LASIK for the correction of high hyperopic astigmatism with the Carl Zeiss Meditec MEL80 and CRS-Master and VHF Digital Ultrasound Epithelial Thickness Monitoring

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Abstract

Purpose: To evaluate outcomes of high hyperopic LASIK using the MEL 80 excimer laser.

Methods: Retrospective analysis of 785 consecutive high hyperopic LASIK procedures using the MEL 80 excimer laser (Carl Zeiss Meditec) and either the VisuMax femtosecond laser (Carl Zeiss Meditec) or zero compression Hansatome (Bausch & Lomb) microkeratome. Inclusion criteria were attempted maximum hyperopic meridian ≥+4.00D and CDVA 20/20 or better. Patients were followed for a minimum of 1 year. Epithelial thickness monitoring by Artemis VHF digital ultrasound (ArcScan Inc) was used to evaluate potential for further steepening as a retreatment. A full review of the peer-reviewed literature was carried out for comparative purposes.

Results: Mean attempted SEQ was +4.52±0.84D (+2.00 to +6.96D) and mean cylinder was 1.05±0.86D (0.00 to 5.25D). Mean age was 50±12 (18 to 70) with 61% female patients. Postoperative SEQ was ±0.50 D in 50% and ±1.00 D in 77% of eyes, after primary treatment. After retreatment, 67% of eyes were ±0.50 D and 89% were within ±1.00 D. UDVA was 20/20 or better in 76% of eyes after final treatment. One line of CDVA was lost in 25% of eyes and two lines were lost in 0.4%. There was a clinically insignificant but statistically significant decrease (P<.05) in contrast sensitivity (CSV-1000) by less than 1 log unit at 3 and 6 cpd, and by 1 log unit at 12 and 18 CPD. Diurnal fluctuation in refraction was identified in 2 eyes, proven by VHF digital ultrasound to be due to diurnal epithelial remodelling overnight and unrelated to maximum postoperative keratometry induced.

Conclusions: LASIK for hyperopia by cumulative treatment of up to +9.00 D with the MEL80 excimer laser was found to satisfy accepted criteria for safety, efficacy and stability.

Introduction

Excimer lasers have been used as a treatment for high hyperopia since Dausch et al[1] first reported the results of PRK for hyperopia up to +7.50 D in 1993 using the MEL60 excimer laser (Carl Zeiss Meditec, Jena, Germany). Numerous reports followed with results of high hyperopia correction with first generation excimer lasers, but many of these were associated with significant regression, undercorrection, and loss of corrected distance visual acuity (CDVA)[1-5] leading a number of clinicians to suggest that safe and effective excimer laser correction of hyperopia might be limited to treatments below +4.00 D or +5.00 D.[2, 3] However, there are more recent reports of safe, effective and stable outcomes for hyperopia above +5.00 D using these first generation excimer lasers.[6, 7]

The first major improvement in hyperopic corneal ablation surgery came relatively early on as different groups found improved results, in particular improved stability, by increasing the optical zone and transition zone size.[3, 8, 9] The second major improvement was observed with the introduction of flying spot lasers to replace the broad beam scanning slit lasers, with an improvement in outcomes noted with the a variety of different lasers.[7, 10-18] Thirdly, alongside the development of excimer laser technology, significant progress has been made with ablation profile design. Finally, results have been improved by changing the protocol for ablation centration from the entrance pupil center to the corneal vertex[16, 19] or coaxially sighted corneal light reflex.[18, 20, 21] (Further references for the introduction are available in appendix A)

The purpose of the present study was to report the refractive outcomes of LASIK with the MEL80 excimer laser (Carl Zeiss Meditec, Jena, Germany) in a large number of eyes with high hyperopic refractive error of +4.00 D or more.

Methods

Patients

This was a retrospective non-comparative consecutive case series including 835 eyes of 681 hyperopic primary LASIK procedures between 14/05/2003 to 20/12/2011 at London Vision Clinic.

Inclusion criteria were: attempted maximum hyperopic correction of ≥+4.00 D, medically suitable for LASIK, no previous ocular, eyelid or orbital surgery, no visually significant cataract, CDVA 20/20 or better, age ≤70 years old, and a minimum follow-up of 1 year. Informed consent and permission to use their data for general analysis and publication was obtained from each patient prior to surgery as part of our routine protocol. Because this was a retrospective study, institutional review board approval was not required. One patient did not provide permission, so was excluded from the analysis.

A full ophthalmologic examination was performed by an in-house optometrist as described previously.[11] This included a manifest refraction and a cycloplegic refraction according to a standardized protocol.[22] The manifest refraction was repeated on a later date by the surgeon, which was used to plan the treatment.

Planning

In our protocol for high hyperopia, the following criteria must be met before the primary procedure. Firstly, the predicted post-operative residual stromal thickness must be greater than 250 µm. Secondly, the attempted correction was limited such that the predicted postoperative keratometry was less than 51.00 D. Finally, an arbitrary maximum laser data entry of +7.00 D was applied. Therefore, some patients were treated using a planned two-stage protocol where the primary procedure was an intentional undercorrection, followed by retreatment at a later date.

Surgical Protocol

All treatments were performed as bilateral simultaneous LASIK using the MEL80 excimer laser. The zero compression Hansatome microkeratome was used between 14/05/2003 and 10/07/2009 in 38% of eyes and the VisuMax femtosecond laser was used between 05/10/2007 and 20/12/2011 in the other 62% of eyes. The procedure was performed by author DZR in 71% of eyes and by author GIC in 29% of eyes. The CRS-Master software platform was used to generate the ablation profiles.

The standardized surgical technique followed has been described previously.[23] Both the flap and corneal ablation were centered on the coaxially sighted corneal light reflex (CSCLR).[20] During surgery, the CSCLR was determined before the flap was lifted as the first Purkinje reflex, seen as the patient fixated coaxially with the aiming beam and the view of the surgeon's contralateral eye through the operating microscope. The CSCLR was used as the best approximation of the intersection of the visual axis with the cornea.

Optical treatment zone diameters were 6.50-mm (in 18%) and 7.00-mm (in 82%). Intended flap thickness was 160 µm in 35% and 180 µm in 2% of eyes (using the Hansatome), and 90-95 µm in 24%, 100 µm in 28%, 110 µm in 8%, and 120 µm in 2% of eyes (using the VisuMax). Flap diameter was 8.5 mm in 0.4% and 9.5 mm in 37% of eyes (using the Hansatome), and 8.0 mm in 16%, 8.5 mm in 0.5%, and 8.8 mm in 45% of eyes (using the VisuMax). For VisuMax flaps, a small contact glass was used for an 8.0-mm flap diameter, otherwise a medium contact glass was used. A 4.5-mm superior hinge was used in all VisuMax cases.

Postoperative Course and Evaluation

Patients were instructed to instill tobramycin with dexamethasone (Tobradex; Alcon Laboratories, Inc., Fort Worth, TX) and ofloxacin (Exocin; Allergan Ltd, Marlow, UK) four times daily and wear plastic shields for sleeping during the first week. The surgeon reviewed the patient at day 1 and flap

adjustments were performed if necessary at the slit-lamp using a surgical spear under topical anesthetic and antibiotic cover. An in-house optometrist examined the patient at 1, 3, and 12 months and yearly thereafter with surgeon review for all outliers. All visits included monocular and binocular UDVA, manifest refraction, and CDVA. Best spectacle-corrected mesopic contrast sensitivity, ATLAS corneal topography and dilated WASCA aberrometry (both Carl Zeiss Meditec) were performed at 3 months, 1 year, and 2 years.

Postoperative complications and dry eye symptoms were assessed at each visit. A 6-grade classification system was used for each parameter: trace, GD I-II (not visually significant), and GD III-V. In this scale, trace refers to any small amount inconsistent with an untreated cornea, even if not visually significant.

Retreatments

Retreatments followed the same protocol in those who had planned retreatments and in those who required retreatment following a full correction. Retreatments were performed once stability was demonstrated over an interval of at least two months, defined as no change in sphere within ±0.25 D and cylinder within ±0.25 D.

In the majority of cases, an Artemis very high-frequency (VHF) digital ultrasound (ArcScan Inc, Morrison, Colo) scan was performed to obtain layered pachymetric maps of corneal, epithelial and residual stromal thickness.[24] When planning a retreatment, the safety was assessed by checking that the predicted residual stromal thickness after the retreatment was greater than 250 µm at the location of the maximum ablation as well as the location of the (peripheral) minimum residual stromal thickness.

Suitability was assessed using an epithelial thickness map to confirm that the minimum epithelium was sufficient to avoid apical syndrome if further steepening was induced. We have previously shown that the central epithelium thins by approximately 2 μm for every diopter of hyperopic correction using the MEL80.[24] This can be used to predict the central minimum epithelial thickness after the retreatment and ensure that this remains greater than 28 μm. This is sufficient given that epithelial breakdown tends to occur for epithelial thicknesses of about 21 μm (personal communication, Dan Z. Reinstein). This method enables us to safely perform further steepening in cases that would otherwise have been excluded based on standard keratometry limits. According to these two safety factors, in some cases the retreatment performed was not a full correction.

Statistical analysis

Outcome analysis was performed according to the Standard Graphs for Reporting Refractive Surgery for both the primary treatment, and after the final treatment. Data from the 2-year visit were used for analysis if available, otherwise 1-year data were used. Stability of keratometry was evaluated as the mean simulated keratometry at 3 months, 1 year, and 2 years. The change in whole eye higher order aberrations was assessed using a 6-mm analysis zone. The incidence of postoperative complications and dry eye symptoms were assessed for the 1 year visit. Microsoft Excel 2010 (Microsoft Corporation, Redmond, WA) was used for data entry and statistical analysis. A *P* value less than .05 was defined as statistically significant.

