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Comparison of laser vision correction outcomes with two excimer laser nomograms

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COMPARISON OF LASER VISION CORRECTION OUTCOMES WITH TWO EXCIMER LASER NOMOGRAMS

by

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ABSTRACT

Background: The human eye is an incredible organ, capable of focusing and detecting light that passes through its specialized structures. These organs are responsible for the sensation of vision and are crucial to the ability to function and operate during daily life. Loss of the sense of vision can result in serious deficits that greatly reduce the quality of a person's life. One of the most prevalent causes of vision impairment in the world is refractive error. Although this is a common and relatively simple problem to fix with modern technology, ophthalmologists are continuously searching for new methods of treating people's eyes to correct refractive errors and improve vision. There are several popular methods for correcting refractive errors, including traditional glasses, contact lenses, and laser vision correction. Laser vision correction is the most modern method for improving visual acuity deficits caused by refractive errors. The two most favored techniques for laser vision correction are laser assisted in situ keratomileusis (LASIK) and photorefractive keratectomy (PRK). The performance of these procedures requires a laser treatment input to be calculated based on the patient's refractive error. These laser treatment inputs are often determined using a nomogram. Nomograms are mathematical functions utilizing a graphical display to calculate a given value based on a set of parameters. Nomograms are crucial for safe and effective LASIK and PRK procedures and there is much interest in enhancing these algorithms to improve the refractive and visual acuity outcomes.

Objectives: The objective of the study was to determine if a newer, more complex laser vision correction nomogram could generate laser treatment inputs better than another more traditional nomogram in terms of refractive and visual acuity outcomes.

Methods: The study included 109 eyes belonging to 59 patients. Fifty-one eyes belonging to 28 patients were operated on using the Wellington nomogram and 58 eyes belonging to 31 patients were operated on using the Internet-based refractive analysis (IBRA) nomogram. Visual acuity and refractive outcomes were recorded at a six-week follow-up evaluation. Data were analyzed using statistical tests to determine significant values.

Results: No statistically significant difference was found between the recorded visual acuity and refractive outcomes of eyes operated on using the Wellington and IBRA nomograms.

Conclusions: The two nomograms were found to perform at equal efficacy and to reach the established standards for safety. Although no significant difference was found between the two nomogram outcomes it is possible that there were variables limiting the external validity of the statistical analysis. With extra time, additional cases, and better sample matching the study could be expanded and developed to provide a more reliable and more representative dataset to elucidate conclusions with greater impact.

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LIST OF ABBREVIATIONS

AMD .... Age-related Macular Degeneration

BCVA .... Best-Corrected Visual Acuity

BEG .... Boston Eye Group

CDVA .... Corrected Distance Visual Acuity

D .... Diopter

DLK .... Diffuse Lamellar Keratitis

DS .... Diopter Sphere

FDA .... Food and Drug Administration

IBRA .... Internet-Based Refractive Analysis

IOL .... Intraocular Lens

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

LogMAR .... Logarithm of the Minimum Angle of Resolution

MRSE .... Manifest Refractive Spherical Equivalent

PRK .... Photorefractive Keratectomy

SEQ .... Spherical equivalents

UCVA .... Uncorrected Visual Acuity

UDVA .... Uncorrected Distance Visual Acuity

UNVA .... Uncorrected Near Visual Acuity

VA .... Visual Acuity

INTRODUCTION

The human eye is a complex organ capable of focusing and detecting light that passes through its specialized structures. These organs are responsible for the sensation of vision. The human eye is highly specialized and effective at forming detailed color images that are crucial to the ability to function and operate during daily life. Loss of the sense of vision can result in serious deficits that greatly reduce a person's quality of life. Ophthalmologists are continuously searching for new methods of treating people's eyes to improve their vision. The ultimate goal of ophthalmology is to maintain a person's vision and eliminate blindness.

A person's ability to see is referred to as visual acuity and is measured based on a Snellen chart score ranging from 20/400 to 20/15, with 20/400 being the lowest visual acuity and 20/15 being the highest. According to a census-based study conducted in 2004, approximately 937,000 Americans experienced blindness at a best-corrected visual acuity (BCVA) less than 20/200 in their better seeing eye, and another 2.4 million adults experienced impaired vision with a best corrected visual acuity (BCVA) of 20/40 or less in their better seeing eye. This means that nearly 3% of the American population is subject to some level of significant vision loss. The same study also predicts that this number will rise approximately 70% by 2020 for both blindness and vision impairment (The Eye Diseases Prevalence Research Group, 2004). The implications of this study necessitate the need for continued research into improving the ways of treating vision loss as the population both grows in number and increases in age.

Anatomy of the Human Eye

The anatomy of the human eye is complex, composed of many small but very specialized tissues and structures that each serves important individual functions. The human eye is an ovular sack separated into an anterior segment containing a watery fluid called the aqueous humor and a posterior segment containing a jelly-like fluid called the vitreous humor. These two regions are separated by the iris (the colored part of the eye), the pupil, and the lens and its suspensory ligaments. Light passes through these regions before interacting with specialized light-sensitive cells located in the retina at the back of the eye called photoreceptors. These signals from the retina are sent to and processed by the brain to give humans the perception of light. Before light can interact with the retina, it must first be focused on the retina by bending or refracting the light through both the cornea at the front of the eye and by the internal crystalline lens located inside the eye (Willoughby et al., 2010).

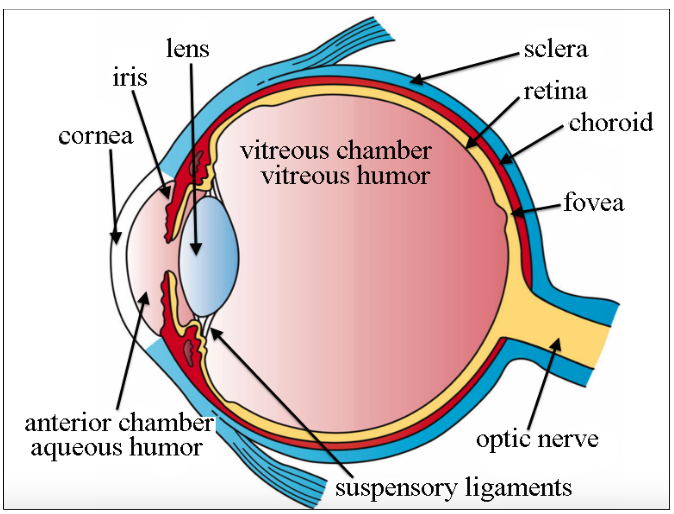


Figure 1. Anatomical representation of the human eye. This graphic depicts the major anatomical features of the human eye including the anterior aqueous chamber and posterior vitreous chamber as well as the cornea, natural lens, retina, optic nerve, choroid, and sclera. Figure taken from Fischer, (2013).

The Cornea

The cornea is the most superficial anterior wall of the eye. Completely transparent in healthy individuals and bathed in a tear film, the cornea is the first structure light must pass through before reaching the retina. The cornea acts as a biconvex lens that bends and focuses distant light rays passing through it. The ability/power of any lens to bend or refract light is quantified as a measurement called the diopter (D), which is defined as the reciprocal of the focal length of the light rays measured in meters. Except for a complete vacuum any medium (gas, fluid, or solid) that light passes through has an index of refraction. The refraction index is a dimensionless unit of measurement that describes the ratio of the velocity of light in a vacuum to its velocity in a specified medium. The higher the refractive index of a material the slower light moves through it relative to its velocity through a vacuum. This reduction in velocity causes the light to change direction and bend as it moves from one medium to another and is described by Snell's law of refraction. The amount of this change in direction is dependent upon the magnitude of the difference between the refractive indices of the two media. Although the cornea represents the first refractive tissue light must pass through, much of the refraction actually occurs as light passes through the air-to-tear film interface. This is because the difference in the index of refraction between the ambient air and the aqueous tear film is much larger than the difference between the tear film and the surface of the cornea. The cornea and its tear film contribute approximately 45 diopters of magnification, or 65% to 70% to the total magnification power of the eye (Meek & Knupp, 2015).

The human cornea is a structure that serves multiple functions and consists of five fundamental tissue layers and a tear film layer, with each layer serving a specific role. Irregularities or pathologies involving any one or more layers can result in significant deficits in optical transparency and visual acuity (Meek & Knupp, 2015).

The first and most superficial layer of the cornea is the corneal epithelium that functions to protect the superficial layers of tissue by acting as a barrier to infection and tear fluid components. This layer is approximately 50 um in thickness and is composed of non-keratinized stratified squamous cells that readily regenerate every 7-10 days. The thickness of this layer, relative to the acellular layers of the cornea, means that these cells must maintain near perfect transparency to maximize visual acuity. Dryness, edema, or inflammation of this layer can result in significant deficits in visual acuity of the eye (Sridhar, 2018; Willoughby et al., 2010).

Just below the corneal epithelium is the acellular Bowman's layer (about 12um thick). Consisting of a condensation of predominantly type-1 and type-5 collagen, Bowman's layer is the sub-epithelial basement membrane for the corneal epithelium and functions to protect the underlying corneal stroma. Bowman's layer has a high tensile strength and helps to maintain the shape of the cornea. However, Bowman's layer lacks the regenerative ability of the corneal epithelium, and damage to it can in some cases result in scarring and opacification of the cornea (Sridhar, 2018).

Layer three is the corneal stroma. Composed of keratocytes and about 200 lamellar layers of specially arranged type-1, type-6, and type-12 collagen, the stroma layer comprises roughly 85% of the total corneal thickness (Meek & Boote, 2004; Sridhar, 2018). Because of its relative thickness, it is crucial for this layer to remain as transparent as possible. To increase transparency, collagen in the stroma is arranged into a particular lattice formation that reduces and counters scattered light. Functionally, the stroma is divided into three parallel lamellar zones, each interwoven with each other and adjacent structural layers (e.g., Bowman's layer). This interwoven lattice of the stroma allows for destructive light interference between the individual collagen fibrils, minimizing scatter and optical degradation (Meek & Boote, 2004; Meek & Knupp, 2015; Radner et al., 1998). Any changes in the shape, thickness, or molecular components that compose the stroma can alter its biomechanics and the way it refracts light. Dysfunction or pathology involving this layer can have serious consequences for vision. Excessive thinning or edema of the stroma can lead to severe loss of visual acuity by changing the shape of the cornea and its refractive index in a way that reduces its optical quality. Structural changes as well as changes to the molecular composition of the stroma can reduce its opacity and lead to visual acuity deficits by disrupting the amount of light reaching the retina in that particular region of vision.

Layer four of the cornea, just superficial to the corneal endothelium and serving as its basement membrane, is a layer called Descemet's membrane. This layer is composed of acellular type-4 and type-8 collagen deposited by the endothelium during development, and it is continuously remodeled by type-4 collagen deposition throughout a person's lifetime. Descemet's membrane functions to support the tightly regulated passage of fluid between the anterior chamber of the eye and the stroma. Descemet's membrane is crucial for this transport by acting as a fluid barrier and by giving the endothelial cells a place to adhere. Damage or dysfunction of this layer can result in corneal edema, opacification, and progressive vision loss (Ali et al., 2016).

The final and deepest layer of the cornea is the corneal endothelium which consists of a layer of simple squamous or low cuboidal cells that have little or no regenerative capability. Endothelial cells adhere to Descemet's membrane in a monolayer that prohibits the diffusion of ions and macromolecules which contribute to osmotic pressures. Osmotic pressure drives aqueous fluid from the anterior eye chamber into the corneal tissues and the function of the endothelial layer is to regulate this fluid movement through active transport of solutes by Na^+/K^+ ATPases. Because there are no stem cells to regenerate the population when these cells are damaged or killed, endothelial cells must stretch and increase in size to maintain this transport barrier. Excessive damage to the endothelium can have severe consequences for vision if the fluid forced into the stroma causes edema (Ali et al., 2016; Sridhar, 2018).

The Natural Lens

The internal crystalline lens which focuses light after it has passed through the cornea and pupil is located behind the iris and suspended by small ligaments called zonules. The lens is a biconvex structure consisting of three structural components; the capsule surrounding the collagen fibers, the collagen fibers that make up the bulk of the lens, and the lens epithelium located between the capsule and the fibers. The crystalline lens bends light in much the same way as the cornea. Because the lens is reasonably elastic it is capable of minor focal adjustments by altering its exact shape to become flatter or more spherical, this capability allows the eye to adjust and focus on images either near or far away (called accommodation). This natural lens can become opacified and cloudy as a result of the natural aging process or certain pathologies and medications. Commonly referred to as cataracts, these opacifications can have severe impacts on visual acuity by reducing the quality and quantity of light reaching the retina. Correction for cataracts requires removal and replacement of the natural crystalline lens with a pseudophakic artificial lens called an intraocular lens (IOL). Replacement of the natural lens with an intraocular lens removes the opacified lens, allowing more light to reach the retina as well as correcting refractive errors. The IOL is designed to do the same job as the natural lens and can be made so that it corrects refractive errors of the cornea. This type of procedure is relatively invasive and requires a full preoperative evaluation before surgery to ensure the patient can undergo it safely.

