Refractive and Corneal Aberrometric Changes after Intracorneal Ring Implantation in Corneas with Pellucid Marginal Degeneration

David P. Piñero, MSc,[1,2] Jorge L. Alio, MD, PhD,[1,3] Hector Morbelli, MD,[4] Antonio Uceda-Montanes, MD,[5,6] Bassam El Kady, MD, PhD,[1,7] Efekan Coskunseven, MD,[8] Inmaculada Pascual, PhD[2]

Purpose: To evaluate refractive, visual, and aberrometric changes in corneas with pellucid marginal degeneration (PMD) implanted with intracorneal ring segments (ICRS) during a 6-month follow-up.

Design: Retrospective, consecutive case series.

Participants: We included 21 consecutive eyes of 15 patients ranging in age from 21 to 73 years old and with a diagnosis of PMD. This diagnosis was made on the basis of slit-lamp (inferior corneal thinning), corneal topography ("butterfly" pattern), and refractive findings (significant against-the-rule astigmatism with best spectacle-corrected visual acuity loss).

Methods: A multicenter, retrospective analysis of patients undergoing ICRS implantation for the management of PMD in 4 ophthalmologic centers was performed. Surgery was indicated in all cases because of reduced best spectacle-corrected visual acuity (BSCVA) and/or contact lens intolerance or dissatisfaction. Mechanical corneal tunnelization was performed in 7 eyes and femtosecond laser-assisted tunnelization in 14 eyes. Intacs were implanted in only 3 eyes whereas KeraRings in 18 eyes. Refractive and corneal aberrometric changes were analyzed during a 6-month follow-up.

Main Outcomes Measures: Uncorrected corrected visual acuity (UCVA) and BSCVA, refraction, keratometry, and root mean square (RMS) for different kinds of corneal aberrations.

Results: The UCVA did not improve at 6 months after surgery ($P = 0.11$). The BSCVA increased from a mean preoperative value of 0.54 to a mean postoperative value of 0.75 ($P = 0.06$). At 6 months, 44.44% of eyes gained ≥2 lines of BSCVA. Sphere ($P = 0.02$), cylinder ($P<0.01$), and spherical equivalent ($P<0.01$) were reduced significantly after surgery ($P\leq 0.02$). Mean keratometry decreased significantly from 44.95 diopters (D) preoperatively to 43.19 D at 6 months postoperatively ($P<0.01$). The RMS values for astigmatism, higher order residual, and coma-like aberrations were significantly reduced with surgery ($P = 0.03$). In addition, significant negative correlations of preoperative RMS astigmatism ($r = -0.90$) and primary spherical aberration ($r = -0.86$) with postoperative BSCVA were also found. Segment ring explantation was performed in a total of 4 eyes owing to poor visual outcome.

Conclusions: Implantation of an ICRS is an effective option for the treatment of 2nd-order and higher aberrations in corneas with PMD. Preoperative corneal astigmatism and spherical aberration seem to be limiting factors for a good visual outcome.

Financial Disclosure(s): The authors have no proprietary or commercial interest in any materials discussed in this manuscript. *Ophthalmology 2009;116:1656–1664 © 2009 by the American Academy of Ophthalmology.*

Pellucid marginal degeneration (PMD) is an idiopathic, progressive, noninflammatory, ectatic disorder characterized by a peripheral band of corneal inferior thinning in a crescent-shaped pattern.[1] The area of thinning is typically found in the inferior cornea, extending from the 4 o'clock to 8 o'clock positions,[1] although PMD cases with areas of superior thinning can also be found.[2] This disease is usually asymptomatic, although a progressive deterioration in uncorrected visual acuity (UCVA) and best-corrected visual acuity can occur owing to the irregular astigmatism induced by the corneal ectasia in the most advanced cases.

Corneal topographic analysis reveals a flattening in the vertical meridian, inducing a significant against-the-rule astigmatism and a significant steepening around the area of maximum thinning.[3] This corneal configuration corresponds with a topographic map that shows the classical "butterfly" pattern. Although corneal topography is an important tool for the diagnosis of this corneal pathology, it should not be used as the only diagnostic criterion. Indeed, it has been demonstrated that a characteristic, claw-like pattern of peripheral steepening on corneal topography is not always associated with the diagnosis of PMD.[4] Pachymetric and biomicroscopic findings must also be considered for a reliable diagnosis.

Published by Elsevier Inc.
ISSN 0161-6420/09/$–see front matter
doi:10.1016/j.ophtha.2009.06.002

Several possible alternatives to manage PMD have been described, such as rigid, gas-permeable contact lenses,[5–7] intracorneal ring segment (ICRS) implantation,[8–14] crescentic lamellar keratoplasty,[15] penetrating keratoplasty,[16] and corneal wedge excision.[17] Regarding the ICRS, it was demonstrated that the addition of extra material at the normal corneal midperiphery induces a displacement of the local anterior surface forward at this area. This modification generates a peripheral steepening and a flattening of the central portion of the anterior cornea owing to the morphologic structure of the corneal lamellae.[18] If it is assumed that changes induced by ICRS in the normal cornea are similar to those generated in the PMD cornea, these ring segments would be able to minimize and center the peripheral corneal protrusion, inducing a significant change in corneal asymmetry and refraction (especially astigmatism). As a consequence, visual acuity would be also expected to improve. Our research group described and reported the first case of PMD implanted successfully with ICRS.[14] Since then, several authors have reported astigmatic reductions[8–10,12] and improvements in best-spectacle corrected visual acuity (BSCVA)[8–14] after ICRS implantation in corneas with PMD. The improvement in BSCVA induced by ICRS in this kind of corneas could be explained by the reduction of corneal aberrations and asymmetry. However, this issue has not still been analyzed and reported.

The aim of the present study was to analyze refractive, visual, and corneal aberrometric changes in a large sample of PMD corneas implanted with ICRS during a 6-month follow-up. To the best of our knowledge, in this study we present the largest series of cases of corneas with PMD treated with ICRS. Furthermore, this study is the first that attempts to analyze the corneal aberrometric changes that occur in these corneas with these kinds of implants.

