

Vector Analysis of Astigmatism in Keratoconic Eyes After Combined Intrastromal Corneal Ring Segments Implantation and Collagen Cross-Linking

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Purpose: To analyze astigmatic changes after intrastromal corneal ring segments (ICRSs) implantation accompanied by corneal collagen cross-linking (CXL) in keratoconic eyes using the Alpíns vectorial method.

Patients and Methods: Twenty-eight eyes of 18 patients with keratoconus were included in this retrospective non-comparative study. All patients had combined femtosecond laser-assisted Keraring implantation and CXL, and completed at least 2 years of follow-up. Both manifest and corneal astigmatic changes were analyzed using the Alpíns vectorial parameters based on 3 vectors; target induced astigmatism (TIA), surgically induced astigmatism (SIA) and difference vector (DV).

Results: Regarding analysis of manifest astigmatism, the TIA arithmetic mean was 5.22 D while the vector mean was 3.13 D Ax 173. The SIA arithmetic mean was 5.41 D while the vector mean was 2.38 D Ax 173. The DV arithmetic mean was 2.10 D while the vector mean was 0.75 D Ax 175. Regarding analysis of corneal astigmatism, the TIA arithmetic mean was 5.22 D while the vector mean was 3.13 D Ax 173. The SIA arithmetic mean was 5.23 D while the vector mean was 1.8 D Ax 12. The DV arithmetic mean was 4.28 D while the vector mean was 2.04 D Ax 157.

Conclusion: Vector analysis of manifest and corneal astigmatism in keratoconic eyes with previous ICRS and CXL reveals more accuracy and predictability of manifest refraction in calculating SIA.

Keywords: Alpíns method, astigmatic correction in keratoconus, kerarings, vector analysis

Introduction

Keratoconus is a relatively common eye condition in upper Egypt where the climate is hot and dry.^{1,2} It is a type of corneal ectasia characterized by thinning of the corneal stroma which assumes a conical shape resulting in progressive deterioration of vision secondary to induced myopia, astigmatism, and high order aberrations.

The onset of keratoconus is usually around puberty but develops earlier in children with chronic eye rubbing. It then shows variable progression before it arrests in the third or fourth decades in most cases. Keratoconus is a bilateral disease but one eye may suffer more than the other.^{3,4}

The management of keratoconus depends on many factors such as age of the patient, stage of keratoconus and presence of other eye diseases. The treatment options include non-surgical lines such as glasses in early cases and hard contact lenses in mild and moderate cases. The surgical options include collagen

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cross-linking, intrastromal corneal ring segments (ICRS), phakic intraocular lenses, and keratoplasty.

Corneal collagen cross-linking (CXL) has become the standard treatment of keratoconus which aims at strengthening the stromal collagen by induction of collagen bonds using ultraviolet light which is applied to riboflavin-soaked cornea. CXL is recommended for mild and moderate stages to halt the progression of ectasia while the visual rehabilitation is done by using glasses, contact lenses or surgical procedures.^{5,6}

ICRS such as Kerarings are increasingly used in the management of non-advanced keratoconus in order to improve the vision by inducing central flattening and regularization of the corneal surface. Their accuracy improved much when assisted by femtosecond laser for tunnel creation. ICRS have been proven to be safe and effective in the management of different forms of corneal ectasia including keratoconus, pellucid marginal degeneration, and iatrogenic ectasia.⁷

The combination of cross-linking with ICRS implantation in the same session has been proven to increase the efficacy of cross-linking by enhancing the penetration of riboflavin through the freshly made tunnels for ICRS implantation.⁸

The conventional description of spherocylindrical errors as sphere, cylinder, and axis gives rise to several problems in statistical analysis as these 3 parameters are not independent. The main problem arises from cylinder axis; rotation of a high power cylinder results in a larger effect than the same rotation of a lower power cylinder.

Vectors are mathematical descriptors of the physics of motion which combine values for magnitude and direction. Astigmatism can be thought of as a vector with a magnitude and an axis. Complete and accurate analysis of any surgery that aims at correcting astigmatism would require analysis of changes in both magnitude and axis of cylinder, ie, vectorial character of astigmatism.^{9,10}

There are 2 major methods for vector analysis of astigmatism; Thibos method which is perfect in descriptive analysis of astigmatism and Alpains method which focuses on analyzing changes in astigmatism or its surgical correction.