Refractive Error

Ideally the cornea and crystalline lens work together to produce a single reduced inverted image that falls directly on a region of the retina called the macula (responsible for the central visual field). If the light does not fall on the retina in this way because of irregularities in the refractive behavior of the eye, it is referred to as a refractive error. Refractive errors result in light that fails to converge to a single focal point directly on the retina - rays converge too soon in front of the retina, too late behind the retina or with two (or more) different focal points. When the refractive error results in rays that converge too soon and in front of the retina, the condition is referred to as myopia or myopic eye. Myopia is most commonly caused by an eye that has an axial length greater than the focal distance of its lenses.

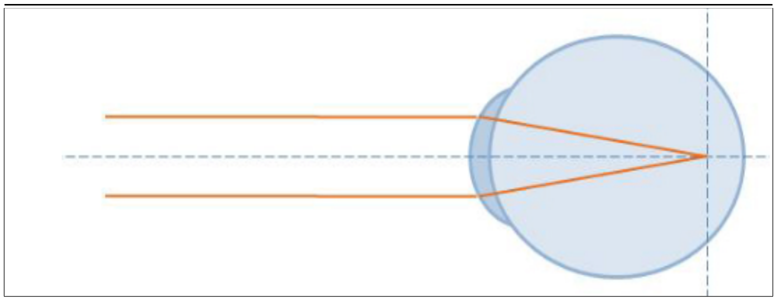


Figure 2. Example of the optics of myopic error. This image is a graphical representation of the way that light is refracted and focused through a myopic or nearsighted eye. The rays of light enter through the cornea and natural lens but are focused to a focal point that is located in front of the retina. This is a result of too great a refractive power or an eye that has an axial length greater than the focal distance of the lenses. Figure taken from Philos 2000 (2017).

When the refractive error results in light rays that converge too late, theoretically behind the retina, the condition is called hyperopia or hyperopic eye. Hyperopia is most often caused by an eye that has an axial length less than the focal distance of its lenses.

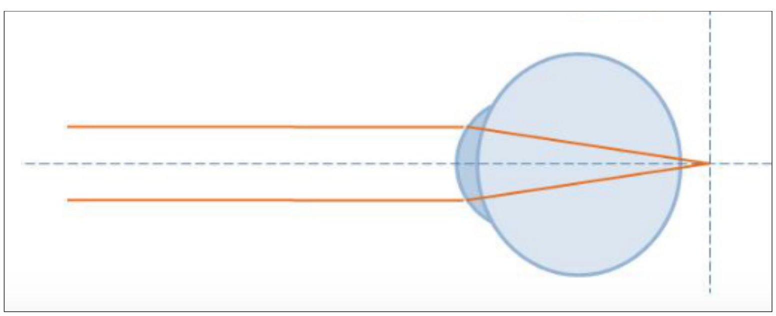


Figure 3. Example of the optics of hyperopic error. This image is a representation of the way that light is refracted and focused through a hyperopic or farsighted eye. The rays of light enter through the cornea and natural lens but are focused to a focal point that is located theoretically behind the retina. This is a result of too low a refractive power or an eye that has an axial length shorter than the focal distance of the lenses. Figure taken from Philos 2000 (2017).

The last refractive error is complex and occurs when the rays do not all converge in the same location on the retina. This condition is known as astigmatism or an astigmatic eye. Astigmatism can be regular or irregular and involve both the anterior and posterior surfaces of the cornea, requiring three-dimensional topography to visualize. Refractive errors can result from any number of events, including changes to the shape of the eye globe, the cornea, or the crystalline lens, or by molecular changes to the tissue comprising these structures that reduce their transparency (Morgan et al., 2012).

Impact of Refractive Error

Refractive errors and their associated complications are the leading cause of vision impairment in the United States. Along with changes in visual acuity, myopia and hyperopia can be characterized by changes in the global structure of the eye. Myopia and hyperopia often result from changes to the axial or global length of the eye and are accompanied by structural changes in the retina and choroid. These structural changes can result in vision-threatening pathologies and complications such as myopic macular degeneration, open-angle glaucoma or retinal detachments (Verhoeven et al., 2015). Macular degeneration is a condition that affects the macular region of the retina that is responsible for the central visual field. The many variations and causes of this condition are not well understood but they generally result in an inflammatory process that gradually thins and alters the vascular and cellular structure of the retina. Degeneration of the retina in this way can lead to severe and possibly permanent central field vision loss (Mitchell et al., 2018). Glaucoma is another common condition that results from progressive damage to the optic nerve innervating the retina and is often caused by increased intraocular pressures or changes to the vasculature closely associated with the nerve itself. Glaucomatous pathology of the optic nerve results in permanent damage that can cause a progressive loss of the peripheral visual field of the eye (Weinreb et al., 2014). These complications are a risk for every myopic eye; however, eyes with a high-grade myopia of -10.00 diopter sphere (DS) or more are at an increased risk for potentially blinding complications. In the case of hyperopic eyes the structural changes are the opposite of myopic and are characterized by a shortening in the axial or global length of the eye. For these eyes, the risks of visual impairments are less well understood than myopic errors. Nevertheless, hyperopic eyes are at a greater risk for amblyopia and closed-angle glaucoma, as well as an association with age-related macular degeneration (AMD). Although these conditions are treatable and manageable with preventative care and medications, they are very prevalent in the global population and currently represent the primary causes of vision impairment. Loss of either the central or peripheral visual field acuities can have severe consequences for a person’s quality of life, making everyday life and complex tasks much more difficult or even dangerous. (Verhoeven et al., 2015).

The Manifest Refraction

Ophthalmologists use a standardized tool for quantifying, recording, and treating these conditions called a manifest refraction. The manifest refraction takes measurements that describe how a person’s eye is refracting light based on the subjective visual acuity.

Ophthalmologists and optometrists use three values from the manifest refraction to quantify the refractive behavior of a person's global eye: the spherical value called the "sphere," the cylindrical value called the "cylinder," and an orientation value dependent upon the presence of a cylinder value called the "axis." The spherical value is measured in diopters (D) and is determined primarily by the distance between the surface of the cornea and the retina called the axial length, as well as the intrinsic refractive biomechanics of the lens itself. This spherical measure can be negative or positive and functionally describes the distance at which light rays converge from the lens. A negative sphere value means that light passing through the eye converges to a focal point too close to the lens (myopic), and a positive value means the light converges too far from the lens (hyperopic). An eye that focuses light to a focal point landing directly on the retina in the macula is said to be "planar" and carries a virtual sphere value of zero. The cylindrical value typically measured in negative diopters for ophthalmology is more complex and is determined by the horizontal and vertical steepness of the anterior and posterior surfaces of the cornea and the crystalline lens. The cylindrical value describes astigmatism and is paired with an axis value to describe how the asymmetry is oriented. The axis value is measured in degrees on a circle between 1 and 180, oriented on a plane parallel to the plane of the cornea. An eye with symmetrical steepness/flatness on the horizontal and vertical meridians of the global eye is said to be "spherical" and carries a virtual cylinder value of zero. Because the axis value is directly dependent upon the cylinder value, a spherical eye carries no axis value and is excluded from the refraction (a value of zero is actually the same as a value of 180 degrees). Along with measurements for proper fitting and comfort, these three values give physicians the ability to design corrective vision devices to adjust the distance and orientation of the focal point on the retina to improve a patient's visual acuity.

Correction of Vision Impairment

The goal of ophthalmologists and optometrists in refractive correction is to alter the way that light rays are bent through the cornea and natural lens to ensure that those rays converge at the correct distance from the lens and at the correct location on the retina. When refractive errors occur as a result of changes or congenital irregularities in the shape of the cornea, there are a number of ways to correct problem. The traditional way to correct these errors is by placing another lens in front of the eye to counteract the refractive irregularity. This can be done with glasses or contact lenses that are placed in front of or in contact with the cornea, respectively. These devices work by altering the refraction of incoming rays before they reach the cornea and adjusting the position of their focal point. Considering that every person's eye is different and has slightly different refractive values, every person requires unique, personalized, refractive correction.

In the case of a myopic eye the required lens is a diverging lens because the person's eye has too much magnification power, converging and focusing light too close to the lens in front of the retina. A diverging lens in front of a myopic eye results in light rays that converge less before reaching the cornea, causing them to meet at a focal point further from the lenses and closer to the retina. In the case of a hyperopic eye, the required lens is a converging lens because the person's eye has too low a magnification power, which focuses light too far from the lens, theoretically behind the retina. A converging lens in front of a hyperopic eye results in light rays that converge more before reaching the cornea meeting at a focal point closer to the lens and on the retina. For a person with astigmatism, a special lens called a toric lens is used because although the rays may converge at the same focal distance, they do not converge at the same focal point. A toric lens works by having two different focal points in the same lens to redirect light rays traveling through structural asymmetries in the cornea. These irregularities can occur in virtually any orientation on the anterior or posterior aspects of the cornea, and so a physician must determine this orientation before a lens can be made to correct astigmatism. A person can have either a myopic or hyperopic eye as well as an astigmatic eye and can require correction for both of these errors.

Benefits and Costs of Traditional Vision Correction

Although these traditional methods of vision correction are well developed and effective at improving visual acuity, they are not without risks or costs. Glasses are the oldest method of correcting refractive errors, and they are effective at reaching this goal. However, they can often be cumbersome or uncomfortable for the wearer. Finding the correct lens fit and frame can be very difficult in some cases and a person searching for the right glasses may be forced into a time-consuming and costly task. Glasses are not expensive but also easy to lose, easy to forget, and difficult to keep clean. They are only effective if they are worn and maintained in good condition, so any factor that reduces the lens clarity or the amount of time wearing the glasses reduces their overall effectiveness.

The second traditional method of vision correction is contact lenses. A large-scale study conducted in 2014 using a United States population-based survey reported that 40.9 million Americans 18 years and older wore contact lenses, with 93% wearing soft contact lenses. This is nearly 17% of the American population (Cope et al., 2015). Contact lenses are small lenses that are placed in direct contact with the eye. They function in the same way that glasses do; however, the close proximity to the cornea results in some differences in the refractive prescription as well as unique complications not associated with glasses. The fact that contact lenses are closer to the cornea than a pair of glasses means that the prescription is slightly different. For myopic eyes, contact lenses generally have slightly less nearsighted magnifying power for lower-order refractive errors because the lenses require less refractive power at a closer distance. The opposite is true for hyperopic eyes. The close proximity of contact lenses to the cornea can also create complications that are both uncomfortable and vision threatening. Some of the common complications associated with contact lens use are irritation, inflammation, and infections. The physical contact of the lens with the cornea can cause irritation and inflammation by damaging the epithelium in a number of ways. Contact lenses cause physical damage by inducing micro-abrasions that disrupt the epithelium and result in release of inflammatory cytokines. Contact lenses can also disrupt the tear film that nourishes the epithelium resulting in deposits and hypoxic stress that damage the epithelial cells. Along with physical trauma and nutrient deprivation, the cleaning solutions used to disinfect extended-wear contacts have been observed to cause cytotoxic reactions in the epithelial cells that further disrupts this protective barrier. More serious than inflammation, however, is the risk of ocular infections. The epithelial and tear film disruptions, which are associated with contact lens use, place the patients wearing them at a much greater risk for ocular infections that can lead to severe complications. An example of a complication is microbial keratitis, a bacterial infection that can be uncomfortable and possibly vision threatening if the cornea is scarred or ulcerated. Patients particularly at risk for these complications are patients who sleep in contacts or do not disinfect them properly. Each of these complications is in most cases preventable with proper hygiene, contact lens care, and maintenance, including yearly exams with a physician to identify any issues before they become visually significant or uncomfortable. If complications do occur there are numerous methods of treatment, such as steroid and antibiotic medications, to counter the inflammation and eliminate microbial infections (Boost et al., 2017).

Apart from medical complications, contact lenses can also be expensive and laborious to obtain. Patients are required to purchase supplies of disposable lenses at regular intervals and to buy solutions to moisturize and disinfect them. Although extended wear lenses are common, they present a greater risk for complications especially infection without proper care. Despite this method of vision correction being effective, contact lenses have a number of costs both medical and financial that may exclude patients from using or obtaining them. A survey study, conducted in 2016 of 1,800 participants who either continued contact lens use or opted for laser vision correction, found that after three years 88% of the participants who opted for laser vision correction were strongly satisfied with their vision compared with 54% of the participants who opted to continue wearing contact lenses (Price et al., 2016). There has been some speculation that the risks for vision loss associated with contact lens use may actually be greater than laser-assisted in situ keratomileusis (LASIK) if considered over a greater period of time. In general the complications associated with contact lenses may accumulate over time to cause greater visually significant complications than a single laser correction procedure.

