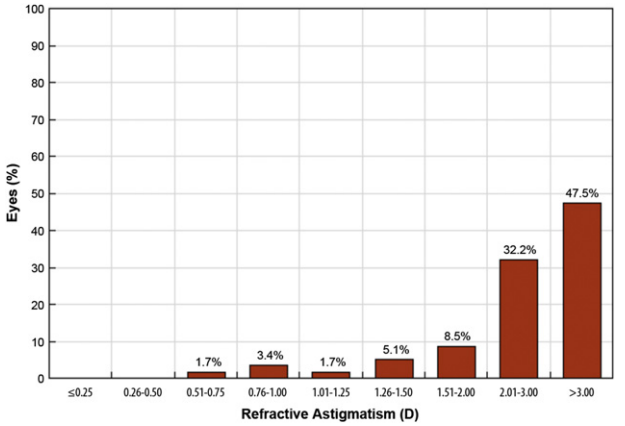

Figure 6. Postoperative refractive astigmatism.

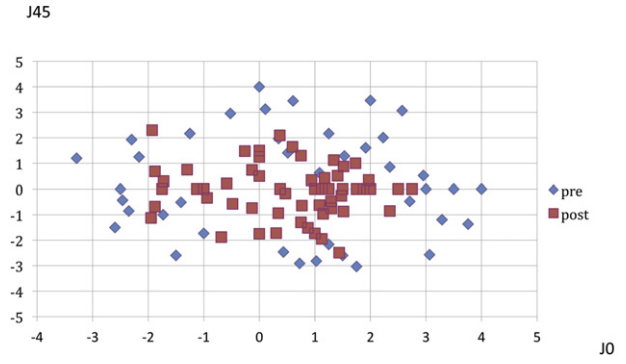

Figure 7. Astigmatic vectors (J_0 and J_{45}) before and 12 months after ICRS implantation. The more central location (0,0) of postoperative data represents the reduction of preoperative astigmatism by the implantation of the ICRS.

DISCUSSION

Post-PKP residual astigmatism and refractive error are frequently observed,[11,18] and their management may be a challenge for anterior segment surgeons. In this retrospective study, we evaluated 59 eyes of 49 patients who had ICRS implantation to correct irregular astigmatism after previous PKP. Despite proper wound healing and good anatomic results, high and/or irregular astigmatism can preclude satisfactory vision in these patients.

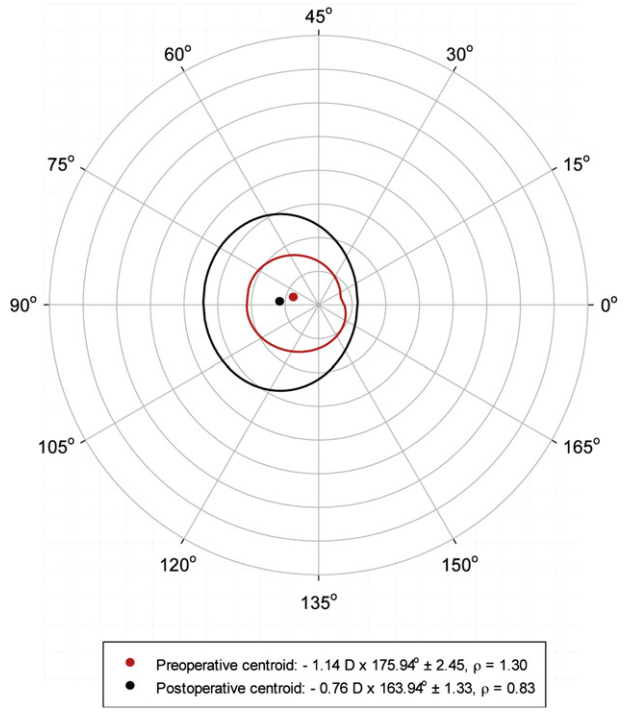

Figure 9. Double-angle plot of keratometric astigmatism.

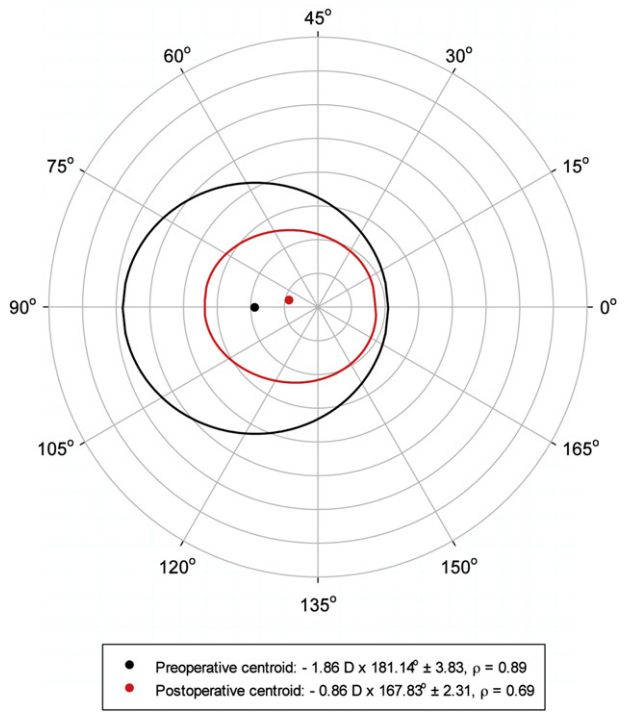

Figure 8. Double-angle plot of refractive astigmatism. Individual cylinders demonstrate the cylinder magnitude (D) and axis (degrees). The radius from the center of the plot to each individual point represents the magnitude of the cylinder.

Many factors inherent to the patient, host cornea, surgical technique, and postoperative management may influence the astigmatism.[2] Peripheral disorders, such as keratoconus,[1] can persist on the corneal host and cause irregular astigmatism. This cause possibly explains the high prevalence of keratoconus patients in our study. Although contact lenses and excimer laser refractive surgery are viable options in this group of eyes,[19–21] contact lens–related problems, such as dry eye, neovascularization, and rejection of donor cornea, must be considered,[22] as well as contraindications to PRK or LASIK because of high ametropia, low baseline corneal thickness, and young age that make these patients unsuitable for corneal laser refractive surgery.[23]

The visual outcomes in our study were satisfactory. The CDVA was unchanged in 16 eyes (27.2%)

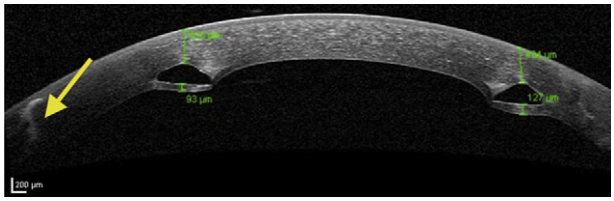

Figure 10. Anterior segment optical coherence tomography shows the ICRS deeply implanted in the cornea stroma and graft–host interface (*yellow arrow*).

postoperatively, whereas 43 eyes (72.8%) improved at least 1 line. The mean SE value decreased from −6.34 ± 3.40 D to −2.66 ± 2.52 D, and the K values also decreased, improving the corneal irregularity.

Alfonso et al.[24] and Morshirfar et al.[12] evaluated the results of pIOL implantation in young patients for the correction of refractive errors after PKP and found safe, predictable, and stable visual and refractive outcomes. Alfonso et al.[24] describe the efficacy, predictability, and safety of Implantable Collamer Lens posterior chamber pIOL implantation for the correction of post-PKP refractive error in 15 eyes of 15 patients; there was a large reduction in the refractive error and CDVA improvement. The postoperative CDVA was 20/40 or better in 12 eyes (80%) and 20/25 in 6 eyes (40%). No eye lost more than 1 line of acuity, 2 eyes gained 1 line, and 5 eyes gained more than 2 lines; 8 eyes were unchanged. Morshirfar et al.[12] evaluated the Artisan iris-supported pIOL to treat high myopia after PKP in 2 patients; there was improvement in uncorrected distance visual acuity and CDVA and no significant endothelial cell density loss 6 months postoperatively.

Our findings are in agreement with results in other studies.[25–27] In a case report, Coskunseven et al.[25] advocate the use of ICRS, a minimally invasive procedure, to correct high astigmatism after PKP. According to Coskunseven et al., eyes with thin corneal grafts and recurrent keratoconus are unsuitable for laser refractive corrections because of the possibility of postoperative complications. In addition, Arriola-Villalobos et al.,[5] in a series of 9 patients, found that ICRS implantation improved the CDVA in all eyes and decreased the topographic mean, minimum, and maximum K values. They conclude that ICRS implantation might be a good surgical choice to correct high astigmatism after PKP and yields good visual, refractive, and topographic outcomes.

Chang and Hardten[27] recommend that ICRS implantation after PKP not be performed until at least 1 year after transplantation and at least 3 months after suture removal. We proceeded as Arriola-Villalobos et al.[5] suggest; that is, we waited at least 2 years after corneal transplantation and a minimum of 6 months after suture removal to avoid damaging the interface by the traction generated by the dissectors used during surgery in the manual technique.

The use of Ferrara ICRS with a 5.0 mm optical zone has 2 advantages over the use of larger optical zone ICRS. First, the central cornea flattening is theoretically greater because the refractive outcome is inversely proportional to the diameter of the segment.[28] The second benefit is that a small diameter ensures greater distance between the rings and the graft–host junction. This reduces the risk for interface dehiscence or vascularization of the stromal channel by vessels extending from the limbus and host cornea. Thus, in patients with a corneal transplant with a diameter of 7.5 mm or smaller, the ICRS with larger optical zones (6.0 or 7.0 mm) should not be used because the segments would be very close to the graft–host junction. Potential disadvantages of ICRS with a small optical zone are halos and glare. Some patients, especially those with large pupil diameters in dim-light conditions, occasionally report halos and glare.

All patients had PKP performed by the same surgeon (S.C.), who always used a discrepancy of 0.50 mm in trephination between the donor graft (8.0 mm) and the host (7.5 mm). Because the Ferrara ICRS is placed at a 5.0 mm optical zone, it is always located far from the graft–host junction, which makes the procedure safer for small-optical-zone ICRS. However, in cases of small trephinations or decentered grafts, care must be taken to avoid excessive torque, which could open the previous keratoplasty wound, thus requiring sutures and postponing ICRS implantation. In our study, ICRS implantation had to be postponed in 5% of cases (3/59 eyes) because wound dehiscence occurred during dissection. All patients had at least 2 years of follow-up after PKP, which indicates that in some cases the graft–host interface strength can be permanently reduced. This may be related to the depth (too shallow or too deep) of the passage of the 10-0 needle during the keratoplasty and early removal of sutures. Tunnel creation using the femtosecond laser in these cases could not only facilitate the surgical procedure but also prevent this type of complication.[26,29]

Implantation of ICRS after PKP may yield results different than those when the technique is used for keratoconus treatment. Keratoconic corneas are thinner and more elastic than healthy corneas, whereas corneas that had PKP are more rigid, with normal thickness and elasticity. Theoretically, this could explain why 73% of eyes presented with undercorrection and there was a low concordance between the attempted refraction and the achieved refraction. The nomogram of the Ferrara ICRS is designed for keratoconus treatment; thus, the ring thickness should be adjusted when using ICRS for post-keratoplasty cases. This means that thicker segments should be implanted in post-PKP patients given the same K values as in keratoconus patients. The main purpose of ICRS implantation is to regularize the corneal surface and improve visual acuity; the refraction reduction after the surgery could be considered a secondary goal.

There are several potential advantages of ICRS implantation over other surgical techniques in eyes with high astigmatism after PKP. First, ICRS implantation avoids excimer laser treatment, eliminating

central corneal wound healing, which could be unsatisfactory in post-PKP corneas. This leaves the optical center of the cornea untouched, enhancing refractive outcomes. Second, the technique is reversible in cases of unsatisfactory refractive or clinical outcomes. Third, adjustment can be performed using thinner or thicker rings. In cases of unexpected corneal shape changes, 1 segment can be removed or exchanged. Fourth, it avoids the complications of intraocular surgery.

The results in our study suggested that ICRS implantation is a promising treatment for post-PKP astigmatism, especially in eyes with thin and irregular corneas. Long-term randomized comparative prospective studies are needed to better evaluate this technique as a treatment for irregular astigmatism in post-PKP patients.

WHAT WAS KNOWN

- Surgical treatments such as wedge resection of the cornea, LASIK, and pIOL implantation are often necessary to manage high astigmatism after PKP when nonsurgical methods fail to achieve satisfactory visual acuity.
- Intrastromal corneal ring segment implantation for the treatment of post-PKP astigmatism has been described in a case report and a 9-patient case series.

WHAT THIS PAPER ADDS

- In a larger clinical series, ICRS implantation improved CDVA in 73% of eyes and produced significant reduction in topographic astigmatism. Dehiscence of the graft–host junction with mechanical dissection occurred in 5% of eyes.

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·Clinical Research·

Clinical outcomes after intrastromal corneal ring segments reoperation in keratoconus patients

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Received: 2013-07-13 Accepted: 2013-08-16

Abstract

• AIM: To evaluate the clinical outcomes after Ferrara intrastromal corneal ring segments (ICRS) reoperation in patients with keratoconus.

• METHODS: A total of 37 keratoconus eyes implanted with intrastromal corneal ring segments, which had an ICRS exchange, addition, reposition or removal were evaluated. Uncorrected visual acuity (UCVA), best corrected visual acuity (BCVA), keratometry (K), asphericity (Q) and pachymetry at the thinnest point (PTP) of the cornea were evaluated using a corneal tomography (Oculus Pentacam, USA)

RESULTS: The mean follow-up time after the reoperation was 30.5±9.7 months. The mean UCVA improved from 20/300 to 20/80 (P=0.005); the mean BCVA improved from 20/160 to 20/50 (P=0.0002), the mean keratometry reduced from 49.33±4.19D to 46.16±3.90D (P=0.0001), the mean pachymetry at the thinnest point increased from 450±42.9μm to 469±40.8μm (P=0.0001). The asphericity increased from −0.84±0.74 to −0.35±0.81 (P=0.15) and the spherical equivalent reduced from −4.64±4.87D to −3.04±3.45D (P=0.137). The changes in the asphericity and spherical equivalent were not statistically significant.

• CONCLUSION: Ferrara ICRS implantation showed to be a reversible and readjustable surgical procedure for keratoconus treatment. Good outcomes can be obtained even after removal, addition, reposition or exchange of ICRS.

KEYWORDS: keratoconus; intrastromal corneal ring segments; reoperation

DOI:10.3980/j.issn.2222-3959.2013.06.10

Torquetti L, Ferrara G, Almeida F, Cunha L, Ferrara P, Merayo-Lloves J. Clinical outcomes after intrastromal corneal ring segments reoperation in keratoconus patients. *Int J Ophthalmol* 2013; 6(6):796-800

INTRODUCTION

Intrastromal corneal ring segments (ICRS) implantation in keratoconus provides favorable visual and refractive results such as decreased corneal surface irregularity, improvement in spectacle corrected vision, and delay or elimination of the need for keratoplasty[1-3].

The Ferrara ICRS are made of polymetilmetacrilate(PMMA) Perspex CQ acrylic segments. They vary in thickness, and are available in 0.15, 0.20, 0.25 and 0.30mm. The segment cross-section is triangular, and the base for every thickness and diameter is 0.60mm. The segments have 90, 120, 160 or 210 degrees of arc.

The reversibility and adjustability of the refractive effect of intracorneal ring segments have been previously studied in myopic eyes and in patients with keratoconus, however only a very small sample of patients was evaluated in theses studies [4,5]. To our knowledge, no studies have demonstrated in detail the behavior of the abnormal keratoconic corneal tissue after different types of reoperation following ICRS implantation.

The purpose of this study is to evaluate the reversibility of the visual, refractive, and topographic changes occurring in keratoconic eyes after ICRS exchange, reposition, addition or removal.

SUBJECTS AND METHODS

This study was approved by the institutional review board of Dr. Paulo Ferrara Eye Clinic, Belo Horizonte, MG, Brazil, and followed the tenets of the Declaration of Helsinki. The procedures were fully explained to each patient, and each provided written informed consent.

Subjects We retrospectively collected the data of 1 073 eyes of 810 consecutive surgical patients that had ICRS implantation from January 2006 to July 2008. Of these eyes,

37 needed a reoperation as follows: ICRS removal (n=6), exchange (n=11), repositioning (n=4), and insertion of an additional ICRS (n=16). The mean age of patients was 29±9.6 (range 17 to 57 years old). Twenty-four patients were male and 13 were female. All patients had uneventful intracorneal ring segment implantation for clear corneal keratoconus; the reoperation was necessary during the follow-up period.

The main indications for the primary surgery were: contact lens intolerance and/or evidence of ectasia progression as measured by worsening of uncorrected distance visual acuity (UCVA) and corrected distance visual acuity (BCVA), progressive intolerance to contact lens wear, and progressive corneal steepening documented by topographical changes. Two or more lines of UCVA and/or BCVA worsening and at least 2 diopters (D) of increase in mean keratometry as measured with a Pentacam (Pentacam HR, OCULUS, Inc., Lynnwood, WA, USA) were required to define progression of the disease. Exclusion criteria included any of the following discovered during the preoperative examination: advanced keratoconus with curvatures over 60D, significant apical opacity and scarring, hydrops, corneas with thickness below 300μm in the ring track as evaluated by Pentacam pachymetry, and intense unresolved atopia.

The main indications for the reoperation were: 1) ICRS removal: superficial segment and/or overcorrection; 2) ICRS exchange: overcorrection or undercorrection; 3) ICRS reposition: migration of segment and/or wrong placement of segment and 4) ICRS addition: undercorrection. Overcorrection was defined as excessive flattening (oblate cornea) after the primary ICRS implantation. Undercorrection was defined as a less than expected cornea flattening, with unsatisfactory UCVA and/or BCVA.

Methods

Clinical measurements A complete ophthalmologic examination was performed before surgery and included UCVA and BCVA assessment, biomicroscopy, fundoscopy, tonometry, corneal topography, pachymetric map, and asphericity measurement using the Pentacam HR. All clinical examinations were performed in a standardized manner by an experienced examiner (PF).

Surgical technique All primary surgeries and reoperations were performed by the same surgeon (PF) using the manual technique, as previously described [3]. The surgery was performed under topical anesthesia after miosis was achieved with 2% pilocarpine. An eyelid speculum was used to expose the eye, and 2.5% povidone iodine eyedrops were instilled onto the cornea and conjunctival cul-de-sac. The visual axis was marked by pressing a Sinskey hook on the central corneal epithelium while asking the patient to fixate on the corneal light reflex of the microscope light. Using a marker tinted with gentian violet, a 5.0mm optical zone and incision site were aligned to the desired axis in which the incision would be made.

The incision site was always the steepest topographic axis of the cornea given by the Pentacam. A square diamond blade was set at 80% of corneal thickness as determined by the pachymetric map at the incision site. It was always considered the pachymetric map obtained after the primary surgery, to define the incision depth. For ICRS removal or exchange, an inverted Sinskey hook was used to engage the segment hole, from beneath, and it was pulled out of the tunnel. For ICRS reposition, the segment was pushed forward into the tunnel after a new dissection. For ICRS addition, a pocket was formed, using the Suarez spreader and the dissecting spatula was inserted through the incision and gently pushed with some, quick, rotary "back and forth" tunneling movements. Following channel creation, the ring segment was inserted using a modified McPherson forceps. The segment was properly positioned with the aid of the Sinskey hook.

The postoperative regimen consisted of moxifloxacin 0.5% (Vigamox®, Alcon, Ft. Worth, TX, USA) and dexamethasone 0.1% (Maxidex®, Alcon) eye drops four times daily for two weeks. The patients were instructed to avoid rubbing the eye and to frequently use preservative-free artificial tears (Systane® 0.4%, Alcon). The patients were examined postoperatively at 1d, 1 month, 3 months, 6 months, and 1 year after the surgery. After the first year, the patients were evaluated annually. The mean follow-up time was based on the time of the last visit.

Statistical Analysis The Statistical Package for the Social Sciences (SPSS, Chicago, IL, USA) was used for descriptive statistics, including means±standard deviations. Student's t-test for paired data was used to compare preoperative and postoperative data. P-values less than 0.05 were considered statistically significant.

RESULTS

One eye each of 37 patients underwent follow-up surgery to remove (n=6), exchange (n=11), reposition (n=4), or insert an additional ICRS (n=16). No patient had reoperation because of subjective complaints (*e.g.* discomfort, dryness, glare, halos). The mean follow-up time after the primary surgery was 7.1±2.8 months. The mean follow-up time between the primary surgery and the reoperation was 8.4±2.2 months. The mean follow-up after the reoperation was 30.5±9.7 months. After the reoperation, the mean UCVA improved from 20/300 to 20/80 (P=0.005); the mean BCVA improved

Table 1 Clinical data according to the type of reoperation (mean values for all data)

	Removal (*n*=6)	Exchange (*n*=11)	Reposition (*n*=4)	Addition (*n*=16)	All cases (*n*=37)
Pre ICRS implantation					
UCVA	20/730	20/700	20/415	20/445	20/570
BCVA	20/130	20/100	20/160	20/115	20/125
Km (D)	49.2	49.8	52.15	46.78	49.48
Post ICRS implantation					
UCVA	20/315	20/260	20/350	20/370	20/325
BCVA	20/110	20/60	20/60	20/60	20/70
Km (D)	43.06	44.93	48.6	45.98	45.64
Post ICRS reoperation					
UCVA	20/150	20/190	20/200	20/450	20/240
BCVA	20/65	20/40	20/50	20/45	20/50
Km (D)	47.63	47.28	49.35	45.12	47.34

Mean values for all data.

from 20/160 to 20/50 (P=0.0002), the mean keratometry reduced from 49.33±4.19D to 46.16±3.90D (P=0.0001), the mean pachymetry at the thinnest point increased from 450±42.9μm to 469±40.8μm (P=0.0001). The changes in the asphericity and spherical equivalent were not statistically significant. The asphericity increased from -0.84±0.74 to -0.35±0.81 (P=0.15) and the spherical equivalent reduced from -4.64±4.87D to -3.04±3.45D (P=0.137).

The data evaluation according with the type of reoperation showed similar results for the different types of surgery (Table 1).

DISCUSSION

Implantation of ICRS is a minimally invasive and reversible surgical procedure that improves the visual acuity by reshaping of the cornea; moreover it prevents or postpones keratoplasty [3]. Successful implantation of ICRS depends on several factors, including correct placement, optical zone diameter, and accurate depth of implantation.

Our postoperative results showed a significant improvement in UCVA and BCVA in reoperation cases. These results are in concordance with most similar papers [1,3,5-10]. In the U.S. Food and Drug Administration phases II and III clinical trials, for Intacs, ICRS removal was required in 4.68% of eyes [11]. The authors of this study concluded that intrastromal ring segments were safely, effectively, and easily extracted, with a return to preoperative refractive status within 3 months. Clinch *et al* [12] evaluated 684 myopic eyes, in which 6.87% needed ICRS removal. The authors concluded that intrastromal corneal ring segment removal was not associated with loss of BCVA, induction of astigmatism, or myopia.

After initial ICRS placement, undercorrection (requiring an additional ICRS implantation, n=16) occurred much more frequently than overcorrection. The reason for insertion of additional ICRS was usually undercorrection, *i.e.* a suboptimal reduction of corneal steepening after implantation of a single ICRS. The causes for these changes (undercorrection and overcorrection) are not well understood but probably are related to corneal biomechanics [13-15]. The cornea rigidity and viscoelasticity can vary in keratoconus and thereby could theoretically be implied in different responses to the ring in patients with similar preoperative topographic patterns. The more elastic the corneal tissue, the greater the ability of intrastromal corneal ring segments to flatten the corneal curvature and correct keratoconus. Studies have shown no change in corneal hysteresis after ICRS implantation, however the use of biomechanic parameters in the nomograms could potentially reduce the risk of undercorrection and overcorrection, thus improving the reproducibility of the technique[15,16]. Moreover, an inaccurate depth of implantation of ICRS can lead to overcorrection and undercorrection.

In all cases, the pre-reoperation UCVA and BCVA was unsatisfactory, with limited improvement after the primary surgery. The mean follow-up time after the primary surgery is relatively short because there are progressive changes after the surgery usually until 6 months postoperatively. Therefore, in most cases we waited up to 6 months to check if any improvement could occur before to proceed to the reoperation. In cases of ICRS removal, the mean keratometry was 43.06D (Table 1) before the reoperation, usually caused by overcorrection, with excessive flattening of the cornea. These patients usually have the worse UCVA and BCVA. This emphasizes the importance of a careful preoperative ring selection, always trying to avoid overcorrection.

We showed that the outcome of patients requiring follow-up surgery due to overcorrection or undercorrection is acceptable. For these patients, there was improvement of UCVA, BCVA, keratometry, and pachymetry. However,

asphericity and spherical equivalent did not improve in these patients undergoing subsequent surgery, perhaps due to the scarring of corneal tissue and/or stroma secondary to the first procedure.