The aim of this study was to detect changes in astigmatism in keratoconic eyes after combined intrastromal corneal ring segments implantation and collagen cross-linking using vector analysis by Alpains method.

Patients and Methods

This retrospective study included 28 eyes of 18 patients with keratoconus who underwent combined femtosecond

laser-assisted Keraring implantation and trans-epithelial accelerated collagen cross-linking in the period from April 2016 to March 2019 at the ophthalmology department of Sohag University Hospital where the patients were recruited and followed in collaboration with Sohag Future Femtolasik center where the surgery was done.

The study followed the declaration of Helsinki and approval was obtained from the ethics committee of Sohag faculty of medicine. Written informed consent was obtained from the patients to review their medical records. The consent was obtained from the parents in patients less than 18 year old.

The inclusion criteria at the time of surgery were patients with progressive keratoconus (one diopter increase in the steepest keratometric value over a 6-month period), stage 2 or 3 keratoconus (Amsler-Krumeich classification), best-corrected visual acuity (BCVA) less than 6/18, clear central cornea and with corneal thickness at the planned site of Keraring implantation of at least 450 μm . After surgery, all patients completed a follow-up period of at least 2 years.

The exclusion criteria at the time of surgery included patients with suspect, mild or advanced keratoconus, corneal opacity, previous ocular surgery or active ocular infection or inflammation.

Preoperative and postoperative assessment of the patients included log MAR uncorrected visual acuity (UCVA) and BCVA, manifest and cycloplegic refraction, slit lamp and fundus examination, and intraocular pressure measurement. A Sirius Scheimflug imaging camera (CSO, Italy) was used to confirm diagnosis of keratoconus in addition to staging of the disease and post-operative follow-up.

Vector analysis of the astigmatism was done using the Alpains method: ASSORT software (ASSORT Pty. Ltd.) was used for analysis of both manifest and corneal astigmatism. The following vectors were calculated; target induced astigmatism (TIA) which represents the intended change in astigmatism, surgically induced astigmatism (SIA) which represents the actual change achieved in astigmatism, and difference vector (DV) which represents the extra change required to achieve the intended target. In addition, 2 values obtained from the relationships between vectors were calculated; Correction index (CI) which is the ratio between SIA magnitude and TIA magnitude (it is ideally 1.0, values more than one indicate over-correction while values less than one indicate under-correction), and angle of error (AE) which is the angle described by SIA and TIA (AE is positive if the axis of achieved correction

is counter-clockwise to axis of intended correction and is negative if the achieved correction is clockwise to intended axis).

Surgical procedure: the surgery was done in all cases under topical anesthesia (Benox, Eipico, Egypt) by 2 surgeons:

(A) femtosecond laser-assisted Keraring implantation: the Keraring nomogram provided by the manufacturer, Mediphacos, was used for the selection of suitable segments. We start by asking the patient to look at the flashing light of the microscope to mark the center of the cornea. The suction ring of the femtosecond laser (iFS Advanced femtosecond laser, Abbott, Chicago, Illinois, USA) is then applied to create the round corneal tunnel and the incision at the steepest keratometry meridian. Then the segments are inserted after assuring patency of the tunnel using a pusher.

(B) Trans-epithelial accelerated corneal cross-linking: was done immediately after insertion of segments by dripping dextran-free hypo-osmolar riboflavin drops containing benzalkonium chloride (ParaCel, Avedro, Waltham, Massachusetts, USA) onto the cornea to increase epithelium permeability every 90 seconds for a duration of 4.5 mins. After that benzalkonium chloride-free riboflavin drops (VibexXtra, Avedro, Waltham, Massachusetts, USA) were dripped every 90 seconds for a duration of 6 mins. Then the accelerated CXL (The KXL accelerated CXL System, Avedro, Waltham, Massachusetts, USA) is applied to the cornea for a duration of 160 seconds using a power of 45 mW/cm² with a pulsed mode (2 seconds on/ 1 second off) and a total energy radiated of 7.2 J/cm². Then a contact lens is inserted and left one week.

Postoperative Treatment

The systemic treatment included analgesics to control pain. The eye drops included the antibiotic moxifloxacin which was dripped hourly for the first 24 hrs, and then reduced to 5 times daily for 10 days, the steroid prednisolone which was dripped hourly for the first 24 hrs, then reduced to 5 times daily for 7 days, and then decreased gradually over one month, and the artificial tears which were dripped hourly during the first 24 hrs and then reduced to 5 times daily for one month.

