Efficacy, Safety, Contrast Sensitivity, Aberration Control and 2 year stability after LASIK for high myopia and astigmatism from -8.00 to -14.25 D

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Abstract

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

Methods: Retrospective analysis of 479 consecutive high myopic LASIK procedures (318 patients) using the MEL 80 excimer laser (Carl Zeiss Meditec) and VisuMax femtosecond laser (Carl Zeiss Meditec) in 77% of cases or zero compression Hansatome (Bausch & Lomb) microkeratome in 23% of cases. Inclusion criteria were preoperative spherical equivalent refraction (SEQ) of between -8.00 D to -14.25 D, and CDVA of 20/20 or better. Patients were followed for a minimum of 1 year. Flap thickness was between 80-160 µm and optical zone was between 5.75-6.50 mm. Standard outcomes analysis was performed.

Results: Mean attempted SEQ was -9.39±1.22 D (-8.00 D to -14.18 D) and mean cylinder was -1.03±0.84 D (0.00 D to -4.50 D). Mean age was 37±9 (21 to 60) with 54% female patients. Of this population 69% were treated by DZR and 31% by GIC. Postoperative SEQ was ±0.50 D in 55% and ±1.00 D in 83% of eyes, after primary treatment. After retreatment, 69% of eyes were ±0.50 D and 95% were within ±1.00 D. UDVA was 20/20 or better in 89% of eyes after final treatment. One line of CDVA was lost in 3% of eyes and no eyes lost two or more lines. Statistically significant increases (p<0.001) were measured in contrast sensitivity (CSV-1000) at 12 and 18 CPD.

Conclusions: The MEL 80 excimer laser was found to achieve high efficacy and safety for treatment of high myopia between -8.00 D and -14.25 D and up to -4.50 D of cylinder.
Introduction

In the 1990s many studies were published reporting PRK and LASIK correction of very high myopia (up to -32.00 D in some cases),\(^1\text{-}^6\) however, these treatments were associated with low predictability, significant regression, and induced night vision disturbances.\(^7\text{-}^9\) During this period, it was found that these issues were in large part due to the use of small optical zones,\(^10\text{-}^11\) and the non-aspheric Munnerlyn ablation profiles leading to significant induction of spherical aberration.\(^12\) By 1998, authors concluded that LASIK was not an appropriate treatment for very high myopia above -15.00 D\(^6\) and were suggesting that phakic intraocular lens (IOL) implantation was more appropriate. Over the next 10 years, consensus shifted towards using phakic IOLs for high myopia and published LASIK studies rarely included myopia above -10.00 D. For example, the German Commission for Refractive Surgery’s guidelines state that laser correction should only be considered up to -8.00 D.\(^13\)

This thinking was further reinforced when a Cochrane review was published in 2010\(^14\) (and updated in 2014\(^15\)), which compared laser refractive surgery and phakic IOLs for the treatment of high myopia. This review concluded that “at one year post surgery, phakic IOLs are safer than excimer laser surgical correction for moderate to high myopia in the range of -6.00 to -20.00 D and phakic IOLs are preferred by patients”. However, by applying the rigorous Cochrane method, only three studies met the inclusion condition of being a randomized control trial (RCT), so the conclusion was based on a total of 114 eyes each for LASIK and phakic IOL. Furthermore, the LASIK studies were for first and second generation excimer lasers, two published in 2002 and one in 2007, in which smaller optical zones and/or non-aspheric ablation profiles had been used.\(^16\text{-}^18\) Therefore, this review had not considered modern flying spot excimer lasers, advances in eye-tracking, and ablation profile design including the use of larger optical zones, wavefront-optimized aspheric profiles,\(^16\text{-}^20\) modern algorithms for compensation for fluence projection and reflection errors,\(^21\) biomechanical factors\(^22\) and the availability of topography-guided ablation profiles.\(^23\) Advances in femtosecond laser technology also allow ultra-thin flaps,\(^24\) thereby preserving stromal tissue and reducing the risk of ectasia.

The comparison should also have been considered in the context of safety. The main risks for high myopic LASIK are inducing night vision disturbances or keratectasia.\(^25\text{-}^28\) However, phakic IOLs can also cause night vision disturbances,\(^29\) and also introduce less common but potentially serious
complications associated with intraocular surgery such as malignant glaucoma, sub-capsular cataract, damage to zonules, macular edema, suprachoroidal hemorrhage, retinal detachment and endophthalmitis. Each type of lens also has specific complications that may require intraocular surgical intervention (over/undersized lens requiring exchange, explantation, cataract, rotation).

