2020

A retrospective analysis of dry eye interventions during the first postoperative year of patients undergoing LASIK versus PRK

BOSTON UNIVERSITY

SCHOOL OF MEDICINE

Thesis

A RETROSPECTIVE ANALYSIS OF DRY EYE INTERVENTIONS DURING THE FIRST POSTOPERATIVE YEAR OF PATIENTS UNDERGOING LASIK VERSUS PRK

by

PAMELA BASTOS RIBEIRO

B.A., Boston University, 2017

Submitted in partial fulfillment of the

requirements for the degree of

Master of Science

2020

Approved by

First Reader

Linda Afifi, Ph.D.
Assistant Professor, Anatomy & Neurobiology

Second Reader

Jason Brenner, M.D.
Ophthalmologist, specialized in Cornea and Refractive Surgery
Boston Eye Group | Boston Laser

ACKNOWLEDGMENTS

I would like to thank the following individuals for their valued insight and assistance with my thesis: Jason Brenner M.D., Linda Afifi Ph.D., and Samir Melki M.D., Ph.D.

A RETROSPECTIVE ANALYSIS OF DRY EYE INTERVENTIONS DURING THE FIRST POSTOPERATIVE YEAR OF PATIENTS UNDERGOING LASIK VERSUS PRK

PAMELA BASTOS RIBEIRO

ABSTRACT

INTRODUCTION: There are two main procedures responsible for correcting refractive error: laser-assisted in situ keratomileusis (LASIK) and photorefractive keratectomy (PRK). The most common postoperative complication of all laser vision correction (LVC) surgeries is keratoconjunctivitis sicca, or dry eye. In addition to physical irritation, dry eye can cause poor visual acuity and reduced quality of life. There are inconsistencies in the literature about which procedure results in higher rates of dry eye thus we explored the likelihood of a dry eye intervention within the first year after surgery.

METHODS: Performing a retrospective chart review of all patients who underwent LVC procedures between 2009-2019 at a private Boston ophthalmology clinic, we were able to quantify the proportion of patients that required postoperative dry eye interventions within the 12 months following surgery. At this clinic, a dry eye intervention was defined as one of two treatments: punctal plug insertion or prescription medication (Restasis or Xiidra) use.

RESULTS: A total of 11,175 LASIK eyes from 5,920 individuals, 1,549 LASEK eyes from 880 individuals, and 2,006 PRK eyes from 1,165 individuals were included in the analysis. Comparing the proportion of LASIK dry eye interventions to the proportion of

PRK/LASEK dry eye interventions via a 2-sample z-test at an alpha level of significance of 0.05, yielded a z-value= 5.7 and a p-value= <0.0001 at a 95% CI (0.0102 - 0.0208). **CONCLUSION:** Our results suggest a greater incidence of postoperative dry eye interventions for PRK/LASEK patients compared to LASIK patients in the 12 months following LVC surgery. This study was limited in regards to both objective and subjective indicators of dryness; therefore future studies should attempt to be more comprehensive in evaluating postoperative dry eye. However, this study should help surgeons in the decision making process of which refractive eye surgery to recommend in order to reduce postoperative dry eye incidence and improve overall patient quality of life and satisfaction.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF ABBREVIATIONS

ALK…… Automated Lamellar Keratoplasty

CAM-1……..……..Intracellular Adhesion Molecule-1

LASIK.....Laser-Assisted In Situ Keratomileusis

LASEK……...……Laser-Assisted Subepithelial Keratectomy

LFA-1……...……. Lymphocyte Function-Associated Antigen-1

LVC……...…..Laser Vision Correction

MMC……Mitomycin C

NGF…….Nerve Growth Factor

PRK.....Photorefractive Keratectomy

PRT……Phenol red test

TBUT……...……...…… Tear film Breakup Time

INTRODUCTION

OCULAR CONDITIONS

The most common ophthalmic disorders in the world are refractive errors: myopia (nearsightedness) and hyperopia (farsightedness) (Hendriks et al., 2017). In myopia the axial length of the eye has elongated beyond normal. In the eye's development, the vitreal chamber has expanded outside the ideal amount, and leads to an eye that is longer than the optimal length. As a result, the image of distant objects will fall anterior to the photoreceptors of the retina and will cause distant objects to be out of focus, hence why myopic individuals tend to see near objects better than far objects (Figure 1 E, Morgan et al., 2012).

Hyperopia is the opposite issue. In hyperopia, the vitreal chamber did not expand enough to meet the optimal eye length and results in an eye that is shorter than the ideal length. In hyperopia, the image of distant objects will fall behind the photoreceptors of the retina (Figure 1 D, Morgan et al., 2012). When the image falls behind the retina, the lens of the eye may be able to move the image forward onto the photoreceptors through a process called accommodation.

Accommodation allows the eye to alter the power of the lens in order to view objects at different distances. In the absence of stimulation, the ciliary muscle is relaxed, zonular fibers are tense, and the lens is stretched thinly to refract light for distant vision. When stimulation causes the ciliary muscle to contract, zonular fibers relax, and cause the lens to thicken and become more spherical to refract light for near vision (F.M.

Toates 1972). Myopia generally necessitates a greater need for correction (i.e. glasses, contact lenses, or refractive surgery) because the image is falling before the retina and therefore cannot be as well accommodated for (Morgan et al., 2012).

Emmetropia refers to an eye that has no visual defects because the length of the eye is precisely the length required to produce a distant object image onto the photoreceptors (Figure 1 A, Morgan et al., 2012). Emmetropic eyes can then accommodate for near objects, because the image of a near object will fall behind the retina (Figure 1 B Morgan et al., 2012) and can utilize accommodation to bring the image forward onto the photoreceptors (Figure 1 C, Morgan et al., 2012). Emmetropia is the ideal visual status.

Astigmatism is another common visual disorder that leads to blurred vision. In astigmatism, either the cornea is irregularly shaped on the surface of the eye, or the lens inside of the eye is irregularly curved. Either of these abnormalities can lead to the redirection of light from properly focusing onto the photoreceptors of the retina resulting in the blurring of images and decreased visual acuity. In regular astigmatism, there is consistent steepening of the cornea along one axis of the eye (Corneal topography and astigmatism). This steady corneal elevation can be corrected through the application of a cylindrical lens, aligned to the axis of steepening (Corneal topography and astigmatism). On the other hand, in irregular astigmatism, there is inconsistent steepening of the cornea or curving of the lens, which cannot be corrected through the application of a cylindrical lens (Corneal topography and astigmatism). Irregular astigmatism can result in visual aberrations and reduce best-corrected visual acuity (Corneal topography and

astigmatism). The application of a rigid gas-permeable contact lens may help in flattening these irregular elevations by making the surface more uniform thereby improving visual acuity (Corneal topography and astigmatism). Since traditional excimer laser ablation can correct spherocylindrical errors, it is important to differentiate regular from irregular astigmatism (Corneal topography and astigmatism). Traditional excimer laser ablation, however, cannot effectively treat irregular astigmatism; topography-guided ablation may be more useful instead. As long as the irregularities are not caused by early ectatic disorders, which would be absolute contraindications for refractive surgery, topography-guided ablation may be performed (Corneal topography and astigmatism) (Table 2).

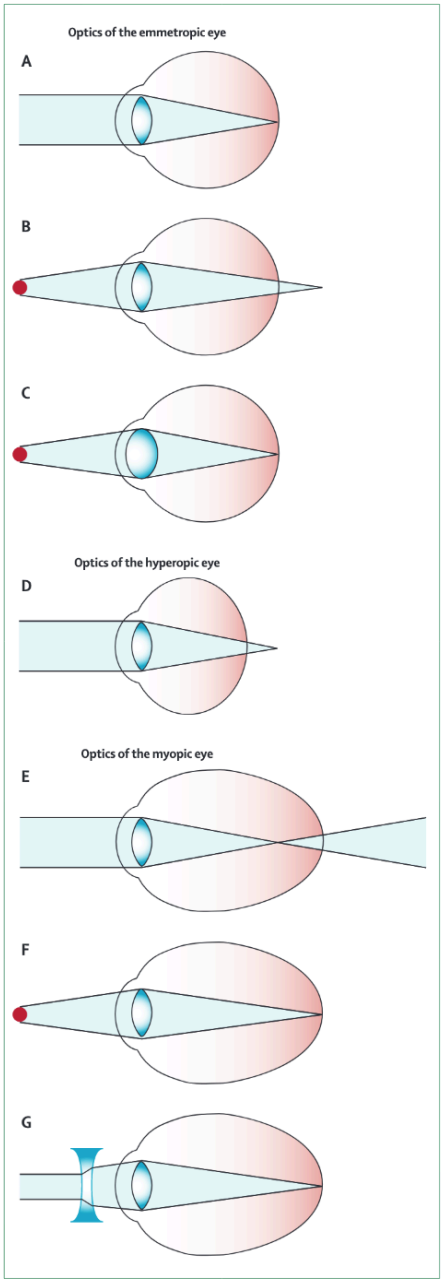

Figure 1. The Optics of Various Ocular Conditions. A: illustrates the emmetropic eye focusing on a distant object perfectly onto the photoreceptors of the retina. B: illustrates how the emmetropic eye focusing on a near object will produce an image that falls behind the photoreceptors of the retina. C: illustrates the emmetropic eye accommodating a near object onto the photoreceptors by contracting the ciliary muscle, relaxing the zonular fibers, and thickening the lens to refract light for near vision. D: illustrates the shorted axial length of a hyperopic eye, and how a distant object will produce an image behind the photoreceptors. E: illustrates the elongated axial length of a myopic eye, and

how a distant object will produce an image in front of the photoreceptors. F: illustrates the myopic eye focusing on a near object and how that brings the image backward onto the photoreceptors. G: illustrates the application of a diverging contact lens to bring the image onto the photoreceptors (Morgan et al., 2012).

LASER EYE SURGERY

Laser vision correction (LVC) procedures allow for the correction of myopia, hyperopia, and astigmatism. Utilizing LVC procedures comes with both advantages and disadvantages. Since 81% of young adults and 88% of older adults admit to falling short of contact lens hygiene recommendations, they run the risk of several complications ranging from discomfort, to pain, to microbial keratitis, and even blindness (Risky Contact Lens Use, 2017) (Improper Contact Lens Use Associated with Increased Risk of Infections, 2018). In addition to complications resulting from improper care, contact lens wearers are also at risk of developing contact lens-induced dry eye (CLIDE) and contact lens-induced limbal stem cell deficiency (LSCD). CLIDE may result from a number of different factors including ocular surface anatomy, lubricity, contact lens material and design, as well as hormonal changes, environmental hazards, and pre-existing conditions (Alzahrani et al., 2017). LSCD is the dysfunction and/or destruction of stem cell precursors within the corneal epithelium (Rossen et al., 2016). LSCD hinders the ability of the corneal epithelium to heal and repair in both normal and disease states (Rossen et al., 2016). The mechanical trauma to the ocular surface from contact lens use can lead to LSCD (Rossen et al., 2016).

