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Visual outcomes in refractive surgery outlier candidates

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VISUAL OUTCOMES IN REFRACTIVE SURGERY OUTLIER CANDIDATES

by

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DEDICATION

I would like to dedicate this work to my mother Patricia and my father Thierry,

I would not be the man I am today without their love and support.

ACKNOWLEDGMENTS

I would like to thank Drs. Melki and Brenner for their continual support and mentorship.

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VISUAL OUTCOMES IN

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ABSTRACT

BACKGROUND: Refractive surgery has become a popular method of treating and reducing refractive errors. Some of the most common types of corneal-based refractive surgery are Laser In Situ Keratomileusis (LASIK), Laser Epithelial Keratomileusis (LASEK), and Photorefractive Keratectomy (PRK). Advanced Surface Ablation (ASA) is an umbrella term which refers to both LASEK and PRK. The current literature lacks analysis of high refractive errors with controls.

OBJECTIVES: To fill gaps in the current literature regrading outliers with high refractive errors by comparing their outcomes to those with low-moderate refractive errors. Additionally, to determine if LASIK or ASA offers superior results for those with high refractive errors and to determine those with different high refractive errors have similar refractive surgery outcomes.

METHODS: A retrospective chart review identified 46 eyes with a preoperative spherical component ≤ -8.50D, 63 eyes with preoperative spherical component ≥ + 3.50D, and 54 eyes with a preoperative cylindrical component ≥ -3.50D which met the criteria for inclusion in the high refractive error cohorts. Each eye was age-matched to a control with a low-moderate amount of its respective refractive error. Quantitative variables were analyzed with t-tests and single-factor analysis of variance. Qualitative variables were analyzed with chi-squared tests. Postoperative uncorrected distance

visual acuity (UCDVA) was used as the primary determinant of visual outcomes and postoperative best corrected visual acuity (BCDVA) was used as the secondary determinant of visual outcomes. Postoperative manifest refractions supplemented the analysis. Changes in BCDVA between pre- and postoperative measurements, with particular attention to loss of Snellen lines, were used as determinants of safety.

RESULTS: The postoperative UCDVA and BCDVA of the myopia cohort was significantly worse than that of the myopia control group (**p = 0.038 and p = 0.0029).** There was no significant difference the safety profiles of the myopia cohort and control group (p = 0.99). The postoperative UCDVA of the hyperopia cohort was significantly worse than that of the hyperopia control group (**p = 0.0069).** There was no significant difference in the safety profiles of the hyperopia cohort and control group (p = 0.96). The postoperative UCDVA of the astigmatism cohort was significantly worse than that of the astigmatism control group (**p = 0.0014).** There was no significant difference the safety profiles of the myopia cohort and control group (p = 0.99). There was no difference between postoperative UCDVA and BCDVA between the cohorts. Neither LASIK nor ASA were superior to the other in terms of UCDVA or BCDVA for all of the cohorts.

CONCLUSION: Refractive surgery, while safe, is not as effective for those requiring high amounts of visual correction compared to those requiring low amounts. Neither surgery type, LASIK nor ASA, offer superior results to those with high refractive errors.

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LIST OF ABBREVIATIONS

ASA ..... Advanced Surface Ablation

BCDVA ..... Best Corrected Distance Visual Acuity

DVA ..... Distance Visual Acuity

LASEK ..... Laser Epithelial Keratomileusis

LASIK ..... Laser In Situ Keratomileusis

PRK ..... Photorefractive Keratectomy

PTA ..... Percent of Tissue Altered

RSB ..... Residual Stromal Bed

UCDVA ..... Uncorrected Distance Visual Acuity

VA ..... Visual Acuity

INTRODUCTION

In the United States, over half of the adult population has some form of refractive error (Vitale et al.). Refractive errors are a group of conditions relating to the eye which impair an individual's sight. The main types of refractive error are myopia, hyperopia, astigmatism, and presbyopia. Traditionally, refractive errors have been treated with spectacle lenses which are placed in front of the eye and correct for the error. Contact lenses may also treat refractive error, if deemed appropriate for an individual. Since 1948, refractive surgery procedures have been developed to reduce an individual's reliance on corrective lenses and with the aid of advances in laser technologies have become a safe, effective, and popular choice for many with refractive errors (Reinstein, Archer, et al.).

Refractive Errors

In normal vision, also known as emmetropia, light passes through the structures of the eye and are focused onto the retina. The human eye is primarily a two-lens system in which the refractive power of the cornea and crystalline lens work in concert to focus light directly onto the retina. The cornea is responsible for the majority of the eye's refractive power. The lens's shape can be modified by the ciliary body which leads to adjustment of the lens's refractive power. This process is known as accommodation. Once light rays reach the retina, rod and cone cells are stimulated to generate electrical impulses which are transmitted to the brain. The brain in turn perceives these impulses as an image (*How Your Eyes Work*). Refractive errors occur when light entering the eye is

not focused properly by the cornea and/or lens onto the retina. This leads to the brain perceiving a blurry image.

Myopia is colloquially known as nearsightedness; myopes, individuals with myopia, see objects close to them (~14") well and objects further from them (>~20') appear to be blurry. Myopia occurs when rays of light are focused in front of the retina (Figure 1). This is due to the refractive power of the eye is too high which moves the focal point anterior to the retina. Typically, an increased axial length, the distance anterior to posterior, of the eye and an increase in the "steepness", curvature, of the cornea are related to myopia (Bastawrous et al.). Treatment of myopia traditionally involves the use of a spherical, divergent (concave) lens placed in front of the eye to shift the focal point posteriorly onto the retina. This lens would have a negative power in diopters (D), and thus myopes are described as having a negative spherical prescription (Stein et al.). The 1999–2004 National Health and Nutrition Examination Survey estimated the prevalence of myopia to be 33.1% (Stein et al.).

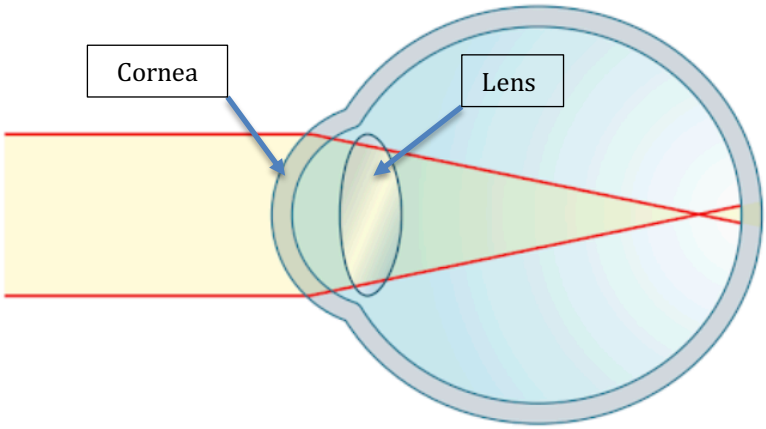


Figure 1. The Myopic Eye. Light rays passing through the eye are focused to a point anterior to the retina. The cornea and crystalline lens are labeled (Stein et al.).

In contrast, individuals with hyperopia, hyperopes, can typically see objects in the distance (>20' from the eye) clearly while objects nearby appear to be blurry. This can vary between individuals dependent upon their age and degree of hyperopia. The structures of the eye focus rays of light too weakly producing a focal point posterior to the retina (Figure 2). Hyperopes are typically described as having a short eye, one with a decreased axial length, or a "flat" cornea, one with decreased curvature (Bastawrous et al.). When a spherical converging (convex) lens is placed in front of a hyperopic eye the focal point is shifted anteriorly onto the retina. Hyperopes are said to have a positive spherical prescription as the lens used to correct their vision has a positive power in diopters (Stein et al.). It has been estimated that 3.6% of Americans are affected by hyperopia (Vitale et al.).

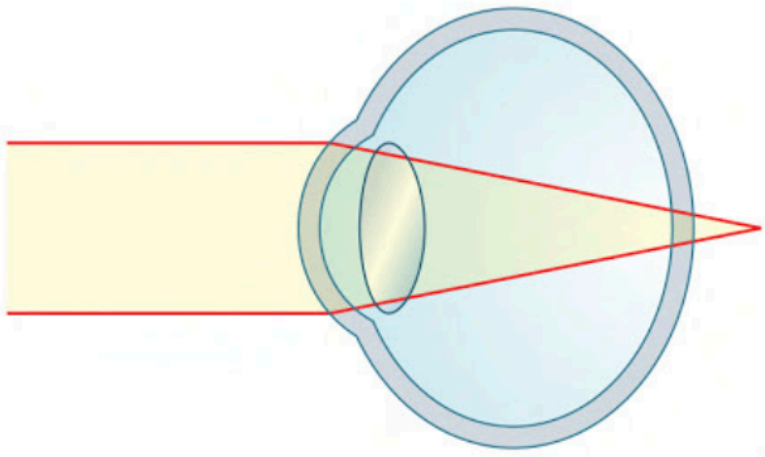


Figure 2. The Hyperopic Eye. Light rays passing through the eye are focused to a point posterior to the retina (Stein et al.).

Astigmatism arises when light rays are not refracted equally in all directions while passing through the eye, in these cases a single focal point is not achieved. Typically, an individual with uncorrected astigmatism will complain of blurriness of both near and far

objects. The unequal refraction is typically due to the radius of curvature of the cornea is not uniform in all directions (Figure 3). Regular astigmatism can be defined as an astigmatism which is able to be corrected by a cylindrical lens. There are various subtypes of regular astigmatism in which an astigmatism may be compounded with myopia and/or hyperopia. In simple astigmatism one meridian of light is focused onto the retina while the complimentary meridian is focused either in front of the retina (simple myopic astigmatism) or behind the retina (simple hyperopic astigmatism). In compound astigmatism both meridians' focal points land in front of the retina (compound myopic astigmatism) or behind the retina (compound hyperopic astigmatism). In mixed astigmatism on meridian's focal point is in front of the retina while the complimentary meridian's focal point lands behind the retina (Stein et al.). Individuals with astigmatism have a cylindrical component to their prescription. Historically, optometrists have used negative cylindrical power and ophthalmologists have worked with positive cylindrical power. However, due to the belief that it is easier to mistakenly overcorrect a myope when working with positive cylinder, refractive surgeons typically use negative cylinder. Approximately 36.2% of Americans are effected by some form of astigmatism (Vitale et al.).

