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The effect of postoperative keratometry on visual acuity after corneal refractive laser surgery

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THE EFFECT OF POSTOPERATIVE KERATOMETRY ON VISUAL ACUITY AFTER CORNEAL REFRACTIVE LASER SURGERY

by

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DEDICATION

I dedicate this work to my family, specifically my parents and sister, for their unwavering support of all of my endeavors.

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THE EFFECT OF POSTOPERATIVE KERATOMETRY ON VISUAL ACUITY AFTER CORNEAL REFRACTIVE LASER SURGERY

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ABSTRACT

PURPOSE: To determine if there is a relationship between eyes with flat corneas (as defined by calculated postoperative keratometry values of <38D) undergoing either LASIK (Laser-assisted in Situ Keratomileusis), LASEK (Laser-assisted Subepithelial Keratectomy), or PRK (Photorefractive Keratectomy) corneal refractive surgery and loss of 1 or more lines of postoperative BCVA, and if there is an advantage to undergoing either LASIK or ASA in eyes meeting flat cornea criteria.

METHODS: A retrospective analysis of 191 candidate eyes with calculated postoperative keratometry values <38D were identified and matched by manifest refraction and surgery type to 191 control eyes with calculated postoperative keratometry values ≥38D. Both candidate groups and control groups were further stratified into subgroups based on degree of calculated postoperative keratometry. Candidate subgroups: Subgroup 1a (K<35D), Subgroup 2a (K=35-35.99D), Subgroup 3a (K=36-36.99D), and Subgroup 4a (K=37-37.99D). Control subgroups: Subgroup 1b (K=38-38.99D), Subgroup 2b (K=39-39.99D), Subgroup 3b (K=40-40.99D) and Subgroup 4b (K≥41D). All patients had undergone corneal refractive eye surgery procedures LASIK, LASEK, or PRK at Boston Eye Group/Boston Laser in Brookline MA between December 2008 and November 2016. All LASIK flaps were created using the

femtosecond laser IntraLase iFS60 Laser (Abbott Medical Optics Inc.). All surface ablation procedures were performed using the excimer lasers VISX STAR S4 IR Excimer Laser System (Abbot Medical Optics Inc.) or WaveLight EX500 Excimer Laser (Alcon Laboratories Inc.). Visual acuity outcomes measuring preoperative and postoperative BCVA and loss of BCVA were recorded as part of the patient's medical chart and were statistically analyzed to determine correlations.

RESULTS: Our data showed no significant differences between overall candidate ($K<38D$) and control ($K\geq38D$) group mean preoperative BCVA ($p<0.23$) or mean postoperative BCVA ($p<0.13$). A total of 15 out of 191 (7.9%) candidate eyes lost 1 or more lines of BCVA in comparison to 23 total control eyes (12.0%) that lost 1 or more lines of BCVA postoperatively. When evaluating subgroup data, Candidate Subgroup 1a ($K<35D$) showed a significant ($p<0.02$) decrease in BCVA when compared to other candidate subgroups. Additionally, Control Subgroup 1b ($K=38=38.99D$) and Control Subgroup 2b (39-39.99D) showed a significant ($p<0.001$ and $p<0.02$ respectively) decrease in BCVA compared to other control subgroups. A total of 231 total candidate and control eyes underwent LASIK and a total of 151 total candidate and control eyes underwent ASA. Overall, 17 out of the 231 (7.4%) eyes undergoing LASIK lost BCVA compared to the 21 out of 151 (13.9%) eyes undergoing ASA that lost BCVA which was significant ($p<0.04$).

CONCLUSION: This study did not find evidence to support that the overall flat cornea group ($K<38D$) lost postoperative BCVA when compared to a control group of eyes with normal keratometry values. However, our data indicated that when the candidate group

was stratified by degree of corneal curvature, patients with very flat corneas (K<35D) may be at increased risk of losing BCVA though further studies are needed. Additionally, eyes undergoing ASA may be at increased risk of losing BCVA though further studies are needed.

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LIST OF ABBREVIATIONS

AC.....Anterior Chamber

ASA.....Advanced Surface Ablation

BCL.....Bandage Contact Lens

BCVA.....Best Corrected Visual Acuity

BSS.....Balanced Salt Solution

CDVA.....Corrected Distance Visual Acuity

CRLS.....Corneal Refractive Laser Surgery

D.....Diopters

DES.....Dry Eye Syndrome

FDA.....Food and Drug Administration

ICL.....Implantable Contact Lens

IOL.....Intraocular Lens

IOP.....Intraocular Pressure

K.....Keratometry Value (in Diopters)

LASEK.....Laser-assisted Subepithelial Keratectomy

LASIK.....Laser-assisted in Situ Keratomileusis

MMC.....Mitomycin C

NSAID.....Nonsteroidal Anti-Inflammatory Drug

OCT.....Ocular Coherence Tomography

PRK.....Photorefractive Keratectomy

PTA.....Percentage of Tissue to be Altered

RSB.....Residual Stromal Bed

UCVA.....Uncorrected Visual Acuity

VA.....Visual Acuity

INTRODUCTION

It is estimated that over 1 billion people worldwide currently suffer from poor vision related to correctable refractive errors, also known as ametropia (Durr et al., 2014). With approximately 75% of Americans currently requiring some sort of corrective eyewear, and that number expected to grow due to an aging population and increasing prevalence of chronic diseases linked to unhealthy lifestyles ("NHIS - Tables of Summary Health Statistics," 2015), correcting ocular refractive errors will continue to be essential in the United States. The four most common types of refractive error in the US are myopia, hyperopia, presbyopia, and astigmatism.

Types of Refractive Error

In a normal healthy eye with no refractive error, beams of distant light enter the eye through the cornea where they are refracted through the lens in such a way so the focal point of those beams of light sits directly on the retina. This normal vision is also known as emmetropia.

Myopia, also called nearsightedness, is a condition where the individual can see close objects clearly but experiences blurred vision when looking at objects farther away. This occurs because the refracting power of the cornea and lens is too strong, causing the beams of distant light entering the eye to be refracted too strongly so the focal point of those beams of light sits in front of the retina. In many cases, a contributing factor to this increased refracting power is a change in shape of the eyeball itself in such a way that the axial length is increased (Bastawrous, Silvester, & Batterbury, 2011). Myopia can be corrected by placing a spherical diverging (concave) lens in front of the ocular surface to

bend the entering beams of distant light in such a way as to move their focal point back to rest normally on the retina.

Hyperopia, also called hypermetropia or farsightedness, is a condition where the individual can see objects that are far away clearly, but experiences blurred vision when looking at near objects. This occurs because the refracting power of the cornea and lens is too weak, causing the beams of distant light entering the eye to be refracted too weakly so the focal point of those beams of light sits theoretically behind the retina. In many cases, a contributing factor to this decreased refracting power is a change in shape of the eyeball itself in such a way that the axial length is decreased (Bastawrous, Silvester, & Batterbury, 2011). Hyperopia can be corrected by placing a spherical converging (convex) lens in front of the ocular surface to bend the entering beams of distant light in such a way as to move their focal point forward to rest normally on the retina.

Presbyopia, also called age-related farsightedness, is a condition similar to hyperopia in that individuals can see objects that are far away clearly, but experiences blurred vision when looking at near objects. This occurs when the lens of the eye loses elasticity and becomes more rigid with age (Michael & Bron, 2011). This loss of elasticity correlates with an inability for the lens to change shape, also called accommodation, and thus loses refracting power (Cochrane, du Toit, & Le Mesurier, 2010). This weak refracting power results in the same condition as hyperopia with the focal point of entering beams of distant light sitting behind the retina (Bastawrous, Silvester, & Batterbury, 2011). Presbyopia typically onsets in the mid-40s and worsens until age 65 (Boyd, 2013). It is corrected in the same manner as hyperopia by placing a

spherical converging (convex) lens in front of the ocular surface to bend the entering beams of distant light in such a way as to move their focal point forward to rest normally on the retina (Dowling & Dowling, 2016).

Astigmatism is a condition that affects individuals suffering from by myopia or hyperopia where either the corneal surface of the eye or the curvature of the lens within the eye is irregularly shaped (Marcos et al., 2015). These two defects are called corneal astigmatism and lenticular astigmatism respectively. Shape irregularities in either the cornea or lens cause the beams of distant light entering the eye to refract in an irregular way, producing multiple focal points that do not all sit directly on the retina. This causes vision to become blurred at any distance. Astigmatism can further be divided into additional subgroups: regular and irregular astigmatism.

Regular astigmatism includes: simple (one focal point always resting on the retina with one focal point resting behind the retina), compound (both focal points resting either in front or behind the retina), and mixed astigmatism (one focal point resting in front of the retina and one focal point resting behind the retina). Irregular astigmatism is astigmatism that is caused by some sort of irregularity of the cornea either by trauma, inflammation, scarring, or a developmental defect, which causes the cornea to deviate and change shape away from its normally expected curvature (Stein, Stein, & Freeman, 2013).

Regular astigmatism can be corrected by placing a special cylindrical lens in front of the ocular surface, which compensates for the irregular shape of the cornea or the lens and helps to focus the beams of distant light into a line instead of a point on the retina

(Stein, Stein, & Freeman, 2013). Irregular astigmatism, however, is much more difficult to treat and is often times not fully correctable using a cylindrical lens.

Types of Vision Correction

By far, the most common type of refractive error correction is corrective eyewear, or glasses. Over 150 million Americans currently wear some sort of corrective eyewear ("Eye Health Statistics," n.d.). This is a very effective first step in vision correction, however, users can experience problems with wearing glasses. Depending on how high the prescription is, users can experience image distortion (Silberner, 1980) including image shrinking. Additionally, glasses can be cumbersome, expensive, and can break or be lost easily.

Another popular way to correct refractive errors is by utilizing prescription contact lenses. Contact lenses commonly come in two varieties: silicone or fluoropolymer soft lenses and rigid gas-permeable lenses (RGP). Contact lenses can be an excellent option to improve quality of life for individuals since they are easy to use and reduce dependence on glasses. However, contact lens users are also at risk for a number of complications. If contact lenses fit incorrectly, they can put an abrasive force on the ocular surface and increase the risk of corneal abrasion and neovascularization of the cornea (Boyd, 2016). Additionally, improper care can lead to increased risk for contact lens associated dry eyes and eye infections including conjunctivitis, keratitis and blepharitis (Stuart, 2012). These conditions can cause trauma or inflammation of the cornea, which can change the anterior corneal curvature, also called keratometry of the cornea, and lead to irregular astigmatism.

A semi-permanent way to correct refractive errors can be found in Implantable Contact Lenses (ICLs). While glasses and contact lenses are a good choice for the entire prescription spectrum from mild to strong lens prescriptions, ICLs are usually only recommended for moderately severely myopic (less than -4D) or hyperopic (less than +4D) individuals (Koivula & Zetterström, 2009). ICLs work by surgically opening the eye and implanting a phakic intraocular lens (IOL) either in front or behind the iris (Koivula & Zetterström, 2009). In either case, the ICL is placed in front of the natural lens. One positive aspect of ICLs is that if an individual's visual acuity worsens, a new ICL of different refractive strength may be exchanged for the previously implanted one. However, ICLs present an increased risk of development of cataracts due to the ICL rubbing on the natural lens. Additionally, ICL users are at increased risk of infection and inflammation at the surgical site, pupillary block, endothelial cell death, as well as potential decrease in best corrected vision and onset of glares and halos (Stein, Stein, & Freeman, 2013).

Since the 1960s, corneal refractive laser surgery (CRLS) has emerged as an extremely popular and effective way to permanently treat refractive errors (Silberner, 1980). With the worldwide satisfaction rate after laser-assisted in situ keratomileusis (LASIK) surgery currently averaging 95.4% (Solomon et al., 2009), it is understandable that nearly 800,000 refractive surgical procedures were performed in the US in 2010 (Helzner, 2010). The underlying idea behind refractive surgery is that since the cornea exerts the greatest influence on ocular refractive power, the corneal tissue can thus be re-

shaped to increase or decrease the refractive power and allow for the focal point of distant light entering the eye to be moved to sit directly on the retina (Shah & Dua, 2000).

During refractive surgery, the corneal tissue is re-shaped via a technique known as surface ablation using an excimer laser. Excimer lasers are a type of pulsed gas discharge laser that are set to produce an optical output in the ultraviolet spectrum of light (Basting, Dejeu, & Jain, 2005). These beams of light from the laser are fired toward a treatment zone on the cornea in a pulsatile fashion causing the molecular bonds of the surface tissue to be break and a certain amount of corneal tissue to be ablated (Alio, Rosman, & Mosquera, 2010). For correction of myopia, laser treatment with the intent to flatten or straighten the cornea is performed while in contrast, correction of hyperopia involves laser treatment with the intent to steepen the cornea (Adib-Moghaddam et al., 2016).

Anatomically, the cornea is avascular and made up of five distinct layers. From superficial to deep positioning those layers are: an external stratified squamous nonkeratinized epithelium, an anterior limiting membrane known as Bowman's membrane, a thick bed of corneal stroma composed of type 1 collagen lamellae making up 90% of the corneal thickness, a posterior limiting membrane known as Descemet's membrane, and an internal simple squamous endothelium sitting just superiorly to the anterior chamber of the eyeball (Mescher, 2016).