Laser Vision Correction

For patients who are unwilling to continue with glasses or contacts there are more advanced, surgical methods, to improve vision. The most modern intervention for refractive errors involves the use of lasers to remove tissue from the corneal stroma, precisely altering its biomechanical structure and improving its refractive behavior. These procedures can be fundamentally divided into three major categories: corneal surface ablation, corneal stromal ablation and corneal lenticule extraction. Surface ablation laser treatments are done directly on the anterior surface of the cornea, usually involving removal of the corneal epithelium and Bowman's layer. Corneal stromal ablation techniques require the creation of a corneal flap with a mechanical microkeratome or a femtosecond laser before laser treatment and ablation of tissue from the underlying stromal bed, after which the flap is put back in place. Refractive corneal lenticule extraction procedures are stromal ablation techniques that remove tissue in the stroma but do not require the creation of a corneal flap (Wen et al., 2017). The two laser correction procedures used most in the United States are a stromal ablation procedure called laser-assisted in situ keratomileusis (LASIK) and a surface ablation procedure called photorefractive keratectomy (PRK). Although using slightly different methods, both of these procedures utilize specially designed lasers to modify the corneal tissue structure in a way that corrects the refractive errors causing deficits in visual acuity.

Mono-vision Correction

A large majority of people eventually require vision correction for focusing on near objects. This is commonly referred to as reading vision and many people will require reading glasses by the age of 45, particularly as individuals lose their ability to accommodate. Although the primary goal of laser vision correction is to restore functional and satisfactory distance vision, it can be used to correct near vision as well. This type of procedure is called mono-vision and requires that one eye, preferably the non-dominant eye, be left under corrected or over corrected to preserve the ability of the eye to focus clearly on near objects, such as text in a book. Thus one eye can focus on distance vision, the mono-vision eye can focus on near vision, and both eyes work together for a full range of distance and near vision. The goal of a mono-vision correction is to spare the patient the need for reading glasses later in life after laser vision correction when the capacity to accommodate between near and far is lost. The patient typically undergoes mono-vision contact lens trials to determine if this correction option would be satisfying. A mono-vision trial requires the patient to wear extended use contact lenses with one contact correcting an eye for distance and the other contact with a slightly different prescription correcting the other eye for near vision. The reasoning behind preoperative trials is that mono-vision may not be a comfortable modality of binocular vision for some patients, and they must test this comfort level before undergoing surgery that permanently alters their vision. While mono-vision procedures are less frequent than traditional laser vision corrections, they are still effective and safe when performed with proper preoperative patient counseling.

LASIK and PRK

LASIK, as it is seen today, is a result of the combination and adaptation of older refractive surgeries and developing laser technology that gave refractive surgeons the tools to predictably and safely reshape the human cornea. This procedure has become the preferred method of surgical correction for both ophthalmologists and patients. LASIK procedures are characterized by the creation of a lamellar corneal flap as the first step. This flap is folded back before the treatment laser is used and is returned to its original position after the ablation is complete (Pallikaris et al., 1991). The LASIK flap is created using a surgical microkeratome which uses a surgical blade to cut the cornea or a specialized femtosecond laser that generates millions of closely arranged microscopic bubbles at a predetermined depth and at a diameter that encompasses the patient's optical zone. These bubbles allow the surgeon to separate the delicate flap from the stromal bed with relative ease, while leaving a hinge at one end that remains attached. The surgeon uses a sterile tool to separate the LASIK flap and fold it over, revealing the underlying stroma in an area of exposed tissue that can now serve as the treatment zone for the laser.

After a flap is created and the stromal bed is exposed an excimer laser is used to remodel the corneal structure. By vaporizing tissue in a finely controlled manner the laser is capable of altering the shape of the cornea while minimizing unnecessary tissue destruction. The excimer laser is capable of tracking the patient's eye position up to 4,000 times per second, redirecting laser pulses for precise placement within the treatment zone and avoiding damage to the adjacent stroma. Laser pulses are about 1 millijoule of energy firing 10 to 20 nanoseconds. After the laser has reshaped the stromal layer, the LASIK flap is carefully repositioned over the treatment area by the surgeon and checked for the presence of air bubbles, debris, or folds. Proper placement of the flap after treatment is crucial for a successful surgery. A flap that is not repositioned correctly can result in new, surgically induced, refractive errors. Once the flap is replaced, it remains in position by natural adhesion (cohesion, friction and osmotic forces) until healing is completed.

LASIK is effective at treating myopia, hyperopia, and astigmatism (Salah et al., 1996). A retrospective study done at a single facility found that of 37,932 eyes treated with LASIK procedures for a myopic error that averaged approximately -5.90 D, 91% of the eyes reached an uncorrected distance visual acuity (UDVA) greater than or equal to a Snellen score of 20/30 with 72.8% reaching a UDVA of 20/20 or greater (Yuen et al., 2010). A study done in 2018 analyzing refractive and visual outcome data for 1,350 eyes diagnosed with hyperopia averaging about +2.77 D of spherical equivalents found that 73% of postoperative spherical equivalents were within 0.50 DS of their target and 93% were within 1.00 D of their target refraction. This study also found that postoperative UDVA was 20/20 or better in 75% of eyes (Reinstein et al., 2018a). Another study completed by the same research team in 2018 found that for 108 eyes corrected for astigmatism with a mean cylinder value of -2.93 D, 89% had a preoperative corrected distance visual acuity (CDVA) of 20/20 or better, and after LASIK correction 69% achieved a postoperative UDVA of 20/20 or better with 83% within 0.50 D of their target refraction. Although these results for astigmatism fulfilled the standards for safety, efficacy, and predictability the study concluded that about 12% of patients were overcorrected. A nomogram was suggested as a way to help reduce the amount of overcorrection (Reinstein et al., 2018b)**.** Two U.S. Food and Drug Administration (FDA) studies conducted in 2017 using patient-reported outcomes analyzed the frequency and incidence of patient reported complications and complaints after having LASIK surgeries. The study found that 46% of patients who did not have visual symptoms before LASIK reported at least one visual symptom after surgery which was most often halos. Although this frequency of visual symptoms after surgery appeared rather high, the study noted that of these patients who reported new visual disruptions after surgery, less than 1% reported experiencing difficulty or inability to perform daily activities because of any one symptom. Overall, 95% of patients were satisfied with their vision following LASIK (Eydelman, Hilmantel, et al., 2017; Eydelman, Taryer, & Ferris, 2017)**.**

Another very popular laser vision correction procedure commonly done in the United States is photorefractive keratectomy (PRK). PRK is very similar to LASIK in that it uses an excimer laser to ablate corneal tissue; however, there is no creation of a flap before the treatment laser is used. Instead of creating a flap and ablating the underlying stromal bed, the corneal epithelium is removed using isopropyl alcohol with a blade or a brush to reveal the stroma. This procedure is done by using a ring that prevents the alcohol from dispersing across the entire surface of the eye. The ring is held in place for about 45 seconds before it is removed, and the alcohol is washed away with sterile saline solution. The 20% alcohol solution partially dissolves the epithelium and Bowman's layer, which are then removed using a sterile tool and discarded. Once the epithelium is removed and the stroma has been exposed, a surface ablation is performed. The PRK ablation occurs in much the same way as the LASIK procedure, using the same excimer laser and treatment calculation inputs. After the laser ablation treatment, a sponge coated with mitomycin-C is typically applied to help reduce the development of haze during healing. Once the treatment zone has been dosed with mitomycin a bandage contact lens is placed over the eye and left in place until the epithelium can heal. Compared to LASIK, the recovery time following a PRK procedure is longer. This longer recovery time is due to the removal of the corneal epithelium which can take several days to fully regenerate.

Although the recovery time for PRK is longer, the procedure eliminates the need for a LASIK flap (Ambrósio & Wilson, 2003). This is an important distinction. LASIK may not be an option for people who cannot safely undergo the flap creation step or who live a lifestyle that puts them at risk for eye trauma after treatment (for example, law enforcement or military service). Creation of the flap in LASIK requires the use of a scleral negative suction ring to immobilize the eye, and applanate, or flatten the cornea. This vacuum ring technique can cause pressure in the eye to increase by nearly 60 mmHg. Patients with thin corneas or glaucomatous eye problems may not be candidates for LASIK laser vision correction because the pressure increase puts them at risk for complications that can damage the optic nerve and result in permanent vision loss.

There are many reasons to choose LASIK over PRK, and vice versa; The choice is a combination of the patient's preferences and the medical judgment of the operating surgeon to determine the procedure with the best possible outcome. A patient must be in agreement with the vision correction offered, and the surgeon must protect the patient from unnecessary harm or cost. Although PRK and LASIK utilize different methods, studies have shown that the refractive outcomes for both procedures are very similar. A meta-analysis conducted in 2017 on the various refractive procedures found that there was no statistically significant difference in visual outcomes or visual quality between LASIK and PRK. (Ambrósio & Wilson, 2003; Wen et al., 2017)

LASIK and PRK Complications

Both LASIK and PRK procedures when done correctly and with proper patient counseling are safe and effective. Nevertheless, no surgical intervention is without risks. There are a number of complications associated with these two methods of laser vision correction. Many of the complications are shared with relative equality between LASIK and PRK, but some are unique to the specific method. One of the most common postoperative complications of LASIK surgery is keratoconjunctivitis sicca, more commonly known as dry eye. Dry eye results when there is insufficient production or increased evaporation of the tear film that covers and nourishes the cornea and conjunctiva. Symptoms of dry eye include burning, itching, irritation, and a gritty foreign body sensation. Patients may also experience pain, photosensitivity, and blurred vision; however, permanent vision loss is rare. LASIK surgery induces dry eye complications through the ablation and flap formation that can result in damage to the corneal nerve plexus which branches from the peripheral stromal nerves and penetrates the Bowman's layer and epithelium. These nerves communicate information about the osmolality of the corneal tissue and tear film to induce production of tears and maintain a moisture content necessary for proper refractive biomechanics and corneal health. Symptoms of dry eye may fluctuate in intensity, are usually intermittent, and can be managed well with lubricating artificial tears or punctal plugs that prevent drainage of the tear film. (Hovanesian et al., 2001; Shaheen et al. 2014).

Other common complications of LASIK involve infection, incorrect flap position, flap damage, or irregularities with the interface between the flap and the stromal bed that can result in scarring, opacification, epithelial ingrowth or striae. Infections are prevented prophylactically with antibiotic drops administered immediately after surgery and for 4 days afterward. Scarring, opacification, and diffuse lamellar keratitis (DLK) are prevented by a course of steroid drops in unison with the antibiotic drops, whereas epithelial ingrowth is avoided primarily through better surgical techniques. Aside from complications associated with flap formation and healing, there are also increased risks for patients more likely to experience ocular trauma, such as military servicemen and servicewomen, law enforcement officers, firefighters, or professional athletes. The LASIK flap never actually heals completely. The flap is held in place by minuscule scar tissue at the margin of the flap, but it will never completely bond to the underlying stromal bed. The presence of incomplete bonding means that extreme blunt force trauma or abrasions by moderately sharp objects such as a fingernail to an eye treated with LASIK could dislodge the corneal flap, resulting in potentially serious vision-threatening complications and blindness. This is one important reason why patients may opt to have PRK over LASIK (Sridhar et al., 2002).

Many of the complications associated with PRK are similar to LASIK, including infection, scarring, and opacification. As with LASIK, the most common postoperative complication of PRK is dry eye. Although there is no flap formation for PRK, the surface ablation and removal of corneal epithelium can result in damage to the corneal nerve plexus, causing a reduction in the amount of tear film produced. Dry eye for PRK is treated in the same way as for LASIK with artificial lubricating tears and punctal plugs. Another common visually significant complication of PRK is corneal haze. Corneal haze results from the preliminary debridement and postoperative healing of the corneal epithelium that causes the production of inflammatory cytokines and the proliferation of fibroblasts which can induce hazy opacities within the laser treatment zone. These hazy opacities can take one month to a year to resolve completely, but they rarely result in permanent vision impairment. Intraoperative use of mitomycin-C and postoperative use of ocular steroid drops have been proven to be effective at preventing haze. Regardless, corneal haze remains a risk of PRK.