Undergoing refractive eye surgery means eliminating these risks associated with wearing contact lenses. Also to the benefit of the patient, correcting vision through the

use of LVC procedures means that they will no longer spend money on replacing lenses, frames, and/or repairing loosened or damaged glasses. For contact lens wearers, this means eliminating the recurring cost of ordering new lenses, contact solution, cases, and the like. For many, in addition to the elimination of these costs, the procedure also allows for increased convenience in sports activities like swimming and skiing, which require the use of goggles and make wearing glasses more challenging. For others, LVC allows them to pursue certain career fields like police enforcement and military roles, where vision requirements need to be met without the use of optical correction (i.e. without glasses or contact lenses) (Reilly et al., 2010). LVC is also in high demand simply because it allows the patient to eliminate glasses as part of one's aesthetic, which can be desirable especially for those who struggle to use contact lenses.

Two of the major techniques used in laser eye surgery today include laser-assisted in situ keratomileusis (LASIK) and photorefractive keratectomy (PRK). According to current literature, there is great similarity between the two procedures. Refractive eye surgery in general is bolstered as one of the safest and most efficacious procedures (Gomel et al., 2018).

PRK

PRK is primarily used in the treatment of myopia, hyperopia, and astigmatism. PRK is a procedure that allows for reshaping of the cornea, via excimer laser, which then allows for the appropriate focusing of light onto the retina to correct refractive error. Prior to reshaping, a thin outer layer of the cornea is removed with the application of a

20% ethanol solution, and then the epithelium is wiped away and discarded (Wilkinson et al., 2017). The laser is then fired to reshape the newly exposed cornea. The epithelial defect heals over the newly reshaped cornea over a few days after the procedure (Wilkinson et al., 2017). In the meantime, a bandage contact lens is place over the newly exposed cornea along with an application of antibiotic and steroid drops in order to protect the cornea from pathogens, inflammation, and desiccation. The bandage contact lens will act as a substitute epithelium for a few days postoperatively and will require reapplication of the antibiotic and steroid drops to prevent infection, as the lens will not be removed until the epithelium has healed.

PRK may be recommended as the corrective procedure for patients who anticipate a future potential for facial trauma (Iskander et al., 2001). This could include police enforcement, military personnel, and professional athletes. Since there is no flap creation involved in PRK, there is no risk of traumatic flap displacement (Reilly et al., 2010). PRK thereby reduces the risk of having to correct for a dislocated flap, which can cause pain and reduce vision until readjusted by an ophthalmic professional (Iskander et al., 2001) (Reilly et al., 2010).

PRK WITH MMC

Mitomycin C is an antimetabolite often utilized during PRK procedures. MMC functions in two ways to prevent corneal haze after laser ablation. Firstly, MMC impedes corneal keratocyte activation (Sia et al., 2014). Secondly, MMC initiates corneal kertatocyte apoptosis (Sia et al., 2014). Combining both of these functions, MMC acts to

disrupt the normal wound healing process of the cornea, thus aiding in the reduction of new cell development and clouding of the tissue. MMC has been shown to work most effectively in preventing both corneal and stromal haze for patients with moderate to high myopia, that is, greater than -6.00 diopters (Sia et al., 2014).

LASEK

Laser-Assisted Subepithelial Keratectomy is considered to be a subcategory of PRK. Instead of using a highly concentrated amount of alcohol, LASEK requires the use of dilute alcohol as to keep the epithelium intact as a flap, but loose enough to separate it from the underlying corneal tissue (Sia et al., 2014). LASEK also requires the salvation of this epithelium, where instead of discarding the layer in PRK, LASEK requires actually carefully placing this tissue back onto the surface of the eye after laser correction of the cornea beneath. This may allow the patient's epithelium to function comparably to a bandage contact lens made out of one's own cellular matter.

LASIK

LASIK is a more recently developed technique compared to PRK. LASIK is performed to correct the same visual issues as PRK. LASIK itself is a combination of automated lamellar keratoplasty (ALK) and PRK (Lindstrom et al., n.d.). In LASIK surgery, instead of completely removing the epithelium, a thin flap of cornea is outlined, sliced, and peeled back. This flap of cornea will remain attached and is later flipped down

and repositioned over the newly laser-corrected cornea (Mori et al., 2017). Flaps can be generated in one of two ways: mechanical microkeratome or femtosecond laser.

Traditional mechanical microkeratomes use an oscillating-blade to physically slice a flap in the cornea for LASIK surgery (Goel & Pathak 2015). The femtosecond laser, on the other hand, is a bladeless method that utilizes short pulses of free electrons to photodisrupt corneal tissue to generate microscopic gas bubbles (Patel et al., 2007). These bubbles are lined up side-by-side and can thereby be cleaved and separated using a LASIK spatula to connect the bubbles and flip down the flap (Patel et al., 2007).

According to Moshirfar et al. (2010), LASIK with mechanical microkeratomes results in significantly more epithelial defects than femtosecond laser LASIK, but femtosecond laser LASIK has significantly more diffuse lamellar keratitis than microkeratome LASIK. However, femtosecond laser technology may be safer than mechanical microkeratomes because it allows for greater precision and predictability in flap thickness execution (Patel et al., 2007). And in regards to dryness, femtosecond flaps had a lower incidence of LASIK-associated dry eye compared to mechanical microkeratome flaps (Salomão et al., 2009). Therefore both flap-generating methods have advantages and disadvantages, but it seems that the femtosecond laser is overall more favorable.

The flap created from the LASIK procedure, though thin, slices deeper into the cornea than both PRK and LASEK. As a result, LASIK requires patients to have a specific range of corneal thickness in order for the procedure to be successful. At the

Boston Eye Group | Boston Laser, only the bladeless method of femtosecond laser is used to generate LASIK flaps.

PRK VS LASIK

Main differences between the two categories of LVC highlight that LASIK tends to provide a faster recovery time, and that the surgical technique is less painful than PRK (Reilly et al., 2010). There are also some considerations as to why a patient may be a good candidate for one procedure type over another. Two of the major preoperative criteria evaluated are corneal thickness and dry eye status.

Generally, the cornea ranges between 530-560μm in a normal adult, however it can fluctuate from person to person (Sutton et al., 2014). In order to reduce the risk of central or peripheral corneal thinning, otherwise known as ectasia, surgeons must aim to leave the stromal bed with 250-300μm of thickness after flap creation and photo-ablation (Sutton et al., 2014). Since the flap itself requires a thickness of 90-110μm for the femtosecond laser and 100-150μm for the microkeratome, surgeons must ensure preoperative corneal thickness is between 490-500μm to safely execute a LASIK procedure (Sutton et al., 2014). In the case that a patient does not have this degree of corneal thickness, LASIK would not be recommended, and the patient would be encouraged to pursue PRK or another corrective procedure.

Preoperative dryness may also impact the decision of which LVC procedure to select. Since most patients who develop dry eye post-LASIK do not show preoperative symptoms, it can be useful to note those who are already predisposed to dryness prior to

operating. For example, patients with the autoimmune condition Sjögren's syndrome, may present with inflamed lacrimal glands, reduced tear levels, and therefore be at greater risk of developing significant dry eye irritation postoperatively (Sutton et al., 2014). These aforementioned considerations are just a couple of the relative contraindications of LASIK surgery (Table 1, Sutton et al., 2014), but there are several absolute contraindications that apply specifically to LASIK, and should be noted (Table 2, Sutton et al., 2014).

Table 1. Relative Contraindications of LASIK Surgery. Major considerations that must be acknowledged, accounted for, and perhaps readjusted in order to perform the LASIK procedure in a safe and efficacious manner (modified from: Sutton et al., 2014).

Moderate/Severe Dry eye symptoms (may be managed postoperatively with artificial tears or punctal plugs)
Recurrent corneal erosions (mild cases may be eligible, otherwise PRK is recommended)
Atopic disease
Autoimmune disorders
Thin cornea
Glaucoma
Breastfeeding

Table 2. Absolute Contraindications of LASIK Surgery. Exclusion criteria that would make a patient ineligible to pursue LASIK surgery (modified from: Sutton et al., 2014).

Unstable refraction (>0.5 diopter change over the past 1yr)
Insufficient central corneal thickness (reliant on depth of ablation)
History of keratoconus
History of herpes simplex keratitis or herpes zoster ophthalmicus
Abnormal corneal topography
Significant corneal scarring
Visually significant cataract

Pregnancy
Uncontrolled systemic or ocular disease
Unrealistic patient expectations

In the end, regardless of whether the treatment type selected is LASIK or PRK, results from both procedures become comparable after one year (Shortt et al., 2013). It has been noted that patients of younger age, low myopia, and male gender experience greatest efficacy for their refractive treatments, but overall there is no difference between the safety and efficacy of PRK compared to LASIK (Gomel et al., 2018).

DRY EYE

Development of keratoconjunctivitis sicca, or dry eye, is one of the most commonly reported postoperative complications of both PRK and LASIK eye surgery. It is noted in up to 50% of patients (Schallhorn et al., 2019). Photo-ablation of sensory nerve plexuses in the cornea after both PRK and LASIK, is the main contributor to dry eye, but alterations to lacrimal gland function as well as dysfunction between the ocular surface and upper eyelid can also result in dry eye (Bower et al., 2015). There have been many postulations as to why dry eye develops in refractive surgery patients, some of which are highlighted in Figure 2 (Toda 2018).

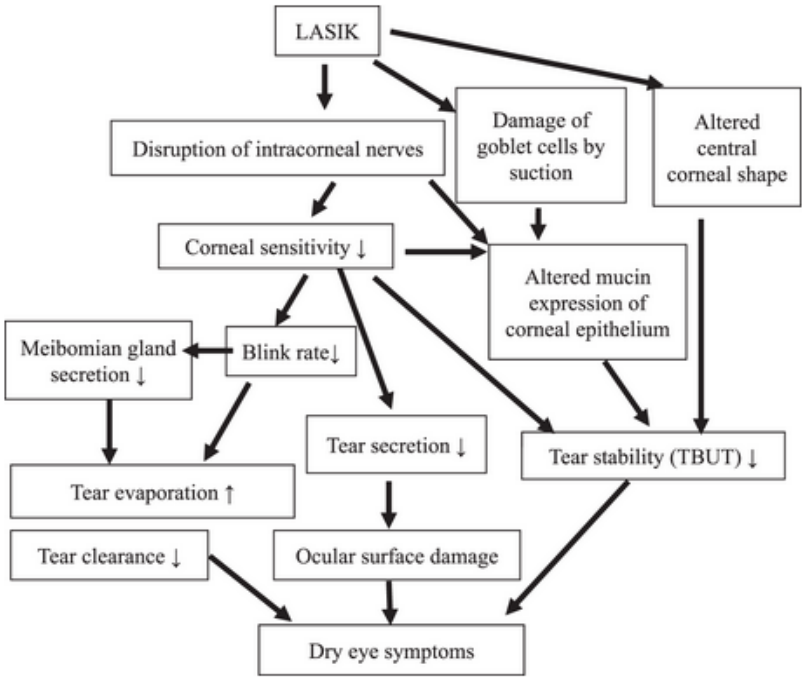

Figure 2. The Possible Mechanisms Involved in Post-LASIK Dry Eye. This network model illustrates the various contributing factors that can lead to a result of dry eye symptoms after LASIK surgery (Toda, 2018).

