Sixteen year follow-up of Hyperopic Photorefractive Keratectomy


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Key Words: Photorefractive Keratectomy, Hyperopia

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Abstract

Purpose: To assess the long-term stability, efficacy and safety of hyperopic laser in situ Keratomileusis (H-LASIK).

Setting: University Hospital

Design: Prospective case series

Methods: Nineteen patients (33 eyes) underwent H-LASIK, using a Moria LSK One microkeratome and a Summit SVS Apex Plus Excimer laser with an optical zone of 6.5mm and a blend zone of 1.5mm. Only simple hyperopia was treated with no astigmatic correction. Mean follow-up was 16.5 years.

Results: Mean age at time of surgery was 51.6 years (range 34 to 60). Mean pre-operative spherical equivalent (SEQ) was +3.74 diopters (D) (range +1.25 to +6.5D). Mean attempted correction was +3.64D (range +1.5 to +6.0D). At 12 months mean SEQ was +0.28D (range -1.0 to +1.5D), with 90% of eyes within +/-1.0D of emmetropia and 68% within +/-0.5D. At 5 years the mean SEQ was +0.84D (range -0.75 to 3.35D), while at 16 years the mean SEQ was +1.74D (range -0.75 to +4.125D) with 24% of eyes within +/- 1.0D and 6% within +/-0.5D. This represented a +1.47 +/- 1.43D increase in hyperopia between 1 and 16 years (p<0.0001) and a +1.13D +/- 0.8D increase between 5 and 16 years (p<0.03). Uncorrected distance visual acuity (UDVA) improved at 16 years compared to pre-operative values (p<0.0001), while corrected distance visual acuity (CDVA) remained unchanged (p<0.2). The efficacy index was 0.5 and safety index was 1.09. Only 1 eye (3%) lost 2 lines of CDVA. Keratometry remained stable between 1 and 17 years (p<1.0). Four eyes (12%) had
undergone cataract surgery and 2 (6%) laser iridotomy at 16 years. There was no evidence of ectasia.

Conclusions: H-LASIK showed a significant increase in hyperopic SEQ between 1 and 5 years and 16 years. At 16 years the efficacy was limited but no sight threatening complications attributable to the LASIK treatment were detected.
Introduction

Refractive surgery for hyperopia remains problematic, with multiple procedures, such as hexagonal keratotomy, keratophakia, keratomileusis, thermokeratoplasty and corneal inlays, having been proposed and developed but associated with poor predictability and sight-threatening complications (1-6). However, over the past quarter of a century, the introduction and refinement of excimer laser (7-11), refractive lens exchange, multifocal (12) and phakic intraocular lens technologies (13) have heralded a new era in refractive surgery and offer promise for the correction of hyperopia. Published studies of hyperopic laser photorefractive keratectomy (H-PRK) and hyperopic laser in situ keratomileusis (H-LASIK) have demonstrated both efficacy and safety and such procedures are now in widespread clinical usage (7-11). However, compared to myopic excimer laser kerato-refractive procedures, results for hyperopic treatments are inferior (14). Clinical studies of H-PRK and H-LASIK report acceptable efficacy for corrections up to approximately +4.0 diopters (D) but with diminished predictability, refractive stability and safety for higher order corrections (7-11, 15-16).

For any surgical intervention to be practicable it is crucial to scrutinize long term stability, efficacy and safety. This is of particular relevance in the case of refractive surgery, which is directed at treating natural physiological variants rather than disease processes and especially important with the correction of hyperopia, as this condition not only tends to progress with age but becomes more symptomatic with developing presbyopia (17). However, despite millions of
corrections having been performed world-wide over the past two decades, studies examining the long-term follow-up of hyperopic excimer laser procedures beyond 5 years are few with none beyond 10 years (18-19). The refractive and biomechanical stability of the cornea decades after such procedures, where the ablation and removal of tissue is in the corneal mid-periphery, nearer to the limbus than in myopic corrections, is unknown. Possible long-term corneal biomechanical impairment, stromal remodeling, neo-vascularization and limbal stem cell damage cannot be excluded. In order to investigate such questions we re-examined our original cohort of subjects who participated in one of the first clinical trials of H-LASIK in the United Kingdom (18) and report the results in 19 patients (33 eyes) who attended for follow-up with a mean follow-up of 16.5 years.