Chan and Khan [17] evaluated the results of ICRS exchange procedures and found satisfactory outcomes, with improvement of at least 1 line of UCVA in all postexchange eyes. As stated in their paper, this enables the surgeon to have a significant "second chance" of obtaining a successful result in patients whose eyes do not have the expected change after the first ICRS placement.

When comparing our reoperation results with studies of primary surgeries, we found slightly worse outcomes in the reoperation cases. Alió *et al* [18] performed a retrospective study to evaluate the long-term (up to 48 months) results after Intacs implantation in patients with keratoconus. After 6 months, the mean UCVA increased significantly (P<0.01), from 0.46 (20/50) preoperatively to 0.66 (20/30), and the average keratometry decreased by 3.13D. Coskunseven *et al* [19] evaluated the results Keraring ICRS in 50 eyes of patients with keratoconus. Of these, 47 had UCVA of 20/40 (range: counting fingers to 20/30). At the last follow-up examination, 14 of the 50 eyes had a UCVA of 20/40 or better (range: counting fingers to 20/25).

Regarding the surgical technique for the reoperation, due to corneal scarring, these procedures can be more demanding to the surgeon. For the ICRS removal, when the primary procedure was recent (less than 10d), the incision can be easily opened, and the segment retrieved using an inverted Sinskey hook, which engages the ICRS hole from below. In longstanding cases, a new incision should be made, over the hole of the ring. For ICRS repositioning, which is usually required soon after the primary surgery because of migration, the segment should be pulled or pushed (according to the desired position), using the Sinskey hook. In cases of ICRS addition, a new incision and a new tunnel should be made, as in primary procedures. In cases of ICRS exchange, the procedure can be made in a single step, *i.e.* removal of the segment followed by immediate insertion of a new segment, or in two separate procedures, removal, followed by insertion in another time. When the reason for ICRS exchange is undercorrection or overcorrection, if the primary segment is well positioned, deeply located in the stroma, the exchange can be made in a single procedure. However, in cases of stromal thinning over a thick segment, it is advisable to remove the segment first, wait at least 3 months, and then proceed to a new ICRS implantation. The choice of the segment to be implanted in a reoperation is based on the surgeon experience, as there are no specific nomograms for reoperations.

In this series of cases, only the manual technique was used for the primary surgery and reoperation. However, reoperation after ICRS implantation assisted by the femtosecond laser has been described [20-23]. The use of the femtosecond laser in corneal tunnel creation makes the procedure easier (especially for inexperienced surgeons). The main advantages of femtosecond-assisted channel creation over the mechanical technique seem to be the precise depth of implantation and symmetry of segments [24,25]. However, these advantages are minimized when the procedure is done by high-volume, experienced surgeons, as in our paper (PF).

In conclusion, ICRS reoperation showed to provide favorable clinical outcomes in keratoconus. The procedure is minimally invasive and yields good visual and keratometric outcomes. Moreover it is a safe technique and does not preclude any future additional treatment or adjustments, if necessary. This study, adds evidence to support the claim of reversibility, readjustability and exchangeability of the ICRS. Further randomized, multi-centric studies, are needed to confirm the results found in the current paper.

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Intrastromal Corneal Ring Segments Implantation in Patients With Keratoconus: 10-Year Follow-Up

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ABSTRACT

PURPOSE: To evaluate the long-term safety and efficacy of Ferrara intrastromal corneal ring segments (ICRS) (Ferrara Ring; AJL, Boecillo, Spain) in patients with keratoconus.

METHODS: The chart records of 36 eyes of 30 patients with keratoconus implanted with ICRS, operated on between July 1996 and January 2002, were retrospectively reviewed. The following parameters were studied: uncorrected distance visual acuity (UDVA), corrected distance visual acuity (CDVA), keratometry (K), and central corneal thickness. The outcomes were evaluated at 5 and 10 years after ICRS implantation.

RESULTS: The mean UDVA (logMAR) improved from 1.01 ± 0.28 (20/200 Snellen) to 0.71 ± 0.38 (20/100 Snellen) at 5 years ($P < .05$) and 0.67 ± 0.25 (20/90 Snellen) at 10 years ($P = .735$). The mean CDVA (logMAR) improved from 0.45 ± 0.45 (20/55 Snellen) to 0.24 ± 0.19 (20/35 Snellen) at 5 years ($P < .05$) and 0.29 ± 0.09 (20/38 Snellen) at 10 years ($P = .292$). The mean maximum K value decreased from 54.99 ± 6.33 to 50.58 ± 5.11 D at 5 years ($P < .05$) and 50.65 ± 5.17 D at 10 years ($P = .854$). The mean minimum K value decreased from 48.85 ± 5.70 to 46.90 ± 5.08 D at 5 years ($P < .05$) and 47.12 ± 4.22 D at 10 years ($P = .945$). The central corneal thickness decreased from 457.42 ± 58.21 to 421.34 ± 74.12 μm at 5 years ($P = .039$) and 434.32 ± 77.65 μm at 10 years ($P = .427$).

CONCLUSIONS: Intrastromal corneal ring segments can effectively improve UDVA and CDVA 10 years after implantation in patients with keratoconus.

[*J Refract Surg.* 2014;30(1):22-26.]

Intrastromal corneal ring segments (ICRS) have been used as an additive surgical procedure for keratoconus correction, which provides an alternative to delay if not avoid corneal grafting in patients with keratoconus.[1,2] ICRS act by an "arc-shortening effect" on the corneal lamellae and flatten the central cornea.[3] The main advantages of ICRS are safety,[4,5] reversibility,[6,7] stability,[8] and the fact that the surgical process does not affect the central corneal visual axis.

There are some reports in the literature regarding the long-term follow-up of eyes with keratoconus implanted with ICRS. These reports, with a variable period of follow-up (2 to 5 years), evaluated a small sample of patients.[2,6-8]

In the current study, we evaluated the long-term safety and efficacy after implantation of the Ferrara ICRS (Ferrara Ring; AJL, Boecillo, Spain) in patients with keratoconus. To our knowledge, this study has the largest follow-up period for eyes implanted with ICRS for correction of keratoconus in the literature.

PATIENTS AND METHODS

This retrospective study included 36 eyes of 30 patients with keratoconus implanted with the Ferrara ICRS, operated on between July 1996 and January 2002. Six patients had a single eye treatment, whereas 15 patients had both eyes treated. There were 18 women and 12 men with a mean age of 39.44 ± 10.18 years (range: 25 to 66 years). The evolutive grade of keratoconus was classified according to Amsler–Krumeich classification: 2 eyes were grade I, 13 eyes were grade II, 14 eyes were grade III, and 7 eyes were grade IV.

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Submitted: June 2, 2013; Accepted: September 18, 2013; Posted online: January 10, 2014

Drs. P. Ferrara, G. Ferrara, and Merayo-Lloves have a financial interest in the Ferrara intrastromal cornea ring. The remaining authors have no financial or proprietary interest in the materials presented herein.

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doi:10.3928/1081597X-20131217-02

All patients were informed about the possible intraoperative and postoperative complications and gave written informed consent in accordance with institutional guidelines and the tenets of the Declaration of Helsinki. The following parameters were studied: uncorrected distance visual acuity (UDVA), corrected distance visual acuity (CDVA), keratometry (K), and central corneal thickness. The outcomes were evaluated at 5 and 10 years after ICRS implantation.

The main indication for ICRS implantation was contact lens intolerance and/or progression of the ectasia. The progression of the disease was defined by worsening of UDVA and CDVA, progressive intolerance to contact lens wear, and progressive corneal steepening documented by the topography (more than 1 diopter [D] increase of mean keratometric values in 1 year). Patients were excluded if any of the following criteria applied after preoperative examination: advanced keratoconus with curvatures greater than 60 D and significant apical opacity and scarring, hydropsis, thin corneas, thickness less than 300 µm in the ring track, intense atopia, and any ongoing infectious process, local or systemic. Patients who did not meet the inclusion criteria were not evaluated for this study. There was contact lens intolerance in 24 eyes and evidence of disease progression in 12 eyes.

The nomograms used for surgical planning were based on the position of the area of ectasia on the cornea, spherical equivalent, and topographic astigmatism.[8]

Surgical Technique

All surgeries were performed using the manual technique, by the same surgeon (PF). The surgery was performed under topical anesthesia after miosis was achieved with 2% pilocarpine. The visual axis was marked by pressing the Sinskey hook on the central corneal epithelium while asking the patient to fixate on the corneal light reflex of the microscope light. Using a marker tinted with gentian violet, a 5.0-mm optical zone and incision site were aligned to the desired axis in which the incision would be made. This incision site was always at the steepest topographic axis of the cornea given by the topographer.

A square diamond blade was set at 80% of corneal thickness at the incision site and this blade was used to make the incision. Using a "stromal spreader," a pocket was formed in each side of the incision. Two (clockwise and counterclockwise) 270° semicircular dissecting spatulas were consecutively inserted through the incision and gently pushed with some quick, rotary "back and forth" tunneling movements. Following channel creation, the ring segments were inserted using a modified McPherson forceps. The rings were properly positioned with the aid of a Sinskey hook.

The postoperative regimen consisted of tobramycin 0.3%–dexamethasone 0.1% eye drops four times a day for a week, after which the dose was tapered over 3 weeks. In addition, patients received topical lubricants (Lacrima; Alcon Laboratories, Inc., Fort Worth, TX) four times a day for at least 3 months.

Postoperative examinations were performed at postoperative days 1 and 7, after 1 and 6 months, and then every year. The UDVA, CDVA, slit-lamp evaluation, corneal topography, funduscopy, and tonometry were performed at each control visit. The corneal topography was obtained from EyeMap (Alcon Laboratories, Inc.) and Pentacam (Oculus Optikgeräte, Wetzlar, Germany).

We evaluated only the clinical outcomes at 5 and 10 years after the surgery because some patients missed some postoperative visits during the period of follow-up.

Statistical Analysis

Statistical analysis was done using the GraphPad Instat 3 for Macintosh (version 3.1a; GraphPad Software, Inc., La Jolla, CA). Student's *t* test for paired data was used to compare preoperative and postoperative data.

RESULTS

Acuity and keratometry results are listed in **Table 1** and **Figures 1-2**. Seventy percent of patients gained two or more lines of UDVA and 10% of patients lost two or more lines of UDVA. We found that 56.5% of patients gained two or more lines of CDVA at 5 years and 66.7% of patients gained two or more lines of CDVA at 10 years of follow-up (**Figure 3**).

Regarding the reoperation rate, ICRS exchange was required in 2 eyes and keratoplasty in 2 eyes. These eyes were excluded from the study.

To illustrate, we present a case of a patient who was contact lens intolerant and had a visual acuity of 20/80 (-5.00 -2.00 × 120). She received two ring segments in December 1997. Her last follow-up visit was in May 2011, at which time she presented with a CDVA of 20/30 (plano -2.50 × 90) and a stable topography (Pentacam) (**Figures A-B**, available in the online version of this article).

DISCUSSION

Implantation of ICRS is a minimally invasive and reversible surgical treatment that reduces refractive error by improving the corneal shape and delaying or preventing keratoplasty.[1,8,9] Successful implantation of ICRS depends on several factors, including correct placement, optical zone diameter, and accurate depth of implantation.[6,7,10]

TABLE 1

Preoperative and 5- and 10-Year Follow-up Examination Data of Eyes Implanted With Ferrara Intrastromal Corneal Ring Segments

Parameter	Preoperative	5-Year Postoperative	*P*	5-Year Postoperative	10-Year Postoperative	*P*
K1 (D)	48.85 ± 5.70	46.90 ± 5.08	< .05	46.90 ± 5.08	47.12 ± 4.22	.945
K2 (D)	54.99 ± 6.33	50.58 ± 5.11	< .05	50.58 ± 5.11	50.65 ± 4.70	.873
Km (D)	51.83 ± 5.66	48.70 ± 5.02	< .05	48.70 ± 5.02	48.82 ± 4.38	.953
UDVA (logMAR)	1.01 ± 0.28	0.71 ± 0.38	< .05	0.71 ± 0.38	0.67 ± 0.25	.735
CDVA (logMAR)	0.45 ± 0.45	0.24 ± 0.19	< .05	0.24 ± 0.19	0.29 ± 0.09	.292
Pach (μm)	457.42 ± 58.21	421.34 ± 74.12	< .05	421.34 ± 74.12	434.32 ± 77.65	.427

K1 = minimum keratometry; D = diopters; K2 = maximum keratometry; Km = mean keratometry; UDVA = uncorrected distance visual acuity; CDVA = corrected distance visual acuity; Pach = pachymetry

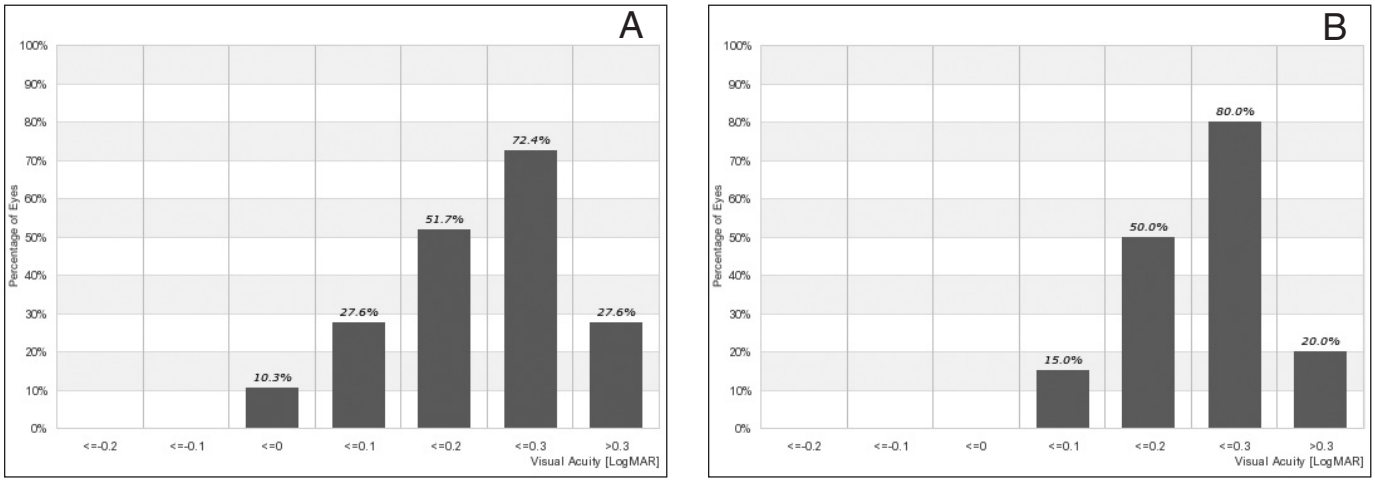

Figure 1. Snellen corrected distance visual acuity (logMAR) at (A) 5 and (B) 10 years postoperatively.

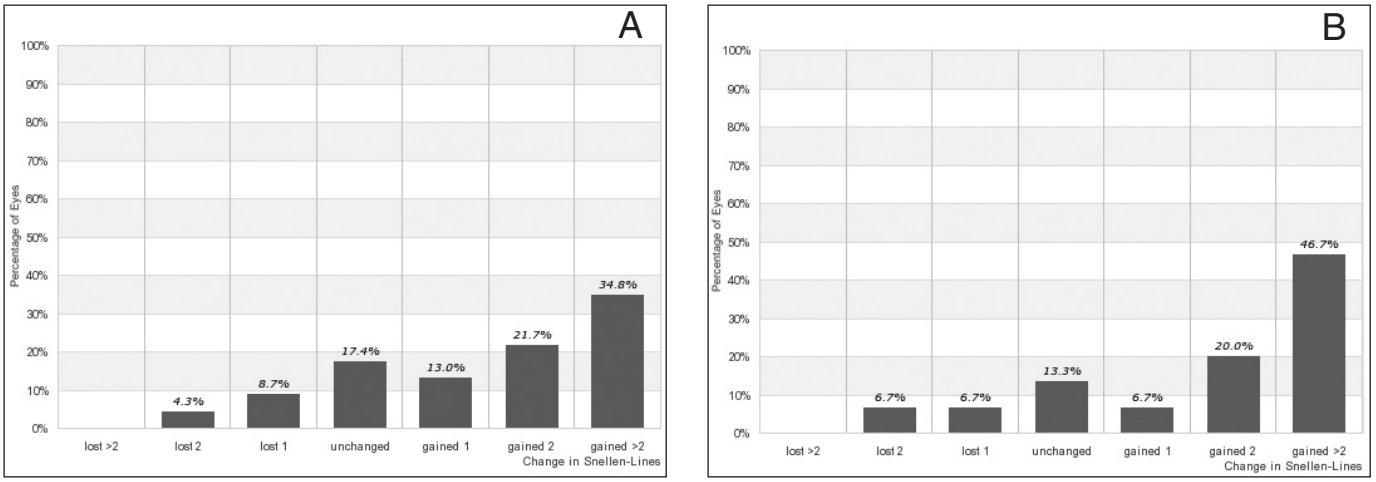

Figure 2. Change in lines of Snellen corrected distance visual acuity at (A) 5 and (B) 10 years postoperatively.

Our postoperative results showed a significant improvement in UDVA and CDVA. Our data reinforce the reproducibility and efficacy of the technique.[10,11] There are few studies regarding the long-term follow-up after ICRS implantation. Alió et al.[2] and Torquetti et al.[8] described results after 4 and 5 years, respectively, but most studies have relatively short follow-ups, between 6 months and approximately 1 year.[12,13] To the best of our knowledge, this study has the longest follow-up of eyes implanted with ICRS ever published.

The results of our study agree with those of other studies. Alió et al.[2] performed a retrospective study to evaluate the long-term (up to 48 months) results after Intacs implantation in patients with keratoconus. After 6 months, the mean UDVA increased significantly ($P < .01$) from 0.46 (20/50) preoperatively to 0.66 (20/30), and the average keratometry decreased by 3.13 D. Coskunseven et al. evaluated the results of Keraring ICRS in 50 eyes of patients with keratoconus.[13] Of these, 47 had UDVA of 20/40 (range: counting fingers to 20/30). At the last follow-up examination, 14 of the 50 eyes had a UDVA of 20/40 or better (range: counting fingers to 20/25). Nine eyes maintained the preoperative CDVA, whereas 39 eyes experienced a CDVA gain of one to four lines.

Kwitko and Severo[14] reported that CDVA after Ferrara ICRS implantation in eyes with keratoconus improved in 86.4%, was unchanged in 1.9%, and was worse in 11.7%. UDVA improved in 86.4%, was unchanged in 7.8%, and was worse in 5.8%. The mean corneal curvature decreased from 48.76 ± 3.97 D preoperatively to 43.17 ± 4.79 D postoperatively.

In a 2-year follow-up study after implantation of Intacs, Colin and Malet[15] described a gain of one or more lines of CDVA in 61.0% eyes at 1 year and 68.3% eyes at 2 years. Fewer than 15% of eyes experienced a CDVA loss of one or more lines during the 2 years following Intacs implantation. There was loss of one or more lines of CDVA in 14.63% of eyes.

Regarding the number of lines gained and lost after ICRS implantation, we found that 10% of patients lost UDVA and 20.7% lost CDVA. All of these patients had grade III or IV keratoconus. The patients who lost UDVA and CDVA but had grade II keratoconus had reoperation due to ring repositioning, removal, or exchange. Therefore, advanced keratoconus and the reoperation could be considered as risk factors for loss of visual acuity after ICRS implantation. Due to the limited size of our sample, we could not statistically establish these two factors as predictors of a bad outcome.

The nomogram used for ring selection in the patients studied was based on the preoperative spherical equivalent.[8] We no longer use this nomogram because newer nomograms provide better reliability and predictability of results. However, because the main purpose of this study was to evaluate the long-term safety and efficacy of ICRS, we do not consider the use of that nomogram as bias factor.

There are some limitations to this study. First, the mean age of patients at the time of surgery was 39 years. We agree that keratoconus tends to be stable after approximately 30 years of age.[16,17] Therefore, the results regarding stability could be influenced by the mean age of the studied patients. However, we could include in this study only patients who came back for revision at 5 and 10 years after the surgery. Because we are a referral center for ICRS implantation in Brazil and receive patients from all over the country, some patients are lost to follow-up. This could be considered a bias of selection, but only the patients who came back for follow-up could be included in this study.

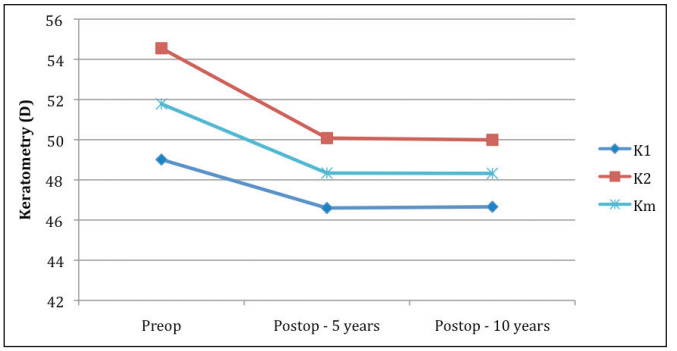

Figure 3. Keratometric values preoperatively and at 5 and 10 years postoperatively.

Other interesting data to be studied would be the stratification of results according to the evolutive grade of keratoconus. Due to the small sample of patients, our analysis could not provide reliable results. Prospective, multicentric, randomized studies with a larger sample of patients would be useful to show the long-term differences (if any) of outcomes in different grades of keratoconus.

As shown in previous studies, the ICRS flattens the cornea and the effect persists for a long period.[2,8] There is no significant resteepening of the cornea over time, in most cases, except when the ring is implanted in advanced cases of keratoconus or in very young patients (unpublished data).

Our study demonstrated that Ferrara ICRS implantation is a safe and efficacious option for the treatment of patients with keratoconus. The improved functional vision associated with this treatment modality can postpone or potentially eliminate the need for corneal transplantation. In patients whose visual outcomes following ICRS implantation are unsatisfactory or decrease due to disease progression, the segments can be removed easily and safely and corneal transplantation performed. Further randomized studies with larger samples are needed to confirm the stability of outcomes following Ferrara ICRS implantation, particularly in young patients and those with progressive disease.

AUTHOR CONTRIBUTIONS

Study concept and design (GF, PF, LT); data collection (FA, LC); analysis and interpretation of data (LPNA, APM, JML, JM-L, LT); drafting of the manuscript (GF, PF, LT); critical revision of the manuscript (FA, LPNA, LC, PF, APM, JML, JM-L, LT); statistical expertise (LPNA, APM); supervision (LT)

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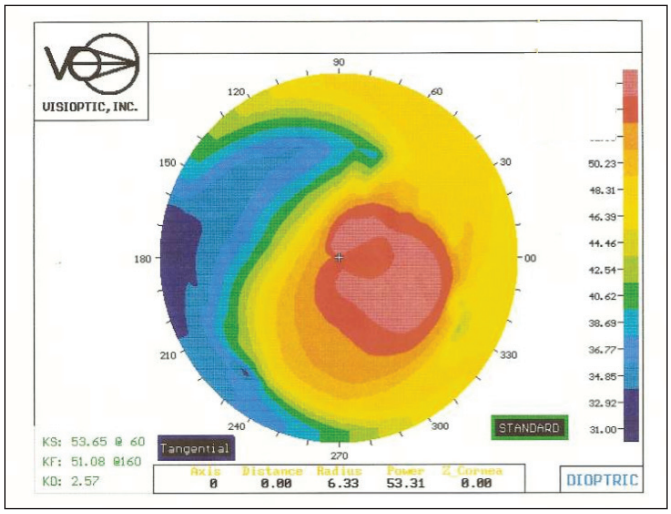

Figure A. Preoperative corneal topography (Alcon Laboratories, Inc., Fort Worth, TX) of an eye with keratoconus implanted with intrastromal corneal ring segments in 1997.