Currently, it is widely believed that LASIK procedures result in greater amounts of postoperative dry eye diagnoses. This is based on the idea that the femtosecond laser slices through more nerve plexuses during flap formation than the epithelium removal does during PRK. Since LASIK must cut the eye at a greater depth than the alcohol penetrates during PRK, it is thought to lead to more dryness (He & Bazan, 2010). As explained by Toda 2018, the denervation is thought to contribute to a greater amount of dryness by reducing the sensitivity of the cornea to air and other irritants thus leading to a decreased blinking reaction, and ultimately resulting in greater evaporation of the surface tear film and exposing the eye to increased levels of dryness (Figure 2).

Although dry eye can result from both PRK and LASIK procedures, according to Schallhorn et al. (2019), patients who underwent PRK were more likely to report an increase in dry eye symptoms 3-months postoperatively compared to those who underwent LASIK. This is contrary to the widely held belief that LASIK results in greater dry eye symptoms.

During both LASIK and PRK, the anterior stromal nerves are disrupted because of the excimer laser photo-ablation sustained to reshape the cornea (He & Bazan, 2010). However, specifically during LASIK both the epithelial nerve bundles and the superficial stromal nerve branches in the flap are severed, whereas in PRK only the epithelial nerve bundles incur damage (He & Bazan, 2010). This would suggest that LASIK is more disruptive to the nerves that supply the lacrimal glands, and therefore impact tear levels more significantly than PRK.

The results of the Schallhorn et al. (2019) study indicated however, that at least in the near postoperative term, less than 12 months after surgery, it was PRK rather than LASIK that left patients feeling greater amounts of dry eye discomfort. Schallhorn et al. (2019) contributed their findings to a variety of potential contributing factors such as delayed corneal nerve healing after LASIK and perhaps due to epithelial instability causing a dryness sensation after PRK.

In addition to the above explanations for dryness after refractive surgery, there is also a loss of conjunctival goblet cells reported after LASIK surgery (He & Bazan, 2010). This results directly from utilization of the suction equipment applied to the eye during flap creation. These conjunctival goblet cells are composed mainly of mucins, which help

adhere the tear film to the superficial epithelium (He & Bazan, 2010). Maintaining the tear film is crucial in preventing dry eye as it protects the outer surface of the eye from desiccation.

Another potential factor contributing to postoperative dry eye is simply the inflammatory changes that occur from the ablation of laser-mediated procedures (He & Bazan, 2010). Inducing inflammation at or near nerve endings could lead to cytokine-mediated irritation, resulting in damage of the nerves and surrounding eye tissue leading to dysfunction (He & Bazan, 2010). Inflammation could also lead to further aggravation of a previously existing dry eye condition (He & Bazan, 2010). General postoperative inflammation can lead to prolonged nerve recovery time, reduced tear film quality, and ultimately increase ocular surface exposure. Whatever the exact reason may be, it is clear that this more recent literature suggests short-term dry eye to be more prominent in PRK rather than LASIK, rebutting the current views on refractive surgery and postoperative dryness.

DRY EYE INTERVENTIONS

In the event that a patient develops dry eye, there are a handful of current treatment options available to mediate the symptoms. The initial treatment is always to utilize over-the-counter preservative-free artificial tears. If symptoms persist and patients find themselves applying artificial tears more often than four times a day, doctors may recommend more aggressive forms of treatment (Shtein, 2011). Physical punctal occlusion, prescription immunosuppressants, application of scleral gas-permeable contact

lenses, and/or utilization of autologous serum tears are all potential ways to alleviate persistent dry eye discomfort.

PUNCTAL OCCLUSION

Punctal plugs can be inserted into either the upper or lower lid puncta. Occluding the nasolacrimal canaliculi in patients with moderate tear levels effectively mimics the placement of a plug into a sink drain. Instead of allowing the tears to quickly wash away from the ocular surface, insertion of punctal plugs act to keep the tears collecting on the corneal surface allowing for the maintenance of a proper hydration level (Shtein, 2011). Punctal plug insertion thereby also functions to extend the time required before another application of artificial tears (Melton & Randall, 2004). Punctal plugs are a safe, reversible, and effective way to preserve the ocular tear film during the treatment of dry eye (Shtein, 2011).

There are two main kinds of punctal plugs: dissolvable temporary plugs and permanent plugs. Dissolvable plugs can be used to assess the need for permanent plug insertion since they only last between three days and six months, they can help determine if symptoms improve prior to permanent occlusion (Baxter & Laibson, 2004). These absorbable, temporary plugs are most commonly made out of collagen (Baxter & Laibson, 2004; Figure 3).

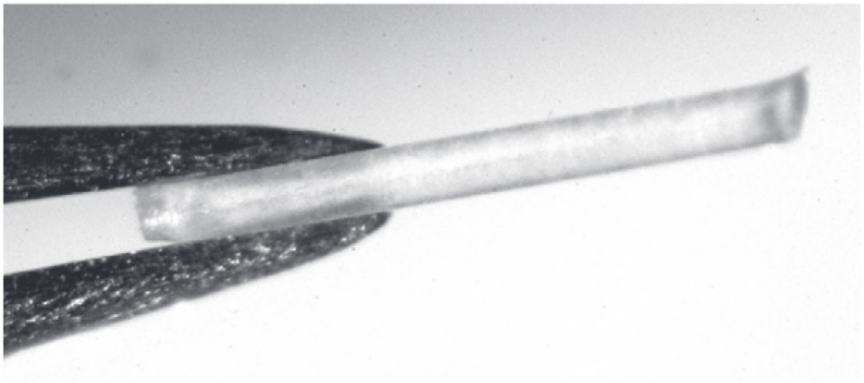

Figure 3. Dissolvable Punctal Plug. Photographed above is a temporary collagen plug, which is typically inserted to prevent short-term nasolacrimal drainage of tears in patients with persistent dry eye (Baxter & Laibson, 2004).

Permanent plugs are non-absorbable and will maintain punctal occlusion indefinitely unless removed by an ophthalmic professional. The permanent plugs are most commonly made out of silicone (Baxter & Laibson, 2004; Figure 4). Permanent plugs may be removed after long-term resolution of symptoms, or if they become bothersome for the patient (Baxter & Laibson, 2004; Figure 5).

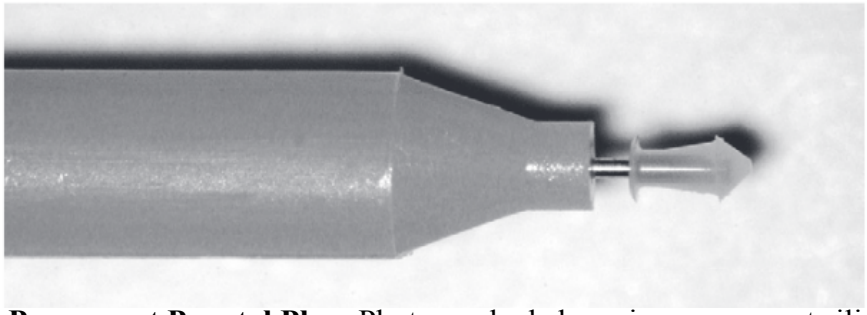

Figure 4. Permanent Punctal Plug. Photographed above is a permanent silicone plug on its insertion device. Permanent plugs are typically inserted to prevent long-term nasolacrimal drainage of tears in patients with a good response to puncta occlusion for alleviation of persistent dry eye symptoms (Baxter & Laibson, 2004).

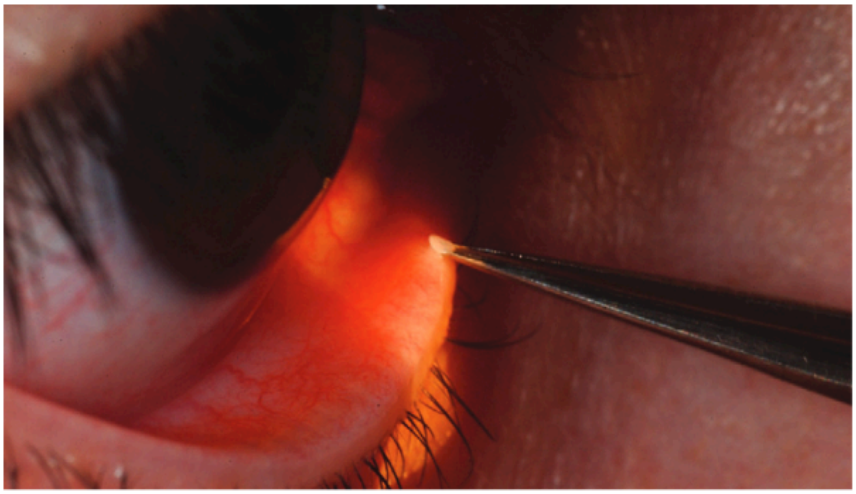

Figure 5. Punctal Plug Removal. Photographed above is the removal of a punctal plug from the lower lid nasolacrimal tear duct by means of surgical jewelers (Baxter & Laibson, 2004).

In patients with compromised tear levels and punctal plugs, frequent reapplication of artificial tears is necessary to prevent tear film stagnation (Melton & Randall, 2004). If these tears are left to buildup, pro-inflammatory cytokines may concentrate and worsen the symptoms of dry eye (Melton & Randall, 2004). Dry eye is therefore not simply exacerbated by tear drainage and desiccation of the ocular surface, but also has an inflammatory component, and as such, can be mediated through the use of anti-inflammatory medications (Shtein, 2011).

