# Computational Models for Optimization of the Intrastromal Corneal Ring Choice in Patients With Keratoconus Using Corneal Tomography Data

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## ABSTRACT

**PURPOSE:** To evaluate the predictability of asphericity and average keratometry in patients with keratoconus after implantation of intrastromal corneal ring segments (ICRS) using artificial intelligence.

**METHODS:** This study included 209 eyes of 160 patients with keratoconus (grades I, II, and III) who had ICRS implanted. The 160 arc length Ferrara ICRS was implanted in all patients. ICRS thickness varied from 150 to 250 $\mu$m. Pentacam (Oculus Optikgeräte, Wetzlar, Germany) corneal tomography parameters, clinical data, and ICRS data formed the basis of the 39 studied parameters. Linear regression was used to create the models.

**RESULTS:** The best mean absolute error value found was 0.19 for asphericity and was 1.18 for mean keratometry. Comparing the mean absolute error values of the nomogram with the average absolute error of the algorithm, there was an improvement of 0.11 for asphericity and 0.09 for mean keratometry in relation to the current nomogram.

**CONCLUSIONS:** The current study showed that the use of computational models could lead to more accurate results and contribute to better surgical decision-making to improve the clinical outcomes in patients with keratoconus implanted with ICRS.


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Intrastromal corneal ring segments (ICRS) have been used to treat ectatic corneal diseases by reducing corneal steepening, decreasing irregular astigmatism, and improving visual acuity. Moreover, as an alternative surgical procedure, they can delay or avert the need for corneal transplantation in patients with clear corneas and contact lens intolerance.[1-3]

Several nomograms were proposed for ICRS implantation in keratoconic eyes. Some are intuitive and based on empirical data (manifest refraction and topographic profile only). Good visual and refractive outcomes have been reported with the use of all nomograms. However, there are cases in which there is minimal keratometry reduction or no keratometric effect despite performing the surgical planning exactly as indicated by the nomogram. Accordingly, and taking into account biomechanical and aberrometric parameters,[4] there is a need for readjusting them to attain more predictable outcomes.

The purpose of this study was to evaluate the predictability of asphericity and average keratometry in eyes with keratoconus after ICRS implantation by creating computational models based on machine learning and the use of corneal tomography data.

## PATIENTS AND METHODS

### Technical Procedures

A total of 209 eyes in 160 patients with keratoconus who underwent Ferrara ICRS implantation were retrospectively assessed between 2012 and 2015. The mean age was 28 ±

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*Dr. Ferrara has a proprietary interest in the Ferrara ring. The remaining authors have no financial or proprietary interest in the materials presented herein.*

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7.56 years (range: 18 to 49 years) and there were 91 (56.87%) men and 69 (43.12%) women. According to the Krumeich classification,[5] the patients had oval keratoconus stages I, II, and III. Follow-up time ranged from 5 to 72 months, with median follow-up of 28 months.

The main recommendation for ICRS implantation was for patients who had contact lens intolerance or unsatisfactory visual acuity with contact lenses. Patients with advanced keratoconus (stage IV), significant opacity at the apex of the cone, scarring, hydropsis, corneal thickness less than 300 µm at the ICRS track, severe atopy, or systemic or local infection were excluded from the study.

Data were collected from patients' medical records. All patients had undergone a thorough ophthalmological examination, which included their personal health records, assessment of corrected visual acuity, biomicroscopy, and funduscopy. Additionally, patients had corneal topography examinations using the EyeMap system (Alcon Laboratories, Inc., Fort Worth, TX) and corneal tomography (Pentacam; Oculus Optikgeräte, Wetzlar, Germany). After the examination and a thorough discussion of the risks and benefits of the surgery, the patients signed an informed consent form based on the tenets of the Declaration of Helsinki.