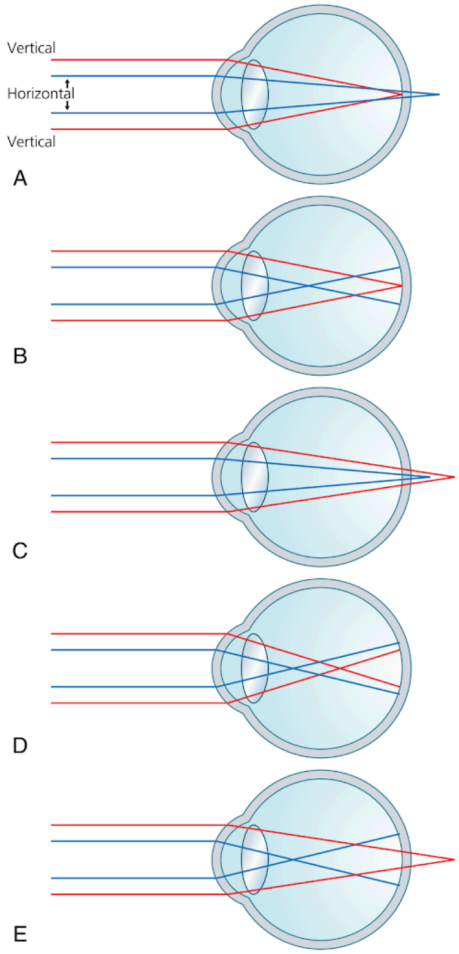


Figure 3. Types of Regular Astigmatism. The red lines represent light rays in the vertical meridian and the blue line represent light rays in the horizontal meridian. A) Simple hyperopic astigmatism, the vertical rays are emmetropic while the horizontal rays are focused behind the retina. B) Simple myopic astigmatism, the vertical rays are emmetropic while the horizontal rays are focused in front of the retina. C) Compound hyperopic astigmatism, both the vertical and horizontal rays are focused behind the retina. D) Compound myopic astigmatism, both the vertical and horizontal rays are focused in front of the retina. E) Mixed astigmatism, vertical rays are focused behind the retina and horizontal rays are focused in front of the retina. (Stein et al.)

Presbyopia is similar to hyperopia, in that it causes objects nearby to appear blurry but objects in the distance are not affected. It is caused by a loss of accommodative power, that is the crystalline lens becomes less flexible as an individual ages and the eye loses the ability to focus on nearby objects. Presbyopia effects virtually all adults over 40 years old.

Refractive Surgery

Refractive surgery is a popular alternative to corrective lenses for the treatment of refractive errors. Typically, this group of procedures is focused on the cornea, but can also involve the crystalline lens. The cornea is the most anterior structure of the eye and is comprised of three main layers: anteriorly the epithelium, the corneal stroma, and posteriorly the endothelium. Bowman's membrane separates the epithelium from the stroma while Descemet's membrane separates the stroma and the endothelium. The epithelium provides a smooth refractive surface for the eye while serving as an immunologic barrier (Huang and Chen). The corneal epithelium is stratified squamous non-keratinized and is regenerated by stem cells from the corneal limbus around its periphery. The stromal layer comprises a majority of the cornea's thickness. Due to its composition, mainly connective tissue, it is responsible for the cornea's integrity. The endothelium separates the cornea from the anterior chamber and aqueous fluid; it is responsible for the cornea's relative dehydration via an active sodium potassium-adenosine triphosphatase pump which allows the cornea to remain transparent (Huang and Chen).

Three common types of corneal-based refractive surgery are Laser In Situ Keratomileusis (LASIK), Laser Epithelial Keratomileusis (LASEK), and Photorefractive Keratectomy (PRK). These are laser based refractive surgeries which utilize an excimer laser to re-shape the corneal stroma. The laser utilizes excited gas dimers to produce photons which are fired in a pulsatile fashion at the corneal stroma. This breaks molecular bonds and causes a controlled amount of tissue to be ablated (Huang and

Chen). In general, the aim of a treating a myopic eye is to flatten the cornea, reducing its radius of curvature. The aim of treating a hyperopic eye is to steepen the cornea, increasing its radius of curvature.

Originally the amount and pattern of ablation was governed by the patient's spherical and cylindrical correction. Wavefront-guided and wavefront-optimized treatment patterns have been utilized to "customize" a patient's treatment. Wavefront based treatments measure light as it passes through the eye to determine a patient's refractive error due to lower-order aberrations (sphere and cylinder) as well as higher-order aberrations. Wavefront systems reportedly offer improved visual outcomes, such as visual acuity (VA) and halos/starbursts, over traditional treatments (Netto et al.).

LASIK, LASEK, and PRK surgeries mainly differ in how the corneal stoma is accessed (Figure 4). In LASIK, a microkeratome or femtosecond laser are utilized to create a flap of tissue with a hinge. This flap can range from 90 to 150 microns in thickness and is comprised of the corneal epithelium and part of the stromal layer. Flap creation with the femtosecond laser, so-called "bladeless LASIK", is preferred as it offers better flap thickness predictability as well as a faster recovery time (Huang and Chen). After ablation the flap is laid back in place over the reshaped stroma. LASEK also involves the use of a flap, however it is much thinner than a LASIK flap as it is solely comprised of the epithelium and does not invade the corneal stroma. A LASEK flap is created via controlled application of an alcohol solution to the cornea which loosens the epithelium so that the surgeon may lift it as a either a single flap or in parts (Taneri et al.). The epithelium is replaced after ablation and a bandage contact lens is placed over the

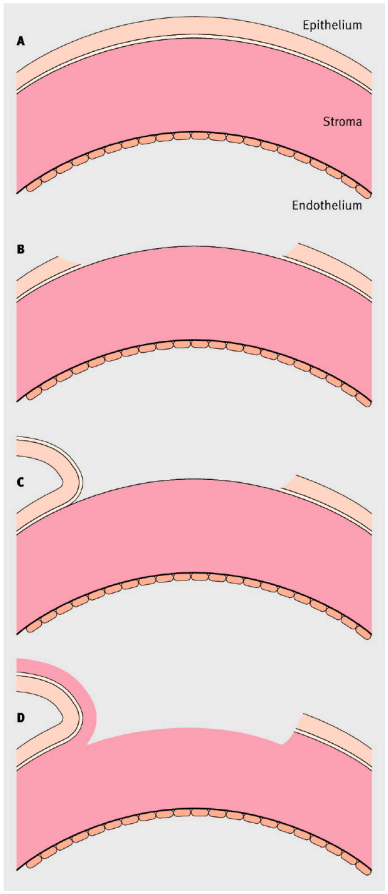


Figure 4. The Cornea in Refractive Surgery A) An intact cross section of the cornea. B) PRK: The epithelium has been completely removed, exposing the corneal stroma for ablation. C) LASEK: The epithelium is removed but preserved as a sheet to be replaced after ablation of the stromal layer. D) LASIK: A partial thickness flap, consisting of the epithelium and some of the stroma, is cut with a hinge. Subsequent to ablation the flap is laid back down over the corneal stroma (Bastawrous et al.).

cornea while a new epithelial layer grows. PRK does not involve the use of a flap, instead the epithelium is completely removed with an alcohol solution, blade, and/or brush. A bandage contact lens is placed over the cornea subsequent to ablation. Due to their similarities, LASEK and PRK surgeries will be grouped and referred to as Advanced Surface Ablation (ASA) for the remainder of this thesis (Taneri et al.).

Candidacy for Refractive Surgery

All patients with refractive errors are not candidates for refractive surgery. Preoperative screening and testing are paramount to selecting proper candidates for the proper procedure type. A good candidate for surgery will have a stable refraction myopia ≤ -12.00D or hyperopia ≤ +6.00D, and/or astigmatism ≤ 5.00D (Huang and Chen). Absolute ocular contraindications to surgery are an unstable refraction (>0.50D change in sphere or cylinder in the past year), keratoconus, herpetic keratitis, corneal dystrophy or degeneration, cataract, uncontrolled glaucoma, active infection or inflammation, and other pre-existing corneal or anterior segment pathologies. Absolute medical contraindications include history of keloid formation, pregnancy or lactation, uncontrolled autoimmune disease, and immunosuppression or immunocompromised status (Huang and Chen). A stable refraction is imperative because if a patient's prescription is fluctuating, they are more likely to require re-treatment (enhancement) after surgery. Keratoconus is a non-inflammatory disorder which causes progressive thinning of the cornea. It is a contraindication for refractive surgery due to the risk of postoperative keratectasia, increasing myopia/astigmatism due to progressive steepening of the cornea (Ormonde). Preoperative corneal topography is essential to the screening for sub-clinical keratoconus. Patients with a history of herpes keratitis are advised against surgery as it may reactivate their infection.

Not all patients are candidates for both LASIK and ASA. Due to the creation of the flap during LASIK, there is less of the stromal bed available for alteration in comparison to ASA. Important considerations for the refractive surgeon in choosing a

surgery type are the percent of tissue altered (PTA) and residual stromal bed (RSB). The PTA is defined as $\frac{Flap\ Thickeness\ (if\ applicable) + Thickness\ of\ Cornea\ Ablated}{Central\ Corneal\ Thickness}$ and the RSB is the thickness of the stromal layer after surgery. If patient has a theoretical PTA > 40% of theoretical RSB < 300 microns they are at an increased risk of corneal ectasia (Santhiago et al.). The surgeon must use corneal pachymetry, a measurement of the cornea's thickness via either a pachymeter or corneal topographer, to determine if a patient is a candidate for LASIK.

If a patient is a candidate for both LASIK and ASA, the question becomes which surgery would provide the patient the best outcome. The current literature is lacking in good evidence randomized control trials comparing LASIK and ASA surgeries for myopia and hyperopia (Kuryan et al.; Li et al.; Settas et al.; Shortt et al.). The literature is even more so lacking in trials comparing different surgery types specifically in patients with high degrees of refractive error. A literature review revealed no studies comparing LASIK to either PRK or LASEK for eyes with high hyperopia, one study comparing LASIK to PRK for high astigmatism, and three comparing LASIK to ASA surgeries for high myopia (Katz et al.). The studies comparing LASIK to ASA surgeries vary greatly in their results, with 19.1% to 60% of eyes achieving 20/20 vision or better and 55.7% to 76% achieving 20/40 vision or better uncorrected (Hersh et al.; Kim et al.; Helmy et al.). They also disagree if there is a superior surgery for highly myopic eyes, with Hersh et al. finding no difference in efficacy between LASIK and PRK, while Kim et al. and Helmy et al. found LASIK to be superior to ASA surgeries. Katz et al. found LASIK and PRK to be similarly effective for the treatment of high astigmatism.

Similarly, while general reports of visual outcomes of various groupings of patients are plentiful, there is a great lack in the literature of high refractive error groups being directly compared to low refractive error groups of the same population. The individual reports of high refractive error groupings vary greatly in outcomes, as do reports of low-moderate refractive error groups. Huang and Chen report ranges for moderate to high myopia 10% to 47% of eyes achieve 20/20 vision or better and 55% to 94% of eyes achieve 20/40 vision or better uncorrected. This thesis aims to fill in these gaps in the current literature.