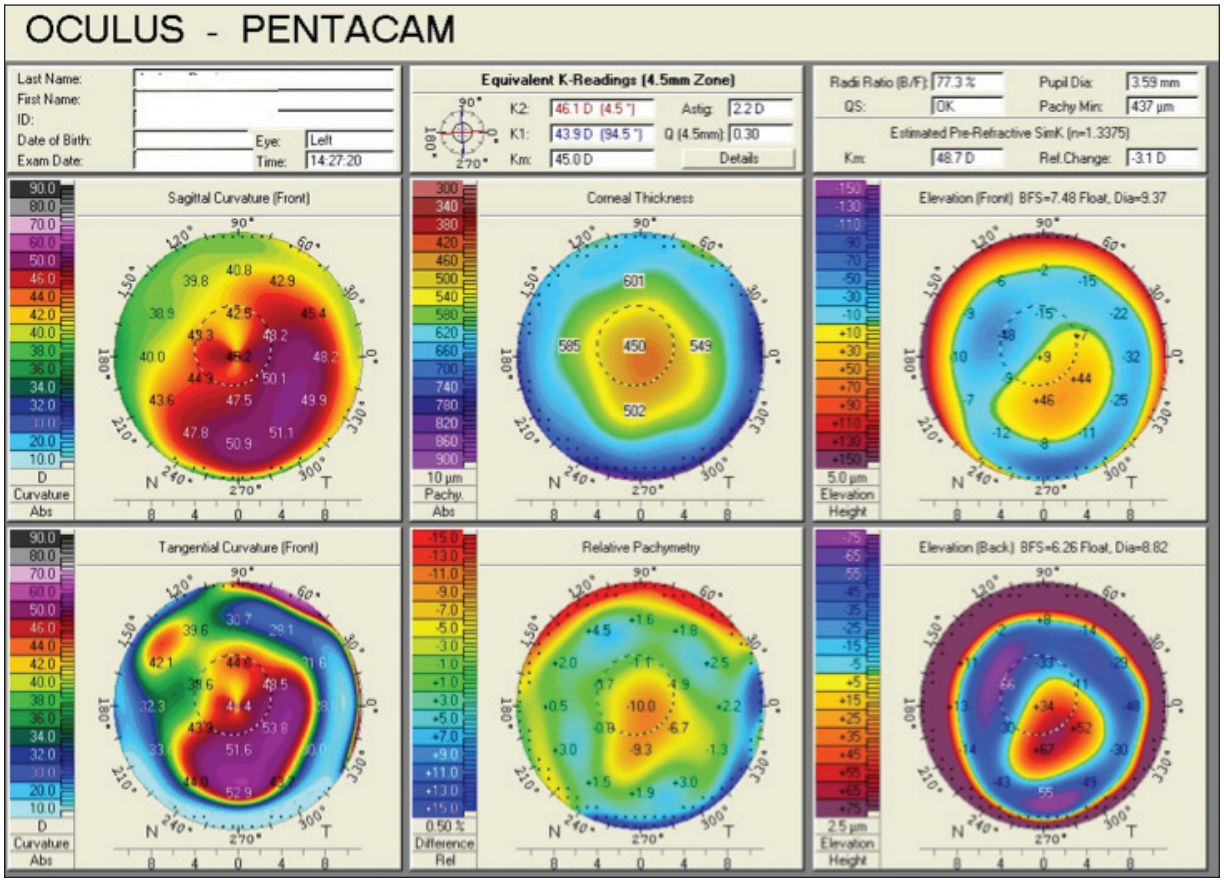

Figure B. Postoperative Pentacam corneal topography (Oculus Optikgeräte, Wetzlar, Germany) of an eye with keratoconus implanted with intrastromal corneal ring segments in 1997 (examination data from 2011).

·Clinical Research·

Evaluation of anterior and posterior surfaces of the cornea using a dual Scheimpflug analyzer in keratoconus patients implanted with intrastromal corneal ring segments

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Received: 2015-07-05 Accepted: 2015-09-25

Abstract

• AIM: To evaluate corneal parameters measured with a dual Scheimpflug analyzer in keratoconus patients implanted with intrastromal corneal ring segments (ICRS).

• METHODS: Fifty eyes of 40 keratoconus patients had Ferrara ICRS implantation from November 2010 to April 2014. Uncorrected visual acuity (UCVA), best corrected visual acuity (BCVA), refraction, keratometry, asphericity, elevation, pachymetry, root mean square (RMS), spherical aberration and coma were studied. All patients were evaluated using a dual Scheimpflug system.

• RESULTS: The mean follow-up time after the procedure was 12.7mo. The mean UCVA improved from 0.82 to 0.31 (P<0.001); the mean BCVA improved from 0.42 to 0.05 (P<0.0001), the mean spherical refraction changed from -3.06±3.80 D to -0.80±2.5 D (P<0.0001) and the mean refraction astigmatism reduced from -4.51±2.08 D to -2.26±1.18 D (P<0.0001). The changes from preoperative to postoperative, in parameters of the anterior and posterior surface of the cornea, were statistically significant except the elevation posterior at the apex of the cornea and posterior asphericity.

• CONCLUSION: The implantation of Ferrara ICRS induces changes in both anterior and posterior surfaces of the cornea.

• KEYWORDS: keratoconus; intrastromal corneal ring segments; dual Scheimpflug.
DOI:10.18240/ijo.2016.09.08

Torquetti L, Arce C, Merayo-Lloves J, Ferrara G, Ferrara P, Signorelli B, Signorelli A. Evaluation of anterior and posterior surfaces of the cornea using a dual Scheimpflug analyzer in keratoconus patients implanted with intrastromal corneal ring segments. *Int J Ophthalmol* 2016;9(9):1283-1288

INTRODUCTION

Intrastromal corneal ring segments (ICRS), which were initially designed to correct mild to moderate myopia[1], have been successfully used for the treatment of keratoconus in cases with a clear cornea and contact lens intolerance[2-5]. The main advantages of ICRS are safety, reversibility, and stability [6-8]. In addition, the surgery preserves the integrity of the central cornea. The efficacy of ICRS implantation for keratoconus has been widely described in the literature[5-7]. The main goals of segment implantation are to improve visual acuity and to delay or avoid corneal grafts in patients with keratoconus.

The Galilei dual Scheimpflug analyzer (Ziemer Ophthalmic Systems AG, Port, Switzerland) is a relatively new dual Scheimpflug imaging system combined with Placido-disk technology, which allows for an extensive evaluation of corneal features[9].

The aim of the present study was to evaluate changes in the anterior and posterior corneal surfaces, pachymetry, visual and refractive outcomes after implantation of Ferrara ICRS (AJL, Vitoria, Spain) using a dual Scheimpflug imaging system.

SUBJECTS AND METHODS

This retrospective case series study enrolled patients examined at Campineiro Microsurgery Eye Center, Campinas, Brazil, between November 2010 and April 2014. All patients were informed about inclusion in the study and provided informed consent in accordance with the Declaration of Helsinki.

The study comprised 50 eyes of 40 patients that had Ferrara ICRS implantation by the manual technique. Twenty-eight operated eyes were right and the remainder (22) were left eyes. Twenty patients were male and 20 patients were female. The mean age of patients was 30.2 years old [range

16 to 53, standard-deviation (SD): 8.3]. The mean follow-up time was 12.7±10.9mo.

The main indication for ICRS implantation was contact lens intolerance and/or progression of the ectasia. The progression of the disease was defined by: worsening of uncorrected visual acuity (UCVA) and best corrected visual acuity (BCVA) and/or progressive intolerance to contact lens wear and/or progressive corneal steepening.

Inclusion criteria were keratoconic eyes with clear central corneas, contact lens intolerance and a BCVA of 20/800 or better. Eyes with advanced keratoconus (mean keratometry higher than 60 D) and apical scarring were excluded.

The selection of the thickness and arch length of the ICRS to be implanted was made based on the Ferrara ring nomogram, third generation (topographic astigmatism)[5]. This nomogram is based on the position of the ectasia area on the cornea, topographic astigmatism, and the pachymetric map.

Clinical Measurements All patients had a complete ophthalmologic examination that included logMAR UCVA, logMAR BCVA, manifest refraction (spherical and astigmatism), spherical equivalent (SE), and slit-lamp and fundus evaluations. Corneal evaluation was performed using a dual Scheimpflug imaging system (Galilei 2, SW version 6.1.3, Ziemer Ophthalmic Systems AG, Port, Switzerland). This noninvasive system measures and characterizes the anterior segment. The Galilei combines and integrates Placido topography and the Scheimpflug photographic system. When both technologies complement each other, 122 000 points are recognized in the anterior segment of the eye. Simultaneously to each pair of Scheimpflug images, in a 180° rotating movement, 17 frontal images are routinely taken on the same alignment, 2 of them with the reflection of Placido rings. The first is taken with cameras at 12 and 6 o'clock and the second at 3 and 9 o'clock, so that the defects of the first are covered by the second. On the anterior curvature maps, everything that Placido topography does not achieve is being deduced from the Scheimpflug images. Meanwhile, the elevation and pachymetry are more dependent on the dual Scheimpflug slits. After processing the information, the internal software provides several calculations and parameters centered to the first Purkinje defined as the center of four dots reflected on the anterior corneal surface. The system may also provide all data aligned to the pupil.

Simultaneously, the system allows for corneal aberration analysis separately from aberrations of the lens and displays the total higher order corneal wavefront aberrations calculated from the front and back surface. Both the displayed wavefront maps and the RMS indices are recalculated re-centered on the pupil center over optical zones from 3- to 6-mm-diameter.

The following anterior and posterior corneal surface parameters were evaluated with the dual Scheimpflug system: anterior (flat SimK) and posterior (flat Kpost) corneal dioptric power in the flattest meridian of the 3.0 mm central zone, anterior (steep SimK) and posterior (steep Kpost) corneal dioptric power in the steepest meridian in the 3.0 mm central zone anterior (SimK) and posterior (Kpost) median corneal power in the 3.0 mm zone, anterior (TopoAstig) and posterior (PostAstig) anterior corneal astigmatism in the 3.0 mm zone, best-fit sphere (BFS) anterior and posterior elevation at the center of the cornea (ElevAnt), BFS anterior and posterior at the thinnest point of the cornea (ElevThin), asphericity in the 8-mm-diameter central zone aligned to the first Purkinje, pachymetry at the center of the cornea, and at the thinnest point. The root mean square (RMS), total coma and spherical aberration (SA) were also analyzed in the 6-mm-diameter central zone aligned to the pupil. All clinical examinations were performed in a standardized manner by an experienced examiner (Signorelli A).

Surgical Technique Corneal tunnels for ICRS segment insertion were performed by the manual technique. The incision was located on the steepest meridian of the anterior corneal surface in all patients. The visual axis was marked by pressing a Sinskey hook on the first Purkinje identified as the corneal light reflex on the central corneal epithelium while asking the patient to fixate at the microscope light. For the incision, a calibrated diamond knife was set at 80% of the corneal thickness at the incision site determined by the pachymetry map of Galilei. Two semicircular dissectors were placed sequentially into the lamellar pocket to be advanced steadily by a rotational movement (counterclockwise and clockwise dissectors). The ICRS was then placed inside the tunnel using a McPherson forceps. All surgeries were performed by the same surgeon (Signorelli A).

The postoperative regimen consisted of gatifloxacin 0.5% (Zymar®, Allergan, USA) and dexamethasone 0.1% (Maxidex®, Alcon) eye drops four times daily for two weeks. The patients were instructed to avoid rubbing the eye and to frequently use preservative-free artificial tears (Fresh Tears® 0.4%, Allergan). The patients were examined postoperatively at 1d, 1, 3, 6mo, and 1y after the surgery. The mean follow-up time was based on the time of the last visit.

Statistical Analysis The Graph Pad Prism (GraphPad2014, Chicago, IL, USA) was used for descriptive statistics, including means ±standard deviations. Student's t-test for paired data was used to compare preoperative and postoperative data. A two-tailed probability of 5% or less was considered statistically significant.

RESULTS

The mean UCVA improved from 0.82 to 0.31 (P<0.001); the mean BCVA improved from 0.42 to 0.05 (P<0.0001), the mean spherical refraction changed from -3.06±3.80 D to -0.80±2.5 D (P<0.0001) and the mean refractive astigmatism reduced from -4.51±2.08 D to -2.26±1.18 D (P<0.0001) (Table 1). The change in coma was not statistically significant. The SA reduced from 0.14±0.59 μm to -0.20±

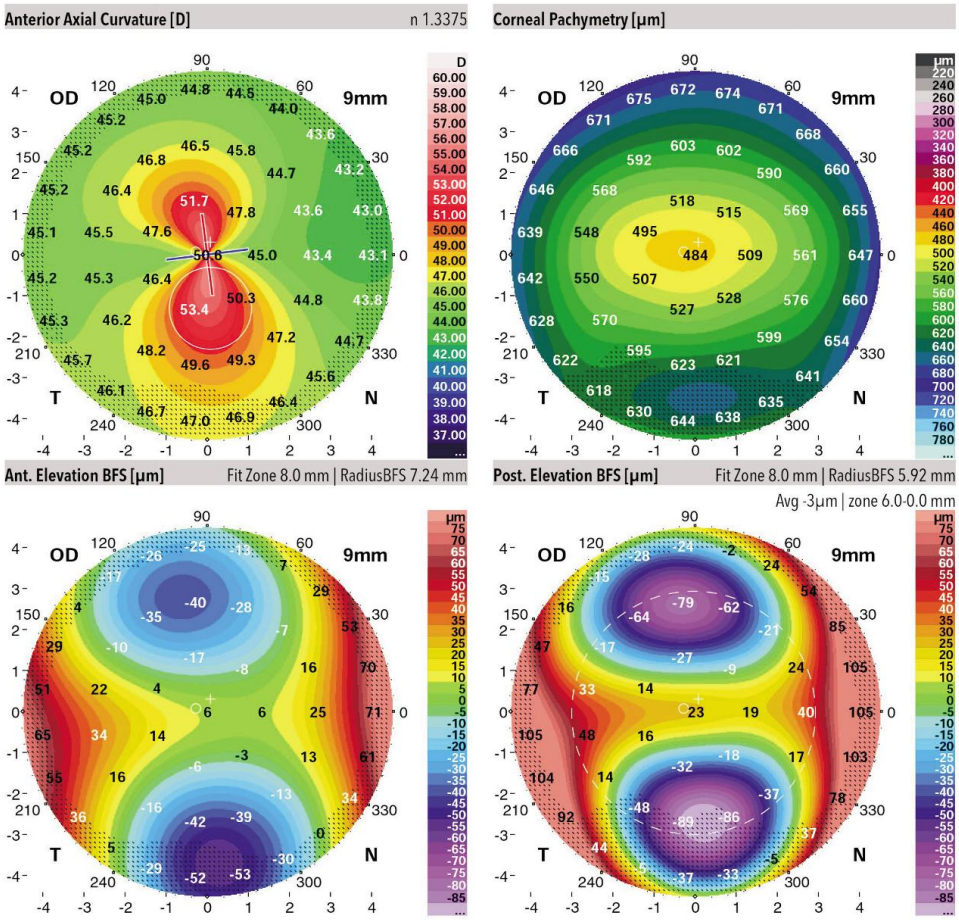

Figure 1 Preoperative axial anterior and elevation map.

0.78 μm (P=0.0003) and RMS reduced from 4.43±2.19 D to 3.88±1.83 D (P=0.0017). The pachymetry at the center of the cornea increased from 482±49.6 D to 519±53.8 D (P<0.0001) and the thinnest pachymetry increased from 461±37.7 D to 473±35.5 D (P<0.0001).

The results of the parameters of the anterior surface of the cornea are summarized in the Table 2. The mean flat SimK reduced from 47.28±4.71 D to 43.31±3.61 D (P<0.0001), the mean steep SimK reduced from 50.89±6.32 D to 47.11±5.19 D (P<0.0001) (Figures 1, 2). The anterior BFS elevation increased from 21.1±27.8 μm to 27.7±22.5 μm (P=0.036). The anterior BFS elevation at thinnest point reduced from 18.2±20.5 μm to 5.8±15.6 μm (P<0.0002). The anterior asphericity changed from -1.23±1.08 to -0.41±1.24 (P=0.0019).

The results of the parameters of the posterior surface of the cornea are summarized in the Table 3. The mean flat Kpost become flatter from -6.93±0.97 D to -6.60±0.96 D (P<0.0001), as well as the mean steep Kpost from -7.89±0.98 D to -7.31±0.96 D (P<0.0001). The posterior BFS elevation increased from 31.3±33.4 μm to 35.4±27.6 μm, however this change was not statistically significant (P=0.47). The posterior BFS elevation at thinnest point reduced from 35.4±33.5 μm to 21.7±20.7 μm (P<0.0014). The posterior asphericity did not change (from -1.48±1.30 to -1.47±1.58, P=0.97).

We stratified the main parameters according with the implanted ICRS. All the patients had implanted 5 mm

Table 1 Preoperative and last follow-up examination data of patients implanted with Ferrara intrastromal corneal ring segments implantation $\bar{x} \pm s$

Parameters	Preoperative	Postoperative	P
UCVA	0.82±0.12	0.31±0.25	<0.0001
BCVA	0.42±0.25	0.05±0.16	<0.0001
Spherical refraction (D)	-3.06±3.80	-0.80±2.57	<0.0001
Refractive astigmatism (D)	-4.51±2.08	-2.26±1.18	<0.0001
SE (D)	-4.48±3.90	-1.54±2.42	<0.0001
SA (μm)	0.14±0.59	-0.20±0.78	0.0003
RMS (μm)	4.43±2.19	3.88±1.83	0.0017
Coma (μm)	1.96±1.33	1.64±1.02	0.0095
Pach (μm)	482±49.6	519±53.8	<0.0001
PachThin (μm)	461±37.7	473.6±35.5	<0.0001

UCVA: Uncorrected visual acuity; BCVA: Best corrected visual acuity; SE: Spherical equivalent; SA: Spherical aberration; RMS: Root mean square; Pach: Pachymetry at the center of the cornea; PachThin: Minimal pachymetry.

Table 2 Comparison of preoperative and postoperative data of anterior cornea $\bar{x} \pm s$

Parameters	Preoperative	Postoperative	P
Flat SimK (D)	47.28±4.71	43.31±3.61	<0.0001
Steep SimK (D)	50.89±6.32	47.11±5.19	<0.0001
SimK (D)	49.10±4.81	44.31±7.91	<0.0001
AntBFSElev (μm)	21.1±27.8	27.7±22.5	0.036
AntBFSElevThin (μm)	18.2±20.5	5.8±15.6	0.0002
QAnt	-1.23±1.08	- 0.41±1.24	0.0019

Flat SimK: Keratometry at the flattest meridian; Steep SimK: Keratometry at the steepest meridian; SimK: Mean keratometry; AntBFSElev: Elevation anterior at the apex of the cornea; AntBFSElevThin: Elevation anterior at the thinnest point of the cornea; QAnt: Asphericity anterior.

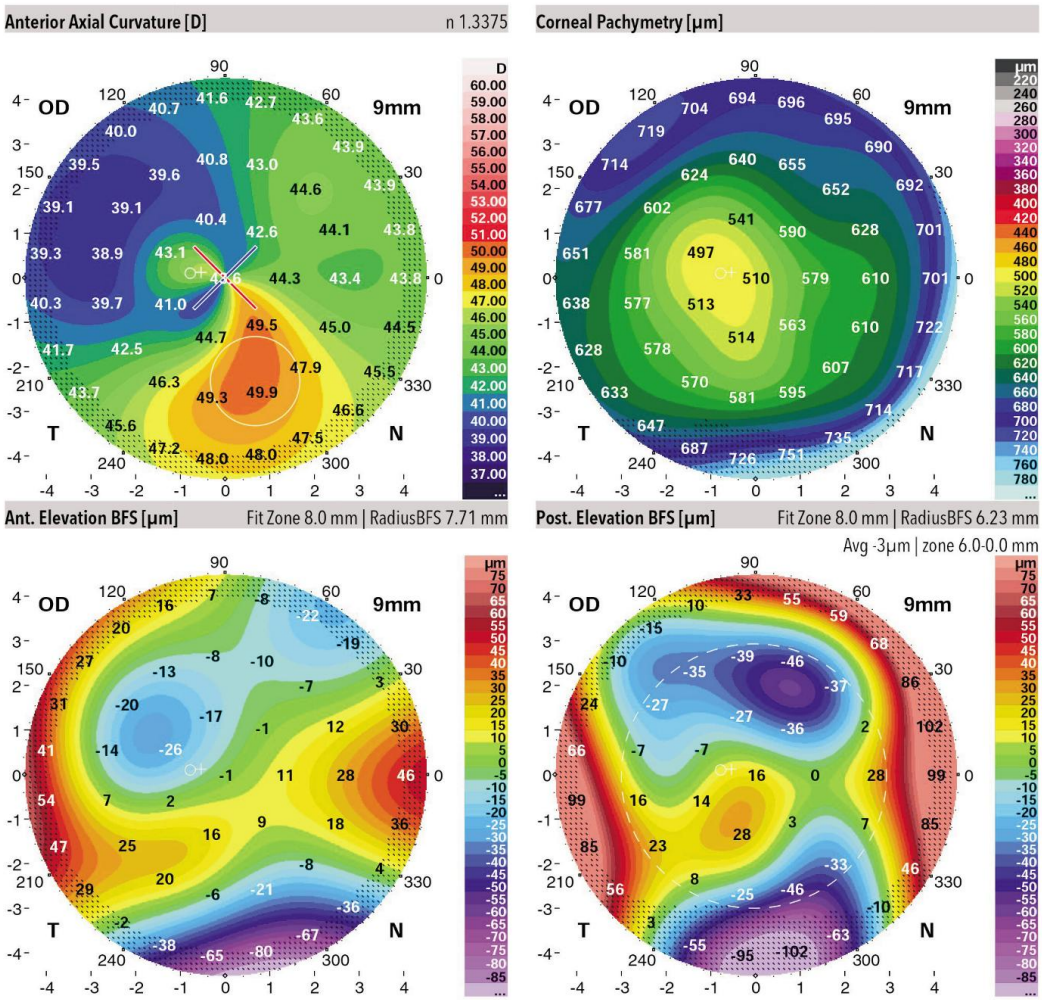

Figure 2 Postoperative axial anterior and elevation map.

Table 3 Comparison of preoperative and postoperative data of posterior cornea $\bar{x} \pm s$

Parameters	Preoperative	Postoperative	*P*
Flat Kpost (D)	-6.93±0.97	-6.60±0.96	<0.0001
Steep Kpost (D)	-7.89±0.98	-7.31±0.96	<0.0001
SimKpost (D)	-7.41 ± 0.95	-6.82±1.35	0.0004
PostBFSElev (µm)	31.3±33.4	35.4±27.6	0.47
PostBFSElevThin (µm)	35.4±33.5	21.7±20.7	0.0014
Qpost	-1.48±1.30	-1.47±1.58	0.97

Flat Kpost: Keratometry at the flattest meridian; Steep Kpost: Keratometry at the steepest meridian; Kpost: Mean keratometry; PostBFSElev: Elevation posterior at the center of the cornea; PostBFSElevThin: Elevation posterior at the thinnest point of the cornea; QPost: Asphericity posterior.

(optical zone) Ferrara segments, of different arch length: 140° (140-ICRS) (13 eyes), 160° (160-ICRS) (25 eyes) and 210° (210-ICRS) (12 eyes). The parameters evaluated for the types of segments were: keratometry, asphericity and astigmatism (Table 4). The flattening effect (keratometry reduction) was more significant in cases implanted with 210° -ICRS. The asphericity change induced was similar among the segments. The cylinder induction was less with the 210°-ICRS.

DISCUSSION

Complete characterization of the corneal structure that includes analysis of the anterior and posterior corneal surface and other objective factors is important for better comprehension of visual performance after ICRS implantation. The purpose of the current study was to evaluate and characterize the anterior segment parameters given by a dual Scheimpflug analyzer in keratoconus patients implanted with Ferrara ICRS.

The visual outcomes in our study were satisfactory and similar to the reported in the literature [10-12]. There was improvement of UCVA, BCVA, spherical and astigmatism refraction. The mean SE value decreased from -4.48±3.90 D to -1.54 ±2.42 D as well as keratometric and anterior asphericity values, reducing the corneal irregularity.

In this study there were significant decreases in sphere and cylinder after ICRS implantation, agreeing with results of other studies. Shabayek and Alio [10] reported a mean difference of 3.37 D in anterior keratometry power and 2.23 D in SE with Keraring ICRS (Mediphacos, Belo Horizonte, Brazil). Coskunseven *et al* [11] reported a mean decrease in anterior K power of 3.07 D. In a study by Ertan *et al* [12], the mean SE decreased from - 7.57 D to - 3.72 D and the mean anterior keratometry value decreased from 51.56 D to 47.66 D, 1y after Intacs ICRS (Addition Technology, Chicago, USA) implantation.