Patients and Methods

Patients

A retrospective analysis of outcomes of all patients who underwent ICRS implantation for the management of PMD from September 2005 to February 2008 in 4 different ophthalmologic centers (Spanish centers: Vissum Alicante, Vissum Sevilla and Vissum Albacete; Turkish center: Dunya Eye Hospital from Istanbul) was performed. Table 1 summarizes the contribution of each center to the present study. Twenty-one consecutive eyes from 15 patients with a diagnosis of PMD (9 unilateral and 6 bilateral) were included. This diagnosis was made on the basis of slit-lamp (inferior corneal thinning and ectasia above the area of maximum thinning), corneal topography ("butterfly" pattern, very steep contour in the peripheral inferior cornea with high keratometric powers radiating toward the center from the inferior oblique meridians), and refractive findings (significant against-the-rule astigmatism with BSCVA loss).[9] In all cases, ICRS implantation was indicated because of reduced BSCVA (>2 lines BSCVA) and/or contact lens intolerance or dissatisfaction.

A comprehensive examination was performed in all cases before the ICRS implantation, which included Snellen UCVA (decimal notation), Snellen BSCVA (decimal notation), manifest refraction, slit-lamp biomicroscopy, Goldman tonometry, fundus evaluation, ultrasonic pachymetry, and corneal topographic analysis. Because topographic data were collected from different periods and from 2 different centers, a total of 3 different corneal topography systems were used for corneal examination: CMS 100 Topometer (G. Rodenstock Instrument GmbH, Ottobrunn, Germany), CSO (CSO, Firenze, Italy), and Orbscan IIz system (Bausch & Lomb, Rochester, NY). The first 2 devices are Placido-based systems and the Orbscan II is a combined scanning-slit and Placido-disc topography system. Although agreement between these specific devices has not been reported, Orbscan and Placido-based devices have been demonstrated to provide similar accuracy and precision on calibrated spherical test surfaces.[19] In this study, the following topographic data were evaluated and recorded with all corneal topographic devices: corneal dioptric power in the flattest meridian for the 3-mm central zone (K1), corneal dioptric power in the steepest meridian for the 3-mm central zone (K2), mean corneal power in the 3-mm central zone (KM) and the inferosuperior asymmetry index, calculated as the difference between the dioptric power at 3 mm below and above the corneal geometric center. Additional topographic parameters were analyzed and recorded in patients examined with the CSO topographic system (15 eyes): corneal astigmatism in the 3-mm central zone (AST3), corneal astigmatism in the 6-mm central zone (AST6), mean asphericity for a corneal area of 4.5-mm diameter (Q45), and mean asphericity for a corneal area of 8-mm diameter (Q8).

During the process of consent for this surgery, consent was taken to later include clinical information in scientific studies. Ethical board committee approval of our institution was obtained for this investigation. For all cases, a 6-month follow-up was completed.

Corneal Aberrations of the Anterior Surface

Corneal aberrometry was also recorded and analyzed only in those patients examined at all visits with the CSO topography system (10 eyes), because this device was the only one with the capability to calculate directly this specific information. This topographic system analyses a total of 6144 corneal points of a corneal area enclosed in a circular annulus defined by an inner radius of 0.33

Table 1. Contribution of Each Participating Ophthalmologic Center

Investigator	Surgeon	Ophthalmologic Center	Eyes Implanted with ICRS
1	Dr Alió	Vissum Alicante (Spain)	10
2	Dr Morbelli	Vissum Albacete (Spain)	7
3	Dr Uceda	Vissum Sevilla (Spain)	3
4	Dr Çoşkunseven	Refractive Surgery Department of Dunya Eye Hospital, Istanbul (Turkey)	1

ICRS = intracorneal ring segments.

Table 2. KeraRings Nomogram Used for the Present Study: Segment Distribution and Thickness According to Area of Ectasia and Spherical Equivalent

Spherical Equivalent (D)	All Ectasia Is Limited to One Half of the Cornea	75% of the Ectasia in One Half of the Cornea and 25% Situated in the Other Half	Two thirds of the Ectatic Area in One Half of the Cornea and One Third in the Other Half	The Ectasia is Distributed Evenly in Both Corneal Halves
> −10	25/35	25/35	30/35	35/35
−8 to −10 D	20/30	20/30	25/30	30/30
−6 to −8 D	15/25	15/25	20/25	25/25
−2 to −6 D	0/20	0/20	15/20	20/20

D = diopters.
For defining the distribution of the ectasia the cornea was divided into 2 halves using the steepest meridian as axis of separation. Example: 25/35 = upper segment thickness/lower segment thickness (0.25 mm/0.35 mm).

and an outer radius of 10 mm with respect to the corneal vertex. The software of the CSO, the EyeTop2005, automatically performs the conversion of corneal elevation profile into corneal wavefront data using the Zernike polynomials with an expansion up to the 7th order. In this study, aberration coefficients and root mean square (RMS) values were calculated for a 6-mm pupil in all cases. The following parameters were analyzed and recorded: total RMS, RMS for corneal astigmatism primary coma RMS (computed for the Zernike terms $Z_3^{\pm 1}$), coma-like RMS (computed for third-, fifth-, and seventh-order Zernike terms), spherical-like RMS (computed for 4th- and 6th-order Zernike terms) and higher order residual RMS (computed considering all Zernike terms except those corresponding with primary coma and spherical aberration). The corresponding Zernike coefficient for primary spherical aberration (Z_4^0) was also reported with its sign.

Surgery

Operative procedures were performed by a total of 4 different surgeons, one from each participating center (JLA, HM, AUM, EC). In all cases, an antibiotic prophylaxis before surgery consisting of topical ciprofloxacin (Oftacilox; Alcon Cusí, Barcelona, Spain) to be applied every 8 hours for 2 days was prescribed. All procedures were performed under topical anesthesia.

Corneal tunnelization for facilitating the ring segment insertion was performed using the mechanical procedure in a total of 7 eyes (33.3%) and by means of femtosecond technology in 14 eyes (66.6%). Incision was located on the steepest meridian of the anterior corneal surface in all patients. A tunnel with inner and outer diameters of 6.6 and 7.8 mm, respectively, was always planned for Intacs implantation, whereas inner and outer diameters of 4.8 mm and 5.7 mm, respectively, were planned for KeraRings implantation. No complications occurred intraoperatively.

The mechanical operative procedure was initiated marking a reference point for centration (pupil center) and performing a radial incision of approximately 1.8 mm long. After this, a calibrated diamond knife was set at approximately 70% of the mean corneal thickness determined by ultrasonic pachymetry. From the base of the incision, pocketing hooks were used to create corneal pockets on each side of the incision, taking care to maintain a uniform depth. A device containing a semiautomated suction ring was placed around the limbus, guided by the previously marked reference point on the cornea. Two semicircular dissectors then were placed sequentially into the lamellar pocket to be steadily advanced by a rotational movement (counterclockwise and clockwise dissectors).[20] In the femtosecond laser-assisted operative procedure, the disposable glass lens of the laser system was first applanated to the cornea to fixate the eye and help to maintain a precise distance from the laser head to the focal point.[21] Then, a continuous circular stromal tunnel was created at approximately 80% of corneal depth within 15 seconds with no corneal manipulation.[21] The 30-kHz IntraLase femtosecond system was always used (IntraLase Corp, Irvine, CA).