Materials and Methods

Subjects and Patient Assessment

The materials and methods employed in this study have been published previously (18). Fifty-two patients underwent H-LASIK from February 1998 to July 1999 as part of a prospective, ethics approved study. All individuals were over 18 years. Those with pre-existing ocular pathology, previous anterior segment surgery, diabetes or connective tissue disorders were excluded. Following ethics committee approval (REC reference 13/NI/0165), 19 patients (37%) (33 eyes) were traced and agreed to attend for long-term follow-up. Five patients (10%) were deceased, 2 declined follow-up, 1 did not attend and 25 (48%) could not be traced. The mean age at time
of correction of the 19 patients (33 eyes) who attended for long-term follow-up was 51.6 years (range 34 to 60 years). Thirteen were female and 6 were male. The mean preoperative manifest distance spherical equivalent (SEQ) refraction was +3.73 diopters (D) (range +1.25 to +6.5D). Mean follow-up was 16.5 years (range 15 to 17.5 years, median 16.6 years). There were no statistically significant differences between the 19 patients that attended for follow-up at 16.5 years and the 33 (53 eyes) that did not attend in terms of age, pre-operative SEQ, pre-operative cylindrical refractive error, attempted hyperopic correction (p<0.5) and achieved refractive correction at 12 months.

Prior to surgery a detailed ocular examination was performed, including subjective and cycloplegic refraction, keratometry, biomicroscopy, corneal pachymetry, tonometry and mydriatic fundoscopy. All cylinders were refracted in negative cylinders. During subjective refraction, reliance was placed on fogging techniques, in particular the +1.00D blur test, to ensure that an accurate end point was reached consistently. Corneal topography was assessed using a computerized photokeratoscope, Computed Anatomy, TMS-1 (Computed Anatomy, Inc., New York, NY, USA).

Operative Procedure

The operative procedure has been described in detail elsewhere (18). In each case a LSK One, Moria, microkeratome was used with a 180 micrometer (um) head (Moria, Antony, France) to fashion a flap approximately 10.0mm in diameter with a
nasal hinge of 1.0 to 1.5mm. A Summit Technology SVS Apex Plus laser (Summit Technology, Waltham, MA, USA) with an emission wavelength of 193 nanometers (nm), a pulse repetition rate of 10Hz and an irradiance of 180mJ/cm² at the cornea was used to fashion the hyperopic ablation. This laser used an ablatable mask with an Axicon, loaded into a cassette and placed in the path of the excimer laser beam, to create a hyperopic correction with an optical zone of 6.0mm and an overall diameter of 9.50mm.

The aim of the study was not to fully correct each patient’s refractive error, but to assess the predictability, safety and stability of H-LASIK. On the basis of their preoperative refraction, patients were assigned to receive a simple hyperopic correction between +1 and +6.00D in half diopter steps. The corrections were based on the Munnerlyn algorithm (20), with a mean attempted correction of +3.64D (range +1.5 to +6.0D).

Postoperative Treatment and Assessment

Preservative free Chloramphenicol 0.5% eye-drops were applied immediately after the procedure and patients were examined at the slit-lamp to assess flap position and interface clarity. No steroid or anti-inflammatory drops were given. Patients instilled Chloramphenicol 0.5% 4 times a day for 1 week.

Postoperative examinations were carried out at 1 day, 1, 2 and 4 weeks, 3, 6, 9, 12 months and 5 and at a mean follow-up of 16.5 years. At each visit a full refraction,
slit-lamp biomicroscopy and corneal topography were performed. Corneal
topography was assessed using a computerized photokeratoscope, Computed
Anatomy, TMS-1 at 1, 3, 6 and 12 months, by Keraton Scout Corneal Analyzer
(Optikon 2000, Rome, Italy) at 5 years and at 16.5 years by corneal tomography
with the Pentacam Scheimpflug camera system (Oculus Optikgeräte GmbH,
Wetzlar, Germany).

At 16.5 years patients were asked whether they were happy they had undergone
the procedure and were asked to score their satisfaction with the procedure from 0
(completely unsatisfied) to 10 (completely satisfied) on a visual analogue score.