IMMUNOSUPPRESSANTS

A number of factors can elicit a disruption of the ocular tear film stability and osmolarity. Imbalances can lead to stress-associated activation of pro-inflammatory kinases, cytokines, chemokines, matrix metalloproteinases, and eventually propagate an immune signaling cascade resulting in T-cell activation and proliferation (Stevenson et

al., 2012). Once activated, T-cells can stimulate secretion of interleukin 17, which promotes epithelium destruction by further promoting cytokines, chemokines, and matrix metalloproteinases (Stevenson et al., 2012). This cycle of inflammation then epithelium destruction, can be deleterious if left uncontrolled. Corticosteroids, cyclosporine, and lifitegrast are all immunosuppressants used to mediate inflammation in dry eye disease.

CORTICOSTEROIDS

Corticosteroids are a class of hormones that act to alleviate inflammation through the inhibition of pro-inflammatory molecules (Stevenson et al., 2012). Nerve growth factor (NGF) is one such molecule that has been detected in elevated concentrations in the tears of patients diagnosed with dry eye disease (Yang et al., 2006). NGF may thereby play a role in perpetuating inflammation (Yang et al., 2006). Corticosteroids may help to reduce ocular surface nerve growth factor and increase conjunctival goblet cell density thus mitigating causes of dryness (Yang et al. 2006). As previously stated, the conjunctival goblet cells and mucins help in stabilizing the tear film to the corneal surface. Aiding to maintain tear viscosity and prevent breakup during the blink response, loss of these cells and mucins can lead to perpetuation of dry eye symptoms (Pflugfelder et al., 2008).

Two common corticosteroids prescribed to treat dry eye are prednisolone acetate and loteprednol etabonate. Patients treated with corticosteroids exhibited rapid anti-inflammatory activity and significantly decreased dry eye complaints within one week of treatment (Yang et al., 2006). However, long-term therapy of patients with topical

corticosteroids should not be advised. Due to risk factors involved with extended use of corticosteroids, healthcare providers should avoid prescribing corticosteroids as they can lead to increased susceptibility to infection, increased intraocular pressure, and cataract formation (Shtein, 2011).

CYCLOSPORINE

An alternative to corticosteroids is cyclosporine. Cyclosporine 0.05% is a topical immunosuppressive agent shown to inhibit T-cell proliferation (Stevenson et al., 2012). Cyclosporine acts to inhibit calcineurin, an enzyme that activates T-cells, and therefore through its inhibition, will aid in preventing the inflammatory cycle from reigniting (Colligris et al. 2014). It not only inhibits this vicious cycle of inflammation, but it has also been shown to increase conjunctival goblet cell density as well (Pflugfelder et al., 2008). Cyclosporine thereby manages dry eye through multiple avenues, similar to corticosteroids, but without the added risk for long-term damage.

The commonly prescribed brand of topical 0.05% cyclosporine for the treatment of dry eye is Restasis. Approved by the FDA in 2003, Restasis has been the primary choice of topical cyclosporine for dry eye, and functions mostly as described above. More recently however, in 2018, the FDA approved a drug called Cequa, also for the treatment of dry eye. Cequa is similar to Restasis in that they both utilize cyclosporine as their active ingredient, but Cequa 0.09% cyclosporine ophthalmic solution differs from Restasis 0.05% cyclosporine ophthalmic solution in one major way. Cequa utilizes a

novel nanomicellar delivery vehicle allowing it to provide a higher concentration of cyclosporine into the eye.

Nanomicelles are 10-100nm in size, and are composed of a hydrophobic center, encased by a hydrophilic outer coat (Vadlapudi & Mitra, 2013). This specific arrangement allows hydrophobic cyclosporine to be transported within what is essentially a hydrophilic bubble, which can then directly penetrate hydrophilic structures in the eye like the stroma (Vadlapudi & Mitra, 2013). In doing so, nanomicelles allow for increased concentrations of active ingredient to be delivered since the cyclosporine is protected from degradation inside of this transportation vesicle (Vadlapudi & Mitra, 2013).

LIFITEGRAST

Although cyclosporine has been determined to be both safe and efficacious by the FDA, it may take upwards of 3 months to achieve its full therapeutic effect, and can cause patient discomfort via instillation site burning (Perry et al., 2008). So another option used to treat dry eye is lifitegrast. Lifitegrast is a lymphocyte function-associated antigen 1 (LFA-1) antagonist ("Lifitegrast (Xiidra) for Dry Eye Disease", 2017). Lifitegrast utilizes another inflammation pathway to reduce ocular surface irritation. By binding to LFA-1, lifitegrast prevents leukocyte binding to intracellular adhesion molecule-1 (ICAM-1), and inhibits its ability to activate the T-cell pro-inflammatory cascade (Perez et al., 2016). Lifitegrast is also soluble and rapidly absorbed due to its aqueous sodium salt formulation, allowing it to be isotonic with human tears, and

permeable at therapeutic concentrations through all ocular tissues (Perez et al., 2016).

GAS-PERMEABLE SCLERAL CONTACT LENSES

A method for alleviating severe, post-LASIK dry eye symptoms is through the use of gas-permeable scleral contact lenses (Shtein, 2011). Scleral contact lenses are larger than standard soft contact lenses. Instead of covering just the iris of the eye, scleral lenses also cover the whites of the eyes and therefore provide a barrier against air exposure and lock in moisture over a larger surface area than standard contact lenses. Scleral lenses also have a reservoir space between the inside of the lens and actual contact with the surface of the eye. This reservoir space is therefore ideal to fill with aqueous hydrating solutions in order to provide a continuous source of moisture for those with dry eye (Doan & Delcampe, 2016). Scleral contact lenses also offer another benefit for dry eye in the fact that they provide a physical shield against frictional irritation from the eyelids rubbing against the epithelial surface of the eye (Doan & Delcampe, 2016). This reduction in mechanical aggravation may allow the corneal epithelium to regenerate and heal from dry eye inflammation (Doan & Delcampe, 2016). In a study conducted by Kok & Visser (1992), improvement in visual acuity was also noted after the use of scleral lenses for the treatment of dry eye (Kok & Visser, 1992).

AUTOLOGOUS SERUM TEARS

As an alternative to over-the-counter and prescription artificial tears, some patients may be recommended autologous serum tears to treat dry eye. Since many

commercially available artificial tears contain preservatives and emulsifiers, patients with sensitivities may find them to be irritating especially if applying tears more often than four times a day (Fox et al., 1984). Autologous serum tears are a way to avoid these unnecessary additives because they are created from a patient's own blood. After drawing a sample, the blood is allow to coagulate, and is then spun down using a centrifuge to separate the cellular matter and clotting factors from the liquid portion of the blood, otherwise known as the serum (Fox et al., 1984). An amount of sterile, preservative-free saline solution is then added to dilute the serum to a proper consistency.

The benefit of the autologous serum tear is not only the removal of aforementioned additives and irritants, but also the additional source of epithelial growth factors and anti-inflammatory agents present in our blood serum (Shtein, 2011). Autologous serum tears have been shown to be both safe and efficacious in the treatment of post-LASIK dry eye (Noda-Tsuruya et al., 2006). Compared to traditional artificial tears, autologous serum tears were shown to prolong tear film breakup time (TBUT) at six months postoperatively, and reduce rose Bengal ocular surface staining at both one and three months postoperatively (Noda-Tsuruya et al., 2006).

Longer TBUT time indicates improved adhesion and reduced desiccation of the epithelial tear film, while reduced rose Bengal staining indicates fewer damaged corneal cells. Although improvements in both of these categories suggest that autologous serum tears offer a multifaceted approach to objectively improving dry eye, in subjective scoring for dryness, patients did not report significant differences between autologous serum and traditional artificial tears (Noda-Tsuruya et al., 2006).

IMPLICATIONS OF POSTOPERATIVE DRY EYE

As previously stated, dry eye is one of the most common complications of photorefractive surgery (Schallhorn et al., 2019). The development of chronic dry eye after PRK or LASIK, however, is rare (Bower et al., 2015). According to a study conducted by Bower et al. (2015), after 12 postoperative months only 5% of PRK and 0.8% of LASIK participants developed chronic dry eye. Although *chronic* dry eye is uncommon after LVC, symptoms of mild short-term dryness *are* common (Hovanesian et al., 2001). This study will therefore focus on cases of postoperative dry eye interventions prior to the 12-month mark.

A small prospective study (n= 68 eyes) conducted by Murakami and Manche (2012) found that patients self-reported dry eye symptoms most notably in the first month after surgery. There were no statistical differences between the LASIK and PRK first-month dryness, however, and symptoms appeared to be temporary as dryness returned to preoperative levels in both patients at 12 months postoperatively (Murakami & Manche, 2012). The study did recognize its small sample size as a limitation to their analysis.

Impeding on normal daily activities like reading and using a computer, the effects of dry eye can prove devastating. The impact of dry eye has been shown to not only decrease patients' quality of life, but it can also reduce workplace productivity and negatively impact patients' financial wellbeing as it prevents them from performing otherwise standard workforce responsibilities (Uchino & Schaumberg, 2013). The aim of this study is to thus expand the cohort size and objectively quantify whether there is a difference in short-term postoperative dry eye between LASIK and PRK patients.

SPECIFIC AIMS

Since the safety and efficacy results between PRK and LASIK eye surgeries are comparable, it is reasonable to further examine differences in the developed complications between these two procedures. Given that dry eye is one of the most common complications of refractive eye surgery, it will be the focus of this study. Due to the adverse effects on quality of life associated with dry eye, patient dissatisfaction prompts this investigation to determine whether one refractive laser therapy yields less of this undesirable outcome than the other. By evaluating which patients required more postoperative dry eye interventions, we may be able to determine whether it is LASIK or PRK that is responsible for more dry eye diagnoses, and can thereby make more informed decisions in patient treatment options.

METHODS

STUDY DESIGN

A retrospective chart review of patients' electronic medical records from a private ophthalmology clinic, Boston Eye Group | Boston Laser, was conducted. The data was extracted using the electronic health record system NextGen, and the information was de-identified to make patient protected health information anonymous. The review included surgical and postoperative follow-up data from the time interval of January 1, 2010 through December 16, 2019. This dataset yielded 182 LASIK eyes, 80 LASEK eyes, and 33 PRK eyes that received dry eye interventions from a total of 14,730 eyes.

For the analysis, a dry eye intervention was defined as having either a medication prescribed or a punctal plug placed within 1 year of the patient's procedure date. The two most commonly prescribed medications for dry eye at this clinic during this time period were Xiidra and Restasis, therefore these were the only medications accounted for in this analysis.

All patients outside of these parameters were excluded. There was no additional inclusion criterion. At this clinic, LASEK was performed prior to the more recent conversion to PRK; therefore LASEK and PRK values will be combined and classified as surface ablation procedures. Considering the large sample sizes, a 2-tailed, 2-sample z-test statistical analysis was performed (Sergeant, 2018) to determine any quantifiable differences in dry eye intervention proportions between the two types of LVC procedures: surface ablation versus LASIK (Sergeant, 2018).