Two different kinds of ICRS were used: Intacs (Addition Technology, Inc, Fremont, CA) in only 3 eyes (14.29%) and KeraRings (Mediphacos, Belo Horizonte, Brazil) in 18 eyes (85.71%). All Intacs cases were implanted using the femtosecond technology, whereas KeraRings were implanted using this same technology only in 11 eyes (52.38%). The remaining KeraRings cases were implanted using the mechanical procedure (cases from Vissum Albacete, where this technology was not yet available). Intacs were always implanted following the protocol described and used by several authors[9,10,20]: a 0.25-mm implant placed superiorly and a 0.45-mm implant placed inferiorly. Regarding KeraRings, the nomogram defined by the manufacturer[21] was used for defining the modality of implant (Table 2). In the analyzed sample, only 2 cases were implanted with a single ring segment (9.52%).

Topical tobramycin and dexamethasone eye drops (TobraDex; Alcon Laboratories, Inc, Fort Worth, TX) were used postoperatively every 6 hours for 1 week and stopped. Topical lubricants were also prescribed to be applied every 6 hours for 1 month (Systane, Alcon Laboratories, Inc, Fort Worth, TX).

Follow-up Evaluation

Postoperative visits were scheduled for the first postoperative day and for months 1, 3, and 6 postoperatively. On the first postoperative day, UCVA measurement and slit-lamp examination (ICRS position and corneal integrity) were performed. We performed UCVA and BSCVA measurement, manifest refraction, slit-lamp biomicroscopy, and corneal topographic analysis at the rest of postoperative visits.

Main Outcome Measures

We collected UCVA, BSCVA, spherocylindrical refraction, keratometry, and corneal aberrometry measurements.

Statistical Analysis

The SPSS statistics software package version 10.1 for Windows (SPSS, Chicago, IL) was used for statistical analysis. Normality of all data samples was first checked by means of the Shapiro-Wilk test. When parametric analysis was possible, the Student *t* test for paired data was used for comparison between preoperative and postoperative data and the Student *t* test for unpaired data was performed to compare the outcomes of specific groups (mechanical vs femtosecond; explanted vs nonexplanted). When parametric

Table 3. Summary of Refractive Outcomes during Follow-up*

Parameter (range)	Preoperatively	1 Month	3 Months	6 Months	P (preoperatively to 6 mos)
UCVA	0.12±0.19 (0.02 to 0.70)	0.23±0.29 (0.02 to 1.20)	0.20±0.13 (0.05 to 0.40)	0.29±0.19 (0.05 to 0.60)	0.11 (Wilcoxon)
Sphere (D)	−0.74±3.41 (−9.00 to +5.00)	0.63±4.07 (−6.00 to +9.00)	0.78±3.93 (−6.00 to +8.00)	0.75±3.90 (−5.50 to +7.50)	0.02 (Paired Student *t* test)
Cylinder (D)	−5.36±1.59 (−8.25 to −2.50)	−3.53±2.06 (−8.00 to −0.75)	−3.52±2.01 (−6.50 to −1.00)	−3.21±1.80 (−6.00 to −1.00)	<0.01 (Paired Student *t* test)
SE (D)	−3.42±3.25 (−11.00 to +2.25)	−1.14±4.02 (−7.25 to +7.25)	−0.97±3.73 (−6.50 to +7.25)	−0.87±3.55 (−6.00 to +6.25)	<0.01 (Wilcoxon)
BSCVA	0.54±0.32 (0.02 to 0.95)	0.63±0.33 (0.10 to 1.20)	0.68±0.28 (0.40 to 1.20)	0.75±0.31 (0.30 to 1.20)	0.06 (Wilcoxon)
Efficacy	—	0.53±0.52 (0.02 to 1.67)	0.76±0.82 (0.08 to 3.00)	0.84±1.33 (0.11 to 5.00)	—
Safety	—	1.29±0.91 (0.23 to 3.33)	1.46±0.88 (0.44 to 3.33)	1.87±2.27 (0.78 to 9.00)	—
No. of eyes†	21	17	15	18	

BSCVA = best spectacle-corrected visual acuity; D = diopters; SE = spherical equivalent; UCVA = uncorrected visual acuity.
*The UCVA, sphere, cylinder, spherical equivalent, BSCVA, efficacy, and safety outcomes are shown. Ranges are shown in brackets below each mean value. Below each p-value the statistical test used is indicated.
†No data from explanted eyes were included after explantation to avoid biasing the final outcomes.

analysis was not possible, the Wilcoxon rank sum test was used to assess the significance of the differences between preoperative and postoperative data and the Mann-Whitney test was used for the comparison between groups. Statistical significance was considered when $P<0.05$.

Correlation coefficients (Pearson or Spearman depending if normality condition could be assumed) were used to assess the correlation between different variables. The efficacy index was calculated as the ratio of the postoperative UCVA to the preoperative best-corrected visual acuity and safety index as the ratio of the postoperative best-corrected visual acuity to the preoperative best-corrected visual acuity.

Results

A total of 21 eyes of 15 patients with a mean age of 44.19±15.78 years (range, 21–73) were analyzed in this study. There were 13 male (86.68%) and 2 female (13.33%) patients. Nine implanted eyes were right eyes (42.9%) and 12 were left eyes (57.1%). No cone opacity was observed in any case.

Refractive Outcomes

Refractive outcomes are summarized in Table 3. A statistically significant reduction was observed in spherical equivalent at 6 months which changed from a mean value of −3.84 diopters (D) preoperatively to a mean value of −0.87 D postoperatively ($P<0.01$; Wilcoxon test). This change was consistent with the significant reduction also found in sphere ($P = 0.02$; paired Student *t* test) and cylinder ($P<0.01$; paired Student *t* test; Table 3). Mean cylinder decreased from a mean preoperative value of −5.36 D to a mean postoperative value of −3.21 D. Mean sphere changed from a mean preoperative value of −0.74 D to a mean postoperative value of +0.75 D (hyperopic shift). No significant correlations were found between postoperative BSCVA and preoperative sphere ($r = -0.32$; $P = 0.31$) or cylinder ($r = 0.49$; $P = 0.10$).