OBJECTIVES

The purpose of this thesis was to fill gaps within the current literature on the visual outcomes of outlier candidates for refractive surgery; those with high degrees of either myopia, hyperopia, or astigmatism. The specific objectives were to: 1) Compare those with high refractive errors with those with low-moderate refractive errors in terms of efficacy and safety of treatment 2) Determine if LASIK or ASA is more efficacious to those with high refractive errors 3) Determine if those with different high refractive errors have similar refractive surgery outcomes.

The hypothesis tested was that refractive surgery for the high refractive error groups would not be as efficacious nor as safe as for their low refractive error peers. Furthermore, it was hypothesized that ASA surgery would be more beneficial for the high astigmatism cohort, LASIK surgery would be more beneficial for the high myopia and high hyperopia cohorts. Lastly, no difference in outcomes was expected between the high refractive error cohorts.

METHODS

Study Design

A retrospective chart review was performed via NextGen electronic health record software (Version 5.9.1.92) on all patients who underwent laser vision correction (LASIK, LASEK, or PRK) at Boston Eye Group/Boston Laser from December 2008 – December 2018. The follow-up period for the study was selected to be 12 months ±3 months from the date of surgery. All eyes were identified via their preoperative manifest refraction. Manifest refraction is the standard, if subjective, measurement of a patient's refractive error using a series of lenses with a phoropter. Myopia cohort candidates were identified as having a preoperative manifest refraction with a spherical component ≤ -8.50D. Myopia control candidates were identified as having a preoperative manifest refraction with a spherical component < -0.50D and ≥ -4.00D. Hyperopia cohort candidates were identified as having a preoperative manifest refraction with a spherical component ≥ + 3.50D. Hyperopia control candidates were identified as having a preoperative manifest refraction with a spherical component > +0.50D and < +2.00D. Astigmatism cohort candidates were identified as having a preoperative manifest refraction with a cylinder component ≥ -3.50D. Astigmatism control candidates were identified as having a preoperative manifest refraction with a cylinder component < -0.25D and ≥ -1.50D. Control eyes were selected to match each cohort eye for age on day of surgery; if a control eye of the same age was unavailable or did not meet inclusion criteria, the next closest control eye in age was selected. If a candidate had multiple follow-ups within the follow-up period data from the visit closest in time to 12 months

from surgery was used. If a candidate for one of the high refractive error cohorts underwent an enhancement surgery prior to 9 months after their initial surgery the results of their original surgery were included using a "last observation carried forward" technique. The last postoperative data available prior to enhancement surgery was used as their one-year endpoint data. These patients were included to reduce bias against poor results that would be introduced by excluding them. Follow-up time was determined in days using https://www.timeanddate.com/date/duration.html.

Exclusion Criteria

- No follow-up visit within 12 ± 3 months from day of surgery
- Previous eye surgery on the operative eye
- Missing pre- or postoperative data from the Electronic Health Record
- Eyes that underwent phototherapeutic keratectomy
- Eyes that required initial treatment in two stages (two surgical dates for the initial treatment of one eye)
- Patient age <18 years old
- Eyes with a target post-operative refraction other than a 0.00 spherical equivalent

Preoperative Consultation

All patients underwent a preoperative consultation with a board-certified ophthalmologist or optometrist. This consultation is standardized for all patients who wish to pursue refractive surgery with Boston Eye Group/Boson Laser. It is typically

carried out by staff at Boston Eye Group and referrals for surgery still undergo the testing at Boston Eye Group. All patients are asked to refrain from soft-contact use for 1 week and hard-contact use for 3 weeks prior to consultation. Initial testing includes an auto-refraction, auto-keratometry, ocular dominance, corneal topography, corneal pachymetry, ZoneQuick Phenol Red Thread Tear Test, ocular tonometry (via non-contact tonometry, Tono-pen, or Goldman applanation), and scotopic pupillometry.

Spectacle-corrected distance visual acuity (DVA) is measured with a Snellen chart, as well as uncorrected distance visual acuity (UCDVA) and uncorrected near visual acuity. A manifest refraction is performed to determine the patient's preoperative prescription as well as their best-corrected distance visual acuity (BCDVA). Wavescans are performed as ordered by the attending physician. All patients are dilated and undergo a cycloplegic refraction, slit-lamp examination, and dilated fundus exam. The physician uses all available information, including personal judgment, to determine what, if any, refractive surgery a particular patient may be a candidate for (Figure 5).

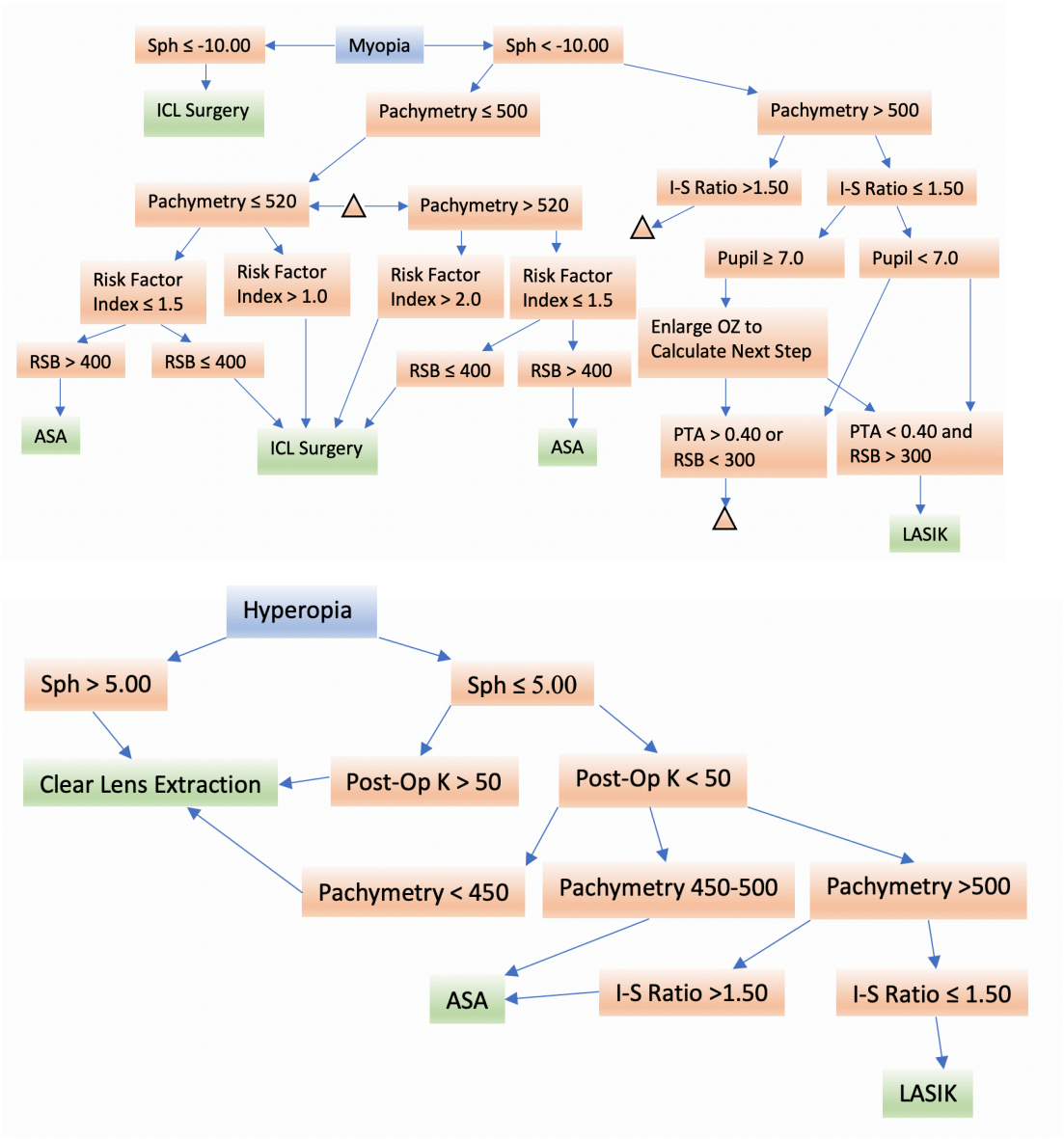


Figure 5. Refractive Surgery Algorithms. These flow charts are an example of a conservative practice pattern of Samir Melki M.D. Ph.D. Not all steps or cut off values are evidenced based nor absolute contraindications, they merely generalize the thought process a surgeon may take when deciding what surgery type a patient is a candidate for. (Sph = spherical power, ICL = implantable collamar lens, I-S Ratio = inferior to superior corneal power ratio, Risk Factor Index = proprietary risk gauging index (Patient Age < 26 years old = 0.5; max preoperative keratometry > 46 = 1.0; difference between right and left eye keratometry > 1.5 = 1.0; positive family history of keratoconus = 1.0; I-S Ratio > 1.5 = 2.0), RSB = residual stromal bed, OZ = optical zone, PTA = Percent of Tissue Altered, ASA = advanced surface ablation, LASIK = Laser In Situ Keratomileusis, Post-Op K = Maximum Calculated Postoperative Keratometry,)

Day of Surgery

All patients met with their surgeon either prior to the day of surgery or when they arrive to the surgery site; they were also given the opportunity to meet with their surgeon again at any point during the preoperative process. All patients signed informed consent forms detailing the potential benefits, risks, and alternatives of laser vision correction. Patients were instructed to discontinue soft-contact lens use one week and hard-contact lens use three weeks prior to the surgical date. Any repeat testing was performed as ordered by the surgeon, e.g. repeat manifest refraction due to discrepancies in earlier refractions and repeat corneal topography due to contact lens use prior to previous topography. Patients were educated on the steps of their specific procedure, postoperative care, and postoperative medication use. A time-out was called with the patient to confirm the operative eye(s), the procedure(s), the aim for each eye, all the patient's questions have been answered, the patient's postoperative transportation, the patient has their postoperative medication, and the patient has discontinued contact lens use for the appropriate time period. Eye(s) not being operated upon were covered with an eye shield. Patients who were scheduled for different procedures on each eye had their forehead marked to denote the correct procedure for each eye. Patients were given preoperative medication 20 minutes prior to the anticipated surgical time: Ciprofloxacin Hydrochloride Ophthalmic Solution 0.3% One drop instilled into the operative eye(s), Ketorolac Ophthalmic Suspension 0.5% One drop instilled into the operative eye(s), and Diazepam 5mg one tablet by mouth. If the patient's refraction contained more than 1.25D

of cylinder their eye was marked with a sterile surgical marker to ensure proper laser alignment.

Each patient was asked to confirm their full name and date of birth prior to being brought into the surgical suite. Patients were laid on supine on the operative bed with a surgical cushion placed below their knees and a hairnet was placed over their head. Proparacaine Hydrochloride Ophthalmic Solution 1% was instilled into the operative eye(s) as a topical anesthetic. The operative eye(s) were sterilized by topical application of Betadine 5% to the periocular area. A time-out was called and patients confirmed their last name, date of birth, operative eye(s), procedure per eye, if they desired monovision, and the aim of each eye. The time-out was continued by the surgeon and assistant who confirmed the patient's identity via a photograph on file and the treatment plan inputted to the laser. The following describes the different intra-operative procedures for LASIK and ASA.