We found a significant increase in corneal thickness after the

Table 4 Preoperative and last follow-up examination data of patients implanted with Ferrara ICRS implantation, according with the arch length of segment $\bar{x} \pm s$

Parameters	140º-ICRS	160º-ICRS	210º-ICRS	*P*
SimK (D)				
Preop.	48.49±3.50	48.37±1.87	50.92±1.97	0.33
Postop.	44.88±3.82	44.39±2.62	45.45±1.81	0.56
Mean change	3.61±2.78	3.98±2.51	5.47±1.47	0.27
P	0.0005	<0.0001	< 0.0001	
Asphericity anterior				
Preop.	-1.34±0.80	-1.19±0.93	-1.69±0.75	0.059
Postop.	-0.13±1.47	-0.39±1.11	-0.52±1.05	0.23
Mean change	1.21±1.27	0.80±1.53	1.17±0.90	0.44
P	0.0069	0.015	0.0047	
Refractive astigmatism (D)				
Preop.	-7.25±2.69	-4.21±1.83	-5.96±1.53	0.032
Postop.	-2.93±1.45	-2.14 ± 1.33	-3.24±1.45	0.19
Mean change	2.77±3.01	2.06±1.98	1.40±1.60	0.33
P	0.026	<0.0001	0.12	

ICRS implantation. This can be explained by a theoretically corneal collagen remodeling induced by the implantation of ICRS. As acting as "spacers" the ring segments could interfere in corneal collagen turnover, with consequent increase in corneal pachymetry[13].

The actual Ferrara ICRS nomogram [14-15] is based on the corneal asphericity, measured by the Pentacam (Oculus Optikgerate GmbH). Most current videokeratoscopes mainly consider asphericity a unique parameter. Meridian differences in asphericity have been pointed out using Scheimpflug imaging [16], and some corneal topographers and autokeratometers provide different asphericity values for the main corneal meridians [17]. Significant variability in asphericity values between different corneal topographers is expected; the values depend on where the peripheral reference points are taken, the area analyzed, the alignment of data to different referential centers, and how many meridians are involved in the calculation. Recently, Read *et al* [18] using a method that combines several corneal topography images to provide a full cornea topography map, observed marked differences in corneal asphericity depending on the annular area taken as reference.

According to this nomogram, the asphericity should be the first parameter to be considered in the ring selection. However, all other parameters are considered as well, secondarily (topographic astigmatism and pachymetry). A target postoperative asphericity value equal to -0.23 is the goal after Ferrara ring implantation[19].

A significant change in asphericity values after implantation of ICRS has been demonstrated in some studies [14-15]. In our study, there was a significant change in the anterior asphericity, after the surgery, however the magnitude of this change was not in agreement with previous studies in which the asphericity change was evaluated by the Pentacam[20]. Due to the size of the studied sample we could not predict the asphericity change according with every ICRS thickness. For these reasons, we advise that the actual Ferrara ICRS nomogram based on cornea asphericity should not be used in patients that the asphericity values were obtained with Galilei.

According to the mechanism of action of ICRS, it is expected that the shorter the segment, the larger the cylinder reduction and the lesser the asphericity change and keratometry reduction (140°-ICRS, for example)[21]. Moreover, the longer the arch segments, the lesser cylinder reduction and the larger the asphericity change and keratometry reduction (210°-ICRS, for example)[22]. The 160º-ICRS can induce moderate changes in these 3 parameters (keratometry, astigmatism and asphericity). The results obtained in our study confirm these mechanism of action (Table 4).

It was expected, in the analysis, that the 140°-ICRS had more effect on cylinder reduction when comparing these data with the 160°-ICRS. However, if we remove the 140°-ICRS sample from patients with astigmatism less than 1.50 D, the mean astigmatism reduced even more in 4.10 ±1.82 (P= 0.001). In all cases implanted with 140°-ICRS, which the preoperative astigmatism was equal or less than 1.50 D, there was increase of the postoperative astigmatism, *i.e.* induction of astigmatism. For this reason, it is strongly advised to avoid implant short arch segments in patients with low astigmatism, due to the risk of increasing the postoperative cylinder.

The SA, coma and RMS significantly changed after ICRS implantation in the present study. Pinero *et al* [23] in a study comparing two different types of ICRS (Intacs and Keraring), found that coma-like aberrations tended to decrease after ICRS implantation, and the change occurred more rapidly with the Keraring. They also compared the visual and wavefront outcomes between the manual and the

femtosecond laser, and found that both procedures provided similar visual and refractive outcomes. A more limited aberrometric correction was observed in the manual technique. They found that the use of mechanical tunnelization specifically for Intacs implantation in eyes with early to moderate keratoconus limited the potential aberrometric correction of these implants because the procedure itself generated new aberrations, especially negative primary SA and primary coma.

The magnitude of change in parameters in the posterior surface of the cornea was less when compared with the anterior surface of the cornea. The only two parameters that did not show a statistically significant change alter ICRS implantation were posterior BFS elevation and posterior asphericity.

Anterior segment parameters determination is important for surgical planning in keratoconus patients and to determine the effect of ICRS implantation. The actual Ferrara nomogram based on the corneal asphericity should not be used in patients evaluated solely by Galilei. The presented data could be used, in future studies, to aid in the development of more predictable ICRS nomograms. Moreover, it emphasizes the need of development of a nomogram that would be universal to any device used to image the cornea.

In summary, we showed that the implantation of Ferrara ICRS induces changes in both anterior and posterior surfaces of the cornea. A limitation of this study is the relatively small sample of patients studied and its retrospective nature. Future studies with larger samples should be done in order to confirm the results obtained.

ACKNOWLEDGEMENTS

This abstract was presented at the European Congress of Cataract and Refractive Surgeons, held in Barcelona, in 2015.

Conflicts of Interest: Torquetti L, None; **Arce C,** Consultant of Ziemer Ophthalmic Systems AG; **Merayo-Lloves J,** Shareholders of Ferrara Ophthalmics; **Ferrara G,** Shareholders of Ferrara Ophthalmics; **Ferrara P,** Shareholders of Ferrara Ophthalmics; **Signorelli B,** None; **Signorelli A,** None.

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10.5005/jp-journals-10025-1005

ORIGINAL ARTICLE

Predictors of Clinical Outcomes after Intrastromal Corneal Ring Segments Implantation

Leonardo Torquetti, Guilherme Ferrara, Paulo Ferrara

ABSTRACT

Purpose: To evaluate the influence of age and severity of keratoconus in the clinical outcomes of implantation of Ferrara intrastromal corneal ring segments (ICRS).

Methods: A total of 1,073 eyes of 810 patients, consecutively operated from January 2006 to July 2008, were evaluated. Two independent analysis were made according to the age of patients and keratoconus staging. Four groups were created according to the age of patients: < 20 years old, 20 to 30, 30 to 40 and >40 years old. The patients were also evaluated according to the keratoconus stage (I to IV). The outcome analysis included uncorrected distance visual acuity (UDVA), corrected distance visual acuity (CDVA), keratometry (K), asphericity (Q), corneal volume (CV) and pachymetry. All patients were evaluated using the Pentacam.

Results: The postoperative increase in UDVA and CDVA was statistically significant in all groups ($p < 0.05$). The magnitude of improvement of CDVA was larger for patients between 21 and 30-year-old (CDVA = 20/40) and patients with keratoconus grade I (CDVA = 20/35) ($p < 0.05$). There was a statistically significant increase in CV and pachymetry postoperatively in all groups. The keratometry (3.95D) and asphericity (–0.77) reduction were larger in patients younger than 20-year-old and in patients with keratoconus grade IV ($p < 0.05$).

Conclusion: The best clinical outcomes are seen in patients between 20 and 30-year-old and initial cases of keratoconus (grade I). The more advanced the keratoconus, the larger magnitude of K and Q reduction after ICRS implantation.

Keywords: Keratoconus, Intrastromal corneal ring segments, Age, Severity of keratoconus.

How to cite this article: Torquetti L, Ferrara G, Ferrara P. Predictors of Clinical Outcomes after Intrastromal Corneal Ring Segments Implantation. Int J Keratoco Ectatic Corneal Dis 2012;1(1):26-30.

Source of support: Nil

Conflict of interest: None declared

INTRODUCTION

Intrastromal corneal ring segments (ICRS), which were initially designed to correct mild to moderate myopia,[1,2] have been evaluated as a way to manage keratoconus in cases with a clear cornea and contact lens intolerance. The main advantages of ICRS are safety,[3-5] reversibility and stability.[6-8] In addition, the surgery preserves the integrity of the central cornea.

The ICRS implantation has been reported to provide effective outcomes for the treatment of patients with corneal thinning disorders like keratoconus,[7,8] pellucid marginal degeneration[9,10] and post-LASIK ectasia.[11,12] The goal of ring segment implantation is to improve visual acuity and to delay or avoid corneal grafts in patients with keratoconus.

The age of patients can, theoretically, interfere in visual and topographic results after ICRS implantation. A recently published paper showed that the stiffness of the human cornea increases by a factor of approximately two between the ages of 20 and 100 years.[13] Moreover, the stage of keratoconus can also influence the outcomes after ICRS implantation, as in more severe cases it is expected suboptimal results, when compared to initial cases.[14]

The purpose of this study is to evaluate the influence of age and severity of keratoconus in the clinical outcomes of implantation of Ferrara ICRS.

PATIENTS AND METHODS

In the present study, 1073 eyes of 810 consecutive surgical patients from January 2006 to July 2008 were evaluated. In 972 eyes, one or two segments of an ICRS with 160° of arc were implanted. In 101 eyes, one ICRS with 210° of arc was implanted. We have done two independent analysis according to: (1) Age of patients and (2) keratoconus staging. The patients were divided into four groups according to its age: <20 years old, 21 to 30 years old, 31 to 40 years old and >40 years old (Table 1). Moreover, patients were divided into four groups regarding the stage of keratoconus, according to the mean keratometry (Km): Grade I (Km < 46D), grade II (46 < Km < 52D), III (52 < Km < 60D) or IV (Km > 60D).

Inclusion criteria were contact lens intolerance and/or evidence of ectasia progression as measured by worsening of uncorrected distance visual acuity (UDVA) and corrected distance visual acuity (CDVA), progressive intolerance to contact lens wear and progressive corneal steepening documented by topographical changes. Two or more lines of UDVA and/or CDVA worsening and at least 2 diopters (D)

Table 1: General data of patients

Age (years)	*Eyes (n)*	*Age (Y)—(range)*	*Sex (F/M)*
<20	98	17 ± 2.25 (10-19)	68/30
20-30	546	23 ± 3.93 (20-29)	224/302
30-40	292	33 ± 2.96 (30-39)	107/195
>40	142	47 ± 6.85 (40-74)	88/59

p-values = mean ± SD

of increase in mean keratometry (K) as measured with a Pentacam (Oculus Optikgerate GmbH), were required to define progression of the disease. Exclusion criteria included any of the following discovered during the preoperative examination: Advanced keratoconus with curvatures over 62D, significant apical opacity and scarring, hydrops, corneas with thickness below 300 µm in the ring track as evaluated by Pentacam pachymetry and intense unresolved atopia, which is more appropriately treated before implantation.

CLINICAL MEASUREMENTS

A complete ophthalmologic examination was performed before surgery and included UDVA and CDVA assessment, biomicroscopy, fundoscopy, tonometry, corneal topography, pachymetric map and asphericity (Q) measurement using the Pentacam HR. All clinical examinations were performed in a standardized manner by an independent, experienced examiner (PF). At the last follow-up examination, manifest refraction, UDVA, CDVA, slit-lamp and topographic examinations were performed.

SURGICAL TECHNIQUE

All surgeries were performed by the same surgeon (PF) using the manual technique. The arc and thickness of the ICRS were selected according to a previously described nomogram that is based on the position of the keratoconus on the cornea, topographic astigmatism and the pachymetric map.[4,5] The nomogram determines the ring thickness to be implanted. The surgery was performed under topical anesthesia after miosis was achieved with 2% pilocarpine. An eyelid speculum was used to expose the eye, and 2.5% povidone iodine eyedrops were instilled onto the cornea and conjunctival cul-de-sac. The visual axis was marked by pressing a Sinskey hook on the central corneal epithelium while asking the patient to fixate on the corneal light reflex of the microscope light. Using a marker tinted with gentian violet, a 5.0 mm optical zone and incision site were aligned to the desired axis in which the incision would be made. This incision site was always the steepest topographic axis of the cornea given by the Pentacam.

A square diamond blade was set at 80% of corneal thickness as determined by the pachymetric map at the incision site. Using a 'stromal spreader', a pocket was formed in each side of the incision. Two 270° semicircular dissecting spatulas, clockwise and counterclockwise, were consecutively inserted through the incision and gently pushed with some, quick, rotary 'back and forth' tunneling movements. Following channel creation, the ring segments were inserted using a modified McPherson forceps. The rings were properly positioned with the aid of the Sinskey hook.

The postoperative regimen consisted of moxifloxacin 0.5% (Vigamox®, Alcon, Ft Worth, TX, USA) and dexamethasone 0.1% (Maxidex®, Alcon) eye drops four times daily for 2 weeks. The patients were instructed to avoid rubbing the eye and to frequently use preservative-free artificial tears (Oftane® 0.4%, Alcon). The patients were examined postoperatively at 1 day, 1, 3 and 6 months and 1 year after the surgery. After the first year, the patients were evaluated annually. The mean follow-up time was based on the time of the last visit.

STATISTICAL ANALYSIS

The GraphPad Instat software was used for descriptive statistics, including means ± standard deviations and to test group differences for continuous variables. Student's t-test for paired data was used to compare preoperative and postoperative data. Statistical analysis was done using independent sample t-tests to compare variables between groups. p-values less than 0.05 were considered statistically significant.

RESULTS

The mean follow-up time of operated patients was 23.8 ± 12.2 months. The majority of patients were between 21 and 30-year-old (Table 1).

The preoperative keratometry values were similar for all age groups. There was a statistically significant reduction of keratometry for all groups, and the amount of this reduction was larger for patients < 20 years old (Table 2). The asphericity values were more negative for patients <20 years old, however, the postoperative Q values were similar between groups. The change in Q value was larger for patients < 20 years old than for older patients ($p < 0.05$).

Table 2: Preoperative and postoperative K and Q, according to the age

Age (years)	*Preoperative Km (D)*	*Postoperative Km (D)*	*p-value*	*ΔKm (D)*	*Preoperative Q (µm)*	*Postoperative Q (µm)*	*p-value*	*ΔQ (µm)*
<20	49.75 ± 4.83	45.80 ± 3.80	<0.01	3.95	–1.09 ± 0.63	–0.36 ± 0.63	<0.01	–0.73
21-30	49.43 ± 4.54	45.86 ± 3.82	<0.01	3.57	–0.90 ± 0.45	–0.38 ± 0.51	<0.01	–0.52
31-40	49.51 ± 4.13	46.11 ± 3.62	<0.01	3.40	–0.85 ± 0.48	–0.39 ± 0.55	<0.01	–0.46
>40	49.54 ± 4.60	46.40 ± 4.30	<0.01	3.14	–0.77 ± 0.57	–0.29 ± 0.70	<0.01	–0.48

p-values = mean ± SD

There was a statistically significant increase in corneal volume and corneal thickness in all groups, postoperatively, however, there was no difference intergroup ($p > 0.05$) (Table 3). The mean UDVA and CDVA increased in all groups ($p < 0.01$, Table 4). The magnitude of improvement of CDVA was larger for patients between 21 and 30-year-old (CDVA = 20/40) and in patients with keratoconus grade I (CDVA = 20/35) ($p > 0.05$). The changes in keratometry and as phericity were statistically significant in all keratoconus grades (Table 5).

DISCUSSION

Improvement in visual acuity and refraction after ICRS implantation is accomplished by shortening the path length of the portion of the collagen lamellae that are central to the segments. Redistribution of corneal curvature leads to a redistribution of corneal stress, interrupting the biomechanical cycle of the keratoconus progression and in some cases reversing the stress.[15]

The goal of ICRS implantation is to stabilize and reinforce the ectatic cornea. It takes approximately 6 months for ICRS implantation to show an effect on the cornea and improve the visual acuity because of the viscoelastic nature of the cornea.[16]

Alió et al[17] have reported good outcomes in a similar group to our study, with a mean age of 29.5 ± 7.05 years and consisting of 75% males. Poorer outcomes and higher complication rates have been reported in older patient populations with a female predominance by Alió et al[17] and Kanellopoulos et al.[18] The preoperative predictors of a good outcome have been reported to be lower initial keratometric readings ($K < 53D$), better preoperative CDVA, lower astigmatism and spherical myopia.[17] Our study results confirm some of these data, as the best clinical outcomes were found in stage I keratoconus, in which the keratometry readings are low and the UDVA and CDVA are better.

We found a significant increase in corneal thickness in all groups. In theory, this can be explained by corneal collagen remodeling induced by the implantation of the ICRS.[19,20] By acting as 'spacers', the ring segments could interfere with corneal collagen turnover, with consequent increases in the corneal pachymetry.

There was a significant decrease in asphericity values after implantation of the ICRS. Most studies agree that

Table 3: Preoperative and postoperative CV and TCT

Age (years)	*Preoperative CV (mm^3)*	*Postoperative CV (mm^3)*	*p-value*	*ΔCV (mm^3)*	*Preoperative TCT (μm)*	*Postoperative TCT (μm)*	*p-value*	*ΔTCT (μm)*
>20	58.2 ± 4.0	59.0 ± 4.3	<0.01	0.86	459.6 ± 48.2	470.8 ± 50.2	<0.01	11.1
21-30	57.2 ± 3.3	58.3 ± 3.3	<0.01	1.1	450.0 ± 41.8	465.8 ± 49.8	<0.01	15.8
31-40	56.1 ± 3.8	57.5 ± 3.8	<0.01	1.4	437.1 ± 47.9	458.8 ± 50.0	<0.01	21.7
>40	56.9 ± 4.2	58.0 ± 4.1	<0.01	1.1	440.0 ± 48.5	457.8 ± 47.4	<0.01	17.8

p-values = mean ± SD

Table 4: Preoperative and postoperative UDVA and CDVA, according to the age and severity of keratoconus

Age (years)	*Preoperative* UDVA	*Postoperative* UDVA	*p-value*	*Preoperative* CDVA	*Postoperative* CDVA	*p-value*
>20	20/240	20/100	<0.01	20/110	20/55	<0.01
21-30	20/240	20/80	<0.01	20/105	20/40	<0.01
31-40	20/170	20/70	<0.01	20/110	20/47	<0.01
>40	20/270	20/70	<0.01	20/105	20/50	<0.01
Grades						
I	20/210	20/60	<0.01	20/60	20/35	<0.01
II	20/220	20/80	<0.01	20/94	20/40	<0.01
III	20/250	20/100	<0.01	20/400	20/55	<0.01
IV	20/800	20/200	<0.01	20/400	20/90	<0.01

p-values = Mean ± SD

Table 5: Preoperative and postoperative K and Q, according to the severity of keratoconus

Grade (I-IV)	*Preoperative Km (D)*	*Postoperative Km (D)*	*p-value*	*ΔKm (D)*	*Preoperative Q (μm)*	*Postoperative Q (μm)*	*p-value*	*ΔQ (μm)*
I	45.50 ± 2.35	43.0 ± 2.61	<0.01	2.5	–0.52 ± 0.27	–0.08 ± 0.43	<0.01	–0.44
II	48.50 ± 2.87	45.3 ± 2.71	<0.01	3.2	–0.84 ± 0.32	–0.33 ± 0.49	<0.01	–0.51
III	52 ± 4.11	47.7 ± 3.69	<0.01	4.3	–0.85 ± 0.37	–0.55 ± 0.34	<0.01	–0.58
IV	61.5 ± 4.83	54.10 ± 479	<0.01	7.4	–1.96 ± 0.55	–1.3 ± 0.60	<0.01	–0.66

p-values = mean ± SD

human cornea asphericity values range from –0.01 to –0.80.[21-23] Currently, the most commonly accepted value in a young adult population is approximately –0.23.[24] The asphericity can be considered as one of the markers of visual quality. Thus, returning it closer to 'normal' or at least reducing the excess prolateness usually found in keratoconus, could be a predictor of improved visual quality.

Most patients of this study were between 21 and 40 years old. There was no statistically significant ($p > 0.05$) change in ΔKm, ΔCV and ΔTCT when compared among the different age groups. The ΔQ was larger ($p < 0.05$) for patients younger than 20 years old. As the corneal asphericity has been considered as a more reliable parameter for corneal remodeling,[25] the larger changes in this parameter in younger patients can be a result of a less stiff cornea, more prone to changes induced by ICRS.

There was improvement of UDVA and CDVA, from preoperative to postoperative, in all age groups. There was no statistically significant difference in UDVA and CDVA among the groups ($p > 0.05$). However, the CDVA was better for patients between 21 and 30 years old. Concerning the stage of the keratoconus, the more initial the stage the better the UDVA and CDVA ($p < 0.05$).

Miranda et al[14] obtained a significant reduction in the postoperative central corneal curvature, the CDVA and UDVA improved in 87.1 and 80.6% of the eyes respectively. Siganos et al[3] showed an increase of the UDVA from 20/285 preoperatively to 20/100 and 20/60 after 1 and 6 months respectively. The BDVA improved from 20/55 preoperatively to 20/40 and 20/33 after 1 and 6 months respectively. We found similar results in our study, which confirms the reproducibility of the technique.

The more advanced the keratoconus the larger the amount of K reduction and Q increase. This seems to be related to the biomechanics of the cornea, i.e. the steeper the cornea, the larger the response to a given implanted ICRS.

The variation of corneal biomechanics with age, may play a role in different clinical outcomes after ICRS implantation, when an age-matched analysis is performed. Elsheikh et al,[26] conducted an experimental study to determine the stress-strain behavior of human corneal tissue and how the behavior varies with age. They found a strong statistical association between stiffness and age ($p < 0.05$). A recent study showed that corneal biomechanical parameters are significantly decreased by aging without significant changes in central corneal thickness, suggesting that age-related structural changes resulting from collagen cross-linking may lead to a reduction of corneal biomechanical variables independent of central corneal thickness.[27]

CONCLUSION

ICRS implantation was effective in reducing the keratometry, corneal asphericity, increasing corneal volume and thickness and improving UDVA and CDVA. Patients with age between 21 and 30 years old and with grade I keratoconus can benefit more from ICRS implantation. The role of age, gender, cone position and evolutive grade as predictors of better outcomes, needs to be better evaluated. Further studies and long-term follow-up reports are required to determine other predictors of a good visual outcome and to develop criteria for patient selection.

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10.5005/jp-journals-10025-1041

ORIGINAL ARTICLE

The Influence of Corneal Volume in Surgical Planning: Insights for a New Parameter for the Ferrara Ring Nomogram

Leonardo Torquetti, Guilherme Ferrara, Wagner Gomes Dias, Paulo Ferrara

ABSTRACT

Purpose: To evaluate the corneal volume (CV) before and after Ferrara intrastromal corneal ring segments (ICRS) implantation and its influence in clinical outcomes in keratoconus patients.

Materials and methods: A total of 77 eyes of 42 keratoconus patients consecutively implanted with the Ferrara ICRS were evaluated with a Pentacam (Oculus Optikgerate GmbH). The following parameters were obtained: Anterior corneal asphericity (Q), CV and thinnest corneal thickness (TCT). The inter-relation between Q and CV was evaluated.

Results: In patients with CV inside two standard deviation (SD: 53.51-60.65) of the mean CV, the postoperative asphericity values roughly agreed with expected asphericity values. In patients with CV outside two SD intervals (<53.51 and >60.65) of the mean CV, the postoperative asphericity values did not agreed with expected asphericity values. Corneas with high volumes (>60.65) had less change of asphericity than corneas with low volumes.

Conclusion: The CV is a new parameter, to be better studied, as it seems to be important in ICRS selection. Corneas with high volumes may require more tissue to get flattened and properly reshaped.

Keywords: Corneal volume, Pentacam, Tomography, Keratoconus.

How to cite this article: Torquetti L, Ferrara G, Dias WG, Ferrara P. The Influence of Corneal Volume in Surgical Planning: Insights for a New Parameter for the Ferrara Ring Nomogram. Int J Kerat Ect Cor Dis 2013;2(1):12-15.

Source of support: Nil

Conflict of interest: None declared

INTRODUCTION

Keratoconus is a bilateral, progressive noninflammatory corneal ectasia that tends to affect young age groups in their late teens.[1] Despite intensive clinical and laboratory investigations, its precise etiology is unknown.[2,3] In keratoconus, corneal changes result in a mild to severe decrease in the corrected distance visual acuity (CDVA) as a result of progressive myopia, regular and irregular astigmatism, in addition to apical scarring in advanced cases.[4]

One of the goals of treatment of keratoconus with intrastromal corneal ring segments (ICRS) is to improve quality of vision beyond the simple corneal flattening and stabilization of the disease. Significant asphericity changes can occur after any corneal surgery[5,6] and these changes may explain the increase in spherical aberration and deterioration in the quality of monocular and binocular vision.[7,8]

The actual Ferrara ICRS nomogram is based on corneal asphericity.[9] Previously published studies have shown that is possible to predict the final Q-value after ICRS implantation.[10] This is important, once the quality of postoperative vision is linked to, besides the corneal flattening, the corneal shape (oblate or prolate). It is well known that not only the excess of prolateness of the cornea found in keratoconus but also the cornea oblate can cause unsatisfactory visual quality. Therefore, the surgical plan should be aimed to achieve a normal, physiologic Q-value (-0.23 ± 0.08).[11]

Corneal volume (CV) was recently identified as an additional screening factor for keratoconus.[12-14] Significant differences in CV have been reported between normal and moderate keratoconic eyes (Pentacam system: 60.83 ± 3.27 mm^3 controls *vs* 57.98 ± 2.65 mm^3 moderate keratoconus),[12] suggesting the potential role for CV as a diagnostic factor for corneal ectatic disorders. However, there is not enough scientific evidence of the potential usefulness of CV as a screening factor for keratoconus suspect.