No statistically significant changes were observed in UCVA at 6 months ($P = 0.11$; Wilcoxon test). On the contrary, BSCVA improved progressively during the postoperative follow-up, with a change in the limit of statistical significance at 6 months ($P = 0.06$; Wilcoxon test). At 6 months after surgery, 44.44% of eyes gained ≥2 lines of BSCVA (Fig 1). Losses of lines of BSCVA were observed in 2 eyes at 3 months (14.28%) and in 3 eyes (16.67%) at 6 months (Fig 1). In one of these eyes, ring segments were explanted at 6 months owing to the poor visual outcome.

The mean efficacy and safety indices at 6 months were 0.84±1.33 (range, 0.11–5.00) and 1.87±2.27 (range, 0.78–9.00), respectively. There was an improvement of both parameters between months 1 and 3 after surgery, although with no statistical significance (efficacy, $P = 0.07$; safety, $P = 0.99$; Wilcoxon test; Table 3).

Corneal Changes

Mean keratometry decreased significantly from 44.95 D preoperatively to 43.19 D at 6 months postoperatively ($P<0.01$; paired Student *t* test; Fig 2). A significant reduction was also observed for the steepest central curvature (K2 $P<0.01$; paired Student *t* test), but not for the flattest (K1 $P = 0.70$; paired Student *t* test; Fig 2).

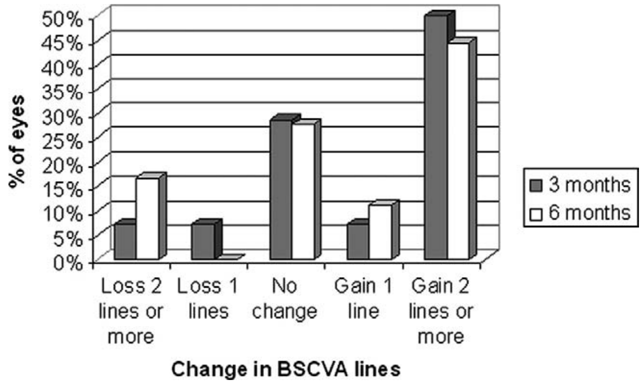

Figure 1. Changes in lines of best spectacle-corrected visual acuity (BSCVA) postoperatively. At 6 months after surgery, 44.44% of eyes gained ≥2 lines of best spectacle-corrected visual acuity.

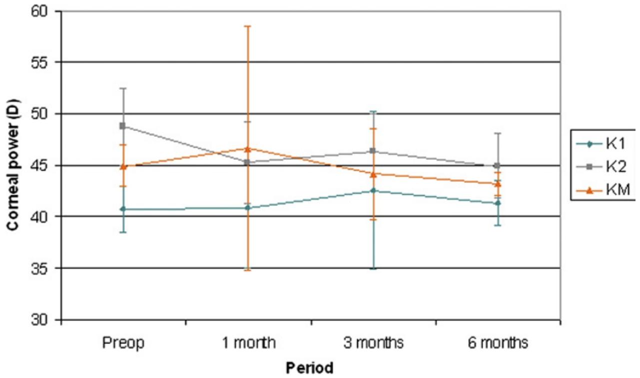

Figure 2. Changes in keratometric parameters during the follow-up: corneal dioptric power in the flattest meridian for the 3-mm central zone (K1; green line), corneal dioptric power in the steepest meridian for the 3-mm central zone (K2; gray line), and mean corneal power in the 3-mm zone (KM; orange line). A statistically significant reduction was observed in K2 and KM, but not in K1. D = diopters.

The inferosuperior asymmetry index decreased from a mean preoperative value of 10.37±11.34 D to a mean postoperative value of 7.60±10.03 D at 6 months. This change did not reach statistical significance ($P = 0.40$; Wilcoxon test). Regarding the topographic corneal parameters provided by the CSO system (Table 4), statistically significant changes were found in Q8 at 6 months (Q8 $P = 0.01$; paired Student *t* test) and in corneal astigmatism calculated in the central 3- and 6-mm zones (AST3, $P = 0.01$; AST6, $P = 0.01$; paired Student *t* test).

The K2 ($r = -0.86$; $P<0.01$) and KM ($r = -0.76$; $P<0.01$) were significantly correlated with postoperative BSCVA at 6 months, but not K1 ($r = 0.05$; $P = 0.91$). In addition, a correlation in the limit of statistical significance was found between inferosuperior asymmetry index and postoperative BSCVA ($r = -0.70$; $P = 0.05$).

Corneal Aberrations of the Anterior Surface

A detailed report of the corneal aberrometric outcomes is shown in Table 5. At 6 months after surgery, a statistically significant reduction was found in the RMS for corneal astigmatism ($P = 0.03$, Wilcoxon test) and also in the higher order residual ($P = 0.03$; paired Student *t* test) and coma-like RMS ($P = 0.03$; paired Student *t* test). However, no statistically significant changes were observed in the spherical-like RMS ($P = 0.50$; Wilcoxon test) and primary spherical aberration coefficient ($P = 0.74$; Wilcoxon test), which maintained the positive sign during all the follow-up (Table 5).

The preoperative RMS value for corneal astigmatism ($r = -0.90$; $P<0.01$) and primary spherical aberration Zernike term ($r = -0.86$; $P = 0.01$) were significantly correlated with postoperative BSCVA at 6 months. However, primary coma showed a very weak correlation with postoperative BSCVA ($r = -0.07$; $P = 0.88$).

Comparison between Mechanical and Femtosecond-Guided Procedures

Table 6 shows a comparative analysis of the preoperative and early postoperative refractive data for the 2 kind of operative procedures used in this study for corneal tunnelization, mechanical and femtosecond-assisted procedures. Sphere was increased (hyperopic shift) at 1 month postoperatively using the mechanical tunnelization, whereas it was reduced when the femtosecond technology was used (Table 6). It should be considered that statistically significant differences between mechanical and femtosecond groups were present preoperatively, with a higher percentage of cases with positive sphere in the group of eyes implanted using the mechanical dissection (Fig 3).

The cylinder was effectively reduced using both procedures. No significant differences in postoperative cylinder were found between operative techniques (Mann–Whitney test; $P>0.70$; Table 6). Comparison of aberrometric data was not feasible because all patients evaluated with the CSO topography system were operated on using the femtosecond-assisted tunnelization.