Results

Patient Population

During the study period, 835 eyes were treated and a minimum of 1-year timepoint examination data were available for 790 eyes (95% follow-up), for which the last time point after the primary procedure was the 2 year visit in 57% (n = 448), the 1 year visit in 38% (n = 303), and the 6 month visit in 5% (n = 39) of eyes. All eyes where the last timepoint after the primary procedure was earlier than 1 year had undergone retreatment at that time. For these eyes, 1-year follow-up data after the retreatment were used to analyse the final outcome. Table 1 shows demographic data for the study population.

Retreatments

The primary procedure was performed as a partial correction in 20% (n = 158) of eyes, of which 51% (81/158) had undergone a retreatment to date. Of the 632 eyes intended for full correction, 35% (220/632) have undergone a retreatment. In total, including two stage protocol cases, 38% (301/790) of eyes have undergone a retreatment. Of these 301 eyes, a second retreatment was performed in 6 eyes (2%) within the two year follow-up period. Retreatments were performed at the 6 month visit in 13% (n = 39), at the 1 year visit in 55% (n = 164), at the 2 year visit in 28% (n = 83), and after the 2 year visit in 4% (n = 12) of eyes. The mean attempted spherical equivalent of the retreatments was +1.08±0.96 D (-1.88 to +3.88 D), of which 6% (n = 18) were myopic, 82% (n = 243) were hyperopic, and 12% (n = 37) were mixed cylinder.

Standard Outcomes

Figure 1 presents the standard graphs for reporting refractive surgery after the primary treatment. Figure 2 presents the standard graphs for reporting refractive surgery after all treatments. Table 2 shows the normalized mesopic contrast sensitivity data. There was a clinical insignificant but statistically significant decrease in contrast sensitivity ($P < .001$) representing less than half a patch at

3 and 6 cpd, and almost one patch at 12 and 18 cpd. Table 3 summarizes the ocular aberrations preoperatively and after the primary treatment. Table 4 summarizes the change in keratometry over time.

Complications

In the 298 eyes treated using the zero compression Hansatome microkeratome, there were two flap complications. In the 492 eyes treated using the VisuMax femtosecond laser, there was 1 suction loss (0.2%), 1 peripheral buttonhole (0.2%), 1 peripheral cryptic buttonhole (0.2%), and 1 case of incomplete sidecut creation (0.2%). None of these complications resulted in abortion of the procedure or a loss of more than one line CDVA. Appendix B (available in the online version of the article) provides details of these complications.

Table A (available in the online version of the article) provides the incidence of postoperative complications that required either a flap lift or Nd:Yag treatment (for epithelial ingrowth). There were also two cases of diurnal refractive fluctuations, with a myopic shift from morning to evening. These cases have been described in detail in a previous publication for an estimated overall incidence for this complication of 0.3%.[25] Table B (available in the online version of the article) summarizes the incidence of postoperative complications as measured at the 1-year postoperative appointment. There were no visually significant complications (GD III-V). Table C (available in the online version of the article) summarizes the dry eye parameters both before and 1-year after surgery. All instances where a patient presented preoperatively with a form of dry eye of GD II or higher were actively managed prior to any surgery.

Discussion

The current study found the treatment of high hyperopia between +4.00 and +9.25 D using the MEL 80 excimer laser to be safe and effective by using a two stage treatment protocol employing epithelial thickness mapping and monitoring. Although there was an increase in higher order aberrations, as expected for a high hyperopic correction, this increase was not visually harmful as demonstrated by only a very small decrease in contrast sensitivity, and only a 0.4% loss of 2 lines in CDVA. The two stage treatment protocol enabled a safer and more accurate final correction for high hyperopia in cases of undercorrection by regression but also enabling us to capitalise on cases that overcorrected after the primary procedure. These results show that LASIK is a safe and effective option for high hyperopia as an alternative to intraocular surgery, although the balance of risks and benefits must be carefully considered between these options.

To compare the current study to published LASIK and intraocular lens studies, we performed a literature review for studies reporting results of hyperopia greater than +4.00 D. The main outcome parameters are shown in Table D for LASIK and Table E for intraocular lens procedures (tables and references available in online version of the article). Chronological examination of the LASIK studies shows a clear trend in improvement over time with modern excimer laser platforms showing a loss of 2 lines CDVA rate of between 0 and 6%. Further, some loss of CDVA would be expected as a matter of course due to the minification effect produced by corneal correction compared to spectacle correction. These rates are similar to the safety reported for refractive lens exchange where the loss of 2 or more lines ranged from 0 to 6.7%[26] and in one study 11%.[27] Such CDVA comparisons must also be considered in context of the more unusual but potentially catastrophic visual complications of intraocular surgery, which cannot be adequately assessed by studies with small populations. For example, refractive lens exchange has been associated with endophthalmitis,[28] posterior capsule opacification,[29] cystoid macular edema,[30] retinal detachment,[31] and suprachoroidal haemorrhage.[32] Equally, phakic intraocular lens implantation is associated with

cataract formation,[33] pupil ovalization,[34] pigment dispersion,[35] endothelial cell loss,[36] and retinal complications.[37] Long term safety of intraocular procedures should also be taken into account given that many of these patients are 50 or younger. Complications such as long term IOL dislocation,[38] capsular fibrosis, and posterior capsule opacification are often underreported.

Postoperative dry eye exacerbation is another factor that should be considered when comparing corneal and intraocular interventions, given that LASIK involves disturbing the corneal nerve plexus. However, intraocular surgery also leads to exacerbation of meibomian gland dysfunction, dry eye and ocular discomfort albeit less so.[39] In the present study, the only dry eye parameter that was greater at 1 year than before surgery was SPK.

Corneal and intraocular approaches to treating high hyperopia are also differentiated in terms of possible achievable refractive correction, refractive stability over the medium and long term, and hence also refractive predictability. It is possible to achieve a larger degree of correction with intraocular surgery simply by changing the power of the lens, whereas hyperopic correction by LASIK has to abide by the limits of corneal steepening, epithelial thinning and potential regression. Therefore, the balance shifts toward intraocular surgery for very high hyperopia as reflected by the treatment range in the published studies compared to LASIK. However, some patients may opt for an undercorrection by LASIK as a compromise to completely avoid the more serious albeit unusual visually compromising complications of intraocular lens surgery.

Intraocular lens procedures are inherently speaking more stable than corneal hyperopic procedures, but the refractive regression generally reported after hyperopic LASIK has been significantly reduced with the use of modern excimer laser systems and ablation profiles. In the present study, there is an initial over-correction which returned to target at 3 months, after which there was a hyperopic shift of about 0.10 D every 6 months. However, it is worth noting that hyperopic refractions progress with

time regardless of whether refractive surgery has been performed; progression of 0.42 D across five years (0.08 D per year) has been reported in patients of 50 or older.[40]

Refractive changes that may occur over many years after LASIK are often identified as a reason to opt for an intraocular procedure in high hyperopia given the perception that this would translate to better refractive predictability. However, a review of refractive predictability data between LASIK and IOL surgery shows that the percentage of eyes within ±0.50 D of the intended target was similar between modern LASIK and the intraocular procedures in the short to medium term. Whereas it might be expected for further hyperopic shift in the long term after LASIK, longer term studies on the stability of clear lens exchange surgery in younger non-cataract patients are lacking.

In this series, two cases of a rare, idiosyncratic diurnal refractive fluctuation syndrome we have previously described were identified by VHF digital ultrasound layered anatomical imaging and shown to be due to epithelial remodelling from morning to evening following compression by the eyelid overnight.[25] This phenomenon was found to also occur in eyes with hyperopia as low as +3.25 D and in postoperative keratometry as low as 41.20 D, with a total incidence of 0.3%. In cases where persistent fluctuation remains, it may be necessary to reverse some of the steepening achieved in order to stabilise the corneal epithelial layer and hence address the root cause for the induced diurnal refractive fluctuations.

Analysis of ocular higher order aberrations showed a significant increase in coma, spherical aberration and higher order RMS. However, the increase in coma can be largely attributed to the difference in where the treatment was centered and where the aberrations were measured, meaning that coma will be measured postoperatively when measured on the entrance pupil center. Spherical aberration induction on average was -0.52 μm, however this was offset by the spherical aberration being positive in the majority of eyes before surgery, meaning that the postoperative

level of spherical aberration was not visually compromising. Induction of negative spherical aberration also carries the benefit of increasing the depth of field,[11, 41, 42] something that can be taken advantage of if cataract surgery is required in the future enabling high quality monofocal lenses to be used in conjunction with micro-monovision rather than employing light transmission reducing multifocal IOLs. In the present study, there was a small decrease in contrast sensitivity, however this was no greater than the drop associated with multifocal intraocular lenses that are currently and commonly used world-wide for patients with this degree of high hyperopia.

In summary, the treatment of high hyperopia within +4.00 to +7.50 D by LASIK with the MEL80 employing epithelial thickness mapping and monitoring represents an equivalent and less-invasive alternative to an intraocular procedure in patients without visually significant cataract. Characterisation and comparison of long-term stability differences between LASIK and intraocular surgery needs further study in order to balance stability benefits against quality of life costs of the rare but more severe visual complications that may occur with intraocular procedures.

Legends

Figure 1: Nine standard graphs for reporting refractive surgery showing the visual and refractive outcomes for 792 high hyperopic eyes after initial treatment with the MEL 80 excimer laser and the VisuMax femtosecond laser (both Carl Zeiss Meditec) or the zero compression Hansatome microkeratome (Bausch & Lomb). UDVA = uncorrected distance visual acuity; CDVA= corrected distance visual acuity; D = diopters; Postop = postoperative; Preop = preoperative; SEQ = spherical equivalent refraction; TIA = target induced astigmatism; SIA = surgically induced astigmatism.

Figure 2: Nine standard graphs for reporting refractive surgery showing the visual and refractive outcomes for 792 high hyperopic eyes after final treatment with the MEL 80 excimer laser and the VisuMax femtosecond laser (both Carl Zeiss Meditec) or the zero compression Hansatome microkeratome (Bausch & Lomb). UDVA = uncorrected distance visual acuity; CDVA= corrected distance visual acuity; D = diopters; Postop = postoperative; Preop = preoperative; SEQ = spherical equivalent refraction; TIA = target induced astigmatism; SIA = surgically induced astigmatism.

