Sequential Topography-Guided Photorefractive Keratectomy and Iris-Claw Phakic IOL Implantation in the Management of Postkeratoplasty Astigmatism

Fotoqueratectomia Refrativa Guiada por Topografia e Implante de Lente Fáquica de Fixação Iridiana Sequencial no Tratamento do Astigmatismo Após Queratoplastia

Bruno Barbosa Ribeiro [1], João Romano [2], Ana Sofia Martins [1], Francisca Bragança [1], Miguel Mesquita Neves [1], Miguel Gomes [1], Luís Oliveira [1]

[1] Serviço de Oftalmologia, Centro Hospitalar Universitário de Santo António - Unidade Local de Saúde Santo António, Porto, Portugal
[2] Serviço de Oftalmologia, ULS Leiria, Leiria, Portugal

Recebido/Received: 2025-10-18 | **Aceite/Accepted:** 2026-02-03 | **Published online/Publicado online:** 2026-07-11

DOI: https://doi.org/10.48560/rspo.43664

ABSTRACT

INTRODUCTION: Keratoplasty is an effective procedure in the management of corneal diseases. However, residual astigmatism limits visual recovery. Our goal was to demonstrate the benefit of sequential topography-guided photorefractive keratectomy (tgPRK) followed by iris-claw phakic intraocular lens (pIOL) in the treatment of post keratoplasty astigmatism.

METHODS: Retrospective analysis of patients submitted to sequential tgPRK and pIOL implantation after previous penetrating keratoplasty (PK) or deep anterior lamellar keratoplasty (DALK) between January 2013 and September 2023 at the Cornea Unit of a tertiary hospital. Patients submitted to other refractive procedures and without a minimum 2-year follow-up were excluded. Demographic data, spherical equivalent (SEQ), uncorrected (UDVA) and corrected (CDVA) distance visual acuity were registered preoperatively, after tgPRK, and 2 years after pIOL implantation. Endothelial cell density (ECD) was evaluated using the same specular microscope. Results are plotted according with standard nomenclature.

RESULTS: We enrolled 20 eyes of 17 patients submitted to Keratoplasty due to Keratoconus (65.0% [n=13] DALK). Ten (58.8%) patients were male, with a mean age of 31.7 ± 7.6 years. Mean preoperative SEQ was -5.0 ± 3.4 diopters (D), with a mean refractive astigmatism of -6.4 ± 3.3 D. At the last visit, 10 eyes (50%) had postoperative UDVA at least 20/32, and 3 (15%) had at least 20/20. Efficacy index was 1.2 ± 0.5. After sequential treatment, all eyes achieved refractive correction without loss of CDVA, and 18 (90.0%) eyes gained ≥ 1 lines of vision. Safety index was 1.3 ± 0.7 at the last follow-up. 14 (70%) eyes were within ±0.50 D of plano refraction. There was a tendency for hypocorrection (α<1), with residual final SEQ of -0.13 ± 0.9 D. A significant annual decline of 26.7 ± 155.6 [-417.6 to 168] cells/mm^2 (4.0%) was found (p<0.001). No significant differences were found between type of keratoplasty (3.9% *vs* 4.2% for DALK and PK, respectively, p=0.989).

CONCLUSION: Sequential tgPRK and pIOL implantation is effective in the treatment of keratoplasty astigmatism. Nomogram adjustment may be beneficial to improve outcomes. Given the risk of endothelial cell loss, strict follow-up is mandatory.

KEYWORDS: Astigmatism; Keratoconus; Lens Implantation, Intraocular; Phakic Intraocular Lenses; Keratoplasty, Penetrating; Photorefractive Keratectomy.

RESUMO

INTRODUÇÃO: A queratoplastia é eficaz no tratamento da disfunção corneana. Contudo, o erro refrativo residual limita a recuperação visual. O objetivo foi demonstrar o benefício do tratamento sequencial queratectomia fotorefrativa guiada por topografia (tgPRK) e implante de lente intra-ocular fáquica de fixação iridiana (pIOL) no tratamento do astigmatismo após queratoplastia.

MÉTODOS: Análise retrospetiva de pacientes submetidos a tratamento sequencial tgPRK e pIOL após queratoplastia penetrante (QP) ou queratoplastia lamelar anterior profunda (DALK) entre Janeiro 2013 e Setembro 2023 na Unidade de Córnea num hospital terciário. Pacientes submetidos a outros procedimentos refrativos e sem seguimento mínimo de 2 anos foram excluídos. Foram colhidos dados demográficos, equivalente esférico (SEQ), acuidade visual para longe não corrigida (UDVA) e corrigida (CDVA) no pré-operatório, após tgPRK, e 2 anos após implante de pIOL. A densidade celular endotelial foi avaliada pelo mesmo microscópio especular. Os resultados estão explanados de acordo com a nomenclatura padrão.

RESULTADOS: Foram incluídos 20 olhos de 17 pacientes submetidos a queratoplastia (65,0% DALK). Dez (58,8%) pacientes são homens, com idade média de 31,7 ± 7,6 anos. O SEQ pré-operatório foi -5,0 ± 3,4 dioptrias (D), com astigmatismo refrativo médio -6,4 ± 3,3 D. Na última visita, 10 olhos (50%) tinham UDVA ≥ 20/32, e 3 (15%) tinham ≥ 20/20. O índice de eficácia foi 1,2 ± 0,5. Após tratamento sequencial, todos os olhos alcançaram correção refrativa sem perda de CDVA, e 18 (90,0%) olhos ganharam ≥ 1 linha de visão. O índice de segurança foi 1,3 ± 0,7 à data da última avaliação. Catorze (70%) dos olhos obtiveram SEQ residual dentro de ±0,50 D. Existiu uma tendência para hipocorreção (α<1), com SEQ residual final -0,13 ± 0,9 D. Existiu uma perda celular endotelial média anual de 26,7 ± 155,6 [-417,6 a 168] céls/mm^2 (4,0%) (p<0,001). Não foram registadas diferenças estatisticamente significativas entre tipos de queratoplastia (3,9% *vs* 4,2% para DALK e QP, respectivamente, p=0,989).