Complications

Segment ring explantation was performed in a total of 4 eyes (19.0%). In all these cases, ring segments were explanted owing to significant visual deterioration during the follow-up. In this series, all the explanted ring segments were KeraRings. Table 7 shows a comparative analysis of preoperative refractive and keratometric data of explanted and nonexplanted eyes. A difference between groups in the limit of statistical significance was only found for cylinder (Table 7). Ring extrusion or migrations were not observed in any case. No severe complications, such as infections, occurred.

Figure 4 shows the topographic changes occurred in 2 specific cases, a successful and an explanted case. As shown, ring segments induced no effect in corneal profile in the explanted case. In this specific unsuccessful case a significant against-the-rule astigmatism was present preoperatively (8 D).

Discussion

Pellucid marginal degeneration is a progressive ectatic corneal disease that can lead to a significant visual deteriora-

Table 4. Summary of Changes Found in the Costruzione Strumenti Oftalmici Topographic Corneal Parameters after Intracorneal Ring Segment Implantation

Parameter	Preoperatively	3 Months	6 Months	P (preoperatively to 6 mos)
AST3 (D)	8.68±4.95	5.38±5.10	4.77±4.42	0.01 (paired Student *t* test)
AST6 (D)	7.21±4.58	4.21±4.15	3.91±3.76	0.01 (paired Student *t* test)
Q45	0.20±0.76	−0.33±0.99	−0.56±0.87	0.11 (paired Student *t* test)
Q8	−0.04±0.63	0.28±0.65	0.24±0.65	0.01 (paired Student *t* test)
No. of eyes*	10	8	8	—

AST3 = corneal astigmatism in the 3-mm zone; AST6 = corneal astigmatism in the 6-mm zone; D = diopters; Q45 = mean asphericity for a corneal area of 4.5-mm diameter; Q8 = mean asphericity for a corneal area of 8-mm diameter.
*No data from explanted eyes were included after explantation to avoid biasing the final outcomes.

Table 5. Summary of Corneal Aberrometric Outcomes*

Parameter	Preoperatively	1 Month	3 Months	6 Months	*P* (preoperatively to 6 mos)
Total RMS (microns)	12.76±11.75 (4.36 to 42.04)	8.90±7.17 (2.41 to 24.30)	11.26±15.98 (3.23 to 47.35)	11.63±15.76 (3.35 to 47.19)	0.50 (Wilcoxon)
Astigmatism RMS (microns)	6.29±5.05 (1.66 to 17.50)	4.74±4.50 (0.83 to 15.13)	3.96±5.15 (0.39 to 14.89)	3.99±4.76 (0.28 to 14.13)	0.03 (Wilcoxon)
Primary coma RMS (microns)	1.40±0.87 (0.25 to 3.14)	1.68±1.75 (0.27 to 6.33)	1.19±0.51 (0.38 to 1.90)	1.34±0.37 (0.85 to 1.90)	0.37 (Paired Student t)
Z_4^0 (microns)	0.60±0.43 (0.11 to 1.41)	0.77±1.01 (−0.11 to 3.43)	0.50±0.55 (−0.21 to 1.31)	0.55±0.78 (−0.05 to 2.14)	0.74 (Wilcoxon)
Residual RMS (microns)	2.38±1.03 (0.83 to 4.41)	2.41±1.72 (0.40 to 6.43)	1.43±0.69 (0.75 to 2.64)	1.32±0.50 (0.62 to 1.98)	0.03 (Paired Student t)
Spherical-like RMS (microns)	1.22±0.59 (0.44 to 2.22)	1.36±1.49 (0.44 to 5.40)	0.95±0.44 (0.51 to 1.53)	0.96±0.80 (0.35 to 2.50)	0.50 (Wilcoxon)
Coma-like RMS (microns)	2.72±0.80 (1.48 to 4.14)	2.64±2.14 (0.45 to 8.00)	1.79±0.62 (0.90 to 2.59)	1.73±0.56 (0.95 to 2.45)	0.03 (Paired Student t)
No. of eyes†	10	8	8	—	

Coma-like = terms third and fifth order; primary coma = terms Z3 ± 1; primary spherical aberration = term Z_4^0; residual aberrations = all Zernike terms except $Z_3^{\pm 1}$ and Z_4^0; RMS = root mean square; spherical-like = terms 4th and 6th order.
*Changes in total RMS, astigmatism RMS, primary coma RMS, primary spherical aberration coefficient, spherical-like RMS and coma-like RMS are shown. Ranges are given in brackets below each mean value.
†No data from explanted eyes were included after explantation to avoid biasing the final outcomes.

tion. As topographic changes progress, large amounts of against-the-rule astigmatism and coma-like aberrations are induced.[22] As in other corneal ectatic disorders,[23–27] it was demonstrated that the use of ICRS is very effective for reducing astigmatism[8–10,12] and improving BSCVA.[8–14] The insertion of these ring segments (extra material) in the deep stroma induces a modification of the central corneal curvature and corneal shape. These changes are in direct proportion to the thickness of the implant and in inverse proportion to its diameter.[18] In a healthy cornea, these implants located on the midperipheral cornea generate a central flattening due to the configuration of the stromal collagen structure.[18] However, this stromal configuration is altered in the ectatic cornea, with a nonorthogonal lamellar architecture.[28,29] Relative centration and minimization of the peripheral corneal protrusion were observed after ICRS implantation in corneas with PMD.[12–14] The present study attempts to characterize the refractive and aberrometric effect of ICRS in this specific group of ectatic corneas, namely, corneas with PMD. These changes would be the result of the modification of corneal biomechanical behavior induced by the implants as a consequence of changes in the distribution of corneal peripheral lamellae.

Case reports or studies including a limited number of cases of PMD implanted with ICRS were only reported previously due to the complexity of finding such cases in clinical practice.[8–14] In this study, we collected data retrospectively from 4 ophthalmologic centers to obtain a significant number of cases. To the best of our knowledge, the current study includes the largest reported series of cases of PMD implanted with ICRS (21 eyes).