Common visually significant complications of both laser vision correction procedures include glare, halos, and starbursts that result from small residual refractive errors and the natural healing process. Glare is particularly bothersome at night while driving because vehicle headlights, taillights, and traffic signs can produce large, visually disruptive halos and starbursts that can reduce a person's visual acuity temporarily, making driving more dangerous. Patients may experience fluctuations in their vision as the tissue heals and stabilizes, and excessive glare usually resolves in weeks to months. Glare and halos can in some cases persist for extended periods of time after surgery, but it is possible to correct these residual refractive errors for night driving using glasses or contacts. Although the ultimate goal of laser vision correction is to eliminate or greatly reduce the need for glasses or contacts, a small number of patients require some traditional vision correction after surgery in particular circumstances, such as night driving. The surgery, however, can still be considered effective at reaching its goal.

Another shared complication of PRK and LASIK procedures is that both involve the removal of corneal tissue from the stroma. Average ablations can leave the cornea 50-120um thinner, and this reduction in thickness can, in some cases; result in a progressive corneal thinning condition called ectasia. Ectasia is a rare, potentially vision-threatening condition that more commonly occurs after secondary LASIK and PRK enhancement procedures but is also prevalent in populations having primary LASIK and PRK treatment. The avoidance of these postoperative complications requires that patients are screened and proper preoperative evaluations are performed in order to determine if patients are at risk for ectasia or other corneal thinning-related complications. Patients are required to undergo corneal topography imaging to visualize and measure the thickness of the cornea and, the dimensions of the anterior and posterior faces of the cornea as well as the anterior chamber. These results help to ascertain if the patients have thin corneas or corneal abnormalities that may put them at risk for ectasia.

Corneal thickness can be measured by using a pachymeter or by analyzing the information from the corneal topographic map. Patients with corneas thinner than 500um may be discouraged from having LASIK and may opt for PRK. Patients with corneas thinner than 450um may be discouraged from having either laser vision correction procedure because of the risks of excessive thinning. Based on the patient's level and category of refractive error, the surgeon is able to calculate the depth of tissue ablation required to reach the desired refractive correction as well as the residual stromal bed. Using this information, the surgeon determines if the patient's cornea can achieve a postoperative corneal thickness that retains the integrity of the cornea. Thickness as well as the physical dimensions of the cornea can give insight into underlying corneal disorders. Patients exhibiting corneal steepening or asymmetry between the anterior and posterior surfaces of the cornea may be indicative of underlying or pathological ectasia disorders. These patients are discouraged or denied from having LASIK or PRK procedures. These possible complications of secondary LASIK and PRK enhancements necessitate the need for maximally precise laser corrections with minimal tissue removal. One way this is accomplished is by adjusting the laser treatment input values to slightly alter the treatment design itself and the amount of tissue removed (Spadea & Giovannetti, 2019)**.**

Laser Vision Correction Nomograms

Before a LASIK or PRK laser procedure can be performed, the surgeon must first calculate the patient's true refractory target and enter it into the treatment laser. This refractive correction target is called the laser treatment input, and the excimer laser uses this input value to perform the desired level of treatment. To make this calculation many surgeons use a nomogram, an algorithm or differential chart that utilizes a diagram to approximate the computation of a mathematical function. This calculation is important because it is the primary parameter that the laser uses to conduct the treatment. Nomogram calculations assist surgeons in designing laser correction treatments that reach the desired refractory target and visual acuity for as long as possible. Miscalculations in this laser input could result in less than acceptable refractive outcomes.

Traditional laser vision correction treatment nomograms generate laser inputs based on a combination of factors, including the preoperative refraction, the target refraction, and the amount of tissue ablation required to reach the target. The algorithms used to create the nomograms are based on the observation and analysis of thousands of compiled real-life visual outcomes from previous laser correction procedures. These algorithms pull together massive data pools to mathematically fine-tune the laser treatments generated by their calculations and alter the amount of tissue removed.

Nomograms are particularly useful for high-order refractive errors because they require greater amounts of tissue ablation and therefore require more adjustments to the amount of correction being administered. The refractive stability of higher-order ablations are less predictable than lower-order ablations as a result of the greater amount of removed tissue. This situation results in increased biomechanical instabilities, and a nomogram can assist the surgeon in making adjustments. Although the surgeon is aware of the patient's preoperative manifest refraction, a decision may be made to under treat or over treat an eye in certain situations. This is because the human eye has a tendency to physically change over time to varying degrees depending on the patient's age, type of refractive error, and general eye health. For example, if a patient has a hyperopic eye that is prone to a myopic regression, the surgeon can choose to slightly under correct the eye with the prediction that the patient's vision will continue to improve as the eye continues to change after surgery (Yan et al., 2018). If the surgeon were to ignore this prediction, it is possible that the patient would have satisfactory vision for a short period of time, after which the patient would again require vision correction with additional laser enhancements or traditional lenses.

Along with the natural tendency of the eye to change, alterations to the corneal structure through laser vision correction often result in biomechanical instabilities that can take months to resolve. These instabilities are a result of the natural healing process of the body as it copes with the tissue damage and structural changes involved in the surgery, and it is one reason why people with a history of unstable refractions are discouraged from electing to have laser vision correction. Patients free of these congenital or surgically induced instabilities are able to undergo secondary or even tertiary laser corrections enhancements; however, these additional treatments come with further risks of their own (Yan et al., 2018).

Besides the financial burden, a major issue and possible complication with having additional laser treatments is that each procedure permanently removes corneal tissue that has no capacity to regenerate. This lack of regenerative capability with a finite amount of corneal tissue means that repeated laser corrections progressively thin the cornea and can place the patient at risk for ectasia. Excessive thinning of the cornea that results in ecstasia or unstable keratoconus can have severe consequences for the visual acuity of the person. Because the goal of these procedures is to eliminate or greatly reduce the need for vision correction, surgeons are obligated to perform a treatment that is as safe and effective as possible at reaching this goal with a minimum of procedures. For this reason, it is crucial for newer, innovative nomogram treatment protocols to be generated and explored.

The Boston Eye Group (BEG) is a comprehensive ophthalmologic care facility in Brookline, MA, that specializes in corneal ophthalmology, laser vision correction, cataract extraction, and general ophthalmology. The corneal surgeons at the BEG are performing LASIK and PRK procedures using a laser treatment nomogram called the Wellington nomogram. The Wellington nomogram utilizes a simple linear regression to determine laser inputs based on varying severity of refractive error. The surgeon must look at the nomogram chart and generate the required laser input based on the given calculations. For example, if a patient has between -2.00 DS and -6.00 DS of spherical error, the Wellington nomogram dictates that there should be no adjustment to the input to reach a target refraction of 0.00 DS. However, if a patient has greater than -6.00 DS of spherical error, then the Wellington instructs the surgeon to subtract -0.25 DS from the laser input to achieve a refractory target of 0.00 DS. Although generally effective, the Wellington way of calculating may not account for variables that are specific to the patient or the surgeon or the facility. Thus, the patient’s eyes may not, with desired predictability, reach the target refraction based on the calculation parameters from the

Wellington nomogram.

A nomogram that has been in development and use since 2007, called the Internet-based refractive analysis (IBRA), has been implemented at the BEG with the goal of improving LASIK and PRK outcomes. The IBRA nomogram is unique in its calculation parameters in that it utilizes outcome data from numerous refractive surgeries, tracking data on the patients and the surgeons performing the procedure to calculate a laser treatment input that results in more predictable and more stable refractive outcomes. Important parameters used by the IBRA nomogram for treatment calculations are the type of laser ablation device and its laser mode, the preoperative and target manifest refractions (spherical, cylindrical and axial values), the K values, the date of the operation, the treatment method (LASIK or PRK), and the chosen optical zone.

The laser ablation device being used is an important parameter to the calculation because different excimer lasers have varying energy outputs and ablation profiles that can change the expected visual outcomes. The preoperative manifest and the target refraction are important specifications because they direct the laser to perform the required refractive correction for that specific case. The K values are measurements that define the horizontal and vertical curvature of the cornea and help to describe the dimensions of a regular astigmatism. These two curves are aligned on a parallel plane with the cornea and are oriented perpendicular to each other to visualize fundamental curvature of the cornea. Optical zones determine the diameter of the treatment zone and affect the amount of tissue ablation required. A larger optical zone requires more tissue ablation, whereas a smaller optical zone requires less. A larger optical zone reduces the chances of complications such as glare and halos, but a greater amount of ablation increases the possibility of complications related to excessive thinning of the cornea like ectasia. For this reason, optical zones are chosen based on the patient's scotopic pupil diameter and the amount of tissue that can be safely ablated in that specific case. To maximize visual acuity and minimize visually significant complications, the largest but safest optical zone possible is chosen for each patient. The type of treatment method is crucial for the calculation of different laser vision correction modalities; however, the LASIK and PRK calculations are virtually identical, so the method chosen has no impact on the calculations provided for this study.

As stated by the proprietary owners of the IBRA software:

> The nomogram calculation derives a linear regression curve from refractive data. The results are two formulas, one for the spherical and one for the astigmatic data. The formulas are a mean value of the effective result. These formulas can be mathematically compared with a theoretical formula, derived by the perfect outcome. The difference between the effective and the theoretical formula is the refractive error, the deviation from the optimal result. This difference also can expressed by a formula. This formula was implemented in IBRA and offers preoperative calculations to optimize the effective outcome (Zuberbuhler et al., 2007)

Surgeons use the IBRA software to calculate the laser inputs as well as to track the refractive and visual acuity outcomes that the program compiles in a user-friendly format. This compiled data from one or more surgeons can be analyzed and displayed by the program with a best-fit regression algorithm which can be used to enhance the calculation parameters. Refractive and visual data, such as preoperative and postoperative manifest refractions and visual acuity scores, are recorded and analyzed by the IBRA software, which can then be displayed in standardized outcome graphs used for the reporting of refractive data. The IBRA software is capable of being personalized and augmented for a specific surgeon or surgical facility to account for treatment variables associated with a specific protocol. This is important because although the fundamental protocol of the procedure is well established, a particular surgeon's proficiency, technique, and equipment can vary greatly from surgeon to surgeon or facility to facility. These variables are accounted for by IBRA to achieve maximal visual acuity and to minimize complications through enhancement of the calculation parameters. Enhancement of the calculation parameters results in changes to the total amount of tissue being ablated and to the amount of under correction or over correction being administered.

With these small corrections, a surgeon may be able to better predict the outcome of the procedure while simultaneously tracking all other case outcomes. Being able to predict how the structure of the cornea and its refractive behavior will change following surgery is critical to performing effective LASIK and PRK procedures. Functional excimer laser treatment nomograms are a crucial part of effective refractive laser vision correction surgeries. The predictability of these laser treatment nomograms and their associated visual outcomes remain an important field of study in refractive ophthalmology (Zuberbuhler et al., 2007).

OBJECTIVES OF STUDY

The goal of this study is to improve the effectiveness of laser vision correction by determining if a new method of calculating laser inputs (IBRA nomogram) is more effective than a more traditional method (Wellington nomogram). The hypothesis of the work is that the IBRA nomogram with a more comprehensive set of parameters will have better visual and refractive outcomes than the Wellington.

The objectives of this study are:

(1) To carry out a retrospective data analysis comparing the laser vision correction outcomes using two different excimer laser nomograms (Wellington and IBRA).

(2) To compare visual acuity and refractive outcomes for patients before laser surgery and at a six-week follow-up evaluation.

METHODS

This study was a retrospective data analysis comparing the laser vision correction outcomes using two different excimer laser nomograms – the IBRA nomogram and the Wellington nomogram.

The ablative excimer laser platform used in this study was the Alcon Laboratories WaveLight EX500 excimer laser (Alcon Laboratories, Fort Worth, TX), utilizing a wavefront-optimized laser ablation profile. LASIK flaps were created with the Johnson & Johnson Intralase iFS femtosecond laser (Johnson & Johnson Vision, Jacksonville, FL). The IBRA Nomogram software was provided by its proprietary owners at Zubisoft Inc. (Niederhasli, Switzerland) and operated by the conducting surgeon, fellow surgeons and surgical staff.

Candidates for LASIK or PRK correction at the BEG were determined based on an evaluation protocol and counseling carried out in a preliminary exam by an ophthalmic technician and a final evaluation by the surgeon. Candidates were chosen or denied using information and measurements collected in the preliminary tests as well as a slit-lamp examination of the patient's cornea. Individuals included in the analysis were patients undergoing primary laser vision correction using LASIK or PRK methods done by two different surgeons. Patients were chosen at random for data collection based on who elected to have the procedure done during the standard surgery schedule.