CONCLUSÃO: O tratamento sequencial tgPRK e pIOL é eficaz na correção do astigmatismo após queratoplastia. O ajuste com nomograma pode ser benéfico para melhorar resultados. Dado o risco de perda endotelial, o seguimento rigoroso é obrigatório.

PALAVRAS-CHAVE: Astigmatismo; Implante de Lente Intraocular; Lentes Intraoculares Fáquicas; Queratectomía Fotorrefractiva; Queratocono; Queratoplastia Penetrante.

INTRODUCTION

Keratoplasty is a safe and effective tissue transplant procedure to treat several corneal diseases. Current indications include corneal ectasias, scarring, and resistant infections.[1-4]

However, residual refractive error and irregular astigmatism remain one of the main causes to impair visual rehabilitation. In fact, up to a third of patients after Penetrating Keratoplasty (PK) have over 5.0 diopters (D) of corneal astigmatism.[5]

Most patients will require some form of optical correction (spectacles and/or contact lenses) after keratoplasty. While it may treat regular astigmatism, it is seldom effective in ameliorating irregular astigmatism. Its management can be challenging and requires a stepwise approach involving surgical and laser vision correction.[6-12]

Excimer laser photoablation can be used to treat residual refractive error after keratoplasty. Topography-guided photorefractive keratectomy (tgPRK) is a customized ablation profile that specifically focuses on anterior corneal regularization. Several studies have shown its benefits in the treatment of post-keratoplasty astigmatism.[13-21]

However, customized laser ablations may increase refractive error given its asymmetric profile across the corneal stroma. Thus, additional procedures (subsequent laser correction, phacoemulsification with toric intraocular lenses, or phakic intraocular lens (pIOL) implantation) are commonly required.[6–8,10,12]

Given the paucity of evidence regarding this matter, the purpose of this study was to study the efficacy and safety of sequential tgPRK followed by iris-claw pIOL implantation in the treatment of post keratoplasty astigmatism.

MATERIAL AND METHODS

A retrospective medical chart review of patients who underwent sequential tgPRK and iris-claw pIOL (Artiflex or Artisan, Ophtec, The Netherlands) implantation after previous PK or deep anterior lamellar keratoplasty (DALK)

between January 2013 and September 2023 at the Cornea Unit of a tertiary hospital was performed.

Patients with less than 24 months of follow-up after pIOL implantation, a history of uveitis or ocular hypertension, and patients submitted to previous refractive procedures (such as arcuate keratotomy, intracorneal ring segments implantation, and photorefractive/phototherapeutic keratectomy) were excluded.

Criteria for laser vision correction included unsatisfactory visual acuity not amenable for correction with spectacles and/or contact lens, significant corneal irregularity with associated refractive error at least 6 months after removal of all keratoplasty sutures, and no ocular procedures 6 months prior to ablation. Inclusion criteria are summarized in Table 1.

The study followed the tenets of the Declaration of Helsinki for the protection of human subjects in medical research and was approved by our institution's review board and ethics committee (Departamento de Ensino, Formação e Investigação – Santo António Local Health Unit).

The data collected in this study included demographic characteristics, uncorrected (UDVA) and corrected (CDVA) distance visual acuity, manifest refraction, keratoplasty data, corneal topography and ocular aberrometry (Pentacam, Oculus, Germany).

Keratoplasty data included diagnosis, date, and type of keratoplasty, presence of complications, number of sutures, history of past keratoplasty, number of rejection episodes, presence of graft neovascularization, and need for re-suture.

Analyzed aberrometry indices included total root mean square (RMS), high-order aberrations (HOA-RMS), defocus, astigmatism, trefoil, and spherical aberration (Z40). Corneal wavefront analysis was performed within a 5 mm zone centered in the corneal vertex.

Endothelial cell density (ECD) was evaluated using the same specular microscopy device (Tomey EM-4000). Total (preoperative ECD – final ECD) and annual endothelial cell loss after implantation were calculated.

Refractive surgery data included date of surgery, ablation depth, model, and power of implanted pIOL, and length of incision. Intraoperative and postoperative surgical complications were noted.

SURGICAL PLANNING

Preoperative scans were obtained using the Wavelight Oculyzer II (Alcon, TX). The device should obtain at least 8 consecutive scans - at least 4 should be of high quality. The consistency and reliability of the device should obey to the following criteria: the successfully analysed area must be at least 90% of the 6.5 mm optic zone; adequate caption of the pupillary area; no more than 0.75 D deviation at the 4-mm central area between any of the 8 analysed scans. In cases of insufficient caption or reproducibility, a tgPRK could not be performed (and thus was not included in this analysis).[22]

FIRST STEP – EXCIMER ABLATION

After adequate imaging acquisition, the first step consisted of tgPRK using the WaveLight EX500 excimer laser (Alcon, TX). To minimize tissue ablation, the effective optical zone (OZ) was decreased to 5.5 mm with a 2.0 mm transition zone.

If there was strong correlation between refractive and topographic astigmatism, correction of refractive error was performed (Refractive tgPRK). In these cases, up to 70% of the spherical error and up to 70% of the cylinder error were allowed.[23]

In cases with no correlation between refractive and topographic astigmatism, a significant irregular component is assumed to exist. Therefore, no attempted refractive correction was performed, aiming only at the regularization of the anterior corneal surface (Neutral tgPRK).

Given the magnitude of pre-existing refractive error, all patients were counselled regarding the expected need for additional refractive procedures, even if partial correction of refractive error was performed.

After postoperative stability of manifest refraction, additional refractive procedures were performed, if needed. Fig. 1 summarizes our algorithm to a stepwise approach to topography-guided ablations. Subsequent treatment approaches were used according to the magnitude of residual refractive error and relative regularity: cases with substantial topographic irregularity (refractive tgPRK); cases with topographic regularity and good wavefront acquisition (WG-PRK); and cases with topographic regularity without adequate wavefront (WFO-PRK). A minority of patients with topographic regularity and magnitude of refractive error not amenable to correct by laser ablation were pro-

Table 1. Criteria for sequential TG-PRK and phakic IOL implantation after previous corneal graft.