CORNEAL REFRACTIVE LASER SURGERY CONSULTATION

When patients present to the clinic for an LVC evaluation, there are specific criteria that must be met in order to determine which procedure type will elicit the best results. Information collected prior to the physical examination includes: basic demographics, referrals, co-management status, and patient profession. A history is also obtained to determine whether patients have undergone previous refractive or other eye surgeries, have any eye diagnoses, have any allergies to medications, take any current medications, or have any systemic health conditions. Patients are also asked to disclose whether they wear glasses, how often they use their glasses, and the age of their most recent pair. Patients are also asked whether they wear contact lenses, date of their last

use, and whether or not they experience dryness in and out of their lenses. The date of last contact lens use is important as contact lenses can alter the shape of the cornea and lead to discrepancies in topographical data.

After the background information has been collected, patients proceed to a physical examination. First, patients are asked to extend their arms out fully in front of themselves, forming a triangle with their thumbs and index fingers. The 20/400 large "E" is placed on the eye chart and patients are asked to center the "E" in the middle of their triangle. Patients are told to focus on the "E" and not move their hands at all. The technician will then cover each of the patient's eyes, one at a time, and ask the patient whether or not they are still able to see the "E". If executed correctly, only one eye will be able to see the "E", and the other eye will not. The eye that can still see the "E" is labeled as the patient's dominant eye.

Eye dominance is particularly useful for LVC when patients are opting for monovision. Monovision is when the dominant eye is corrected for distance vision, while the non-dominant eye is corrected for near vision. Most candidates for monovision are approaching 40 years of age and are hyperopic. This combination of features is regarded as presbyopia. Monovision helps presbyopic patients to delay their need for reading glasses as they age. The majority of younger patients will not receive monovision, and will be corrected for distance in both eyes.

Uncorrected distance and uncorrected near (if over 40 years of age) visual acuity is recorded for each individual. Patients will then be evaluated again with correction (contact lenses, or preferably glasses). Contact lens prescriptions will be recorded based

on patient recollection, existing medical records, or from their contact lens box. Glasses prescriptions can more accurately be determined utilizing a lensometer.

Patients are then tested for an objective refraction using a Nidek Tonoref II combination auto refractometer and auto keratometer. The objective refraction values from the Nidek Tonoref I, or comparable equipment, serve as a baseline for the patient's manifest refraction, which is then fine-tuned to obtain the patient's best-corrected visual acuity using the patient's preferences in lenses for a final prescription. The auto keratometer provides both the flattest and steepest corneal curvatures, known as the flat K and steep K respectively. Preoperative and postoperative kertatometry are important indicators of refractive outcome and visual prognosis (Mostafa, 2015) (Christiansen et al., 2012).

Next, pachymetry values for central and thinnest corneal thickness are collected using a Ziemer Ophthalmology Galilei G4 or Pentacam. As previously stated, corneal thickness is a crucial measurement to the determination of whether a patient is a good candidate for LASIK since the flap generation requires a substantial amount of corneal tissue. Surgeons must ensure preoperative thickness is at least 500μm to safely execute LASIK (Sutton et al., 2014).

Preoperative dry eye is also assessed by means of an Oasis Medical Zone-Quick phenol red test (PRT). Administration of a PRT involves the technician requesting the patient to stare straight ahead, and one eye at a time beginning with the right, will lower the patient's lower eyelid and place a small yellow thread inside approximately 1/3 from the patient's lateral canthus. The patient is directed to shut both eyes for fifteen seconds,

and then the thread is removed. A chemical reaction occurs between the patient's tears and the originally yellow thread, turning it red. The volume of residual tear film in the inferior conjunctival sac is thought to be measured as the liquid travels down the length of the thread turning it red on a scale of 1-30 millimeters (Sakamoto et al., 1993). However, in a study conducted by Tomlinson et al. (2001), there was no clear experimental evidence to indicate that PRT measures tear production or tear volume. Instead they proposed that PRT reflects some other aspect of tears that allows for the determination of a dry eye patient as a result of different thread absorption based on biophysics and tear composition (Tomlinson et al., 2001). The PRT value should thus be considered a supplemental tool for determining preoperative dryness in addition to patient self-reported dryness and current patient medications. PRT alone should not be recognized as a diagnostic tool for determining dry eye.

Scotopic pupil diameter is another measurement recorded during evaluation. Scotopic pupil diameter determines the full size of the optical zone. The optical zone is the diameter of cornea that receives the laser correction treatment. Historically, scotopic pupil diameter has been used as a marker to determine whether a patient may experience more visual aberrations or night vision complaints like halos, glare, and starbursts (Salz & Trattler, 2006) (Figure 6) (Chang, 2016).

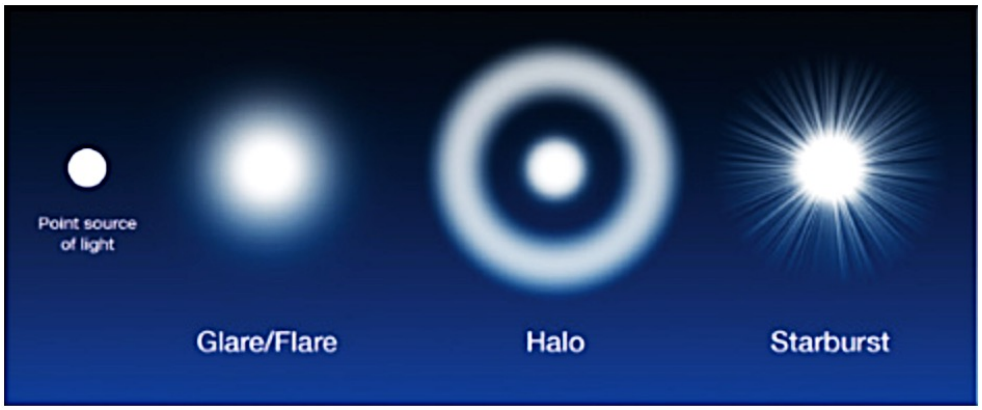

Figure 6. **Night Vision Complaints Illustrated**. When looking at a point source of light (i.e. the first image above), patients with larger scotopic pupils may experience more visual aberrations at nighttime like: glare—which expands light and makes it appear more fuzzy, halos—where a point source appears to have a defined ring of light around it, or starbursts—where lines of light appear to shoot out and surround a point source. All of these visual disturbances can make driving or other nighttime activities more challenging and uncomfortable (Chang, 2016).

Scotopic pupil diameter is measured by turning off the lights in the exam room, closing window blinds, and turning off computer monitors. Patients are then instructed to cover their left eye with their left hand, but to keep both eyes open. The Oasis Medical Colvard Pupilometer is then pressed against the patient's right eye, and the patient is told to look for a small infrared light. As the patient focuses on this light, the pupilometer essentially functions as a ruler and the technician records the pupil diameter to the closest increment of 0.5mm. Patients then switch sides and the left pupil diameter is also recorded.

Literature regarding whether large pupil size is a risk factor for visual aberrations and night vision complaints is conflicting, but the conservative practice is to warn patients that large pupil diameter may pose potential disturbances, as recommended by the United States Food and Drug Administration (Salz & Trattler, 2006).

Next, preoperative intraocular pressure is measured using one of three devices: the non-contact Nidek Tonoref II, the Reichert Technologies Tono-Pen, or the Goldmann applanation tonometer. For the Tono-Pen and Goldmann tonometer, patients have one drop of 0.5% proparacaine hydrochloride ophthalmic solution instilled in each eye to numb the cornea and diminish the blinking reflex.

After pressure is recorded, patients are determined as either requiring or not requiring dilation. Patients who are either co-managed with a recorded dilation in the past 12 months, or hold a diagnosis of presbyopia do not require dilation. For all other patients, one drop of 1% tropicamide ophthalmic solution is instilled in each eye. Dilation requires 10-15 minutes for the anticholinergic properties of tropicamide to relax the iris sphincter muscles and ciliary muscles responsible for accommodation. Once full dilation is achieved, patients undergo a cycloplegic refraction to determine changes in manifest prescription now that the accommodation muscles have been paralyzed and cannot adjust the vision.

Lastly the surgeon performs a fundus and slit-lamp examination. After reviewing all of the compiled information, evaluating the risks and benefits of each procedure, while keeping the goals of the patient in mind, the surgeon is proposes the best treatment option.

LASEK/PRK SURGICAL PROCEDURE

For patients undergoing PRK/LASEK at the Boston Eye Group | Boston Laser, a 20% ethanol solution is prepared using 2cc of 100% ethanol, and 8cc of sterile water. The

solution is then injected into a trephine using a 23-gauge cannula. Patient's lids are taped back using tegaderm and held open using a surgical speculum. The trephine containing alcohol is then held onto the cornea for 40 seconds before a Weck-Cel Eye Spear soaks it up. The eye is then dowsed in saline solution before epithelium displacement. For LASEK, the epithelium is gently lifted using a LASEK spatula. For PRK, a spatula and Weck-Cel Eye Spear are used to gently wipe away and remove the epithelium.

The Alcon EX500 wavelight excimer laser is then fired for the designated treatment length; typically taking 1.4 seconds per diopter of correction. After both LASEK and PRK, a 0.2mg/mL MMC soaked corneal light shield is applied for a length of time based on ablation depth. The shield is removed and cold saline rinses the eye again before re-applying the epithelium (LASEK), or placing a bandage contact lens (PRK) onto the freshly treated eye, protecting the cornea until the one-week postoperative follow-up visit. One drop of steroid and one drop of antibiotic are each administered onto the eye as: 1% prednisolone and 0.5% moxifloxacin. Finally, the eye is dilated with 1% cyclopentolate, and the patient is either discharged from surgery or has the same procedure repeated for the other eye.

LASIK SURGICAL PROCEDURE

For patients undergoing LASIK at the Boston Eye Group | Boston Laser, a suction device is placed into the patients eye and connected to the Intralase femtosecond FS laser to prepare for flap generation. The laser thinly cuts a sheath of cornea, leaving a superior hinge in place to allow the cornea to peel back, while remaining connected to the eye.

Once the suction device is removed, the patient's eyelid is taped back using tegaderm and a surgical speculum is inserted to keep the eyelids open. The surgeon marks the edge of the patient's flap using a McKesson Regular Tip Latex-Free Sterile Marker so that it can be correctly repositioned after the procedure. The surgeon then gently flips back the newly generated flap, and positions the patient beneath the Alcon EX500 wavelight excimer laser for treatment. After completion, the flap is flipped back down and adjusted using the pre-treatment markings for alignment, before rinsing the eye with saline solution. The same two drops are then administered onto the eye as: 1% prednisolone and 0.5% moxifloxacin. Patients are then guided to an exam room to wait for 30 minutes for a flap positioning check before being discharged home.