All patients had their ICRS implanted by the same surgeon (PF) using the standard manual technique. All cases had ectasia with oval cones and one or two 160° arc ring segments of variable thickness (150, 200, and 250 µm) were implanted. The intrastromal segments were implanted according to the fourth generation Ferrara ring nomogram, which is based on corneal asphericity.[6] There were no intraoperative complications during the procedures. After the surgery, dexamethasone 0.1% (Maxidex; Alcon, Laboratories, Inc.) and moxifloxacin 0.5% (Vigamox; Alcon Laboratories, Inc.) eye drops were used four times a day for 2 weeks. Patients were told not to rub their eyes and to make frequent use of preservative-free artificial tears.

### Statistical Analysis

Our aim was to improve the predictability of postoperative asphericity and average keratometry by increasing the accuracy of the current nomogram through the construction of computer models based on machine learning. The study was performed in four distinct phases.

***First Phase.*** A database was prepared comprising 39 parameters, 37 of which had been obtained with the Pentacam. Patient age and characteristics of the Ferrara ICRS were also taken into account. The 37 Pentacam parameters were chosen for having had statistically significant postoperative changes ($P < .05$) based on the Wilcoxon test (**Table A**, available in the online version of this article).

ICRS features were converted into one numerical variable based on thickness and the presence of one or two segments. Based on these features, nine groups were created (**Table 1**).

***Second Phase.*** The nomogram error was assessed by calculating the difference between asphericity variation and average keratometry, as predicted by the Ferrara nomogram (**Table 2**), and the actual preoperative and postoperative variation of the sample.

***Third Phase.*** The 39 parameters were input into the machine learning algorithms to create a predictive model for average keratometry and asphericity. The linear regression algorithm was used for analysis of data. The aim was to select the best parameters and thus automatic selection techniques were employed. RapidMiner software (version 5.3; RapidMiner, Boston, MA) was used for creation of the computational models. Sample validation was performed using the leave-one-out technique. Computational error was calculated by measuring the difference between variation in asphericity and mean keratometry, as predicted by the model, and the actual preoperative and postoperative variation of the sample.

***Fourth Phase.*** The computational model error and the Ferrara nomogram error were compared.

## RESULTS

After running the computational models, the results were assessed by comparing the nomogram error and the machine learning algorithm error for asphericity and mean keratometry.

The Ferrara nomogram error for asphericity was 0.30. The algorithm results for asphericity were 0.28 with linear regression and no selection and 0.19 with select parameters. This result was obtained when selecting 16 of 39 initial parameters: ICRS group, Age, D3.2mm Pachy (pachymetry 3.2 mm), D5.2mm Pachy (pachymetry 5.2 mm), Asph Q Back (asphericity back) (30°), F Ele Avg (front elevation average) Zone5mm, F Ele Avg (front elevation average) Ring4mm, F Ele Avg (front elevation average) Ring5mm, F Ele Avg (front elevation average) Ring6mm, B Ele Avg (back elevation average) Zone 4mm, B Ele Avg (back elevation average) Zone6mm, B Ele Avg (back elevation average) Ring4mm, B Ele Avg (back elevation average) Ring5mm, K2 F (D), K2 B (D), and BFS (best fit sphere) Back 8mm.

The Ferrara nomogram error for mean keratometry was 1.27. The algorithm result for mean keratometry was 1.47 with linear regression and selection param-

TABLE 1
**Groups Divided According to Thickness and Number of Segments Implanted**

| Thickness | Group |
|---|---|
| 1 segment (μm) | |
| 150 | 1 |
| 200 | 2 |
| 250 | 3 |
| 2 segments (μm) | |
| 150 to 150 | 4 |
| 150 to 200 | 5 |
| 150 to 250 | 6 |
| 200 to 200 | 7 |
| 200 to 250 | 8 |
| 250 to 250 | 9 |