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Table 1 – demographic and refractive data

Number of eyes	785
Number of patients	644
Gender (% male / female)	39 / 61
Age (years)	50.4±12 (18 to 70)
Preoperative spherical equivalent refraction (D)	+3.84±1.35 (+0.63 to +8.38)
Preoperative refractive astigmatism (D)	1.05±0.86 (0.00 to 5.25)
Intended postoperative spherical equivalent refraction after primary treatment (D)	-0.68±0.89 (-1.88 to +2.75)
Attempted spherical equivalent refraction correction in primary treatment (D)	+4.52±0.84 (+2.00 to +6.96)
Attempted maximum hyperopic meridian correction in primary treatment (D)	+5.04±0.84 (+4.00 to +7.00)
Spherical equivalent refraction relative to intended target after primary treatment (D)	+0.30±0.85 (-3.63 to +4.25)
Refractive astigmatism after primary treatment (D)	0.77±0.58 (0.00 to 3.50)
Intended postoperative spherical equivalent refraction after all treatments (D)	-0.82±0.82 (-2.38 to +2.50)
Attempted spherical equivalent refraction correction including all treatments (D)	+4.65±0.98 (+2.00 to +8.33)
Attempted maximum hyperopic meridian correction including all treatments (D)	+5.18±0.99 (+4.00 to +9.00)
Spherical equivalent refraction relative to intended target after all treatments (D)	+0.09±0.67 (-2.38 to +2.50)
Refractive astigmatism after all treatments (D)	0.61±0.47 (0.00 to 3.25)
Pre-operative corneal thickness (µm)	547±33 (467 to 662)
Scotopic pupil size (mm)	5.10±0.96 (2.05 to 7.85)
Preoperative average keratometry (D)	43.25±1.49 (38.70 to 47.81)
Average keratometry after primary treatment (D)	46.64±1.90 (40.99 to 51.85)
Average keratometry after all treatments (D)	46.80±1.99 (41.50 to 54.50)

Table 2 - Mean normalized mesopic contrast sensitivity ratio for before and after the primary treatment

cpd	Pre	Post	p-value
3	0.97	0.95	↓ <0.001
6	0.94	0.90	↓ <0.001
12	0.92	0.85	↓ <0.001
18	0.83	0.72	↓ <0.001

cpd: cycles per degree, ↓: indicates a decrease in mesopic contrast sensitivity

Table 3: Change in ocular aberrations

	Pre	Post	Change	t-test
Coma (µm)	0.22±0.13	0.77±0.32	0.54±0.33	p<0.001
Spherical Aberration (µm)	024±0.14	-0.28 ±0.21	-0.52±0.18	p<0.001
High Order Root Mean Square (µm)	0.43±0.13	0.90±0.26	0.48±0.27	p<0.001

Table 4: Change in mean simulated keratometry

	n	Mean K (D)	P-value
3 months	635	46.9 ± 1.9 41.3 to 52.4	
1 year	451	46.6 ± 2.0 41.0 to 51.8	
2 years	313	46.6 ± 1.8 41.0 to 51.5	
3-12 months change	371	-0.34 ± 0.51 -3.32 to 1.22	<.01
1-2 years change	211	-0.13 ± 0.47 -1.60 to 1.97	<.01

Table A: Incidence of postoperative complications requiring surgical intervention

Postoperative complications after primary treatment requiring intervention (out of n = 785)	Occurrence	Percentage of Total
Flap lift for trauma	3	0.38%
Flap lift for inflammation	2	0.25%
Postoperative complications after retreatment requiring intervention (out of n = 298)		
Flap lift for epithelial ingrowth	4	1.34%
Nd:Yag for epithelial ingrowth	8	2.68%

Table B – Incidence of postoperative complications at 1 year

	Nil	Trace	1	2	3	4	5
Microfolds	99.9%	0.1%	-	-	-	-	-
Epithelial ingrowth	95.9%	3.1%	1.0%	-	-	-	-
Interface haze	97.1%	2.9%	-	-	-	-	-
Infection	100%	-	-	-	-	-	-
Interface debris	99.5%	0.5%	-	-	-	-	-
Diffuse lamellar keratitis	100%	-	-	-	-	-	-

Table C – Incidence of dry eye parameter before and 1 year after surgery

Data indicated as percentages		Nil	Trace	1	2	3
SPK (exposure, inferior SPK)	Pre	91.7	6.2 (1.0)	1.9 (0.6)	0.1 (0.0)	0.0
SPK (exposure, inferior SPK)	1 year	72.4	18.0 (5.7)	7.5 (2.8)	2.2 (0.3)	0.0
MGD	Pre	67.5	22.2	8.0	2.2	0.1
MGD	1 year	70.1	20.0	7.1	2.8	0.0
Anterior blepharitis	Pre	93.4	4.5	2.0	0.1	0.0
Anterior blepharitis	1 year	96.4	2.4	1.1	0.0	0.0
Posterior blepharitis	Pre	95.3	2.4	2.0	0.1	0.1
Posterior blepharitis	1 year	95.7	2.9	1.3	0.1	0.0
Mixed blepharitis	Pre	94.6	4.5	0.8	0.1	0.0
Mixed blepharitis	1 year	98.1	1.5	0.4	0.0	0.0
ABMD	Pre	96.6	2.9	0.5	0.0	0.0
ABMD	1 year	97.1	2.9	0.0	0.0	0.0
Lash deposits	Pre	99.9	0.1	0.0	0.0	0.0
Lash deposits	1 year	99.7	0.1	0.0	0.0	0.1
Meibomitis	Pre	99.7	0.3	0.0	0.0	0.0
Meibomitis	1 year	100.0	0.0	0.0	0.0	0.0
Scurf	Pre	99.7	0.3	0.0	0.0	0.0
Scurf	1 year	99.6	0.4	0.0	0.0	0.0
		Nil	Present			
Entropion	Pre	99.9	0.1			
Entropion	1 year	100.0	0.0			
Ectropion	Pre	99.9	0.1			
Ectropion	1 year	99.9	0.1			
Chalazion	Pre	100.0	0.0			
Chalazion	1 year	99.9	0.1			
Pitted lid margins	Pre	100.0	0.0			
Pitted lid margins	1 year	99.9	0.1			
Lid thickening	Pre	100.0	0.0			
Lid thickening	1 year	99.9	0.1			
Blocked meibomian glands	Pre	99.9	0.1			
Blocked meibomian glands	1 year	99.9	0.1			
Band keratopathy	Pre	99.9	0.1			
Band keratopathy	1 year	100.0	0.0			

Appendix A – Complete Introduction and References for Literature Review

Introduction

Excimer lasers have been used as a treatment for high hyperopia since Dausch et al[1] first reported the results of PRK for hyperopia up to +7.50 D in 1993 using the MEL60 excimer laser (Carl Zeiss Meditec, Jena, Germany). Numerous reports followed with results of high hyperopia correction with first generation excimer lasers, but many of these were associated with significant regression,[1-13] undercorrection,[14-16] and loss of corrected distance visual acuity (CDVA)[1, 3, 6, 7, 9-11, 16, 17] leading a number of clinicians to suggest that safe and effective excimer laser correction of hyperopia might be limited to treatments below +4.00 D or +5.00 D.[5-7, 12, 16, 18, 19] However, there are more recent reports of safe, effective and stable outcomes[20] for hyperopia above +5.00 D using these first generation excimer lasers.[8, 21-26]

The first major improvement in hyperopic corneal ablation surgery came relatively early on as different groups found improved results, in particular improved stability, by increasing the optical zone and transition zone size.[7, 8, 21, 23, 27, 28] The second major improvement was observed with the introduction of flying spot lasers to replace the broad beam scanning slit lasers, with an improvement in outcomes noted with the MEL70[29-31] and MEL80[32, 33] (Carl Zeiss Meditec, Jena, Germany), the LADARVision[26, 27, 34] (Alcon, Fort Worth, TX), the EC-5000[35] and NAVEX[36] (NIDEK Co Ltd, Gamagori, Japan), the ESIRIS[37-40] and Amaris[41-46] (Schwind GmbH, Kleinostheim, Germany), and the Allegretto,[47, 48] Eye-Q[49] and EX500[50] (Alcon, Fort Worth, TX). Thirdly, alongside the development of excimer laser technology, significant progress has been made with ablation profile design. Finally, results have been improved by changing the protocol for ablation centration from the entrance pupil center to the corneal vertex[41-43, 51, 52] or coaxially sighted corneal light reflex.[49, 53-56]

Literature Review

A literature review was conducted to identify published LASIK[3, 4, 6-8, 10-14, 16, 20, 22-27, 29, 31-39, 41-50, 57-59] (PRK studies were not included) and intraocular lens studies (clear lens exchange, phakic IOLs)[60-76] reporting results of hyperopic greater than +4.00 D. The main outcome parameters are shown in Table D for LASIK and Table E for intraocular lens procedures (references in the tables are according to the reference list included in this appendix, not the main article).