Anterior chamber lenses can cause chronic endothelial cell loss with an incidence of 0.8% in one study, although another study showed no change in endothelial cell count over 10 years, but concluded this might be related to surgeon expertise. Cataract formation in posterior chamber lenses has been reported to occur in 8.48% of myopic eyes, requiring lens explantation in 3.4% of all eyes.

The aim of our study was to report outcomes for a large high myopic LASIK population using the MEL 80 excimer laser (Carl Zeiss Meditec, Jena, Germany). We also set out to compare other methods for high myopia correction with respect to safety and efficacy.
Methods

Patients
This was a retrospective case series of consecutive high myopic LASIK procedures by two experienced surgeons (DZR & GIC) using the MEL 80 excimer laser and VisuMax femtosecond laser (both Carl Zeiss Meditec) or zero compression Hansatome microkeratome (Bausch & Lomb) at the London Vision Clinic, London, UK. Inclusion criteria were attempted spherical equivalent refraction correction of -8.00 D or higher for the primary procedure, medically suitable for LASIK, no signs of keratoconus, no previous ocular, eyelid or orbital surgery, no visually significant cataract, and corrected distance visual acuity (CDVA) 20/20 or better. A minimum follow-up of 1 year was applied. Informed consent and permission to use their data for analysis and publication was obtained from each patient prior to surgery as part of our routine preoperative protocol.

A full ophthalmologic examination was performed before surgery by an in-house optometrist, as has been described previously. Manifest refraction was performed using a standardized and validated protocol. The manifest refraction was repeated on or before the day of surgery by the surgeon, which was used for treatment planning. Laser data entry was calculated using a multivariate regression derived nomogram including sphere, spherical aberration precompensation level (see below), cylinder, age, and flap thickness.

Planning
In our protocol for treating high myopia, the predicted residual stromal thickness (RST) must be greater than 250 µm. For some eyes, this meant planning the treatment to be performed in two stages, so that the RST available for further correction could be accurately assessed before planning the second procedure. RST was calculated including safety biases for corneal thickness, flap thickness and ablation depth. The minimum of 10 central handheld ultrasound pachymetry measurements was used, less a further 15 µm to allow for the mean overestimation based on our comparison to Artemis very high-frequency digital (VHF) ultrasound (Personal communication, Dan Z Reinstein, 01/09/2006). For flaps created with the zero compression Hansatome using the 160 µm head, we had previously measured our mean central flap thickness to be 119±13 µm. By using a 160 µm flap thickness in the safety calculation, this incorporated a safety bias of 41 µm, meaning that...
the achieved central flap thickness would be thicker than 160 µm in only 0.8% of eyes. Similarly, a
bias of 18 µm was added to the programmed VisuMax flap thickness, based on our previous study
that found the mean central flap thickness to be 2 µm thicker than programmed with a standard
deviation of 7.9 µm.38 Finally, ablation depth was adjusted according to our previous study which
found the MEL 80 ablation depth readout overestimated achieved ablation depth by approximately
20%,39 plus an additional 5 µm bias. Postoperative keratometry was not included as part of the
suitability assessment; this parameter was formerly used because it acts as a surrogate for induced
spherical aberration, but we can now measure the spherical aberration directly.

Patients in whom full correction could not be achieved using the above RST calculations, a two-stage
protocol was used where the primary procedure was an intentional undercorrection, followed by a
retreatment according to the criteria set out below.

All patients were given extra consent forms that described the greater risks associated with treating
high myopia by LASIK relative to lower corrections, including discussion of night vision disturbances,
and refractive accuracy and stability. If a full correction was not possible or the RST indicated that
further treatment would be unlikely, another extra consent form was used to clarify that only one
treatment might be possible. The alternative of phakic IOL surgery was explained to all patients and
that this would enable a full correction. Patients then decided which option to take after weighing up
the relative risks and benefits.