LASIK

All LASIK flaps were created using the IntraLase iFS60 or FS150 Femtosecond Laser. The standard parameters were a superior hinge position, 9.2 mm in diameter, and a thickness of 100 microns. These parameters may have been changed at the surgeon's discretion due to corneal topography and/or pachymetry. Suction was applied to the eye prior to docking into the laser interface. The patient's cornea was applanated flat and the pupil was centered with fine adjustments to the laser's position. The patient was undocked from the laser and the patient interface was discarded.

The operative bed was repositioned under the excimer laser, either the VISX STAR S4 IR or WaveLight EX500. A Tegaderm (3M^{TM}) was placed over the upper eyelid to hold the eyelashes away from the eye and a speculum was placed to ensure the eye remained open. A mark was placed at the edge of the LASIK flap at the 5 o'clock with a sterile surgical marker. The eye was irrigated with balanced salt solution and proparacaine hydrochloride ophthalmic solution 1% was instilled to maintain proper anesthetization. The eye was dried with a Weck-Cell sponge (BVI). Corneal pachymetry was measured either with a handheld pachymeter or with the excimer laser system and was read out loud to the surgeon. The LASIK flap was lifted with a LASIK spatula and the exposed stroma was dried with a Weck-Cell sponge. A "flap-lift" pachymetry was measured in the same manner as previously described and verbally called out. The surgeon confirmed that the surgery was safe to proceed. The surgeon centered the pupil and adjusted the head as needed. The surgeon then fired the excimer laser to ablate the corneal stroma. After completion of the treatment, the surgeon repositioned the LASIK flap and irrigated the corneal surface and stromal bed with balanced salt solution. A Weck-Cell sponge was used to dry the excess fluid and remove fluid from the LASIK flap "gutter". Two drops of Gatifloxacin- Prednisolone 0.5%-0.1% ophthalmic solution were instilled in the operative eye. The patient was escorted to a dimly lit exam room where they remained at rest for 30 minutes. The operative eye was examined with a silt-lamp to ensure the LASIK flap was in position. An eye shield was placed over the operative eye and the patient was discharged from the surgical site to the care of their

postoperative transportation. All patients were instructed with lie down with their eyes closed for a minimum of four hours once they arrived home.

ASA

The operative bed was repositioned under the excimer laser, either the VISX STAR S4 IR or WaveLight EX500. A Tegaderm was placed over the upper eyelid to hold the eyelashes away from the eye and a speculum was placed to ensure the eye remained open. Proparacaine hydrochloride ophthalmic solution 1% was instilled to maintain proper anesthetization. The eye was dried with a Weck-Cell sponge. A 9mm ring well was positioned centrally on the cornea and filled with a previously prepared 20% ethanol solution. The solution was applied to the cornea for 40 seconds before being absorbed with a Weck-Cell sponge. The eye was irrigated with 5 mL of 0.9% saline and dried with a Weck-Cell sponge.

Eyes undergoing LASEK had their epithelium repositioned outside of the treatment area. The surgeon centered the pupil and adjusted the head as needed. The surgeon the fired the excimer laser to ablate the corneal stroma. The epithelium was then repositioned to cover the exposed stromal layer.

Eyes undergoing PRK had their epithelium completely removed. The surgeon centered the pupil and adjusted the head as needed. The surgeon the fired the excimer laser to ablate the corneal stroma. If indicated, a corneal light shield soaked with mitomycin-C was applied for an amount of time dependent on the amount of tissue ablated. The eye was irrigated with 5 mL of cold 0.9% saline and dried with a Weck-Cell sponge.

Regardless of procedure type, a bandage contact lens was placed on the eye. Two drops of Gatifloxacin- Prednisolone 0.5%-0.1% ophthalmic solution and one drop of cyclopentolate hydrochloride ophthalmic solution 1% were instilled in the operative eye. The patient was discharged from the surgical site to the care of their postoperative transportation.

Postoperative Care

All patients were given printed postoperative care instructions. Postoperative limitations and precautions included but were not limited to: no squinting, squeezing, or rubbing the operative eye and no heavy lifting for 24 hours; keep exercise light and no sunscreen, lotion, or moisturize near the operative eye(s) for one week; no contact sports, swimming, hot tub, sauna, or jacuzzi for two weeks. Patients were instructed to wear an eye shield over their operative eye(s) while sleeping for one week.

For eyes which underwent LASIK the following postoperative regiment was prescribed. Prednisolone Acetate 1% Ophthalmic Suspension one drop every hour on the day of surgery and the two following days, then four drops per day for two days, then stop. Moxifloxacin hydrochloride ophthalmic solution 0.5% four drops per day the day of surgery and following 4 days, then stop. Liberal use of preservative-free artificial tears was strongly encouraged. Patients were instructed to wait 5 minutes before instilling a drop a different medication into the same eye. Patients were instructed to only using the drops during their waking hours.

For eyes which underwent ASA the following postoperative regiment was prescribed. Prednisolone acetate 1% ophthalmic suspension four drops per day for one week, then three drops per day for one week, then two drops per day for one week, then one drop per day for one week, then stop. Moxifloxacin hydrochloride ophthalmic Solution 0.5% four drops per day until instructed to stop (typically after one week and removal of the bandage contact lens). Nepafenac 0.1% ophthalmic suspension 1 drop as needed for discomfort, up to two times per day. Vitamin C 1,000 mg per day for three months to aid in corneal healing and prevent scar formation. Liberal use of preservative-free artificial tears was strongly encouraged. Patients were instructed to wait 5 minutes before instilling a drop a different medication into the same eye. Patients were instructed to only use eyedrops during their waking hours. Patients were also offered a prescription for acetaminophen-codeine phosphate 300-30mg tablets for postoperative discomfort for use up to four times a day.

All patients had follow-up appointments scheduled for one day after surgery. If a patient was "co-managed", meaning they were under the concurrent care of an outside optometrist, they were returned to their optometrist's care subsequent to their one-day follow-up. For all other patients, one-week, six-week, six-month, and one-year follow-ups were recommended and attempted to schedule.

At follow-up visits patients were asked if they had any complaints such as blurry vision, dryness, trouble driving, trouble reading, or halos. Patients' uncorrected distance visual acuity (UCDVA) was checked monocularly and binocularly. If the patient underwent LASIK/ASA monovision, near visual acuity was checked. All patients had

auto-refraction performed at each follow-up visit. From the one-day follow-up for LASIK eyes and from the six-week follow-up for ASA eye, if the patient could not successfully read the 20/20 line on a Snellen chart or complained of blurry vision, a manifest refraction was performed. From the six-week follow-up onward intra-ocular pressure was measured. Additional testing was performed as ordered by the attending physician.

Statistical Analysis

Prior to analysis, all patient data was de-identified and assigned a reference number. The spherical equivalent of manifest refractions were calculated via the following formula: $SE = (Sph) + \left({}^{Cyl}/_{2}\right)$. Visual acuity (VA) data measured by the Snellen Chart were converted to log(MAR) for proper statistical analysis using Table 1 (Holladay). Eyes with a postoperative UCDVA of 20/20, or better, that did not have a postoperative manifest refraction noted were considered to have a plano-spherical refraction (+0.00 -0.00x180) with a BCDVA the same as their UCDVA. Eyes that underwent an enhancement surgery prior to the study period had their last postoperative data available prior to enhancement surgery used as the data with a follow-up time of 365 days.

Table 1. Conversation Chart: Snellen to log(MAR). The log(MAR) values corresponding to relevant lines of the Snellen Visual Acuity Chart, as described by Holladay, 1997.

Snellen Equivalent (feet)	log(MAR) Equivalent
20/15	-0.125
20/20	0
20/25	0.1
20/30	0.176
20/40	0.3
20/50	0.4
20/60	0.477
20/70	0.544
20/80	0.6
20/100	0.7
20/150	0.875
20/200	1.0
20/400	1.3

The data analysis toolpak in Microsoft Excel for Mac 16.16.13 was used for all statistical analysis. Microsoft Excel for Mac 16.16.13 was also used for the creation of graphs. Quantitative variables were analyzed with t-tests and single-factor analysis of variance (ANOVA). Qualitative variables were analyzed with chi-squared tests. Two-sample assuming unequal variances two-tailed t-tests were used to determine if there was a significant difference between different groups in the following variables: age at surgery, spherical power, cylindrical power, spherical equivalent, follow-up visit time, UCDVA, and BCDVA. Paired two-sample for means two-tailed t-tests were used to determine if there were significant differences between a group's preoperative BCDVA and postoperative UCDVA as well as preoperative BCDVA and postoperative BCDVA. Chi-squared tests of independence were used to determine if there was a significant difference in distribution of sexes, surgery type, and gain/loss of BCDVA. Single-factor ANOVA tests were used to compare UCDVA and BCDVA between the cohorts.

The null hypothesis for all tests assumed equal means for continuous variables or equal distribution for categorical variables. A p-value of $p < 0.05$ was considered statistically significant. A p-value of $p < 0.01$ was considered very statistically significant. Any significant p-value led to rejection of the null hypothesis.

Postoperative UCDVA was used as the primary determinant of visual outcomes and postoperative BCDVA was used as the secondary determinant of visual outcomes. Postoperative manifest refractions supplemented the analysis. Changes in BCDVA between pre- and postoperative measurements, with particular attention to loss of Snellen lines, were used as determinants of safety (Huang and Chen). Visual acuities of 20/20, or better, were considered to be optimal results. While visual acuities worse than 20/40 were considered unsatisfactory. Visual acuities worse than 20/20 but 20/40 or better were considered satisfactory.

RESULTS

Myopia

There were 187 eyes (91 right and 96 left eyes) identified with a preoperative spherical power ≥ -8.50D. Of these, 48 eyes (22 right and 26 left eyes) met the criteria for inclusion in the myopia cohort. Excluded eyes are broken down in Table 2. There was a total of three eyes in the myopia cohort that underwent an enhancement procedure within the year following their surgery, accounting for 1.6% of the total eyes that were identified. The mean time after the original surgery that the enhancement procedure was performed was 266 ± 23 days.

Table 2: Myopia: Excluded Eyes. A breakdown of the eyes excluded from the myopia cohort and for what reason.

Exclusion Criteria	Number of Eyes Excluded
Non-Zero Target Refraction	5
Previous Surgical Procedure	1
Age < 18 Years Old	1
Missing Data	3
No Follow-Up in Study Period	129

Preoperative

Of the 48 eyes included, 21 belonged to men and 27 belonged to women. Average preoperative manifest values and visual acuities are presented in Table 3. The myopia cohort had 4 eyes correctable to 20/15 on the Snellen scale, 40 eyes correctable to 20/20, three eyes correctable to 20/25, and one eye correctable to 20/30.