In order for the excimer laser to reach the corneal stroma to ablate and change the shape of the stromal tissue bed, the superficial layer of external stratified squamous nonkeratinized epithelium and the associated Bowman's membrane must be temporarily

displaced or removed. This epithelium is lifted in laser-associated in situ keratomileusis (LASIK) and laser epithelial keratomileusis (LASEK) and removed entirely in photorefractive keratectomy (PRK).

LASIK

LASIK involves creating a flap in the cornea. This flap is usually created using a very small blade (microkeratome) or a femtosecond laser. A femtosecond laser is a type of infrared laser that works in conjunction with a suction ring and docking system to align the laser parallel with the ocular surface (Soong & Malta, 2009). Upon initiation, the laser generates microscopic gas bubbles within a horse-shoe shaped plane of cleavage under the ocular surface epithelium (Soong & Malta, 2009). Typical placement creates a superior flap hinge. After flap creation, the ophthalmologist performing the surgery is then able to loosen and lift the flap, exposing the underlying corneal stroma for ablation with an excimer laser. After ablation, the flap is re-positioned back in place and functional vision recovery can be expected within less than 24 hours with refractive stability achieved within 1 week to 3 months (Taneri, Weisberg, & Azar, 2011).

LASEK

LASEK involves displacing the superficial epithelium overlying the laser treatment zone by means of producing an epithelial detachment by weakening the intercellular bonds within corneal epithelium with exposure to alcohol. Typically, 18-20% medical grade ethanol is used and the epithelium is displaced with a superior or nasal hinge (Taneri, Zieske, & Azar, 2004). After laser ablation, the corneal epithelium is replaced over the treatment zone and a bandage contact lens is placed over the ocular

surface to help protect and facilitate healing (Taneri, Zieske, & Azar, 2004). Functional vision recovery can be expected within 3-7 days with full refractive stability achieved between 3 weeks to 3 months (Taneri, Weisberg, & Azar, 2011).

PRK

PRK involves completely removing and discarding the superficial epithelium overlying the laser treatment zone by means of weakening the intercellular bonds within the corneal epithelium with exposure to alcohol. As with LASEK, typically 18-20% medical grade ethanol is used but in this case the epithelium is removed entirely with no intent to replace (Luger, Ewering, & Arba-Mosquera, 2012). After laser ablation the area is sometimes treated with Mitomycin C (MMC). MMC is a mitotic inhibitor that has been shown to help facilitate healing and prevent scarring by inhibiting keratinocyte and myofibroblast differentiation while the epithelium regenerates (Pinheiro et al., 2016). Though MMC is effective in preventing corneal subepithelial fibrosis and scarring, it has known carcinogenic properties and its use is decided on a case by case basis. Functional vision recovery can be expected within 3-7 days with full refractive stability achieved between 3 weeks to 3 months (Taneri, Weisberg, & Azar, 2011).

Candidates for Refractive Surgery

According to Bastawrous, Silvester, & Batterbury (2011), the absolute criteria that must be met for candidacy for refractive surgery are: patients over 18 years of age with myopia up to 10 diopters or hyperopia up to 4 diopters and a stable lens prescription with less than 0.5 diopter change over one year. Absolute contraindications include unstable refraction, keratoconus, active infection or inflammation, and uncontrolled

glaucoma (Bastawrous, Silvester, & Batterbury, 2011). A stable refraction is essential for candidacy for refractive surgery as individuals with unstable refractions are more likely to need re-treatment or enhancement surgery in the future. Keratoconus is a condition in which the cornea experiences progressive central thinning leading to a central protrusion which may contribute to progressive myopia and irregular astigmatism (Ormonde, 2012). Patients with keratoconus are not candidates for refractive surgery as studies have demonstrated keratoconus patients who have undergone refractive surgery are at an increased risk of postoperative progressive ectasia (a non-inflammatory eye disorder characterized by central thinning of the cornea) and extension of the cornea (Ormonde, 2012). Refractive surgery should only be performed on healthy eyes and as such, patients experiencing any sort of infection or inflammation should be treated prior to surgery. Lastly, studies have shown that refractive surgery can cause a transient rise in intraocular pressure and as such, patients with uncontrolled glaucoma are not good candidates for CRLS (Bastawrous, Silvester, & Batterbury, 2011).

Additional consideration should be given to patients with dry eye syndrome, think corneas, blepharitis, cataracts, glaucoma, history of herpes simplex keratitis, ocular trauma, or previous ocular surgery as all of these can increase a patient's probability of experiencing refractive surgery complications (Melki and Azar, 2001).

The Cornea and Corneal Refractive Laser Surgery

As outlined above, there are several absolute criteria and contraindications for LASIK surgery relating to the cornea. Due to the nature of laser vision correction surgery re-shaping the cornea, it is imperative to perform multiple diagnostic and screening tests

to obtain as much information about the shape of the preoperative cornea so appropriate predictions can be made about the expected postoperative cornea. These screening criteria include: corneal topography, central corneal thickness, tear production, and corneal curvature.

Corneal topography, also known as photokeratoscopy, is commonly measured using either an OCULUS Pentacam or Ziemer Ophthalmology Galilei G4 machine. These non-invasive medical imaging devices utilize a an advanced placido disc system where a digital camera to focus on the anterior segment of the eye and quantify the corneal thickness pattern that is reflected back from the cornea (Luz et al., 2016). Each machine can collect up to 100,000 points of data across the surface of the cornea with a computer analyzing the results and presenting the information in a color-coded geographical formula, usually a sagittal map, according to the value of the corneal curvature (Stein, Stein, & Freeman, 2013). This information can then be used to determine any corneal shape irregularities, such as keratoconus or irregular astigmatism that could be contributing to refractive error. Additionally, the information can be used as a diagnostic tool to determine any irregularities that may arise or be exacerbated by CRLS and the corneal ablation that entails.

Corneal thickness is a measure of the amount of corneal stroma present in the eye in question and is usually measured by either a pachymeter or corneal topographer (such as the OCULUS Pentacam or Ziemer Ophthalmology Galilei G4). Values are given in diopters with a normal peripheral thickness of approximately 950μm and a normal central thickness of approximately 450μm (Stein, Stein, & Freeman, 2013). Central corneal

thickness is essential in screening for corneal dysfunction including keratoconus. Depending on the patient's manifest refraction and accompanying planned treatment of corneal stroma ablation to correct the refractive error, the actual thickness of residual stromal bed (RSB) is essential to know if the eye can withstand the planned ablation treatment. The amount of corneal stroma removed varies depending on the planned treatment and the surgeon must be cautious in screening the prospective patient, as too much thinning of the RSB increases the probability of the patient developing progressive ectasia or keratoconus postoperatively.

Due to the cornea being an avascular structure, it is entirely dependent on the diffusion of nutrients from the anterior chamber of the eye and tear film over the ocular surface. As such, tear production is important in maintaining the health of the cornea and contributes to its refractive power (Khurana, 2007). Laser vision correction surgery's manipulation of the corneal surface and corneal stromal bed thus have an effect on the postoperative tear production and nourishment of the cornea. One of the possible side effects of refractive surgery is surgery-induced Dry Eye Syndrome (DES) with studies estimating that between 0.25% to 48% of patient's undergoing CRLS experience DES either transiently or indefinitely after surgery (Bower et al., 2015). Tear production is always tested during initial surgery screening protocols and is usually done using a Schirmer Test or Oasis Medical ZoneQuick Test. Both of these tests evaluate normal tear production. Though patients with a lower than normal tear production can still undergo refractive surgery, they must be informed about the higher probably of them developing DES postoperatively.

Lastly, corneal curvature as defined by flat and steep keratometry values are important because it is the corneal curvature that determines the refractive power of the cornea. Keratometry, also known as ophthalmometry, values can be given either in diopters when discussing the refractive power, or in millimeters when discussing the radius of curvature of the eye. Keratometry is an objective method to estimate the corneal astigmatism of the eye by measuring the central corneal curvature (Khuarana, 2007). It can be measured in multiple ways including manually using a keratometer, via an autorefractor, or via a corneal topographer (such as the OCULUS Pentacam or Ziemer Ophthalmology Galilei G4). Keratometers work by utilizing internal doubling prisms that reflect an image from two pairs of points on the cornea; the anterior corneal curvature and corneal power is then calculated using Snell's Law of Refraction (assuming an Index of Refraction of 1.3375) from these four total reflected points (Stein, Stein, & Freeman, 2013). On average, normal keratometry values range from 42-44 diopters indicating that is the normal refractive power of the central cornea ("Shape Curvature, and Power," n.d.). Due to keratometry being an indicator of the refractive power of the cornea, keratometry values are thus related and important to understanding visual acuity.

Visual Acuity and Keratometry

Visual acuity (VA) is a test that has been developed over the years to accurately gauge how well a person can read at given distances based on a standardized chart. The standardized chart utilized most often for visual assessment is the Snellen Visual Acuity Chart consists of letters and/or numbers presented at a 5-minute angle to the eye at 20 feet (6 meters). It is important to only use this chart at 20 feet as at that distance, the

distant rays of light entering the eye are parallel to each other and require very little accommodation by the lens (Stein, Stein, & Freeman, 2013). The actual VA testing result is expressed as a fraction, see Table 3. The numerator represents the distance between the patient and the chart letters while the denominator represents the distance between the patient and the chart letters at which a person with normal vision can see the chart letters. For example, if a person reads the 20/20 line at 20 feet, VA is 20/20 but if a person reads the 20/200 line at 20 feet, VA is 20/200. Normal distance vision is considered to be 20/20.

If a patient is not able to read the 20/20 line clearly, they will be refracted using a phoropter (Figure 1). This phoropter, also called a refractor, contains many trial spherical and cylindrical trial lenses mounted on circular wheels that can be interchanged quickly. An ophthalmic technician will determine the patient's manifest refraction based on which lenses make the lines of the Snellen Visual Acuity Chart more clear.

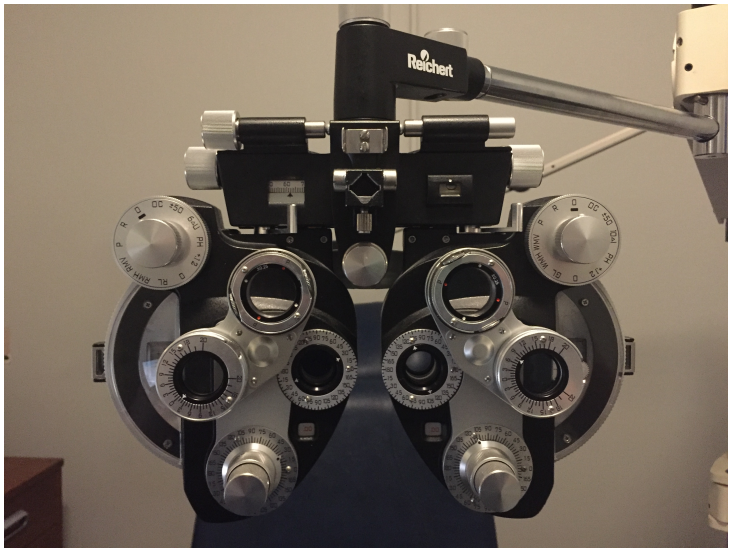

Figure 1: Phoropter (Refractor). Image showing both spherical and cylindrical trial lenses mounted internally on circular wheels for easy adjustment. Photo taken at Boston Eye Group/Boston Laser in Brookline, MA.

It has long been a longstanding belief in the ophthalmology community that if the cornea is re-shaped during vision correction surgery to such a degree that the postoperative keratometry falls below a certain value (historically given as <35D) rendering the cornea too "flat" that the best corrected (either surgically or surgically plus additional refraction) postoperative visual acuity will be diminished (Varssano et al., 2013). Though literature and peer-reviewed journal articles are unclear in exactly how this idea came about since there is little evidence published to support the claim, there are several possible explanations for how this idea gained traction in the medical community. When specifically discussing LASIK procedures, multiple sources report that eyes with flat corneas can be at increased risk of developing flap complications including buttonholed flap or free cap.

A buttonholed flap, also called a thin flap, is defined as when a flap is created within or above the Bowman's membrane. In a normal flap, the bowman's membrane will be lifted up with the overlying epithelium. However, in a buttonholed flap, the Bowman's membrane (and thus full thickness of the ocular epithelium) is not lifted and is subsequently exposed to the excimer laser during ablation (Melki and Azar, 2001). This is problematic as the incomplete lifting of the epithelium can provide an easy route for epithelial cells to migrate along the corneal flap/stroma interface during the healing process and lead to epithelial ingrowth. Buttonhole flaps are a common complication leading to loss of BCVA postoperatively (Stulting et al., 1999).

A free cap is the unintended complete dissection (removal) of the corneal flap. As with buttonhole flaps, patient's with flat corneas (K<42D preoperatively) are at an

increased risk of developing a free cap due to the flat angle of the cornea exposing less tissue during flap creation (Melki and Azar, 2001). In the best case scenario, if the cap can be retrieved it can be replaced in a manner similar to LASEK surgery. If the flap cannot be retrieved the epithelium will re-grow in a manner similar to PRK surgery. However, free caps can sometimes lead to a detrimental hyperopic shift (a weakening of the cornea's refractive ability) that can greatly influence a patient's postoperative BCVA (Amano et al., 2016).