Candidates in the first group (Wellington group) had LASIK or PRK done by one surgeon using the Wellington nomogram calculations between June and July of 2019. Candidates in the second group (IBRA group) had LASIK or PRK done by another surgeon using the IBRA nomogram calculations between November and December of 2019. Both physicians operated with identical equipment and BEG staff with a significant number of procedures performed by their fellows in training to help reduce surgeon bias. Patients who exhibited preoperative corneal abnormalities affecting visual acuity or pathologies affecting procedure safety, such as glaucoma, cataracts, keratoconus, myopia greater than -12.00 DS, hyperopia greater than +5.00 DS, or unstable refractive errors, were discouraged or denied from having laser vision correction and were excluded from this study. Patients who had undergone a previous laser refractive surgery were excluded from using the IBRA nomogram and were also excluded from the study.

For entry of each patient into the IBRA program several measures were important for procedure outcomes and patient data tracking. The first set of values consisted of the preoperative examination values that dictated the fundamental laser correction: sphere, cylinder, and axial manifest refraction values; K values for flat, steep and axis; central corneal thickness; flap thickness (if LASIK); and scotopic pupil diameter. The second set of values were the operational parameters consisting of the operation date, laser vision correction method, laser ablation platform, laser mode, intervention type (primary or otherwise), chosen optical zone, flap creation laser platform, and target sphere and cylinder measurements that were the intended postoperative refraction values.

Once these values were entered the program generated a refractive correction which represented the nomogram calculation and the numbers used as input for the treatment laser. IBRA gave values that were exact to the refractive correction; however, the excimer laser ablation platform used by the BEG required an input in minimal increments of +\-0.25 diopters. To work around this, the treatment correction was rounded to the nearest quarter diopter: IBRA might give a refractive correction of 2.68 diopters, but because the decimal 0.68 was not accepted by the laser, it was rounded to 2.75 diopters. For calculations in this study, the IBRA reference database was used for the regression analysis and the final treatment input. Based on the chosen calculation the program also gave measures of the estimated depth of tissue ablation (in microns) as well as the amount of residual stromal bed after the treatment was completed.

Postoperative visual acuity, manifest refraction, spherical equivalents and complications were recorded and tracked at the six-week postoperative evaluation conducted by one of the surgeons, an in-house optometrist, or by the patient's primary ophthalmologist or optometrist. Patients experiencing visually significant post-operational complications at this six-week follow-up were excluded from the study to control for confounding variables in the visual acuity analysis. Examples of postoperative complications warranting study exclusion included striae in the optical zone, haze, flap folds or severe dry eye. Patients unable to return for a six-week evaluation or unable to have their values sent by their co-managing physician were also excluded for lack of data. Results were calculated and displayed using the standard reporting graphs provided by the *Journal of Refractive Surgery* and the *Journal of Cataract and Refractive Surgery*. The standard reporting graphs were the following: (1) the efficacy graph for distance eyes only which gave information about whether or not the treatments were actually improving the distance vision of patients having laser vision correction (see Figure 4 in Results); (2) the preoperative CDVA to postoperative UDVA comparison graph, which gave insights into how well the correction treatments approached their intended or desired visual acuity (see Figure 5 in Results); (3) the safety graph, which was used to ensure that the treatments were not reducing the CDVA of the patients (see Figure 6 in Results); (4) the accuracy of spherical equivalent refraction histogram, which displayed information on the resulting accuracy of the refractive corrections and how close they were to the target refraction after six weeks (see Figure 7 in Results); (5) the attempted versus achieved spherical equivalent refraction regression plot, which displayed the amount of under correction or over correction administered during the treatment (see Figure 8 in Results); and (6) the amplitude of astigmatism graph, which showed how well the treatments were able to correct astigmatic refractive errors (see Figure 9 in Results). These values were entered into the provided Microseoft Excel sheets (Version 2007-2016 XML, Microsoft Corporation, Redmond, WA) and organized into the graphs based on their embedded formulas.

Visual acuity, measured UDVA and CDVA given by the Snellen visual acuity chart for distance vision and measured UNVA given by the Jaeger visual acuity chart for near vision, were converted to logarithm of the minimum angle of resolution (logMAR) and decimals for more accurate statistical analysis and representation in the study. All manifest refraction values were converted to manifest refraction spherical equivalents (MRSE) values for more accurate statistical analysis. Statistical analyses were performed with IBM SPSS Statistics for Macintosh software (Version 26.0, IBM Corp., Armonk, NY).

RESULTS

Outcomes were divided and grouped by the nomogram (Wellington or IBRA) that the surgeons used in their procedures. In total, 109 eyes belonging to 59 patients were included in the study: 51 eyes belonging to 28 patients operated on using the Wellington nomogram, and 58 eyes belonging to 31 patients operated on using the IBRA nomogram. Patients were chosen at random, and their treatments were not matched between the two groups. Table 1 summarizes the mean scores from the study.

Table 1. Mean logMAR Visual Acuity Scores and Mean Manifest Refraction Spherical Equivalents.

	Wellington Nomogram	IBRA Nomogram
Mean Preoperative logMAR BCVA	-0.03 (0.05)	-0.02 (0.05)
Mean Postoperative logMAR UCVA	0.006 (0.05)	0.03 (0.08)
Mean Preoperative MRSE	-4.3 D (2.7 D)	-2.9 D (2.09 D)
Mean Postoperative MRSE	0.02 D (0.4 D)	-0.2 D (0.5 D)

This table displays some of the key data points collected and analyzed in the study using the Wellington nomogram (n = 51) and the IBRA nomogram (n = 58). The table lists each value as the mean (standard deviation) for each group for better comprehension. BCVA = Best-corrected visual acuity; D = Diopter; IBRA = Internet-based refractive analysis; logMAR = Logarithm of the minimum angle of resolution; MRSE = Manifest refractive spherical equivalent; n = Number of sample cases; UCVA = Uncorrected visual acuity.

As Table 1 shows, data collected from the Wellington nomogram group showed a mean logMAR score for preoperative BCVA of (-0.03) with a standard deviation of (0.05), a mean logMAR score for postoperative UCVA of (0.006) with a standard deviation of (0.05), a mean preoperative MRSE of (-4.3 D) with a standard deviation of

(2.7 D), and a mean postoperative MRSE of (0.02 D) with a standard deviation of (0.4 D). Data collected from the IBRA nomogram group showed a mean logMAR score for preoperative BCVA of (-0.02) with a standard deviation of (0.05), a mean logMAR postoperative UCVA of (0.03) with a standard deviation of (0.08), a mean preoperative MRSE of (-2.9 D) with a standard deviation of (2.09 D), and a mean postoperative MRSE of (-0.2 D) with a standard deviation of (0.5 D).

For comparison of the two laser vision correction nomograms, a decision was that the two fundamental outcomes to be analyzed would involve a comparison of the postoperative UCVA and a comparison of the number of patients within 0.50 diopters of their spherical equivalent target refraction. These values were the most pertinent data points to base the goal of improving the efficacy and safety of laser vision correction through LASIK and PRK treatment methods.

For analysis visual acuity outcomes, a two-sample, two-tailed t-test assuming unequal variance was used to compare the Wellington and IBRA postoperative visual acuity outcomes at their six-week postoperative evaluation (df = 50) (P = 0.57). No statistically significant difference between the two groups was found.

For analysis of the refractive correction outcomes of the Wellington and IBRA groups, a Fisher exact test was used to compare the postoperative MRSE values that fell within 0.50 diopters of their target refraction at the six-week postoperative follow-up evaluation (df = 57)(P = 0.075). No statistically significant difference was found between the two groups.

An additional Fisher exact statistical analysis was done comparing the data collected for Standard Outcome Reporting Safety Graphs from both Wellington and IBRA nomograms to determine if there were significant differences in the changes in BCVA. The test was done because the two graphs visually appeared to have a significant difference between the number of Snellen chart lines lost and the number of Snellen chart lines unchanged or greater. No statistically significant difference in change in CDVA at the six-week postoperative evaluation was found (P = 0.2054).

Standard Outcome Reporting Graphs

Figures 4–9 show the standard outcome reporting graphs for this study after six weeks from laser vision correction. In each figure, panel (A) represents the results using the Wellington nomogram, and panel (B) represents the results using the IBRA nomogram.

Figure 4 displays the efficacy graphs for distance eyes only by presenting the postoperative UDVA and preoperative CDVA. These graphs give general information about the how effectively the treatments improved visual acuity. The values indicated that both laser treatment nomograms were able to generate laser treatment inputs that resulted in visual acuity outcomes reaching the desired level of efficacy.

Figure 5 displays the comparison graphs presenting the difference between postoperative UDVA and preoperative CDVA. These graphs give insight into how closely the correction treatments approach their intended visual acuity target. The values indicated that both laser treatment nomograms were able to generate laser treatment inputs that resulted in acceptable six-week uncorrected visual acuity outcomes.

Figure 6 displays the safety graphs for laser vision correction by presenting the change from preoperative CDVA to postoperative CDVA. The function of the safety graphs is to track the CDVA and ensure that the laser vision correction treatments are not reducing the overall best-corrected visual acuity that can be achieved by patients. Even if the surgery is not completely successful, it is important that the patient can still return to using traditional vision correction without significant changes in best-corrected visual acuity. The values indicated that both laser treatment nomograms were capable of generating laser treatment inputs that achived an acceptable level of safety by avoiding significant reductions in postoperative CDVA. The values appeared to have a significant difference in loss of postoperative Snellen chart lines however a Fisher exact test showed no statistical significance ($P = 0.2054$).

Figure 7 displays the graphs for spherical equivalent refraction accuracy by presenting how much patients postoperative spherical equivalent refraction differed from their intended spherical equivalent refraction. These graphs give insight into how accurate the treatments were at reaching the intended refractive values. The collected values indicated that both laser treatment nomograms were able to generate effective laser treatment inputs that achieved an acceptable level of refractive adjustment.

Figure 8 displays the attempted versus achieved spherical equivalent graph by presenting the intended versus achieved spherical equivalent refractions utilizing a regression plot. These graphs are intended to illustrate the amount of unintended, under correction or over correction administered during the treatment. The presented values indicate that both laser treatment nomograms generated laser treatment inputs that resulted in acceptable levels of under correction or over correction.

Figure 9 displays the change in amplitude of astigmatism by presenting the preoperative and postoperative cylindrical astigmatic values. The amplitude of astigmatism graphs are used to display how well the treatments corrected astigmatic refractive errors. The presented values indicated that both laser treatment nomograms were capable of generating laser treatment inputs that achieved acceptable levels of refractive astigmatism correction.