							Accuracy			UDVA		Safety	
First Author	**Year**	**N (eyes)**	**Technique**	**Preop SEQ**	**Age (years)**	**Timepoint**	**Mean±SD (range)**	**±0.50D**	**±1.00D**	**≤20/20**	**≤20/40**	**1 line**	**≥2 lines**
de Ortueta[42]	2016	38	LASIK Amaris Carriazo-Pendular	+4.07±0.90 +2.38 to +5.75	40±10 18 to 57	6 months	+0.28±0.58	61	96	18	84	8	8
Arba Mosquera[43]	2016	46	LASIK Amaris Carriazo-Pendular	+3.64±1.42 +1.27 to +6.18	45±11 18 to 62	6 months	+0.39±0.43	61	93	30	85	13	6.5
Plaza-Puche[44]	2016	51	LASIK Intralase & Amaris OZ 6.2-6.9mm	+6.33±0.83 +5.00 to +8.50	33±9 21 to 54	6 months	+0.50±1.06 -0.50 to +3.38		71	53	98	11	6.5
Amigo[48]	2015	24	Allegretto 400 Hz & Hansatome Wavefront Optimised	+3.66±0.61 +2.75 to +5.00	39±9 20 to 49	6 months	+0.08± 0.56 -0.75 to +1.25	57	96	67	92	21	4
		16	Aspheric Customised Profile OZ 6.5 mm	+4.05±0.59 +2.75 to +5.13			+0.21±0.44 -0.50 to +1.00	100	100	81	100	12	0.0
Plaza-Puche[45]	2015	86	LASIK Intralase & 500kHz Amaris excimer OZ 6.3-7.0mm	+2.66±1.68 -1.38 to +5.75	40±10 23 to 64	36 months	+0.40±0.65 -1.63 to +2.00	70	85	76	99	6.2	1.2
Antonios[46]	2015	53	LASIK Moria M2 & Amaris	+2.25±1.06 +0.75 to +5.00	45±12 19 to 61	6 months	+0.22±0.75 -1.25 to +1.75	43	72	85	92	0.0	0.0
		72	LDV femto & Amaris	+2.24±0.95 +0.50 to +4.75	46±10 18 to 66		-0.32±0.76 -2.13 to +1.50	65	90	88	100	0.0	0.0
Alio[41]	2013	27	LASIK Intralase & 500kHz Amaris excimer OZ 6.2-6.9mm	+6.33±0.83 +5.00 to +8.50		6 months	+0.55±1.09 -0.50 to +3.38	70		44	92	8	0.0
Kanellopoulos[50]	2012	34	LASIK Xtra IntraLase / FS200	+3.40±1.78 +0.25 to +8.00		2 years	+0.20±0.40						
		34	LASIK Xtra EX500	+3.15±1.46 +0.25 to +8.00			-0.20±0.56						
Kanellopoulos[49]	2012	202	LASIK Eye-Q	+3.04±1.75 +0.75 to +7.25 (sphere)	40±12 19 to 62	2 years	-0.39±0.30 (sphere)	76	94	59	96	2.9	2.4
Kermani[36]	2009	52	LASIK NAVEX OZ 6.5mm (TZ 9mm) (visual axis group)	+2.57±1.26 +0.13 to +5.63		3 months	+0.29±0.70 -1.00 to +1.75	81	96	51	95	21	10
de Ortueta[39]	2009	33	LASIK Carriazo-Pendular ESIRIS OZ 6.25mm	+2.61±1.39 +0.75 to +6.00	52 34 to 65	3 months	+0.26±0.51 -0.38 to +1.88	88	94				0.0
Llovet[32]	2009	49	LASIK Moria I MEL80 OZ 6mm	+3.30±1.30 +3.60 to +6.25	36.9 20 to 56	1 year	+0.40±0.60	63	90			8	4

Reinstein[33]	2009	258	LASIK Hansatome MEL80	+2.54±1.16 +0.25 to +5.75	56 44 to 66	1 year	+0.09±0.48	79	95	86	100	17	0.0
Young[57]	2009	Sub-group of 1659 eyes	LASIK IntraLase FS60 S4	+4.00 to +5.50		1 month				38			20
Alio[38]	2008	51	LASIK ESIRIS	+4.45±1.08 +2.50 to +7.25		6 months	+0.88±1.10 -0.50 to +3.50	80	88	54	95	4	0.0
Waring[35]	2008	279	LASIK EC-5000 OZ 6mm (TZ 9mm)	+3.51±1.45 +0.50 to +6.75	50±9 23 to 69	1 year	+0.35±0.54 -1.63 to +2.00	61	99	63	90	15	1.4
Desai[16]	2008	12	LASIK Hansatome Star S2 OZ 5mm (TZ 9mm)	+4.10±0.69 +4.00 to +5.50	54±14	≥3 years	+0.59±1.18	32	68	17	67	0	9
Alio[58]	2006	41	LASIK Incl. retreatments Keracor 217C OZ 6mm	5.30±0.90 +4.00 to +7.75	31±11	1 year	+0.30±1.30 -2.50 to +3.50	46	63				
Alio[37]	2006	55	LASIK Carriazo Pendular ESIRIS ≥6mm	+5.10±0.90 +4.00 to +7.00		6 months	+0.40±0.50 0.00 to +2.00	86	91			5.5	1.8
Spadea[31]	2006	100	LASIK Hansatome MEL70 OZ 6mm	+4.49±1.20 +2.25 to +7.25	40±8 22 to 55	2 years	+0.29±0.66	70	92	64	96	6	0
Kanellopoulos[47]	2006	23	LASIK Moria M2 Allegretto Wave	+2.24±1.18 +0.25 to +6.50		1 year	+0.69±0.92 0.00 to +1.50	71				8	0
Jaycock[13]	2005	47	LASIK Microkeratome (180um) Summit Apex Plus OZ 6.0mm	+3.58±1.48 +0.75 to +7.00	51.5 32 to 66	5 years	+0.89±0.94	32	60	43	87	2.1	0
Oral[26]	2004	39	LASIK S2	+2.98±1.60 +0.87 to +6.50	51±10	6 months	+0.51±0.51	63	88	67	100	2.5	0.0
		25	S3	+2.71±1.36 +1.00 to +5.37	58±9		+0.35±0.58	68	88	48	100	12	0.0
		41	LADARVision	+2.59±1.28 +0.62 to +5.62	53±10		+0.24±0.57	76	86	76	100	0.0	0.0
Esquenazi[12]	2004	18	LASIK ACS Keracor 117C OZ 5.5mm (8.5mm TZ)	+5.48±1.23 +4.25 to +7.25		5 years	+2.24±1.00	22	33	10	42		
Zadok[11]	2003	26	LASIK ACS Keracor 117CT OZ 5.0-8.5	+4.29±0.89 +3.00 to +5.90	45 19 to 65	1 year	+0.21±0.60		92	23	92	11	0.0
		22		+7.52±1.36 +6.00 to +10.00			+1.62±1.50		36	14	59	4	13

El-Agha[25]	2003	40	S2 LASIK	+2.86±1.28 +1.38 to +6.50	41±9 35 to 63	9 months	+0.44±0.57		86	68	100	22	0.0
Carones[27]	2003	53	LASIK SKBM LADARVision OZ 7mm	+2.34±2.09 +0.50 to +6.00	40±10 20 to 58		-0.22±0.41 -1.75 to +0.75	79	98	53	100	4	0.0
Lian[24]	2002	54	LASIK ACS Keracor 117C PZ 5-5.5 (TZ 8.5-9.5)	+3.12 +1.00 to +5.75	38±13 18 to 55	1 year	+0.29±0.78	61	83	63	93	12	1.9
Ditzen[29]	2002	23	LASIK Hansatome MEL70 Spherical	+4.88±2.13 +2.13 to +9.63	28 20 to 42	1 year	+0.30±0.90 -0.75 to +2.50	78		39	83	6	0.0
		44	Astigmatic	+4.33±2.15 +0.50 to +9.50	30 25 to 43		+0.29±1.27 -3.25 to +3.25	42		4	63	4	4
Cobo-Soriano[10]	2002	74	LASIK Moria LSK-One Keracor 217CT	+4.40±0.30 +4.00 to +4.90	35.5 18 to 65	8 months			82	-	-	-	2.8
		56		+5.30±0.20 +5.00 to +5.90					80				5.8
		47		+6.50±0.50 +6.00 to +7.90					80				16.6
Salz[34]	2002	39	LASIK Hansatome LADARVision OZ 6mm (TA 9mm) Spherical	+3.00 to +6.00		6 months		41	69	29	79		2.6
		48	Astigmatic	+3.00 to +5.75				46	79	32	84		8.5
Choi[20]	2001	32	LASIK Hansatome S2	+4.00±4.50 +1.50 to +8.75	55 35 to 71	6 months	+0.30±1.70 -3.00 to +2.70	34	53		66	25	9
Tabbara[14]	2001	80	LASIK ACS Keracor 117C	+3.40±2.00 +0.50 to +11.50	42±13 18 to 65	6 months	+0.26±0.80 -2.00 to +3.50	58	84	44	98		1.25
Argento[8]	2000	251	LASIK Microkeratome (160um) Keracor 117CT 4.5-5.5mm OZ	+5.28±0.69 +5.50 to +8.50	30.9% <40 69.1% >40	1 year	+0.88±0.96	52	81		78	5	0.0
		32	5.9mm OZ	+5.13±0.61 +5.00 to +8.50	19.1% <40 80.9% >40		-0.48±0.45	52	93		77	5	0.0
Esquenazi[7]	1999	58	LASIK Chiron Keracor 117CT OZ 5-7mm	+4.50±1.73 +1.75 to +8.50	47 20 to 63	1 year	+0.88±1.87 -1.25 to +2.50	61	73	35	81	6	6
Barraquer[23]	1999	30	LASIK Chiron Schwind-Keratom II OZ 7mm	+4.67 +3.51 to +6.00		6 months	+0.82 0.00 to +2.50		80				0.0
		18		+7.44 +6.01 to +10.00			+1.10 -0.50 to +3.00		77				0.0

Arbelaez[6]	1999	20	LASIK ACS Keracor 117C 4.5-5.5mm (TZ 8mm)	+3.10 to +5.00		1 year		43	83	28	93	24	0.0
		16		+5.10 to +9.00				38	50	0	50	24	12
		14		+3.10 to +5.00				41	58	10	81	21	7
		13		+5.10 to +9.00				17	17	0	15	61	15
Argento[4]	1998	95	LASIK Chiron Keracor 117CT 5.0-5.5mm OZ	+5.28±0.69		6 months	+0.88±0.96	10	71	45		6	0.0
Goker[22]	1998	54	LASIK ACS Keracor 116 OZ 8.5mm	+6.50±1.33 +4.25 to +8.00	24 21 to 64	18 months	+0.44±1.95	39	76	15	67		6.8
Ditzen[3]	1998	23	LASIK ACS MEL60 OZ 5mm	+5.28±1.92 +4.25 to +8.00	33±12	1 year	+1.91 -0.08 to +3.71				13	4.3	7.3