Vector Analysis
To investigate vectoral astigmatic change in the manifest refraction, vector analysis
was performed in all eyes according to the system described by Retzlaff et al\(^{(21)}\).

Statistical Methods
Paired student t-tests were used to compare refractive changes pre- and post-
operatively. F-tests were used to test the differences between variances at 1 and
18 years. Chi squared analysis was used to compare qualitative data, such as
the corneal haze scores. Results with p<0.05 were considered statistically
significant.
Results

Refractive Outcome and Stability

The mean changes in refraction with time are shown figures 1 and 2 and table 1.

One eye of one patient (3%) had undergone cataract surgery between 5 and 16.5 years after H-LASIK. In the 32 eyes that had not had cataract surgery, at 1 year the mean SEQ was +0.28D +/- 0.55D standard deviation (SD) (range -1.0 to +1.5D), with 90% of eyes within +/- 1.0D of emmetropia and 68% within +/- 0.5D (figure 1, table 1). At 5 years the SEQ had increased to +0.84D +/- 1.02D SD (range -0.75 to +3.25D) (p<0.03). At 16.5 years the mean SEQ was +1.74D +/- 1.32D (range -0.875 to +4.125D) with a mean achieved correction of -2.06D and 24% of eyes within +/- 1.0D of emmetropia and 6% within +/- 0.5D. This represented a significant increase in hyperopic refractive error compared to 1 year (p<0.0001) and 5 years (p<0.0001) and an increase in variance between one year and 16.5 years (p<0.001) (figures 1 and 2, table 1). The increase in hyperopic refractive error was >1.00D in 19 eyes (58%) from 1 to 16.5 years.

In eyes which had not undergone cataract surgery during the follow-up period and underwent low order hyperopic treatments of +2.0, +2.5 and +3.0D (n=16) (mean attempted correction +2.56D), mean SEQ at 1 and 5 years was +0.35D and +0.72D respectively. At 16.5 years it was +1.61D (range -0.875 to +4.0D), which
represented a significant increase in hyperopic refractive error compared to 1 year (p<0.001) and at 5 years (p=0.001) (figure 3, table 1).

In eyes which had not undergone cataract surgery during the follow-up period and underwent high order hyperopic treatments of +3.5, +4.0, 5.0 and +6.0D (n=16), mean SEQ at 1 and 5 years was +0.22D and +1.0D respectively. At 16.5 years it was +1.87D (range -0.75 to +4.125D), which represented a significant increase in hyperopic refractive error compared to 1 year (p<0.005) and 5 years (p<0.005) (figure 3, table 1).

Figure 4 and table 1 shows the refractive change with time for those patients 53 years of age or over (n=15 eyes) (mean age 56.7 years, range 53 to 60 years) and 52 years of age or under (n=17 eyes) (mean age 46.9 years, range 34 to 52 years) at the time of surgery. Pre-operatively there was no difference in SEQ or attempted refractive correction between these two groups (p=1.0). At 1, 6, and 12 months and 5 and 16.5 years the hyperopic refractive error was similar between the two age groups (p<0.05) (figure 4), although the increase in hyperopic refractive error was less in the older (mean +1.96D, range -1 to 4.875D) compared to the younger age group (mean +0.89D, range -0.875 to +2D) (p<0.03).

**Astigmatic Change and Vector Analysis**

The mean preoperative manifest refractive cylindrical correction was -0.72DC +/- standard deviation (SD) 0.67D (range 0 to -2.5D) at a mean axis of 94°. At 16.5
years post-operatively, the mean manifest refractive cylindrical correction was –
0.88D +/- SD 0.85D (range 0 to -3.25D) at a mean axis of 84°. In 25 (78%) eyes the change in manifest refractive cylinder was 1.00D or less. In two eyes (6%) the change in manifest refractive cylinder was greater than -2.0D

Vector analysis demonstrated a mean change in the manifest refractive cylinder at 16.5 years post-operatively of 0.97D (range 0.13 to 3.29D), with a change of 1.0D or less in 23 eyes (72%).