Table 3. Myopia: Preoperative Data. Mean preoperative data for the myopia cohort and control groups. Significance values for statistical analysis between groups are included below the respective data. (BCDVA = best corrected distance visual acuity)

	Myopia Cohort	Myopia Control Group
Age (Years)	34 ± 8	35 ± 8
p-value	0.96	
Spherical Power (D)	-8.77 ± 0.58	-1.14 ± 0.62
p-value	**1.4×10^{-76}**	
Cylindrical Power (D)	-0.71 ± 0.52	-1.06 ± 0.83
p-value	**0.027**	
Spherical Equivalent (D)	-9.13 ± 0.70	-1.67 ± 0.71
p-value	**4.9×10^{-70}**	
BCDVA (log(MAR))	0.00 ± 0.05	0.00 ± 0.03
p-value	0.75	

The average age of the myopia control group at time of surgery did not differ from the myopia cohort, $t(92) = 0.05$, $p = 0.96$. Of the 48 eyes, 33 belonged to men and 15 belonged to women; this distribution was not significantly different than the myopia cohort, $\chi^2(1, N=96) = 0.01$, $p = 0.91$. The myopia control group was very significantly more myopic than the myopia cohort, $t(92) = -61.60$, **$p = 1.4 \times 10^{-76}$**. The myopia control group had significantly more preoperative cylindrical power than the myopia cohort, $t(78) = 2.25$, **$p = 0.027$**. The mean preoperative spherical equivalent of the myopia control group was very significantly less than the myopia cohort, $t(92) = -52.04$, **$p = 4.9 \times 10^{-70}$**. The myopia cohort and control group's mean preoperative BCDVA did not differ significantly, $t(73) = 0.31$, $p = 0.75$.

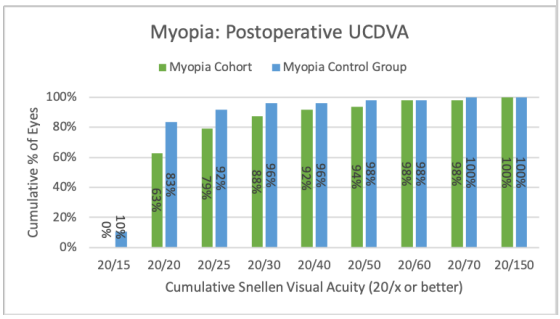
Postoperative

Table 4. Myopia: Postoperative Data. Mean postoperative data for the myopia cohort and control groups. Significance values for statistical analysis between groups are included below the respective data. (UCDVA = uncorrected distance visual acuity, BCDVA = best corrected distance visual acuity)

	Myopia Cohort	Myopia Control Group
Follow-up Time (Days)	361 ± 62	406 ± 42
p-value	**1.2×10^{-4}**	
Spherical Power (D)	0.03 ± 0.62	-0.08 ± 0.29
p-value	p = 0.18	
Cylindrical Power (D)	-0.29 ± 0.47	-0.13D ± 0.29
p-value	**p = 0.034**	
Spherical Equivalent (D)	-0.11D ± 0.63	-0.14D ± 0.32
p-value	0.65	
UCDVA (log(MAR))	0.09 ± 0.17	0.02 ± 0.12
p-value	**0.038**	
BCDVA (log(MAR))	0.02 ± 0.06	-0.01 ± 0.04
p-value	**0.0029**	

Average postoperative manifest values and visual acuities are presented in Table 4. The mean follow-up time was very significantly later for the myopia control group, t(80) = -4.06, **$p = 1.2 \times 10^{-4}$**. The myopia cohort had a very significant decrease in VA between the mean preoperative BCDVA and mean postoperative UCDVA, t(47) = -3.58, **$p = 8.2 \times 10^{-4}$**. The myopia control group had no significant difference between mean preoperative BCDVA and mean postoperative UCDVA, t(47) = -1.54, p = 0.13. The UCDVA of the myopia cohort was significantly worse than that of the myopia control group, t(83) = 2.11, **p = 0.038**. The myopia cohort's mean BCDVA was significantly worse postoperatively when compared to the preoperative mean, t(47) = -2.52, **p = 0.015**. There was no significant change to the myopia control group's mean postoperative BCDVA when compared to their preoperative mean, t(47) =1.63, p = 0.11. The mean postoperative BCDVA of the myopia control group was very significantly better than the

myopia cohort, t(80) = 3.07, **p = 0.0029**. The breakdown of postoperative visual acuities is presented in Figure 6.



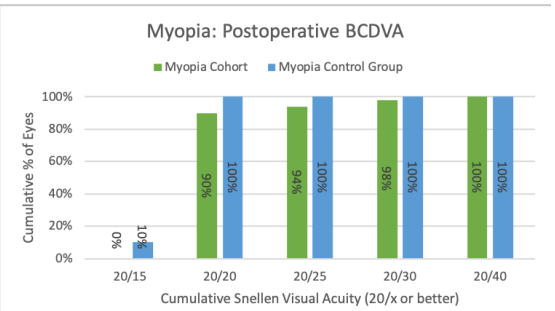


Figure 6. Myopia: Cohort vs Control Visual Acuities. Representations of the postoperative UCDVA and BCDVA of myopia cohort and myopia control group. The data are in terms of the percentage of eyes that achieved that VA or better.

The mean postoperative spherical power and spherical equivalents did not differ significantly between the myopia cohort and the myopia control group, t(67) = 1.37, p = 0.18 and t(70) = 0.45, p = 0.65. The mean postoperative cylindrical power did differ significantly higher for the myopia cohort, t(75) = -2.16, **p = 0.034**.

Safety

Changes in BCDVA are presented in Figure 7. There was no significant difference in the distribution of change of BCDVA between the myopia cohort and myopia control group, $\chi^2(3, N=96) = 0.01$, p = 0.99.

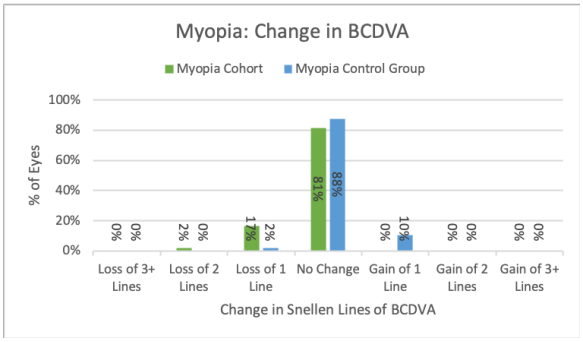


Figure 7. Myopia: Change in BCDVA. Representation of the safety profile for both the myopia cohort and myopia control group. The data are presented in terms of the percentage of eyes that underwent that change in BCDVA.

Surgery Type

In the myopia cohort there were 16 eyes that underwent LASIK and 32 eyes that underwent ASA. There was no significant difference in mean follow-up time between the surgery groups in the myopia cohort, $t(26) = -1.47$, $p = 0.15$. In the myopia control group, 39 eyes underwent LASIK and 9 eyes underwent ASA; this was not significantly different from the surgery type distribution of the myopia cohort, $\chi^2(1, N=96) = 0.00$, $p = 0.99$. There was no significant difference in mean follow-up time between the surgery groups in the myopia control group, $t(11) = 2.05$, $p = 0.06$.

Within the myopia cohort, the mean postoperative UCDVA did not differ significantly between the eyes that underwent ASA (0.10 ± 0.18) and the eyes that underwent LASIK (0.05 ± 0.15), $t(41) = 1.05$, $p = 0.30$. In contrast, the mean postoperative UCDVA was significantly better in eyes the underwent ASA (-0.05 ± 0.08) than eyes that underwent LASIK (0.04 ± 0.11) within the myopia control group, $t(13) = -2.50$, **$p = 0.03$**. The mean postoperative BCDVA did not differ significantly between ASA eyes (0.02 ± 0.06) and LASIK eyes (0.03 ± 0.05) within the myopia cohort, $t(31) = -$

0.54, p = 0.59. In the myopia control group, again eyes that underwent ASA performed significantly better than those that underwent LASIK with mean postoperative BCDVAs of -0.06 ± 0.07 and 0.00 ± 0.00 respectfully, t(7) = -2.65, **p = 0.03**.

When comparing eyes that underwent LASIK within the myopia cohort to LASIK eyes in the myopia control group, there was no significant difference between their mean postoperative UCDVA, t(26) = 0.31, p = 0.76. Nor was there a difference in the mean postoperative BCDVAs when comparing the myopia cohort and control group's LASIK eyes, t(14) = 1.78, p = 0.10. The eyes that underwent ASA in the myopia control group had a very significantly better mean postoperative UCDVA compared to those in the myopia cohort, t(25) = 3.26, **p = 0.003**. Likewise the ASA eyes in the myopia control group had a significantly better mean postoperative BCDVA compared to those in the myopia cohort, t(10) = 3.00, **p = 0.013**.

Hyperopia

There were 148 eyes (70 right and 78 left eyes) identified with a preoperative spherical power ≥ + 3.50D. Of these, 63 eyes (31 right and 32 left eyes) met the criteria for inclusion in the hyperopia cohort. Excluded eyes are broken down in Table 5.There was a total of 14 eyes in the hyperopia cohort that are known to have undergone an enhancement procedure within the year following their surgery, accounting for 9.5% of the total eyes that were identified. The mean time after the original surgery that the enhancement procedure was performed was 305 ± 120 days.

Table 5: Hyperopia: Excluded Eyes. A breakdown of the eyes excluded from the hyperopia cohort and for what reason.

Exclusion Criteria	Number of Eyes Excluded
Non-Zero Target Refraction	6
Phototherapeutic Keratectomy	2
Missing Data	1
No Follow-Up in Study Period	76

Preoperative

Of the 63 eyes included, 30 belonged to men and 33 belonged to women. Average preoperative manifest values and visual acuities are presented in table 6. The hyperopia cohort had 52 eyes correctable to 20/20 on the Snellen scale, six eyes correctable to 20/25, four eyes correctable to 20/30, and one eye correctable to 20/50.