The aim of the present study was to evaluate changes in the CV and asphericity before and after ICRS implantation and the correlation between these parameters.

MATERIALS AND METHODS

In the present study, 77 eyes of 42 consecutive surgical patients from January to March 2011 were evaluated. The preoperative and postoperative data of patients, which had a Ferrara ICRS implantation, were used for analysis. This study was approved by the institutional review board of Dr Paulo Ferrara Eye Clinic, Belo Horizonte, Minas Gerais, Brazil and followed the tenets of the Declaration of Helsinki. The procedures were fully explained to each patient, and each provided written informed consent.

All operated patients had the diagnosis of keratoconus based on clinical findings and tomographic parameters. The patients had progressive intolerance to contact lens and/or clinical and topographic evidence of disease progression and/or unsatisfactory CDVA.

Participant exclusion criteria were any previous corneal or ocular surgery, any eye disease other than keratoconus and chronic or continuous use of topical medications. Contact lenses (soft or rigid) had to be removed at least 72 hours before the examination.

We evaluated the asphericity changes after ICRS implantation and the expected asphericity[9,10] change based on preoperative CV.

PENTACAM MEASUREMENTS

The Pentacam is a combined device consisting of a slit illumination system and a Scheimpflug camera, which rotates around the eye.

A thin layer within the eye is illuminated through the slit. Being not entirely transparent the cells scatter the slit light. In doing so, they create a sectional image, which is then photographed in side view by a camera. This camera is oriented according to the Scheimpflug principle, thus creating an image of the illuminated plane, which appears completely sharp from the anterior surface of the cornea right up to the posterior surface of the crystalline lens.

After correction for Scheimpflug distortion and light refraction at tissue interfaces the exact of location of image edge points in the eye is determined by means of raytracing.[15] Eye movements during image acquisition are captured by a second camera (pupil camera) and also taken into account in the mathematical evaluation. This produces a set of three-dimensional (3D) measurement data, which gives a precise geometric description of the anterior eye segment. This data in turn can be used to generate data on elevation, curvature, pachymetry and depth of the anterior chamber in the well known form of color maps. We used the HR version of Pentacam, which has a precision and reproducibility of 0.1 D for keratometry measurements.

The following parameters were evaluated with the Scheimpflug system: Mean corneal power in the 3.0 mm zone, topographic astigmatism, CV at 10 mm, minimum pachymetry and mean asphericity at 4.5 mm diameter corneal area.

STATISTICAL ANALYSIS

All data were analyzed using the SPSS software (SPSS, Chicago, IL) and reported as means ± standard deviation. The Student's t-test for paired sample was used for comparison of the variables. A p-value less than 0.05 was considered statistically significant.

RESULTS

The mean preoperative CV was 57.08 (SD: standard deviation ± 3.57) and 58.92 postoperatively (Table 1). The keratometry decreased from 56.3 to 51.4 D ($p < 0.001$). The mean asphericity increased from –0.86 to –0.33 ($p < 0.001$). We evaluated the asphericity changes after ICRS implantation and the expected asphericity change based on preoperative CV. The Table 2 shows, in a sample of patients, the preoperative and postoperative Q and CV, and the ΔQ and expected ΔQ. In patients with CV inside two SD (53.51-60.65) of the mean CV, the postoperative asphericity values roughly agreed with expected asphericity values. In patients with CV outside two SD interval (<53.51 and >60.65) of the mean CV, the postoperative asphericity values did not agreed with expected asphericity values. Corneas with high volumes (>60.65) had less change of asphericity than corneas with low volumes.

Table 1: Preoperative and postoperative parameters

	Preoperative	*Postoperative*
Q-value	–0.86	–0.33
Corneal volume	57.08	58.92
Pachymetry (thin)	454	470
Km	56.3	51.4
Top. astigmatism	–2.68	–1.09

Student's t-test for paired sample, $p < 0.001$ for all parameters

DISCUSSION

Among the numerous morphologic parameters that can be measured by modern examination techniques is the CV. It reflects topographical and pachymetric changes and characterizes corneal morphometric changes with a single value.[16] The Pentacam, a 3D analyzer equipped with a rotating Scheimpflug camera, allows CV assessment. Because the CV is a numerical value, it may be useful for a statistical assessment of the entire cornea.

CV has been proposed as a new index to diagnose keratoconus and screen refractive candidates.[12] However, most published papers found no significant differences in CV among different grades of keratoconus.[13,17]

Mannion et al have found that CV was significantly decreased in keratoconus, particularly in the central and paracentral area explained by loss of corneal tissue. The reduction in CV was in moderate and severe cases of keratoconus, but not in the early cases. One likely explanation for this finding could be that in early stages of keratoconus, a redistribution of CV occurs with no loss of tissue.[18]

Most studies agree that the human cornea Q (asphericity) values ranges from –0.01 to –0.80.[11-13] Currently, the most commonly accepted value in a young adult population is approximately –0.23 ± 0.08.[14] As the asphericity can be considered as one of markers of quality of vision,[15] turning it closer to 'normal' or at least reducing the excess of prolateness usually found in keratoconus, could be a

Table 2: Preoperative and postoperative Q and CV; achieved and expected

Patient	*Q preop*	*CV preop*	*Q postop*	*Delta Q achieved*	*Delta Q expected*	*CV postop*	*Ring used*
ARF	–1.21	63.7	–1.19	–0.02	–1.02	64.3	160/250 and 160/200
BGFG	–0.51	52.4	–0.1	–0.41	–0.26	54.3	160/150
CMFT	–0.87	64.8	–0.95	0.08	–0.34	64.8	160/250
EB	0.34	60.6	0.45	–0.11	–0.31	59.3	140/150
LMA	–1.85	61.6	–1.61	–0.24	–0.86	68.8	160/200 × 2
LRJ	–0.61	52.3	–0.17	–0.44	–0.26	54.1	160/150
MFAS	–0.85	62.1	0.25	–1.1	–0.57	63.7	160/150
MFAS	–0.64	61.8	0.18	–0.82	–0.57	63.4	160/15 × 20
MLOF	–0.28	50	0.02	–0.3	–0.26	50	160/150
RMM	–1.15	51.9	–0.36	–0.79	–0.73	52.7	160/200 and 160/150
RM	–1.1	62.5	0.7	–1.8	–0.8	64.1	160/250 and 160/150
SDMS	0.02	51.4	–0.05	0.07	–0.26	54.3	160/150
THQV	–1.71	51.9	–0.61	–1.1	–0.86	53	160/200 × 2
VRC	0.03	61.1	–0.26	0.29	–0.86	61.8	160/150

predictor of improvement of visual. The Q-value has been used as an important parameter for ICRS selection.[16,17]

A recently published paper has shown how much each thickness of ICRS (single or paired) can change the cornea asphericity.[10] Based on this data we can expect the asphericity change based on the thickness of the segment implanted. In the present paper we evaluated the asphericity change and the expected asphericity change after ICRS implantation and correlated this data with the preoperative CV in order to evaluate its influence in the outcomes based on Q.

We found that in patients with the CV inside two SD (53.51-60.65) of the mean CV, the postoperative asphericity values roughly agreed with expected asphericity values. In patients with CV outside two SD intervals (<53.51 and >60.65) of the mean CV, the postoperative asphericity values did not agreed with expected asphericity values. Moreover, patients with cornea volume higher than 60.65 may have worse outcomes based on corneal asphericity.

Tu et al[19] implanted symmetrical segments of the same thickness in a sample of keratoconus patients with different grades of the disease. They reported that the refractive and keratometric surgical effect of ICRS appeared to be positively associated with the stage of keratoconus; that is, the effect was greater the more advanced the keratoconus stage. Considering that the CV is lower in more advanced cases of keratoconus, the results of that study agrees with the results of the present paper.

Ambrosio et al[12] showed that the corneal-thickness spatial profile, corneal-volume distribution, percentage of increase in thickness, and percentage of increase in volume are different in keratoconic eyes and normal eyes. Keratoconic eyes have thinner corneas than normal corneas, with less volume and a more abrupt increase in these parameters from the thinnest point toward the periphery. In that paper, the authors described the corneal thickness and volume in different optical zones.

The CV is a new parameter, to be better studied, as it seems to be important in ICRS selection. Corneas with high volumes may require more tissue to get flattened and properly reshaped. The presented data could be used, in future studies, to aid in the development of new nomograms for ICRS implantation.

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10.5005/jp-journals-10025-1091

CASE SERIES

Intrastromal Corneal Ring Segments Implantation in Patients with Mild Keratoconus

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ABSTRACT

Purpose: The purpose of this study is to evaluate the topographic, topometric and visual changes after implantation of Ferrara intrastromal corneal ring segments (ICRS) in grades I and II keratoconus patients.

Materials and methods: The chart records of 50 consecutively operated keratoconus patients were reviewed. The patients were operated on by the same surgeon, with the manual technique. All patients were preoperatively and postoperatively evaluated with the Pentacam (OCULUS Optikgeräte, Wetzlar, Germany). The studied parameters were: uncorrected distance visual acuity (UDVA), corrected distance visual acuity (CDVA), keratometry, corneal asphericity and corneal volume.

Results: Fifty eyes of 42 patients (26 males and 16 females) were analyzed. The mean preoperative UDVA was 0.91 ranging from LogMAR 0.10 to 1.30. The mean postoperative CDVA was 0.19 ranging from 0.00 to 0.54 LogMAR. The postoperative CDVA was equal or better than 0.18 in 37 cases (74%). The mean K1 decreased from 45.80D (±2.52) preoperatively to 44.27D (± 2.10) postoperatively and the mean K2 value, from 49.06D (± 2.09) to 46.22D (±1.89). The mean asphericity increased from –0.71 preoperatively to –0.29 postoperatively. The average preoperative corneal volume was 56.89 ± 3.11 mm^3 while the average postoperative corneal volume was 57.64 ± 3.05 mm^3.

Conclusion: The study supports the early indication of implantation of Ferrara ICRS in mild to moderate keratoconus cases in order to achieve good visual, keratometric and ashpericity outcomes.

Keywords: Mild keratoconus, Intrastromal corneal ring segment, Corneal volume, Asphericity.

How to cite this article: Rodrigues PF, Ferrara G, Ferrara P, Dias WG, Torquetti L. Intrastromal Corneal Ring Segments Implantation in Patients with Mild Keratoconus. Int J Kerat Ect Cor Dis 2014;3(3):122-126.

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Source of support: Nil

Conflict of interest: None

INTRODUCTION

Keratoconus is a noninflammatory corneal condition in which there is thinning and protrusion of the cornea. It is commonly bilateral, involving two-third of the cornea, with its central apex just below the visual axis. The condition, along with pellucid marginal degeneration, keratoglobus and posterior keratoconus represents phenotypical variations of the same pathogenic mechanism. Asides from a significant variability in prevalence, it has an estimated incidence of 50 to 230 cases per 100,000.[1] Initially, it is usually managed with the correction of ametropia through the use of glasses. In cases which glasses do not provide a satisfactory corrected visual acuity, rigid gas permeable contact lenses are used. They, in turn, create a new anterior refractive surface; however, they do not stop the progression of the disease. The use of intracorneal implants for high myopia correction was initially described at the beginning of the 60 seconds.[1,2] Its application is an important tool for keratoconus patients who are intolerant to contact lenses. The Ferrara ring implant (1986) was first used in the correction of myopia of up to 15 diopters. Its applicability and reproducibility allowed for its use in keratoconus patients, irregular astigmatism and after corneal transplants.[3-6]

There is an important debate regarding the best moment in which intrastromal corneal ring segments (ICRS) should be implanted. Levinger et al[7] showed significant reduction in myopia with improvement in regular astigmatism in initial and moderate keratoconus; Fahd et al[8] also demonstrated good results in moderate and advanced keratoconus. Kahn et al demonstrated significant corneal flattening and improved patient contact lens tolerance after ICRS implants in advanced keratoconus. At this moment, there is no consensus in the current literature about the best moment to implant the ICRS in keratoconus patients.

The purpose of this study is to evaluate the topographic, topometric and visual changes after implantation of Ferrara (ICRS) in grades I and II keratoconus patients.

MATERIALS AND METHODS

The chart records of 50 consecutively operated keratoconus patients were reviewed. The patients were operated on by the same surgeon (Paulo Ferrara) from February to November 2011. This study was approved by the Ethics Committee of the Instituto Suel Abujamra (Plataforma Brasil) [Suel Abujamra Institute (Brazil Platform)], and follows the tenets of the Declaration of Helsinki. All patients signed an inform consent allowing the procedure to be done.

Inclusion criteria utilized: Topographic diagnosis of grades I and II keratoconus (Amslwer-Krumeich), absence of any other previous ocular disease or surgery, absence of corneal opacity, pachymetry greater than 450 micra at the incision site and minimal age of 16 years.

All patients were preoperatively and postoperatively evaluated with the Pentacam (OCULUS Optikgeräte, Wetzlar, Germany) for evaluation of anterior segment parameters.

All patients were operated using the manual surgical technique as previously described.[9]

INTRASTROMAL RING (ICRS) IMPLANTATION METHOD

Surgical Planning

The selection of ICRS was done according to the Ferrara asphericity nomogram.[9] The most commonly accepted value of normal corneal asphericity is about –0.23 ± 0.08.[10] In patients with unilateral keratoconus, the asphericity of the fellow eye should be used as the postoperative target. Thus, it will be calculated from the algebraic expression of the preoperative asphericity –0.23. This will be the target postoperative asphericity.

Surgical Technique

All surgeries were performed according to the standard manual technique.

A reference point was marked in the center of cornea, while asking to the patient to look to a red light attached to surgical microscope (while turned off). The incision was made at the steepest meridian of the anterior cornea surface, using a calibrated diamond knife was set at approximately 80% of the mean corneal thickness determined by Pentacam. Corneal pockets were then created using the spreader hook. One semicircular dissector was placed sequentially into the lamellar pocket to be steadily advanced by a rotational movement (counterclockwise and clockwise dissectors). After completion of the tunnelization the ring was inserted inside the tunnels.

Postoperative evaluations were performed on the first day, 1 week, 1 and 3 months postoperatively.

Table 1: Correlation between the preoperative Q and preoperative and postoperative CDVA (mean)

Q (30°) Pre	*CDVA Pre*	*Eyes*	*CDVA Post*	*Q (30°) Post*
Q up to –0.3	0.84	4	0.28	0.09
–0.3 ≤Q < –0.5	0.81	8	0.15	–0.17
–0.5 ≤Q < –0.7	0.80	13	0.22	–0.25
–0.7 ≤Q < –0.9	0.79	11	0.16	–0.34
–0.9 ≤Q < –1.1	1.07	9	0.19	–0.35
Less than or equal to –1.1	1.18	5	0.23	–0.77
Total	0.91	50	0.19	–0.29

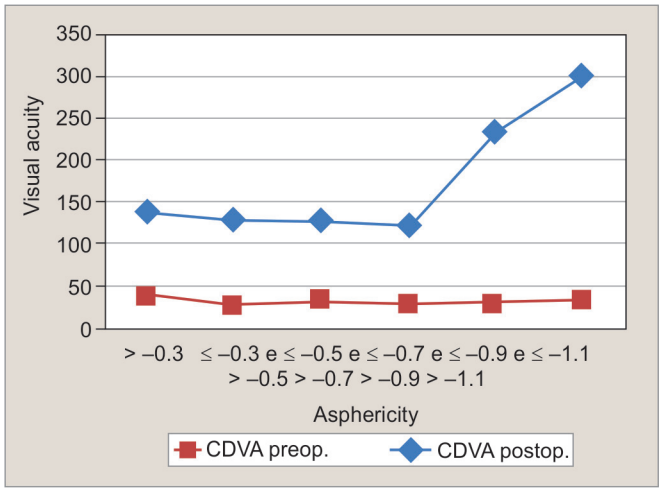
DATA ANALYSIS

Evaluation of preoperative collected data and evaluation on the 1st and 3rd months of cornea analysis. The studied parameters were: corneal asphericity, volume, keratometry and visual acuity. The paired student t-test was used for statistical analysis.

RESULTS

Fifty eyes of 42 patients (26 males and 16 females) were analyzed. Of all of the surgeries performed 25 were on right eyes and 25 on left eyes. The results present preoperative and last follow-up data. The age of patients ranged from 13 to 63 years (the mean age was 30.40 years old ±9.15). The mean preoperative corrected distance visual acuity (CDVA) was 0.91 (LogMAR) ranging from 0.10 to 1.30. The mean postoperative CDVA was 0.19 ranging from 0.00 to 0.54. The postoperative CDVA was equal or better than 0.18 in 37 cases (74%).

An observation between preoperative and postoperative asphericity and CDVA was described (Table 1). Forty-eight percent of the eyes present asphericity between –0.5 and –0.9 and achieve a mean CDVA post 0.19 LogMAR.



Graph 1: Correlation between corrected distance visual acuity and pre- and postoperative asphericity

Table 2: K variation, Q variation and CV from preoperative to postoperative

	K1 (D)	*K2(D)*	*Km (D)*	*Q (30º)*	*CV*	*p-value*
Preop	45.80 ± 2.52	49.06 ± 2.09	47.10 ± 2.18	–0.71 ± 0.32	56.89	< 0.05
Postop	44.27 ± 2.10	46.22 ± 1.89	45.18 ± 1.88	–0.29 ± 0.29	57.64 ± 3.05	< 0.05

Table 3: Volume of each segment from thickness and its respective arc length

Volume	*Thickness*	*Arc angle (º)*
0.75	0.15	140
0.94	0.20	140
1.14	0.25	140
0.85	0.15	160
1.08	0.20	160
1.30	0.25	160
1.13	0.15	210
1.42	0.20	210
1.71	0.25	210

Table 4: Volumetric comparison after discounting ICRS volume

	Volumetric comparison	
Keratometry	*Reduction (%)*	*Increase (%)*
Km ≥ 48D	52	48
Km < 48D	71	29
Total	60	40

There is great difficulty in measuring medical visual acuity (LogMAR chart) in patients with Q (30º) equal to or less than 0.7 (Graph 1). The average CDVA in these patients was 1.0 still with a mean CDVA of 0.20. A CDVA better or equal to 0.18 occurred in 74% of all patients.

The mean K1 decreased from 45.80D (±2.52) preoperatively to 44.27D (± 2.10) postoperatively and the mean K2 value, from 49.06D (± 2.09) to 46.22D (±1.89) ($p < 0.05$). The mean asphericity increased from –0.71 preoperatively to –0.29 postoperatively ($p < 0.05$) (Table 2). Currently, the most commonly accepted value in a young adult population is approximately –0.23 ± 0.08 measured at a 4.5 mm optical zone.[10]

Corneal volume (CV) was recently identified as an additional screening factor for keratoconus.[11-13] Significant differences in CV have been reported between normal and mode-rate keratoconic eyes (Pentacam system: 60.83 ± 3.27 mm^3 controls *vs* 57.98 ± 2.65 mm^3 moderate keratoconus).[11]

The average preoperative corneal volume was 56.89 ± 3.11 mm^3 while the average postoperative corneal volume was 57.64 ± 3.05 $mm.^3$ For better analysis of this additional screening, we divided the eyes into three groups: group 1—patients with corneal volume lower than normal and group 2—patients with normal corneal volumes. The study included 19 cases, 38% of total cases, already showed a volume lower than normal before the procedures. Twenty-five eyes were in the normal corneal volume range before (ICRS implantation). The group 3 (comprised of 6 eyes) shows eyes that had an upper limit of normality before the ICRS.

We analyzed the volumetric behavior of the cornea after surgeries and obtained 22 eyes with normal corneal volume (*vs* 25 eyes before surgeries). This total included 21 eyes, which maintained of normal range corneal volume after the surgeries and originally belonged to group 2 (with normal range corneal volume), and one eye from group 1 (corneal volume lower than normal). Regarding the group 1, 11 cases increased the final volume being nine eyes were introduced in the normal corneal volume with normal asphericity in eight eyes of them (Table 3).

The group 1 showed a presurgical average keratometry of 46.45 *vs* of 42.33D after ICRS implantation with an average final asphericity of –0.29 (Qval preoperative –0.32). The group 2 reach an average keratometry 45.84D (*vs* a preoperative 47.89D) but the initial asphericity already were –0.76 and presented the final asphericity –0.32. The group 3 showed a presurgical average keratometry of 46.22D *vs* an average keratometry of 44.53D after ICRS implantation with an average final asphericitiy of –0.21 (*vs* –0.67 preoperative).

The mean volume of the ICRS implants was 1.31 mm^3 ± 0.39 µm, with a variation between 0.75 to 1.71 mm^3. The volumetric data of each ICRS segment were supplied by the company AJL (Miñano, Álava-Spain) manufacturer of the FerraraRings® orthoses (Table 3).

In the group 1 (19 eyes), 11 eyes presented a final volume larger than initial plus the ICRS implants being nine reached the normal range of volume, and eight presented final volume lower than initial plus the ICRS.

On the other hand, the group 2 (25 eyes) presented seven eyes a final volume bigger than initial plus the ICRS implants with asphericity of –0.34 but CDVA 0.15 *vs* 18 final volume lower than initial plus the ICRS with asphericity of –0.29 but CDVA 0.23.

In the group 3 (6 eyes), two eyes presented a final volume bigger than initial plus the ICRS implants with asphericity of –0.08 but VA 0.09 *vs* four eyes wich final volume lower than initial plus the ICRS implants with asphericity of –0.27 but VA 0.18.

An interesting relationship between volume and keratometry mean was observed from a 48D. In 71% of patients that underwent surgery who presented a Km less or equal that 48D had a reduction in the final corneal volume (Table 4).

DISCUSSION

Aydin et al demonstrated the low visual quality in keratoconus patients.[14] This disease is progressive and vision may be seriously impaired, causing an important negative impact on patients' quality of life (QoL).[15] A study conducted by the CLEK concluded that QoL is seriously affected in keratoconus patients and continues to decline over time, but an earlier study by our group showed that ICRS implantation improves visual QoL (V-QoL).[16] The correlation between with quality of life (V-QoL) following ICRS implantation in these patients was established.[17]

The results demonstrated the low visual acuity present in patients suffering from keratoconus already in the initial grades (0.90 with a variability of ±0.74). The patients evaluated in the study presented a significant improvement in visual acuity (from 1.30 to 0.18 LogMAR), and significant corneal flattening, with the mean keratometry decreasing from 47.14 to 45.18D. We believe that all of this is corroborated by the reduction in optical aberration indices, and consequently improvement in visual quality.[18]

Some studies agree that the human cornea Q (asphericity) values range from −0.01 to −0.80.[19] However, in our studies, we observed that if we adopted such values as a reference we would have 56% of the patients within 'normality' with a mean visual acuity of 0.79 LogMAR before ICRS, i.e. completely outside of normality. The asphericity showed an important and direct relationship with the visual acuity. The Figure 1 demonstrates the progressive worsening of visual acuity preoperative and asphericity. This characteristic is more easily measured up to approximately 20/125. Beyond this point, we believe the quantification of visual acuity (LogMAR chart) is relatively compromised. After ICRS implantation, 28% of eyes turn to the normal range of asphericity, and among these eyes, 71.42% had a final visual acuity better than or equal 20/30.

Asphericity before and after surgery is an important parameter to measure, as it allowed us to assert the significant change and variability, in the initial cases of keratoconus as well as their improvement after the surgical procedure. This data supports the predictability and effectiveness of the nomogram based on asphericity also in mild keratoconus cases.

The correlation between keratometry and asphericity is evident with a strong correlation,[20] however, no such corresponding correlation was shown with the corneal volume.

We measured the cornea volume after the procedure in all cases and, 58% of cases, the corneal volume turned to normal values and, in these cases, we obtained a final asphericity −0.28 with a mean visual acuity 0.15 being better or equal to 0.10 LogMAR in 41%.

For the volumetric evaluation, we considered the volume of each ICRS in the cornea and therefore calculate the difference between the final (Vf) and initial volume (Vi) plus the ICRS volume (Vic). The result we call 'volume error' (Ver). If the result was positive after the surgery, the final volume is higher than initial. On the other hand, if 'the volume error' was negative, it means that the cornea was lower than initial.