Age ≥ 21 years with unsatisfactory visual acuity not amenable for correction with spectacles and/or contact lens
Significant irregular corneal astigmatism at least 6 months after removal of all keratoplasty sutures
No other refractive procedures 6 months prior to laser ablation
Absence of corneal scarring
ACD ≥ 3.00 mm
ECD ≥ 2000 cells/mm^2 for DALK and ≥ 1000 cells/mm^2 for PK[a]

ACD = anterior chamber depth (measured from the corneal endothelium); DALK = deep anterior lamellar keratoplasty; ECD = endothelial cell density; PK = penetrating keratoplasty.

a Patients with previous PK were allowed lower ECD if best-tolerated corrected visual acuity was inferior to 20/200 and subjective refraction sphere and/or cylinder was ≥ -6.0 D. Strict medical advice was given regarding higher-risk for adverse events.

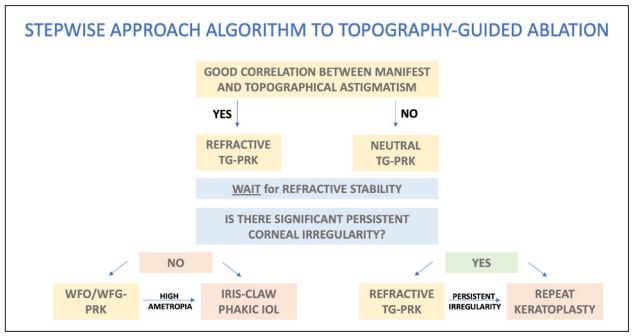

Figure 1. Proposed algorithm to a stepwise approach to irregular astigmatism and topography-guided ablations.

TGPRK = topography-guided photorefractive keratectomy; WFO = wavefront optimized; WFG = wavefront guided

posed to iris-claw pIOL implantation (the ones described in this study).

SURGICAL TECHNIQUE AND PATIENT EVALUATION PROTOCOL

All tgPRK procedures were transepithelial and performed using the WaveLight EX500 (Alcon, TX). Under topical anesthesia with 0.4% oxibupracaine chlorhydrate, the excimer laser was used to ablate 45 to 60 µm of epithelium, followed by stromal ablation. Epithelial ablation depth was determined based on corneal epithelial thickness, when available.

In cases where epithelial thickness mapping was not available, epithelial ablation was performed according to clinical impression: initial ablation of 30 µm (8.0 mm OZ) followed by a second ablation 10 to 30 µm deep (7.5 mm OZ).

In all procedures, a mitomycin C 0.02% soaked cellulose sponge was applied over the stromal bed for 30 to 60 seconds, followed by copious cold saline irrigation. At the conclusion of the case, a bandage contact lens was applied, followed by instillation of 1 drop of 0.3% ofloxacine and 1% cyclopentolate.

The BCL was removed in postoperative day 3 or until complete re-epithelization. Postoperative medication included 0.3% ofloxacine qid for 1 week, followed by 0.1% dexamethasone tapered over a 3-month period. Postoperative appointments were scheduled at 3 days, 1 month, 3 months, 6 months, and as needed.

SECOND STEP – IRIS-CLAW PHAKIC IOL IMPLANTATION

Surgery was performed by three experienced corneal surgeons (LO, MG, and MMN). The procedure was performed under general anesthesia after preoperative induction of miosis by instillation of 2% pilocarpine. The surgical technique has been extensively described elsewhere by our group.[12]

In summary, pIOL implantation was implanted via a 5.2 or 6.2 mm (Artisan) or 3.2 mm (Artiflex) superior corneoscleral incision with a lens spatula (Artiflex) or implantation forceps (Artisan) after anterior chamber injection of cohesive viscoelastic (1% sodium hyaluronate, Provisc, Alcon, TX). A surgical iridectomy was performed at 12 o'clock in all cases to avoid pupillary block glaucoma. The main incision was sutured with 10-0 single interrupted polyamide sutures.

Postoperative medication for all patients included topical application of 0.3% ofloxacin qid for 10 days, 0.1% dexamethasone 1 mg/mL qid tapered over 3 weeks, and 0.03% flurbiprofen qid for 4 weeks. Oral prednisolone 0.5 mg/kg/d was given in a tapered regimen over the first 15 days in patients without contraindications. Patients were scheduled for observation at the first day, first week, first month and third month. Additional visits were scheduled according to clinical indication.

OUTCOMES

The outcome parameters included efficacy (cumulative percentage of preoperative CDVA and postoperative UDVA); efficacy index (ratio of mean postoperative UDVA and mean preoperative CDVA); safety (intraoperative and postoperative adverse events and loss in CDVA); safety index (ratio of mean postoperative CDVA and mean preoperative CDVA); predictability (percentage of eyes within ±0.50 D and ±1.00 diopters of the attempted refraction); percentage of ECL, annualized (preoperative ECD – postoperative ECD/preoperative ECD).

STATISTICAL ANALYSIS

Statistical analysis was performed using the SPSS software (SPSS Statistics, version 26.0.0 for Mac OS, IBM Corporation). The Kolmogorov-Smirnov test was used to assess normality. Comparisons between independent continuous variables were evaluated using the Mann-Whitney U test and the Student's t-test. Fisher's exact test was used for nominal-scaled data. Spearman's bivariate correlation test was applied to study correlations. A *p*-value of less than 0.05 was considered statistically significant. All measurements are expressed as mean ± standard deviation.

Calculation of mean gain in VA and VA line change was made based on VA values obtained with a Snellen chart and rounded to the nearest line and were converted into logarithm of the minimum angle of resolution (logMAR). Conversion of decimal VA values according to Snellen decimal into logMAR was made using the following formula: logMAR = -log (decimal VA).