Statistical Analysis

Data were analyzed using IBM SPSS Statistics for Windows version 20.0. (SPSS Inc, Chicago, Illinois, USA). All data were quantitative and so expressed as means $\pm$ standard

deviation and its normality was checked by the Kolmogorov–Smirnov test. For normally distributed data (e.g, keratometry values) The paired samples *t*-test was used to compare the means while the nonparametric Wilcoxon Signed Ranks test was used for data which were not normally distributed (e.g, UCVA and BCVA). In all statistical tests, a 5% level was chosen as a level of significance. Simple linear regression model of SIA magnitude versus TIA magnitude was calculated.

Results

Twenty-eight eyes of 18 patients (14 males and 4 females) with keratoconus who underwent combined femtosecond laser-assisted Kerarings implantation and trans-epithelial accelerated collagen cross-linking were included in this retrospective non-comparative study. The age ranged from 14 to 31 years with a mean of 18.6 ± 1.9 years. Ten patients underwent bilateral surgery while the remaining 8 patients underwent a unilateral surgery.

On comparing the preoperative and postoperative parameters, we noted significant improvement (*p*-value < 0.001) in the mean visual, refractive, and topographic parameters. The UCVA (log MAR) decreased from 0.88 ± 15 preoperatively to 0.64 ± 13 postoperatively while the BCVA (log MAR) decreased from 0.59 ± 17 to 0.35 ± 14 . The spherical error decreased from -6.55 ± 3.79 preoperatively to -2.49 ± 2.36 postoperatively, while the cylindrical error decreased from -6.12 ± 2.02 to -2.71 ± 1.35 and the spherical equivalent decreased from -9.61 ± 3.97 to -3.50 ± 2.87 . The preoperative and postoperative refraction of individual cases was shown in Table 1. Regarding topographic parameters; the preoperative values of K1, K2, and Kmax were 46.95 ± 3.46 , 51.71 ± 3.39 , and 61.03 ± 4.23 respectively while their postoperative values were 44.19 ± 3.37 , 47.35 ± 3.45 , and 56.09 ± 4.44 respectively.

Regarding analysis of manifest or refractive astigmatism (Figure 1); the TIA arithmetic mean was 5.22 D while the vector mean was 3.13 D Ax 173. The SIA arithmetic mean was 5.41 D while the vector mean was 2.38 D Ax 173. The DV arithmetic mean was 2.10 D while the vector mean was 0.75 D Ax 175. The correction index geometric mean was 1.03 and the percentage of eyes with angle of error from +5 to -5 degrees was 50%.

Simple linear regression model between SIA magnitude versus TIA magnitude revealed that $Y = 0.71X + 1.69$ with $R^2 = 0.41$.

Regarding analysis of corneal astigmatism (Figure 2); the TIA arithmetic mean was 5.22 D while the vector mean was

Table I Preoperative and Postoperative Refraction of the 28 Eyes

Case ID	Preop Sphere (D)	Preop Cylinder (D)	Preop Axis (°)	Postop Sphere (D)	Postop Cylinder (D)	Postop Axis (°)
1	-18.00	-11.00	8	-16.00	-2.00	110
1	-6.00	-5.00	155	-3.00	-3.00	49
2	-10.00	-7.00	34	-6.50	-4.00	129
2	-6.00	-8.00	143	-2.00	-3.00	150
3	-7.00	-10.00	26	-1.00	-3.50	171
3	-3.00	-7.00	143	0.00	-1.50	54
4	-4.00	-5.00	155	-1.50	-3.00	51
4	-6.00	-7.00	110	-4.00	-2.00	11
5	-5.00	-11.00	168	-1.00	-3.00	2
6	-1.50	-5.00	15	0.00	-1.00	167
6	-7.50	-8.00	172	-3.00	-1.00	149
7	-2.00	-8.00	180	0.00	-1.50	10
7	-1.50	-7.00	177	0.00	-2.00	165
8	-10.00	-6.00	59	-6.00	-3.00	162
9	-6.00	-4.00	171	-1.50	-1.00	170
9	-2.50	-2.00	20	0.00	-0.25	155
10	-4.00	-11.00	15	-1.25	-3.00	114
11	-14.00	-10.00	17	-10.00	-8.00	180
12	-9.00	-3.00	137	-2.00	-2.00	50
13	-4.00	-2.50	46	0.00	-1.00	90
13	-4.00	-5.00	150	-1.00	-0.50	93
14	-2.00	-2.00	14	0.00	-2.00	94
15	-1.00	-3.00	18	0.00	-0.50	106
15	-2.00	-9.00	165	0.00	-1.50	165
16	-4.00	-5.00	120	-1.50	-3.00	50
16	-5.00	-5.00	140	-3.00	-3.00	160
17	-9.00	-6.00	148	-5.00	-3.00	162
18	-2.00	-9.00	171	-1.00	-3.50	20