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							Accuracy			UDVA		Safety	
First Author	**Year**	**N (eyes)**	**Technique**	**Preop SEQ**	**Age (years)**	**Timepoint**	**Mean±SD (range)**	**±0.50D**	**±1.00D**	**≤20/20**	**≤20/40**	**1 line**	**≥2 lines**
Hua[60]	2013	19	CLE + piggyback IOL	+9.81±2.62 +6.00 to +14.50	45±8 32 to 55	2 years	-0.20±1.39	31.6	68.4		21	21	11
Ferrer-Blasco[61]	2012	30	CLE (ReSTOR)	+4.52±1.14 +3.00 to +7.00	52 44 to 60	6 months	-0.04±0.46	33	97			0.0	6.67
Alfonso[62]	2011	45	CLE (AcriLISA)	+3.53±2.29 +0.25 to +10.00	55 45 to 64	6 months	-0.15±0.40 -0.50 to +1.25	87	93			24	0.0
Alfonso[63]	2009	41	LASIK + CLE (ReSTOR)	+2.71±1.61 +1.25 to +5.50	51±6 45 to 65	6 months	-0.06±0.51 -1.25 to +1.25	73				22	2.4
Fernandez-Vega[64]	2007	158	CLE (ReSTOR)	+3.86±2.52 +0.75 to +8.50	53±6 45 to 70	6 months	+0.23±0.32	89	100			11	0.0
Pop[65]	2004	19	CLE (Acrysof / PMMA)	+2.75 to +7.50	26 to 46	2 month	+0.18±0.71	55	91		82	0.0	0.0
Preetha[66]	2003	20	CLE (Staar IOL / Rayner)	+6.66±2.17 +4.75 to +13.00	36 19 to 50	16 months	+0.68±0.67 0.00 to +2.50	70	90	10	50	10	0.0
Dick[67]	2002	26	CLE (Array IOL)	+3.04±1.04 +1.63 to +5.75	52 44 to 62	6 months	+0.04±0.45 -0.83 to +1.00	88	100	31	100	0.0	0.0
Fink[68]	2000	24	CLE (SurgiAA-4203V)	+6.32±1.32 +4.75 to +10.25	54.7	10 months	+1.02±0.16 +0.67 to +1.25	71	88	25	63	29	0.0
Siganos[69]	1998	35	CLE (Coburn)	+9.19±0.34 +6.75 to +13.75	40 19 to 55	5 years	+0.02±0.82 -2.50 to +3.00	74	91	14	100	0.0	0.0
Lyle[70]	1997	20	CLE (Chiron / Ioptex)	+4.73±1.98 +2.38 to +7.63	49±6 37 to 60	2 years	-0.21±0.95 -2.25 to +1.88		75		85	15	0.0
Guell[71]	2008	41	Artisan	+4.92±1.70	32	4 years	-0.11±0.74	35	64	0	43		
Munoz[72]	2005	39	Artisan + LASIK	+7.39±1.30 +5.25 to +9.75	26 23 to 31	1 year	+0.06±0.52 -1.50 to +0.75	80	95	17	90	23	0.0
Pop[65]	2004	19	Artisan	+2.75 to +9.25	20 to 41	2 month	-0.03±0.75	50	78		89	0.0	0.0
Saxena[73]	2003	26	Artisan	+6.80±1.97 +3.00 to +11.00	44 28 to 60	6 months	-0.08±0.74 -1.50 to +1.38	59	86	50	96	11	0.0
Alio[74]	2002	29	Artisan	+6.06±1.26 +3.00 to +9.00	34 19 to 54	1 year	0.10±0.57 -1.00 to +2.00	79	97	7	66	3.4	0.0
Pesando[75]	1999	15	ICL	+7.77±2.08 +4.75 to +11.75	38 22 to 56	1 year	+0.02±0.64 1.00 to +1.50	69	92	0	46	8	0.0
Davidorf[76]	1998	24	ICL	+6.51±2.08 +3.75 to +10.50		8 months	-0.39±1.29 +1.25 to -3.88	58	79	8	63		4

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Appendix B – Intraoperative and postoperative complications

Intraoperative complications for Hansatome treated eyes

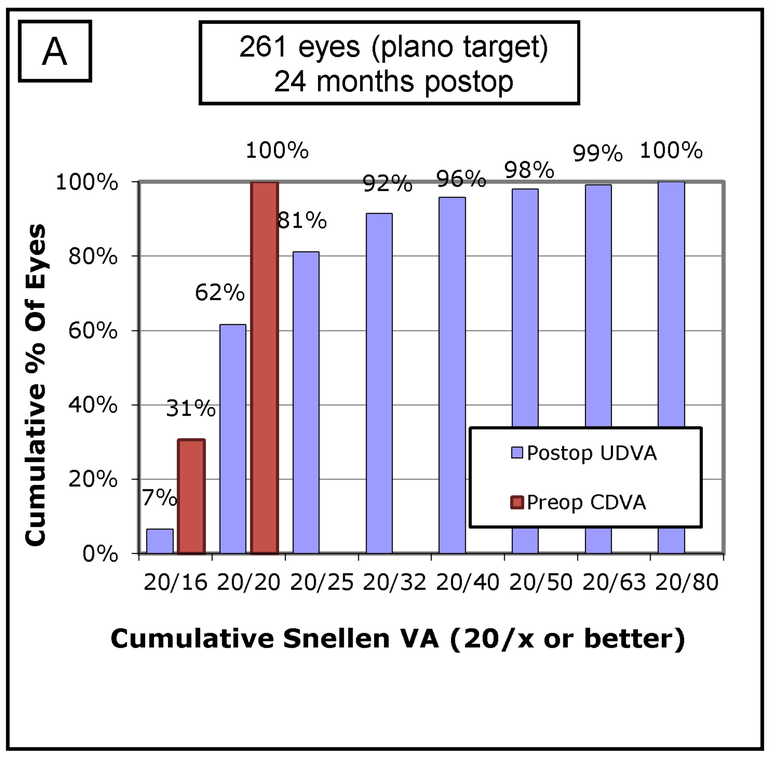
The first case was of an irregular bed in one eye of the patient, where a shallow linear step in the bed was noted, but ablation was carried out as planned with no subsequent impact on the final refractive or visual outcome. In the second case, there was a very small (0.25 mm) “button” on the stromal surface with no associated defect in the flap overlying this – a cryptic buttonhole. The epithelium was manually removed from the “button” to reveal the shiny aspect of Bowman’s layer prior to the ablation, after which the flap was replaced with excellent edge apposition. The patient was prescribed fluorometholone 0.1% eye drops (FML; Allergan, Irvine, CA) for four weeks, however this eye developed trace interface haze associated with a -1.50 D overcorrection in outcome (this was the outlier overcorrection in the population). A PRK retreatment with mitomycin-C 0.02% for 60 seconds was performed 6 months after the primary surgery. Postoperatively, there was no indication of interface haze after this retreatment and the final CDVA was 20/25, one line less than preoperatively.

Intraoperative complications for VisuMax treated eyes

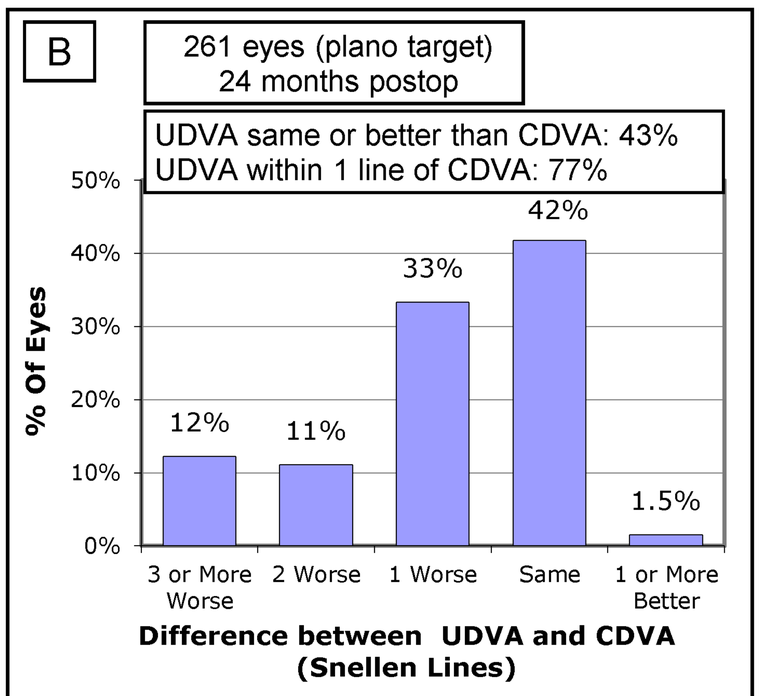
In one eye, there was incomplete protection of the hinge, which meant that part of the peripheral hyperopic ablation profile was inadvertently applied to the edge of the hinge resulting in ablation through the stromal component of the flap in this area. This was recognised when checking the flap at the slit-lamp immediately after surgery and managed conservatively with a bandage contact lens until the epithelial defect had healed without consequences. At 5 months after surgery, this eye recovered the preoperative CDVA of 20/16.