Though corneal thickness and anterior corneal curvature are not the same thing, they are undoubtedly linked as you cannot change the thickness of the cornea without associatively changing the degree of curvature. Therefore, the amount of corneal stroma that can be removed by ablation can be limited by the predicted postoperative anterior corneal curvature and conversely. This has special importance for patients suffering from high degrees of myopia (spherical equivalent of -6D or greater) as the higher the prescription the greater the amount of corneal stroma that will need to be ablated. Several studies have reported greater incidence of under-correction (patients still remain myopic to some degree after surgery) in patients who ended up with flat corneas (K<38D) postoperatively (Mostafa, 2015 and Rao et al., 2001). This has been attributed to the possible loss of ablation efficiency for patients at corneal curvature extremes (flat or steep) as recommended by the current laser FDA guidelines (Mostafa, 2015).

Several papers have explored the relationship between measured preoperative keratometry values and VA outcomes after myopic CRLS. In 2001, Rao et al. examined preoperative keratometry's relationship to postoperative VA in highly myopic (spherical

equivalent -6 to -13D) patients, followed by Christiansen et al. in 2012 who extended the investigation of preoperative keratometry and postoperative VA to moderately myopic (spherical equivalent -2 to -5.99D) patients. Additionally, whether preoperative keratometry has an influence on postoperative VA after hyperopic CRLS has also been explored (Cobro-Soriano et al., 2002; Williams, Dave, and Moshifar, 2008). However, current literature exploring the effect of either predicted postoperative keratometry values calculated using preoperative data, or measured postoperative keratometry values on postoperative visual acuity has not been extensively explored.

Three studies (Kim et al., 2011; Christiansen et al., 2012; Williams et al., 2008) looked at the overall change in keratometry values after myopic LASIK and PRK and any associated effect on visual acuity but did not explore if this change in keratometry left the patients with flat corneas after surgery. In 2013, Varssano et al. 2013 investigated the relationship between eyes that ended up with significantly flat corneas (K<35D) postoperatively and loss of BCVA in PRK patients, however they did not investigate if the degree of corneal flatness had any effect on BCVA or include any patients undergoing LASIK or LASEK surgery. In 2015, E. M. Mostafa explored the relationship between the degree of change in keratometry after CRLS and VA, however, he only investigated patients undergoing LASIK and limited his patient population to highly myopic (spherical equivalent -6 to -12D) patients. Also in 2015, Schallhorn et al. looked at postoperative keratometry but only investigated if there is a relationship with patient-reported satisfaction and night-vision phenomena.

Therefore, based on current literature searches, additional exploration of any relationship between postoperative keratometry including the degree of corneal flatness in any degree of myopic eyes undergoing any type of CRLS and loss of postoperative BCVA is warranted and will be explored in this thesis.

SPECIFIC AIMS

As reviewed in the introduction, there are many ways refractive errors can be corrected to improve vision. Furthermore, significant evidence shows that corneal refractive laser surgery (CRLS) is a safe and effective way to permanently correct these refractive errors. However, due to the pervasive idea in ophthalmology suggesting that patients with "flat corneas" or calculated predicted postoperative keratometry values of <35D, many of these patients are told they cannot be candidates for CRLS.

The main objective of this paper was to retrospectively examine clinical data across all types of CRLS including LASIK, LASEK, and PRK to determine if there is evidence to substantiate this currently held idea that patients with a too flat anterior corneal curvature should not undergo CRLS. If there is in fact no demonstrated correlation between patients with flat corneas and loss of BCVA, this could have an impact on preoperative guidance for that patient population when considering candidacy for CRLS.

The Specific Aims of the study are:

1. To test if there is a correlation between candidate patients undergoing CRLS with predicted postoperative keratometry values of <38D and loss of best corrected visual acuity (BCVA).
2. To test if there is a significant difference in visual acuity outcome between the degree of corneal flatness as measured by keratometry by placing patients into designated subgroups: Subgroup 1 (K<35D), Subgroup 2 (K=35-35.99D), Subgroup 3 (K=36-36.99D0 and Subgroup 4 (K=37-37.99D).

3. To examine the relationship between the type of surgery (LASIK, LASEK, or PRK) and patients who experienced a loss of BCVA after CRLS.

We expect this study will show:

1. There is no significant difference between patients with calculated predicted postoperative keratometry values <38D and patients with calculated predicted postoperative keratometry values of ≥38D with respect to loss of BCVA after CRLS.
2. There is no significant difference between candidate patients placed further stratified groups based on the degree of corneal curvature: Subgroup 1 (K<35D), Subgroup 2 (K=35-35.99D), Subgroup 3 (K=36-36.99D) and Subgroup 4 (K=37-37.99D).
3. There is no significant difference between type of CRLS (LASIK, LASEK, or PRK) candidate patients underwent and subsequent postoperative BCVA.

METHODS

Study Design Overview

A retrospective chart review through the electronic health record, NextGen, was conducted for eyes that underwent LASIK, LASEK, or PRK corneal refractive laser surgery between December 2008 and November 2016. All reports were collected for patients undergoing surgery at the private ophthalmic practice Boston Eye Group/Boston Laser in Brookline, Massachusetts.

The inclusion criteria for the study included patients with myopia who underwent LASIK, LASEK, or PRK between December 2008 and November 2016 and patients with mathematically calculated postoperative corneal curvature as measured by both flat and steep keratometry values estimated to be <38 diopters (see below for calculation). A manifest refraction matched control group of patients, meeting the same surgical and time frame period, with mathematically calculated postoperative corneal curvature values estimated to be equal to or greater than 38 diopters was included for control purposes.

The exclusion criteria for the study was patients who underwent hyperopic laser vision correction surgery, patients who had undergone any other ocular surgeries prior to their LASIK, LASEK, or PRK with surface ablation screening evaluation, and patients who underwent enhancement surgery after the original LASIK, LASEK, or PRK laser vision correction surgery.

Postoperative Keratometry Calculation

Postoperative Keratometry values were calculated using a modified version of the mathematical formula suggested by Holladay et al. (2001) and Varssano et al. (2013).

The preoperative spherical equivalence was calculated using the preoperative manifest sphere and preoperative manifest cylinder and the formula: sphere + (cylinder/2). The spherical equivalence was then multiplied by 0.7. This calculation was performed to yield the approximate expected amount of corneal stroma to be ablated during surgery according to the 1:0.7 ratio as commonly accepted by the ophthalmological community. This estimated amount of corneal stroma expected to be removed via ablation was then subtracted from the measured preoperative keratometry values to yield the suggested calculated postoperative keratometry values.

Clinical Laser Vision Correction Surgical Consultation Procedures

As part of the preoperative laser vision correction surgery screening evaluation, all patients were required to undergo a thorough ocular examination to determine visual acuity including uncorrected visual acuity (UCVA) and best-corrected visual acuity (BCVA) along with both a manifest refraction using either an electronic or manual phoropter. Additional testing and imaging as part of the routine screening process included autorefraction with a Nidek Autorefractor (NIDEK ARK-530A, Fremont, California), ocular dominance, pupillometry using a handheld Oasis Medical Colvard Pupillometer (Oasis Medical Inc., San Dimas, California), tear production using Oasis Medical ZoneQuick (Oasis Medical Inc., San Dimas, California) Phenol Red Thread Tear Test, ocular tonometry using a Reichert Technologies Tono-Pen (AMETEK Inc., Depew, New York) or Nidek TONOREF II Non-Contact Tonometer (NIDEK Inc., Fremont, California), corneal pachymetry using a Corneo-Gage Plus pachymeter (Sonogage Inc., Cleveland, Ohio) and corneal topography using an OCULUS Pentacam (OCULUS Inc.,

Arlington, Washington) prior to February 2014, or Ziemer Ophthalmology Galilei G4 (Ziemer USA, Inc., Alton, Illinois) since February 2014. All tests were performed by ophthalmic technicians. Additionally, each patient underwent a cycloplegic refraction, dilated fundus examination, and slit-lamp examination by an ophthalmologist per Boston Eye Group/Boston Laser protocol. A total of 191 candidate eyes were identified to fit the inclusion criteria for this analysis within the study period which were subsequently matched with 191 control eyes for comparison.

The following procedures are standard protocol for patients receiving laser vision correction surgery at Boston Eye Group/Boston Laser under the direction of ophthalmologist Dr. Samir Melki, MD, PhD.

Pre-Operative Workup

All patients were instructed to remain out of contact lenses for at least one week prior to surgery. Each patient was given the opportunity to meet with his or her surgeon either prior to surgery day or on the day of surgery to have all questions answered and addressed. On the day of surgery, upon check-in at Boston Eye Group/Boston Laser, each patient was instructed to fill out and sign all informed consent forms including medication consent(s) and all potential risks of each procedure via DocuSign and in-person. Repeat testing of a manifest refraction or corneal topography were repeated if three months or more had elapsed since the initial surgery consultation, or if the patient had been wearing contact lenses on the day of initial surgery consultation. All repeat testing was performed by an ophthalmic technician and checked by the surgeon. Next, all patients were given both an oral and written outline of what each surgery entails and what

to expect before, during, and after that procedure. Patients were walked through all at-home care instructions, follow-up eye drop regimens, and what to expect at each follow-up appointment. Finally, 20-minutes prior to the expected surgery time, each patient was given 1-drop of the antibiotic Ciprofloxacin Hydrochloride Ophthalmic Solution 0.3% (Sandoz Inc., Princeton, New Jersey) and 1-drop of the anti-inflammatory Ilevro Nepafenac Ophthalmic Suspension 0.3% (Alcon Laboratories Inc, Fort Worth, Texas) to each pre-operative eye and one 5mg valium tablet by mouth to ease any day-of-surgery anxiety.

Intra-Operative LASIK Procedure

Each patient was brought into the Laser Suite at Boston Eye Group/Boston Laser (1101 Beacon Street Suite 6, Brookline, MA) and provided with a hair net prior to having them lay flat on the surgical bed with a surgical positioner placed under both knees. Sterile draping was performed with sterilization of the ocular surface of each surgical eye achieved using Betadine 5% Sterile Ophthalmic Prep Solution (Povidone-Iodine Ophthalmic Solution, Alcon Laboratories Inc., Fort Worth, Texas). Topical anesthesia of the ocular surface was achieved using 1% Proparacaine Hydrochloride Ophthalmic Solution (Alcon Laboratories Inc., Fort Worth, Texas). A Time-Out call was verbally called with patient name, date of birth, type of treatment and specific eye treatment was verified.

Laser-assisted in situ keratomileusis (LASIK) flap formation involved using a femtosecond laser (IntraLase iFS60 Laser, Abbott Medical Optics Inc., Santa Ana, California) to create a corneal flap to allow for access to the corneal stromal tissue for

ocular surface laser ablation. Each corneal flap creation was set with an aim of a 9mm diameter flap and a superior hinge-position. Corneal flap depth, approximately between 90 to 110 microns, is unique for each patient and determined using corneal topography and corneal thickness measurements (Kim et al., 2011) obtained at the patient's initial surgical screening evaluation. Each of the patient's measurements for flap position, diameter, and depth were double checked on the day of surgery.

After corneal flap creation, the patient was rotated around and securely placed under an excimer laser (VISX STAR S4 IR Excimer Laser System, Abbot Medical Optics Inc., Santa Ana, California or WaveLight EX500 Excimer Laser, Alcon Laboratory Inc., Fort Worth, Texas). The patient's upper eyelid was secured with a sterile Tegaderm Film (3M Health Care, St. Paul, Minnesota), a second drop of 1% Proparacaine Hydrochloride Ophthalmic Solution was applied, and an ocular speculum (Model OR 018, Titan Surgical, Kazan, Russia) placed to ensure the surgical eye remained open throughout the procedure. The surgical flap was then marked with a Regular Tip Latex-Free Sterile Marker (McKesson Medical Surgical, Richmond, Virginia) to ensure proper re-placement after laser application. The ocular surface was then irrigated with Balance Saline Solution (Alcon Laboratories Inc., Fort Worth, Texas) via a 25-gauge cannula (Model OC 022, Titan Surgical, Kazan, Russia) with a 3cc syringe (McKesson Medical Surgical, Richmond, Virginia) and dried with a Weck-Cel Cellulose Fluid Control Sponge (Xiomed, Jacksonville, Florida). If the planned surgical treatment cylinder was 1.5 or greater, the eye axis was marked on the ocular surface so laser crosshairs could be initiated to ensure accurate placement of the laser during

treatment. Pre-operative pachymetry was verbally called out. The corneal flap was then lifted using a LASIK spatula (Model OE 041, Titan Surgical, Kazan, Russia).

The exposed corneal stromal tissue was then ablated, i.e. treated for vision correction with the excimer laser (VISX STAR S4 IR Excimer Laser System or WaveLight EX500 Excimer Laser) to remove a certain amount of corneal stroma, measured in micrometers, from a set area of the ocular surface known as the ocular zone given in millimeters.

Three-drops of a practice-specific steroid-antibiotic mixture of equally matched Prednisolone Acetate 0.1% Ophthalmic Solution (Sandoz Inc., Princeton, New Jersey) and Ciprofloxacin Hydrochloride Ophthalmic Solution 0.3% (Sandoz Inc., Princeton, New Jersey) was applied to the postoperative ocular surface. Gauze was taped over each surgical eye and the patient was taken out of the Laser Suite and to a dark examination room to rest for 30-minutes. After 30-minutes, each postoperative eye was thoroughly examined via slit-lamp examination to ensure proper flap placement and approximation of wound edges.