We observed a final volume lower than the initial volume in 38% of all patients. Therefore, in 60% of cases we obtained a corneal remodeling whose final volume was lower than the initial volume, being the preoperative Km was 47.42 and 45.58 after the surgery and average final asphericity of −0.31. That suggests that the ICRS promote indirectly a kind of reorganization by collagen lamellas of corneal stroma contributing for better values of keratometry, asphericity and visual acuity, which raises the possibility of corneal shrinkage after the procedure. Such a presumption is corroborated based on other studies that demonstrated the formation of collagen and other extracellular matrix components[21] after ICRS implantation.

Such characteristics lead us to consider the possible role of the ICRS in relation to the reorganization of collagen fibers allowing these ectasic corneas to resemble their primary form and, in this way, improve their visual performance.

The Ferrara ICRS demonstrates its effectiveness in the treatment of initial and moderate keratoconus. This ability can be verified through the application of the proposed nomogram based on an analysis and observation of asphericity as a remodeling parameter and corresponding corneal visual function.

CONCLUSION

The study supports the early indication of Ferrara ICRS in mild to moderate keratoconus cases in order to achieve good visual, keratometric and asphericity outcomes.

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10.5005/jp-journals-10025-1132

REVIEW ARTICLE

Ferrara Intrastromal Corneal Ring Segments

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ABSTRACT

The Ferrara intrastromal corneal ring segments (ICRS) are designed to treat ectatic corneal disorders, especially keratoconus. They have been used to reshape keratoconic corneas to improve uncorrected visual acuity, best-corrected visual acuity, contact lens tolerance and to delay or prevent the need for keratoplasty. Intrastromal corneal ring segments have several distinct and important advantages. The Ferrara ICRS have been used largely in several countries for the treatment of primary and secondary ectatic corneal disorders. This article reviews the latest data published and the clinical experience/findings on the treatment of keratoconus by the Ferrara ICRS implantation.

Keywords: Ferrara, Intrastromal corneal ring segments, Keratoconus.

How to cite this article: Torquetti L, Sandes J, Ferrara G, Ferrara P. Ferrara Intrastromal Corneal Ring Segments. Int J Kerat Ect Cor Dis 2016;5(3):114-127.

Source of support: Nil

Conflict of interest: Dr. Paulo Ferrara and Guilherme Ferrara have proprietary interest in the Ferrara ICRS. Dr. Leonardo Torquetti does not have financial interest in any device cited in this review.

INTRODUCTION

The implantation of intrastromal corneal ring segments (ICRS) is a minimally invasive surgical option for reshaping the cornea in keratoconus and other secondary ectasias. Intrastromal corneal ring segments have been used to correct ectatic corneal diseases in order to reduce corneal steepening and irregular astigmatism and improve the visual acuity.[1-6] Besides, the ICRS are a surgical alternative to at least delay, if not eliminate, the need for lamellar keratoplasty or penetrating keratoplasty (PKP).[7]

In 1986, Ferrara started implanting modified polymethylmethacrylate (PMMA) ICRS in rabbit corneas, and in 1994, he developed a better technique of corneal tunnel construction for implanting the ICRS.[8]

The Ferrara ICRS are made of PMMA Perspex camphorquinone (CQ) acrylic segments. They vary in thickness and are available in 0.15, 0.20, 0.25, and 0.30 mm. The segment cross-section is triangular, and the base for every thickness and diameter is 0.60 mm. The segments have 90, 120, 140, 160, or 210° of arc.

Many studies have demonstrated the efficacy of ICRS to treat many corneal conditions as keratoconus,[1-7] post-LASIK corneal ectasia,[9,10] postradial keratotomy ectasia,[11] astigmatism,[12] and myopia.[13-15] The changes in corneal structure induced by additive technologies can be roughly predicted by Barraquer's thickness law, which states that when material is added to the periphery of the cornea or an equal amount of material is removed from the central area, a flattening effect is achieved. The corrective result varies in direct proportion to the thickness of the implant and in inverse proportion to its diameter. The thicker and smaller is the diameter of the device, the higher is the corrective result.[16]

Preliminary investigations have demonstrated that ICRS are effective in the treatment of astigmatism and myopia with astigmatism, with the preservation of corrected distance visual acuity (CDVA) and stable results over time.[2,17-20] The objective of the addictive technology is to reinforce the cornea, decrease the corneal irregularity, and provide improvement of visual acuity in affected patients.

The research about the Ferrara ICRS began in 1985. In 1986, Dr. Paulo Ferrara (P.F) realized that to keep the implant in place, a large hole was needed in the center of the lens which resulted in an annular prostheses. Since then, several annular shapes and diameters were tried. From these researches, it was concluded that the best design would be the one, i.e., used nowadays, made of PMMA, with a total diameter of 5.0 mm, arch length ranging from 90 to 210°, and thickness ranging from 150 to 300 μm.

The ICRS were implanted in rabbit eyes, through a free hand dissection technique, at 50% depth of measured central corneal thickness. The eyes were examined for 12 months, and the animals were sacrificed for histopathological exams. The histopathological results revealed excellent tolerance of the cornea to the orthesis since there was only slight inflammatory reaction surrounding the implant and no evidence of extrusion.

The techniques, traditionally, used for the implant of corneal prostheses, free hand dissection, and keratectomy with a microkeratome showed some negative points, such as interface deposits, delay in refractive stability,

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besides the high costs of microkeratomes and slow learning curves.

In order to improve the ICRS implantation technique, reduce its complications, and make it accessible to a large number of anterior segment surgeons, we (P.F) developed in 1994 a stromal tunnel and ICRS implantation technique, which completely eliminates the disadvantages of the conventional techniques.

In 1995, we (P.F) implanted the first patient who had undergone PKP and radial keratotomy. This patient was forwarded to the Cornea Service at Hospital Sao Geraldo in Federal University of Minas Gerais (UFMG) for a new transplantation. We decided, with formal authorization of the patient, to test the ICRS before performing the PKP. The result was satisfactory, yielding ametropia correction and good corneal tolerance to the orthesis.

The excellent tolerance to the implant by the transplanted cornea gave us the needed confidence to apply the technique in keratoconic corneas. Therefore, we decided in 1996, to implant the ICRS in patients' intolerant to contact lenses that had the PKP indicated.

MECHANISM OF ACTION

The ICRS complies with Barraquer and Blavatskaya postulates, according to which, an addition in the cornea periphery results in its flattening, and the ICRS diameter determines how much the cornea will be flattened. Thus, the more tissue is added (increasing ICRS thickness), and the smaller is the diameter, the greater will be the myopia correction obtained.[21,22]

Besides these mechanisms of action, there are some additional changes induced by the ICRS:

- Regularization of the corneal surface through a tilting movement caused by the flatness in the surface of the ICRS base, making the cornea flattened at the areas corresponding to the segment extremities and making it curve at the ICRS body area.
- Interruption, or at least delay of keratoconus evolution,[17,19] reduction of opacity on the cone apex, and reduction of related symptoms as itching, photophobia, and pain/ocular discomfort.
- Lack of correspondence between uncorrected visual acuity after the ICRS implantation and residual ametropia. Sometimes, good visual acuity coexisting with high residual refractive errors can be observed.
- The prisma effect generated by the triangular section reduces halos and glare, which could result from the small diameter of the orthesis.
- The yellow filter introduced in the plastic prevents the ultraviolet (UV) light to go into the eye, reducing the halos and reflections at night.

Table 1: Ferrara ICRS indications

1	Keratoconus
2	High irregular astigmatism after PKP or lamellar keratoplasty
3	Irregular astigmatisms after radial keratotomy
4	Pellucid marginal degeneration
5	Corneal ectasia after excimer laser

INDICATIONS

The main indication for the Ferrara ICRS implantation is keratoconus. In patients with keratoconus, the Ferrara ICRS should be indicated when: (1) There is an evidence of progressive worsening of the disease, with the gradual decrease of UDVA and CDVA; (2) progressive corneal steepening, and (3) progressive contact lens intolerance.

In post-LASIK corneal ectasia,[9] the Ferrara ICRS implantation is indicated when there is worsening of the condition. The main indications for the Ferrara ICRS implantation are listed in Table 1.

CONTRAINDICATIONS

The main contraindications for the Ferrara ICRS implantation are the presence of apical opacities in very advanced keratoconus, usually with K readings above 60 Diopters (D). The postoperative results in these cases are usually poor, and the best treatment for these cases is lamellar keratoplasty or PKP.[8,23] The main contraindications for the Ferrara ICRS implantation are listed in Table 2.

NOMOGRAM

The nomogram has evolved as the knowledge about the predictability of results has grown. Initially, surgeons implanted a pair of symmetrical segments in every case. The incision was always placed on the steep meridian to take advantage of the coupling effect achieved by the ICRS.

First, only the grade of keratoconus was considered for the ICRS selection, which means that in keratoconus grade I, the more suitable Ferrara ICRS for implantation was that of 150 µm, and in keratoconus grade IV, the more appropriate ICRS was of 350 µm (Table 3). However, some cases of extrusion could be observed in keratoconus grade IV in which the cornea is usually very thin, and the thick ICRS sometimes were not properly fitted into the corneal stroma.

Table 2: Ferrara ICRS contraindications

1	Very advanced keratoconus with curvatures over 60 D and significant apical opacity and scar ICRS
2	Hydropsis
3	Thin corneas, with thickness below 300 µm in the ICRS track
4	Patients with intense atopia (these should be treated before the implant)
5	Any ongoing infectious process, local or systemic

Table 3: Ferrara ICRS first-generation nomogram

Diameter 5.00 mm	*Thickness (mm)*	*Diopters to be corrected*
Fruste	0.150	–2.00 to –4.00
Cone I	0.200	–4.25 to –6.00
Cone II	0.250	–6.25 to –8.00
Cone III	0.300	–8.25 to –10.00
Cone IV	0.350	–10.25 to –12.00

The second generation of the nomogram considered the refraction for ICRS selection, besides the distribution of the ectatic area on the cornea. Therefore, as the spherical equivalent increased, the selected ICRS thickness also increased. However, in many keratoconus cases, the myopia and astigmatism could not be caused by the ectasia itself but by an increase in the axial length of the eye (axial myopia). In these cases, hypercorrection by implanting a thick ICRS was observed in a keratoconus in which a thinner segment should be indicated.

In the third generation of the Ferrara ICRS nomogram, the ICRS selection depends on the type of keratoconus, its location in the cornea (Table 4), topographic astigmatism (Tables 5 to 7), and pachymetry.[17,24]

Table 4: Distribution of the area of corneal ectasia

Map	*Distribution of ectasia*	*Description*
	0/100%	All the ectatic area is located at one side of the cornea
	25/75%	75% of the ectatic area is located at one side of the cornea
	33/66%	66% of the ectatic area is located at one side of the cornea
	50/50%	The ectatic area is symmetrically distributed on the cornea

Table 5: Segment thickness choice in symmetric bow-tie keratoconus

Topographic astigmatism (D)	*Segment thickness*
<1.00	150/150
1.25–2.00	200/200
2.25–3.00	250/250
>3.25	300/300

Table 6: Asymmetrical segment thickness choice in sag cones with 0/100 and 25/75% of asymmetry index (Graph 1)

Topographic astigmatism (D)	*Segment thickness*
<1.00	none/150
1.25–2.00	none/200
2.25–3.00	none/250
3.25–4.00	none/300
4.25–5.00	150/250
6.25–6.00	200/300

For symmetric bow-tie patterns of keratoconus, two equal segments are selected. For the nipple type of keratoconus, a single 210 µm segment is chosen based on the nomogram (Table 8). For peripheral cones, the most common type asymmetrical segments are selected. It is important to emphasize that the ICRS thickness cannot exceed 50% of the thickness of the cornea on the track of the ICRS.

Using this third generation of the nomogram, we usually found that in some patients, there was significant corneal flattening without considerable improvement of visual acuity. We realized that, in these cases, the cornea usually presented oblate (positive Q values) postoperatively, what could explain the lack of significant improvement in these cases.[25-27]

This finding led us to retrospectively review the charts of 147 eyes operated in 2008, and we evaluated the asphericity changes induced by the implantation of each thickness of ICRS (or pair of ICRS). Surprisingly, we found a direct correlation between ICRS thickness and change of Q values; i.e., the thicker is the ICRS the more is the effect in the change of Q value.

One paper published by our group[27] showed that, using the previous nomograms, the CDVA was 20/60 or better in 70% of patients. When using the Q-based nomogram, we found a CDVA of 20/40 or better in 70% of patients.

The asphericity should be the first parameter to be considered in the ICRS selection. However, all the other parameters are considered secondarily (topographic astigmatism and pachymetry).

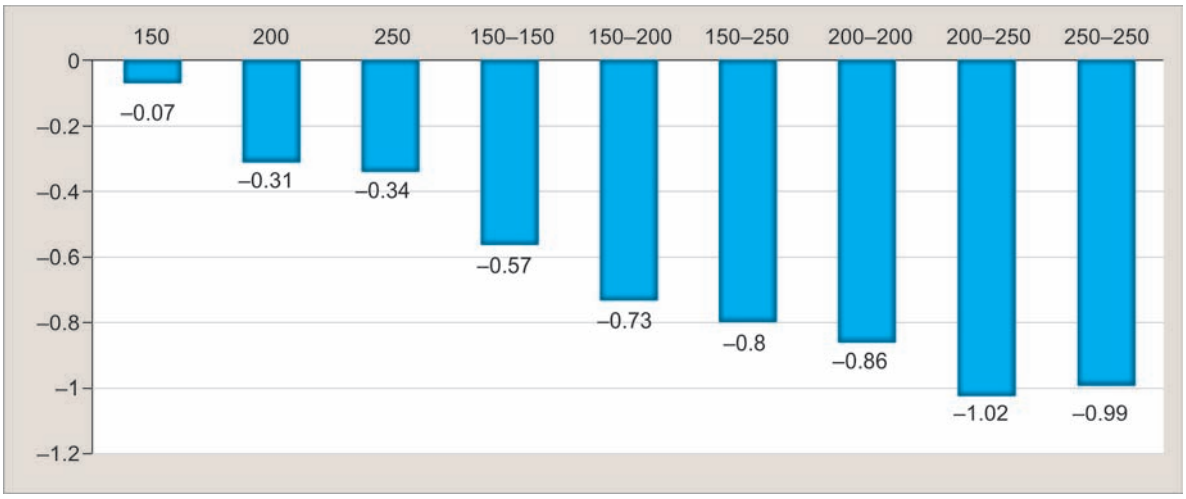
We have described[27] that for each ICRS segment, there is a correspondent Q value change (Graph 1). A target postoperative Q value as close as possible of –0.23 is the goal after the Ferrara ICRS implantation.[28-30] Based on this nomogram, one could predict the Q value change after the implantation of a specific ICRS (or pair of ICRS)

Table 7: Asymmetrical segment thickness choice in sag cones with 0/100 and 33/66% of asymmetry index (Graph 1)

Topographic astigmatism (D)	*Segment thickness*
<1.00	none/150
1.25–2.00	150/200
2.25–3.00	200/250
3.25–4.00	250/300

Table 8: Segment thickness choice in Nipple cones (210 µm ICRS)

Spherical equivalent (D)	*Segment thickness*
Up to 2.00	150
2.25–4.00	200
4.25–6.00	250
>6.25	300



Graph 1: Q (asphericity) variation according to the ICRS thickness (160-arc ICRS)

Table 9: Actual Ferrara ICRS nomogram (Q-based): step-by-step

1	Define the keratoconus type: sag, bow-tie, or nipple
2	Corneal asphericity (Q)
3	Pachymetry at incision site and ICRS track

thickness; e.g., a single segment of 200 µm changes the asphericity as 0.31 (Graph 1); therefore, this segment would be the most appropriate in patients with a preoperative Q value of –0.54, to achieve a postoperative Q value close to –0.23 (theoretical normal value).[28-30]

The pachymetry at the incision site (steep axis of the cornea) must be determined. The incision depth must be 80% of the corneal thickness at the incision site. The pachymetry should be measured in all ICRS track to avoid superficial ICRS, which could lead to future extrusion.

The actual guidelines for ICRS selection are described in Table 9.

SURGICAL TECHNIQUE

Manual Technique

The surgery is performed under topical anesthesia after miosis is achieved with 2% pilocarpine. An eyelid speculum is used to expose the eye, and 2.5% of povidone-iodine eye drops is instilled in the cornea and conjunctival cul-de-sac. The visual axis is marked by pressing the Sinskey hook on the central corneal epithelium while asking the patient to fixate on the corneal light reflex of the microscope light. Using a marker tinted with gentian-violet ink, a 5.0-mm optical zone and incision site are aligned to the desired axis in which the incision will be made. This site can be the steepest topographic axis of the cornea (in case of implantation of two segments) or 90° (in case of implantation of only one segment – one of the tips of the ICRS must be located on the steepest axis).[17]

The depth of a 1.0-mm square diamond blade is set at 80% of corneal thickness at the incision site, and this blade is used to make the incision. Using a "stromal spreader," a pocket is formed in each side of the incision. Two (clockwise and counterclockwise) 270° semicircular dissecting spatulas are consecutively inserted through the incision and gently pushed with some, quick, rotary "back and forth" tunneling movements. Following channel creation, the ICRS are inserted using a modified McPherson forceps. The ICRS are properly positioned with the aid of a Sinskey hook.

Femtosecond Laser Technique

The femtosecond laser (IntraLase Corp.) has recently been introduced in clinical practice whose surgical effect through photodisruption can be used as an alternative to the traditional mechanical techniques. Several recent articles[31-36] have reported its efficacy and safety for tunnel creation and intrastromal ICRS implantation. The femtosecond laser can easily and quickly create a predetermined depth and channel size.

There is a controversy over channel size nomograms with the technique. Some authors conclude that more effect can be achieved by making the stromal channels narrower than the ICRS size, leading to faster visual results.[37]

The use of the femtosecond laser in corneal tunnel creation made the procedure faster, easier (especially for inexperienced surgeons), and more comfortable for the patient. However, the main advantage of IntraLase-assisted channel creation over the mechanical technique seems to be the precise depth of implantation. The only disadvantage of this technique is the cost of the equipment, which is still relatively high.

The technique: Tunnel depth is set at 80% of the thinnest corneal thickness on the tunnel location in the femtosecond laser. Special attention must be given in centralizing the disposable suction ICRS to mark the

central point to minimize decentration. The channel's inner diameter is set to 4.4 mm, the outer diameter is 5.6 mm, the entry cut thickness is 1 m (at the steepest topographic axis), the ICRS energy used for channel creation is 1.30j, and the entry cut energy is 1.30j. Channel creation timing with the femtosecond laser is 15 seconds. The intracorneal ICRS are implanted immediately after the channel creation before the disappearance of the bubbles, which reveals the exact tunnel location. The segments are placed in the final position with a Sinskey hook through a dialing hole at both ends of the segment.

The postoperative regimen, for both techniques, consists of moxifloxacin 0.5% (Vigamox®, Alcon, USA) and dexamethasone 0.1% (Maxidex®, Alcon, USA) eye drops four times per day for 2 weeks. The patients were instructed to avoid rubbing the eye and to use preservative-free artificial tears frequently – polyethylene glycol 400 0.4% (Oftane®, Alcon, USA).

Manual × Femtosecond Laser Technique

Initially, the tunnel for ICRS implantation was created manually with a mechanical spreader in every case. The complications of ICRS implantation with mechanical devices include epithelial defects, perforation, asymmetric segment placement, and extension of the incision toward the central visual axis or the limbus.[38-41]

More recently, surgeons began using a femtosecond laser to create the tunnel. It has been proposed that this method results in precise tunnel and keratotomy depth, width, and location as well as a uniform 360° channel; causes minimum haze and edema; and minimizes surgical complications. The femtosecond laser acts through photodisruption and can be programmed to create tunnels for segment placement at predictable corneal depths. Studies show that tunnel creation with the femtosecond laser is easier, more precise, and more predictable than with the traditional mechanical spreaders.[36]

Some studies have compared the visual and refractive outcomes and the complications of mechanical tunnel creation and femtosecond-assisted tunnel creation for ICRS implantation to manage keratoconus.[31,33,42,43]

The results of these clinical trials suggest that visual and refractive results of femtosecond-assisted tunnel creation are comparable to those of mechanical tunnel creation.[31] However, the femtosecond method is faster, easier, and more comfortable for both patient and surgeon. Another potential advantage of the femtosecond method is the precise depth of implantation, especially in thinner corneas.

LONG-TERM FOLLOW-UP AFTER FERRARA ICRS IMPLANTATION IN KERATOCONUS

We retrospectively reviewed patient records of 94 eyes of 76 patients, which were consecutively operated (Ferrara ICRS implantation).[17] There were 33 females and 61 males. The average age of the patients was 28.1 years. All procedures were performed by the same surgeon (P.F) between June 1996 and September 2007. Patients included in the study presented clear cornea and a minimal corneal thickness of 300 µm at the ICRS track. Patients were intolerant to contact lens and/or showed progression of ectasia.

Fifty-eight subjects underwent a single eye treatment, whereas 18 subjects had both eye treated. Seventy-three eyes had a 2-year follow-up, 66 eyes had a 3-year follow-up, 48 eyes had a 4-year follow-up, and 34 eyes had a 5-year follow-up. All patients completed at least a 2-year follow-up. No intraoperative complications occurred. All patients returned for ocular examination on day one, 1 week and a month after the surgery, and then 3, 6, and 12 months. Thereafter, the following eye examinations occurred yearly.

Preoperative and postoperative UDVA, CDVA, and keratometry data were collected from all patients. The mean UDVA (decimal) at the preoperative period was 0.12, and the mean CDVA (decimal) was 0.41. At the first month, the mean UDVA improved to 0.25, and the mean CDVA improved to 0.56. At 2-year follow-up, the mean UDVA improved from 0.12 preoperatively to 0.29. At 3-year follow-up, the mean UDVA improved to 0.34, at 4-year follow-up, the mean UDVA improved to 0.42, and at 5-year follow-up, the mean UDVA decreased to 0.31 postoperatively. The mean CDVA, at the first month, improved to 0.56. At 2-year follow-up, the mean CDVA improved from 0.41 preoperatively to 0.68. At the third-year follow-up, the mean CDVA decreased to 0.63; at the fourth-year follow-up, the mean CDVA improved to 0.65; and at the fifth-year follow-up, the mean CDVA decreased to 0.59 postoperatively.

The mean keratometry decreased significantly from the preoperative to the last postoperative follow-up. Preoperative mean keratometry was 50.36, which decreased to 47.29 at the first-month postoperative follow-up. The mean keratometry follow-up along the second to fifth years was 45.96, 45.83, 46.44, and 46.24 respectively.

As shown in previous studies, the intrastromal ICRS flatten the cornea and keep this effect for a long period of time. There is no significant resteepening of the cornea over time.

A study published by Pesando et al[44] found similar results in a 5-year follow-up. A total of 93.84% (122 patients) of the eyes gained lines of UDVA, and only 1.53% (2 eyes) lost them. A total of 97.69% (127 patients) of the treated eyes gained lines of CDVA, and no eyes lost them. The values of K1 and K2 were considerably reduced over 5 years. The preoperative value of K average of 49.27 D became 4.68 D postoperatively. Both UDVA and the CDVA

showed an increase. The UDVA changed from 0.14 lines preoperatively to 0.32 lines postoperatively, while the best-corrected visual acuity (BCVA) changing from 0.40 to 0.59. The spherical equivalent changed from –8.34 D before the operation to –2.83 D after the operation.

In 2014, we published a paper[19] with the longest follow-up ever described, after ICRS implantation. The mean UDVA (logMAR) improved from 1.01 ± 0.28 to 0.71° ± °0.38 at 5 years (p = 0.000) and 0.67° ± °0.25 at 10 years (p = 0.735). The mean CDVA (logMAR) improved from 0.45° ± °0.45 to 0.24° ± °0.19 at 5 years (p = 0.004) and 0.29° ± °0.09 at 10 years (p = 0.292). The mean maximum K value decreased from 54.99° ± °6.33 to 50.58° ± °5.11 D at 5 years (p = 0.000) and 50.65° ± °5.17 D at 10 years (p = 0.854). The mean minimum K value decreased from 48.85° ± °5.70 to 46.90° ± °5.08 D at 5 years (p = 0.000) and 47.12° ± °4.22 D at 10 years (p = 0.945). The central corneal thickness decreased from 457.42° ± °58.21 to 421.34° ± °74.12 µm at 5 years (p = 0.039) and 434.32° ± °77.65 µm at 10 years (p = 0.427).

These studies showed that the Ferrara ICRS could be a valuable tool to provide topographic and visual stability, delay the progression of keratoconus, and postpone a corneal grafting surgery to more physiological position.[4,18]

THE 140 FERRARA ICRS

There are different models of Ferrara ICRS with varying sizes and arc thickness. These segments induce an arch shortening effect in the lamella, leading to central flattening of the cornea. There are three main corneal ring arc diameters, 140, 160, and 210°. The shorter the segment, the greater the astigmatic correction, the lesser the asphericity change.[27] A new Ferrara intrastromal ring model has a short arc length of 140° (140-ICRS) and has been recently used. The main advantage of this 140 arc length is its effect in astigmatism reduction. That is why, they have as a main indication, pellucid marginal degeneration,[45] which leads to high astigmatism, besides corneal deformity. It has also been used in cases of astigmatic cones. These are central cones with high astigmatism and high keratometry.