Table 6. Hyperopia: Preoperative Data. Mean preoperative data for the hyperopia cohort and control groups. Significance values for statistical analysis between groups are included below the respective data. (BCDVA = best corrected distance visual acuity)

	Hyperopia Cohort	Hyperopia Control Group
Age (Years)	42 ± 12	42 ± 13
p-value	0.54	
Spherical Power (D)	+4.11 ± 0.64	+1.33 ± 0.40
p-value	**3.93×10^{-51}**	
Cylindrical Power (D)	-1.62 ± 1.40	-1.62 ± 1.3
p-value	0.88	
Spherical Equivalent (D)	+3.30 ± 0.65	+0.53 ± 0.80
p-value	**5.2×10^{-41}**	
BCDVA (log(MAR))	0.024 ± 0.070	0.013 ± 0.043
p-value	0.30	

The average age of the hyperopia control group at time of surgery did not differ significantly from the hyperopia cohort, $t(121) = -0.23$, $p = 0.82$. Of the 63 eyes, 35 belonged to men and 28 belonged to women; this was not significantly different than the hyperopia cohort, $\chi^2(1, N=126) = 0.37$, $p = 0.54$. The hyperopia cohort was very

significantly more hyperopic than the hyperopia control group, t(103) = 28.84, **p = 3.93 x 10^{-51}**. The mean preoperative cylindrical did not differ significantly between the groups, t(121) = -0.15, p = 0.88. The mean preoperative spherical equivalent of the hyperopia control group very significantly less than the hyperopia cohort, t(119) = 20.58, **p = 5.2 x 10^{-41}**. The hyperopia control group and the hyperopia cohort did not differ in mean preoperative BCDVA, t(101) = 1.04, p = 0.30.

Postoperative

Table 7. Hyperopia: Postoperative Data. Mean postoperative data for the hyperopia cohort and control groups. Significance values for statistical analysis between groups are included below the respective data. (UCDVA = uncorrected distance visual acuity, BCDVA = best corrected distance visual acuity)

	Hyperopia Cohort	Hyperopia Control Group
Follow-up Time (Days)	351 ± 92	369 ± 66
p-value	0.29	
Spherical Power (D)	+0.25 ± 0.73	0.060 ± 0.42
p-value	**0.045**	
Cylindrical Power (D)	-0.38 ± 0.46	-0.28 ± 0.39
p-value	0.20	
Spherical Equivalent (D)	+0.06D ± 0.78	-0.08D ± 0.43
p-value	0.15	
UCDVA (log(MAR))	0.14 ± 0.18	0.044 ± 0.11
p-value	**0.0069**	
BCDVA (log(MAR))	0.03 ± 0.07	.00 ± 0.06
p-value	0.050	

Average postoperative manifest values and visual acuities are presented in table 7. The mean follow-up time did not differ significantly between the groups, t(113) = -1.06, p = 0.29. The hyperopia cohort had a very significant decrease in VA between the mean preoperative BCDVA and mean postoperative UCDVA, t(62) = -5.47, **p = 8.6 x 10^{-7}**. There was also a very significant decrease in VA between the hyperopia control group's mean preoperative BCDVA and mean postoperative UCDVA, t(62) = -3.03, **p = 0.0036**.

However, the hyperopia control group's mean postoperative UCDVA was very significantly better than the hyperopia cohort, t(109) = 2.75, **p = 0.0069**. There was not a significant difference between the hyperopia cohort's mean preoperative and postoperative BCDVA, t(62) = -0.61, p = 0.61. There was no significant change to the hyperopia control group's postoperative BCDVA compared to their preoperative BCDVA either, t(62) = 1.17, p = 0.27. The mean postoperative BCDVA was not significantly different between the groups, t(121) = 1.98, p = 0.050. The breakdown of postoperative visual acuities is presented in Figure 8.

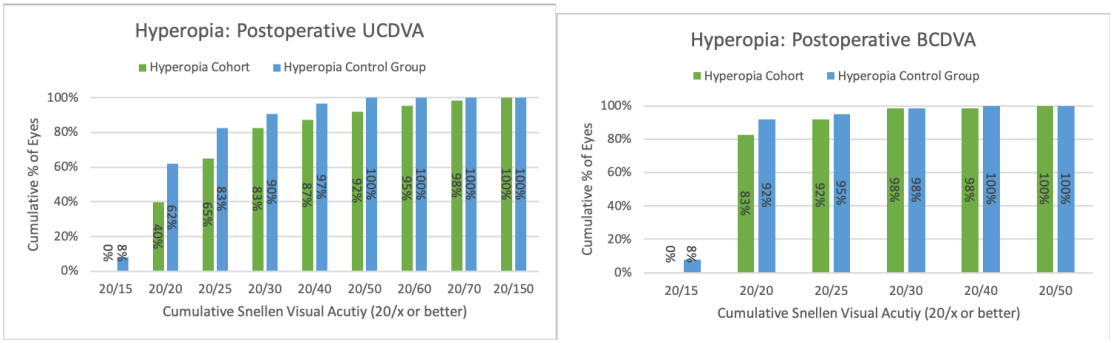


Figure 8. Hyperopia: Cohort vs Control Visual Acuities Representations of the postoperative UCDVA and BCDVA of hyperopia cohort and hyperopia control group. The data are in terms of the percentage of eyes that achieved that VA or better.

The mean postoperative spherical power differed significantly between the groups, t(99) = 2.03, **p = 0.045**. The mean postoperative cylindrical power and spherical power did not differ significantly between the groups, t(119) = -1.30, p = 0.20 and t(96) = 1.45, p = 0.15.

Safety

Changes in BCDVA are presented in Figure 9. There was no significant difference in the distribution of change of BCDVA between the myopia cohort and myopia control group, $\chi^2(3, N=126) = 0.31$, $p = 0.96$.

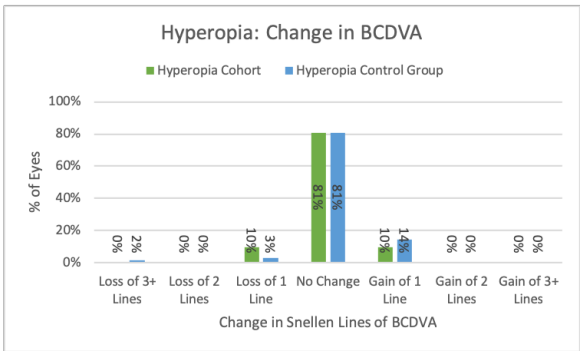


Figure 9. Hyperopia: Change in BCDVA. Representation of the safety profile for both the hyperopia cohort and hyperopia control group. The data are presented in terms of the percentage of eyes that underwent that change in BCDVA.

Surgery Type

In the hyperopia cohort here were 53 eyes that underwent LASIK and 10 eyes that underwent ASA. There was no significant difference in mean follow-up time between the surgery groups in the hyperopia cohort, $t(10) = -1.66$, $p = 0.13$. In the hyperopia control group, 48 eyes underwent LASIK and 15 eyes underwent ASA; this was not significantly different from the surgery type distribution of the hyperopia cohort, $\chi^2(1, N=126) = 0.26$, $p = 0.61$. There was no significant difference in mean follow-up time between the surgery groups in the hyperopia control group, $t(18) = 0.79$, $p = 0.4$.

Within the hyperopia cohort, the mean postoperative UCDVA did not differ significantly between the eyes that underwent ASA (0.19 ± 0.18) and the eyes that underwent LASIK (0.12 ± 0.17), $t(11) = 1.03$, $p = 0.32$. The mean postoperative UCDVA

also did not differ between eyes that underwent ASA (0.07 ±0.13) than eyes that underwent LASIK (0.11 ± 0.05) within the hyperopia control group, $t(21) = 0.54$, $p = 0.60$. The mean postoperative BCDVA did not differ significantly between ASA eyes (0.03 ± 0.06) and LASIK eyes (0.03 ±0.07) within the hyperopia cohort, $t(12) = 0.14$, $p = 0.89$. In the hyperopia control group, again eyes that underwent ASA (0.02 ± 0.05) did not significantly differ than those that underwent LASIK (0.00 ± 0.07) in regard to mean postoperative BCDVA, $t(27) = 1.21$, $p = 0.23$.

Eyes that underwent LASIK within the hyperopia control group had a significantly better mean postoperative UCDVA compared to LASIK eyes in the hyperopia cohort, $t(89) = 2.49$, **$p = 0.015$**. Likewise, there was a significant difference in the mean postoperative BCDVAs when comparing the hyperopia cohort and control group's LASIK eyes, $t(97) = 2.04$, **$p = 0.044$**. When comparing eyes that underwent ASA within the hyperopia cohort to ASA eyes in the hyperopia control group, there was no significant difference between their mean postoperative UCDVA, $t(12) = 1.77$, $p = 0.10$. Nor was there a difference in the mean postoperative BCDVAs when comparing the hyperopia cohort and control group's ASA eyes, $t(15) = 0.43$, $p = 0.67$.

Astigmatism

There were 244 eyes (117 right and 127 left eyes) identified with a preoperative cylindrical power ≥ -3.50D. Of these, 54 eyes (27 right and 27 left eyes) met the criteria for inclusion in the astigmatism cohort. A breakdown of excluded eyes is provided in Table 8. There was a total of 15 eyes in the astigmatism cohort that are known to have

undergone an enhancement procedure within the year following their surgery, accounting for 6.1% of the total eyes that were identified. The mean time after the original surgery that the enhancement procedure was performed was 229 ± 123 days.

Table 8. Astigmatism: Excluded Eyes. A breakdown of the eyes excluded from the astigmatism cohort and for what reason.

Exclusion Criteria	Number of Eyes Excluded
Non-Zero Target Refraction	16
Previous Surgical Procedure	3
Two-Stage Treatment	14
Missing Data	8
No Follow-Up in Study Period	149

Preoperative

Of the 54 eyes included, 29 belonged to men and 25 belonged to women. Average preoperative manifest values and visual acuities are presented in Table 9. The myopia cohort had three eyes correctable to 20/15 on the Snellen scale, 47 eyes correctable to 20/20, one eye correctable to 20/25, one eye correctable to 20/30, one eye correctable to 20/40, and one eye correctable to 20/70.

Table 9. Astigmatism: Preoperative Data. Mean preoperative data for the astigmatism cohort and control groups. Significance values for statistical analysis between groups are included below the respective data. (BCDVA = best corrected distance visual acuity)

	Astigmatism Cohort	Astigmatism Control Group
Age (Years)	34 ± 9	34 ± 9
p-value	0.98	
Spherical Power (D)	0.03D ± 2.78	-3.14D ± 2.52
p-value	**3.4×10^{-8}**	
Cylindrical Power (D)	-4.18D ± 0.86	-1.28D ± 0.26
p-value	**2.7×10^{-32}**	
Spherical Equivalent (D)	-2.06 ± 2.69	-3.78D ± 2.51
p-value	**0.0016**	
BCDVA (log(MAR))	0.051 ± 0.12	-0.01 ± 0.03
p-value	**0.0013**	

The average age at time of surgery did not differ significantly between the hyperopia cohort and control group, $t(103) = -0.02$, $p = 0.98$. Of the 54 eyes, 27 belonged to men and 27 belonged to women; this was not significantly different than the astigmatism cohort, $\chi^2(1, N=108) = 0.70$, $p = 0.40$. The astigmatism control group was very significantly more myopic than the astigmatism cohort, $t(103) = 5.97$, **$p = 3.4 \times 10^{-8}$**. The mean preoperative cylindrical power of the astigmatism cohort was very significantly higher than that of the astigmatism control group, $t(61) = -23.52$, **$p = 2.7 \times 10^{-32}$**. The mean preoperative spherical equivalent of the astigmatism control group very significantly more myopic than the hyperopia cohort, $t(104) = 3.25$, **$p = 0.0016$**. The mean preoperative BCDVA of the astigmatism control group was very significantly better than that of the astigmatism cohort, $t(58) = 3.38$, **$p = 0.0013$**.