Surgically induced astigmatism (SIA) was calculated for all eyes. Preoperative keratometry (K) readings and subjective refraction data were gathered to yield the double-angle plots of refractive astigmatism at the corneal plane (including centroid values, standard deviations, and 95% confidence interval ellipses of the data set) according to the method published by Holladay *et al*.[24] Results are reported following the Standard for Reporting Refractive Surgery Outcomes.[25]

RESULTS

Preoperative characteristics are shown in Table 2. Final analysis comprised 20 eyes of 17 patients submitted to Keratoplasty due to Keratoconus. Mean age was 31.7 ± 7.6 [20, 46] years, and ten (58.8%) patients were male, with no difference between type of keratoplasty. Thirteen patients (65.0%) were

Table 2. Preoperative characteristics (n=20).	
Variable	
Age, years	31.7 ± 7.6 [20, 46]
Male sex, n(%)	10 (58.8)
DALK, n(%)	13 (65.0)
Time after keratoplasty, months	69.5 ± 72.3 [16, 325]
No previous keratoplasty, n(%)	17 (85.0)
Need for corneal re-suture, (%)	2 (10.0)
UCVA	1.4 ± 0.5 [0.3, 2.0]
CDVA	0.4 ± 0.4 [0.1, 1.8]
Sphere (D)	-2.5 ± 3.2 [-8.0, 2.5]
Cylinder (D)	-6.4 ± 3.3 [-14, -3]
Spherical equivalent (D)	-5.0 ± 3.4 [-11.0, 0.9]
K1 (D)	45.4 ± 2.8 [39.8, 50.4]
K2 (D)	50.4 ± 3.4 [45.5, 56.7]
ACD (mm)	3.7 ± 0.3 [3.0, 4.3]
ECD (cells/mm²)	1920.9 ± 578.9 [861, 2518]

ACD = anterior chamber depth; CDVA, corrected distance visual acuity; DALK = deep anterior lamellar keratoplasty; D = diopters; ECD = endothelial cell density; UCVA = uncorrected distance visual acuity;

submitted to DALK, and 7 (35.0%) were submitted to PK. Sixteen eyes (80.0%) were implanted with Artiflex pIOL, and four eyes (20.0%) were implanted with Artisan pIOL. Preoperatively, mean manifest spherical equivalent was -5.0 ± 3.4 diopters (D), and mean refractive astigmatism was -6.4 ± 3.3 D. The results following the Standard for Reporting Astigmatism Outcomes are shown in Fig. 2.

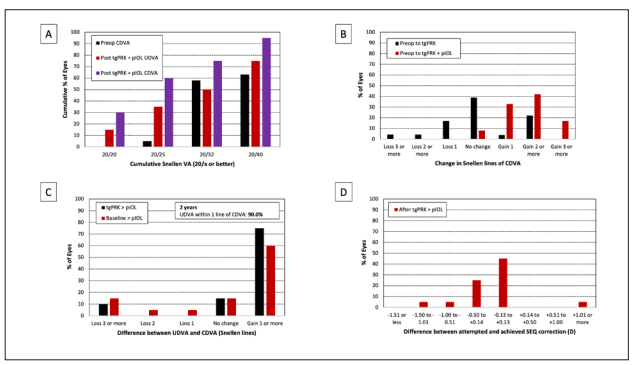

Figure 2. Visual and refractive outcomes of sequential topography-guided photorefractive keratectomy and iris-claw phakic intraocular lens implantation.

CDVA = corrected distance visual acuity; UDVA = uncorrected distance visual acuity; D = diopters; VA = visual acuity; tgPRK = topography-guided photorefractive keratectomy; pIOL = iris-claw phakic intraocular lens

ABLATION PARAMETERS

Epithelial ablation was 59.3 ± 9.3 [50.0 to 75.0] µm. On average, maximum stromal ablation depth was 81.3 ± 42.2 [12.0 to 138.0] µm. Tissue consumption was below 25% in 19 (95.0%) eyes, and the percentage of tissue altered inferior to 40% in 19 (90.0%) eyes. Average residual stromal bed was 387.8 ± 50.8 [264.0 to 454.0] µm. Optic zone ranged from 5.0 to 6.5 [5.7 ± 0.3] mm.[26,27]

EFFICACY

Efficacy is shown as the cumulative proportion of UDVA in Fig. 2 (panel A). After sequential treatment, 3 eyes (15.0%) had UDVA ≥ 20/20, 7 had UDVA ≥ 20/25, 10 (50.0%) had UDVA ≥ 20/32, and 15 (75.0%) had ≥ 20/40. Efficacy index was 1.2 ± 0.5 at the last follow-up. The cumulative proportion of preoperative CDVA to postoperative UDVA is shown in Fig. 2 (panel C). At the end of follow-up, 18 (90%) eyes had UDVA within 1 line of CDVA.

SAFETY

After tgPRK, CDVA was within 1 line of preoperative CDVA in 14 (60.0%) eyes. Two eyes (8.6%) lost > 1 line of vision. After sequential treatment, all eyes achieved refractive correction without loss of CDVA, and 18 (90.0%) eyes gained ≥ 1 line of vision. Safety index was 1.3 ± 0.7 at the last follow-up.

ACCURACY AND PRECISION

Accuracy of spherical equivalent refraction (SEQ) to the intended target is shown in Fig. 2 (panel D). Fourteen (70.0%) and fifteen (75.0%) and eyes obtained a postoperative SEQ within ±0.50 D and ±1.00 D of plano refraction, respectively.

There was a positive correlation between attempted and achieved SEQ refraction. There was a tendency for hypocorrection (α<1), more pronounced with more myopic refractive error. Fig. 3 depicts the proportion of attempted to achieved correction in SEQ (panel A) and SEQ variation (panel B).

Mean refractive error increased from -4.5 ± 3.4 D preoperatively to -10.0 ± 3.7 D after tgPRK. Average residual SEQ (postoperative achieved SEQ – target SEQ) was -0.13 ± 0.9 D at the last follow-up.

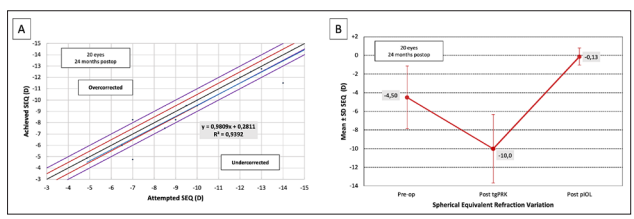

Figure 3. Proportion between attempted and achieved spherical equivalent refraction and residual refractive error.