A

B

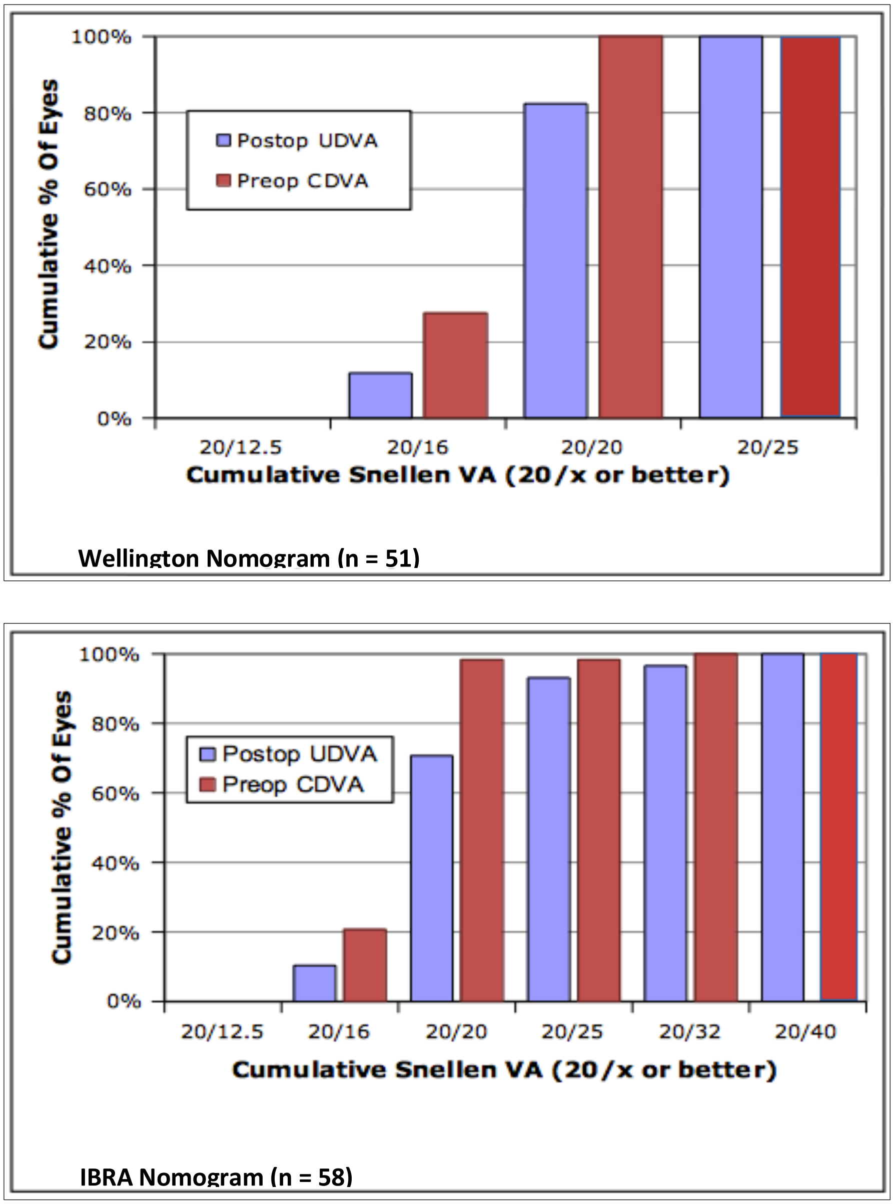
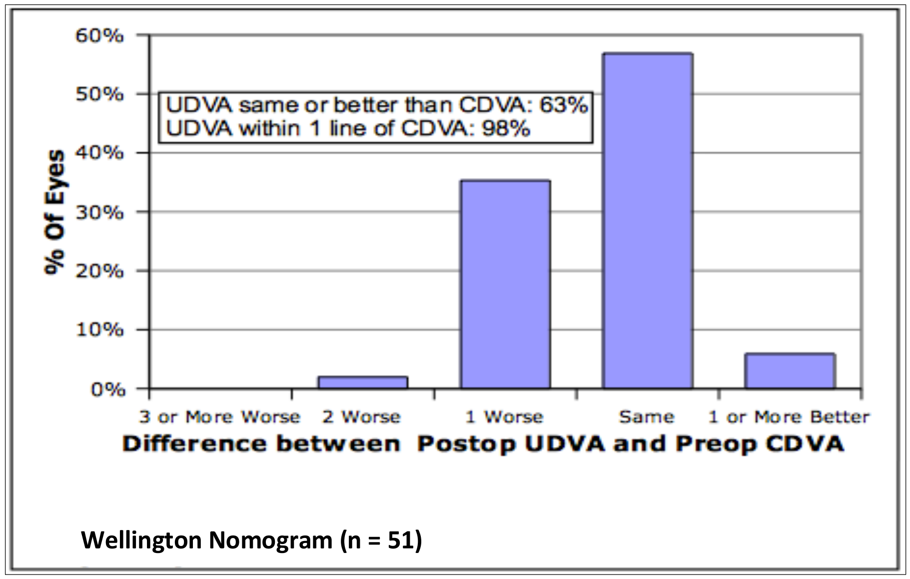


Figure 4. Six-week uncorrected distance visual acuity using Wellington and IBRA nomograms. This figure shows the efficacy graph for distance eyes only after six weeks from laser treatment using either the **(A)** Wellington nomogram or the **(B)** IBRA nomogram. These graphs display general information about how effectively the treatment corrections were at improving visual acuity by comparing preoperative CDVA and postoperative UDVA. CDVA = Corrected distance visual acuity; IBRA = Internet-based refractive analysis; n = Number of sample cases; UDVA = Uncorrected distance visual acuity; VA = Visual acuity.

A



B

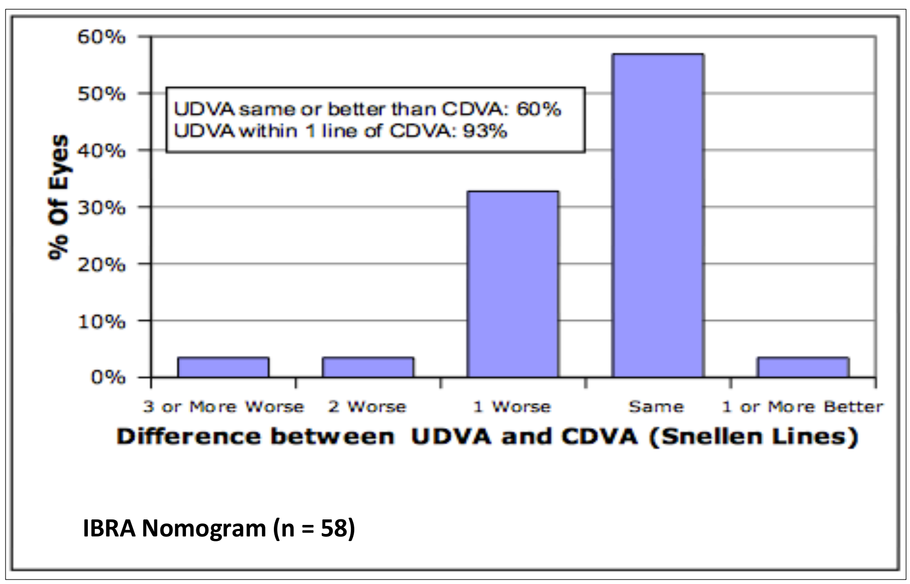
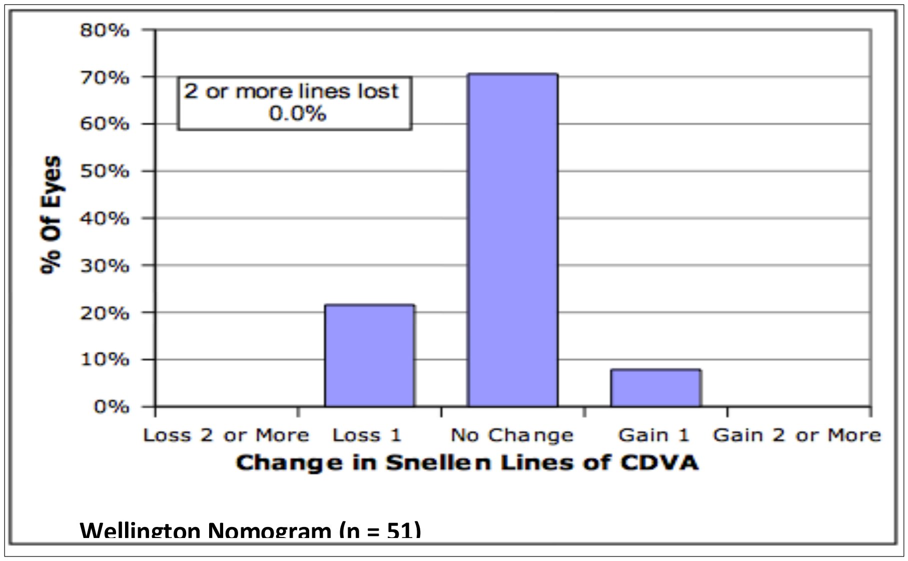


Figure 5. Six-week uncorrected distance visual acuity versus corrected distance visual acuity using Wellington and IBRA nomograms. This figure shows the comparison graph for the difference between postoperative UDVA and preoperative CDVA after six weeks from laser treatment using either the **(A)** Wellington nomogram or the **(B)** IBRA nomogram. These graphs function to display information about how well the corrections improved visual acuity by comparing their preoperative CDVA and postoperative UDVA. CDVA= Corrected distance visual acuity; IBRA = Internet-based refractive analysis; n = Number of sample cases; UDVA = Uncorrected distance visual acuity.

A



B

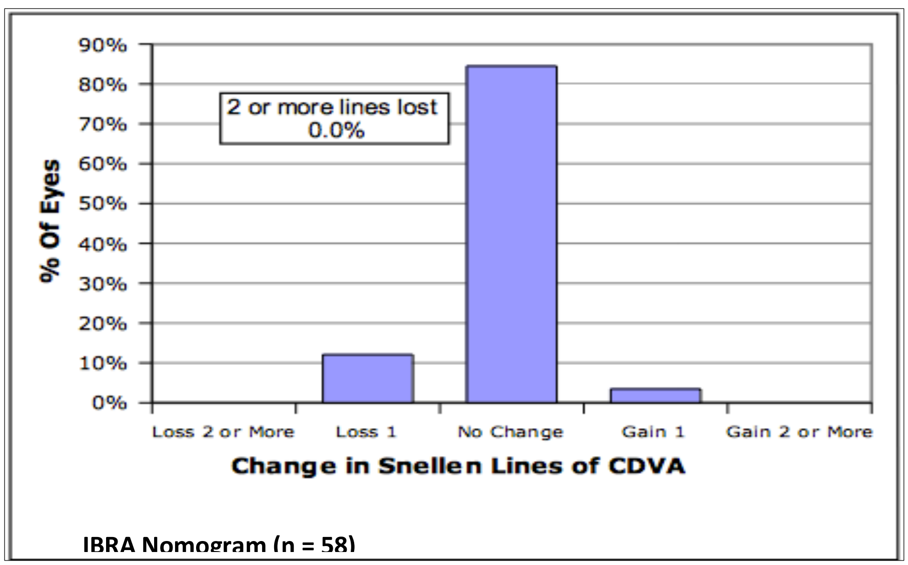


Figure 6. Six-week change in corrected distance visual acuity using Wellington and IBRA nomograms. This figure shows the safety graph with the change in CDVA after six weeks from laser treatment using either the **(A)** Wellington nomogram or the **(B)** IBRA nomogram. The graphs display information about how safely the treatments corrected vision in terms of reductions in postoperative CDVA by comparing the postoperative CDVA with the preoperative CDVA. Significant reductions in postoperative CDVA would mean the treatments reduced the patients best-corrected visual acuity and their ability to return to traditional vision correction. Although the graphs seem to have a significant difference, a Fisher exact test concluded that there was no statistically significant difference between the two groups (P = 0.2054).

A

B

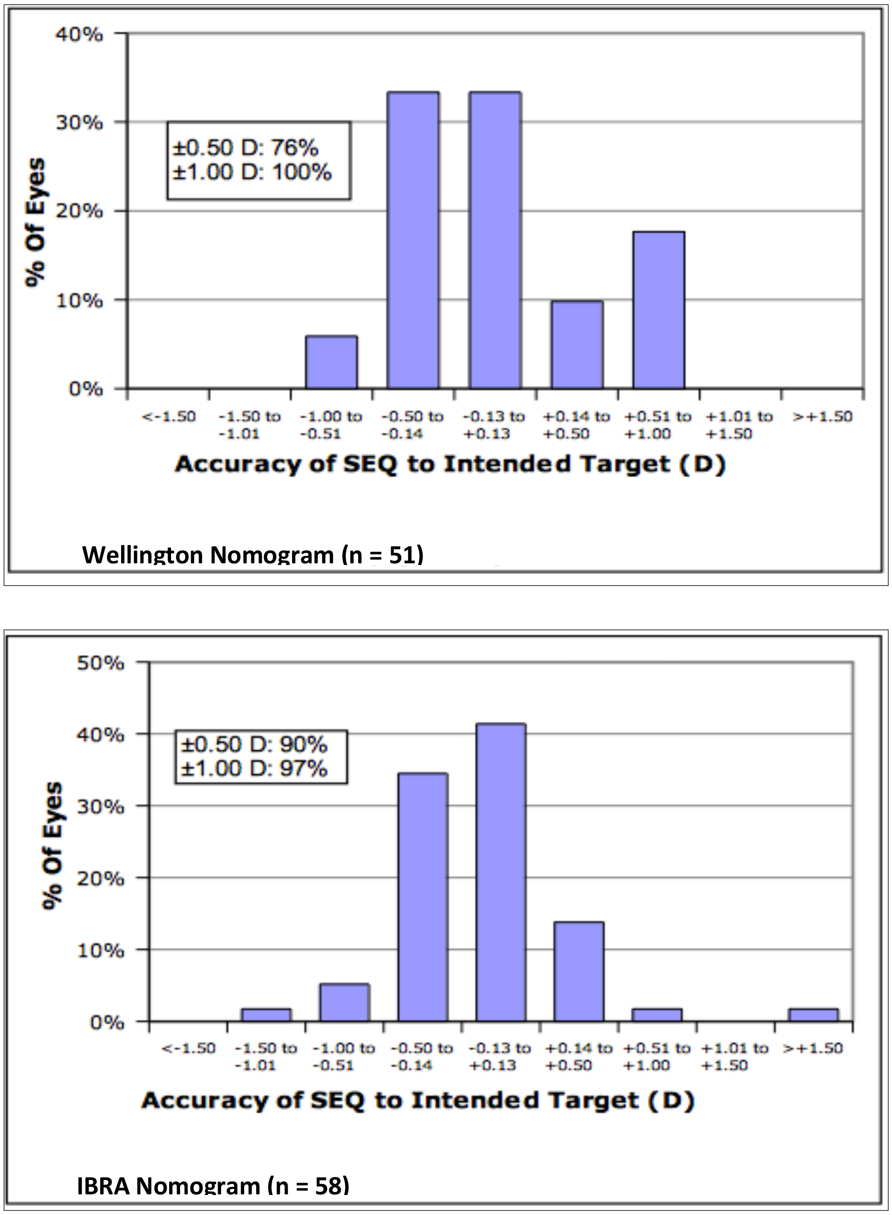
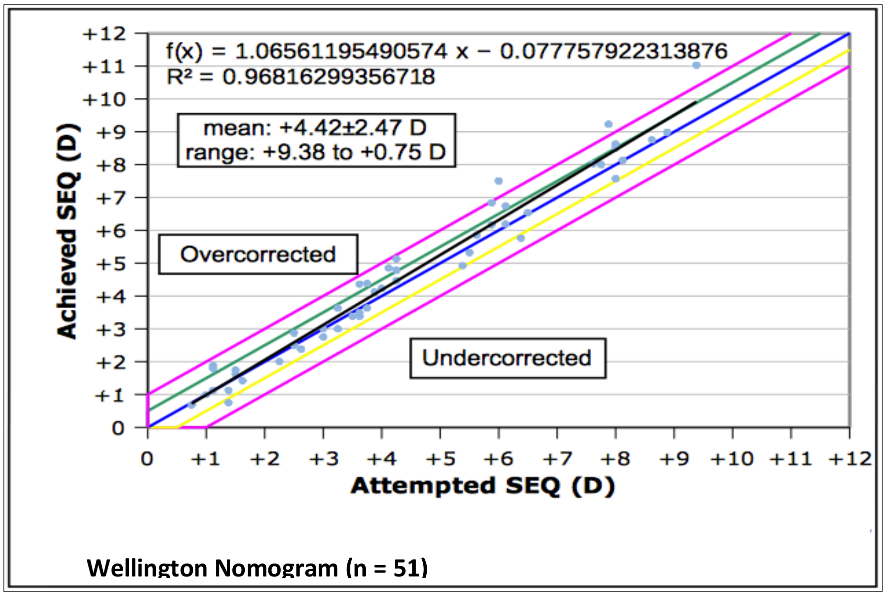