In our series, a statistically significant reduction was found in sphere and cylinder after ICRS implantation. On average, manifest astigmatism was reduced with the implants by 50%. This reduction in spherocylindrical error was consistent with changes reported in previous studies and case reports.[8–13] Furthermore, a trend toward postoperative increasing hyperopia after ICRS implantation was observed. This seems logical because it is supposed that ring segments induce a central corneal flattening and then a reduction of

Table 6. Summary of Refractive Outcomes Depending on the Operative Procedure Used for Intracorneal Ring Segment Implantation*

	Mechanical (7 eyes)		Femtosecond (14 eyes)		*P*	
Parameter	*Preoperatively*	*1 Month Postop*	*Preoperatively*	*1 Month Postop*	*Preoperatively*	*Postoperatively*
UCVA	0.07±0.07	0.14±0.16	0.17±0.27	0.29±0.34	0.73	0.17
Sphere (D)	+1.75±2.46	+5.00±3.16	−2.08±3.14	−1.19±2.85	0.01	<0.01
Cylinder (D)	−5.39±0.76	−3.25±1.70	−5.35±1.92	−3.65±2.25	0.70	0.88
SE (D)	−0.95±2.55	+3.35±3.38	−4.75±2.83	−3.01±2.52	0.01	<0.01
BSCVA	0.35±0.31	0.49±0.20	0.64±0.29	0.69±0.36	0.08	0.26

BSCVA = best spectacle-corrected visual acuity; D = diopters; SE = spherical equivalent; UCVA = uncorrected visual acuity.
*A comparative analysis of the preoperative and early postoperative data obtained using the mechanical and femtosecond-guided procedures is shown. Statistical significance of differences between groups preoperatively and postoperatively is provided in this table for each refractive parameter (all Mann–Whitney tests).

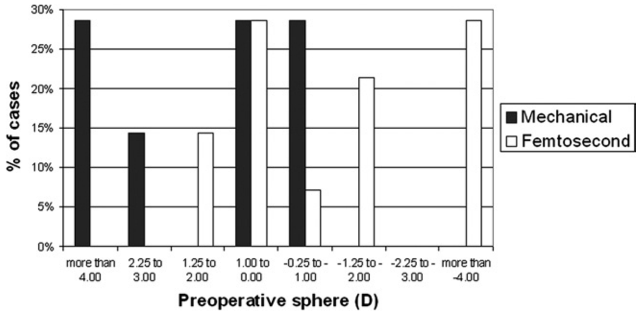

Figure 3. Distribution of preoperative sphere in the group of eyes operated using the mechanical dissection and in the group of eyes operated using the femtosecond laser technology. As shown, a higher percentage of cases with positive sphere was present in the group of eyes implanted using the mechanical dissection.

the corneal and ocular refractive power, leading theoretically to a postoperative hyperopia. However, this fact was not confirmed in our series. There were cases with myopic astigmatism and very important postoperative hyperopic shift. In addition, no significant correlation was found between preoperative sphere and postoperative visual outcome.

Mean corneal curvature was reduced significantly with the ICRS, as in previous experiences.[8–14] This flattening effect was due to the significant reduction of curvature that occurred in the steepest meridian. This fact could be explained by the combination of 2 flattening factors, the insertion of the midperipheral implants, and the weakening effect induced by corneal incision. This significant flattening was consistent with the significant reduction observed in sphere.

A reduction, although not significant, was found in inferosuperior asymmetry, which implies that ring segments were inducing a relative centration of the peripheral corneal protrusion. In addition, all corneal astigmatic coefficients (only obtained with the CSO topography system) were significantly reduced after ICRS implantation. A significant change was also found in corneal asphericity, with a trend toward oblateness (in concordance with central flattening and spherical reduction).

To the best of our knowledge, this is the first report on anterior corneal aberrometric outcomes after ICRS implantation in corneas with PMD. It should be remembered that anterior corneal aberrometric analysis is a very important tool in the clinical practice for evaluating the ocular optical quality because the first refractive interface (air–cornea) is the most important contributor to the total power of the eye because of the large difference in refractive index existing at this point. In highly aberrated corneas, such as in PMD, the corneal aberrations of the anterior corneal surface are the most important sources of optical errors in the eye. In the current study, we found that astigmatism, higher order residual, and coma-like aberrations were significantly reduced with surgery. In addition, a reduction in spherical-like aberrations was also observed, but this change did not reach significance. All these changes in corneal aberrations were consistent with the improvement in BSCVA (55.55% of eyes gaining lines of BSCVA) and also with the reduction in inferosuperior asymmetry. These findings supports the conclusions reached by Shabayek and Alió,[21] who found a significant reduction in higher order RMS for those eyes with a relatively high preoperative RMS (≥3.0 microns) and implanted with KeraRings using the femtosecond laser for corneal tunnelization. Furthermore, it should be remarked that primary spherical aberration was not modified significantly with the implants, maintaining the positive sign during all follow-up.

When comparing operative techniques for corneal tunnelization, no significant differences in cylindrical correction were found between techniques. On the contrary, the eyes implanted with the mechanical procedure experienced an increase in sphere in the early postoperative period, whereas a reduction of this parameter was observed in those eyes implanted using the femtosecond technology. A statistically significant difference between techniques was found in sphere postoperatively, but this difference was also present preoperatively. A significantly higher percentage of cases with positive sphere was present in the group of eyes implanted using the mechanical dissection. It is logical to think that an increase in sphere could have happened in these cases with hyperopic astigmatism as a consequence of the central flattening induced by the segments. However, we found several hyperopic shifts in eyes with myopic astigmatism. Therefore, we cannot extract general conclusions regarding sphere in this comparative analysis. Carrasquillo et al[30] did not find previously statistically significant differences in refractive and visual acuity outcomes between mechanical and femtosecond-guided procedures when implanting ICRS in corneas with keratoconus and post-LASIK ectasia. Differences in corneal aberrometric changes induced by each operative procedure could not be analyzed

Table 7. Comparative Analysis of Preoperative Refractive and Keratometric Data of Explanted and Nonexplanted Eyes*

Parameter	Explanted (4 eyes)	Nonexplanted (17 eyes)	P
UCVA	0.08±0.09 (0.02 to 0.15)	0.12±0.20 (0.02 to 0.70)	0.99
Sphere (D)	+1.56±2.13 (0.00 to +4.50)	−1.31±3.48 (−9.00 to +5.00)	0.10
Cylinder (D)	−6.81±1.72 (−8.25 to −4.50)	−5.00±1.38 (−8.00 to −2.50)	0.05
SE (D)	−1.84±2.81 (−4.00 to +2.25)	−3.81±3.31 (−11.00 to +2.00)	0.34
BSCVA	0.59±0.35 (0.10 to 0.95)	0.53±0.32 (0.02 to 0.95)	0.68
K1 (D)	39.64±2.09 (37.26 to 41.16)	41.01±2.24 (37.17 to 44.90)	0.66
K2 (D)	50.60±2.29 (49.15 to 53.24)	48.24±3.94 (42.00 to 55.60)	0.23
KM (D)	44.96±0.25 (44.72 to 45.21)	44.74±2.29 (40.85 to 48.40)	0.64

D = diopters; BSCVA = best-spectacle corrected visual acuity; K1 = corneal dioptric power in the flattest meridian for the 3 mm central zone; K2 = corneal dioptric power in the steepest meridian for the 3 mm central zone; KM = mean corneal power in the 3-mm zone; SE = spherical equivalent; UCVA = uncorrected visual acuity.