We retrospectively reviewed the chart records of 65 consecutive patients implanted with Ferrara ICRS, which has a 140° arch length (unpublished study). Patients included in the study presented with clear corneas and minimum corneal thickness of 300 µm at the ring track. Patients were contact lens intolerant and/or showed progression of ectasia. The average follow-up was 16 months. The average age was 33.38 (±13.25), 54 females (80.6%) and 13 males (19.4%).

The UDVA improved from 0.22 (decimal) preoperatively (±0.15) to 0.42 postoperatively (±0.42) (p < 0.001). The CDVA improved from 0.38 (±0.20) to 0.59 (±0.21) (p < 0.001). The mean minimum keratometry (K1) did not change significantly; it reduced from 45.49 (±6.38) to 45.14 (±5.10) (p = 0.354). The mean K2 decreased from 54.11 (±8.40) to 49.54 (±5.11) (p < 0.001). The average keratometry reduced from 49.87 (±7.018) to 47.34 (±4.90) (p < 0.001). The average asphericity changed from –0.60 (±0.86) to –0.23 (±0.67) (p < 0.001). The refractive astigmatism decreased from –4.95 (±1.61) to –2.55 D (±1.31) (p < 0.001). The mean preoperative astigmatism topography decreased from –8.00 (±3.45) to –4.53 (±2.52) (p < 0.001).

In selected cases of keratoconus with high astigmatism, the short arch segments (140 arch) seem to be more effective, in order to get a significant astigmatic reduction.

THE 210 FERRARA ICRS

The 210° of arc Ferrara intrastromal ICRS have three major advantages over the conventional ICRS (160°): (1) Minimal astigmatic induction; (2) corneal flattening, and (3) implantation of a single segment. These ICRS are especially useful for the nipple type of keratoconus. The 210-ICRS are an efficient method for keratoconus correction, significantly decreasing the keratometric values and spherical equivalent and improving UDVA and CDVA.

We retrospectively reviewed patient records of 80 eyes of 76 patients, which were consecutively operated, in which the 210-ICRS were implanted.[24] Statistical analysis included preoperative and postoperative UDVA, BCVA, spherical equivalent, and keratometry.

The mean follow-up time was 6.65 months. The mean UDVA increased from 20/350 to 20/136 (p° = °0.001). The mean CDVA increased from 20/125 to 20/55 (p° = °0.0001). The mean preoperative spherical equivalent decreased from –5.22 D, preoperative, to –2.26 D (p° = °0.050), postoperative.

Corneal tomography (Pentacam®) showed corneal flattening in all eyes. The mean K_1 decreased from 51.49 D to 47.40 D (p° = °0.00014), and the mean K_2 decreased from 54.33 D to 49.14 D (p° = °0.00022). The mean keratometric astigmatism decreased from 3.65 D (preoperative) to 2.69 D (postoperative) (p° = °0.0001).

IMPLANTATION OF FERRARA ICRS IN POSTREFRACTIVE SURGERY CORNEAL ECTASIA

We evaluated 25 eyes of 20 patients with corneal ectasia (13 males [15 eyes] and 7 females [10 eyes]) who underwent Ferrara intracorneal ICRS implantation.[46]

The mean follow-up time was 39.8° ± °21.1 months (Table 1). All patients had implanted only one segment of ICRS. A 160° arc ICRS (160-ICRS) was implanted in 18 eyes, and the 210° arc ICRS (210-ICRS) was implanted in 7 eyes.

The mean UDVA increased from 20/185 to 20/66 (p = 0.005). The mean CDVA increased from 20/125 to 20/40 (p = 0.008) (Graph 1). The mean asphericity values

decreased from –0.95, preoperatively, to –0.23 (p = 0.006), postoperatively.

The mean pachymetry at the apex of the cornea increased from (mean) 457.7 ± 48.7 µm (361–542) to 466.2 ± 49.8 µm (381–559) (p = 0.025), and the pachymetry at the thinnest point of the cornea increased from 436.3 ± 46.2 µm (348–533) to 453.9 ± 49.3 µm (370–548) (p = 0.000). A significant reduction in keratometric values was found at the last follow-up examination; mean preoperative keratometry was decreased from 45.41 ± 5.63 D (37.3–55.5) and changed significantly to 42.88 ± 4.44 D (31.2–54.1) (p = 0.000).

Our postoperative results show a significant improvement in UDVA and CDVA. Moreover, there was significant increase in corneal thickness. This can be explained by a theoretical cornea collagen remodeling induced by the implantation of ICRS.

We found a significant increase in asphericity values after the implantation of ICRS in this study. Interestingly, the mean postoperative value was –0.23, which is considered the "normal" value for the general population.[25,28-30,47] This value means that the normal physiologic asphericity of the cornea shows a significant individual variation ranging from mild oblate to moderate prolate. In an unpublished study, where we evaluated the corneal asphericity changes induced by the ICRS in keratoconus, we found that the Ferrara intrastromal ICRS implantation significantly increased the mean corneal asphericity from –0.85 to –0.32. It is well known that most corneas after ablation laser procedures tend to become oblate, and when ectasia develops these corneas usually become prolate. However, the excess of prolatism usually found in keratoconus (primary) is usually of a much larger amount that that found in postrefractive surgery ectasia. The probable reason is that the Q value after Ferrara ICRS becomes much closer to "normal" values than when the ICRS is used for keratoconus. As asphericity is one of the markers of visual quality, turning it "normal" can be a predictor of improvement of visual quality.

The keratometry values reduced significantly in all eyes. It can be realized that the mean preoperative values are usually lower than ones found in keratoconus (primary). This can be explained somewhat by the corneal flattening induced by the refractive procedure, usually in an optic zone of greater extent than the location of the ectasia.

Most of the implanted ICRS were 160-ICRS, the "conventional" ICRS. The remainder of eyes received the 210-ICRS. The latter is usually reserved for central cones of nipple type.[24] Some ectasia assume the same topographical pattern of nipple cones, in which we usually use the 210-ICRS with excellent results. These ICRS are reserved for cases with low astigmatism, in which we desire to flatten the cornea with minimal astigmatic induction.

The potential advantages of ICRS implantation over keratoplasty in eyes with post-LASIK ectasia are many.[23,48] First, it avoids further laser treatment, eliminating central corneal wound healing. This leaves the optical center of the cornea untouched, enhancing the refractive outcome. Second, the technique is reversible in cases of an unsatisfactory refractive or clinical outcome, and minimal postoperative care is required. Third, adjustment can be performed using thinner or thicker ICRS. In cases of unexpected corneal shape changes, one segment can be removed or exchanged.[49] Fourth, it avoids the complications of intraocular surgery.

These data are confirmed by several studies.[9,50-52] Some long-term studies (ICRS in ectasia after LASIK) showed that ICRS yielded improvements in visual acuity, refractive status, and keratometric values without any progression in cases with post-LASIK corneal ectasia.[53]

ENDOTHELIUM EVALUATION AFTER FERRARA ICRS IMPLANTATION

We retrospectively reviewed patient records of 102 eyes of 81 patients, which were followed for a period of at least 1 year (mean follow-up: 45.7 months, standard deviation: 16.4 months; range: 13–71 months).[54] All patients had the diagnosis of keratoconus, post-LASIK ectasia, or pellucid degeneration. Statistical analysis included preoperative and postoperative keratometry and endothelial characteristics (cell count, average cell size, and coefficient of variation).

All patients completed at least 1 year of follow-up (13–71 months). Mean age was 30.5 ± 8 years. The mean cell count decreased from (mean ± standard deviation [SD]) 2714 ± 372 to 2562 ± 406 cells/mm^2 (p < 0.001). The calculated exponential cell loss rate over the mean interval of follow-up (4 years) was 1.4% per year. The average cell size increased from (mean ± SD) 375 ± 56 to –399 ± 61 µ^2 (p < 0.001). The coefficient of variation increased from (mean ± SD) 0.22 ± 0.075 to 0.26 ± 0.010 (p = 0.001).

The mean maximum cell size increased from (mean ± SD) 529 ± 116 to 639 ± 225 µ^2 (p < 0.001). The mean minimum cell size varied from (mean ± SD) 225 ± 36 to 226 ± 54 µ^2 (p = 0.936).

There was significant corneal flattening as shown by keratometry changes. The mean K decreased from 47.70 ± 2.29 (43.70–53.80) to 44.86 ± 2.02 (41.20–51.20) (p = 0.0001).

In our study, we found a 1.4% loss of endothelial cells per year. Considering that most of the studied patients were young, the rate of endothelial cell loss was slightly higher than in normal eyes (1.1%).[55,56] Moreover, there is no study in the current literature that shows the profile of the "normal" endothelial loss in keratoconus corneas, which could be higher than in normal corneas. The only report in the literature regarding the endothelium profile of keratoconus is nonprospective and studied only 12 eyes.[57]

Endothelial cell loss after PKP is known to be an ongoing process even years after surgery. It is well known that the cell loss is higher than in the early time course after surgery and decreases 3 to 5 years after surgery. There is a great variation of rates of cell loss after PKP, ranging from 4.2[30] to 9.4% per year, at the long-term follow-up.[58-60] Even after deep anterior lamellar keratoplasty (DALK), which is a surgical technique that spares the receptor endothelium, cell loss has been reported. In one study, a decrease in average preoperative endothelial cell count of approximately 200 cells/mm^2 was observed during the first 12 months of surgery.[61,62]

The only study that assessed the endothelial after intrastromal ICRS (Intacs, Addition Technology Inc.) implantation reported that after 24 months of surgery, all corneal regions had a slight decrease in cell density.[63] In all eyes, mean central and peripheral endothelial cell counts remained above 2,495 cells/mm^2. Our results are similar, we obtained a higher average postoperative cell count (2,562 cells/mm^2), and we had a longer follow-up (4 years).

Wollensak et al,[64] in a collagen cross-linking study in keratoconus, showed that the corneal transparency and the endothelial cell density ($p = 0.45$) remained unchanged. The follow-up was 23 months, and the sample was only 23 eyes. The same author, in an experimental study in rabbits,[23] showed that riboflavin–ultraviolet A (UVA) treatment should be safe as long as the dose is less than the endothelial cytotoxic dose of 0.65 J/cm^2. In human corneas, the endothelial cytotoxic UVA dose is reached in corneas thinner than 400 µ, which is not uncommon in keratoconus patients. Moreover, the data obtained from normal corneas of rabbit cannot be extrapolated to human keratoconic corneas, which can have a different metabolism and response to cross-linking. The study has a limitation of measure the endothelial toxicity only at 4 and 24 hours after treatment. The long-term endothelial cytotoxicity was not evaluated by the study.

Our study suggests that some endothelial changes occur after Ferrara ICRS implantation. However, these changes are minimal and nonclinically significant, since the endothelial cell loss rate is not much higher than that normally expected for normal corneas. In contrast, the long-term endothelial cell loss after other therapies for keratoconus is much higher (as in PKP, or even DALK, in which the receptor endothelium is spared) or unknown (as in cross-linking).

CONTACT LENS FITTING AFTER FERRARA ICRS IMPLANTATION

Contact lens fitting in keratoconus patients can be considerably facilitated after Ferrara ICRS implantation. Once there is corneal surface regularization with reduction of the excess of prolatism, the majority of patients can be well fitted with contact lens after the surgery.

The contact lens trial must be done after 3 months of surgery, which is the period required for keratometry and refraction stabilization. It is very common that patients that usually were intolerant to rigid gas-permeable contact lens in the preoperative period become tolerant after the surgery. It is frequently possible to fit soft contact lenses in these patients. Moreover, there is a very good stability of the contact lenses after the surgery, with "losses of lenses" caused by instability (a common complaint before the surgery) not occurring anymore.

There are a few studies about contact lens fitting after ICRS implantation. One study evaluated the fitting of a lathed soft toric contact lens (STCL) after the implant of ICRS to treat keratoconus. It was found that STCL fitting was successful in 75, 66.66, and 0% of the ICRS implanted eyes with stages I–III keratoconus respectively. Spectacle-CDVA was 1.5 lines better, and mean corneal power was 3.62 D lower in the successful STCL group. Piggy-back (PB) refitting achieved a PB-CDVA ≤0.2 logMAR in all cases. A similar difference in the CDVA change achieved by contact lenses *vs* spectacles was observed in the successful STCL and PB refitted groups. They concluded that STCL fitting is a feasible option in a large proportion of patients implanted with ICRS. When these lenses are unsatisfactory, a PB system is a good alternative.[65]

Scleral contact lenses (ScCl) are used for improving vision in patients with high or irregular astigmatism, such as keratoconus, pellucid marginal degeneration, keratoglobus, and post-keratoplasty astigmatism (Fig. 1).[66] Scleral lenses are lenses with bearing only on the sclera with diameter of the lens being 15 mm and above. Mini-scleral lenses have diameters between 15 and 18 mm, and true scleral lenses have 18 mm diameter (more than 6 mm bearing on sclera). Mini-scleral lenses have less corneal clearance as compared with true sclerals. They were

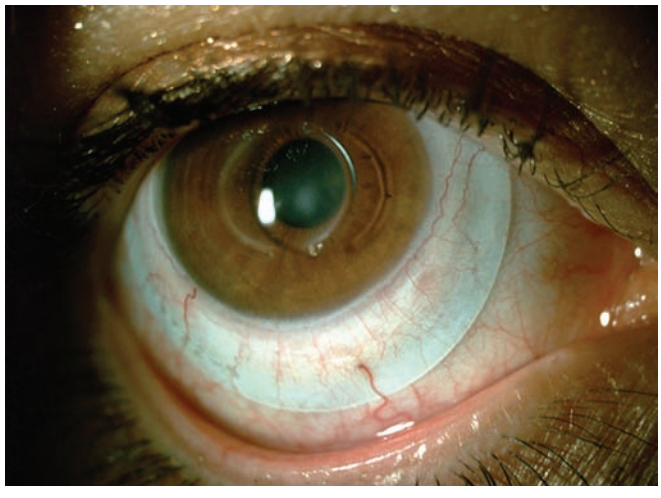


Fig. 1: Scleral contact lens in a patient implanted with Ferrara ICRS

used for a long time and then abandoned. Recently, after significant improvement in its manufacturing process, it has been used with great success in keratoconus patients with or without previous ICRS implantation.

High cost and the special training required in assessing the fitting and then modifying the design is quite challenging. Still, with the advances in technology, the field of ScCl has led to its resurgence as specialized lenses. Despite these challenges, improvement in visual acuity with scleral lenses is significant and worth its fitting.[66]

SURGICAL CORRECTION OF RESIDUAL AMETROPIA AFTER FERRARA ICRS IMPLANTATION

Keratoconus patients frequently have high myopia. Although the corneal shape in these eyes may improve after ICRS implantation, most patients require contact lenses or spectacles to correct the residual refractive error. Some studies[67-69] found that implantation of a phakic intraocular lens (pIOL) was a safe, effective, and predictable way to correct myopia associated with keratoconus (Figs 2A and B).

The success of the sequential procedure (ICRS followed by pIOL) requires knowledge of when the refraction is stable after ICRS insertion and whether the progression of keratoconus is halted because keratoconus progression leading to a refractive change can be a problem after pIOL implantation. A previous study[18] evaluated the long-term results and stability of ICRS implantation for keratoconus correction. The authors found that CDVA stability was achieved, with no significant differences in refraction from 6 to 36 months after ICRS implantation; there was also an improvement in corneal topography. However, there was a significant increase in K values over time. It has been a consensus that pIOL should be implanted at least 6 months after ICRS implantation.

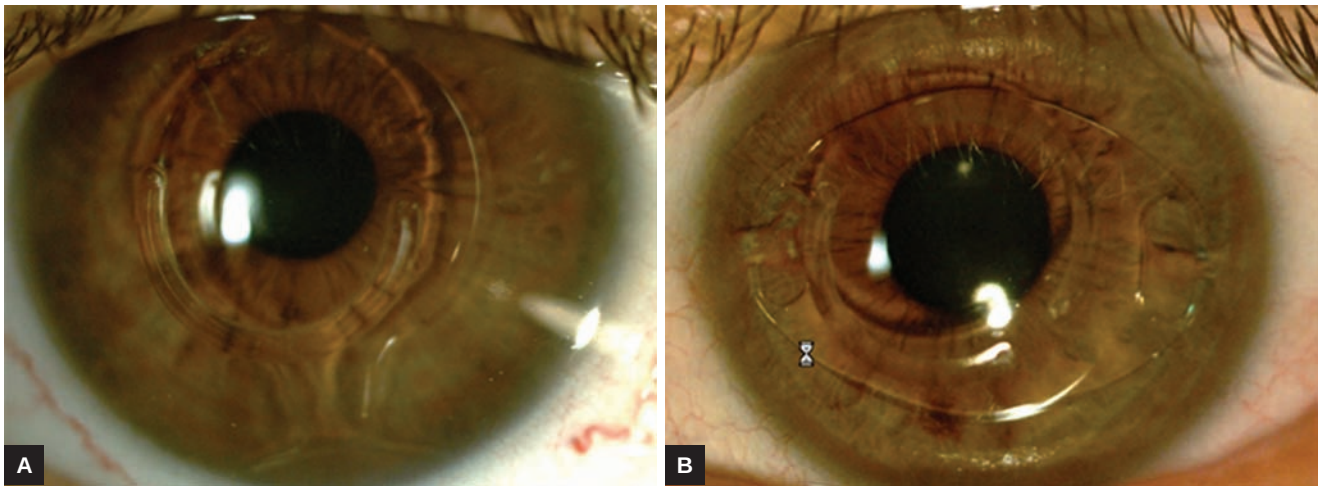
FERRARA ICRS IMPLANTATION FOR CORRECTION OF IRREGULAR ASTIGMATISM AFTER KERATOPLASTY

After keratoplasty, postoperative astigmatism is a common condition in clinical practice. Some studies[32,70] have investigated the use of ICRS as an alternative surgical option for the treatment of astigmatism in patients who underwent keratoplasty for keratoconus (Figs 3A and B).

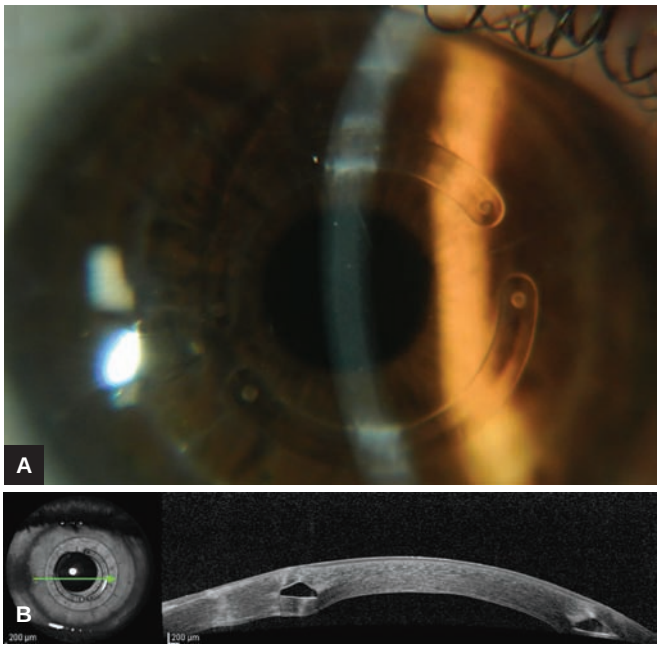
One of these studies[70] found that the mean CDVA (LogMAR) improved from 0.45 ± 0.17 (0.18–1.00) to 0.30 ± 0.17 (0.00–1.00). The mean preoperative standard error was –6.34 ± 3.40 D (0.37 to –16.50 D) and –2.66 ± 2.52 D (0.87 to –10.50 D) postoperatively. The mean spherical refractive error reduced from –7.10 ± 3.07 D (2.15–16.68 D) preoperatively to –3.46 ± 2.05 D (0.88–10.79 D) postoperatively. No patient lost visual acuity. The mean corneal topographic astigmatism decreased from 3.37 ± 1.51 D preoperatively to 1.69 ± 1.04 D postoperatively. The mean maximum K value decreased from 48.09 ± 2.56 to 44.17 ± 2.67 D, and the mean minimum K value decreased from 44.90 ± 2.54 to 42.46 ± 2.63 D. All changes were statistically significant ($p < 0.0001$).

There are several potential advantages of ICRS implantation over other surgical techniques in eyes with high astigmatism after PKP. First, ICRS implantation avoids any excimer laser treatment, eliminating central corneal wound healing, which could be unsatisfactory in post-PKP corneas. This leaves the optical center of the cornea untouched, enhancing refractive outcomes. Second, the technique is reversible in cases of an unsatisfactory refractive or clinical outcome. Third, adjustment can be performed using thinner or thicker rings. In cases of unexpected corneal shape changes, one segment can be removed or exchanged. Fourth, it avoids the complications of intraocular surgery.

The results of these studies suggested that ICRS seem to be a promising treatment for astigmatism after keratoplasty, especially in those with thin and irregular corneas.



Figs 2A and B: Phakic intraocular lens in patients implanted with Ferrara ICRS



Figs 3A and B: Ferrara ICRS implantation in a patient with corneal graft

ABERROMETRY AFTER FERRARA ICRS IMPLANTATION

The wavefront corneal changes induced by the implantation of the Ferrara ICRS have been evaluated by several studies.[33,70] The decrease of vision in patients with keratoconus is caused not only by sphero-cylindrical refractive errors (low-order aberrations), but also to a significant extent by high-order ones. This is clearly explained by the fact that spectacles in most cases are not able to provide full correction. The predominant defect is in the coma aberration, specifically its vertical component.

The studies describe a statistically significant reduction of all evaluated aberrations, not only the reduction of wavefront aberrations, but also the prediction of possible surgical-induced aberrations. These data (reduction and induction of aberrations) could be considered in a nomogram to assist in the ring (or pair of rings) selection for the best visual quality results.

FERRARA ICRS×KERATOPLASTY

Barbara and Barbara[71] have published the only paper that compares the clinical outcomes between ICRS implantation and keratoplasty in keratoconus patients. They found better UDVA and CDVA in the ICRS group of patients; the PKP group has more myopia and astigmatism but lower keratometry readings; all these differences were not statistically significant. intrastromal corneal ring segments implantation has been shown to be a less invasive procedure with less postoperative complications than PKP.

COMPLICATIONS

The incidence of complications after the learning curve is very low.[72] Postoperative complications can be related to (1) The surgical technique, (2) the nomogram, and (3) the ICRS itself. The complications related to the surgical technique are as follows: Extrusion (due to a shallow tunnel), infection, bad centration of the segment (wrong placement of the ICRS), migration, and misplacement or asymmetry of the segments.

The complications related to the nomogram are linked to the corneal biomechanics and can be (1) Overcorrection and (2) undercorrection. Although the predictability of postoperative results is high, in some cases, overcorrection and undercorrection can occur due to viscoelastic and biomechanic profile of the different keratoconic corneas.