Surgical Protocol
All treatments were performed as bilateral simultaneous LASIK. The Hansatome was used between
08/08/2003 and 23/07/2010 in 23% and the VisuMax between 13/04/2007 and 29/12/2011 in 77% of
eyes. The procedure was performed by surgeon DZR in 69% and by surgeon GIC in 31% of eyes.
The CRS-Master software platform (Carl Zeiss Meditec, Jena, Germany) was used to generate the
ablation profiles (version 1.1 until 08/11/2004, version 1.3 until 01/03/2007, version 2.1.6 until
01/11/2009, version 2.3.0 thereafter).
The standardized surgical technique has been described previously. Both the flap and corneal ablation were centered on the coaxially sighted corneal light reflex (CSCLR), used as the best approximation of the intersection of the visual axis with the cornea.43

The ablation profile used the Tissue Saving Ablation (TSA) profile for the correction of sphere and cylinder, but also included a predetermined level of spherical aberration pre-compensation with a $Z_4$ value ranging up to 1.21 µm (6 mm zone equivalent). Optical treatment zone diameter for first (TSA) profiles was 5.75 mm in 7%, 6.00 mm in 87%, 6.25 mm in 3%, and 6.50 mm in 3% of eyes. The spherical aberration component was treated at the same diameter as the base ablation in 30% and at a 7.00 mm diameter in 70% of eyes. In patients with thinner corneas, the optical zone was reduced to less than 6.00 mm in order to maximize the correction, with the patient counselled for greater risk of night vision disturbances. In patients with very large dark pupil diameter, the optical zone was increased if possible according to corneal thickness.

Intended flap thickness was 160 µm in 23% with the Hansatome, and 80-85 µm in 47%, 90-100 µm in 29%, and 110 µm in 2% of eyes using the VisuMax. Flap diameter ring used was 8.5 mm in 14% and 9.5 mm in 9% of eyes using the Hansatome, while flap diameters with the VisuMax were 8.0 mm in 70%, 8.5 mm in 1%, and 8.8 mm in 5% of eyes. For VisuMax flaps, a small (S) contact glass was used for a 8.0 mm flap diameter otherwise a medium (M) contact glass was used. A 5 mm superior hinge was used in all VisuMax cases.

Where a full correction was performed, we included an age dependent target hyperopic spherical refraction for all patients younger than 42 years according to a linear function whereby the target sphere was +0.66 D for a 21 year old decreasing to plano for a 42 year old. Our micro-monovision protocol was used for all patients older than 42 years, where the target sphere is plano for the dominant eye and -1.50 D for the non-dominant eye for the majority of patients.

Postoperative Course and Evaluation

Patients were instructed to instill tobramycin & dexamethasone (Tobradex: Alcon, Fort Worth, TX, USA) 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 one and measured spherical
refraction and uncorrected distance visual acuity (UDVA); if necessary, flap adjustments were
performed at the slit-lamp using a surgical spear under topical anesthetic and antibiotic cover. An
optometrist examined the patient at one, three, and twelve months and then yearly thereafter. All
visits included measurements of monocular and binocular UDVA, manifest refraction, and corrected
distance visual acuity (CDVA). Best-spectacle-corrected mesopic contrast sensitivity was performed
at the 3 month visit to compare to baseline. ATLAS corneal topography (Carl Zeiss Meditec, Jena,
Germany) and WASCA aberrometry (Carl Zeiss Meditec, Jena, Germany) were performed at 3
months, 1 year and 2 years.

Retreatments
Retreatments followed the same protocol full correction and two-stage patients. Retreatments were
performed once stability was demonstrated after at least 6 months, defined as no change in sphere
and cylinder within ±0.25 D over an interval of at least two months. A topography-guided ablation23
was used if the patient reported significant night vision disturbances and it was demonstrated that full
spectacle correction alone did not improve night vision disturbances whereas spectacles plus one
drop of brimonidine 0.5% did improve night vision disturbances.

In the majority of cases (66%), where the predicted RST was less than 275 µm, a VHF digital
ultrasound scan was performed to obtain layered pachymetric maps of corneal, epithelial and residual
stromal thickness.44 The RST map was used to identify the thinnest point and applied in the RST
safety calculation. The retreatment was planned such that the predicted RST after the retreatment
was at least 250 µm at the location of the maximum ablation as well as the location of the minimum
RST. Therefore, in some cases, the retreatment was not necessarily a full correction.

Statistical Analysis
Outcome analysis was performed according to the Standard Graphs for Reporting Refractive
Surgery.45 Outcomes were analyzed separately for primary treatment data only, and after the final
treatment. Data from the 2 year visit were used for analysis if available, otherwise 1 year data was
used. Stability of keratometry was evaluated by calculating the mean simulated keratometry at 3
months, 1 year and 2 years. The change in higher order aberrations was assessed by the change in coma, spherical aberration and higher order RMS, using a 6 mm analysis zone. Student’s t-tests were used to calculate the statistical significance of changes in log contrast sensitivity. Microsoft Excel 2010 (Microsoft Corporation, Seattle, WA, USA) was used for data entry and statistical analysis. A p-value <0.05 was defined as statistically significant.
Results

Patient Population

During the study period, 527 eyes were treated and one year data were available for 479 (91% follow-up), for which the last timepoint after the primary procedure was 2 years in 48% (n=230), 1 year in 46% (n=221), and 6 months in 6% (n=27) 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 after the retreatment were used to analyze the final outcome. Table 1 shows the demographic data for the study population.