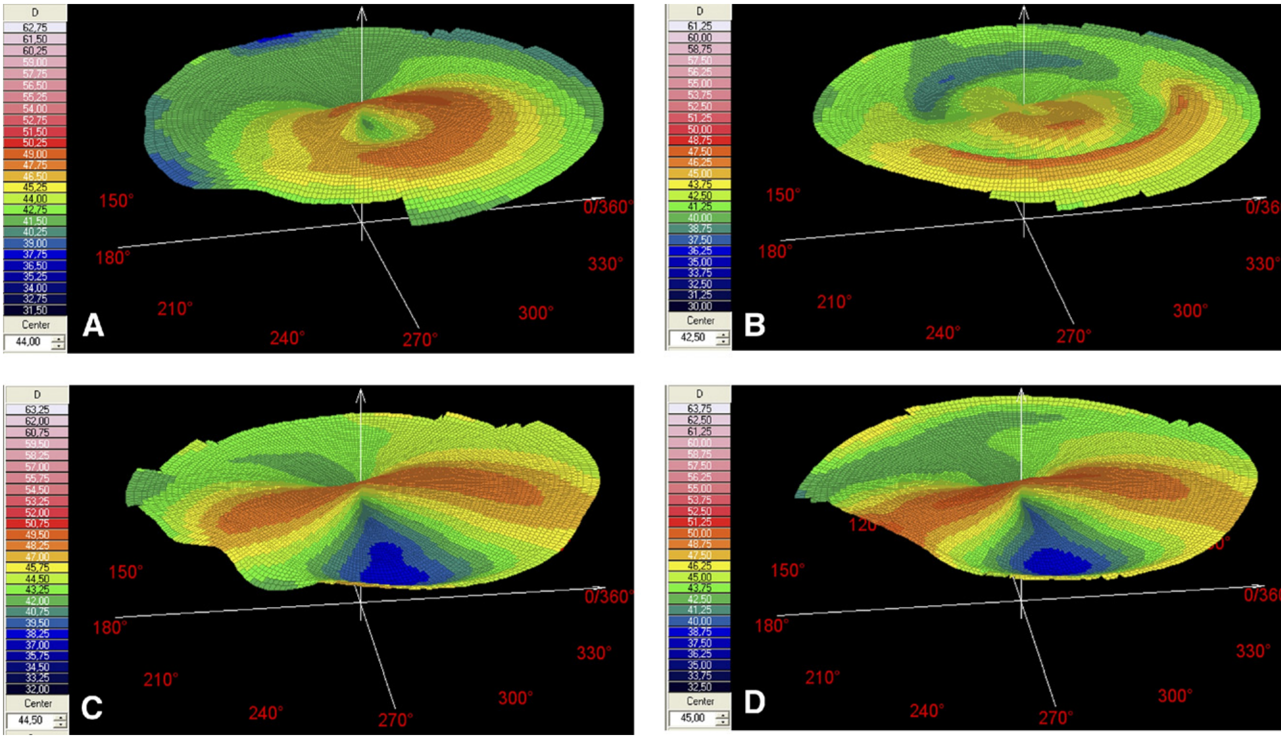

Figure 4. Topographic changes occurring after intracorneal ring segments (ICRS) implantation in a successful (**A** and **B**) and in an explanted case (**C** and **D**). The upper figures show the preoperative (**A**) and 1-month postoperative (**B**) corneal topographies in a case with a successful outcome (reduction of 3.25 diopters in cylinder and postoperative best spectacle-corrected visual acuity [BSCVA] of 0.9). The lower figures show the preoperative (**C**) and 1-month postoperative (**D**) corneal topographies in a case with an unsuccessful outcome (loss of 2 lines of BSCVA and increase in astigmatism). In this last case, ring segments were finally explanted.

because all corneas examined with the CSO system were operated on using the femtosecond technology.

No severe complications were observed during the 6-month follow-up of this study. Explantation of the ICRS was performed in 4 eyes owing to the poor visual quality outcome. A significantly higher level of astigmatism was found in this group of explanted eyes. Therefore, the magnitude of manifest astigmatism seems to have an important role in the success of this treatment option. Corneas with PMD and a significant astigmatic configuration could be associated to a specific corneal structure limiting the effect of ring segments and providing poorer outcomes. It was demonstrated that lamellar structure of ectatic corneas is different compared with normal corneas with regions of more highly aligned collagen intermixed with regions in which there was little aligned collagen (distortion of the orthogonal lamellar matrix).[28,29] Probably in these cases with PMD and a significant astigmatic configuration the distribution of corneal lamellae is highly irregular with poor or unpredictable response to a peripheral addition of tissue. In any case, future studies are required to understand how the configuration of ectatic corneal structure is modified or altered with the ICRS.

Furthermore, we found some factors correlated with the postoperative BSCVA outcome. The RMS for corneal astigmatism and primary spherical aberration were found to be in linear relation with postoperative BSCVA. Specifically, the larger the preoperative RMS for astigmatism or spherical aberration term, the poorer the postoperative visual outcomes was. Therefore, corneal and manifest astigmatism seem to be limiting factors for a good visual prognosis after ICRS implantation. All these limiting factors should be considered before any ICRS implantation in corneas with PMD to establish the convenience of the operative procedure.

In conclusion, ICRS implantation—Intacs or KeraRings—is an effective option for the treatment of 2nd-order and higher aberrations in corneas with PMD. Anterior corneal higher order aberrations (higher order residual and coma-like) are reduced significantly after ICRS implantation in concordance with an improvement in BSCVA. The magnitude of corneal astigmatism and primary spherical aberration seem to be important limiting factors for a good visual outcome with this operative therapeutic option. In this study, only a 6-month follow-up could be completed. Future studies of the outcomes with ICRS in corneas with PMD in the long term are required to corroborate the stability of these implants.

References

1. Rabinowitz YS. Keratoconus. Surv Ophthalmol 1998;42:297–319.
2. Sridhar MS, Mahesh S, Bansal AK, Rao GN. Superior pellucid marginal corneal degeneration. Eye 2004;18:393–9.