Figure 7. Six-week spherical equivalent refraction accuracy using Wellington and IBRA nomograms. This figure shows the histogram for accuracy of spherical equivalent refraction after six weeks from laser treatment using either the **(A)** Wellington nomogram or the **(B)** IBRA nomogram. These graphs are intended to show the number of patients who deviated from their intended postoperative refraction values and by how much by comparing the intended postoperative SEQ and the achieved SEQ. D = Diopter; IBRA = Internet-based refractive analysis; n = Number of sample cases; SEQ = Spherical equivalent.

A



B

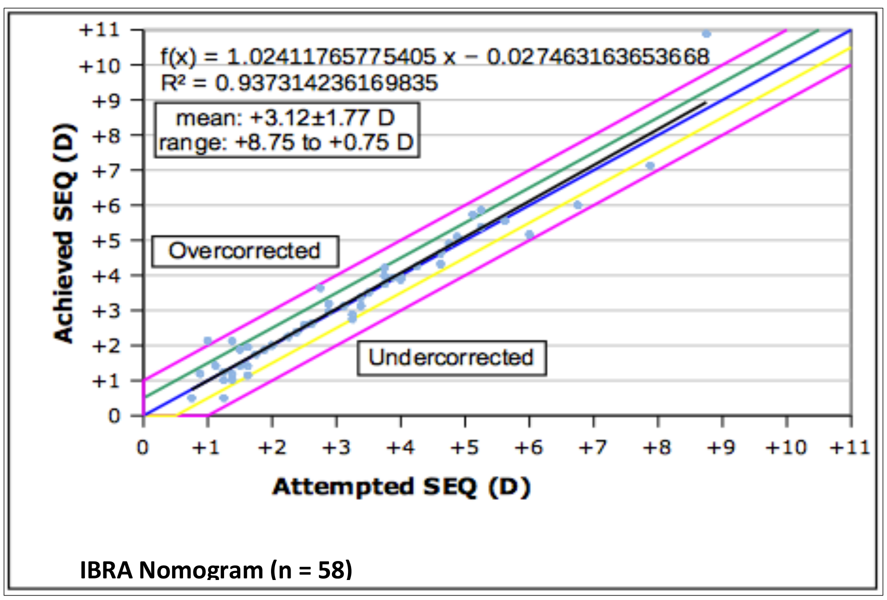
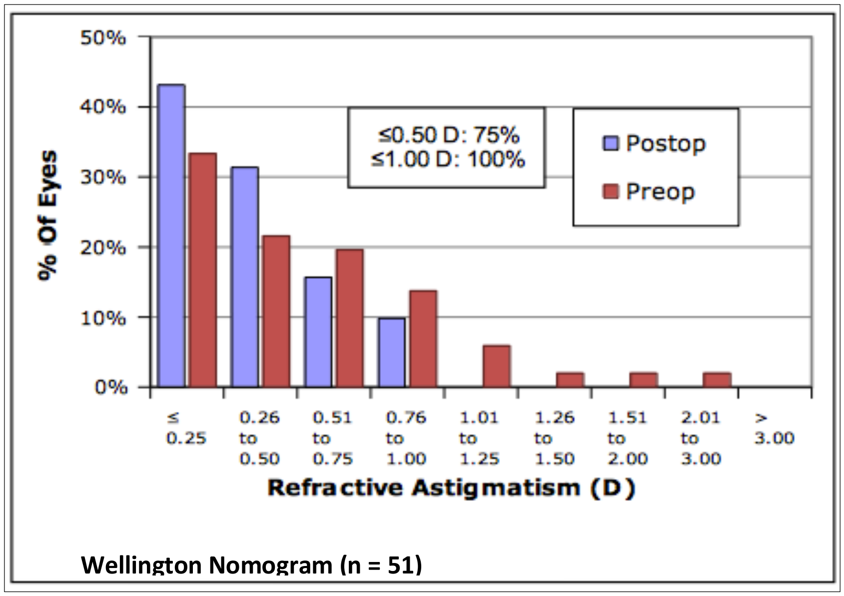


Figure 8. Six-week spherical equivalent refraction attempted versus achieved using Wellington and IBRA nomograms. This figure shows the linear regression plot for attempted versus achieved spherical equivalent refraction after six weeks from laser treatment using either the **(A)** Wellington nomogram or the **(B)** IBRA nomogram. These graphs display data on how much under correction or over correction was administered for each treatment by comparing the attempted SEQ and the achieved SEQ, similar to Figure 7. D = Diopter; IBRA = Internet-based refractive analysis; n = Number of sample cases; SEQ = Spherical equivalent.

A



B

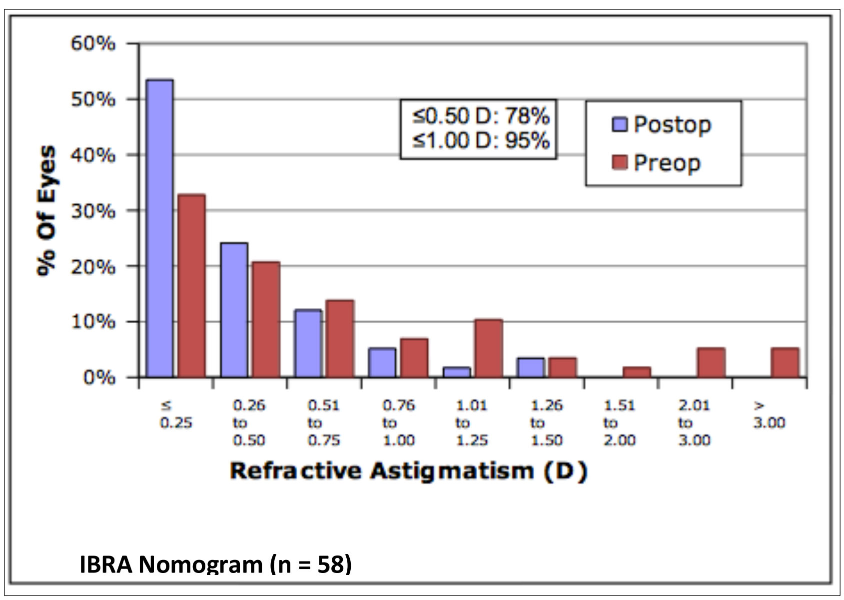


Figure 9. Preoperative amplitude of astigmatism versus six-week postoperative amplitude of astigmatism using Wellington and IBRA nomograms. This figure shows the change in amplitude of refractive astigmatism after six weeks from laser treatment using either the **(A)** Wellington nomogram or the **(B)** IBRA nomogram. These graphs display how well the laser treatments corrected refractive astigmatism by comparing the preoperative and postoperative refractive cylindrical values. D = Diopter; IBRA = Internet-based refractive analysis.

DISCUSSION

The goal of this study was to determine if the Internet-based refractive analysis (IBRA) and its nomogram software could outperform the traditional Wellington nomogram protocol for calculating the input values for excimer laser vision correction treatment in terms of its ability to reach better visual acuity outcomes and spherocylindrical error corrections. This study found that there was no statistically significant difference between the two nomograms when compared on the following data points: (a) six-week postoperative uncorrected visual acuity outcomes and (b) number of patients whose postoperative manifest refraction spherical equivalent reached a refraction within 0.50 diopters of the intended target at six-weeks.

The study has several limitations that undermined the value of the results. The sample population of laser vision correction procedures was too small to accurately represent the general population of patients undergoing laser vision correction. With only 51 Wellington cases and 58 IBRA cases included in the final analysis, the small sample sizes limited the ability of the study to be confidently applied to the general public which shows much greater variation in category and severity of refractive error.

The functions that nomograms serve for laser vision correction are more pertinent and necessary in cases of high spherocylindrical errors, such as myopia higher than -6.00 diopters, hyperopia greater than +4.00 diopters, and astigmatism greater than -3.00 diopters. The reason is that these levels of refractive error require greater amounts of ablation and greater calculation adjustments. In the sample, there were 14 patients from the Wellington group who qualified as high-order myopic error compared with only 3 patients in the IBRA group. For better sample matching, it would be necessary to accumulate more high-order myopic cases in the IBRA group to more accurately represent the population and to perform a more in-depth statistical analysis. Due to this issue, the results are limited by external validity. The same could be said for the number of hyperopic cases. Hyperopic treatments can be more unpredictable and more difficult to perform than myopic cases because of the nature of the required ablative correction. This means that the efficacy of the nomogram is even more crucial in reaching the desired visual and refractive outcomes. There were only 2 hyperopic cases in the Wellington group and 4 cases in the IBRA group. This number was too small to accurately represent the general population of patients with hyperopic eyes and thus limited the external validity of the study results. If there were more cases involving these higher-order or more difficult refractive errors a much more accurate analysis could be performed.

Along with a lack of a representative sample population there was also trouble controlling variables for visual acuity analysis of mono-vision cases. Because reading vision is not as well standardized as a manifest refraction for distance vision which has closely controlled distances from the Snellen chart, a decision was made to consider a Jaeger chart score conversion to Snellen chart score equivalent in reliance even though this may not necessarily be the case for every exam. This is due to the fact that this test is significantly more subjective, based heavily on where the patient decides to hold the reading card and their accommodative ability.

An issue with data collection was attrition bias through patient drop-out from the IBRA candidate group because of a failure to show up at their six-week postoperative evaluation. One major reason for this failure is that patients were not required to book a six-week follow-up appointment before they left the BEG clinic the day of their one-week postoperative evaluation. Patients who did not book an appointment at this time often never called back to schedule the six-week appointment and were therefore excluded from the study. In relation to the possible bias of the study, patients who were experiencing minor complications may have been more likely to show up at their six-week postoperative visit, whereas patients who were happy with their vision or free of complications may have been less likely to show up for the visit. If more patients with possible complications were showing up for their follow-up visit, it is possible that the results were skewed toward more negative visual acuity or refractive outcomes for the IBRA candidate group.

Even though LASIK and PRK procedures have been proved to have statistically no difference in visual acuity and refractive outcomes, PRK has a much longer recovery time (Wen et al., 2017). It is possible that if the recovery time for PRK patients in either nomogram groups was longer than six weeks on average for the preliminary sample populations before exclusion, then patients experiencing visually significant complications that resolved after the six-week period were excluded before their true representative visual acuity and refractive outcome could be recorded and included in the study. If the study continued with a three-month postoperative evaluation and with less patient dropout, the results might have been different, if not statistically significant, in terms of overall visual acuity and refractive outcomes. There are many complications not uncommon to LASIK and PRK procedures that eventually clear up and result in much improved vision. Common complications such as haze and dry eye can affect vision for up several to months before complete resolution.