Intra-Operative Advanced Surface Ablation (LASEK and PRK) Procedure

Each patient was brought into the Laser Suite at Boston Eye Group/Boston Laser and provided with a hair net prior to having them lay flat on the surgical bed with a surgical positioner placed under both knees. Sterile draping was performed with sterilization of the ocular surface of each surgical eye achieved using Betadine 5% Sterile Ophthalmic Prep Solution. Topical anesthesia of the ocular surface was achieved using 1% Proparacaine Hydrochloride Ophthalmic Solution. A Time-Out call was verbally

called with patient name, date of birth, type of treatment and specific eye treatment was verified.

Using the microscope of an excimer laser (VISX STAR S4 IR Excimer Laser System or WaveLight EX500 Excimer Laser), the upper eyelid of the surgical eye was draped with a sterile Tegaderm Film, a second drop of 1% Proparacaine Hydrochloride Ophthalmic Solution was applied, and an ocular speculum (Model OR 018, Titan Surgical, Kazan, Russia) was placed to ensure eye opening throughout the procedure. One edge of a 9mm LASEK trephine (Model OK 048; Titan Surgical, Kazan, Russia) was marked with a Regular Tip Latex-Free Sterile Marker to visualize the ocular surgical treatment zone and for epithelium replacement after surface ablation. The LASEK trephine was then placed on the ocular surface and the central barrel filled with 20% ethanol solution (prepared with 2mL 100% medical grade ethanol mixed with 8mL sterile water) injected via 25-g cannula (Model OC 022, Titan Surgical, Kazan, Russia) for 40 seconds. The 20% ethanol solution was applied with the intent to loosen and weaken the epithelium of the surface of the eye and removed using a Weck-Cel Cellulose Fluid Control to prevent spillage outside the trephine. After alcohol and trephine removal, the ocular surface was irrigated with Balanced Saline Solution (BSS) to wash away any remaining residual alcohol and re-hydrate the epithelium. During LASEK surgical procedures, the epithelium was lifted and displaced toward the limbal area and away from the optical ablation zone using a LASIK PVA Spear (Beaver-Visitec International Inc., Waltham, Massachusetts). During PRK surgical procedures, the epithelium was removed using another LASIK PVA Spear and Weck-Cel Cellulose Fluid Control Sponge.

The exposed corneal stromal tissue was then ablated with the excimer laser (VISX STAR S4 IR Excimer Laser System or WaveLight EX500 Excimer Laser) to remove a certain amount of corneal stroma, measured in micrometers, from a set area of the ocular surface known as the ocular zone given in millimeters. If the planned surgical treatment cylinder was 1.5 or greater, the eye axis was marked on the ocular surface so laser crosshairs could be initiated to ensure accurate placement of the laser during treatment.

For LASEK surgeries, the epithelium was repositioned back into place using a LASIK PVA Spear with a bandage contact lens (Acuvue; Johnson & Johnson Vision Care Inc., Jacksonville, Florida) placed after surgery completion.

For select patients undergoing PRK and laser vision correction, a bvi Merocel corneal light shield (Beaver-Visitec International Inc., Waltham, Massachusetts) saturated with the DNA crosslinking compound Mitomycin C (MMC) was applied to the corneal stroma after laser ablation for a variable time. Mitomycin C has been found to help facilitate healing and decrease corneal scarring (Hashemi et al., 2017). After ablation and/or MMC removal, the ocular surface was irrigated once again with BSS, the epithelium was not replaced, and a bandage contact lens was placed on the surface of the eye.

After LASEK, three-drops of a practice-specific steroid-antibiotic mixture of equally matched Prednisolone Acetate 0.1% Ophthalmic Solution and Ciprofloxacin Hydrochloride Ophthalmic Solution 0.3% was applied to the postoperative ocular surface.

After PRK, three drops of the same mixture of Prednisolone Acetate 1% Ophthalmic Solution and Ciprofloxacin Hydrochloride Ophthalmic Solution 0.3% in addition to one drop of the dilation solution Cyclopentolate Hydrochloride Ophthalmic Solution USP 1% (Bausch + Lomb Incorporated, Tampa, Florida) was applied to the postoperative ocular surface.

Gauze was then taped over each surgical eye and the patient was taken out of the Laser Suite and to a dark examination room to rest for 30-minutes. After 30-minutes, each postoperative eye was thoroughly examined via slit-lamp.

Post-Operative Procedure and Directions for LASIK

Immediately following slit-lamp examination, clear plastic eye shield(s) were placed over the patient's surgical eye(s) prior to leaving the office. Patients were instructed to keep their eyes closed for 4 hours after surgery upon arrival at home, and keep the clear plastic eye shields in place every night for 1 week.

The daytime Boston Eye Group/Boston Laser eye drop regimen for 5 days after surgery is the following:

- Pred Forte (Prednisolone Acetate 1% Ophthalmic Suspension USP), a topical anti-inflammatory agent.
- Vigamox (Moxifloxacin Hydrochloride Ophthalmic Solution 0.5% as base), a fluoroquinolone antibiotic.

Table 1: Boston Eye Group/Boston Laser Postoperative LASIK Eye Drop Regimen

	Day of Surgery	**Day 1**	**Day 2**	**Day 3**	**Day 4**	**Day 5**
Pred Forte	1 drop every hour	1 drop every hour	1 drop every hour	4 drops per day	4 drops per day	STOP!
Vigamox	4 drops per day	4 drops per day	4 drops per day	4 drops per day	4 drops per day	STOP!

Patients were instructed to wait 5 minutes between applying drops to prevent drops washing each other away. Due to the importance of keeping the ocular surface lubricated to prevent rough interaction with the eyelid, patients were encouraged to use preservative-free lubricating tears as needed. Additional instructions included:

24 Hours: No squinting, squeezing, or rubbing the surgical eye(s) and no heavy lifting or strenuous physical activity.

1 Week: no eye makeup, sunscreen, or lotion directly around the eyes.

2 Weeks: no contact sports, swimming, hot tub, or Jacuzzi.

Post-Operative Procedure and Directions for Advanced Surface Ablation

Immediately following slit-lamp examination, clear plastic eye shield(s) were placed over the patient's surgical eye(s) prior to leaving the office. Patients were instructed to keep their eyes closed for 4 hours after surgery upon arrival at home, and keep the clear plastic eye shields in place every night for 1 week.

The daytime Boston Eye Group/Boston Laser eye drop regimen for 5 days after surgery is the following:

- Pred-Gati (50:50 Mixture of Prednisolone Acetate 1% Ophthalmic Suspension USP and Gatifloxacin Ophthalmic Solution 0.5%), a topical anti-inflammatory agent and fluoroquinolone antibiotic.

- Nevanac (Nepafenac 0.1% Ophthalmic Suspension), a nonsteroidal anti-inflammatory drug (NSAID).

Table 2: Boston Eye Group/Boston Laser Postoperative LASEK and PRK Eye Drop Regimen

	Week 1 (including surgery day)	**Week 2**	**Week 3**	**Week 4**
Pred-Gati	4 drops per day	2 drops per day	1 drop per day	1 drop per day until out
Nevanac	2 drops per day if experiencing discomfort			
Vitamin C	1 gram/100mg per day for 3 months to help prevent scarring			

Patients were instructed to space the drops evenly throughout the day and to wait 5 minutes between applying drops to prevent drops washing each other away. Due to the importance of keeping the ocular surface lubricated to prevent rough interaction with the eyelid, patients were encouraged to use preservative-free lubricating tears as needed. Additional instructions included:

- 24 Hours: No squinting, squeezing, or rubbing the surgical eye(s) and no heavy lifting or strenuous physical activity.
- 1 Week: no eye makeup, sunscreen, or lotion directly around the eyes. Bandage contact lenses will be removed in office at Boston Eye Group/Boston Laser.
- 2 Weeks: no contact sports, swimming, hot tub, or Jacuzzi.

Additionally, each patient was given a prescription for Tylenol #3 with codeine to be taken as needed for postoperative discomfort.

Follow-Up Procedures

All patients regardless of refractive surgery type were instructed to return to Boston Eye Group/Boston Laser for postoperative follow-up examinations at 1-day, 1-

week, 6-weeks for LASIK or 9 weeks for Advanced Surface Ablation, 6-months, and 1-year after surgery date.

LASIK Follow-Up

At each LASIK postoperative examination, the patient was asked if they were experiencing any complaints including blurry vision, dryness, halos, trouble driving or trouble reading, and their right eye (OD), left eye (OS), and both eyes together (OU) distance visual acuity was checked. If the patient underwent LASIK Monovision, near visual acuity was also checked. At the 1-day postoperative examination, no intraocular pressure (IOP) or manifest refraction was performed. At the 1-week LASIK postoperative examination, a manifest refraction of both eyes was performed if the patient was not seeing 20/20 but no IOP was checked. Beginning at the 6-week LASIK postoperative examination, in addition to a manifest refraction of both eyes if not seeing 20/20, the patient's IOP was checked using either Tono-Pen or Nidek TONOREF II Non-Contact Tonometer. Additionally, autorefraction, corneal topography, and/or Optical Corneal Tomography (OCT) of the macula were taken if patient not seeing 20/20.

Advanced Surface Ablation Follow-Up

At each LASEK/PRK postoperative examination, the patient was asked if they were experiencing any complaints including blurry vision, dryness, halos, trouble driving or trouble reading, and their OD, OS, and OU visual acuity was checked. At the 1-day postoperative examination, no IOP or manifest refraction was performed. At the 1-week LASIK postoperative examination, no IOP was taken and bandage contact lenses were removed. All patients were given a manifest refraction if not seeing 20/20. Beginning at

the 9-week LASIK postoperative examination, in addition to a manifest refraction of both eyes if not seeing 20/20, the patient's IOP was checked using either a Tono-Pen or Nidek TONOREF II Non-Contact Tonometer. Additionally, autorefraction, corneal topography, and/or Macular Optical Corneal Tomography (OCT) were taken if patient not seeing 20/20.

Data and Statistical Analysis

All data was de-identified. Visual acuity, as measured as best corrected distance visual acuity (BCVA) given by the Snellen Visual Acuity Chart was converted to logMAR(BCVA) for more accurate statistical analysis (Holladay, 1997), see Table 3.

Table 3: Snellen Visual Acuity Chart Conversion to LogMAR Equivalent. Adapted from Holladay, 1997.

Snellen Visual Acuity Chart Conversion to LogMAR	
Snellen Equivalent	**LogMAR 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

Candidate patients with calculated keratometry values <38D were separated from control patients with calculated keratometry values 38D and over. The candidate population data was further stratified with regard to calculated postoperative keratometry into four subgroups: Subgroup 1a (K<35D), Subgroup 2a (K=35-35.99D), Subgroup 3a (K=36-36.99D) and Subgroup 4a (K=37-37.99D). Accordingly, the control population data was also stratified with regard to calculated postoperative keratometry into four

subgroups: Subgroup 1b (K=38-38.99D), Subgroup 2b (K=39-39.99D), Subgroup 3b (K=40-40.99D) and Subgroup 4b (K≥41D).

The Data Analysis tool in Microsoft Excel 15.26 was used for statistical analysis. The quantitative variables (means) were analyzed using the following tests: t-test, z-test, and ANOVA. A Two-Sample Assuming Unequal Variances two-tailed t-test was used to determine significance between candidate and control means of the preoperative manifest refraction, spherical equivalence, and total follow-up duration. To determine if there was a significant difference in preoperative vs. postoperative visual acuity outcomes between the overall candidate and control groups, a Two-Sample for Variances F-Test was used to determine equal or unequal variance and that variance was used to compute a Two Sample for Means z-test. To determine if there was a significant difference in preoperative vs. postoperative visual acuity outcomes between the candidate and control subgroups, a Single Factor Analysis of Variance (ANOVA) test was used to compare the multiple means. The qualitative variables (number of eyes that lost BCVA and number of eyes undergoing different surgery types) were analyzed using a Chi-Square Test for Independence.

The null hypothesis of all analysis tests assumed equal means or equal qualitative distribution. A $p \leq 0.05$ (probability less than 5%) was considered statistically significant and $p \leq 0.01$ (probability less than 1%) was considered very statistically significant leading to a rejection of the null hypothesis.

RESULTS

Data information was collected from Boston Eye Group/Boston Laser chart records between December 2008 and January 2017. A total of 191 eyes (104 OD, 87 OS) belonging to 124 patients were identified as candidates. A control population of 191 candidate eyes (104 OD, 87 OS) belonging to 123 individuals were selected by matching manifest refraction sphere and cylinder values with candidate patients.

Preoperative Data

Data collected from the overall candidate group showed a mean preoperative manifest sphere refraction of -6.6D ± 1.95, mean manifest cylinder refraction of -1.23D ± 1.03, mean spherical equivalence of -7.22D ± 1.86, mean flat keratometry of 41.46D ± 1.24, and mean steep keratometry of 42.78D ± 1.41. Data collected from the corresponding overall control group showed a mean preoperative manifest sphere refraction of -6.49D ± 1.84, mean manifest cylinder refraction of -1.09D ± 0.90, mean spherical equivalence of -7.03D ± 1.68, mean flat keratometry of 44.31D ±1.32, and mean steep keratometry of 45.52D ± 1.29. A Two-Sample t-Test assuming Unequal Variance was used to compare candidate and control mean preoperative manifest sphere refraction ($t(379) = -0.58$, $p = 0.55$, two-tailed.), mean preoperative manifest cylinder refraction ($t(373) = -1.46$, $p = 0.15$, two-tailed.), and mean preoperative spherical equivalence ($t(376) = -1.03$, $p = 0.30$, two-tailed.). No significance was found between any of the previously mentioned comparisons.