3.13 D Ax 173. The SIA arithmetic mean was 5.23 D while the vector mean was 1.8 D Ax 12. The DV arithmetic mean was 4.28 D while the vector mean was 2.04 D Ax 157. The correction index geometric mean was 0.99 and the percentage of eyes with angle of error from 5 to 15 degrees was 29%.

Simple linear regression model between SIA magnitude versus TIA magnitude revealed that $Y=0.28X+3.78$ with $R^2=0.07$.

Discussion

The use of ICRS for correction of spherocylindrical errors in keratoconus is challenging with many cases showing postoperative under-correction or over-correction. The adjustments of the nomograms used to select the suitable ring segments for different cases of keratoconus require accurate analysis of preoperative and postoperative refraction in every case.

Regarding the spherical error, the analysis is quite simple and direct in contrast to the cylindrical error

which is difficult and requires the use of vector analysis for better understanding of the changes induced by the ICRS.

Alpins method of vector analysis is recommended to detect the effectiveness of any type of astigmatic treatment. This method is readily understood by using a golfing analogy because a golf putt resembles a vector which creates corneal steepening or flattening, possessing both magnitude and direction.

In this study, we used the Alpins vectorial analysis to detect the efficacy of combined femtosecond laser-assisted Keraring implantation and trans-epithelial accelerated collagen cross-linking in correcting the cylindrical error in keratoconic eyes. On comparing the changes in manifest and corneal astigmatism, we noted that both revealed undercorrection and misalignment, however the degree of inaccuracy was more apparent in corneal astigmatism (DV arithmetic mean of 4.28 D and vector mean of 2.04 D Ax 157) versus DV arithmetic mean of 2.10 D and vector