Retreatments

The primary procedure was performed as a partial correction (two-stage protocol) in 16% (79/479) of eyes, of which 71% (56/79) have undergone a retreatment. Of the 400 full correction eyes, 16% (64/400) have undergone a retreatment. Including all eyes, 25% (120/479) of eyes have undergone a retreatment, of which 95% (114/120) were performed as a flap lift, 2.5% (3/120) as a PRK procedure, 1.7% (2/120) as a VisuMax LASIK procedure, and 0.8% (1/120) using the VisuMax sidecut only option (to create a flap within the original flap to avoid a zone of epithelial ingrowth scarring). A topography-guided custom ablation profile was used for 8 eyes, which constitutes 1.7% of all 479 eyes treated (6.7% of the 120 retreatments performed), and was used to correct for a decentration in 5 eyes, and to enlarge the optical zone in 3 eyes. The scotopic pupil diameter (mean 6.04 mm, range: 5.34 to 7.10 mm) of this sub-group was not different to that of the population (p=0.282).
Standard Outcomes

Figure 1 shows the outcomes for primary treatments only. Figure 2 shows the final outcomes, including retreatments.

Table 2 shows the normalized contrast sensitivity data preoperatively and after the final treatment. There was no change at 3 and 6 cpd, and small but statistically significant increase at 12 and 18 cpd (p<0.001). Table 3 summarizes the ocular aberrations preoperatively and after the primary treatment. Coma and higher order RMS were increased, as well as spherical aberration which increased by an average of 0.49 µm. ATLAS keratometry data showed that the mean keratometry was 38.09±1.65 D (range: 32.85 to 42.75 D, n=374) at 3 months, 38.27±1.46 D (range: 34.57 to 42.51 D, n=297) at 1 year, and 38.36±1.47 D (range: 34.06 to 41.98 D, n=168) at 2 years. For 238 eyes with keratometry data at both 3 and 12 months, the mean change was 0.22±0.43 D (range: -1.72 to 1.67 D, p<0.01). For 116 eyes with keratometry data at both 1 and 2 years, the mean change was 0.11±0.33 D (range: -0.88 to 1.43 D, p<0.01).

Complications

In the 109 eyes with flaps created using the Hansatome there were no intraoperative complications other than small epithelial defects requiring bandage contact lenses in 3 eyes (2.8%). The appendix details intraoperative complications for VisuMax flaps and postoperative complications in all eyes. Overall, across the 31 eyes that had intraoperative and/or postoperative complications, 1 eye lost 1 line of CDVA and none lost more than 1 line.
Discussion

The present study found the treatment of myopia between -8.00 D and -14.25 D using the MEL 80 excimer laser and either the VisuMax femtosecond laser or zero compression Hansatome microkeratome to be safe and effective. While there was an increase in higher order aberrations, as expected for a high myopic correction, this increase was not excessive as demonstrated by no reduction in contrast sensitivity. Safety in terms of change in CDVA was also excellent with no eyes losing 2 lines, 3% losing one line, and 50% gaining one line. While night vision disturbances were not objectively measured, a topography-guided retreatment was available for any patients reporting significant symptoms, but was only used in 8 eyes (1.7%) demonstrating that few patients experienced visually significant night vision disturbances.

In order to compare the current study to published LASIK and phakic IOL studies, we performed a literature review for studies published within the last five years reporting results of myopia above -8.00 D. The main outcome parameters are shown in Table 4, as well as the studies included in the Cochrane review. The results of the present study were similar in terms of accuracy, efficacy and safety to those reported in the last five years for both LASIK and phakic IOLs, although the range treated was much higher for phakic IOLs (e.g. up to -23.00 D). Nevertheless, as discussed earlier, intraocular surgery introduces potential, albeit unusual, serious visual complications. While ectasia can occur many years after surgery, with modern keratoconus screening techniques, inclusion of biases for calculating predicted RST, direct measurement of RST before retreatment surgery, and the availability of corneal cross-linking, the risk of ectasia is significantly lower than 10 years ago.