The mean candidate preoperative visual acuity, given in logMAR(BCVA), was 0.0059 ±0.056 compared to the mean control preoperative logMAR(BCVA) of -2.9E-19

± 0.039. A z-test for means was conducted comparing these overall preoperative candidate and control means (z=1.20, p<0.23, two-tailed). Candidate vs. control preoperative visual acuity data is presented below (Figure 2).

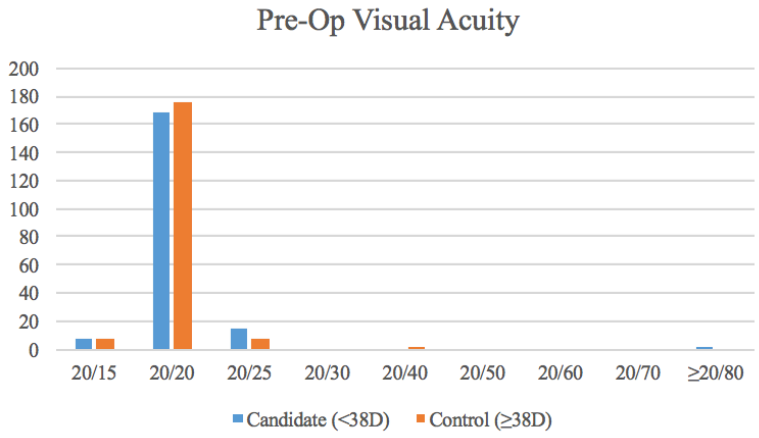

Figure 2: Candidate vs. Control Preoperative Visual Acuity. Graphical representation of the preoperative visual acuity of candidate patients with predicted postoperative keratometry values <38D vs. preoperative visual acuity of control patients with predicted postoperative keratometry values ≥38D. X-axis represents number of eyes; Y-axis represents visual acuity.

The candidate population data was further stratified with regard to calculated postoperative keratometry into four subgroups: Subgroup 1a (K<35D), Subgroup 2a (K=35-35.99D), Subgroup 3a (K=36-36.99D), and Subgroup 4a (K=37-37.99D). Accordingly, the control population data was also stratified with regard to calculated postoperative keratometry into four subgroups: Subgroup 1b (K=38-38.99D), Subgroup 2b (K=39-39.99D), Subgroup 3b (K=40-40.99D), and Subgroup 4b (K=≥41D). See Table 4 for a summary of these stratifications with regard to preoperative data.

Table 4: Candidate and Control Stratified Subgroups and Preoperative BCVA.

Candidate: Preoperative BCVA					
	Subgroup 1a (K<35D) n=25	**Subgroup 2a (K=35-35.99D) n=36**	**Subgroup 3a (K=36-36.99D) n=60**	**Subgroup 4a (K=37-37.99D) n=70**	**P-value between Subgroups**
Mean BCVA: (logMAR(BCVA))	0.008	0.0111	0.0083	0.0004	0.77
SD	0.028	0.032	0.088	0.035	
Range: (logMAR(BCVA))	0-0.1	0-0.1	-0.125-0.6	-0.125-0.1	
Manifest Sphere	-8.2	-6.97	-6.63	-5.81	**5.8E-7**
Manifest Cylinder	-1.33	-1.58	-1.13	-1.10	0.10
Spherical Equivalence	-8.87	-7.76	-7.20	-6.36	**5.0E-9**
Control: Preoperative BCVA					
	Subgroup 1b (K=38-38.99D) n=76	**Subgroup 2b (K=39-39.99D) n=70**	**Subgroup 3b (K=40-40.99D) n=24**	**Subgroup 4b (K≥41D) n=21**	**P-value between Subgroups**
Mean BCVA: (logMAR(BCVA))	-0.003	0.005	0	-0.007	0.53
SD:	0.035	0.047	0	0.045	
Range: (logMAR(BCVA)	-0.125-0.1	-0.125-0.3	0	-0.125-0.1	
Manifest Sphere	-6.74	-6.7	-6.19	-5.20	**0.004**
Manifest Cylinder	-1.04	-1.18	-1.14	-0.90	0.616
Spherical Equivalence	-7.25	-7.29	-6.76	-5.65	**0.0004**

A single factor analysis of variance (ANOVA) test was conducted to compare the following between candidate subgroups 1a, 2a, 3a and 4a: mean preoperative BCVA (no significance between the subgroup means, $F(3, 187) = 0.374$, $p = 0.77$), mean manifest sphere (statistically significant differences between the subgroup means, $F(3, 187) = 11.51$, $p = 5.8E\text{-}7$), mean manifest cylinder (no significance between the subgroup means, $F(3, 187) = 2.10$, $p = 0.10$) and mean spherical equivalence (statistically significant differences between the subgroup means, $F(3, 187) = 15.46$, $p = 5.0E\text{-}9$).

Additional single factor ANOVA test was conducted to compare the following between control subgroup 1b, 2b, 3b and 4b: mean preoperative BCVA (no significance between the subgroup means, $F(3, 187) = 0.741$, $p = 0.53$), mean manifest sphere (statistically significant differences between the subgroup means, $F(3, 187) = 4.65$, $p = 0.004$), mean manifest cylinder (no significance between the subgroup means, $F(3, 187) = 0.616$, $p = 0.61$) and mean spherical equivalence (no significance between the subgroup means, $F(3, 187) = 6.45$, $p = 0.0004$).

Postoperative Data

Data collected from the candidate group showed a mean postoperative flat K of 36.41D ± 1.07 and mean postoperative steep K of 37.73D ± 1.23. Data collected from the corresponding control group showed a mean postoperative flat keratometry of 39.39D ±1.05, and mean postoperative steep keratometry of 40.60D ± 1.24. Candidate vs. control postoperative visual acuity data is presented below (Figure 3).

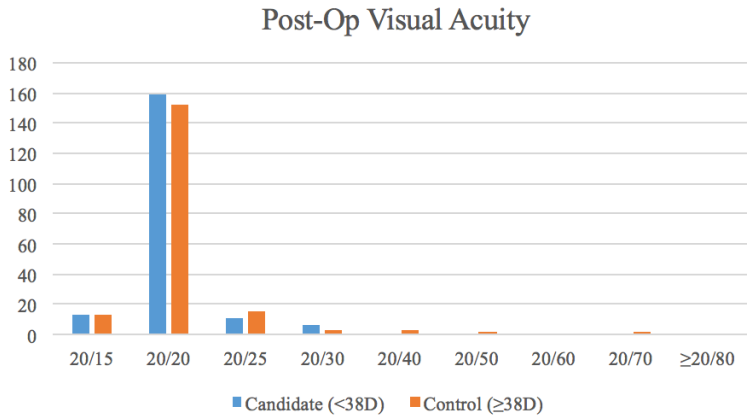

Figure 3: Candidate vs. Control Postoperative Visual Acuity. Visual illustration of the postoperative BCVA of candidate patients with predicted postoperative keratometry values <38D vs. postoperative BCVA of control patients with predicted postoperative keratometry values ≥38D. X-axis represents number of eyes; Y-axis represents visual acuity.

The further stratified control subgroups with regard to postoperative visual acuity are presented below in Table 5.

Table 5: Candidate and Control Stratified Subgroups and Postoperative BCVA. Top: Total number of persons in each stratified group and associated postoperative BCVA. Bottom: Total number of persons in each stratified control group and associated postoperative BCVA.

Candidate: Postoperative BCVA					
	Subgroup 1a (K<35D) n=25	**Subgroup 2a (K=35-35.99D) n=36**	**Subgroup 3a (K=36-36.99D) n=60**	**Subgroup 4a (K=37-37.99D) n=70**	**Total: n=191**
Mean BCVA: (logMAR(BCVA))	0.026	0.001	-0.0004	-0.0032	0.006
SD:	0.056	0.036	0.046	0.070	0.062
Range: (logMAR(BCVA))	0-0.176	-0.125-0.176	-0.125-0.176	-0.125-0.4	-0.125-0.4
Control: Postoperative BCVA					
	Subgroup 1b (K=38-38.99D)	**Subgroup 2b (K=39-39.99D)**	**Subgroup 3b (K=40-40.99D)**	**Subgroup 4b (K≥41D)**	**Total:**
Mean BCVA: (logMAR(BCVA)	0.026	0.029	-0.004	-0.012	0.019
SD:	0.092	0.119	0.067	0.038	0.097
Range: (logMAR(BCVA)	-0.125-0.544	-0.125-0.544	-0.125-0.1	-0.125-0	-0.125-0.544

A single factor ANOVA test was conducted to compare the mean postoperative BCVA, reported in logMAR(BCVA), between candidate subgroups 1a, 2a, 3a and 4a, see Table 5. The analysis of variance showed no significance between the subgroup means, $F(3, 187) = 1.8$, $p = 0.15$. A second single factor ANOVA test was conducted to compare the mean postoperative BCVA between control subgroup 1b, 2b, 3b and 4b, see Table 5. The analysis of variance showed no significance between the subgroup means, $F(3, 187) = 1.58$, $p = 0.20$.

Loss of BCVA

Of the overall candidate patient group, a total of 15 out of 191 eyes (7.85%) lost BCVA with 7 eyes losing 1 line of BCVA and 8 eyes lines losing 2+ lines of BCVA, see Figure 4. Of the overall control patient group, a total of 23 out of 191 eyes (12.04%) lost BCVA with 12 eyes losing 1 line of BCVA and 11 eyes losing 2+ lines of BCVA, Figure 4.

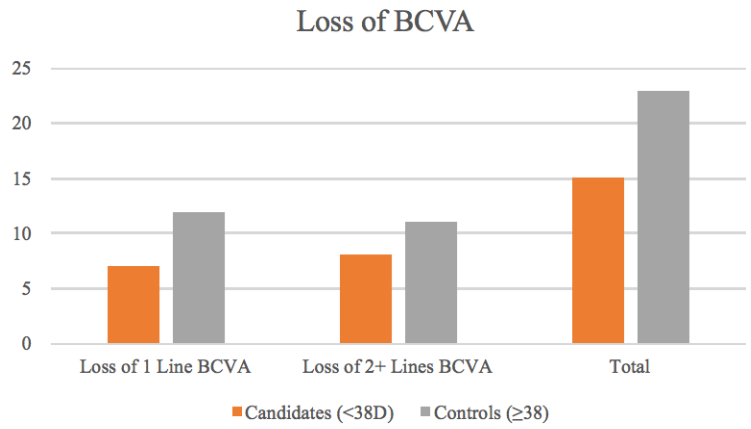

Figure 4: Candidate vs. Control vs. Total Loss of BCVA. Left: Candidate (7 eyes or 46.7% of candidate eyes losing BCVA) and Control (12 eyes or 52.2% of control eyes losing BCVA) Loss of 1 Line BCVA. Middle: Candidate (8 eyes or 53.3% of candidate eyes losing BCVA) and Control (11 eyes or 47.8% of control eyes losing BCVA) Loss of 2+ Lines BCVA. Right: Candidate (15 eyes) and Control (23 eyes) Loss of Total BCVA. X-axis represents number of eyes; Y-axis represents loss of BCVA categories.

Further investigation into loss of postoperative BCVA by individual candidate and control subgroup is presented in Table 6 and Table 7 with both raw data numbers and relative frequencies within each subgroup.

Table 6: Candidate Eyes That Lost BCVA by Subgroup and Relative Frequency of Total Subgroup Population. The number of eyes within each subgroup that lost either 1 line or 2+ lines of BCVA as a percentage of each subgroup population where n is the number of subjects.

	Subgroup 1a (K<35D) n= 25	**Subgroup 2a (K=35-35.99D) n=36**	**Subgroup 3a (K=36-36.99D) n=60**	**Subgroup 4a (K=37-37.99D) n=70**	**Total Candidates: n=191**
Loss of 1 Line BCVA	3 (12.0%)	1 (2.8%)	2 (3.3%)	1 (1.4%)	7 (3.7%)
Loss of 2+ Lines BCVA	4 (16%)	1 (2.8%)	1 (1.7%)	2 (2.9%)	8 (4.2%)
Total Loss of BCVA	**7 (28.0%)**	**2 (5.6%)**	**3 (5.0%)**	**3 (4.3%)**	**15 (7.9%)**
BCVA Not Lost	**18 (72.0%)**	**34 (94.4%)**	**57 (95.0%)**	**67 (95.7%)**	**176 (92.1%)**

Table 7: Control Eyes That Lost BCVA by Subgroup and Relative Frequency of Total Subgroup Population. The number of eyes within each subgroup who lost either 1 line or 2+ lines of BCVA as a percentage of each subgroup population.