In the case of the cryptic buttonhole, the surface of Bowman’s layer was exposed by scraping the epithelium prior to the ablation. A bandage contact lens was applied and the final result was a loss

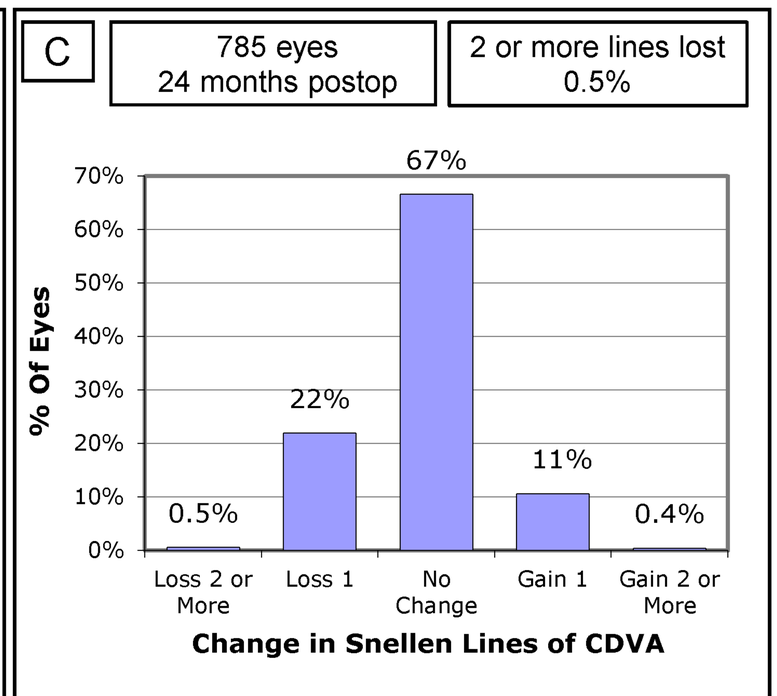
of 1 line CDVA at 2 years. In the case of suction loss, this occurred after about 20% of the interface had been ablated, in the periphery due to the out to in scan direction. The contact glass was reapplied and the flap was created successfully using the same flap settings. Minimal flap slivers were noted in the temporal periphery, which were carefully positioned and the flap was replaced. There was a loss of 1 line CDVA in this eye at 2 years. There was incomplete femtosecond sidecut creation in one eye in the inferior region, which was manually dissected by a rhexis fashion following which the flap was lifted and replaced as normal. There was a loss of 1 line CDVA in this at 2 years, although trace ABMD was noted.



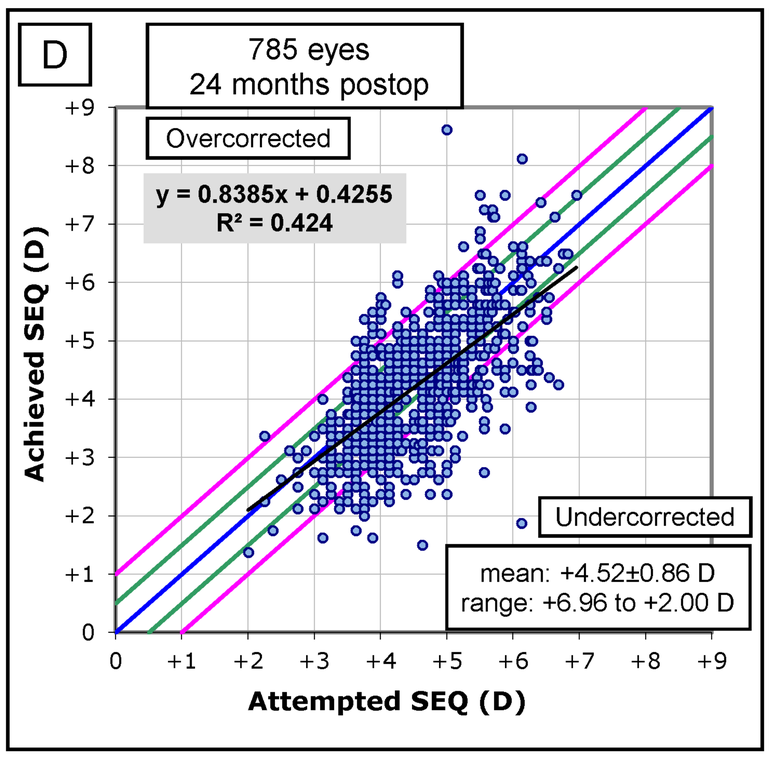
Uncorrected Distance Visual Acuity



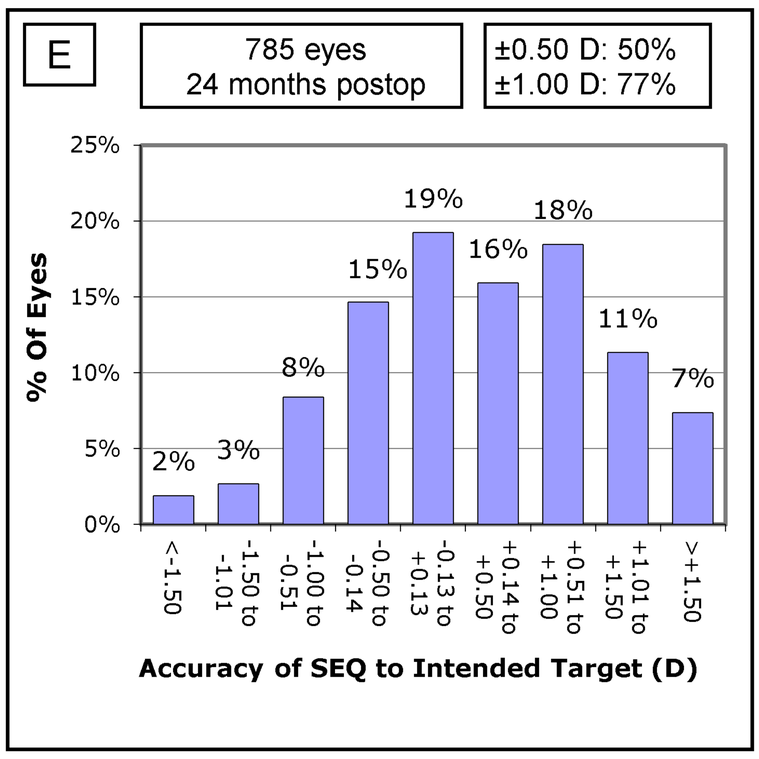
Uncorrected Distance Visual Acuity vs. Corrected Distance Visual Acuity



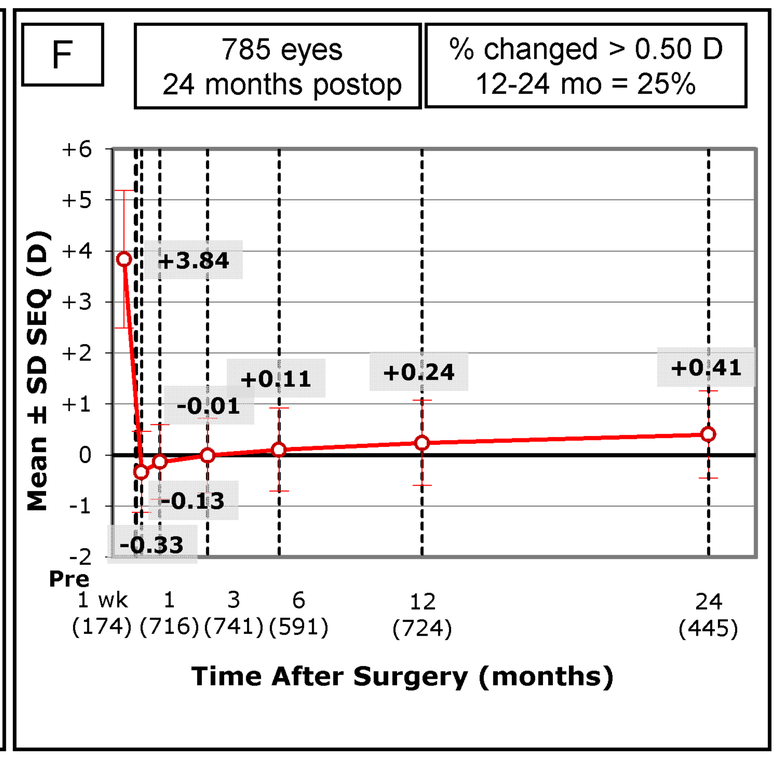
Change in Corrected Distance Visual Acuity



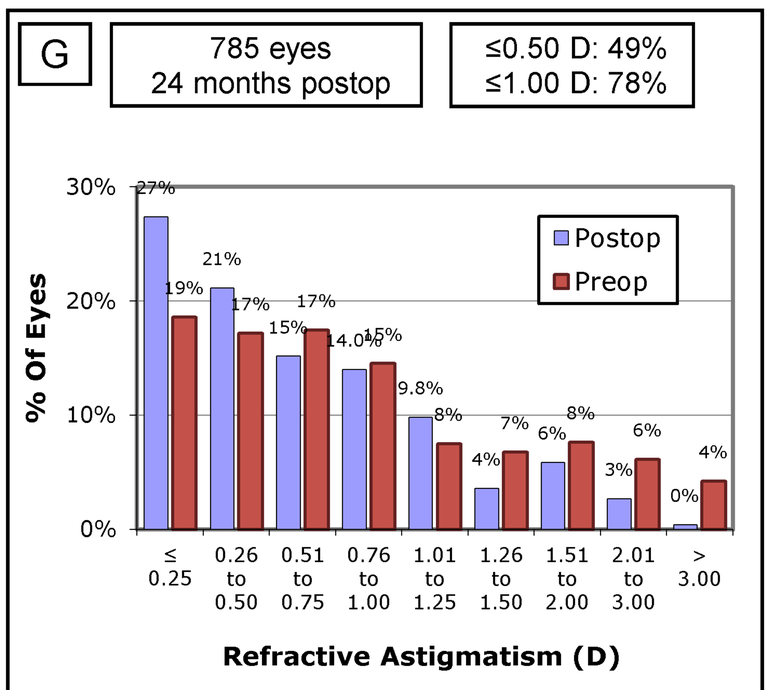
Spherical Equivalent Refraction Attempted vs Achieved