Unaided Visual Acuity

Uncorrected distance visual acuity (UDVA) was improved at 16.5 years post-operatively in the entire cohort (p<0.0001). The efficacy index (post-operative UDVA/post-operative corrected distance acuity (CDVA)) at 1 year was 0.98, while at 16.5 years it was 0.5 (figure 5). Two of the treated eyes were amblyopic and did not have a corrected visual potential of 20/60 preoperatively

Uncorrected near visual acuity (UCNA) was N18 or better in 14 eyes (44%) and only N12 or better in 4 eyes (12.5%) at 16.5 years.

Corrected Distance Visual Acuity

At 16.5 years CDVA in 32 eyes that had not undergone cataract surgery was unchanged or improved in 20 eyes (62.5%) compared to pre-operative levels. It was reduced by one line in 11 eyes (24%). One eye (3%), which had to have a
flap lift for epithelial in growth in the first months after H-LASIK, lost 2 lines (figure 6). CDVA at 16.5 years was unchanged compared to pre-operative levels (p=0.2), but reduced compared to 1 and 5 years (p<0.05). The safety index (post-operative CDVA/pre-operative CDVA) at 16.5 years was 1.09.

Corneal Haze

No eyes showed any disturbance of central corneal transparency. The flap edge could still be easily delineated by a faintly altered light reflex in 6 eyes at 16.5 years.

Corneal Topography

Pre-operative simulated topographic keratometry (simK) values were 42.74 +/- 1.87D SD (range 40.5 to 46.625D). At 12 months mean simK had increased to 45.37D +/- 2.18D SD (41.75 to 49.25D) (p<0.0001). At 16.5 years simK values were unchanged from 12 month values 45.35D +/- 1.89D SD (range 42.3 to 49.5D (p=1.0).

Analysis of tomographic data at 18 years did not reveal any cases of ectasia defined by localized inferior-central/inferior anterior corneal steepening with corresponding changes in the anterior and posterior float maps.

Complications/Ocular Co-morbidity

One eye (3%) lost 2 lines of CDVA. One eye (3%) had undergone cataract surgery during the 16.5 year follow-up and another 4 eyes (12%) have since
undergone cataract surgery, with two of the eyes (6%) having undergone laser iridotomy for narrow angle problems.

Corneal Pachymetry

At 16.5 years corneal pachymetry was 560um +/- 38.4um range 503 to 649um

Patient satisfaction

At 18 years 17 of the 19 patients (89%) were happy they had undergone the procedure. The mean satisfaction score was 8.24 out of 10 (range 4 to 10, median 9).

Discussion

This patient group was one of the first to undergo H-LASIK in the United Kingdom. Treatments were conducted with a broad beam laser, utilizing a prototype delivery system and spherical algorithms, coupled with a mechanical microkeratome and a 180um predicted flap depth. Diagnostics were undertaken with anterior surface topography and hand-held ultrasonic pachymetry. We have previously published efficacy and safety in this cohort in the early and late post-operative periods and reported good safety and moderate efficacy for the correction of low degrees of hyperopia, but uncertain refractive stability over a 5 year follow-up period. Since the introduction of excimer laser refractive surgery, possible late long-term complications such as impairment of
transparency, biomechanical instability, regression and limbal stem cell irregularities have been postulated and reinforced the need for long-term follow-up for decade’s not just years \(^{(22-23)}\). We have recently published studies of myopic and H-PRK and have confirmed refractive stability at the level of the cornea with stable keratometry, maintenance of corneal transparency and biological integrity and no late complications attributable to the treatment at 18-20 years \(^{(24-26)}\). However, such studies investigating the long-term outcomes of H-LASIK have not been published to date and this present investigation was conducted to address these issues.