	Subgroup 1b (K=38-38.99D) n=76	**Subgroup 2b (K=39-39.99D) n=70**	**Subgroup 3b (K=40-40.99D) n=24**	**Subgroup 4b (K≥41D) n=21**	**Total Controls: n=191**
Loss of 1 Line BCVA	8 (10.5%)	0 (0%)	4 (16.7%)	0 (0%)	12 (6.3%)
Loss of 2+ Lines BCVA	8 (10.5%)	3 (4.3%)	0 (0%)	0 (0%)	11 (5.8%)
Total Loss of BCVA	**16 (21.1%)**	**3 (4.3%)**	**4 (16.7%)**	**0 (0%)**	**23 (12.0%)**
BCVA Not Lost	**60 (82.2%)**	**67 (95.7%)**	**20 (83.3%)**	**0 (0%)**	**168 (88.0%)**

A chi-square test for independence was performed to examine if more eyes within the overall candidate group lost BCVA when compared to the overall control group. The relationship between these groups was not significant, X^2 (1, N=382) = 1.87, p = 0.17. A second chi-square test for independence was performed to examine if more eyes within one particular candidate subgroup lost more BCVA when compared to the other respective candidate subgroups. The relationship between these subgroups was significant, X^2 (3, N=191) = 16.19, p=0.001. A third chi-square test for independence was performed to examine if more eyes within one particular control subgroup lost more

BCVA when compared to the other respective control subgroups. The relationship between these subgroups was significant, X^2 (3, N=191), = 13.16, p = 0.004.

To better understand and statistically analyze the loss of BCVA within each subgroup, visual acuities were converted to logMAR(BCVA) and an overall mean visual acuity in logMAR(BCVA) was calculated before and after surgery for each particular subgroup. When comparing mean preoperative BCVA to mean postoperative BCVA within each subgroup, a single factor ANOVA test was conducted with the p-values presented below in Table 8 (candidate) and Table 9 (control).

Table 8: Candidate Subgroup Mean Preoperative and Postoperative BCVA Comparison. Significant p-values are bolded.

	Subgroup 1a (K<35D) n= 25	**Subgroup 2a (K=35-35.99D) n=36**	**Subgroup 3a (K=36-36.99D) n=60**	**Subgroup 4a (K=37-37.99D) n=70**	**Total Candidates: n=191**
P-value:	**0.02**	0.13	0.53	0.74	0.92

Table 9: Control Subgroup Mean Preoperative and Postoperative BCVA Comparison. Significant p-values are bolded.

	Subgroup 1b (K=38-38.99D) n=76	**Subgroup 2b (K=39-39.99D) n=70**	**Subgroup 3b (K=40-40.99D) n=24**	**Subgroup 4b (K≥41D) n=21**	**Total Controls: n=191**
P-value:	**0.001**	**0.02**	0.76	0.33	**0.01**

Follow-Up Data

The overall candidate group had a mean follow-up period of 283.59 days (9.34 months) ranging from 1 day to 1613 days. In contrast, the overall control group's mean follow-up period was 181.72 days (5.98 months) ranging from 1 day to 1455 days. A Two-Sample t-Test assuming Unequal Variance comparing the candidate and control mean follow-up durations was performed and a statistically significant difference was found, t(335) = 3.07, p = 0.002, two-tailed. The candidate and control subgroup data

including subgroup mean and standard deviation are presented below in Tables 10 and 11, respectively.

Table 10: Candidate Subgroup Follow-Up Duration

	Subgroup 1a (K<35D)	**Subgroup 2a (K=35-35.99D)**	**Subgroup 3a (K=36-36.99D)**	**Subgroup 4a (K=37-37.99D)**	**Overall:**
Follow-Up Mean (days):	274.4	257.72	278.83	308.70	283.59
SD:	396.86	361.87	367.70	417.12	378.89
Range (days):	1-1420	1-1420	1-1250	1-1613	1-1630

Table 11: Control Subgroup Follow-Up Duration

	Subgroup 1b (K=38-38.99D)	**Subgroup 2b (K=39-39.99D)**	**Subgroup 3b (K=40-40.99D)**	**Subgroup 4b (K≥41D)**	**Total:**
Follow-Up Mean (days):	207.04	156.37	238.04	110.19	181.72
SD:	295.32	204.39	343.54	110.39	258.12
Range (days):	1-1287	1-1105	1-1455	1-444	1-1455

A single factor ANOVA test was conducted to compare the mean follow-up duration, in days, between candidate subgroups 1a, 2a, 3a and 4a, see Table 12. The analysis of variance showed no significance between the subgroup means, $F(3, 187) = 0.156$, $p = 0.93$. A second single factor ANOVA test was conducted to compare the mean follow-up duration, in days, between control subgroup 1b, 2b, 3b and 4b, see Table 13. The analysis of variance showed no significance between the subgroup means, $F(3, 187) = 1.40$, $p = 0.25$.

Six of the candidate eyes were co-managed, meaning they did not return to Boston Eye Group/Boston Laser after their 1-day post-op and instead received their follow-up care from their regular ophthalmologist or optometrist who referred them for surgery. Seven of the control eyes were co-managed.

Surgery Type

For the purposes of our results, due to the similarities in healing time and vision stabilization, LASEK and PRK were combined together as Advanced Surface Ablation (ASA). Of the 191 candidate patients, 123 (64.4%) underwent LASIK and 68 (35.6%) underwent ASA surgery. In contrast, of the 191 control patients, 108 (56.5%) underwent LASIK, 83 (43.5%) underwent ASA surgery. A chi-square test for independence was performed to examine the relationship between candidate and control groups versus surgery type (LASIK or ASA). The relationship between these groups was not significant, X^2 (1, N=382) = 2.46, p = 0.12.

With regard to the candidate and control subgroups, surgery type is presented below in Table 12 and Table 13.

Table 12: Candidate Surgery Type by Subgroup. Candidate eyes that underwent LASIK surgery (top row) and ASA (bottom row) stratified by subgroup (columns). Results given in raw data and relative frequency.

	Subgroup 1a (K<35D) n=25	**Subgroup 2a (K=35-35.99D) n=36**	**Subgroup 3a (K=36-36.99D) n=60**	**Subgroup 4a (K=37-37.99D) n=70**	**Total Candidates: n=191**
LASIK	15 (60%)	29 (81%)	34 (57%)	44 (63%)	123 (64%)
ASA	10 (40%)	7 (19%)	26 (43%)	26 (37%)	68 (36%)

Table 13: Control Surgery Type by Subgroup. Control eyes that underwent LASIK surgery (top row) and ASA (bottom row) stratified by subgroup (columns). Results given in raw data and relative frequency.

	Subgroup 1b (K=38-38.99D) n=76	**Subgroup 2b (K=39-39.99D) n=70**	**Subgroup 3b (K=40-40.99D) n=24**	**Subgroup 4b (K≥41D) n=21**	**Total Controls: n=191**
LASIK	47 (62%)	42 (60%)	10 (42%)	9 (43%)	108 (57%)
ASA	29 (38%)	28 (40%)	14 (58%)	12 (57%)	83 (43%)

A chi-square test for independence was performed to examine if one particular candidate subgroup contained eyes that underwent a different surgery type distribution. The relationship between these groups was statistically significant, X^2 (1, N=191) = 4.37,

p = 0.04. A second chi-square test for independence was performed to examine if one particular control subgroup contained eyes that underwent a different surgery type distribution. The relationship between these groups was not significant, X^2 (1, N=191) = 4.97, p = 0.27.

Presented another way, the overall data of both candidate and control groups: 231 eyes underwent LASIK with 17 total eyes losing BCVA (7.4%) and 214 (92.6%) not losing BCVA. In contrast, 151 eyes underwent ASA with 21 total eyes losing BCVA (13.9%) and 130 (86.1%) not losing BCVA. A chi-square test for independence was performed to examine the relationship between overall postoperative BCVA (Loss of BCVA or No Loss of BCVA) and surgery type (LASIK or ASA). The relationship between these groups was significant, X^2 (1, N=382) = 4.37, p = 0.04.

Of the 15 candidate eyes that lost 1 or more lines of postoperative BCVA, 7 eyes (46.7%) underwent LASIK and 8 eyes (53.3%) underwent ASA. A chi-square test for independence was performed to examine if there was a difference in loss of BCVA between surgery type. The relationship between these groups was not significant, X^2 (1, N=191) = 2.23, p = 0.14. These 15 candidate eyes had a mean follow-up period of 248.8 days with a range from 1 day to 1420 days. Of the 8 candidate eyes that lost 1 or more lines of BCVA and underwent ASA, five eyes (62.5%) had the last documented follow-up before expected vision stabilization (1 day(x3), 7 days, and 18 days). Normal vision stabilization for ASA is 3 weeks to 3 months (Taneri, Weisberg, & Azar, 2011).

Of the 23 control eyes that lost 1 or more lines of postoperative BCVA, 10 eyes (45.5%) underwent LASIK and 13 eyes (56.5%) underwent ASA. A chi-square test for

independence was performed to examine if there was a difference in loss of BCVA between surgery type. The relationship between these groups was not significant, X^2 (1, N=191) = 1.12, p = 0.29. These 23 control eyes had a mean follow-up period of 39.3 days with a range from 1 day to 473 days. Of the 13 control eyes that lost BCVA and underwent ASA surgery, eight eyes (61.5%) had the last documented follow-up before expected vision stabilization (1 day, 4 days(x2), 6 days(x3), and 7 days(x2)). Normal vision stabilization for ASA is 3 weeks to 3 months (Taneri, Weisberg, & Azar, 2011).

Intraoperative Complications

Of the 191 candidate eyes, 17 eyes experienced intraoperative complications. Three LASEK eyes experienced an Epi Flap <180 (incomplete hemi-dissected flap), 5 LASEK eyes experienced flap removal (this rendered each procedure equivalent to PRK), 6 LASIK eyes experienced bubbles in the anterior chamber (AC) as a result of LASIK flap creation with a Femtosecond laser (requires the surgery be stopped for a length of time to allow the bubbles to dissipate naturally), 1 LASIK eye demonstrated a 2-4mm epithelial defect, 1 LASIK eye experienced a loss of suction during the first pass of docking with the Femtosecond laser with successful second pass, and 1 LASIK eye experienced a VBB (Vertical Gas Bubble Breakthrough) peripheral complication with the femtosecond laser flap creation. See Table 14 for complications within candidate subgroups breakdown. Of the 15 overall candidate eyes that lost BCVA, none experienced intraoperative complications.

Table 14: Eyes Within Candidate Subgroups Experiencing Intraoperative Complications. Raw numbers and relative frequencies

	Subgroup 1a (K<35D) n= 25	**Subgroup 2a (K=35-35.99D) n=36**	**Subgroup 3a (K=36-36.99D) n=60**	**Subgroup 4a (K=37-37.99D) n=70**	**Total Candidates: n=191**
Epi Flap <180	0	0	1 (1.7%)	1 (1.4%)	2 (1.0%)
LASEK Flap Removal	1 (4.0%)	0	3 (5.0%)	1 (1.4%)	5 (2.7%)
Bubbles in AC	0	2 (5.6%)	4 (6.7%)	0	6 (3.1%)
Epi Defect	0	0	1 (1.7%)	0	1 (0.5%)
Loss of Suction 1st Pass	0	0	0	1 (1.4%)	1 (0.5%)
VBB	0	0	1 (1.7%)	0	1 (0.5%)
Total:	1 (4.0%)	2 (5.6%)	10 (16.7%)	3 (4.3%)	16 (8.4%)

Of the 191control eyes, 26 eyes experienced intraoperative complications. Six LASEK eyes experienced an Epi Flap <180 (incomplete hemi-dissected flap), 16 LASEK eyes experienced flap removal, 2 LASIK eyes experienced bubbles in the anterior chamber as a result of LASIK flap creation with a Femtosecond laser, 1 LASIK eye demonstrated a 1mm epithelial defect, and 1 LASIK eye experienced a VBB peripheral complication with the Femtosecond laser flap creation. See Table 15 for complications within control subgroups breakdown. Of the 23 overall control eyes that lost BCVA after CRLS surgery, 18 eyes did not experience any intraoperative complications, 2 eyes experienced an Epi Flap <180, 2 eyes experienced flap removal, and 1 eye experienced a VBB peripheral complication.

Table 15: Eyes Within Control Subgroups Experiencing Intraoperative Complications. Raw numbers and relative frequencies.

	Subgroup 1b (K=38-38.99D) n=76	**Subgroup 2b (K=39-39.99D) n=70**	**Subgroup 3b (K=40-40.99D) n=24**	**Subgroup 4b (K≥41D) n=21**	**Total Controls: n=191**
Epi Flap <180	0	3 (4.3%)	1 (4.2%)	2 (9.5%)	6 (3.1%)
LASEK Flap Removal	1 (1.3%)	4 (5.7%)	4 (16.7%)	4 (19.0%)	13 (6.8%)
Bubbles in AC	0	1 (1.4%)	0	0	1 (0.5%)
Epi Defect	0	0	0	1 (4.8%)	1 (0.5%)
Loss of Suction 1st Pass	0	0	0	0	0
VBB	1 (1.3%)	0	0	0	1 (0.5%)
Total:	2 (2.6%)	8 (11.4%)	5 (20.8%)	7 (33.3%)	22 (11.5%)

DISCUSSION

This study was performed with the objective of exploring if patients undergoing CRLS with mathematically calculated postoperative keratometry values of <38D are at greater risk of losing one or more lines of BCVA after surgery. Furthermore, we wished to examine if the degree of corneal curvature flatness as designated by mathematically calculated postoperative keratometry values (K<35D, 35-35.99D, 36-36.99D, and 37-37.99D) was related to postoperative loss of BCVA, and if type of CRLS (LASIK vs. ASA) had any type of contributing role in predicting postoperative visual acuity.