TABLE 2
**Relationship Between Implanted Ring Thickness and Asphericity Variation and Keratometry in Accordance With the Ferrara Nomogram**

| Segment (μm) | ΔQ | ΔK (D) | *P* |
|---|---|---|---|
| Single | | | |
| 150 | -0.07 | 0.78 | .042 |
| 200 | -0.31 | 1.82 | < .001 |
| 250 | -0.34 | 2.74 | < .001 |
| Double | | | |
| 150 to 150 | -0.57 | 3.40 | < .001 |
| 150 to 200 | -0.73 | 4.35 | < .001 |
| 150 to 250 | -0.80 | 3.86 | .001 |
| 200 to 200 | -0.86 | 5.65 | < .001 |
| 200 to 250 | -1.02 | 6.27 | < .001 |
| 250 to 250 | -0.99 | 5.30 | .001 |

Δ = *change; Q = asphericity; K = keratometry; D = diopters*

eters, and the best reading in the computational model was 1.18. This result was obtained when 30 parameters were selected: Ring, Age, Ele F BFS 8mm Thinnest Ele B BFS 8mm Thinnest, Ele B BFS 8mm Max 4mm Zone, D2.0mm Pachy, D3.2mm Pachy, D4.0mm Pachy, D5.2mm Pachy, Asph Q Front (30°), Asph Q Back (30°), F Ele Avg Zone4mm, F Ele Avg Zone5mm, F Ele Avg Ring4mm, F Ele Avg Ring5mm, F Ele Avg Ring6mm, B Ele Avg Zone4mm, B Ele Avg Zone5mm, B Ele Avg Zone6mm, B Ele Avg Ring3mm, B Ele Avg Ring4mm, B Ele Avg Ring6mm, K1 F (D), K2 F (D), Astig F (D), K2 B (D), Astig B (D), AC Depth, BFS Front 8mm, and BFS Back 8mm.

After comparing the readings for mean error of the nomogram and the algorithm, there was an improvement of 0.11 for asphericity and 0.09 for mean keratometry.

## DISCUSSION

Asphericity and keratometry readings markedly changed after Ferrara ICRS implantation. Torquetti and Ferrara[6] published the first study that showed the changes in asphericity readings in patients with keratoconus in line with the grading scale and the changes in corneal asphericity as a direct result of the implanted ICRS. Mean asphericity increased after ICRS implantation from -0.85 to -0.32, with a statistically significant -0.53 difference. Mean keratometry decreased from 48.60 to 45.30 D, with a statistically significant change of 3.30. Assessment of all 209 patients in this study also yielded a change of -0.42 and 2.10 for mean asphericity and keratometry, respectively.

In a study involving 135 eyes from 123 patients,[7] the mean values for asphericity change and keratometry variation after Ferrara ICRS implantation of different thickness, and on which the current nomogram is based, were established. It was demonstrated that the thicker the segment or pair of segments to be implanted, the greater the change in corneal asphericity. This is important when choosing the segment to be implanted, which is currently based on the preoperative asphericity.

The first results of the fourth generation of the Ferrara nomogram were described in a study evaluating 50 eyes of 42 patients.[8] The main characteristic of this nomogram is to consider the asphericity as the first parameter to be evaluated when selecting the ICRS. In this study, asphericity values changed significantly, from -0.86 preoperatively to -0.42 postoperatively, with a statistically significant difference of -0.44. Mean keratometry decreased from 49.10 to 45.30 D, with a statistically significant difference of 3.20. In our study, we found statistically significant differences in the change of mean asphericity (-0.42) and keratometry (2.10). In 2011, Ferrara et al.[9] studied 972 eyes implanted with ICRS and found an average change of -0.53 and 3.46 for asphericity and keratometry, respectively.

In 2017, Lyra et al.[10] analyzed and compared changes in the anterior and posterior corneal surfaces after ICRS implantation. They studied 37 tomographic corneal parameters derived from the Pentacam and also made correlations with visual outcomes. In a database of 241 eyes from 182 patients, they concluded that both anterior and posterior corneal surface showed statistically significant changes. In the anterior surface, asphericity, steep keratometry (K2), astigmatism, elevation at the apex, elevation at the thinnest point, and the maximum elevation in the central 4-mm central area reduced significantly ($P < .001$) from preoperative to postoperative evaluation. In the posterior surface, the same parameters previously described from the anterior surface showed similar reduction ($P < .001$). Only the posterior asphericity did not show a statistically significant change.