It is important to note that the present study and other recent LASIK studies appear to contradict the conclusion from the Cochrane review; these results are significantly better than those of both LASIK and phakic IOLs reported for studies included in the Cochrane review. The predictability ranged from 29% to 57% within ±0.50 D for the LASIK/PRK groups and from 24% to 76% for the phakic IOL groups in the Cochrane review, whereas the range was from 69% to 100% for recent LASIK studies. Similarly, postoperative UDVA was 20/20 or better in 12% to 84% in the LASIK/PRK groups and 20% to 97% in the phakic IOL groups in the Cochrane review, whereas the range was 77% to 92% for recent LASIK studies. Finally, safety was much worse for the LASIK groups in the
Cochrane review with a loss of 2 or more lines of CDVA between 4%\(^1\)\(^8\) and 12% of eyes\(^1\)\(^6\), whereas no eyes lost even 2 lines in the recent LASIK studies. Therefore, it appears that the Cochrane review\(^1\)\(^4\),\(^1\)\(^5\) only included studies that would be considered out-of-date, and the conclusions while applicable to earlier technology and protocols do not apply to modern LASIK. This demonstrates the limitation of the Cochrane review methodology to refractive surgery, as very few studies meet the strict criteria of being randomized control trials. This is further emphasized by the fact that the 2014\(^1\)\(^5\) update found no new studies meeting the inclusion criteria. While the Cochrane review methodology clearly represents a robust method scientifically, it suffers when applied to refractive surgery as the majority of studies reporting surgical outcomes are retrospective for obvious reasons. This however highlights the paucity of randomized controlled trials, outside of United States Food and Drug Administration trials,\(^5\)\(^5\) as a weakness of the refractive surgery field.

In summary, LASIK for high myopia up to -14.25 D using modern technology was found to have similar outcomes to phakic IOLs, while avoiding the potentially serious complications associated with intraocular surgery.
Legends

Figure 1: Nine standard graphs for reporting refractive surgery showing the visual and refractive outcomes for 479 high myopic 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 479 high myopic 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.
References


41. Reinstein DZ, Archer TJ. Real-time bilateral LASIK procedure. Available at: https://www.youtube.com/watch?v=ncSWnXpgYd0. Accessed 01/12/2014.


47. Stonecipher KGMD, Kezirian GMMD, Stonecipher M. LASIK for -6.00 to -12.00 D of Myopia with up to 3.00 D of Cylinder Using the ALLEGRETTO WAVE: 3- and 6-Month Results with the 200- and 400-Hz Platforms. Journal of Refractive Surgery. 2010;26:S814-818.


49. Hashemi H, Miraftab M, Asgari S. Comparison of the visual outcomes between PRK-MMC and phakic IOL implantation in high myopic patients. Eye. 2014.


Intraoperative complications

<table>
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<tr>
<th></th>
<th>Occurrences</th>
<th>Percentage of Total</th>
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<tbody>
<tr>
<td>Epithelial Defect</td>
<td>8</td>
<td>2.2%</td>
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<tr>
<td>Suction Loss</td>
<td>7</td>
<td>1.9%</td>
</tr>
<tr>
<td>Incomplete Flap (Edge)</td>
<td>2</td>
<td>0.5%</td>
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<tr>
<td>Incomplete Flap (Ablation Zone)</td>
<td>1</td>
<td>0.3%</td>
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<tr>
<td>Buttonhole</td>
<td>4</td>
<td>1.1%</td>
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<tr>
<td>Free Cap</td>
<td>0</td>
<td>0%</td>
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<tr>
<td>Irregular Bed</td>
<td>0</td>
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</tr>
<tr>
<td>Flap Tear</td>
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<td>0.3%</td>
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Postoperative complications requiring flap lift

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<tr>
<td>Flap Lift for Trauma</td>
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<td>0.3%</td>
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<tr>
<td>Flap Lift for Epithelial Ingrowth</td>
<td>2</td>
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<tr>
<td>Flap Lift for Microfolds</td>
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<td>0.3%</td>
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<tr>
<td>Flap Lift for Interface Deposits</td>
<td>1</td>
<td>0.3%</td>
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Intraoperative Complications

**Hansatome treated eyes:** There were no intraoperative complications in the 109 eyes treated using the Hansatome microkeratome other than a small epithelial defect requiring a bandage contact lens in 3 eyes (2.8%). There was no impact on CDVA in any of these cases.