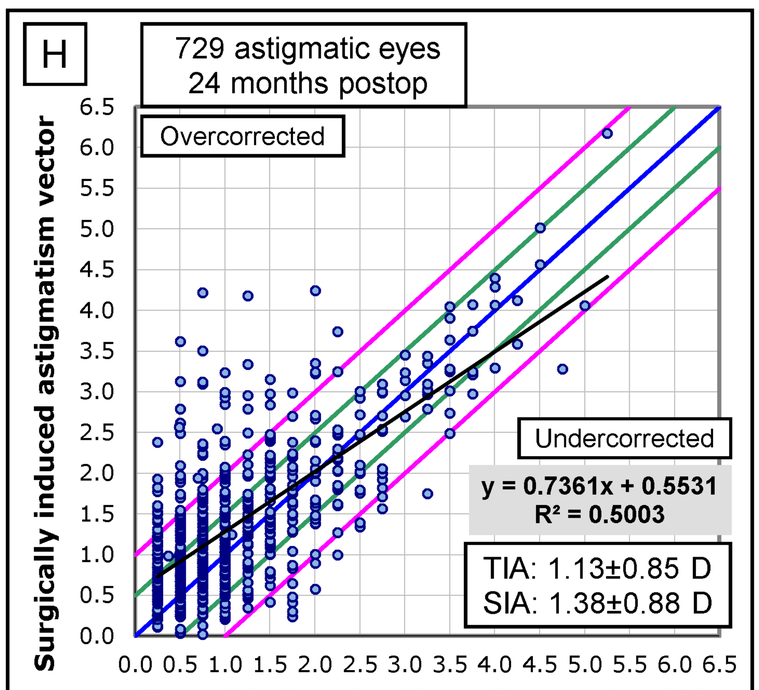
Spherical Equivalent Refraction Accuracy



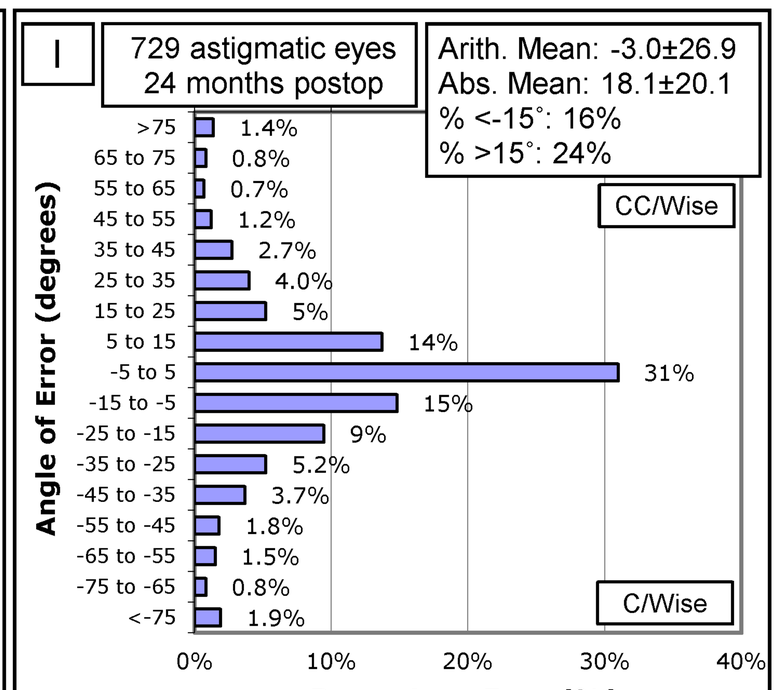
Spherical Equivalent Refraction Stability



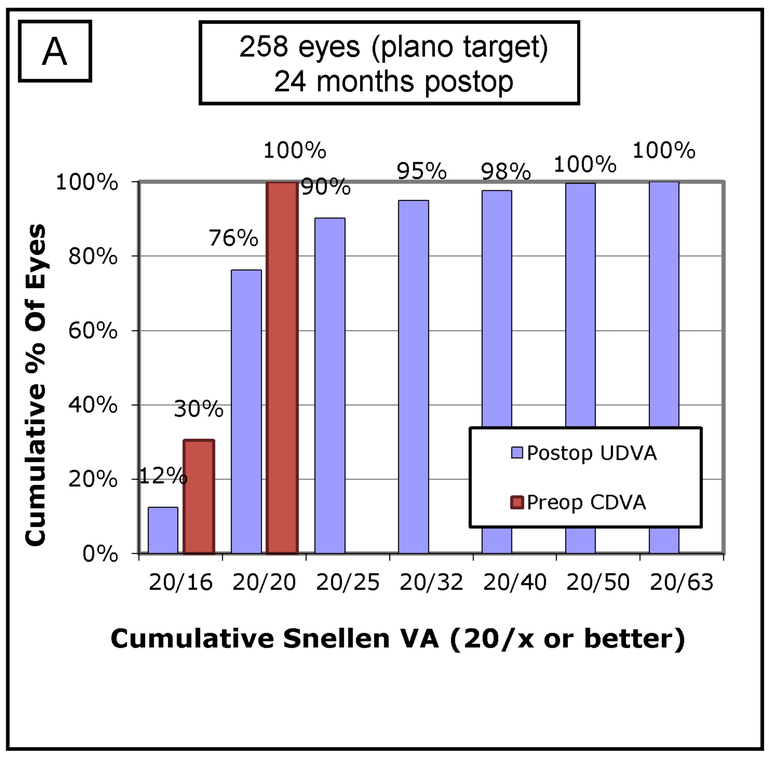
Refractive Astigmatism



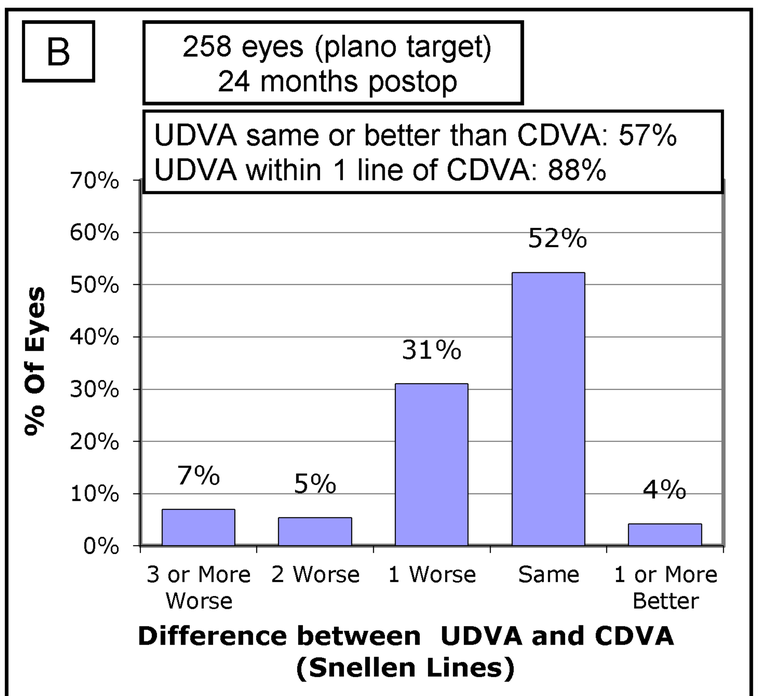
Target Induced Astigmatism vs Surgically Induced Astigmatism