CDVA = corrected distance visual acuity; UDVA = Uncorrected distance visual acuity; D = diopters; pIOL = iris-claw phakic intraocular lens; SEQ = spherical equivalent refraction; tgPRK = topography-guided photorefractive keratectomy

ENDOTHELIAL CELL LOSS

Preoperative to 24 months after pIOL implantation, there was a statistically significant acute decline of 208.3 ± 226.6 [-67.0 to 654.0] cells/mm² (13.2%, p<0.001). No significant differences were found regarding acute decline and type of keratoplasty (179.2 ± 198.1 [9.6%] *vs* 262.3 ± 280.8 [20.0%] cells/mm² for DALK and PK, respectively, p=0.449).

To avoid bias from the effect of surgery on ECD, chronic EC loss was measured from 12 months to the last follow-up.

Table 3. Changes in aberrometry indices (n=20).

	Preoperative	After tgPRK	*p* value	After pIOL	*p* value
Total RMS, µm	15.9 ± 5.6	7.9 ± 2.7	<0.001	8.9 ± 2.8	<0.001
HOA RMS, µm	5.1 ± 1.7	2.8 ± 1.0	<0.001	3.1 ± 1.0	<0.001
Vertical Coma, µm	1.3 ± 3.1	0.1 ± 1.5	0.017	0.1 ± 1.8	0.026
Horizontal Coma, µm	0.7 ± 3.0	0.5 ± 1.5	0.570	0.6 ± 1.6	0.280
Horizontal Trefoil, µm	0.3 ± 1.2	0.1 ± 1.0	0.410	-0.3 ± 1.0	0.097
Oblique Trefoil, µm	-0.5 ± 1.0	0.1 ± 0.8	0.006	0.1 ± 0.9	0.109
Spherical Aberration, Z40, µm	1.5 ± 0.5	0.8 ± 0.6	<0.001	1.0 ± 0.6	0.013

RMS, root mean square; HOA, high order aberrations; values are shown as mean ± standard deviation

Longitudinally, a significant annual decline of 26.7 ± 155.6 [-417.6 to 168] cells/mm^2 (4.0%) was found (p<0.001). No significant differences were found between type of keratoplasty (3.9% *vs* 4.2% for DALK and PK, respectively, p=0.989).

Chronic endothelial cell loss was negatively correlated with preoperative ACD (r=-0.514, p=0.034) but not with time since keratoplasty (r=0.070, p=0.834). Acute endothelial cell loss was positively correlated with preoperative ECD (r=0.763, p<0.001) and negatively correlated with chronic endothelial cell loss (r=-0.716, p<0.001)

Further analysis was made to characterize a possible effect of ACD on ECD loss. Mean ACD was 3.60 ± 0.37 preoperative and 3.46 ± 0.29 mm after pIOL implantation, translating in a mean reduction of 0.14 ± 0.19 mm (p=0.017). Further subgroup analysis was performed according to preoperative and postoperative ACD. No difference in annual chronic endothelial cell was found between subjects in preoperative ACD below or above 3.20 mm (22.2 ± 222.2 *vs* 53.9 ± 135.5 cells/mm^2, respectively, p=0.409). Furthermore, no significant differences were found regarding postoperative ACD (44.0 ± 197.7 cells/mm^2 if <3.2 mm *vs* 75.3 ± 156.7 cells/mm2 if >3.2 mm, p=0.236)

SURGICALLY INDUCED ASTIGMATISM AND OPTICAL ABERRATIONS

Fig. 4 shows double-angle plots of preoperative corneal astigmatism and postoperative refractive astigmatism at the corneal plane for all eyes. There was a reduction in the astigmatic vector from 2.14 ± 5.44 D (preoperative) *vs* 0.47 ± 4.16 D (after sequential treatment). This suggests a significant reduction in both the magnitude and dispersion of astigmatism.

Preoperative and postoperative aberrometry indices were available for all patients. There was statistically significant improvement for Total RMS, HOA RMS, Spherical Aberration, and Oblique Trefoil. Full data is shown in Table 3.

ADVERSE EVENTS

There were no reported severe intraoperative complications. Two patients required a second laser ablation due to persistent irregularity. Two patients developed haze which partly resolved with tapered 0.1% prednisolone acetate. There were no reports regarding the development of cataract. Two patients developed mild corectopia. No spontaneous haptic dislocations of the iris-claw pIOL or iris atrophy were observed. No secondary interventions were required.

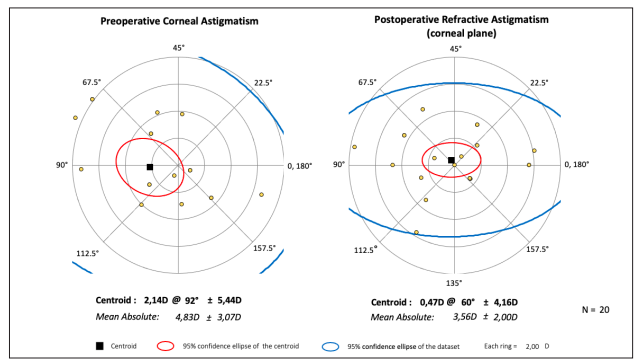

Figure 4. Double-angle plots of preoperative corneal astigmatism and postoperative refractive astigmatism at the corneal plane for all eyes.

DISCUSSION

Solving refractive errors following keratoplasty remains challenging. Predictable refractive outcomes are not always achieved after corneal grafting, being influenced by either the surgical technique or the healing process.

Refractive surgery as visual rehabilitation should be considered after unsuccessful correction with spectacles and contact lens (CL) – limitations may arise due to the presence of irregular astigmatism, peripheral neovascularization, and tear-film instability (all leading to CL intolerance).[28]

Patients should be aware that the refractive error may not fully stabilize even years after suture removal - keratoconus progression in the host cornea and graft ectasia may be putative mechanisms.[29]

The introduction of customized PRK in the past years has broadened the possibilities in the management of irregular astigmatism, especially after corneal surgery. Several studies have shown significant improvement in UDVA and CDVA with a significant reduction in refractive cylinder.[13–19,21,23,26,30–35]

Our study is in line with current evidence – there was a significant reduction in high-order aberrations, and vector analysis demonstrated a reduction in both the magnitude and dispersion of astigmatism after tgPRK.[13,16–18,30]