A possible confounding variable for sampling is that the two surgeons who operated on the patients may have varying levels of skill or less random patient selection. For example, one surgeon may have more years of experience as well as more difficult cases. If one surgeon was more likely to be scheduled with a greater number of high-order refractive errors to correct, then it is possible that the sample groups were not matched well enough to make an accurate comparison. Although this possible variable exists, it should be noted that the Boston Eye Group is a teaching institution and multiple corneal fellows performed a significant number of these surgeries under the supervision of each surgeon which reduced the bias from one category to the other.

One of the goals of this study was to assess the ability of the IBRA software to enhance its nomogram calculation parameters for a specific surgeon or facility performing the procedures. Prior to doing this calculation enhancement, the IBRA program suggests inputting about 30 completed cases to ensure that the regression analysis has enough data to be accurate and applicable. By the end of the data collection process in this study, there were 58 IBRA nomogram cases. To ensure that all of the IBRA nomogram procedures were done using the same set of calculation parameters, a decision was made to use only the IBRA reference database regression for parameter enhancement. This decision was due largely to time limitations for data collection. For the sake of maintaining a more homogenous sample group, procedures done with the IBRA reference database nomogram parameters and procedures done with surgeon-specific IBRA nomogram parameters would be considered two different sample groups. This would have added another sample group or reduced the number of analyzed IBRA nomogram cases to 28, which was considered too few to compare with 51 Wellington nomogram cases. Reducing the number of cases in each group for comparison would have added further limitations to the validity and applicability of the statistical analysis. Due to this issue, the surgeon-specific IBRA nomogram parameter enhancements were not used in this study. The comparison would have been possible if there were more IBRA cases. Although this database is still effective at generating usable treatment laser calculations, it meant that the efficacy of the software to enhance its nomogram calculations for a specific surgeon could not be evaluated. With more time for data collection and analysis, it would be possible to make this assessment.

Although the results pointed to a lack of statistical significance, the study proved that the IBRA nomogram could at least perform as well as the Wellington nomogram. According to the standard reporting graphs that were generated, the Wellington and IBRA nomograms both generated excimer laser correction treatment inputs that fulfilled standards for predictability, safety, and efficacy. Although this study may be limited in scope and external validity, it can be further expanded and developed into an impactful study for the BEG practice and for future publication. There are many more data points that could be collected and tracked using the IBRA software such as the average amount of ablations used or more specific tracking of complications instead of excluding these cases. There would have to be much more control over the variables associated with any one data point or comparison but it could reasonably be done. Another data point that is worth tracking, but difficult to collect without bias, is patient satisfaction. Even if patients do not necessarily reach exact refractive corrections, they may still be satisfied with near-perfect vision or at the very least, greatly improved vision and reduced reliance on glasses or contacts lenses. Often patients have near perfect or functional daytime distance vision, but they may need correction with glasses during night driving or for reading. There could also be more control and better organization for analyzing mono-vision cases. Because these cases are less objective than traditional distance-vision corrections, researchers could implement more standardized methods for measuring and correcting reading vision that could improve the reliability and confidence of a statistical analysis of these cases. In addition, there could be a more detailed, in-depth statistical analysis of the MRSE outcomes as well as the astigmatic axis corrections which were not considered in this study. The statistical test used to analyze the spherical equivalent outcomes could be modified to account for more groups, such as patients within 0.25 diopters of the target refraction, to gain even more insight into the ablative corrections and their predictability.

Expanding the study by increasing its length and sample size as well as modifying and developing a more descriptive statistical analysis could greatly benefit the reliability, validity, and scope of the study. With strict sample matching and precise control of confounding variables, a more developed study could elucidate any number of interesting conclusions about the many subtle intricacies involved in safer, more effective laser vision correction procedures.

REFERENCES

Ali, M., Raghunathan, V., Li, J. Y., Murphy, C. J., & Thomasy, S. M. (2016). Biomechanical relationships between the corneal endothelium and Descemet's membrane. *Experimental Eye Research*, *152*, 57–70. https://doi.org/10.1016/j.exer.2016.09.004

Ambrósio, R., & Wilson, S. E. (2003). Lasik vs lasek vs prk: Advantages and indications. *Seminars in Ophthalmology*, *18*(1), 2–10. https://doi.org/10.1076/soph.18.1.2.14074

Boost, M., Cho, P., & Wang, Z. (2017). Disturbing the balance: Effect of contact lens use on the ocular proteome and microbiome: Contact lens use on ocular proteome and microbiome *Clinical and Experimental Optometry*, *100*(5), 459–472. https://doi.org/10.1111/cxo.12582

Cope, J. R., Collier, S. A., Rao, M. M., Chalmers, R., Mitchell, G. L., Richdale, K., Wagner, H., Kinoshita, B. T., Lam, D. Y., Sorbara, L., Zimmerman, A., Yoder, J. S., & Beach, M. J. (2015). Contact lens wearer demographics and risk behaviors for contact lens-related eye infections – united states, 2014. *MMWR. Morbidity and Mortality Weekly Report*, *64*(32), 865–870. https://doi.org/10.15585/mmwr.mm6432a2

Eydelman, M. B, Hilmantel, G., Tarver, M. E., Hofmeister, E. M., May, J., Hammel, K., Hays, R. D., & Ferris, F. (2017). Symptoms and satisfaction of patients in the patient-reported outcomes with laser in situ keratomileusis (Prowl) studies. *JAMA Ophthalmology, 135*(1), 13.https://doi.org/10.1001/jamaophthalmol.2016.4587

Eydelman, M. B., Tarver, M. E., & Ferris, F. (2017). Listening to the patients—The laser-assisted in situ keratomileusis quality of life collaboration project. *JAMA Ophthalmology, 135*(2), 83. https://doi.org/10.1001/jamaophthalmol.2016.4585

The Eye Diseases Prevalence Research Group. (2004). Causes and prevalence of visual impairment among adults in the United States. *Archives of Ophthalmology*, *122*(4), 477–485. https://doi:10.1001/archopht.122.4.477

Fischer, A. by H. (2013). *English: This image shows the basic structure of the eye with the three main layers visible.* http://open.umich.edu/education/med/resources/second-look-series/materials - Eye Slide 3. https://commons.wikimedia.org/w/index.php?title=File:Three_Main_Layers_of_the_Eye.png&oldid=371960677.

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

Meek, K. M., & Boote, C. (2004). The organization of collagen in the corneal stroma. *Experimental Eye Research*, *78*(3), 503–512. https://doi.org/10.1016/j.exer.2003.07.003

Meek, K. M., & Knupp, C. (2015). Corneal structure and transparency. *Progress in Retinal and Eye Research*, *49*, 1–16. https://doi.org/10.1016/j.preteyeres.2015.07.001

Mitchell, P., Liew, G., Gopinath, B., & Wong, T. Y. (2018). Age-related macular degeneration. *The Lancet*, *392*(10153), 1147–1159. https://doi.org/10.1016/S0140-6736(18)31550-2

Morgan, Ian G., et al. (2012). "Myopia." *The Lancet*, *379*(9827), 1739–1748. doi: 10.1016/S0140-6736(12)60272-4.

Pallikaris, I. G., Papatzanaki, M. E., Siganos, D. S., & Tsilimbaris, M. K. (1991). A corneal flap technique for laser in situ keratomileusis. Human studies. *Archives of Ophthalmology*, *109*(12), 1699–1702. https://doi.org/10.1001/archopht.1991.01080120083031

Philos2000 (2017). *Schematics of refractive errors of the eye, Emmetropia, Myopia (Nearsightedness), Hyperopia (Farsightedness).* This is an edited version of the source image made for use in the "Anatomist" iOS and Android app and shared here under the terms of the source image's Share Alike Creative Commons license.File:Refractive_errors.jpg.https://commons.wikimedia.org/w/index.php?title=File:Refractive_Errors_of_the_Eye.jpg oldid=359958364.

Price, M. O., Price, D. A., Bucci, F. A., Jr, Durrie, D. S., Bond, W. I., & Price, F. W., Jr (2016). Three-Year Longitudinal Survey Comparing Visual Satisfaction with LASIK and Contact Lenses. *Ophthalmology*, *123*(8), 1659–1666. https://doi.org/10.1016/j.ophtha.2016.04.003

Radner, W., Zehetmayer, M., Aufreiter, R., & Mallinger, R. (1998). Interlacing and cross-angle distribution of collagen lamellae in the human cornea: *Cornea*, *17*(5), 537–543. https://doi.org/10.1097/00003226-199809000-00012

Reinstein, D. Z., Carp, G. I., Archer, T. J., Day, A. C., & Vida, R. S. (2018a). Outcomes for mixed cylinder lasik with the mel 90 ® excimer laser. *Journal of Refractive Surgery*, *34*(10), 672–680. https://doi.org/10.3928/1081597X-20180814-01

Reinstein, D. Z., Carp, G. I., Archer, T. J., Day, A. C., & Vida, R. S. (2018b). Outcomes for hyperopic lasik with the mel 90 ® excimer laser. *Journal of Refractive Surgery*, *34*(12), 799–808. https://doi.org/10.3928/1081597X-20181019-01

Salah, T., Waring, G. O., Maghraby, A. E., Moadel, K., & Grimm, S. B. (1996). Excimer laser in situ keratomileusis under a corneal flap for myopia of 2 to 20 diopters. *American Journal of Ophthalmology*, *121*(2), 143–155. https://doi.org/10.1016/S0002-9394(14)70578-1

Shaheen, B. S., Bakir, M., & Jain, S. (2014). Corneal nerves in health and disease. *Survey of Ophthalmology*, *59*(3), 263–285. https://doi.org/10.1016/j.survophthal.2013.09.002

Spadea, L., & Giovannetti, F. (2019). Main complications of photorefractive keratectomy and their management. *Clinical Ophthalmology*, *13*, 2305–2315. https://doi.org/10.2147/OPTH.S233125

Sridhar, M. S. (2018). Anatomy of cornea and ocular surface. *Indian Journal of Ophthalmology*, *66*(2), 190–194. https://doi.org/10.4103/ijo.IJO_646_17

Sridhar, M. S., Rao, S. K., Vajpayee, R. B., Aasuri, M. K., Hannush, S., & Sinha, R. (2002). Complications of laser-in-situ-keratomileusis. *Indian Journal of Ophthalmology*, *50*(4), 265–282.

Verhoeven, V. J. M., Wong, K. T., Buitendijk, G. H. S., Hofman, A., Vingerling, J. R., & Klaver, C. C. W. (2015). Visual consequences of refractive errors in the general population. *Ophthalmology*, *122*(1), 101–109. https://doi.org/10.1016/j.ophtha.2014.07.030

Weinreb, R. N., Aung, T., & Medeiros, F. A. (2014). The pathophysiology and treatment of glaucoma: A review. *JAMA: The Journal of the American Medical Association*, *311*(18), 1901. https://doi.org/10.1001/jama.2014.3192

Wen, D., McAlinden, C., Flitcroft, I., Tu, R., Wang, Q., Alió, J., Marshall, J., Huang, Y., Song, B., Hu, L., Zhao, Y., Zhu, S., Gao, R., Bao, F., Yu, A., Yu, Y., Lian, H., & Huang, J. (2017). Postoperative efficacy, predictability, safety, and visual quality of laser corneal refractive surgery: A network meta-analysis. *American Journal of Ophthalmology*, *178*, 65–78. https://doi.org/10.1016/j.ajo.2017.03.013

Willoughby, C. E., Ponzin, D., Ferrari, S., Lobo, A., Landau, K., & Omidi, Y. (2010). Anatomy and physiology of the human eye: Effects of mucopolysaccharidoses disease on structure and function — a review: Anatomy and physiology of the eye. *Clinical & Experimental Ophthalmology*, *38*, 2–11. https://doi.org/10.1111/j.1442-9071.2010.02363.x

Yan, M. K., Chang, J. S., & Chan, T. C. (2018). Refractive regression after laser *in situ* keratomileusis: Regression in LASIK. *Clinical & Experimental Ophthalmology*, *46*(8), 934–944. https://doi.org/10.1111/ceo.13315

Yuen, L. H., Chan, W. K., Koh, J., Mehta, J. S., & Tan, D. T. (2010). A 10-year prospective audit of Lasik outcomes for myopia in 37932 eyes at a single institution in Asia. *Ophthalmology*, *117*(6), 1236-1244.e1. https://doi.org/10.1016/j.ophtha.2009.10.042

Zuberbuhler, B., Galloway, P., Reddy, A., Saldana, M., & Gale, R. (2007). A web-based information system for management and analysis of patient data after refractive eye surgery. *Computer Methods and Programs in Biomedicine*, *88*(3), 210–216. https://doi.org/10.1016/j.cmpb.2007.09.003

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