3. Maguire LJ, Klyce SD, McDonald MB, Kaufman HE. Corneal topography of pellucid marginal degeneration. Ophthalmology 1987;94:519–24.
4. Lee BW, Jurkunas UV, Harissi-Dagher M, et al. Ectatic disorders associated with a claw-shaped pattern on corneal topography. Am J Ophthalmol 2007;144:154–6.
5. Ozbek Z, Cohen EJ. Use of intralimbal rigid gas-permeable lenses for pellucid marginal degeneration, keratoconus, and after penetrating keratoplasty. Eye Contact Lens 2006;32:33–6.
6. Dominguez CE, Shah A, Weissman BA. Bitoric gas-permeable contact lens application in pellucid marginal degeneration. Eye Contact Lens 2005;31:241–3.
7. Raizada K, Sridhar MS. Nomogram for spherical RGP contact lens fitting in patients with pellucid marginal corneal degeneration (PMCD). Eye Contact Lens 2003;29:168–72.
8. Ertan A, Bahadir M. Management of superior pellucid marginal degeneration with a single intracorneal ring segment using femtosecond laser. J Refract Surg 2007;23:205–8.
9. Ertan A, Bahadir M. Intrastromal ring segment insertion using a femtosecond laser to correct pellucid marginal corneal degeneration. J Cataract Refract Surg 2006;32:1710–6.
10. Mularoni A, Torreggiani A, di Biase A, et al. Conservative treatment of early and moderate pellucid marginal degeneration: a new refractive approach with intracorneal rings. Ophthalmology 2005;112:660–6.
11. Barbara A, Shehadeh-Masha'our R, Zvi R, Garzozi HJ. Management of pellucid marginal degeneration with intracorneal ring segments. J Refract Surg 2005;21:296–8.
12. Akaishi L, Tzelikis PF, Raber IM. Ferrara intracorneal ring implantation and cataract surgery for the correction of pellucid marginal corneal degeneration. J Cataract Refract Surg 2004;30:2427–30.
13. Kymionis GD, Aslanides IM, Siganos CS, Pallikaris IG. Intacs for early pellucid marginal degeneration. J Cataract Refract Surg 2004;30:230–3.
14. Rodriguez-Prats J, Galal A, Garcia-Lledo M, et al. Intracorneal rings for the correction of pellucid marginal degeneration. J Cataract Refract Surg 2003;29:1421–4.
15. Javadi MA, Karimian F, Hosseinzadeh A, et al. Lamellar crescentic resection for pellucid marginal corneal degeneration. J Refract Surg 2004;20:162–5.
16. Rasheed K, Rabinowitz YS. Surgical treatment of advanced pellucid marginal degeneration. Ophthalmology 2000;107:1836–40.
17. MacLean H, Robinson LP, Wechsler AW. Long-term results of corneal wedge excision for pellucid marginal degeneration. Eye 1997;11:613–7.
18. Patel S, Marshall J, Fitzke FW III. Model for deriving the optical performance of the myopic eye corrected with an intracorneal ring. J Refract Surg 1995;11:248–52.
19. González Pérez J, Cerviño A, Giraldez MJ, et al. Accuracy and precision of EyeSys and Orbscan systems on calibrated spherical test surfaces. Eye Contact Lens 2004;30:74–8.
20. Alió JL, Artola A, Hassanein A, et al. One or 2 Intacs segments for the correction of keratoconus. J Cataract Refract Surg 2005;31:943–53.
21. Shabayek MH, Alió JL. Intrastromal corneal ring segment implantation by femtosecond laser for keratoconus correction. Ophthalmology 2007;114:1643–52.
22. Kamiya K, Hirohara Y, Mihashi T, et al. Progression of pellucid marginal degeneration and higher-order wavefront aberration of the cornea. Jpn J Ophthalmol 2003;47:523–5.
23. Coskunseven E, Kymionis GD, Tsiklis NS, et al. One-year results of intrastromal corneal ring segment implantation (KeraRing) using femtosecond laser in patients with keratoconus. Am J Ophthalmol 2008;145:775–9.
24. Kymionis GD, Siganos CS, Tsiklis NS, et al. Long-term follow-up of Intacs in keratoconus. Am J Ophthalmol 2007;143:236–44.
25. Ertan A, Colin J. Intracorneal rings for keratoconus and keratectasia. J Cataract Refract Surg 2007;33:1303–14.
26. Kymionis GD, Tsiklis NS, Pallikaris AI, et al. Long-term follow-up of Intacs for post-LASIK corneal ectasia. Ophthalmology 2006;113:1909–17.
27. Alió JL, Salem TF, Artola A, Osman A. Intracorneal rings to correct corneal ectasia after laser in situ keratomileusis. J Cataract Refract Surg 2002;28:1568–74.
28. Meek KM, Tuft SJ, Huang Y, et al. Changes in collagen orientation and distribution in keratoconus corneas. Invest Ophthalmol Vis Sci 2005;46:1948–56.
29. Daxer A, Fratzl P. Collagen fibril orientation in the human corneal stroma and its implication in keratoconus. Invest Ophthalmol Vis Sci 1997;38:121–9.
30. Carrasquillo KG, Rand J, Talamo JH. Intacs for keratoconus and post-LASIK ectasia: mechanical versus femtosecond laser-assisted channel creation. Cornea 2007;26:956–62.

Footnotes and Financial Disclosures

Originally received: October 2, 2008.
Final revision: May 26, 2009.
Accepted: June 2, 2009.
Available online: July 29, 2009. Manuscript no.: 2008-1177.

[1] Vissum/Instituto Oftalmológico de Alicante, Spain.

[2] Departamento de Óptica, Farmacología y Anatomía, Universidad de Alicante, Spain.

[3] Division of Ophthalmology, Universidad Miguel Hernández, Alicante, Spain.

[4] Vissum Albacete, Spain.

[5] Vissum Sevilla, Spain.

[6] Fundación Andaluza de Imagen, Color y Óptica, Sevilla, Spain.

[7] Ain Shams University, Cairo, Egypt.

[8] Dunya Eye Hospital, Istanbul, Turkey.

Financial Disclosure(s):
The authors have no proprietary or commercial interest in any materials discussed in this manuscript.

Supported in part by a grant from the Spanish Ministry of Health, Instituto Carlos III, Red Temática de Investigación Cooperativa en Salud "Patología ocular del envejecimiento, calidad visual y calidad de vida", Subproyecto de Calidad Visual (RD07/0062).

Correspondence:
Jorge L. Alio, MD, PhD, Avda de Denia s/n, Edificio Vissum, 03016 Alicante, Spain. E-mail: jlalio@vissum.com.