Postoperative

Table 10. Astigmatism: Postoperative Data. Mean postoperative data for the astigmatism cohort and control groups. Significance values for statistical analysis between groups are included below the respective data. (UCDVA = uncorrected distance visual acuity, BCDVA = best corrected distance visual acuity)

	Astigmatism Cohort	Astigmatism Control Group
Follow-up Time (Days)	391 ± 50	340 ± 96
p-value	**7.6×10^{-4}**	
Spherical Power (D)	+0.01 ± 0.72	+0.11 ± 0.52
p-value	0.45	
Cylindrical Power (D)	-0.73 ± 0.97	-0.29 ± 0.40
p-value	**0.0028**	
Spherical Equivalent (D)	-0.35 ± 0.62	-0.04 ± 0.45
p-value	**0.0039**	
UCDVA (log(MAR))	0.12 ± 0.19	0.041 ± 0.09
p-value	**0.0014**	
BCDVA (log(MAR))	0.01 ± 0.09	-0.00 ± 0.024
p-value	0.17	

Average postoperative manifest values and visual acuities are presented in Table 10. The mean follow-up time of the astigmatism control group was very significantly later compared to the astigmatism cohort, t(78) = -3.51, **$p = 7.6 \times 10^{-4}$**. The astigmatism cohort's mean postoperative UCDVA was very significantly worse than its mean preoperative BCDVA, t(53) = -3.36, p = 0.0015. There was also a very significant decrease in VA between the astigmatism control group's mean preoperative BCDVA and mean postoperative UCDVA, t(53) = -3.47, **p = 0.0011**. The mean postoperative UCDVA of the astigmatism control group was very significantly better than that of the astigmatism cohort, t(77) = 3.32, **p = 0.0014**. There was a very significant improvement in VA between the astigmatism cohort's mean preoperative and postoperative BCDVA, t(53) = 3.32, **p = 0.0016**. There no significant change to the astigmatism control group's postoperative BCDVA compared to their preoperative BCDVA, t(53) = -0.44, p = 0.66.

The mean postoperative BCDVA did not significantly differ between the groups, t(59) = 1.40, p = 0.17. The breakdown of postoperative visual acuities is presented in Figure 10.

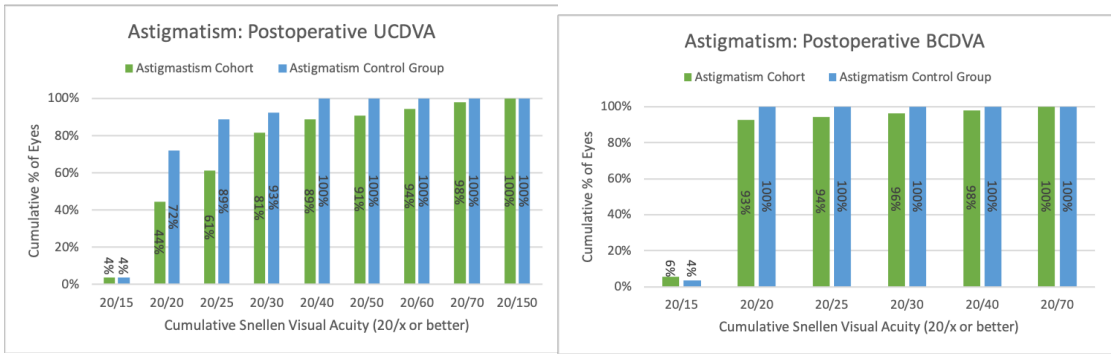


Figure 10. Astigmatism: Cohort vs Control Visual Acuities. Representations of the postoperative UCDVA and BCDVA of astigmatism cohort and astigmatism control group. The data are in terms of the percentage of eyes that achieved that VA or better.

The mean postoperative spherical power did not differ significantly between the groups, t(95) = -0.76, p = 0.45. The mean postoperative cylindrical power of the astigmatism cohort was very significantly higher than that of the astigmatism control group, t(70) = -3.10, **p = 0.0028**. The mean postoperative spherical equivalent of the astigmatism cohort was very significantly higher than that of the astigmatism control group, t(96) = -2.98, **p = 0.0039**.

Safety

Changes in BCDVA are presented in Figure 11. There was no significant difference in the distribution of change in BCDVA between the astigmatism cohort and astigmatism control group, $\chi^2(3, N=108) = 0.00$, p = 0.99.

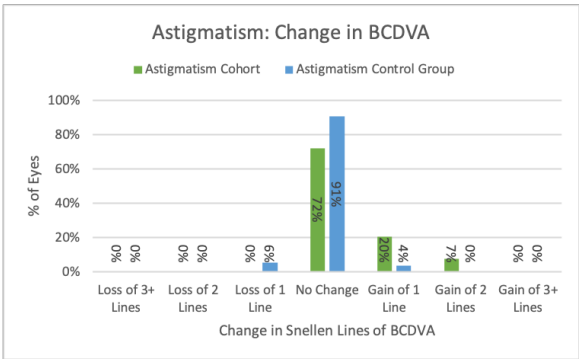


Figure 11. Astigmatism: Change in BCDVA. Representation of the safety profile for both the astigmatism cohort and astigmatism control group. The data are presented in terms of the percentage of eyes that underwent that change in BCDVA.

Surgery Type

In the astigmatism cohort here were 43 eyes that underwent LASIK and 11 eyes that underwent ASA. There was no significant difference in mean follow-up time between the surgery groups in the astigmatism cohort, $t(11) = 0.61$, $p = 0.56$ In the astigmatism control group, 32 eyes underwent LASIK and 22 eyes underwent ASA; this was not significantly different from the surgery type distribution of the astigmatism cohort, $\chi^2(1, N=108) = 0.02$, $p = 0.88$. There was no significant difference in mean follow-up time between the surgery groups in the astigmatism control group, $t(11) = 0.86$, $p = 0.39$.

Within the astigmatism cohort, the mean postoperative UCDVA did not differ significantly between the eyes that underwent ASA (0.05 ± 0.10) and the eyes that underwent LASIK (0.01 ± 0.09), $t(13) = 0.73$, $p = 0.47$. The mean postoperative UCDVA also did not differ between eyes that underwent ASA (0.06 ± 0.09) than eyes that underwent LASIK (0.03 ± 0.09) within the astigmatism control group, $t(44) = 0.94$, $p = 0.35$. The mean postoperative BCDVA did not differ significantly between ASA eyes

(0.05 ± 0.10) and LASIK eyes (0.01 ±0.09) within the astigmatism cohort, $t(13) = 1.14$, $p = 0.27$. The mean postoperative BCDVA did not differ significantly between ASA eyes (0.01 ± 0.04) and LASIK eyes (0.00 ±0.00) within the astigmatism control group, $t(13) = -1.45$, $p = 0.16$.

Eyes that underwent LASIK within the astigmatism control group had a very significantly better mean postoperative UCDVA compared to LASIK eyes in the astigmatism cohort, $t(64) = 2.81$, **$p = 0.0066$**. However, there was no significant difference in the mean postoperative BCDVAs when comparing the astigmatism cohort and control group's LASIK eyes, $t(41) = 0.45$, $p = 0.66$. When comparing eyes that underwent ASA within the astigmatism cohort to ASA eyes in the astigmatism control group, there was no significant difference between their mean postoperative UCDVA, $t(11) = 1.79$, $p = 0.10$. Nor was there a difference in the mean postoperative BCDVAs when comparing the astigmatism cohort and control group's ASA eyes, $t(10) = 1.75$, $p = 0.11$.

Outlier Cohorts

The visual outcomes of the myopia cohort, hyperopia cohort, and astigmatism cohort were compared. There was no significant difference in postoperative UCDVA between the cohorts, $F(2,162) = 2.03$, $p = 0.36$. There was no significant difference in postoperative BCDVA between the cohorts, $F(2,162) = 0.48$, $p = 0.62$. There was no significant difference in the distribution of changes to BCDVA (Figure 12) between pre- and postoperative measurements, $\chi^2(8, N=165) = 2.3 \times 10^{-4}$, $p = 1.00$.

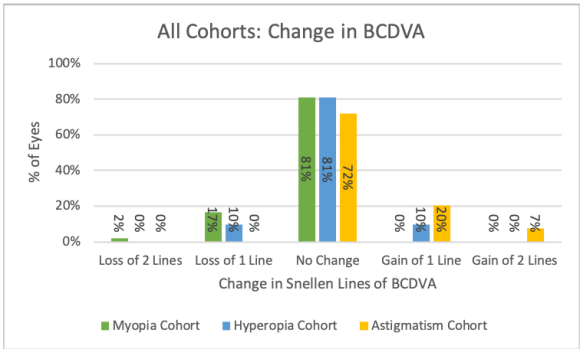


Figure 12. All Cohorts: Change in BCDVA. Representation of the safety profile for both the myopia cohort, hyperopia cohort, and astigmatism cohort. The data are presented in terms of the percentage of eyes that underwent that change in BCDVA.

DISCUSSION

Myopia

The myopia cohort was chosen to include only those with a substantially high degree of myopia (≥ -8.50D) without concern for their degree of astigmatism. The age matching of mild-moderate myopes was successful as their mean age did not differ significantly that of the myopia cohort. The myopia control group did have a significantly longer follow-up time than the myopia cohort. The myopia cohort's mean follow-up time of almost one year (361 days) should have been more than sufficient to allow for stabilization of vision postoperatively (Keskinbora), and thusly the difference in follow-up time should not have affected the comparison of visual outcomes (Keskinbora). As designed, the myopia cohort's preoperative spherical power and spherical equivalent were very significantly more negative than the myopia control group. It should be noted that the myopia control group had significantly higher preoperative mean cylindrical power than the myopia cohort. This was likely due to not controlling for degree of astigmatism when including eyes in either the myopia cohort or control group. Its possible impact is discussed below.

The main goal of refractive surgery being to reduce patient's reliance on glasses, the best outcomes would be to have their postoperative UCDVA match or be better than their preoperative BCDVA. The myopia cohort experienced a very significant decrease in VA when comparing their preoperative BCDVA to their postoperative UCDVA. This differed from the myopia control group which did not experience any significant change when comparing the same variables and had a significantly better postoperative UCDVA

than the myopia cohort. That is, the myopia control group had better vision than the myopia cohort after surgery. Additionally, the myopia cohort did not see as well as they did with their correction prior to surgery. This is a similar result to Kojima et al. that also found that lower myopes achieved a better postoperative UCDVA than high myopes. It is worth mentioning the myopia cohort of this thesis had a more myopic mean preoperative spherical equivalent (-8.77D vs – 7.54D) than that in Kojima et al. It would be expected that the myopia cohort would achieve a less ideal vision postoperatively because of this but the cohort achieved a better mean postoperative UCDVA than Kojima et al.'s myopes.