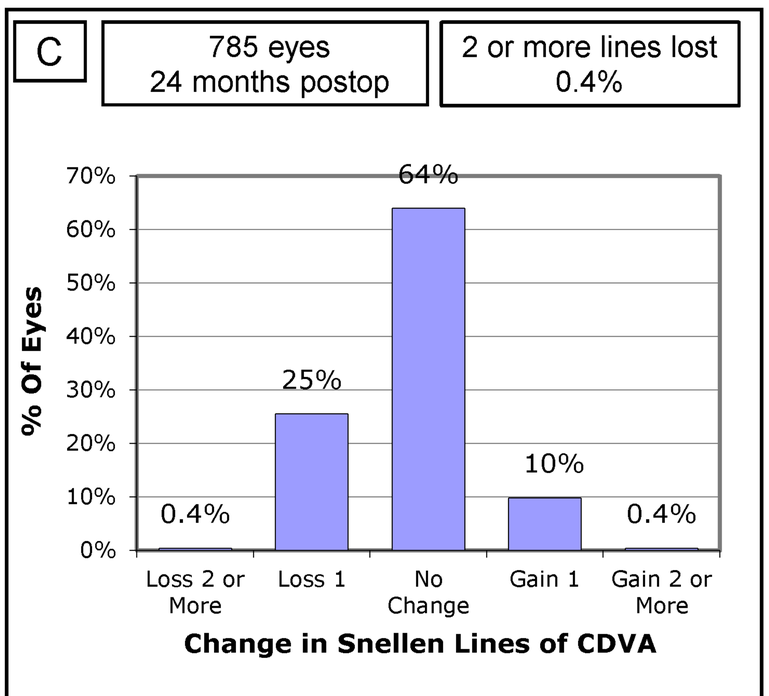
Refractive Astigmatism Angle of Error



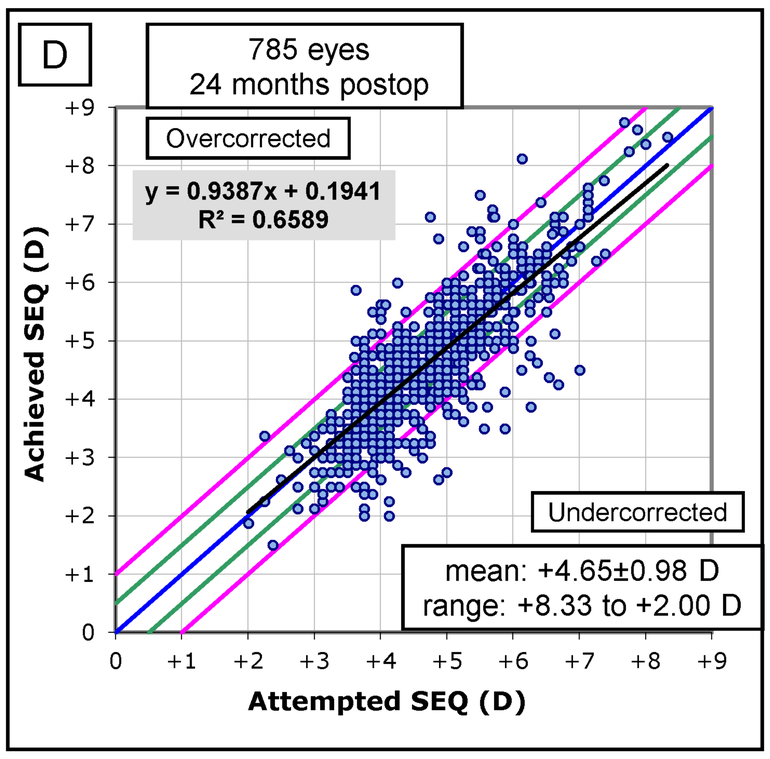
Uncorrected Distance Visual Acuity



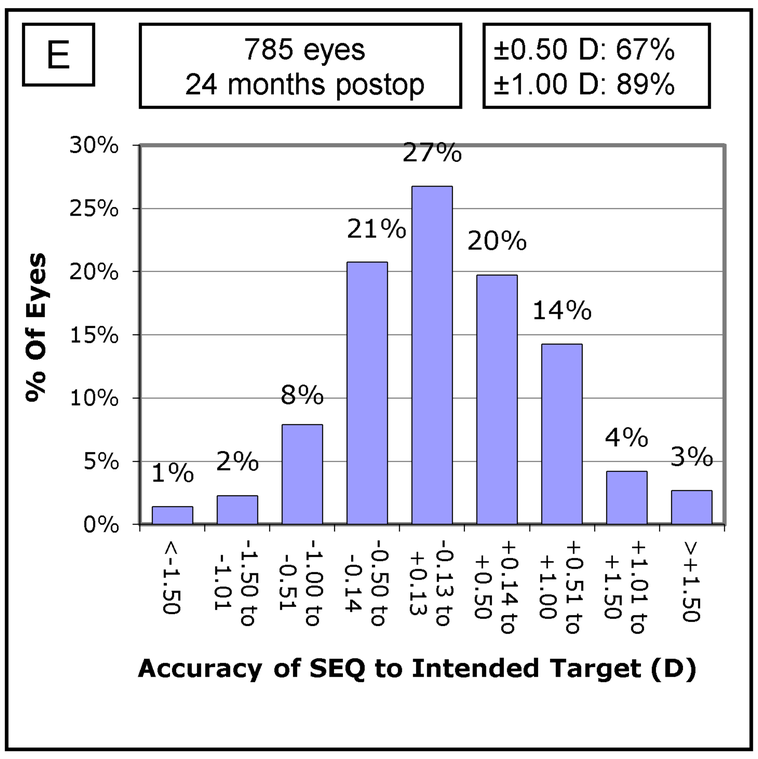
Uncorrected Distance Visual Acuity vs. Corrected Distance Visual Acuity



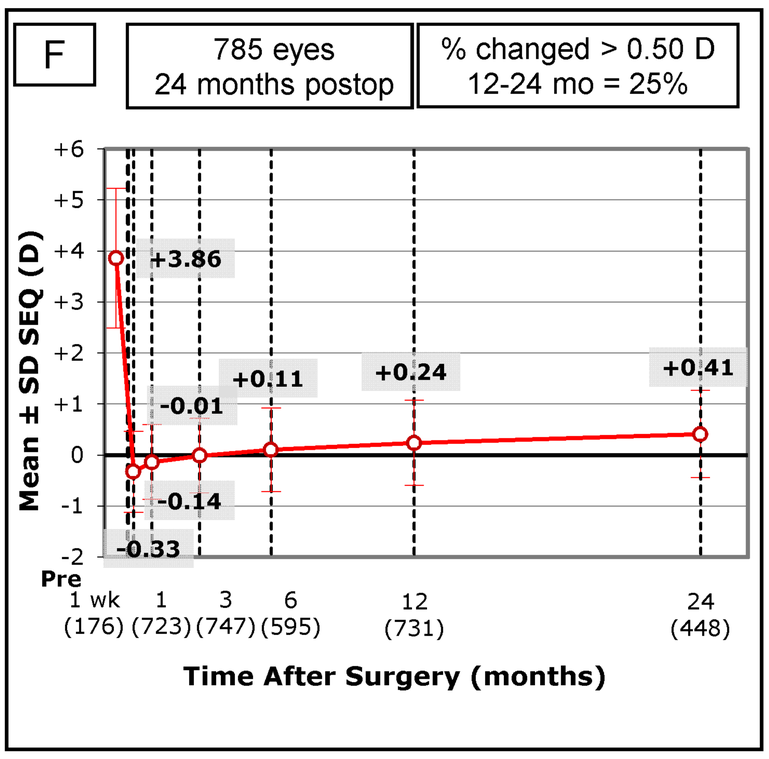
Change in Corrected Distance Visual Acuity



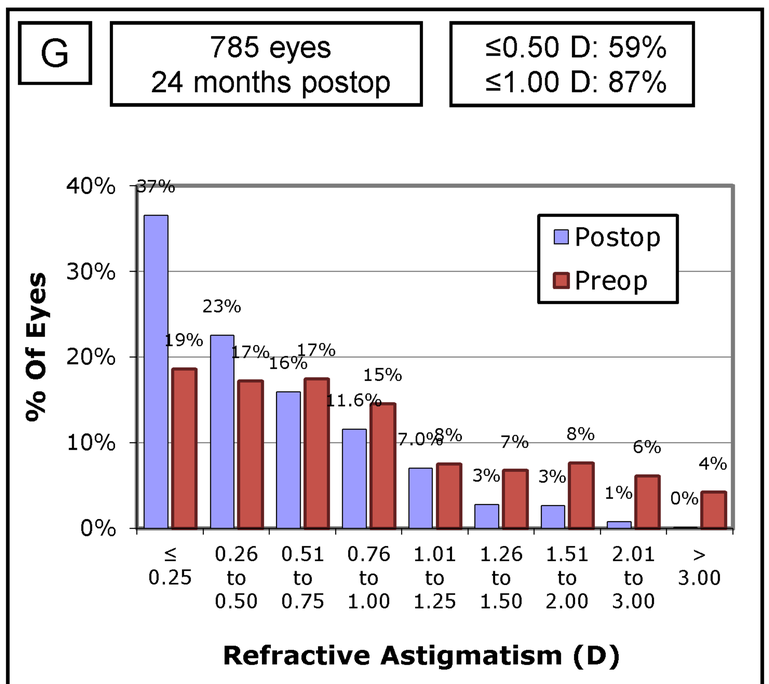
Spherical Equivalent Refraction Attempted vs Achieved



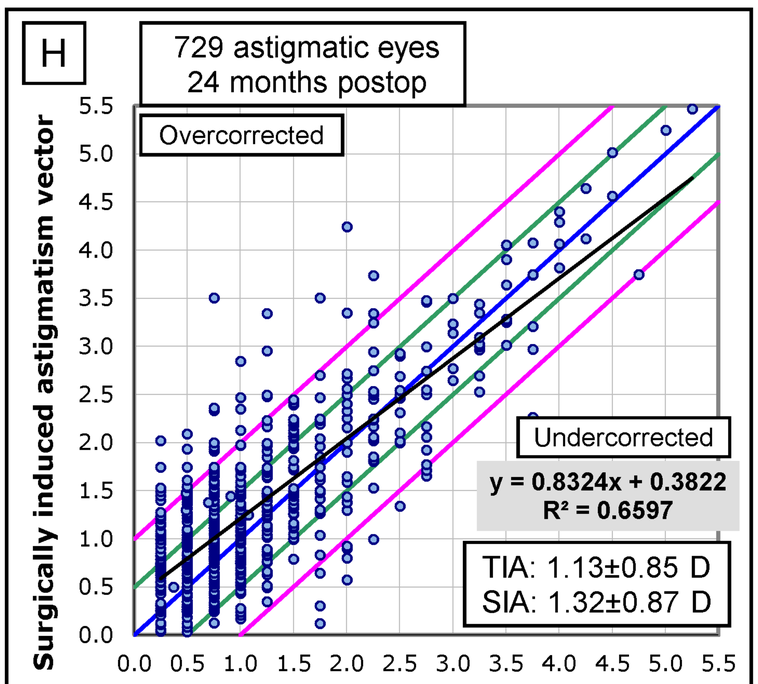
Spherical Equivalent Refraction Accuracy



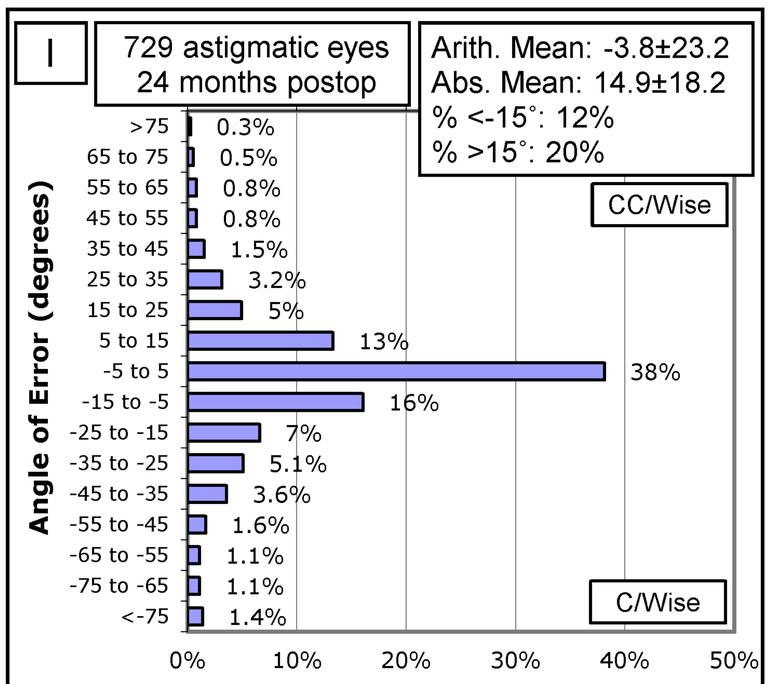
Spherical Equivalent Refraction Stability



Refractive Astigmatism



Target Induced Astigmatism vs Surgically Induced Astigmatism



Refractive Astigmatism Angle of Error