It should be noted that the improvement in HOA did not necessarily correlate with an improvement in CDVA - 8.6% (n=2) of eyes exhibited temporary loss in >1 line of CDVA after customized ablation. We believe this can be explained by the complex interaction between optic aberrations, visual behaviour, and neuroadaptation – Chen et al found that best subjective image quality occurs when some aberrations are left uncorrected.[36] In other words, the best perceived image quality does not necessarily occur when the quality of the retinal image is highest. In fact, each individual subjective blur is adapted to its own wavefront pattern. Thus, after corneal refractive surgery, the brain will remain adapted to the first pattern for some time.[36,37]

This effect can be further explored by the coupling effect of aberrations – the additive effect of several HOAs may positively influence the final retinal image quality. In other words, the customized ablation may influence the positive coupling exerted by the presence of vertical trefoil and coma, thus perceiving worse image quality despite a reduction in HOAs.[38]

We also found high residual refractive error after customised laser treatment – this has been previously described and probably reflects the complex interaction between LOAs and HOAs. Epithelial remodelling, wound healing and biomechanical effects inherently induce HOAs. On the other hand, customized ablation patterns lack symmetry – deeper peripheral hyperopic ablations may induce negative SA and further contribute to overall myopic defocus.[21,39,40]

In this series, customized ablation was performed with the only goal of regularizing the anterior corneal surface. Thus, we did not expect any improvement in UDVA after tgPRK. The value of the efficacy index states that, on average, patients can expect an uncorrected visual acuity up to 120% of their preoperative CDVA. In fact, three quarters of eyes achieved UDVA of 20/40 or better at the last follow-up – thus demonstrating excellent efficacy of the sequential treatment in visual rehabilitation.

It should be noted, however, that patients did not tolerate full refraction due to aniseikonia. Thus, "functional" preoperative CDVA was much lower than reported. After pIOL implantation, all eyes achieved refractive correction without loss of CDVA, and 18 (90.0%) eyes gained ≥ 1 line of vision. The safety index was above 1.00, indicating that CDVA is, on average, better after sequential treatment.

The incidence of haze ranges from 2.9%-19.4% in studies in which MMC was used[14,17,17–19] and from 6.3%-25.0% in which MMC was not used.[20,35,41] As detailed, all our eyes were treated with MMC, and we registered 2 cases (10.0%) of haze. MMC exerts antifibrotic properties and effectively reduces the incidence of postoperative haze.[42,43] Since a higher incidence has been described after corneal graft, intraoperative MMC should always be applied after laser ablation.[15,18,30,33,44]

Some studies have demonstrated the predictability and accuracy of iris-claw pIOL in the management of postkeratoplasty astigmatism.[11,12] There was a strong correlation between attempted and achieved SEQ, with around three-fourths of patients achieving residual SEQ within ±0.5 D of intended refraction.

As previously reported, there seems to be a higher tendency for undercorrection, especially for higher myopic corrections.[12] This probably reflects a combination of epithelial remodelling, progressive graft ectasia, and a more complex interaction between LOAs and HOAs.

As previously mentioned, all treatments were transepithelial. The first step consisted of a phototherapeutic keratectomy targeting the stromal irregularity compensated by the epithelium, followed by the treatment of stromal irregularity not compensated by the epithelium. Thus, our strategy mitigates the possible loss of efficacy induced by epithelial irregularity and remodelling, as suggested by Reinstein *et al*.[45]

The main concern regarding iris-claw pIOL after past keratoplasty is accelerated endothelial cell loss. In our series, there was an approximate cell loss of 4%/year, which is significantly higher than both eyes with keratoplasty without pIOL and virgin eyes with pIOL.[46,47] While this analysis may be underpowered to characterize EC loss according to the type of keratoplasty, current evidence suggests more accelerated EC loss with PK.[12]

As previously mentioned, pIOL implantation was only proposed after failure of conservative measures. Strict counselling was given regarding the risk of endothelial cell loss after pIOL implantation. Patients were informed and accepted the risk. No patient required pIOL explantation or endothelial keratoplasty. However, we acknowledge that these are high-risk patients. Thus, a tailored approach and strict follow-up are essential to prevent adverse events.

The current study demonstrates that sequential treatment with tgPRK and iris-claw pIOL is safe and effective in the treatment of postkeratoplasty astigmatism. We included a subset of patients successfully treated for iatrogenic refractive error. Overall, the correction of SE is very precise, with up to 0.3 D of undercorrection per diopter of attempted treatment.

Despite its strengths, we also acknowledge the limitations of this study. It is a retrospective cohort, thus prone to selection and information bias. It has a small sample size, which may limit external validity. However, patients were examined by the same team of ophthalmologists and treated according with a standardized protocol, minimizing classification bias.

This work included a special subset of patients with high refractive error following tgPRK. Thus, this study is not designed to evaluate the efficacy of customized ablations alone - the possibility of selection bias may underestimate the real-life results after tgPRK in previously grafted corneas.

Sequential tgPRK and pIOL implantation is effective in the treatment of keratoplasty astigmatism. Nomogram adjustment may be beneficial to improve outcomes. Given the risk of endothelial cell loss, strict follow-up is mandatory.

CONTRIBUTORSHIP STATEMENT / DECLARAÇÃO DE CONTRIBUIÇÃO

BBR and JR: Analysis, data collection, study design, and writing.

ASM and FB: Analysis, data collection, and review.

MMN, MG: Study design and review.

LO: Study design, conception, and review.

All authors approved the final version to be published.

BBR e JR: Análise, colheita de dados, desenho do estudo e escrita

ASM e FB: Análise, colheita de dados e revisão.

MMN, MG: Desenho do estudo e revisão.

LO: Desenho do estudo, concepção e revisão.

Todos os autores aprovaram a versão final a ser publicada.

RESPONSABILIDADES ÉTICAS

Conflitos de Interesse: Os autores declaram a inexistência de conflitos de interesse na realização do presente trabalho.

Fontes de Financiamento: Não existiram fontes externas de financiamento para a realização deste artigo.

Confidencialidade dos Dados: Os autores declaram ter seguido os protocolos da sua instituição acerca da publicação dos dados de doentes.

Proteção de Pessoas e Animais: Os autores declaram que os procedimentos seguidos estavam de acordo com os regulamentos estabelecidos pela Comissão de Ética responsável e de acordo com a Declaração de Helsínquia revista em 2024 e da Associação Médica Mundial.