**VisuMax treated eyes:** Of the 371 eyes treated using the VisuMax femtosecond laser, a peripheral epithelial defect requiring a bandage contact lens occurred in 8 eyes (2.2%). Suction loss occurred in 7 eyes (1.9%), 5 eyes in which the contact glass was immediately reapplied and flap creation completed with the same flap parameters; of these, a perfect flap was created in 4 eyes with the stromal bed appearing smooth prior to ablation. In the remaining eye some thin thread-like mid-peripheral stromal slivers were noted on the stromal bed with the central bed of good quality for ablation; the peripheral stromal slivers were repositioned before the excimer laser ablation was performed and the flap was repositioned perfectly with no subsequent loss of best spectacle corrected vision or contrast sensitivity. The remaining 2 eyes with repeated suction loss belonged to the same patient, where after four attempts on the first eye and one attempt on the second eye it was deemed
not possible to adequately create flaps using the VisuMax. After discussion with the patient, the
procedures were performed instead using the zero compression Hansatome microkeratome without
further complication. In all 8 eyes that experienced a suction loss, there was no loss of CDVA nor
contrast sensitivity, and 7 eyes actually experienced a gain of one line of CDVA. Further recorded
complications in VisuMax treated eyes included one eye (0.3%) with a small tear to the hinge of the
flap in an eye that subsequently gained two lines of CDVA; a small peripheral flap tear approximately
1 mm within the flap boundary inferiorly in one eye (0.3%) where the flap lifting instrument perforated
the flap while manually dissecting through a peripheral zone of dense opaque bubble layer (OBL) due
to the presence of a small cryptic buttonhole in an 80 (programmed 98) µm flap – after ablation the
flap was repositioned perfectly, a bandage contact lens was applied and after healing there was no
change in CDVA. There were 3 eyes (0.8%) in which there was inadequate or no femtosecond cutting
within a small area of flap interface (centrally in 1 eye, peripherally in 2 eyes); in each case these
areas could be dissected manually and there was no impact on CDVA or contrast sensitivity. Finally,
there were 4 eyes (1.1%) in which a small buttonhole was discovered on lifting the flap (centrally in 1
eye, peripherally in 3 eyes) probably secondary to previous focal contact lens related infections (with
epithelial plugs). In all cases, after carefully lifting the flap, the residual epithelium overlying Bowman’s
layer was brushed off to reveal the stromal surface and the ablation was performed and flap replaced
carefully followed by an overnight bandage contact lens. The eye with a central buttonhole lost one
line of CDVA.

Postoperative complications requiring flap lift
A flap lift procedure was required at the 1 day visit to reposition the flap in 1 eye (0.3%) following a
flap slip due to trauma to the eye overnight. This eye then also required a second flap lift procedure 1
week later for epithelial ingrowth removal which healed with no ingrowth. One other eye (0.3%)
required a flap lift procedure for epithelial ingrowth following a retreatment procedure. A flap lift
procedure was performed for 1 eye (0.3%) to treat microfolds at the 1 month timepoint. A flap lift
procedure was performed for 1 eye (0.3%) to remove inorganic deposits from the flap interface. There
was no impact on CDVA in any of these cases.
<table>
<thead>
<tr>
<th>Table 1: Study demographics</th>
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<tr>
<td><strong>Number of Eyes (patients)</strong></td>
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<tr>
<td><strong>Age (years)</strong></td>
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<tr>
<td><strong>Gender Ratio (M/F %)</strong></td>
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<tr>
<td>** Attempted Spherical Equivalent Refraction (D)**</td>
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<td><strong>Attempted Cylinder (D)</strong></td>
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<td><strong>Scotopic pupil (mm)</strong></td>
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Table 2: Normalized mesopic contrast sensitivity (CSV-1000)

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<th>6 CPD</th>
<th>12 CPD</th>
<th>18 CPD</th>
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<tr>
<td>Pre</td>
<td>0.99±0.11</td>
<td>0.94±0.09</td>
<td>0.91±0.13</td>
<td>0.84±0.19</td>
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<tr>
<td>Post</td>
<td>0.98±0.11</td>
<td>0.94±0.09</td>
<td>0.93±0.13</td>
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<td>0.249</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