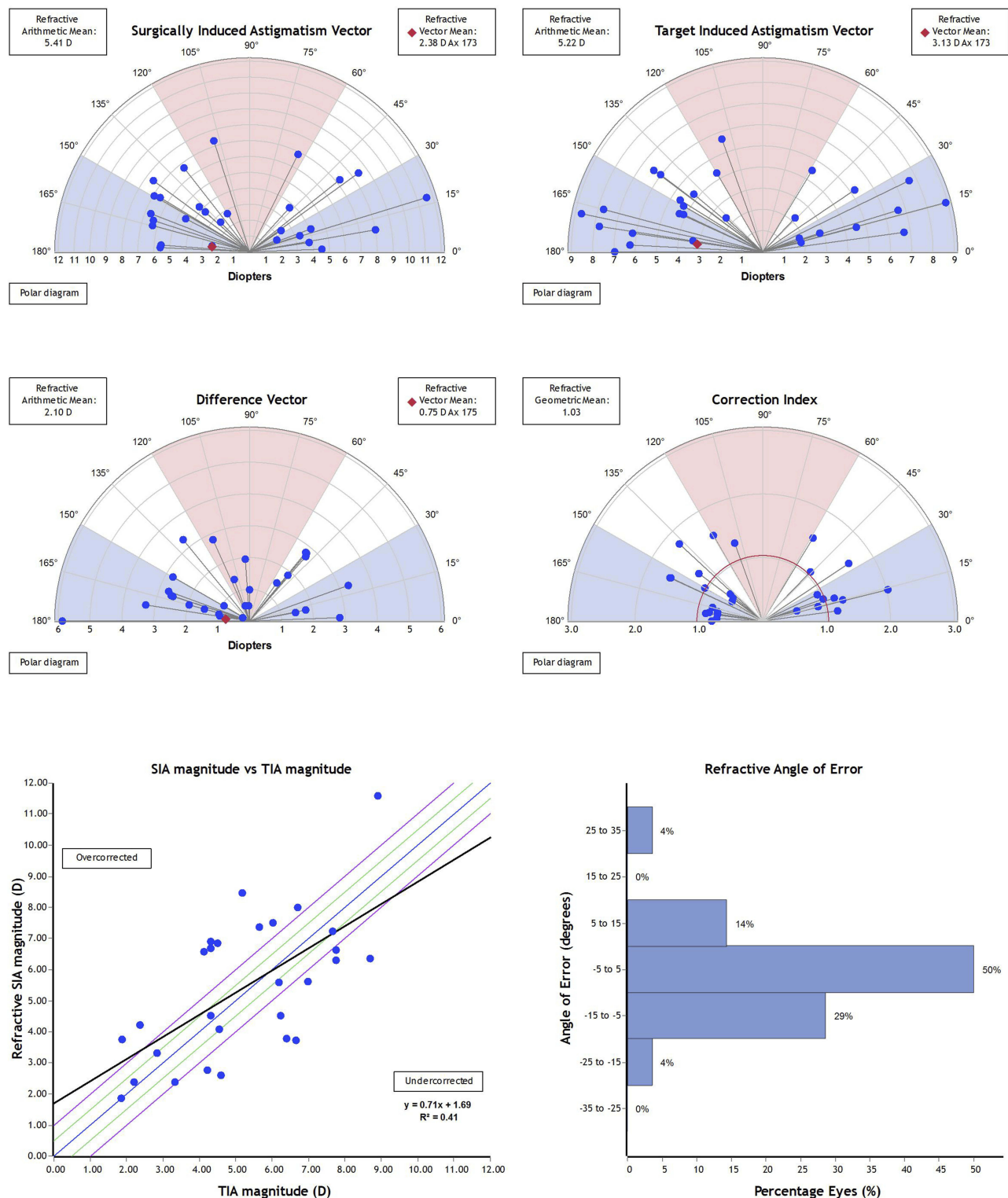


Figure 1 Overview of Alpins vectorial analysis of refractive astigmatism.

mean of 0.75 D Ax 175 in manifest astigmatism. Also, the linear regression model revealed that the predictability of SIA from TIA is relatively better in manifest ($R^2 = 0.41$) than corneal ($R^2 = 0.07$) astigmatism.

Pinero et al¹¹ used the Alpins method to analyze the corneal astigmatic changes after ICRS implantation in keratoconic eyes and found that there was a trend toward undercorrection and misalignment justifying the need for