Other studies[11-13] evaluated keratometry but not asphericity simultaneously because they were based on the third generation nomogram. All of them showed a marked reduction in keratometry with improvement in visual acuity.

Several studies support the safety and efficacy of the Ferrara ICRS implantation, with significant improvement of corneal shape and parameters. However, there have been cases in which the postoperative results are not as expected. Some nomograms for ICRS implantation were developed that showed good results, but there were cases in which the change in asphericity and keratometry was small and not anticipated by the nomograms; hence, the need for adjustments to attain more predictable results. Prior studies[4] had considered the use of more preoperative data as relevant in the selection of the ring segment to be implanted. They also reported the need for further research into the development of new mathematical models designed to achieve more accurate results and to improve nomogram precision for the intrastromal ICRS implantation.

Valdés-Mas et al.[14] used 96 eyes from 74 individuals to create mathematical models for predicting astigmatism in patients who had received ICRS. The study concluded that the most important parameters for predicting astigmatism correction were flat keratometry and segment position; however, the results stress the need for newer data to help improve and validate the models produced.

The study is the first to be performed with the purpose of predicting asphericity and mean keratometry following Ferrara ICRS implantation using computational models based on machine learning and corneal tomography data. This study showed a decrease in asphericity error and mean keratometry error with regard to the current nomogram. Our results support the creation of computational models based on machine learning to improve the predictability of postoperative asphericity and mean keratometry on implantation of intrastromal corneal ring segments in patients with keratoconus.

## AUTHOR CONTRIBUTIONS

Study concept and design (DL, GR, LT, PF, AM, JML); data collection (DL, GR); analysis and interpretation of data (DL, GR, AM, JML); writing the manuscript (DL, GR); critical revision of the manuscript (DL, GR, LT, PF, AM, JML); statistical expertise (AM); supervision (LT, PF, AM, JML)

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TABLE A
## Pentacam Parameters at Baseline

| |
|---|
| Ele F BFS 8mm Thinnest |
| Ele F BFS 8mm Max 4mm Zone |
| Ele B BFS 8mm Apex |
| Ele B BFS 8mm Thinnest |
| Ele B BFS 8mm Max 4mm Zone |
| D2.0mm Pachy |
| D3.2mm Pachy |
| D4.0mm Pachy |
| D5.2mm Pachy |
| Asph Q Front (30°) |
| Asph Q Back (30°) |
| F Ele Avg Zone3mm |
| F Ele Avg Zone4mm |
| F Ele Avg Zone5mm |
| F Ele Avg Zone6mm |
| F Ele Avg Ring3mm |
| F Ele Avg Ring4mm |
| F Ele Avg Ring5mm |
| F Ele Avg Ring6mm |
| B Ele Avg Zone3mm |
| B Ele Avg Zone4mm |
| B Ele Avg Zone5mm |
| B Ele Avg Zone6mm |
| B Ele Avg Ring3mm |
| B Ele Avg Ring4mm |
| B Ele Avg Ring5mm |
| B Ele Avg Ring6mm |
| K1 F (D) |
| K2 F (D) |
| Astig F (D) |
| K1 B (D) |
| K2 B (D) |
| Astig B (D) |
| AC Depth |
| BFS Front 8mm |
| Ele F BFS 8mm Apex |
| BFS Back 8mm |

*ele = elevation; F = front; B = back; BFS = best fit sphere; pachy = corneal thickness; asph Q = asphericity; avg = average; K1 = flat keratometry; K2 = steep keratometry; D = diopters; astig = astigmatism; AC = anterior chamber*
*The Pentacam is manufactured by Oculus Optikgeräte, Wetzlar, Germany.*