POSTOPERATIVE CARE REGIMEN- LASIK

Patients are advised to pickup postoperative eye drops from the pharmacy prior to surgery day. Patients are prescribed both a steroid and an antibiotic drop to be used for the first week after the procedure. Patients are instructed to administer 1 drop of prednisolone acetate 1% every hour the day of surgery, postoperative day 1, and postoperative day 2. On postoperative days 3 and 4, patients taper down to 4 times a day; typically instilled breakfast, lunch, dinner, and bedtime. For the antibiotic, moxifloxacin HCl 0.5% patients will administer drops 4 times a day as described above for the day of surgery, as well as on postoperative days 1, 2, 3, and 4. If two drops must be administered at the same time, patients are directed to wait five minutes between each drop. Drops need only be administered during the waking hours. And all prescription drops are

discontinued on postoperative day 5. Patients are advised to administer over-the-counter, preservative-free, single-use artificial tears for a minimum of 4 times a day for several weeks after surgery to reduce the sensation of dryness and discomfort.

In addition to the drop regimen, patients are advised to adhere to certain rules following LASIK surgery. Patients must not squint, squeeze, or rub their eyes. Patients must avoid swimming, hot tubs, Jacuzzis, saunas, and contact sports for two weeks. No lifting weights above 15 pounds, or heavy exercising. Eye makeup cannot be worn for the first 48 hours after surgery.

POSTOPERATIVE CARE REGIMEN-PRK/LASEK

Similar to the postoperative care instructions for LASIK, PRK follows the same advice regarding activities, but has a more extensive drop regimen. PRK/LASEK patients will be sent home with a prescription for prednisolone acetate 1% and moxifloxacin HCl 0.5%, but they will also be sent home with a prescription for Tylenol-Codeine. Patients are instructed to administer prednisolone 4 times a day for the first postoperative week, including surgery day. Week 2, patients are advised to administer it 3 times a day. Week 3, patients are tapered down to twice a day. And for week 4, they are reduced further down to once a day. For the moxifloxacin, patients will administer the drops four times a day until the removal of the bandage contact lens, typically taken out at the one-week postoperative visit. The Tylenol-Codeine is recommended for preemptive pain control and patients are instructed to start taking it the night of surgery since pain will peak after 24-48 hours, once the cyclopentolate dilation drops have worn off.

If patients are enduring significant pain and discomfort, they can call their surgeon or the emergency phone line at the clinic and also receive a prescription for a third drop called nepafenac 0.1%, an NSAID, which can be administered as needed no more than twice a day. If administered more frequently, nepafenac can lead to corneal ulceration and perforation, hence why patients are warned extensively of drop administration. All PRK/LASEK patients are also advised to take 1gram/1000mg per day of Vitamin C for three months after surgery to help prevent scarring.

POSTOPERATIVE FOLLOW-UP VISITS

At the Boston Eye Group | Boston Laser, every patient, regardless of procedure type, is scheduled for a one day, one week, and six week follow-up after refractive eye surgery. At these visits patients undergo an uncorrected visual acuity test and auto-refraction. (After two weeks, and only if visual acuity is less than 20/20, are patients manifest refracted.) At each visit they will meet with either a fellow or the surgeon to discuss any postoperative complaints and undergo a slit-lamp examination to monitor healing and check for any complications. Only at and after six weeks is intraocular pressure recorded as to not irritate the cornea. It is at these postoperative visits that patients will note dryness and the doctors will recommend a plan of action with either punctal plug insertion or prescription drug recommendations.

RESULTS

The total number of eyes operated on within January 1, 2010 – December 16, 2019 was 11,175 LASIK eyes from 5,920 individuals, 1,549 LASEK eyes from 880 individuals, and 2,006 PRK eyes from 1,165 individuals (Table 3). Performing a 2-sample z-test to compare the sample proportions, led to sample proportion 1 for LASIK dry eye interventions to be 0.0163 with n=11,175 (Table 3). For PRK/LASEK dry eye interventions, sample proportion 2 was 0.0318 with n=3,555 (Table 3). Comparing the difference between the two sample proportions at an alpha level of significance of 0.05, yields a z-value= 5.7 and a p-value= <0.0001 at a 95% CI (0.0102 - 0.0208) (Figure 7).

Table 3. Comparative Postoperative Dry Eye Interventions. Numerical breakdown of the proportion of dry eye interventions necessitated after each kind of LVC procedure within 1 postoperative year at a private Boston ophthalmology clinic (Sergeant, 2018).

LVC Procedure Type	# Of Eyes that Received Postoperative Plugs and/or Medication	# Of Eyes Treated	Proportion of Postoperative Dry Eye Interventions
LASIK	182	11,175	0.0163
LASEK	80	1,549	0.0516
PRK	33	2,006	0.0165
PRK + LASEK	113	3,555	0.0318
TOTAL	295	14,730	

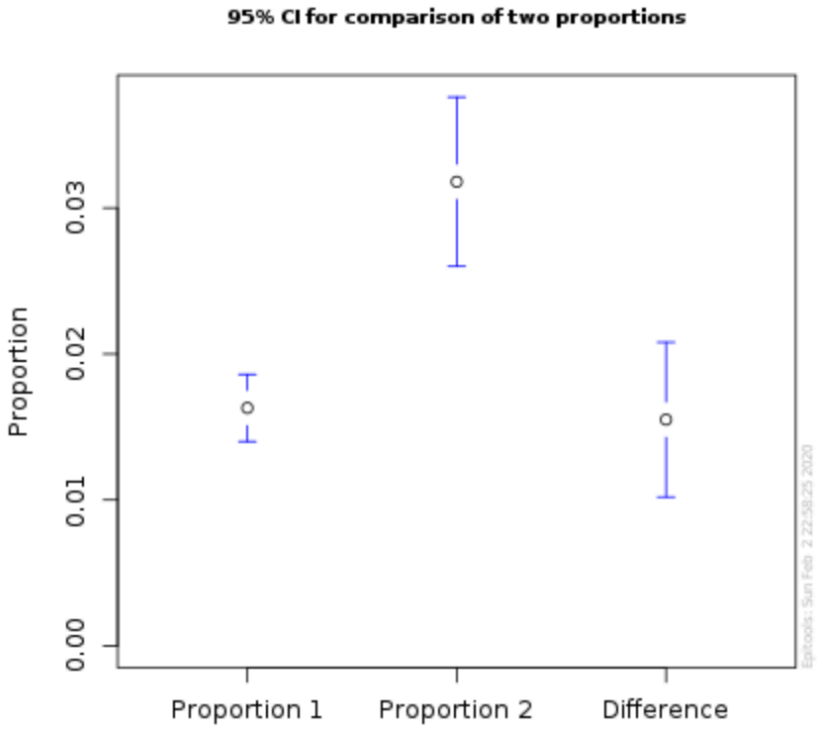

Figure 7. **Confidence Interval Plot Comparing Proportions of Postoperative Dry Eye Interventions in LASIK vs. PRK/LASEK**. Illustrates the confidence limits of the 2-sample z-test, and how the interval does not include the value 0.00, therefore suggesting that there is a significant difference between the proportion of dry eye interventions between LASIK patients and PRK/LASEK patients. Proportion 2 is greater, suggesting that more PRK/LASEK patients received postoperative dry eye interventions (Sergeant, 2018).

This relationship indicates that there is a statistically significant difference between the proportion of LASIK dry eye interventions and PRK/LASEK dry eye interventions performed over the last nine years of refractive surgeries at this private Boston clinic. This suggests a greater incidence of postoperative dry eye interventions for PRK/LASEK patients compared to LASIK patients.

DISCUSSION

DENERVATION IN LASIK VERSUS PRK

The debate between which LVC procedure results in greater dry eye outcomes is ongoing. As described in the introduction, the historical belief is that LASIK is responsible for more postoperative dryness due to a deeper severing of corneal nerves. Since LASIK disrupts both the epithelial nerve bundles and the superficial stromal nerve branches during flap creation and photo-ablation, it is thought to be more responsible for dryness compared to PRK, which only disrupts epithelial nerve bundles (He & Bazan, 2010). As highlighted by Toda (2018), this deeper level of denervation may contribute to more significant dry eye symptoms by reducing corneal sensitivity, decreasing the blinking reaction, and thereby resulting in greater desiccation of the superficial tear film (Figure 2).

DIFFERENCES IN CORNEAL SENSATION RECOVERY

However, the results of the Schallhorn et al. (2019) study support the results of our study. Rebutting that at least in the near postoperative term, less than 12 months after surgery, it is PRK rather than LASIK that results in greater patient dry eye complaints (Schallhorn et al., 2019). Arguing that multiple factors could be responsible for this new turn in view, Schallhorn et al. (2019) suggested a neurotrophic effect could be making LASIK more comfortable than PRK. This would imply that the deeper disruption from LASIK surgery could trigger the release of small biomolecules and peptides that could, in

turn, actually help support nerve healing. Schallhorn et al. (2019) states that these neurotrophic factors could mitigate discomfort during the corneal sensation recovery period, making LASIK less uncomfortable than PRK in the short term. Two, the longer corneal sensation recovery period due to more deeply severed nerves in LASIK could also explain why PRK may be more uncomfortable. Since there is only epithelial nerve disruption, perhaps this instability without deeper denervation can cause more of a dryness sensation for patients compared to LASIK because there is greater corneal sensation (Schallhorn et al., 2019).

MILD RECURRENT EROSION SYNDROME

Another facet to be considered is the misdiagnosis of mild recurrent erosion syndrome for dry eye after LVC procedures. Since dryness and mild recurrent erosions share many common symptoms including: sharp pains, eyelid sticking to the eyeball sensations, and eyelid soreness, patients may be receiving a diagnosis of dryness when in fact they are experiencing mild recurrent erosion syndrome (Hovanesian et al., 2001). This may be a point to consider in the debate of whether LASIK or PRK is worse in regards to postoperative dryness since the Hovanesian et al. (2001) study found that these symptoms were “significantly more common, more severe, and more prolonged after PRK.” This could support the results of our study that patients were experiencing more symptoms after PRK, but could also refute that the symptoms were relating to dryness.

INFLAMMATORY RESPONSE DIFFERENCES

Differences in inflammatory response post-LASIK versus post-PRK must also be considered. The mechanisms that control LASIK healing and PRK healing are not fully understood, but they do demonstrate explicit differences (Alió et al., 2000). For instance, there is less of an inflammatory response after LASIK surgery compared to PRK, and thereby requires a greater healing period to regain sensory function (Alió et al., 2000). It may be possible then that the differences in inflammatory processes between LASIK and PRK could help further explain why patients in our study required greater dry eye interventions with PRK. This is not certain, but there may be a plausible inflammatory role.