In this cohort we documented a statistically significant increase in hyperopic refractive error between 1 and 16.5 years, and 5 and 16.5 years (table 1 figure 1) \((p<0.001)\). In similarity to our recent study of H-PRK \(^{(26)}\), this hyperopic shift was more apparent during the first few years after surgery, with a mean change of +0.56D (+0.14D per year) between 1 and 5 years and +0.9D (+0.08D per year) between 5 and 16.5 years. \(\text{table 1, figure 1}\). When evaluating long-term refractive stability, the expected natural history of physiological age-related refractive changes has to be taken into consideration \(^{(27-29)}\). The mean age at time of surgery of our cohort was 51.6 years. Bengtsson reported a hyperopic shift of 0.6 D (0.06D per year) every 10 years between 50 and 70 years \(^{(25)}\), with a similar trend of hyperopic shift between 50 to 65 yrs followed by myopic drift after 65 years seen in the Blue Mountains Eye Study \(^{(26)}\) and by Saunders \(^{(27)}\). The refractive changes in our study between 5 and 16.5 years fall within this
range of expected age-related hyperopic shift, although as we have reported previously the changes within the first 5 years are higher (almost double) than that expected physiologically \(^1\)\(^8\). The concept that the hyperopic drift after H-LASIK with time is, at least after the first few years after surgery, due to physiological lenticular changes rather than regression of correction at the level of the cornea is supported by the fact that the keratometry remained stable in this cohort between 1 and 16.5 years and is similar to our long-term findings after H-PRK \(^2\)!\(^6\). It should, however, be borne in mind that that 5 eyes (15%) developed visually significant cataract during the 16.5 year follow-up period and that the increase in hyperopic refractive error with time was less in older compared to younger patients (figure 4). This might suggest that with time and advancing patient age any hyperopic drift may be masked by lenticular myopic cataract changes.

At 16.5 years, predictability was limited with an efficacy index of 0.5 and only 24% of eyes within +/- 1.0D of emmetropia and 6% within +/-0.5D. This is similar to the results of H-PRK we reported at 18 years \(^2\)!\(^6\) and is in contrast to the outcomes in this cohort at 12 months when 90% of eyes were within +/-1.0D of emmetropia and 68% within +/-0.5D. This reduction in efficacy with time, given the stable changes in keratometry after 12 months, is probably due to the shift in lenticular hyperopic refractive error as discussed above (figures 1 and 2, table 1). It is of note that variance was increased at 16.5 years compared to 1 year, which might suggest some variability in the physiological lenticular shift in our patients,
perhaps due to their age range and/or the influence of cataract changes as discussed above. As with H-PRK, this restricted longevity of the correction and consequent need to return to spectacle wear and/or undergo further refractive procedures need to be discussed during patient counselling pre-operatively. This is particularly true in light of recent advancements in refractive lens exchange and multifocal intraocular lens technology over the past twenty years\textsuperscript{(12-13)} although the sight-threatening risks associated intraocular surgery and the undetermined long-term complications of refractive lens exchange in terms of decades, also need to be carefully discussed.

In spherical myopic PRK, with first generation broad-beam, iris-diaphragm lasers induction of astigmatism and an increase in pre-existing astigmatism has been documented\textsuperscript{(24, 30)}. Typically these changes were small and insignificant clinically\textsuperscript{(24, 30)}. In this study of H-LASIK, the change in the mean preoperative manifest refractive cylindrical correction at 16.5 years was only -0.16D, with a change of less than -1DC in nearly 78% of eyes. These are results are similar to our reported long-term results after H-PRK using the same delivery system\textsuperscript{(26)}. Given the limitations of the technology used to treat these patients compared to modern laser delivery systems with flying spots, active eye tracking and optimized wave-front ablation profiles, these small astigmatic inductions are encouraging and once again re-enforce the stability of these excimer laser corrections at the level of the cornea. It is of note, however, that vector analysis did indicate a mean change of almost 1D and 2 eyes (6%) experienced astigmatic induction of over 2.0DC. Such changes
are likely to be the result the limitations of technology discussed above and be due to de-centration errors, misaligned laser optics, variability in laser fluencies, irregular epithelial and stromal wound healing, variability in flap creation by first generation LASIK mechanical microkeratomes and the induction of higher order aberrations.

The mean age at time of H-LASIK of our patients was over 50, with only one individual under 40. Therefore, the majority of subjects were hyperopic prebyopes and without refractive correction they typically had no clear point of focus either for distance, near or intermediate. This might clarify why despite limited predictability at 16.5 years with this prototype system, first generation algorithms and continued physiological hyperopic drift, patient satisfaction was relatively high with 89% happy they had undergone the procedure and a mean satisfaction score of over 8 out of 10. At 16.5 years, UDVA was improved (p<0.0001) with 85% of eyes gaining lines of UDVA, while CDVA was unchanged or improved in over 60% and over 40% of eyes could read N18 or better unaided.