While there was no significant difference in residual spherical power, the myopia cohort did have significantly more residual cylindrical power which accounts for the difference in UCDVA. This is interesting due to the myopia control group having higher preoperative cylindrical power. It is possible that the treatment pattern of the higher myopes was less effective in treating astigmatic errors than the treatment pattern of lower myopes. Another possible explanation is that the treatment of higher myopes had a higher probability of inducing a new or different astigmatism to a greater degree than the treatment of low myopes. Further investigation may be warranted to differentiate between these possibilities.

The myopia cohort's mean BCDVA postoperatively was significantly worse than their preoperative mean BCDVA with 13% of eyes losing lines of BCDVA. The myopia control group experienced no corresponding changes to their BCDVA after surgery and had a very significantly better mean BCDVA than the myopia cohort. In other words, the

myopia cohort could not see as well after surgery as they did before, even with the use of corrective lenses.

However, from a safety standpoint, there was no significant difference in the distribution of the change in Snellen lines of BCDVA. This means that eyes in the myopia control group, with low-moderate myopia, were just as likely to lose lines of vision as cohort eyes, with high myopia. Similarly, highly myopic eyes were just as likely to gain vision lines of vision as low-moderate myopic eyes.

The UCDVA and BCDVA results did not differ significantly between eyes that underwent different surgeries for eyes in the myopia cohort. In contrast, eyes underwent ASA in the myopia control group had significantly better outcomes for UCDVA and BCDVA than the eyes that underwent LASIK. This result differed from Helmy et al. and Hashemi et al. which both found LASIK to be superior to PRK (ASA) for high myopes. Their studies included a wider range of high myopes, -6.00D and -10.00D (Helmy et al.) and >-7.00D (Hashemi et al.) than this thesis. The restriction of the myopia cohort to comparatively very high myopes may have influenced this result in that the visual outcomes of both surgery types were poor and a difference in efficacy could not be distinguished.

Refractive surgery was effective in reducing the refractive error of the high myopia cohort of this thesis, 100% of cohort eyes were able to reach 20/40 or better with correction and 92% without correction. However, their results were not as ideal as the control group, with only 63% of eyes reaching 20/20 or better uncorrected vs 83%, and 100% of control eyes being correctable to 20/20 or better. The myopia cohort performed

better than those in Keskinbora which reported a peak of 22.5% of eyes achieving 20/20 or better and 90% achieving 20/40 or better uncorrected. However, Reinstein et al. reported better outcomes for their high myopia group than the high myopia cohort in this thesis with 89% of eyes 20/20 or better and 99% 20/40 or better uncorrected. The cohort reached an UCDVA of 20/~25 and a BCDVA of 20/~21 vs the control group's 20/~21 and 20/~19. Both groups achieved satisfactory results, with the control group achieving better vision.

LASIK and ASA were safe and provided similar, satisfactory results for those with significantly high myopia, but these patients should be counseled as to the risk that their results may not be as ideal as their lower myopia counterparts.

Hyperopia

The hyperopia cohort was chosen to include eyes with a moderately high degree of hyperopia without concern for degree of astigmatism. The age matching of the hyperopia control group was successful. As designed the hyperopia cohort had very significantly more hyperopic mean preoperative spherical power and spherical equvalent than the hyperopia control group.

Both the hyperopia cohort and control group showed a very significant decrease in vision when comparing their preoperative UCDVA and postoperative UCDVA. However, when comparing the two groups' UCDVA postoperatively, the hyperopia control group had very significantly better uncorrected vision. It has been previously demonstrated that visual outcomes in hyperopic LASIK are negatively influenced by the

degree of hyperopic correction (Cobo-Soriano et al.). This study's findings seem to concur, with the hyperopic control group having significantly better mean UCDVA and BCDVA after surgery.

The hyperopia cohort demonstrated a small amount of under-correction with their mean postoperative spherical power being left slightly hyperopic (spherical power = +0.25D). While the hyperopia control group demonstrated an almost negligible amount of over-correction with the spherical power being left slightly myopic (spherical power = -0.060D). The small under-correction of the hyperopia cohort and the over-correction of the hyperopia control group correspond with each groups' respective UCDVA after surgery. These residual refractive errors can be reasonably assumed to be causative of their non-ideal postoperative UCDVAs.

Neither the hyperopia cohort, nor the control group, experienced a significant change in their mean BCDVA when comparing preoperative and postoperative values. There was also no significant difference between the hyperopic groups' postoperative BCDVA. Meaning that with correction both groups saw as well as they did before surgery. There was also no difference in the distribution of Snellen lines gained/lost. Thus, the hyperopia cohort was not at greater risk of losing or gaining vision. Published literature on high hyperopes shows rates of losing BCDVA between 10% (Alió et al.) and 17.5% (Plaza-Puche et al.), consistent with the 10% of eyes in the hyperopia cohort that lost vision. Refractive surgery was as safe for high hyperopes as for low hyperopes.

With only 40% of eyes achieving 20/20 or better and 87% achieving 20/40 or better vision uncorrected, the hyperopia cohort did not have ideal results. In the

hyperopic control group, 62% of eyes achieved 20/20 or better vision and 97% achieved 20/40 or better vision uncorrected, which were not ideal either. The cohort reached an UCDVA of 20/~27 and a BCDVA of 20/~21 vs the control group's 20/~23 and 20/~20. Both groups achieved satisfactory results, with the control group achieving better vision. LASIK and ASA were safe and provided similar, satisfactory results for those with significantly high hyperopia, but these patients should be counseled as to the risk that their results may not be as ideal as their lower hyperopia counterparts.

Astigmatism

The astigmatism cohort was chosen to include eyes with a high degree of astigmatism. The age matching of the astigmatism control group was successful. The astigmatism cohort had a significantly shorter mean follow-up time, but as previously discussed at 340 days it likely did not impact the visual outcomes. As designed, there was a significant difference between the astigmatism cohort and control group's mean preoperative cylindrical power and spherical equivalent. However, there was also a very significant difference between their preoperative spherical power as well, with both groups having an average moderate amount of myopia. This did not likely effect the visual outcomes of the groups.

The astigmatism cohort experienced a very significant loss of vision when comparing their mean preoperative BCDVA to mean postoperative UCDVA. There was a corresponding very significant decrease in the astigmatism control groups vision comparing the same variables. The control group's mean postoperative UCDVA was still

very significantly better than that of the astigmatism cohort. These results correlate to the residual refractive errors of the two groups with the cohort left with an average of -0.73 ± 0.97 cylindrical power and an average spherical equivalent of -0.35D ± 0.62, compared to -0.29D ± 0.40 and -0.04D ± 0.45, respectfully, for the control group. The undercorrection of the astigmatism cohort is similar to previously reported high astigmatism groups (residual cylindrical power = -0.97D & -1.17D) (Ivarsen et al.). Both the astigmatism cohort and control group had worse vision after surgery, but the control group still saw better than the cohort.

With correction the astigmatism control group could see just as well as they did before the surgery. Furthermore, with correction the control group did not see better than the cohort did. The astigmatism cohort had a very significant improvement to their BCDVA. After surgery the cohort was able to be corrected to better vision than they had prior to surgery. This is demonstrated by the 27% of eyes in the astigmatism cohort that gained Snellen lines of BCDVA.

The astigmatism control group had 77% of eyes achieving 20/20 or better and 100% achieving 20/40 or better uncorrected; while in the astigmatism cohort only 44% of eyes achieved 20/20 or better and 89% achieved 20/40 or better uncorrected, 98% of eyes were correctible to 20/40 or better. This was a significant increase from the 96% of eyes correctable to 20/40 or better preoperatively. The cohort reached an UCDVA of 20/~27 and a BCDVA of 20/~21 vs the control group's 20/~22 and 20/~20. Both groups achieved satisfactory results, with the control group achieving better vision.

Within both the astigmatism cohort and control group there was no difference in UCDVA or BCDVA when comparing eyes that underwent ASA vs LASIK. This is consistent with a previous report which found LASIK and PRK to be comparably effective treatment of high astigmatism (Katz et al.). The astigmatism cohort also included those that with higher degrees of astigmatism than Katz et al.'s group, >-3.50D vs >-3.00D.

LASIK and ASA proved to provide similar, satisfactory results for those with high astigmatism. There was also theoretical potential for the astigmatism cohort to gain BCDVA, if repeat surgeries were to be performed. There was no difference in the distribution of loss/gain of BCDVA between the astigmatism cohort and control groups which demonstrated similar safety profiles. However, due to the results of the postoperative UCDVA and BCDVA, those with high astigmatism should be cautioned that they may have worse visual results than their lower astigmatism peers.

Outlier Cohorts

The analysis of postoperative vision between cohorts revealed no significant differences. The cohorts had similar mean postoperative UCDVAs, as well as mean postoperative BCDVAs. The safety profiles of each cohort showed no significant differences. Overall, none of the cohorts were able to gain ideal, uncorrected vision, but they achieved similar satisfactory results.

Limitations and Future Studies

A prominent limitation of this study was that there was no control for confounding refractive errors. This was most obvious in the myopia category. This could be avoided in future investigations by setting limits the preoperative spherical power for astigmatism groups and preoperative cylindrical power for myopia and hyperopia groups.

Another limitation was the limited study period which yielded only moderate sample sizes. Refractive and visual stabilization theoretically should have occurred three to six months after surgery, and inclusion of data from follow-up visits after that time could have yielded larger sample sizes. More significant sample sizes would increase the power of the study, while also reduce the chances of sampling error.

The limited study period may have also skewed the result data for the population. It can be reasonably assumed that happy patients, or those with good visual outcomes, were less likely to attend follow-up appointments. Therefore, the true final visual outcomes for these populations may be better than reported here.

While standard follow-up visits were attempted to be made for all patients, there was a lack of compliance. It is also possible that the follow-up visits were not consistent across all patients; more specifically that during VA testing and manifest refraction the technician may not have asked all patients able to read the 20/20 line to read the 20/15 line. A future prospective study should allow for greater control and standardization over follow-up visits. Any future study should also include manifest refractions at all visits to allow for tracking of the stability of refractions.

In conclusion, LASIK and ASA are safe for outlier candidates with high myopia, high hyperopia, or high astigmatism. Neither surgery type offered superior results for the high refractive error cohorts. There was no difference in visual outcomes or safety for outliers with different refractive errors. While these surgeries offer satisfactory results, the candidates should be properly informed that they may achieve poorer results than counterparts with lower degrees of refractive error.

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CURRICULUM VITAE