Candidate-Control Matching

In terms of preoperative data, the lack of significant differences between overall visual acuity, manifest refraction (sphere and cylinder) and spherical equivalence demonstrates the candidates and controls were not significantly different with regard to planned treatment. Additionally, the lack of significant difference between percentage of eyes undergoing surgery type (LASIK or ASA) provides additional evidence that candidate and control patient populations were well matched. This demonstrates that any differences in postoperative visual acuity outcome between the overall candidate and control groups was not due to candidate-control mismatching and do not need to be considered further as confounding factors.

Overall Loss of BCVA

Numerically, 15 (7.85%) candidate eyes lost 1+ lines of BCVA compared to 23 (12.04%) control eyes that lost 1+ lines of BCVA. This result was not significant

($p<0.17$) indicating there was no evidence of an overall difference between instances of loss of BCVA between candidate eyes (K<38D) and control eyes (K≥38D).

Though not significant, these results indicating the control population actually had more eyes that lost postoperative BCVA compared to the candidate population, is not what we hypothesized and is different that the results found by Varssano et al. (2013). Varssano et al. (2013) found that when comparing the proportion of eyes with flat corneas (K<35D) and control eyes (K≥35D) who lost 1 or more lines of BCVA, there was no significant difference between the groups. There are several possible explanations for this discrepancy between our study and that 2013 study's results. First, our candidate groups were different. Varssano et al. (2013) studied eyes with flat corneas as defined by keratometry values under 35D whereas we studied candidate eyes with flat corneas as defined by keratometry values under 38D. However, we did subdivide our candidate group to include a K<35D subgroup with the results of this division discussed later. Second, Varssano's mean preoperative and mean postoperative data was different than ours. Varssano et al. (2013) found that their control group (K<35D) exhibited significantly worse mean preoperative BCVA and mean postoperative BCVA when compared to the control group (K≥35D) whereas we found no significant difference in overall mean preoperative BCVA and overall mean postoperative BCVA between our candidate and control groups.

Subgroup Loss of BCVA

A significant difference ($p<0.001$) was found between candidate subgroups when comparing loss of BCVA indicating that one or more subgroups contained more eyes that lost BCVA when compared to the other candidate subgroups.

Candidate Subgroup 1a (K<35D) had significantly worse postoperative visual acuity ($p<0.02$) when compared to preoperative visual acuity. This significant difference was not seen within the other candidate subgroups indicating Candidate Subgroup 1a contained significantly more eyes that lost 1 or more lines of BCVA compared to the other candidate subgroups. This is evident in the raw data with 28% of eyes experiencing BCVA loss after CRLS. This data is again different from Varssano et al. (2013). They found that their K<35D group had significantly worse preoperative and postoperative BCVA but no overall greater proportion of eyes that lost BCVA compared to the K≥38D group. Our data was the exact opposite with no significantly worse preoperative or postoperative BCVA compared to other subgroups, but a significantly greater proportion of eyes that lost BCVA. One possible explanation for this is that the data presented in this study is a random sampling of a larger data set. It is possible that the smaller sample size and sampling process could have contributed to our differing data due to sampling error.

A second study carried out by E. M. Mostafa in 2015 discussed visual acuity with regard to flat corneas. He focused on stratification of patients by degree of myopia (-6 to -7.9D, -8 to -9.9D, and -10 to -12D) and measured postoperative corrected distance visual acuity (CDVA) in patients with postoperative keratometry values <35D. His results were: 0.0±0.6 in the -6 to -7.9D group, 0.1±1.2 in the -8 to -9.9D group, and 0.13±1.3 in the -10

too -12D group. This data shows eyes with flat corneas and higher myopia degrees of myopia experienced worse postoperative CDVA outcomes but is difficult to relate to our data due to our project not stratifying patients by degree of myopia and Mostafa not stratifying patients by degree of corneal flatness groups as we did.

One possible explanation for our Candidate Subgroup 1a showing significant differences is that this subgroup had significantly higher myopia with a higher mean preoperative manifest spherical refraction (-8.2D) and mean preoperative spherical equivalence (-8.87D) when compared to the other candidate subgroups (see Table 4 in results section). Several studies over the years have indicated that patients with higher myopia, -8 to -14D, are at increased risk of losing BCVA if they undergo CRLS which were summarized in a recent Cochrane Review paper (Barsam, 2014). Additionally, higher myopia requires a percentage of corneal tissue to be altered (PTA) by laser surgery (Santhiago et al., 2016) and if patients already have flat corneas, a high PTA could put the patient at risk of removing too much corneal tissue, increasing their risk for ectasia postoperatively, and making the cornea too weak to refract effectively.

Another explanation for our Candidate Subgroup 1a showing significant differences could be if those eyes experienced a shorter follow-up duration that did not allow for full vision stabilization. However, analysis of follow-up data did not identify a significant difference in follow-up duration between candidate subgroups with Candidate Subgroup 1a experiencing an average follow-up duration of 274.4 days (see Table 12 in results section). This duration is short when considering patients are normally followed for 1 year after CRLS, but is not significantly different than the follow-up durations of

other candidate subgroups, or the overall candidate group, that did not lose postoperative BCVA.

A third explanation for our Candidate Subgroup 1a showing significant differences could be if those eyes experienced more intraoperative complications. However, again this was not the case as of the 17 candidate eyes that experienced intraoperative complications during CRLS, only 1 eye (LASEK flap removal) was part of the Candidate Subgroup 1a. Furthermore, a LASEK flap removal complication essentially renders the operation equivalent to PRK which does not have an increased risk of visual acuity reduction or BCVA loss.

Varssano et al. (2013) reported a mean follow-up period of 326± 327 days which is significantly longer than our paper which could contribute to our differing results. Mostafa (2015) did not report a follow-up period. Neither of the papers mentioned previously, Varssano et al. (2013) and Mostafa (2015), discussed intraoperative complications. A thorough literature review did not identify any additional studies that explored visual acuity outcomes in patients with flat corneas (either $K<35D$ or $K\geq38D$), therefore we have no other data to compare.

Additionally, a significant difference ($p<0.004$) was found between control subgroups when comparing loss of BCVA indicating that one or more subgroups contained more eyes that lost BCVA when compared to the other control subgroups.

Control Subgroup 1b (K=38-38.99D) and Control Subgroup 2b (K=39-39.99D) exhibited significantly worse postoperative visual acuity ($p<0.001$ and $p<0.02$ respectively) when compared to preoperative visual acuity. In terms of raw data, 21% of

eyes in Control Subgroup 1b experienced BCVA loss after CRLS while 4.3% of eyes in Control Subgroup 2b experienced BCVA loss after CRLS. Additionally, both Candidate Subgroup 3a and Candidate Subgroup 4a experienced higher or similar percentages of intraoperative complications (16.7% and 4.3% respectively), making intraoperative complications leading to loss of preoperative BCVA unlikely.

Again, possible explanations for these groups significant differences could potentially be preoperative myopia, follow-up duration, and intraoperative complications. Both Control Subgroup 1b and Control Subgroup 2b exhibited significantly higher degrees of myopia compared to the other two control subgroups with mean preoperative spherical manifest of -6.74D and -6.7D respectively and mean preoperative spherical equivalence of -7.25D and -7.29D respectively. It is interesting to note these values are nearly identical and they offer evidence that preoperative spherical manifest and spherical equivalence as relating to planned corneal tissue to be altered could account for an important impact on postoperative visual acuity. With regard to follow-up duration, all control subgroup follow-up durations were shorter than candidate durations, however, Control Subgroup 1b and Control Subgroup 2b did not have significantly shorter follow-up durations when compared to their control subgroup counterparts.

Lastly, Control Subgroup 1b contained two eyes that experienced intraoperative complications (flap removal and VBB) and Control Subgroup 2b contained eight eyes that experienced intraoperative complications (3 Epi Flap <180, 4 flap removal and 1 bubbles in AC). Though these raw numbers may seem high, when relative frequency is taken into account, these complications only represent 2.6% of Control Subgroup 1b and

11.4% of Control Subgroup 2b. Additionally, both Control Subgroup 3b and Control Subgroup 4b experienced much higher rates of intraoperative complications (20.8% and 33.3% respectively), making intraoperative complications influencing loss of postoperative BCVA less likely.

A thorough literature review did not identify any additional studies that investigated visual acuity outcomes in patients grouped and stratified by keratometry values over 38D so we have no data with which to compare and contrast.

It is important to note that our finding that the control eyes experienced a higher loss of BCVA postoperatively is different than the majority of articles studying visual acuity and patient satisfaction in post-CRLS patients. As stated previously patient satisfaction after LASIK is approximately 95.4% (Solomon et al., 2009), with patient satisfaction after ASA very similar (Diakonis et al., 2014). A possible explanation for our data's deviation from the accepted norm of LASIK/ASA success rates is that we did not have a true randomized control sample. Our control sample was matched to manifest refraction and spherical equivalence to the control sample who exhibited higher than average treatment plans. Additionally, our control group's significantly shorter follow-up duration when compared to the candidate patients most likely contributed to this apparent loss of BCVA as vision stabilization was not achieved in many patients.

Surgery Type

Given that there was no significance between the overall percentages of candidates undergoing LASIK or ASA and overall percentages of controls undergoing LASIK or ASA, this offers relevant evidence the candidate and control groups were well

matched by surgery type. Additionally, the lack of significance between candidate and control subgroups with regard to choice of surgery shows that not only were the candidate eyes well matched to the control eyes but there was similar breakdown of surgery type across subgroups.

However, when looking at total candidate and control eyes that lost BCVA versus eyes that did not lose BCVA, significantly more eyes that lost BCVA underwent ASA (7.4% LASIK vs. 13.9% ASA). A possible explanation for this lies in the follow-up duration of eyes undergoing ASA. Approximately 62.5% of the candidate eyes and 61.5% of the control eyes that lost BCVA and underwent ASA had follow-up durations shorter than the recommended time for vision stabilization.

The data makes it impossible to rule out choice of surgery (LASIK or ASA) as a confounding factor for loss of postoperative BCVA. However, the inconsistency in follow-up duration indicates no clear conclusion can be made with regard to the influence of type of CLRS on postoperative vision outcomes.

We were not able to find any literature investigating the effect of LASIK or ASA choice on postoperative visual acuity outcomes in flat corneas. Varssano et al. (2013) only investigated patients undergoing PRK whereas Mostafa (2015) only investigated patients undergoing LASIK.

Current Study Limitations and Future Studies

The first major limitation of this study is the use of mathematically calculated predicted postoperative keratometry values. Though the practice of using a mathematical formula and preoperative data to predict if a patient is a good candidate for CRLS from a

corneal curvature point of view is quite commonplace (Varssano et al., 2013), there is still a question of the validity of this mathematical formula as a prediction tool due to lack of studies performed to test the correlation between predicted and measured postoperative keratometry values. Further large-scale controlled studies to test this correlation are warranted.

For the purposes of this thesis, only mathematically calculated postoperative keratometry values were used. To further test the validly of this study, measured postoperative calculations and their correlation with postoperative visual acuity would offer greater evidentiary support to our findings and provide a more accurate exploration of the relationship between postoperative keratometry and visual acuity. Again, further large-scale controlled studies to test this relationship are warranted.

Next, though 191 candidate and 191 control eyes are significant enough to make this thesis study valid, sampling error due to a small sampling size could have possibly skewed our results. Future studies should take steps to avoid this by increasing sample size to include larger and more significant patient population.

Another potential limitation of this thesis is the lack of uniformity in follow-up durations both within and between the candidate and control groups. In future studies, a minimum follow-up duration of 3 weeks should be set as part of the inclusion criteria to ensure all patients have experienced vision stabilization.

Though patients were screened with a questionnaire for past ocular disorders or surgeries, it is possible that some patients suffered from undiagnosed diseases or disorders of the macula. In a future study, candidate screening protocols could include a

Macular Optical Coherence Tomography (OCT) to rule out any retinal changes which could account for a change in vision outcome. Additionally, patients were not evaluated for postoperative complications such as Dry Eye Syndrome (DES) or ectasia. Beyond glare and halos which can reduced patient's satisfaction with CLRS postoperatively but do not necessarily have an impact on visual acuity, both DES and ectasia can reduce visual acuity postoperatively. These could potentially be addressed in future studies to reduce the number of possible confounding factors.

In conclusion, though our study provided evidence that there is no relationship between our overall group of patients who end up with a corneal curvature of K<38D after surgery and loss of BCVA. However, our data did indicate that when the candidate group was stratified by degree of corneal curvature, eyes with very flat corneas (K<35D) may be at in increased risk of losing BCVA after CRLS. Further studies including an expanded patient population and follow-up duration should be carried out in the future. With regard to the relationship between visual acuity outcomes and type of surgery undergone, our data provided evidence that eyes undergoing ASA may be at increased risk of losing BCVA though further studies are needed.

Additionally, the main goal of this thesis was to determine if there is a relationship between flat corneas and loss of postoperative BCVA. Further studies should be conducted to explore in more detail why a loss of BCVA may occur in flat corneas.