In H-LASIK, with the exception of flap creation, the central corneal stroma is spared with the main site of ablation in the mid-periphery. Therefore it is expected that except in the presence of unusual serious adverse events such as de-centration, infection, intra-lamellar inflammation and epithelial in-growth significant disturbances in CDVA attributable to H-LASIK would be unusual.
Indeed, at 16.5 years in our cohort, we found that CDVA was unchanged compared to pre-operative levels and only one eye with epithelial in growth lost 2 lines of CDVA and no eyes lost more than 2 lines.

As excimer laser kerato-refractive surgery is undertaken on healthy eyes, any deterioration in postoperative corneal transparency is of concern. Unlike H-PRK, where a ring of haze is often apparent by the 4th week following surgery, reaching maximal intensity at 6 months and diminishing thereafter (19), no such changes were seen after H-LASIK, where flap creation eliminates the epithelial-stromal wound healing interactions seen with excimer surface ablations. Similarly, we did not see any peripheral Salzmannoid nodular changes associated with the para-central maximal depth of ablation, which we documented in a few patients 18 years after H-PRK (26), using the same excimer laser delivery system.

No late complications associated with H-LASIK were found in this study. Despite the pre-operative use of only anterior surface pachymetry, hand held ultrasonic pachymetry and a mechanical microkeratome with a predicted flap depth of 180um, all eyes appeared to be biomechanically stable on Scheimpflug corneal tomography with no evidence of ectasia at 16.5 years. Similar to our cohort of H-PRK subjects at 18 years, ocular co-morbidity was common with visually symptomatic cataracts requiring surgery in 15% and a number requiring laser iridotomy for problems related to narrow angles. Such potential problems, their relationship to advancing age, should be discussed with these hyperopic patients pre-operatively.
In conclusion H-LASIK showed a significant increase in hyperopic SEQ between 1 and 16.5 years after surgery. The post-operative hyperopic shift after the first 5 years was consistent with the normal physiological lenticular changes expected with age. At 16.5 years the efficacy of the procedure was limited but patients were generally happy they had undergone the procedure. Co-morbidity with cataract was common over the 16.5 year follow-up period in these middle-aged patients.

References


Captions for Figures

Figure 1: Mean spherical equivalent refractive error (diopters) with time after H-LASIK in eyes that had not undergone cataract surgery during the follow-up period (n=32). Error bars = +/- 1 standard deviation.

Figure 2: Scattergram of achieved versus attempted correction after H-LASIK at 16.5 years n=(32).

Figure 3: Mean spherical equivalent refractive error (diopters) with time after H-LASIK in patients receiving +2.0, +2.5 and +3.0D corrections (solid line, n=16) versus patients receiving+3.5, +4.0, 5.0 and +6.0D (n=16). Error bars = +/- 1 standard deviation.

Figure 4: Mean spherical equivalent refractive error (diopters) with time after H-LASIK in patients over 53 years at time of surgery (solid line, n=15) versus patients 52 and under (dotted line, n=17). Error bars = +/- 1 standard deviation.

* statistically significant difference between age groups

Figure 4: Lines of decimal Snellen visual acuity lost or gained at 16.5 years compared to pre-operative values.
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<th>Time</th>
<th>Pre-op</th>
<th>6 months</th>
<th>12 months</th>
<th>5 years</th>
<th>16.5years</th>
<th>P values</th>
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<td>3.79 +/-1.38D</td>
<td>0.22 +/- 0.71D</td>
<td>0.28 +/- 0.55D</td>
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<td>3.11 +/-1.23D</td>
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<td>0.35 +/-0.48D</td>
<td>0.72 +/-0.94D</td>
<td>1.61 +/-1.18D</td>
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<td>4.48 +/-1.19D</td>
<td>0.14 +/-0.79D</td>
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<td>***p=0.005</td>
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<td>3.4 +/-1.6D</td>
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**TABLE 1.** Mean Spherical Equivalent Refraction (SEQ) +/- 1 standard deviation diopters (D) pre-operatively and with time after H-PRK

* Statistically significant change from 1 to 16.5 years

** Statistically significant change from 1 to 5 years

*** Statistically significant change from 5 to 16.5 years