**CPD**: Cycles Per Degree
Table 3: Ocular Aberrations (µm)

<table>
<thead>
<tr>
<th></th>
<th>Pre</th>
<th>Post</th>
<th>Change</th>
<th>t-test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coma</td>
<td>0.169±0.103</td>
<td>0.266±0.201</td>
<td>0.100±0.221</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>Spherical Aberration</td>
<td>0.135±0.148</td>
<td>0.626±0.222</td>
<td>0.491±0.074</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>HORMS</td>
<td>0.324±0.109</td>
<td>0.737±0.198</td>
<td>0.426±0.196</td>
<td>p&lt;0.001</td>
</tr>
</tbody>
</table>

HORMS: High Order Root Mean Square
<table>
<thead>
<tr>
<th>First Author</th>
<th>N (eyes)</th>
<th>Technique</th>
<th>Preop SEQ (D)</th>
<th>Age (years)</th>
<th>FU</th>
<th>Mean±SD (D) (range)</th>
<th>±0.50</th>
<th>±1.00</th>
<th>Pre CDVA ≤20/20</th>
<th>≤20/40</th>
<th>≤20/40</th>
<th>1 line ±2 lines</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reinstein 2014</td>
<td>483</td>
<td>LASIK VisuMax/Hansatome CZM MEL80</td>
<td>-9.57±1.29 (-7.50 to -14.18)</td>
<td>36.8±9.4 (21 to 60)</td>
<td>1-2 years</td>
<td>-0.26±0.47 (-2.25 to +1.13)</td>
<td>69%</td>
<td>95%</td>
<td>100%</td>
<td>89%</td>
<td>99%</td>
<td>3% 0%</td>
</tr>
<tr>
<td>Kanellopoulos 2013</td>
<td>116</td>
<td>LASIK WaveLight FS200 WaveLight EX500</td>
<td>-7.67±1.55 (-6.00 to -13.00)</td>
<td>28.7 ± 7.5 (17 to 51)</td>
<td>3 months</td>
<td>-0.37±0.08</td>
<td>89%</td>
<td>95%</td>
<td>73%</td>
<td>90.5%</td>
<td>97.4%</td>
<td>1.7% 0%</td>
</tr>
<tr>
<td>Vega-Estrada 2012</td>
<td>29</td>
<td>LASIK IntraLase Schwind AMARIS LASIK IntraLase Alcon Allegretto Wave 400Hz</td>
<td>-8.39±0.93 (-6.75 to -11.25)</td>
<td>36.7±10.8 (24 to 61)</td>
<td>6 months</td>
<td>-0.42±0.82 (-3.50 to +0.63)</td>
<td>-</td>
<td>89.6%</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Stonecipher 2010</td>
<td>65</td>
<td>LASIK IntraLase Alcon Allegretto Wave 200Hz</td>
<td>-7.07±0.89 (-6.86 to -12.63)</td>
<td>33.8 (20 to 60)</td>
<td>6 months</td>
<td>-</td>
<td>100%</td>
<td>100%</td>
<td>-</td>
<td>92%</td>
<td>100%</td>
<td>- 0%</td>
</tr>
<tr>
<td>Stonecipher 2010</td>
<td>141</td>
<td>LASIK IntraLase Alcon Allegretto Wave 200Hz</td>
<td>-6.76±1.01 (-6.08 to -11.05)</td>
<td>33.8 (20 to 60)</td>
<td>6 months</td>
<td>-</td>
<td>86%</td>
<td>100%</td>
<td>-</td>
<td>77%</td>
<td>100%</td>
<td>- 0%</td>
</tr>
<tr>
<td>Hashemi 2014</td>
<td>23</td>
<td>PRK-MMC VISX STAR S4</td>
<td>-8.82±1.25 (-8.00)</td>
<td>28.7±5.3 (21 to 60)</td>
<td>1 year</td>
<td>-0.25±0.41</td>
<td>85.7%</td>
<td>-</td>
<td>76.2%</td>
<td>57.1%</td>
<td>-</td>
<td>9.5% 0%</td>
</tr>
<tr>
<td>Hashemi 2014</td>
<td>23</td>
<td>Phakic IOL Artiflex</td>
<td>-9.49±1.94 (-8.00)</td>
<td>27.7±5.3 (21 to 60)</td>
<td>1 year</td>
<td>-0.17±1.17</td>
<td>95.7%</td>
<td>-</td>
<td>95.7%</td>
<td>73.9%</td>
<td>-</td>
<td>0% 0%</td>