SUBJECTIVE VERSUS OBJECTIVE PARAMETERS

The inconsistencies among current research can be attributed to differences in categorizing dryness. Many studies utilize different parameters to determine whether a patient is experiencing dryness or not. Some studies are more objective, focusing on quantifiable indicators of dryness like: Schirmer test, TBUT, visual acuity, and Rose Bengal corneal staining even if patients are not complaining of dryness symptoms. Other studies are more subjective and categorize dryness based primarily on patient-reported sensations of dryness, and lack quantifiable measures of dry eye. These different methods for determining whether a patient is experiencing dryness can thereby be viewed as gray rather than black or white.

In our study, looking at postoperative dry eye interventions, we believe provides a combination of subjective and objective parameters since patients are questioned about whether they are experiencing dryness at their postoperative visits, and the surgeons then examine the patient responses (i.e. complaints of redness, burning, itching, excessive tearing, and foreign body sensations) along with comprehensive physical evaluations (i.e. slit-lamp examinations, tear osmolarity measurements, and uncorrected visual acuity scores) before offering different treatment options. Since the patient and doctor must agree on the level of dryness and the pursuit of plugs or prescription medications, it becomes clear that there are both subjective and objective factors accounted for.

CRITICAL PERIOD FOR DRY EYE DEVELOPMENT

Overall, our results challenge historical beliefs that LASIK is worse for dry eye than PRK/LASEK. And there are recent publications supporting our results that PRK/LASEK is a more significant contributor to dryness in the near postoperative term of less than 12 months after surgery (Schallhorn et al., 2019). Current literature may also suggest postoperative LASIK healing and improvement in dry eye symptoms occurs for most patients between 1-6 months (Shtein, 2011). However, Cohen and Spierer (2018) recognize that there are reasons why some LASIK patients may have more prolonged dryness or more severe dry eye symptoms. For instance, patients who underwent treatment for correction of higher myopia (between -9.1 and -14 diopters) tended to suffer with dry eye symptoms for much longer, ranging anywhere from 2-5 years after surgery (Cohen & Spierer, 2018).

According to Murakami and Manche (2012), the difference between dry eye symptoms after LASIK compared to PRK lose statistical significance after 12 months postoperatively. This suggests that dry eye symptoms are most notably different between the two procedure types during the first year after surgery. This supports our rationale for limiting our analysis to only the first postoperative year. Focusing on this critical period where there is greater variation between LVC procedures, may allow us to provide patients with the most significant recommendation for avoiding postoperative dry eye discomfort.

CONCLUSION

STUDY OUTCOME

Dry eye is the most commonly developed complication status post refractive laser eye surgery (Schallhorn et al., 2019). Although dry eye resolves for most patients by the end of the first postoperative year, the frustration and negative impact on patient-reported quality of life and satisfaction with the procedure continues to be a concern (Murakami & Manche, 2012) (Uchino & Schaumberg, 2013). Determining which LVC procedure type, LASIK versus PRK/LASEK, leads to more postoperative dry eye interventions may allow surgeons to better select a treatment type to avoid this undesirable outcome. Comparing the proportions of patients who required postoperative punctal plug insertion and/or prescription dry eye medications (Xiidra or Restasis) allowed us to determine that

a greater percentage of patients who underwent PRK/LASEK developed postoperative dry eye in the 12 months following surgery.

STUDY LIMITATIONS

Our study does not come without limitations, so the following information should be taken into consideration. All study data was gathered from one private practice ophthalmology clinic in Boston, so the results of our study may not be generalizable to the entire population due to limited patient demographics. Although we took both objective and subjective parameters into consideration during our study design, we did not analyze Schirmer's test for dryness or Rose Bengal corneal staining, which are two commonly used objective indicators of dryness. Other studies also incorporated patient-reported symptoms in the format of questionnaires to quantify not only dryness symptoms, but to also ask about patient satisfaction with the surgery and the impacts on their quality of life. In future studies, we would recommend incorporating all of these tools in the analysis.

Also, since we based our dry eye diagnoses only on the patients who pursued dry eye interventions beyond artificial tear administration there could have been significantly more patients experiencing dryness than our results reflect. Results regarding dry eyes may be even worse as patients were often recorded as being offered punctal plugs and/or dry eye prescription medications and then refusing treatment. This could be the result of poor patient compliance with surgeon recommendations, loss to follow-up as patients stop returning for postoperative visits, and/or patient lack of insurance coverage for

prescription medications. Whatever the reasoning, there were many patients that fell into this category and future studies should make an effort to quantify this outcome.

There is also a question of how compliant patients were with artificial tear administration. Since we could not record frequency of at-home artificial tear administration that may confound our results. We also cannot confirm if patients who were administering artificial tears more often than four times a day were using preservative-free eye drops. Especially considering preservative-free drops are more costly, patients may end up reverting to cheaper products containing preservatives, which can lead to aggravated dry eye symptoms (Gomes et al., 2017).

Certain patient lifestyle behaviors should also be considered during the design of future research. Since a history of heavy alcohol consumption, current and past cigarette smoking, as well as the use of indoor heating systems have all been associated with worse dry eye symptoms, they should be accounted for (Moss et al., 2000). And on the other hand, patient caffeine consumption has been associated with lower dry eye prevalence and should be further investigated (Moss et al., 2000).

DIRECTIVE

In the end, the results of our study should help better direct clinicians in the decision making process of which refractive eye surgery to recommend in order to reduce postoperative dry eye and improve patient satisfaction.

REFERENCES

Alió, J. L., Pérez-Santonja, J. J., Tervo, T., Tabbara, K., Vesaluoma, M., Smith, R. J., Maddox, B., & Maloney, R. K. (2000). Postoperative Inflammation, Microbial Complications, and Wound Healing Following Laser in situ Keratomileusis. *Journal of Refractive Surgery*, *16*(5), 523–538.

Alzahrani, Y., Colorado, L.H., Pritchard, N. and Efron, N. (2017). Longitudinal changes in Langerhans cell density of the cornea and conjunctiva in contact lens-induced dry eye. *Clinical and Experimental Optometry*, 100: 33-40. https://doi-org.ezproxy.bu.edu/10.1111/cxo.12399

Baxter, S. A., & Laibson, P. R. (2004). Punctal Plugs in the Management of Dry Eyes. *The Ocular Surface*, *2*(4), 255–265. https://doi.org/10.1016/S1542-0124(12)70113-1

Bower, K. S., Sia, R. K., Ryan, D. S., Mines, M. J., & Dartt, D. A. (2015). Chronic dry eye in photorefractive keratectomy and laser in situ keratomileusis: Manifestations, incidence, and predictive factors. *Journal of Cataract & Refractive Surgery*, *41*(12), 2624–2634. https://doi.org/10.1016/j.jcrs.2015.06.037

Chang, D. H. (2016, August). Night Vision and Presbyopia-Correcting IOLs. *Cataract & Refractive Surgery Today*. https://crstoday.com/articles/2016-aug/night-vision-and-presbyopia-correcting-iols/

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*, 459. https://doi.org/10.2147/OPTH.S28808

Cohen, E., & Spierer, O. (2018). Dry Eye Post-Laser-Assisted In Situ Keratomileusis: Major Review and Latest Updates. *Journal of Ophthalmology*, *2018*, 1–9. https://doi.org/10.1155/2018/4903831

Colligris, B., Alkozi, H. A., & Pintor, J. (2014). Recent developments on dry eye disease treatment compounds. *Saudi Journal of Ophthalmology*, *28*(1), 19–30. https://doi.org/10.1016/j.sjopt.2013.12.003

Corneal topography and astigmatism. (n.d.). Retrieved February 18, 2020, from https://www.aao.org/bcscsnippetdetail.aspx?id=03192889-6102-4b53-bd0a-ebc0429f1547

Doan, S., & Delcampe, A. (2016). Moderate to severe dry eye - a promising indication for scleral lenses. *Acta Ophthalmologica*, *94*(S256). https://onlinelibrary-wiley-com.ezproxy.bu.edu/doi/abs/10.1111/j.1755-3768.2016.0104

Ervin, A.-M., Law, A., & Pucker, A. D. (2017). Punctal occlusion for dry eye syndrome. *Cochrane Database of Systematic Reviews*. https://doi.org/10.1002/14651858.CD006775.pub3

Fox, R. I., Chan, R., Michelson, J. B., Belmont, J. B., & Michelson, P. E. (1984). Beneficial Effect of Artificial Tears Made With Autologous Serum In Patients With Keratoconjunctiviitis Sicca. *Arthritis and Rheumatism*, *27*(4), 459–461.

Goel, M., & Pathak, A. K. (2015, January 19). Femtosecond lasers and laser assisted in situ keratomileusis (LASIK). Retrieved February 20, 2020, from https://eyewiki.aao.org/Femtosecond_lasers_and_laser_assisted_in_situ_keratomileusis_(LASIK)

Gomel, N., Negari, S., Frucht-Pery, J., Wajnsztajn, D., Strassman, E., & Solomon, A. (2018). Predictive factors for efficacy and safety in refractive surgery for myopia. *PLOS ONE*, *13*(12), e0208608. https://doi.org/10.1371/journal.pone.0208608

Gomes, J. A. P., Azar, D. T., Baudouin, C., Efron, N., Hirayama, M., Horwath-Winter, J., Kim, T., Mehta, J. S., Messmer, E. M., Pepose, J. S., Sangwan, V. S., Weiner, A. L., Wilson, S. E., & Wolffsohn, J. S. (2017). TFOS DEWS II iatrogenic report. *TFOS International Dry Eye WorkShop (DEWS II)*, *15*(3), 511–538. https://doi.org/10.1016/j.jtos.2017.05.004

He, J., & Bazan, H. E. P. (2010). Omega-3 fatty acids in dry eye and corneal nerve regeneration after refractive surgery. *Prostaglandins, Leukotrienes and Essential Fatty Acids (PLEFA)*, *82*(4–6), 319–325. https://doi.org/10.1016/j.plefa.2010.02.004

Hendriks, M., Verhoeven, V. J. M., Buitendijk, G. H. S., Polling, J. R., Meester-Smoor, M. A., Hofman, A., Kamermans, M., Ingeborgh van den Born, L., Klaver, C. C. W., van Huet, R. A., Klevering, B. J., Bax, N. M., Lambertus, S., Klaver, C. C. W., Hoyng, C. B., Oomen, C. J., van Zelst-Stams, W. A., Cremers, F. P., Plomp, A. S., … de Jong-Hesse, Y. (2017). Development of Refractive Errors—What Can We Learn From Inherited Retinal Dystrophies? *American Journal of Ophthalmology*, *182*, 81–89. https://doi.org/10.1016/j.ajo.2017.07.008

Hovanesian, J. A., Shah, S. S., & Maloney, R. K. (2001). Symptoms of dry eye and recurrent erosion syndrome after refractive surgery. *Journal of Cataract & Refractive Surgery*, *27*(4), 577–584. https://doi.org/10.1016/S0886-3350(00)00835-X

Improper Contact Lens Use Associated with Increased Risk of Infections. (2018, August 16). *PR Newswire*. Retrieved from https://link-gale-com.ezproxy.bu.edu/apps/doc/A550422157/AONE?u=mlin_b_bumml&sid=AONE&xid=394800fb

Iskander, N. G., Peters, N. T., Anderson Penno, E., & Gimbel, H. V. (2001). Late traumatic flap dislocation after laser in situ keratomileusis. *Journal of Cataract & Refractive Surgery*, *27*(7), 1111–1114. https://doi.org/10.1016/S0886-3350(01)00752-0

Kok, J. H. C., & Visser, R. (1992). Treatment of Ocular Surface Disorders and Dry Eyes with High Gas-Permeable Scleral Lenses. *Cornea*, *11*(6), 518–522.