Proveniência e Revisão por Pares: Não comissionado; revisão externa por pares.

ETHICAL DISCLOSURES

Conflicts of Interest: The authors have no conflicts of interest to declare.

Financing Support: This work has not received any contribution, grant or scholarship

Confidentiality of Data: The authors declare that they have followed the protocols of their work center on the publication of patient data.

Protection of Human and Animal Subjects: The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical research ethics committee and those of the Code of Ethics of the World Medical Association (Declaration of Helsinki as revised in 2024).

Provenance and Peer Review: Not commissioned; externally peer-reviewed.

REFERENCES

1. Söğütlü Sari E, Kubaloğlu A, Ünal M, Piñero Llorens D, Koytak A, Ofluoglu AN, et al. Penetrating keratoplasty versus deep anterior lamellar keratoplasty: comparison of optical and visual quality outcomes. Br J Ophthalmol. 2012;96:1063–7.
2. Shimazaki J, Shimmura S, Ishioka M, Tsubota K. Randomized clinical trial of deep lamellar keratoplasty vs penetrating keratoplasty. Am J Ophthalmol. 2002;134:159–65.
3. Watson SL, Ramsay A, Dart JKG, Bunce C, Craig E. Comparison of deep lamellar keratoplasty and penetrating keratoplasty in patients with keratoconus. Ophthalmology. 2004;111:1676–82.
4. Henein C, Nanavaty MA. Systematic review comparing penetrating keratoplasty and deep anterior lamellar keratoplasty for management of keratoconus. Cont Lens Anterior Eye. 2017;40:3–14. doi: 10.1016/j.clae.2016.10.001.
5. Javadi MA, Motlagh BF, Jafarinasab MR, Rabbanikhah Z, Anissian A, Souri H, et al. Outcomes of penetrating keratoplasty in keratoconus. Cornea. 2005;24:941–6.
6. Fares U, Sarhan ARS, Dua HS. Management of post-keratoplasty astigmatism. J Cataract Refract Surg. 2012;38:2029–39.
7. Bhayani R, Walkden A. Managing post keratoplasty astigmatism. Clin Ophthalmol. 2024;18:1727–34. doi: 10.2147/OPTH.S393975.
8. Alfonso JF, Lisa C, Abdelhamid A, Montés-Micó R, Poo-López A, Ferrer-Blasco T. Posterior chamber phakic intraocular lenses after penetrating keratoplasty. J Cataract Refract Surg. 2009;35:1166–73.
9. Tiveron MC, Alió Del Barrio JL, Kara-Junior N, Plaza-Puche AB, Abu-Mustafa SK, Zein G, et al. Outcomes of Toric Iris-Claw Phakic Intraocular Lens Implantation After Deep Anterior Lamellar Keratoplasty for Keratoconus. J Refract Surg. 2017;33:538–44. doi: 10.3928/1081597X-20170616-02.
10. Malheiro L, Coelho J, Neves MM, Gomes M, Oliveira L. Phakic intraocular lens implantation after deep anterior lamellar keratoplasty: retrospective case series analysis with long-term follow-up. Clin Ophthalmol. 2019;13:2043–52. doi: 10.2147/OPTH.S202054.
11. Moshirfar M, Barsam CA, Parker JW. Implantation of an Artisan phakic intraocular lens for the correction of high myopia after penetrating keratoplasty. J Cataract Refract Surg. 2004;30:1578–81.
12. Ribeiro BB, Martins AS, Malheiro L, Coelho J, Neves MM, Gomes M, et al. Long term efficacy and safety of iris-claw phakic intraocular lens in the management of post keratoplasty astigmatism. J Cataract Refract Surg. 2025;51:1090-6. doi: 10.1097/j.jcrs.0000000000001748.
13. Bandeira E Silva F, Hazarbassanov RM, Martines E, Güell JL, Hofling-Lima AL. Visual Outcomes and Aberrometric Changes With Topography-Guided Photorefractive Keratectomy Treatment of Irregular Astigmatism After Penetrating Keratoplasty. Cornea. 2018;37:283–9.
14. Laíns I, Rosa AM, Guerra M, Tavares C, Lobo C, Silva MF, et al. Irregular astigmatism after corneal transplantation--efficacy and safety of topography-guided treatment. Cornea. 2016;35:30–6. doi: 10.1097/ICO.0000000000000647.
15. Khan MS, Gonzales AL, Kofi M, Alio JL. Outcomes of photorefractive keratectomy after corneal graft: brief review. Cornea. 2024;43:1592–8. doi: 10.1097/ICO.0000000000003663.
16. Camellin M, Arba Mosquera S. Simultaneous aspheric wavefront-guided transepithelial photorefractive keratectomy and phototherapeutic keratectomy to correct aberrations and re-