REFERENCES

Adib-Moghaddam, S., Arba-Mosquera, S., Walter-Fincke, R., Soleyman-Jahi, S., & Adili-Aghdam, F. (2016). Transepithelial Photorefractive Keratectomy for Hyperopia: A 12-Month Bicentral Study. *Journal of Refractive Surgery*, *32*(3), 172–180. https://doi.org/10.3928/1081597X-20160121-01

Alio, J. L., Rosman, M., & Mosquera, S. A. (2010). Minimally Invasive Refractive Surgery. In *Minimally Invasive Ophthalmic Surgery* (pp. 97–122). Springer Berlin Heidelberg.

Amano, S., Kashiwabuchi, K., Sakisaka, T., Inoue, K., Toda, I., & Tsubota, K. (2016). Efficacy of Hyperopic Photorefractive Keratectomy Simultaneously Performed With Phototherapeutic Keratectomy for Decreasing Hyperopic Shift. *Cornea*, *35*(8), 1069–1072.

Barsam, A., & Allan, B. D. (2014). Excimer laser refractive surgery versus phakic intraocular lenses for the correction of moderate to high myopia. In The Cochrane Collaboration (Ed.), *Cochrane Database of Systematic Reviews*. Chichester, UK: John Wiley & Sons, Ltd. Retrieved from http://doi.wiley.com/10.1002/14651858.CD007679.pub4

Bastawrous, A., Silvester, A., & Batterbury, M. (2011). Laser refractive eye surgery. *British Medical Journal*, *342*(May 2011), d2345–d2345. https://doi.org/10.1136/bmj.d2345

Basting, D., Djeu, N., & Jain, K. (2005). Historical Review of Excimer Laser Development. In D. D. Basting & P. D. G. Marowsky (Eds.), *Excimer Laser Technology* (pp. 8–21). Springer Berlin Heidelberg. Retrieved from http://link.springer.com/chapter/10.1007/3-540-26667-4_2

Bower, K. S., Sia, R. K., Ryan, D. S., Mines, M. J., & Dartt, D. A. (2015). Chronic dr eye in photorefractive keratectomy and laser in situ keratomileusis: Manifestations, incidence, and predictive factors. *Journal of Cataract & Refractive Surgery*, *41*, 2624–2634. https://doi.org/10.1016/j.jcrs.2015.06.037

Boyd, K. (2013, September 1). What Is Presbyopia? Retrieved February 17, 2017, from https://www.aao.org/eye-health/diseases/what-is-presbyopia

Boyd, K. (2016, March 1). Important Things to Know About Contact Lenses. Retrieved February 17, 2017, from https://www.aao.org/eye-health/glasses-contacts/contact-lens-information

Christiansen, S. M., Neuffer, M. C., Sikder, S., Semnani, R. T., & Moshirfar, M. (2012). The effect of preoperative keratometry on visual outcomes after moderate myopic LASIK. *Clinical Ophthalmology*, *6*, 459–464. https://doi.org/10.2147/OPTH.S28808

Cobo-Soriano, R., Llovet, F., Gonzalez-Lopez, F., Domingo, B., Gomez-Sanz, F., & Baviera, J. (2002). Factors that influence outcomes of hyperopic laser in situ keratomileusis. *Journal of Cataract & Refractive Surgery*, *23*, 1530–1538.

Cochrane, G. M., du Toit, R., & Le Mesurier, R. T. (2010). Management of refractive errors. *British Medical Journal*, *340*(apr12 1), c1711–c1711. https://doi.org/10.1136/bmj.c1711

Diakonis, V. F., Kankariya, V. P., Kymionis, G. D., Kounis, G., Kontadakis, G., Gkenos, E., … Pallikaris, I. G. (2014). Long Term Followup of Photorefractive Keratectomy with Adjuvant Use of Mitomycin C. *Journal of Ophthalmology*, *2014*, 1–5. https://doi.org/10.1155/2014/821920

Dowling, J. E., & Dowling, J. L. (2016). *Vision: How It Works and What Can Go Wrong*. MIT Press. Retrieved from http://books.google.com/books?hl=en&lr=&id=JA_XCwAAQBAJ&oi=fnd&pg=PR7&dq=%22Anterior+to+the+lens+is+a+watery+fluid,+the+aqueous%22+%22the+choroid,+a+highly+vascular+tissue+that+supplies+the%22+%22smaller+blood+vessels+that+provide+oxygen+and%22+&ots=wMDiNvMRIY&sig=WGf1X1SfoEbmEy13xXENSjmBq-s

Durr, N. J., Dave, S. R., Lage, E., Marcos, S., Thorn, F., & Lim, D. (2014). From Unseen to Seen: Tackling the Global Burden of Uncorrected Refractive Errors. *Annual Review of Biomedical Engineering*, *16*(1), 131–153. https://doi.org/10.1146/annurev-bioeng-071813-105216

Eye Health Statistics - American Academy of Ophthalmology. (n.d.). Retrieved February 17, 2017, from https://www.aao.org/newsroom/eye-health-statistics#_edn18

Hansen, R. S., Lyhne, N., Grauslund, J., Grønbech, K. T., & Vestergaard, A. H. (2015). Four-year to seven-year outcomes of advanced surface ablation with excimer laser for high myopia. *Graefe's Archive for Clinical and Experimental Ophthalmology*, *253*(7), 1027–1033. https://doi.org/10.1007/s00417-014-2920-z

Hashemi, H., Salimi, Y., Pir, P., & Asgari, S. (2017). Photorefractive Keratectomy With Mitomycin-C for High Myopia: Three Year Follow-Up Results. *Acta Medica Iranica*, 42–48.

Helzner, J. (2010, September 1). Can You Revive Your Refractive Surgery Practice? Retrieved February 17, 2017, from http://www.ophthalmologymanagement.com/issues/2010/september-2010/can-you-revive-your-refractive-surgery-practice

Holladay, J. T. (1997). Proper Method for Calculating Average Visual Acuity. *Journal of Refractive Surgery*, *13*(July/August), 388–391.

Holladay, J. T., Moran, J. R., & Kezirian, G. M. (2001). Analysis of aggregate surgically induced refractive change, prediction error, and intraocular astigmatism. *Journal of Cataract & Refractive Surgery*, *27*(1), 61–79.

Khurana, A. K. (2007). *Comprehensive Ophthalmology (4)*. Daryaganj, IN: New Age International. Retrieved from http://site.ebrary.com/lib/alltitles/docDetail.action?docID=10323376

Kim, C. Y., Song, J. H., Na, K. S., Chung, S.-H., & Joo, C.-K. (2011). Factors influencing corneal flap thickness in laser in situ keratomileusis with a femtosecond laser. *Korean Journal of Ophthalmology*, *25*(1), 8–14. https://doi.org/10.3341/kjo.2011.25.1.8

Koivula, A., & Zetterström, C. (2009). Phakic intraocular lens for the correction of hyperopia. *Journal of Cataract & Refractive Surgery*, *35*(2), 248–255. https://doi.org/10.1016/j.jcrs.2008.10.039

Luger, M. H. A., Ewering, T., & Arba-Mosquera, S. (2012). Consecutive myopia correction with transepithelial versus alcohol-assisted photorefractive keratectomy in contralateral eyes: One-year results. *Journal of Cataract & Refractive Surgery*, *38*(8), 1414–1423. https://doi.org/10.1016/j.jcrs.2012.03.028

Luz, A., Lopes, B., Salomão, M., & Ambrósio, R. (2016). Application of corneal tomography before keratorefractive procedure for laser vision correction. *Journal of Biophotonics*, *9*(5), 445–453. https://doi.org/10.1002/jbio.201500236

Marcos, S., Velasco-Ocana, M., Dorronsoro, C., Sawides, L., Hernandez, M., & Marin, G. (2015). Impact of astigmatism and high-order aberrations on subjective best focus. *Journal of Vision*, *15*(11), 4. https://doi.org/10.1167/15.11.4

Melki, S. A., & Azar, D. T. (2001). LASIK complications: etiology, management, and prevention. *Survey of Ophthalmology*, *46*(2), 95–116.

Mescher, A. L. (2016). *Junqueira's Basic Histology* (Fourteenth). New York, NY: McGraw-Hill Education. Retrieved from http://accessmedicine.mhmedical.com.ezproxy.bu.edu/content.aspx?bookid=1687&sectionid=108453529

Michael, R., & Bron, A. J. (2011). The aging lens and cataract: a model of normal and pathological aging. *Philosophical Transactions: Biological Sciences*, *366*(1568), 1278–1292.

Mostafa, E. M. (2015). Effect of Flat Cornea on Visual Outcome after LASIK. *Journal of Ophthalmology*, *2015*, 1–7. https://doi.org/10.1155/2015/794854

NHIS - Tables of Summary Health Statistics. (2015). Retrieved February 17, 2017, from https://www.cdc.gov/nchs/nhis/SHS/tables.htm

Ormonde, S. (2013). Refractive surgery for keratoconus: Refractive surgery for keratoconus. *Clinical and Experimental Optometry*, *96*(2), 173–182. https://doi.org/10.1111/cxo.12051

Pinheiro, F. I., Araújo-Filho, I., Meneses do Rego, A. C., Pereira de Azevedo, E., Tabosa do Egito, E. S., Oréfice, F., & Alves de Souza Lima Filho, A. (2016). New drug delivery system for corneal administration of mitomycin-C. *Journal of Cataract & Refractive Surgery*, *42*(8), 1216–1223. https://doi.org/10.1016/j.jcrs.2016.04.035

Rao, S. K., Cheng, A. C., Fan, D. S., Leung, A. T., & Lam, D. S. (2001). Effect of preoperative keratometry on refractive outcomes after laser in situ keratomileusis. *Journal of Cataract & Refractive Surgery*, *27*(2), 297–302.

Santhiago, M., Giacomin, N., Smadja, D., & Bechara, S. (2016). Ectasia risk factors in refractive surgery. *Clinical Ophthalmology*, 713. https://doi.org/10.2147/OPTH.S51313

Schallhorn, S. C., Venter, J. A., Hannan, S. J., Hettinger, K. A., & Teenan, D. (2015). Effect of postoperative keratometry on quality of vision in the postoperative period after myopic wavefront-guided laser in situ keratomileusis. *Journal of Cataract & Refractive Surgery*, *41*(12), 2715–2723. https://doi.org/10.1016/j.jcrs.2015.06.034

Shah, S., & Dua, H. S. (2000). The Changing Face of Refractive Surgery: Several Promising Techniques are Already Available. *British Medical Journal*, *320*(7232), 395–396.

Shape, Curvature, and Power. (n.d.). Retrieved February 20, 2017, from https://www.aao.org/bcscsnippetdetail.aspx?id=99d3bbfa-cd4e-4615-9bd9-8119c0d7bc7a

Silberner, J. (1980). The Eyes Have It. *Science News*, *118*(22), 346. https://doi.org/10.2307/3965181

Solomon, K. D., Fernández de Castro, L. E., Sandoval, H. P., Biber, J. M., Groat, B., Neff, K. D., … Lindstrom, R. L. (2009). LASIK World Literature Review: Quality of Life and Patient Satisfaction. *Ophthalmology*, *116*(4), 691–701. https://doi.org/10.1016/j.ophtha.2008.12.037

Soong, H. K., & Malta, J. B. (2009). Femtosecond Lasers in Ophthalmology. *American Journal of Ophthalmology*, *147*(2), 189–197.e2. https://doi.org/10.1016/j.ajo.2008.08.026

Stein, H., A., Stein, R. M., & Freeman, M. I. (2013). *The Ophthalmic Assistant: A Text for Allied and Associated Ophthalmic Personnel* (Ninth). Saunders Elsevier. Retrieved from https://expertconsult.inkling.com/read/stein-ophthalmic-assistant-9th/the-ophthalmic-assistant-a-text

Stuart, A. (2012, August 1). Contact Lenses: When a Solution Is the Problem. Retrieved February 17, 2017, from https://www.aao.org/eyenet/article/contact-lenses-when-solution-is-problem

Stulting, R. D., Carr, J. D., Thompson, K. P., Waring III, G. O., Wiley, W. M., & Walker, J. G. (1999). Complications of laser in situ keratomileusis for the correction of myopia. *Ophthalmology*, *106*(1), 13–20. https://doi.org/10.1016/S0161-6420(99)90000-3

Taneri, S., Weisberg, M., & Azar, D. T. (2011). Surface ablation techniques. *Journal of Cataract & Refractive Surgery*, *37*(2), 392–408. https://doi.org/10.1016/j.jcrs.2010.11.013

Taneri, S., Zieske, J. D., & Azar, D. T. (2004). Evolution, techniques, clinical outcomes, and pathophysiology of LASEK: review of the literature. *Survey of Ophthalmology*, *49*(6), 576–602. https://doi.org/10.1016/j.survophthal.2004.08.003

Varssano, D., Waisbourd, M., Minkev, L., Sela, T., Neudorfer, M., & Binder, P. S. (2013). Visual Acuity Outcomes in Eyes With Flat Corneas After PRK. *Journal of Refractive Surgery*, *29*(6), 384–389. https://doi.org/10.3928/1081597X-20130515-02

Williams, L. B., Dave, S. B., & Moshirfar, M. (2008). Correlation of visual outcome and patient satisfaction with preoperative keratometry after hyperopic laser in situ keratomileusis. *Journal of Cataract & Refractive Surgery*, *34*(7), 1083–1088. https://doi.org/10.1016/j.jcrs.2008.03.018

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