The complications related to the ICRS itself are as follows: (1) Halos and glare, (2) periannular deposits, and (3) neovascularization. Halos are reported by 10% of patients and can be related to the pupil size. This symptom tends to fade or at least diminish over time. In very symptomatic cases, we usually prescribe pilocarpine or brimonidine tartarate at night, to constrict the pupil and alleviate the undesired reflexes. The periannular opacities are small white debris lying along the ICRS internal face (Fig. 4). They do not tend to grow and do not harm visual performance, being only antiesthetical when submitted to biomicroscopic examination. Neovascularization of the stromal tunnel is rare and usually occurs in atopic patients (Fig. 5). Subconjunctival bevacizumab has shown to be an effective option to treat neovascularization of the tunnel.[73,74]

Coskunseven et al[38] reported the complication rate after implantation of ICRS assisted by the femtosecond laser in 850 keratoconus eyes. They found an incidence of 2.7% of incomplete channel formation and 0.6% of endothelial

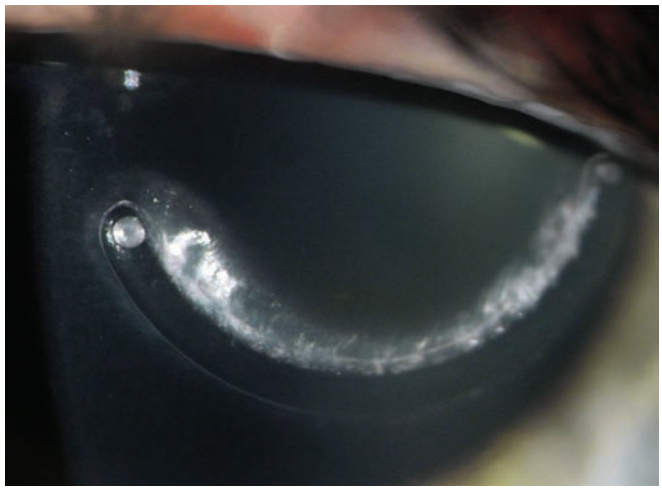


Fig. 4: White deposits in a patient implanted with Ferrara ICRS

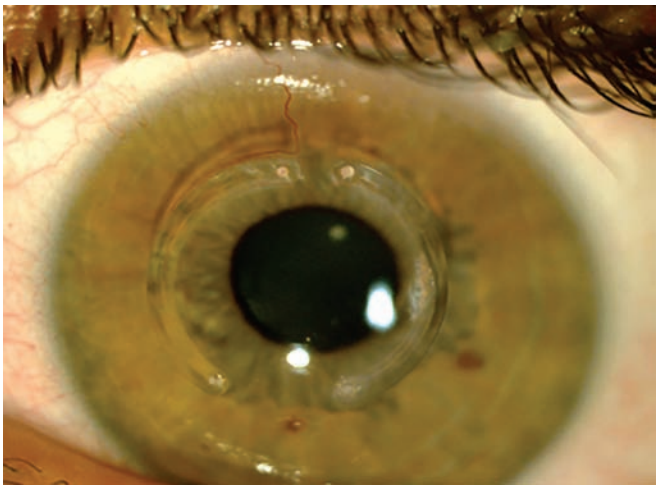


Fig. 5: Neovascularization of the tunnel in a patient implanted with Ferrara ICRS

perforation. About postoperative complications, there were 1.3% cases of segment migration, 0.2% of corneal melting, and 0.1% case of mild infection. The overall complication rate was 5.7% (49 cases out of 850 eyes).

Kwitko and Severo[41] reported ICRS decentration in 3.9% of cases, segment extrusion in 19.6%, and bacterial keratitis in 1.9%. As the author mentioned in his paper, the surgeon's learning curve and different healing processes in keratoconic corneas can cause the majority of complications related to the surgical technique. Once the surgical procedure is mastered, the complication rate related to the surgery itself is very low. The surgical steps must be followed carefully (the stromal tunnel must be constructed with the adjustable diamond knife set at 80% of local corneal thickness to reduce the chance of a shallow tunnel and subsequent ICRS extrusion) to avoid surgery-related complications.

As a general rule, it must be assumed that the thickest segment of a pair of segments cannot exceed half thickness of the cornea in its bed. If this happens, a pair of segments that fit this condition has to be chosen even if the achieved correction is smaller than the desired one.

The majority of the complications can be managed by ICRS exchange, reposition, addition, or removal. One study[49] evaluated the visual, refractive, and topographic changes occurring after reoperation in keratoconic eyes. In this study, the incidence of patients requiring follow-up surgery due to the overcorrection or undercorrection was 3.4%. For these patients, there was improvement of UDVA, CDVA, keratometry, and pachymetry. However, asphericity and spherical equivalent did not improve in these patients undergoing subsequent surgery, perhaps due to the scarring of corneal tissue and/or stroma secondary to the first procedure. The mean follow-up time after the reoperation was 30.5 ± 9.7 months. Uncorrected distance visual acuity improved from 20/300 to 20/80 ($p = 0.005$); CDVA improved from 20/160 to 20/50 ($p = 0.0002$), the mean keratometry reduced from 49.33 ± 4.19 D to 46.16 ± 3.90 D ($p = 0.0001$), and the mean pachymetry at the thinnest point increased from 450 ± 42.9 to 469 ± 40.8 µm ($p = 0.0001$).

Good outcomes can be obtained even after removal, addition, reposition, or exchange of ICRS. Ferrara ICRS implantation has been shown to be a reversible and readjustable surgical procedure for keratoconus treatment.

COMMENTS

Preliminary investigations have demonstrated that intracorneal ICRS are effective in the treatment of astigmatism and myopia with astigmatism,[9] with preservation of CDVA and stable results over time.[10] The objective of the addictive technology is to reinforce the cornea, decrease the corneal irregularity, and provide an improvement of the visual acuity in affected patients.

It is important to note an important reduction of keratometric values after the Ferrara ICRS implantation, with corneal regularization and return to its physiological values when the intervention is made early in the course of the disease.[75,76] However, in a late intervention, with values of keratometry superior to 56 D, a reduction of the K is also shown, high keratometry values remain when compared with a normal corneal keratometry.[77]

Ferrara's ICRS technique has the objective of reshaping the abnormal cornea, flattening the periphery, and decreasing the corneal astigmatism. With the objective to avoid, or at least postpone[2,17-19,39] the keratoplasty, the technique is within the options of visual rehabilitation of patients with keratoconus.

Observing the clinical outcomes of our patients, we could realize that the visual rehabilitation curve and refractive stabilization occurs on average after 3 months of surgery. The visual rehabilitation process follows a certain pattern. In general, vision improvement is quick and on the day following surgery, the patients usually report subjective and objective improvement of the visual acuity. However, it usually reverts within the first weeks, and at the end of the first month, the patient reports his/her vision was better immediately after surgery. The same fluctuation is detected in relation to refraction and keratometry. From the first month on, the vision starts to improve and refractive and keratometric fluctuation decreases. From the third month on, it stabilizes. Then, it is possible to correct the residual ametropia, if necessary, by means of eyeglasses, rigid or soft contact lenses, or even implanting plOL for high myopia correction.

We could notice that patients having central cones show a longer rehabilitation time,[24] which means that the central flattening is slower, while patients with decentralized cones have faster rehabilitation.[39] We believe that this is due to the dislocation or the corneal apex toward

its physiological position in front of the pupil. In some cases, we could observe that after ICRS implantation, there was an increase in myopia and in the keratometric readings, caused by this same phenomenon.

Symptoms, such as photophobia, visual discomfort, eye strain, and itching reduce or disappear after surgery. Most of the keratoconus patients are allergic; therefore, we recommend strongly that they should not rub their eyes, which could displace the segments, and stimulate the disease progression. In addition, rubbing could theoretically change the regularity of the corneal surface leading to visual acuity loss. In some cases, it is necessary to use eye shields at night to prevent the patient from rubbing the eyes compulsively and unwarily.

The satisfaction level is high. We could observe that the fear of becoming blind in those patients, along with the fearsome possibility of a transplant in case of a continuously evolving condition, is very common. The possibility of postponing those eventualities generates great relief in the patients. Our cases show that, besides correcting the corneal deformity, the cone evolution is interrupted. Along with this interruption, we could also observe a decrease in corneal opacity and the other symptoms aforementioned.

The surgery is simple and well reproducible, although it is not an easy procedure. As in any other procedure, it must be well executed to attain a consistent result.

The incidence of complications is very low, around 3 to 5%, compatible with the levels required for refractive procedures. It should be emphasized that the corneal ICRS implant is essentially an orthopedic technique designed to enable the correction of a structural deformity. As an advantage, it provides simultaneous refractive correction, although not well predictable, as with other refractive procedures.

Whenever it was necessary to perform keratoplasty, the ICRS not only helped the procedure, but also provided a better centralization during trephination.

We could also notice that, after surgery, there was a decrease in the corneal sensitivity, resulting in greater comfort in contact lens fitting, which was not possible before the operation.

The incidence of complications is greater in more advanced stages, because the cornea is thinner, and the pressure generated inside the stroma after the ICRS implantation can cause the displacement of segments toward the incisions, eventually extruding the segments.

CONCLUSION

From the results obtained, we can state that this therapeutic approach has the following benefits:

- Low morbidity, because it preserves the corneal structure and has a low rate of complications,[38,39] allowing 95% of the operated patients to quickly reintegrate themselves to their everyday activities.
- Reversibility, because it enables the cornea to revert to the preoperative dimensions when the segments are removed.[49]
- Readjustability through segment replacement. In some cases, it was possible to correct hypercorrection removing just one of the segments.[49]
- Lack of rejection – the acrylic which the ICRS is made of is inert and biocompatible.
- Patients' high satisfaction rate.
- As an orthopedic technique, it corrects corneal deformity and restores the physiologic curvature. After the surgery it is possible to correct the residual ametropia with conventional optical correction or contact lenses.[65]
- Stabilization or delay of cone progression.[19]
- Lack of a minimum age for surgery, thus making it possible to reduce the waitlists for transplants in eye banks (30% of the transplants in eye banks are attributed to keratoconus).
- Possibility of association with other procedures like contact lens fitting and intraocular lenses.
- No interference whatsoever with corneal transplant.

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INTRASTROMAL CORNEAL RING SEGMENTS IN CHILDREN WITH KERATOCONUS

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Int J Kerat Ect Cor Dis Submitted April 5 2017.

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ABSTRACT

Purpose: To evaluate the long-term follow-up of Ferrara intrastromal corneal ring segments (ICRS) (Ferrara Ophthalmics, Belo Horizonte, Brazil) implantation for the management of keratoconus in children.

Setting: Dr. Paulo Ferrara Eye Clinic, Belo Horizonte, MG, Brazil

Methods: Fifty-eight eyes of 37 children with keratoconus were included. One or two ring segments were inserted in the cornea, embracing the keratoconus area. Statistical analysis included preoperative and postoperative uncorrected distance visual acuity (UDVA), corrected distance visual acuity (CDVA), asphericity, pachymetry and keratometry.

Results: Ferrara ICRS implantation significantly improved the mean UDVA and CDVA. Corneal tomography (Pentacam®) showed corneal flattening in all eyes

implanted with the Ferrara ring. The mean K decreased, and the corneal asphericity and pachymetry increased in all cases.

Conclusion: The Ferrara ICRS improved all parameters after two years of implantation in children with keratoconus. There was significant corneal flattening after ring implantation with improvement of the UDVA and the CDVA. All studied parameters remained stable over time.

Key-words: Ferrara ring, keratoconus, children, intrastromal corneal ring segments

INTRODUCTION

Keratoconus is a corneal ectatic disease characterized by non-inflammatory progressive thinning of unknown cause in which the cornea assumes a conical shape.

Intrastromal corneal ring segments (ICRS) have been used to correct ectatic corneal diseases in order to reduce the corneal steepening, reduce the irregular astigmatism and improve the visual acuity. [1-7] Besides, the segments may be a surgical alternative to at least delay, if not eliminate, the need of lamellar or penetrating keratoplasty.

The Ferrara ICRS are made of PMMA Perspex CQ acrylic. They vary in thickness, and are available in 0.15, 0.20, 0.25, 0.30 and 0.35 mm. The

segment cross-section is triangular, and the base for every thickness and diameter is 0.60 mm. The segments have 90, 120, 160 or 210 degrees of arc.

Many studies have demonstrated the efficacy of intrastromal rings to treat many corneal conditions as keratoconus,[1-7] post–LASIK corneal ectasia,[8] post-radial keratotomy ectasia,[9] astigmatism[10] and myopia.[11-14] The changes in corneal structure induced by additive technologies can be roughly predicted by the Barraquer´s thickness law; that is when material is added to the periphery of the cornea or an equal amount of material is removed from the central area, a flattening effect is achieved. The corrective result varies in direct proportion to the thickness of the implant an in inverse proportion to its diameter. The thicker and smaller the diameter of the device, the higher the corrective result.[15]

In order to investigate the long-term visual acuity and mechanical stability after Ferrara ICRS implantation in children with keratoconus, we conducted the current retrospective study.

METHODS

We retrospectively reviewed patient records of 58 eyes of 37 children with keratoconus, which were followed for a period of at least 6 months. The main indication for ICRS implantation was contact lens intolerance and/or progression of the ectasia. The progression of the disease was defined by:

worsening of uncorrected distance visual acuity (UDVA) and corrected distance visual acuity (CDVA) (loss of at least 1 line of VA), progressive intolerance to contact lens wear and progressive corneal steepening documented by corneal topography. Patients were excluded if any of the following criteria applied after preoperative examination: advanced keratoconus with significant apical opacity and scarring, hydropsis, thin corneas, with thickness below 300 μm in the ring track, intense atopia and any ongoing infectious process, local or systemic.

Patients were separated into two groups (initial and advanced) according to Amsler-Krumeich classification*.

Statistical analysis included preoperative and postoperative UDVA, CDVA, keratometry, pachymetry at the thinnest point of the cornea and corneal asphericity. The anterior segment parameters were obtained from Pentacam (Oculus Pentacam®, Germany). Statistical analysis was carried out using the MINITAB software (version .3.3.1). Student´s *t* test for paired data was used to compare preoperative and postoperative data.

All surgeries were performed by the same surgeon (PF) using the manual technique for ICRS implantation, as previously described.[1-5] The segments were implanted according to a previously described Ferrara Nomogram[16].

After surgery Ketorolac drops were used every 15 minutes for 3 hours, and a combination of 0.1% dexamethasone and 0.3% moxifloxacin or ciprofloxacin drops was used every 4 hours for 7 days, as well as hypromelose (Alcon) every 6 hours for 30 days.

RESULTS

Fifty-eight eyes of 37 patients were studied. Thirteen eyes remained untreated and 3 eyes underwent lamellar keratoplasty due to advanced keratoconus. The mean age of patients was 13 ± 2.1 years old (range 8 to 16 years). All patients completed at least 6 months of follow-up (average 20 months, range 6 to 81). No peroperative or postoperative complications occurred.

Preoperative and postoperative UDVA, CDVA, asphericity, pachymetry and keratometry data were collected from all patients. The mean UDVA at the preoperative period was 0.41 LogMAR, and the mean CDVA was 0.36 LogMAR. At the first month, the mean UDVA improved to 0,29 LogMAR and the mean CDVA improved to 0.20 LogMAR. At the first year follow-up, the mean UDVA was 0.30 LogMAR postoperatively. The mean CDVA, at the first year follow-up, the mean CDVA improved to 0.15 LogMAR, at the second year follow-up, the mean UDVA increased slightly 0.25 LogMAR, and the mean CDVA decreased slightly, to 0.16 LogMAR postoperatively (Table 1).

Corneal topography showed corneal flattening in all eye. The mean $K_{minimum}$ and the mean $K_{maximum}$ decreased in all groups and there was an increase of corneal asphericity and pachymetry. One patient needed

crosslinking and one patient needed a lamellar keratoplasty due to progressive steepening despite ICRS implantation.

Minimum Keratometry

Evaluating the results obtained between preoperative and the first month postoperatively, the minimum keratometry reduced, on average, 4 units (range: 3 to 5), with 95% confidence.

Between the first month and the second year of follow up, there was no change in minimum keratometry values (p-value = 0.412). (Graphic 1)

Maximum Keratometry

From the preoperative to the evaluation in the first month, the maximum keratometry decreased, on average, 6 units (range: 4.7 to 7,3), with 95% confidence.

From the first month and the second year of follow up, the maximum keratometry increased (p-value =0,002). At each year evaluated, the maximum keratometry increased, on average, 0.7 units (95%CI: 0.2 to 0.5) (Graphic 2)

Asphericity

From the preoperative to the first month postoperative, there was an increase in asphericity, which was, on average, 0,61 unit (p-values < 0.001).

From the first month and the second year of follow up, the asphericity values remained stable over time (p-value = 0,275) (Graphic 3).

Corneal Thickness Variation

From the preoperative evaluation to the first month postoperative, there was corneal thickening of, on average, 8.5 units (p-values = 0.05).

From the first month to the second year of follow up, the corneal thickness remained stable over time (p-value = 0,112) (Graphic 4).

DISCUSSION

Preliminary investigations have demonstrated that intracorneal rings are effective in the treatment of astigmatism and myopia with astigmatism[15], with preservation of CDVA and stable results over time[16]. The objective of the addictive technology is to reinforce the cornea, decrease the corneal irregularity and to improve the visual acuity in affected patients.

This is the first study to show the long-term follow-up of children with keratoconus in which the Ferrara ICRS was implanted for at least 6 months. This study is in agreement with some other studies: Miranda *et al.* obtained on their study a significant reduction in the mean central corneal curvature postoperatively. CDVA and UDVA improved in 87.1% and 80.6% of the eyes, respectively. Siganos *et al* [4] showed an increase of the mean UDVA from 0.07 $\pm$ 0.08 preoperatively to 0.20 $\pm$ 0.13 and 0.30 $\pm$ 0.21 after 1 and 6 months, respectively, and the mean CDVA improved from 0.37 $\pm$ 0.25 preoperatively to 0.50 $\pm$ 0.43 and 0.60 $\pm$ 0.17 after 1 and 6 months, respectively. Kwitko and Severo[18] reported that, after implantation of Ferrara ring in keratoconus eye, the CDVA improved in 86.4% of eyes, was unchanged in 1.9% and worsened in 11.7%. The UDVA improved in 86.4% of eyes, was unchanged in 7.8%, and worsened in 5.8%. The mean corneal curvature was reduced from 48.76 ± 3.97 to 43.17 ± 4.79.

The minimum and maximum keratometry decreased from the pre-surgical evaluation to the first month, while the values of asphericity and pachymetry increased during this same period. Between the first month of

follow-up to the second year, we observed that minimum keratometry did not change over time, and maximum keratometry had a slight increase over time. The value of asphericity does not change over time; the pachymetry did not change over time. Although there was a slight increase in maximum keratometry over time (0.7 diopters per year, on average), this increase was not clinically significant.

Based on our personal (unpublished) data, about 5% of patients go to penetrating or lamellar keratoplasty due to progressive corneal scarring, despite proper ICRS implantation. It is important to emphasize that these patients usually had ring implantation in very advanced phases of the disease and does not mean necessarily keratoconus evolution but rather an unsatisfactory visual outcome. In our study, two patients (5,4%) underwent keratoplasty, and one patient (2.7%) underwent corneal crosslinking due to keratoconus progression.

Alió *et al*.[20] conducted a retrospective study to evaluate the long-term (up to 48 months) results after implantation of Intacs in patients with keratoconus. They found that the mean CDVA increase significantly ($p<0.01$) from 0.46 (20/50) preoperatively to 0.66 (20/30) 6 months after implantation. Also the mean average K-value decreased significantly ($p<0.01$) by 3.13 D. The comparison of results 6 months and 36 months after implantation showed refraction and topography stability.

Kimionis *et al*.[21] studied 17 eyes of patients with keratoconus that had Intacs implantation for corneal flattening. They found that the pre-Intacs UDVA was 20/50 or worse in all eyes, whereas, at the last follow-up examination 59%

had UDVA of 20/50 or better. Most of eyes (59%) experienced a gain of one up to 8 lines of visual acuity.

Previous studies showed that the intrastromal ring flattens the cornea and keeps this effect for a long period of time. There is no significant re-steepening of the cornea over time, in adults. We found that the preoperative keratometry values were higher in our study when compared with similar studies.[20,21,22] Moreover, the preoperative UDVA and CDVA were worse in our study. This can be explained by the behaviour of keratoconus in some children, which can rapidly evolve, and when the surgery is indicated the disease is more advanced.

There was improvement of all parameters in our study. The pattern of reduction of keratometry parameters was similar to other studies. Despite of that, at 5 years of follow-up we found corneal re-steepening on maximum keratometry, what was not found in the other studies we compared our results. Regarding the visual acuity, there was improvement in UDVA and CDVA, but not as much as in adults.

The present study showed that the Ferrara ring, despite the small sample of patients, could be a valuable tool to provide topographic and visual improvement in children with keratoconus. Corneal re-steepening can occur after ICRS implantation. It plays an important role in delaying the progression of keratoconus and postpones a corneal grafting surgery. Further studies with larger samples and longer follow-up periods must be warranted to confirm the presented results.

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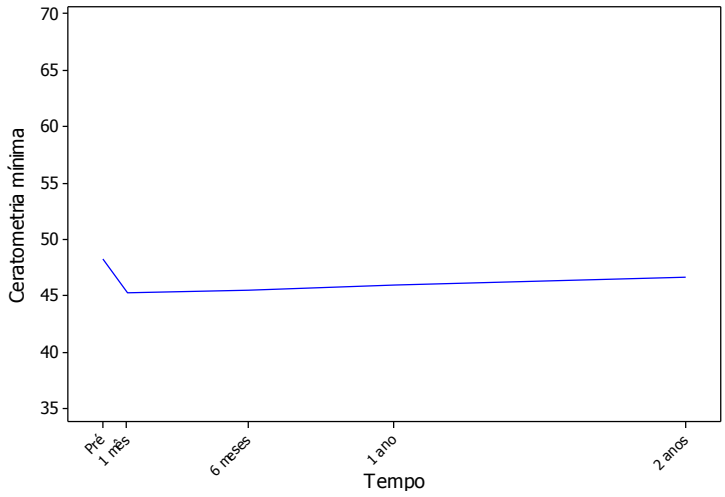
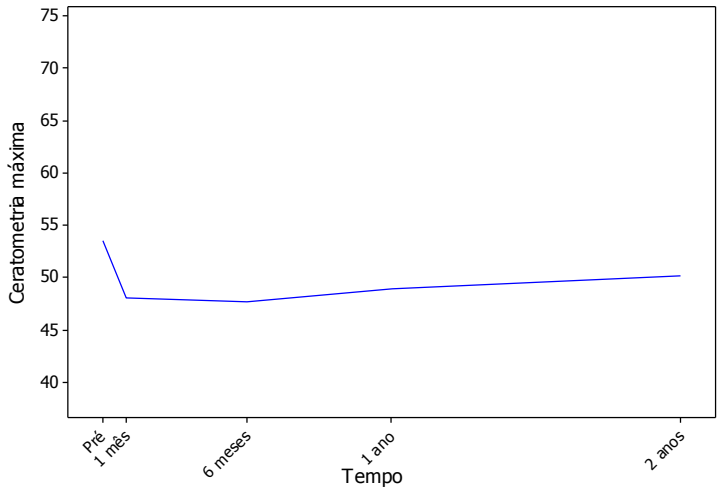
Pre and Post operative data					
		Postoperative			
	Preoperative	1st month	p	2nd year	p
UDVA	0.41	0.29	0.004	0.25	0.262
CDVA	0.36	0.2		0.16	0.983

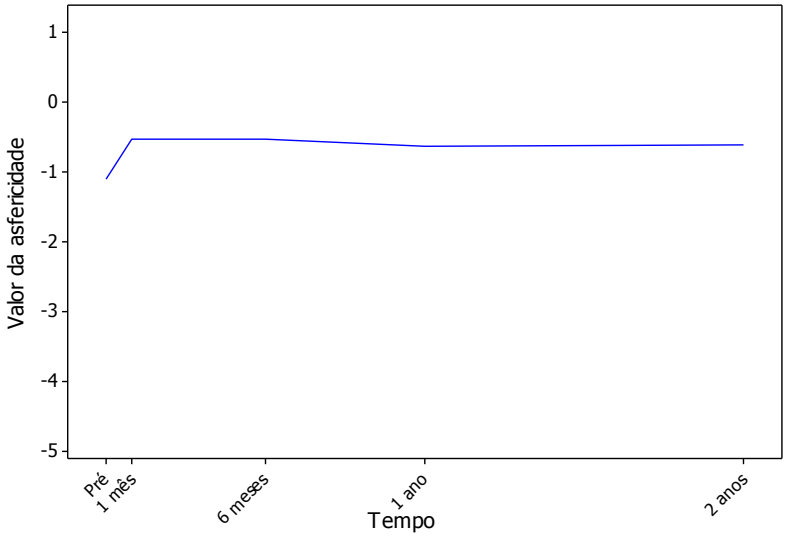
Table 1: UDVA and CDVA variation



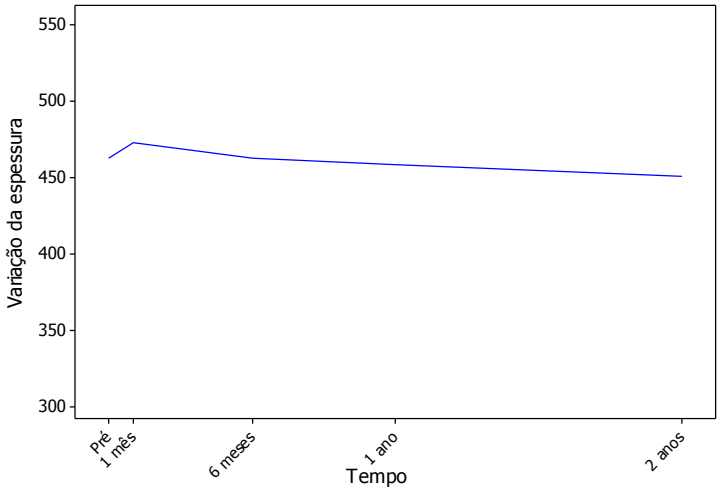
Graphic 1: Variation of minimum keratometry over time



Graphic 2: Variation of maximum keratometry over time



Graphic 3: Variation of asphericity over time



Graphic 4: Variation of pachymetry over time