fractive errors after corneal surgery. J Cataract Refract Surg. 2010;36:1173–80. doi: 10.1097/ICO.0000000000001359.
17. Sorkin N, Einan-Lifshitz A, Abelson S, Boutin T, Showail M, Borovik A, et al. Stepwise guided photorefractive keratectomy in treatment of irregular astigmatism after penetrating keratoplasty and deep anterior lamellar keratoplasty. Cornea. 2017;36:1308–15.
18. Idris L, Khandekar R, Ahad M. Topography guided custom ablation treatment for residual refractive error after keratoplasty. J EuCornea. 2020;9:10–6.
19. Bizrah M, Lin DTC, Babili A, Wirth MA, Arba-Mosquera S, Holland SP. Topography-guided photorefractive keratectomy for postkeratoplasty astigmatism: long-term outcomes. Cornea. 2021;40:78–87. doi: 10.1097/ICO.0000000000002403.
20. Ohno K. Customized photorefractive keratectomy for the correction of regular and irregular astigmatism after penetrating keratoplasty. Cornea. 2011;30:S41-44.
21. Hanna R, Mimouni M, Plaza AB, Alió JL. Factors predicting successful customized excimer laser treatment in irregular corneas. J Cataract Refract Surg. 2020;46:241–9. doi: 10.1097/j.jcrs.0000000000000043.
22. Alcon, Fort Worth, TX. WaveLight EX500 Excimer Laser User Manual. 2022.
23. Kanellopoulos AJ. Combined Photorefractive Keratectomy and Corneal Cross-Linking for Keratoconus and Ectasia: The Athens Protocol. Cornea. 2023;42:1199–205. doi: 10.1097/ICO.0000000000003320.
24. Holladay JT, Wilcox RR, Koch DD, Wang L. Astigmatism analysis and reporting of surgically induced astigmatism and prediction error. J Cataract Refract Surg. 2022;48:799–812. doi: 10.1097/j.jcrs.0000000000000871.
25. Reinstein DZ, Archer TJ, Randleman JB. JRS standard for reporting astigmatism outcomes of refractive surgery. J Refract Surg. 2014;30:654–9.
26. Santhiago MR, Smadja D, Gomes BF, Mello GR, Monteiro MLR, Wilson SE, et al. Association between the percent tissue altered and post-laser in situ keratomileusis ectasia in eyes with normal preoperative topography. Am J Ophthalmol. 2014;158:87-95.e1.
27. Randleman JB, Woodward M, Lynn MJ, Stulting RD. Risk assessment for ectasia after corneal refractive surgery. Ophthalmology. 2008;115:37–50.
28. Genvert GI, Cohen EJ, Arentsen JJ, Laibson PR. Fitting gas-permeable contact lenses after penetrating keratoplasty. Am J Ophthalmol. 1985 ;99:511–4.
29. de Toledo JA, de la Paz MF, Barraquer RI, Barraquer J. Long-term progression of astigmatism after penetrating keratoplasty for keratoconus: evidence of late recurrence. Cornea. 2003;22:317–23.
30. Rajan MS, O'Brart DPS, Patel P, Falcon MG, Marshall J. Topography-guided customized laser-assisted subepithelial keratectomy for the treatment of postkeratoplasty astigmatism. J Cataract Refract Surg. 2006;32:949–57.
31. Spadea L, Visioli G, Mastromarino D, Alexander S, Pistella S. Topography-Guided Trans-Epithelial No-Touch Photorefractive Keratectomy for High Irregular Astigmatism After Penetrating Keratoplasty: A Prospective 12-Months Follow-Up. Ther Clin Risk Manag. 2021;17:1027–35.
32. Ghoreishi M, Peyman A, Koosha N, Golabchi K, Pourazizi M. Topography-guided transepithelial photorefractive keratectomy to correct irregular refractive errors after radial keratotomy. J Cataract Refract Surg. 2018;44:274–9. doi: 10.1016/j.jcrs.2017.12.015.
33. Forseto A dos S, Marques JC, Nosé W. Photorefractive keratectomy with mitomycin C after penetrating and lamellar keratoplasty. Cornea. 2010;29:1103–8.
34. Ohno K. Customized photorefractive keratectomy for the correction of regular and irregular astigmatism after penetrating keratoplasty. Cornea. 2011;30:S41-44.
35. De Rosa G, Boccia R, Santamaria C, Fabozzi L, De Rosa L, Lanza M. Customized photorefractive keratectomy to correct high ametropia after penetrating keratoplasty: A pilot study. J Optom. 2015;8:174–9. doi: 10.1016/j.optom.2013.12.002.
36. Chen L, Artal P, Gutierrez D, Williams DR. Neural compensation for the best aberration correction. J Vis. 2007;7:9.1-9.
37. Applegate RA, Hilmantel G, Howland HC, Tu EY, Starck T, Zayac EJ. Corneal first surface optical aberrations and visual performance. J Refract Surg. 2000;16:507–14.
38. Villegas EA, Alcón E, Artal P. Impact of positive coupling of the eye's trefoil and coma in retinal image quality and visual acuity. J Opt Soc Am A Opt Image Sci Vis. 2012;29:1667–72.
39. Roberts C. Future challenges to aberration-free ablative procedures. J Refract Surg. 2000;16:S623-629.
40. Yoon G, Macrae S, Williams DR, Cox IG. Causes of spherical aberration induced by laser refractive surgery. J Cataract Refract Surg. 2005;31:127–35.
41. Hjortdal JØ, Ehlers N. Treatment of post-keratoplasty astigmatism by topography supported customized laser ablation. Acta Ophthalmol Scand. 2001;79:376–80.
42. Maldonado MJ. Intraoperative MMC after excimer laser surgery for myopia. Ophthalmology. 2002;109:826; author reply 826-828.
43. Netto MV, Mohan RR, Sinha S, Sharma A, Gupta PC, Wilson SE. Effect of prophylactic and therapeutic mitomycin C on corneal apoptosis, cellular proliferation, haze, and long-term keratocyte density in rabbits. J Refract Surg. 2006;22:562–74.
44. Bilgihan K, Ozdek SC, Akata F, Hasanreisoğlu B. Photorefractive keratectomy for post-penetrating keratoplasty myopia and astigmatism. J Cataract Refract Surg. 2000;26:1590–5.
45. Reinstein DZ, Archer TJ, Gobbe M. Improved effectiveness of transepithelial PTK versus topography-guided ablation for stromal irregularities masked by epithelial compensation. J Refract Surg. 2013;29:526–33. doi: 10.3928/1081597X-20130719-02.
46. Cheng YYY, Visser N, Schouten JS, Wijdh RJ, Pels E, van Cleynenbreugel H, et al. Endothelial cell loss and visual outcome of deep anterior lamellar keratoplasty versus penetrating keratoplasty: a randomized multicenter clinical trial. Ophthalmology. 2011;118:302–9.
47. Marta A, Leite J, Abreu AC, Monteiro S, Pinto C. Long-term results in patients with iris-fixated foldable phakic intraocular lenses for myopia and astigmatism. J Cataract Refract Surg. 2022;48:993–8. doi: 10.1097/j.jcrs.0000000000000914.

Corresponding Author/
Autor Correspondente:

Bruno Barbosa Ribeiro
Serviço de Oftalmologia, Centro Hospitalar Universitário de Santo António - Unidade Local de Saúde Santo António,
Largo do Prof Abel Salazar,
4099-001 Porto, Portugal
E-mail: brunot.barbosaribeiro@gmail.com

ORCID: 0000-0002-8079-9101