Lifitegrast (Xiidra) for Dry Eye Disease. (2017). *JAMA*, *317*(14), 1473–1474. https://doi.org/10.1001/jama.2016.12872

Lindstrom, R. L., Hardten, D. R., & Chu, Y. R. (n.d.). *LASER IN SITU KERATOMILEUSIS (LASIK) FOR THE TREATMENT OF LOW, MODERATE, AND HIGH MYOPIA*. 22.

Melton, R., & Randall, T. (2004). A Fresh Look at Dry Eye Intervention. *Review of Optometry; Radnor*, *143*(5), 8A-12A.

Miljanović, B., Dana, R., Sullivan, D. A., & Schaumberg, D. A. (2007). Impact of Dry Eye Syndrome on Vision-Related Quality of Life. *American Journal of Ophthalmology*, *143*(3), 409-415.e2. https://doi.org/10.1016/j.ajo.2006.11.060

Morgan, I. G., Ohno-Matsui, K., & Saw, S.-M. (2012). Myopia. *The Lancet*, *379*(9827), 1739–1748. https://doi.org/10.1016/S0140-6736(12)60272-4

Mori, Y., Miyata, K., Ono, T., Yagi, Y., Kamiya, K., & Amano, S. (2017). Comparison of laser in situ ketatomileusis and photorefractive keratectomy for myopia using a mixed-effects model. *PLOS ONE*, *12*(3), e0174810. https://doi.org/10.1371/journal.pone.0174810

Moshirfar, M., Gardiner, J. P., Schliesser, J. A., Espandar, L., Feiz, V., Mifflin, M. D., & Chang, J. C. (2010). Laser in situ keratomileusis flap complications using mechanical microkeratome versus femtosecond laser: Retrospective comparison. *Journal of Cataract & Refractive Surgery*, *36*(11), 1925–1933. https://doi.org/10.1016/j.jcrs.2010.05.027

Moss, S. E., Klein, R., & Klein, B. E. K. (2000). Prevalence of and Risk Factors for Dry Eye Syndrome. *Archives of Ophthalmology*, *118*(9), 1264–1268.

https://doi.org/10.1001/archopht.118.9.1264

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

Murakami, Y., & Manche, E. E. (2012). Prospective, Randomized Comparison of Self-reported Postoperative Dry Eye and Visual Fluctuation in LASIK and Photorefractive Keratectomy. *Ophthalmology*, *119*(11), 2220–2224. https://doi.org/10.1016/j.ophtha.2012.06.013

Noda-Tsuruya, T., Asano-Kato, N., Toda, I., & Tsubota, K. (2006). Autologous serum eye drops for dry eye after LASIK. *Journal of Refractive Surgery*, *22*(1), 61–66.

Patel, S. V., Maguire, L. J., McLaren, J. W., Hodge, D. O., & Bourne, W. M. (2007). Femtosecond Laser versus Mechanical Microkeratome for LASIK: A Randomized Controlled Study. *Ophthalmology*, *114*(8), 1482–1490. https://doi.org/10.1016/j.ophtha.2006.10.057

Perez, V. L., Pflugfelder, S. C., Zhang, S., Shojaei, A., & Haque, R. (2016). Lifitegrast, a Novel Integrin Antagonist for Treatment of Dry Eye Disease. *The Ocular Surface*, *14*(2), 207–215. https://doi.org/10.1016/j.jtos.2016.01.001

Perry, H. D., Solomon, R., Donnenfeld, E. D., Perry, A. R., Wittpenn, J. R., Greenman, H. E., & Savage, H. E. (2008). Evaluation of Topical Cyclosporine for the Treatment of Dry Eye Disease. *Archives of Ophthalmology*, *126*(8), 1046–1050. https://doi.org/10.1001/archopht.126.8.1046

Pflugfelder, S. C., Paiva, C. S., Villarreal, A. L., & Stern, M. E. (2008). Effects of Sequential Artificial Tear and Cyclosporine Emulsion Therapy on Conjunctival Goblet Cell Density and Transforming Growth Factor-β2 Production. *Cornea*, *27*(1), 64–69. https://doi.org/10.1097/ICO.0b013e318158f6dc

Reilly, C., Panday, V., Lazos, V., & Mittelstaedt, B. (2010). PRK vs LASEK vs Epi-LASIK: A comparison of corneal haze, post-operative pain and visual recovery in moderate to high myopia. *Nepalese Journal of Ophthalmology*, *2*(4), 97–104. https://doi.org/10.3126/nepjoph.v2i2.3715

Risky Contact Lens Use. (2017). *The Journal of the American Medical Association*, *318*(12), 1100. doi: 10.1001/jama.2017.13441

Rossen, J., Amram, A., Milani, B., Park, D., Harthan, J., Joslin, C., … Djalilian, A. (2016). Contact Lens-induced Limbal Stem Cell Deficiency. *The Ocular Surface*, *14*(4), 419–434. https://doi.org/10.1016/j.jtos.2016.06.003

Sakamoto, R., Bennett, E. S., Henry, V. A., Paragina, S., Narumi, T., Izumi, Y., Kamei, Y., Nagatomi, E., Miyanaga, Y., & Hamano, H. (1993). The phenol red thread tear test: a cross-cultural study. *Investigative Ophthalmology & Visual Science*, *34*(13), 3510–3514.

Salomão, M. Q., Ambrósio, R., & Wilson, S. E. (2009). Dry eye associated with laser in situ keratomileusis: Mechanical microkeratome versus femtosecond laser. *Journal of Cataract & Refractive Surgery*, *35*(10), 1756–1760. https://doi.org/10.1016/j.jcrs.2009.05.032

Salz, J. J., & Trattler, W. (2006). Pupil size and corneal laser surgery. *Current Opinion in Ophthalmology*, *17*(4). https://journals.lww.com/co-ophthalmology/Fulltext/2006/08000/Pupil_size_and_corneal_laser_surgery.11.aspx

Schallhorn, J. M., Pelouskova, M., Oldenburg, C., Teenan, D., Hannan, S. J., & Schallhorn, S. C. (2019). Effect of Gender and Procedure on Patient-Reported Dry Eye Symptoms After Laser Vision Correction. *Journal of Refractive Surgery*, *35*(3), 161–168. https://doi.org/10.3928/1081597X-20190107-01

Sergeant, E. (2018). *Epitools Epidemiological Calculators*. Ausvet. http://epitools.ausvet.com.au.

Shortt, A. J., Allan, B. D. S., & Evans, J. R. (2013). Laser-assisted in-situ keratomileusis (LASIK) versus photorefractive keratectomy (PRK) for myopia. *The Cochrane Database of Systematic Reviews*, *1*, CD005135. https://doi.org/10.1002/14651858.CD005135.pub3

Shortt, A. J., Bunce, C., & Allan, B. D. S. (2006). Evidence for Superior Efficacy and Safety of LASIK over Photorefractive Keratectomy for Correction of Myopia. *Ophthalmology*, *113*(11), 1897–1908. https://doi.org/10.1016/j.ophtha.2006.08.013

Shtein, R. M. (2011). Post-LASIK dry eye. *Expert Review of Ophthalmology*, *6*(5), 575–582. https://doi.org/10.1586/eop.11.56

Sia, R. K., Ryan, D. S., Edwards, J. D., Stutzman, R. D., & Bower, K. S. (2014). The U.S. Army Surface Ablation Study: Comparison of PRK, MMC-PRK, and LASEK in Moderate to High Myopia. *Journal of Refractive Surgery*, *30*(4), 256–264. https://doi.org/10.3928/1081597X-20140320-04

Stevenson, W., Chauhan, S., & Dana, R. (2012). Dry Eye Disease: An Immune-Mediated Ocular Surface Disorder. *Archives of Ophthalmology*, *130*(1), 90.

https://doi.org/10.1001/archophthalmol.2011.364

Sutton, G., Lawless, M., & Hodge, C. (2014). Laser in situ Keratomileusis in 2012: A Review. *Clinical and Experimental Optometry*, *97*(1), 18–29. https://doi.org/10.1111/cxo.12075

Toates, F. M. (1972). Accommodation function of the human eye. *Physiological Reviews*, *52*(4), 828–863. https://doi.org/10.1152/physrev.1972.52.4.828

Toda, I. (2018). Dry Eye After LASIK. *Investigative Ophthalmology & Visual Science*, *59*(14), DES109–DES115. https://doi.org/10.1167/iovs.17-23538

Tomlinson, A., Blades, K. J., & Pearce, E. I. (2001). What does the Phenol Red Thread Test Actually Measure? *Optometry and Vision Science*, *78*(3). https://journals.lww.com/optvissci/Fulltext/2001/03000/What_does_the_Phenol_Red_Thread_Test_Actually.5.aspx

Uchino, M., & Schaumberg, D. A. (2013). Dry Eye Disease: Impact on Quality of Life and Vision. *Current Ophthalmology Reports*, *1*(2), 51–57. https://doi.org/10.1007/s40135-013-0009-1

Vadlapudi, A. D., & Mitra, A. K. (2013). Nanomicelles: an emerging platform for drug delivery to the eye. *Therapeutic Delivery*, *4*(1), 1–3. https://doi.org/10.4155/tde.12.122

Wilkinson, J. M., Cozine, E. W., & Kahn, A. R. (2017). Refractive Eye Surgery: Helping Patients Make Informed Decisions About LASIK. *American Family Physician*, *95*(10), 637–644.

Yang, C., Sun, W., & Gu, Y. (2006). A clinical study of the efficacy of topical corticosteroids on dry eye. *Journal of Zhejiang University SCIENCE B*, *7*(8), 675–678. https://doi.org/10.1631/jzus.2006.B0675

CURRICULUM VITAE