</tr>
<tr>
<td>Ju 2013</td>
<td>82</td>
<td>Phakic IOL STAAR ICL</td>
<td>-15.56±4.35 (-9.00 to -23.00)</td>
<td>28.6 ± 7.6 (19 to 45)</td>
<td>3 months</td>
<td>-1.85±0.72</td>
<td>72.5%</td>
<td>88%</td>
<td>45%</td>
<td>58.5%</td>
<td>92.7%</td>
<td>3.7% -</td>
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<tr>
<td>Knorz 2011</td>
<td>104</td>
<td>Phakic IOL AcrySof Cachet</td>
<td>-10.41±2.31 (-6.00 to -16.50)</td>
<td>36.6±8.1 (18 to 53)</td>
<td>3 months</td>
<td>-0.24±0.55 (-2.00 to +1.63)</td>
<td>78.8%</td>
<td>91.3%</td>
<td>100%</td>
<td>71.2%</td>
<td>98.1%</td>
<td>1% 1%</td>
</tr>
<tr>
<td>Alió 2014</td>
<td>40</td>
<td>LASIK VISX 20/20</td>
<td>(-6.00 to -18.00)</td>
<td>51.1±6.7 (35 to 60)</td>
<td>15 years</td>
<td>-1.37±2.21</td>
<td>-</td>
<td>46.2%</td>
<td>-</td>
<td>43.6%</td>
<td>64.1%</td>
<td>10.3% 0%</td>
</tr>
<tr>
<td>Oruçoğlu 2012</td>
<td>143</td>
<td>LASIK Technolas</td>
<td>-21.70±5.80 (-38.00 to -14.13)</td>
<td>-</td>
<td>10 years</td>
<td>-6.09±3.35 (-14.38 to -0.50)</td>
<td>-</td>
<td>14%</td>
<td>-</td>
<td>2.6%</td>
<td>10.3%</td>
<td>-</td>
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<tr>
<td>El Danasoury 2002</td>
<td>45</td>
<td>LASIK NIDEK EC-5000</td>
<td>-13.24±2.30 (-9.13 to -17.50)</td>
<td>33.7±7.1 (21 to 47)</td>
<td>1 year</td>
<td>-0.87±0.8 (-3.00 to -1.00)</td>
<td>29%</td>
<td>56%</td>
<td>-</td>
<td>12.2%</td>
<td>58.5%</td>
<td>- 12.2%</td>
</tr>
<tr>
<td>El Danasoury 2002</td>
<td>45</td>
<td>Phakic IOL Artisan</td>
<td>-13.93±2.90 (-9.50 to -19.38)</td>
<td>33.7±7.1 (21 to 47)</td>
<td>1 year</td>
<td>-0.64±0.8</td>
<td>42%</td>
<td>65%</td>
<td>-</td>
<td>20.9%</td>
<td>88.4%</td>
<td>- 0%</td>
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<tr>
<td>Malecaze 2002</td>
<td>25</td>
<td>LASIK Hansatome Technolas</td>
<td>-9.39±1.47 (-8.00 to -12.00)</td>
<td>38.4±7.6 (31 to 52)</td>
<td>1 year</td>
<td>-0.74±0.67</td>
<td>44%</td>
<td>64%</td>
<td>-</td>
<td>24%</td>
<td>80%</td>
<td>20% 4%</td>
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<tr>
<td>Study</td>
<td>N</td>
<td>Procedure</td>
<td>Mean ± SD</td>
<td>Range</td>
<td>Follow-up</td>
<td>Mean ± SD</td>
<td>Range</td>
<td>成功率 (%)</td>
<td>20%</td>
<td>60%</td>
<td>80%</td>
<td>90%</td>
</tr>
<tr>
<td>--------------</td>
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</tr>
<tr>
<td>Malecaze 2002</td>
<td>25</td>
<td>Phakic IOL Artisan PRK VISX S3</td>
<td>-10.19±1.56 (-8.00 to -12.00)</td>
<td>38.4±7.6 (31 to 52)</td>
<td>1 year</td>
<td>-0.95±0.45</td>
<td>24%</td>
<td>60%</td>
<td>-</td>
<td>20%</td>
<td>60%</td>
<td>12%</td>
</tr>
<tr>
<td>Schallhorn 2007</td>
<td>45</td>
<td>Phakic IOL TICL</td>
<td>-8.04±1.28</td>
<td>30.8±6.0</td>
<td>1 year</td>
<td>+0.27±0.36</td>
<td>76%</td>
<td>100%</td>
<td>93%</td>
<td>97%</td>
<td>-</td>
<td>0%</td>
</tr>
</tbody>
</table>