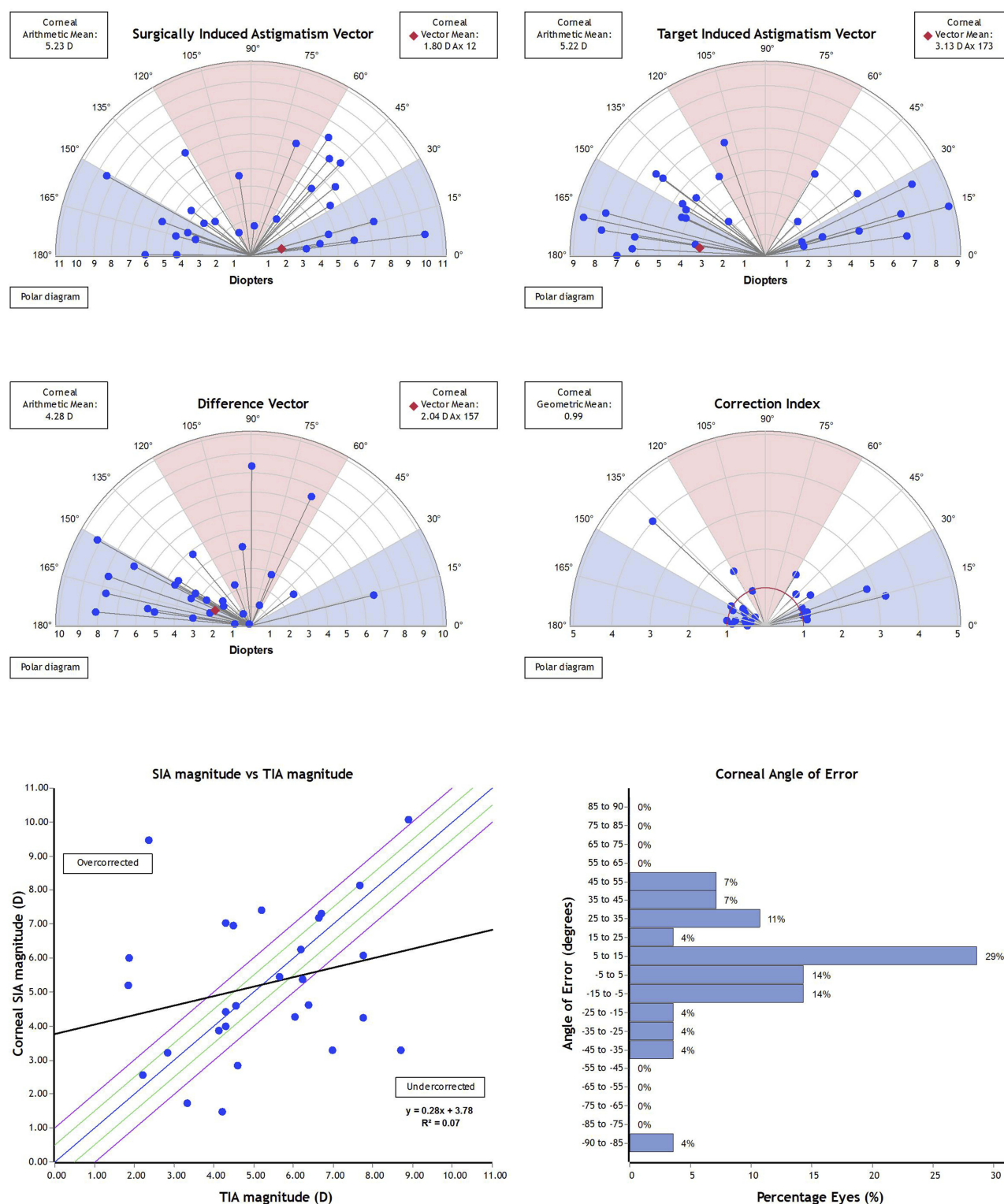


Figure 2 Overview of Alpins vectorial analysis of corneal astigmatism.

nomogram adjustments. Another study by Pinero et al¹² retrospectively evaluated the effect of cross-linking on 16 keratoconic eyes of 12 patients previously treated by ICRS (14 eyes with Kerarings and 2 eyes with Intacs). They

analyzed the corneal astigmatic changes by Alpins vectorial method and noted poor predictability of cross-linking in generating efficacious visual, refractive or topographic changes in these patients.

Unlike these 2 studies, the current study analyzed both corneal and manifest astigmatism and found that the 2 methods yielded different results, however the analysis of corneal astigmatism, in spite of being objective, is associated with less accuracy and less predictability in calculating the SIA than manifest astigmatism.

In a previous study, Abozaid et al¹³ performed vector analysis of astigmatism before and after Kerarings plus CXL in children with keratoconus and vernal keratoconjunctivitis. They used Thibos method for analysis of manifest astigmatism and noted reduction in the mean J0 value indicating improvement in “with-the-rule” astigmatism. Unlike that study, we used Alpains method for vectorial analysis which is more useful than Thibos method in evaluating changes induced by surgery.

Rocha et al¹⁴ compared implantation of 2 types of ICRS in keratoconus (Kerarrings versus Ferrara ring). Corneal and manifest astigmatic changes were analyzed using the double-angle polar plot and the Alpains vectorial method. Both groups showed improvement in visual, keratometric and aberrometric data. Their Alpains vectorial analysis revealed better performance (although statistically insignificant) in the Keraring group. The double-angle polar plot analysis showed a statistically significant difference only in tomographic astigmatism with more significant improvement in the Keraring group. Unlike their study, our study was non-comparative and all cases received Kerarrings.

Fernández-Vega-Cueto et al¹⁵ evaluated the outcomes of implanting ICRS in central “bow-tie”- shaped keratoconus. They used Ferrara rings in 20 eyes of 18 patients with 20 eyes completing one year of follow-up and 14 eyes completing 3 years of follow-up. Using Thibos power vector method, they found that the percentage of eyes with a refractive cylinder $\leq -1.5D$ increased from 25% preoperatively to 100% 6 months postoperatively. Unlike that study, the current study used Kerarrings ICRS in different types of keratoconus and analyzed astigmatism by the Alpains method.

Conclusion

The use of manifest astigmatism in Alpains vectorial analysis of changes after combined ICRS and CXL in keratoconus is more beneficial and more predictable than

corneal astigmatism which justifies paying more attention to the accurate assessment of preoperative manifest astigmatism for better outcome of such procedures.

Disclosure

The authors report no conflicts of interest in this work.

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